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OVERVIEW OF LOCAL ANESTHETICS
Vanessa Loland, M.D.

Chemistry
- Sodium channel blockers
- Weak bases (pKa>7.4)
- Positively charged at physiologic pH
- Composed of a tertiary amine coupled to a benzene ring
- Physicochemical properties of local anesthetics depend on the substitutions in the aromatic ring, the type of linkage in the intermediate chain, and the alkyl groups attached to the amine nitrogen.

- Classified based on intermediate chain
  - AminoESTERS
    - Most commonly used
    - Have two "I"s
  - AminoAMIDES
**Mechanism of Action**

- Voltage-gated sodium channel blockade
  - Only the non-ionized molecule crosses cell membranes
  - Blocks channel from intracellular side
  - Decreases $\text{Na}^+$ conductance
  - Slows the rate of depolarization

- The $\text{Na}^+$/K$^+$ pump actively transports $\text{Na}^+$ out of the cell and $\text{K}^+$ into the cell. The cell membrane is naturally more permeable to $\text{K}^+$ than to $\text{Na}^+$, so a relative excess of negatively charged ions accumulates intracellularly = negative resting potential (-70mV polarization).

- After excitation, if a threshold depolarization of -55mV is reached, $\text{Na}^+$ channels are activated and this allows a sudden influx of $\text{Na}^+$ ions (+35mV depolarization). The changes in axon membrane potential are called the action potential.

- Action is limited to the site of application

- Effect reverses upon diffusion from the site of action
Nerve Sensitivity

- Small diameter nerves > large diameter nerves
  - But slower recovery of large fibers, when the LA wears off
- Myelinated (3 nodes of Ranvier) > unmyelinated
  - A (large myelinated)
    - α: large motor, proprioception
    - β: small motor, pressure, touch
    - γ: muscle tone
    - δ: sharp pain, temperature
  - B (small myelinated): preganglionic sympathetic
  - C (small unmyelinated): pain, temperature, touch
- Frequent firing > infrequent firing
  - LA gains access to its binding site within a pore only when the Na channel is in an activated state
- Autonomic > pain > temp > touch > proprioception > motor
  - Influenced by structural arrangement of nerve bundle (anesthetic diffuses from outside in)
  - Nerves to proximal structures on outside, so proximal structures are blocked first
Pharmacokinetics

• Potency: Determined by lipid solubility

<table>
<thead>
<tr>
<th>Potency</th>
<th>Drug</th>
<th>Octanol/H₂O</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Procaine</td>
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</tr>
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</tr>
<tr>
<td></td>
<td>Ropivacaine</td>
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</table>

• Onset: Determined by pKa
  o Only the lipid-soluble form diffuses across the nerve membrane
  o Local Anesthetics (weak bases) with a lower pKa (closer to physiologic pH) have a higher concentration of the non-ionized form, and have a faster rate of onset
    ▪ The pH at which the amounts of ionized and non-ionized drug are equal is the pKa of the drug
    ▪ Once inside the cell, the non-ionized base will reach an equilibrium with its ionized form
    ▪ Only the charged cation binds to the receptor within the Na⁺ channel

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<thead>
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<th>Onset</th>
<th>Drug</th>
<th>pKa</th>
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<td>Chloroprocaine</td>
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<td>Bupivacaine</td>
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</tr>
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<td></td>
<td>Ropivacaine</td>
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</tr>
<tr>
<td>Slow</td>
<td>Tetracaine</td>
<td>8.4</td>
</tr>
<tr>
<td></td>
<td>Procaine</td>
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</tr>
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</table>

  o Addition of bicarbonate to increase local tissue pH
    ▪ Although LA are weak bases, they are marketed as water-soluble hydrochloride salts, which are acidic
    ▪ Adding bicarbonate makes the LA in solution a non-ionized, lipid soluble base that can penetrate the membrane (the rate limiting step in onset time) - this only works for very soluble LA (lidocaine)
  o Delayed onset in acidic (eg, infected) tissues
  o Other factors affecting onset
    ▪ Total dose (concentration gradient)
    ▪ Increased volume
    ▪ Increased concentration

• Duration: Mainly determined by plasma protein binding
  o Plasma Protein binding
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<th>Duration</th>
<th>Drug</th>
<th>% Protein Binding</th>
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<td></td>
<td>Etidocaine</td>
<td>95</td>
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</table>

- Total dose
- Rate of systemic absorption
  - Vascularity
    - Blood > Intercostal > caudal > epidural > brachial plexus > sciatic > subcutaneous infiltration (BICEPS)
  - Tissue binding
  - Lipophilicity: more lipophilic = more tissue binding
  - Addition of vasoconstrictors ↓ absorption due to ↓ local blood flow
    - More pronounced with less lipophilic drugs
- Rate of elimination
  - Amides
    - Primarily hepatic, by microsomal enzymes
    - Toxicity is dose-related and may be delayed
    - Allergic reactions rare, but usually due to methylparaben preservative, similar to PABA reaction
  - Esters
    - Ester hydrolysis by plasma esterases (pseudocholinesterases), very rapid
    - H₂O soluble metabolites excreted in urine
    - PABA metabolite may lead to allergic reactions
- Liposomal encapsulation
  - Liposomal encapsulation systems for delivery of local anesthetics may significantly prolong their duration of action

**Agents**
- Chloroprocaine (Nesacaine)
  - Ester
  - Rapid onset (high concentration)
  - Short duration
  - Uses: CLE, Caudal
  - Neurotoxicity described when acidic meta-bisulfite preservative-containing solution injected intrathecally
  - When used epidurally, chloroprocaine may decrease the efficacy and duration of action of bupivacaine, morphine, and fentanyl
- Tetracaine
  - Derivative of Procaine (first synthetic LA)
  - Long-acting, potent
  - Slow metabolism, so more toxic
  - Used only for spinals
- Benzocaine (Hurricaine)
Ester does not exist in a charged form, so it probably acts by an alternate mechanism (e.g., expanding the lipid membrane).

- Only used topically as a mucosal spray
- May result in methemoglobin (also prilocaine) by production of its byproduct, o-toluidine
  - Treat with methylene blue, reduces methemoglobin (Fe3+) to hemoglobin (Fe2+)
  - No significant consequences in healthy patients

**Bupivacaine (Marcaine)**
- Amide
- Long-acting
  - Can be further prolonged by epinephrine
  - Unpredictable duration, especially in elderly
- Cardiotoxicity is cumulative and greater than predicted by its potency
- Part of the cardiotoxicity is centrally mediated (malignant ventricular arrhythmias when injected in the medulla)

**Ropivacaine (Naropin)**
- Amide
- Chemical analogue of bupivacaine, with similar potency, onset, duration (more predictable) and toxic doses
- Advertised as less cardiotoxic alternative to bupivacaine, however recent case reports of cardiac arrest when used in equipotent doses (Chazalon 2003, Huet 2003, Reinikainen 2003, Polley 2003)
- Sensory > Motor block

**Levobupivacaine (Chirocaine)**
- Amide
- S isomer of bupivacaine
- Equipotent with less potential for cardiotoxicity
- Not currently available in the United States

**Lidocaine (Xylocaine)**
- Amide
- Intermediate duration
- Transient Neurological Symptoms following SAB (Freedman 1998)
  - Aching pain in buttocks, lower back, legs (no motor)
  - Onset 12-24 hrs, resolution within 4 days
  - Lidocaine > bupivacaine (RR=5.1), > tetracaine (RR=3.2)
  - Lithotomy > other positions (RR=2.6)
  - Outpatients > inpatients (RR=3.6)

**Mepivacaine (Polocaine)**
- Amide
- Equipotent to Lidocaine, same onset time, but longer duration (still intermediate)
- Used for quick surgical onset, or for bolusing peripheral nerve block catheters prior to or during surgery

**EMLA Cream**
- Eutectic (easily melted) Mixture of Local Anesthetic, 1:1 mixture of 5% lidocaine and 5% prilocaine in an oil-in-water emulsion
- Dermal analgesia sufficient for starting an IV requires contact time of at least 1hr, under an occlusive dressing
o Uses: STSG harvesting, laser removal of port-wine stains, lithotripsy, circumcision
o Don’t use on broken skin or mucous membranes
o Side effects: blanching, redness, edema, methemoglobin

Additives
• Vasoconstrictors—prolongs anesthesia with shorter-acting agents by 50% (low protein-binding)
  o Epinephrine—also useful as intravascular marker
  o Phenylephrine
  o Limit to 1:300,000 to limit decrease in nerve blood supply
• Sodium bicarbonate—increases non-ionized fraction of local anesthetic to speed onset
  o 1 mL 8.4%NaCo3 per 10 mL local
• Clonidine: prolongs block by 3 hrs, may produce sedation (Casati 2000)
  o Dose: 50-100 mcg
• Additives for IVRA (Bier block)
  o Ketorolac
    ▪ Reuben et al: lidocaine + 60 mg ketorolac superior to lidocaine alone
    ▪ Tourniquet tolerance
    ▪ Postoperative analgesia
  o Clonidine
    ▪ Gorgias et al: 1 mcg/kg added to lidocaine prolongs tourniquet tolerance and postop analgesia although < ketamine
    ▪ Reuben et al: May be beneficial in CRPS
  o Ketamine
    ▪ Gorgias et al: 0.1 mg/kg added to lidocaine superior to 1 mcg/kg clonidine for tourniquet tolerance and postop analgesia
  o Dexmedetomidine
    ▪ Esmaoqlu et al: 1 mcg/kg improves intraop and postop analgesia with no effect on onset or regression
    ▪ Memis et al: 0.5 mcg/kg improves analgesia with no side effects

Toxicity
• CNS Toxicity
  o Excitation (selective blockade of inhibitory pathways)
    ▪ Tinnitus, circumoral numbness, vertigo
    ▪ Anxiety, disorientation
    ▪ Seizures (benzodiazepines and low pCO₂ lowers seizure threshold)
      ▪ Lidocaine: 10-12 mcg/mL
      ▪ Bupivacaine: 4 mcg/mL
  o Depression
    ▪ Slurred speech, drowsiness
    ▪ Respiratory arrest, coma, death
      ▪ Lidocaine: 20-25 mcg/mL
      ▪ Bupivacaine: 4-6 mcg/mL
  o CNS effects usually precede cardiac
• Cardiac Toxicity
  o Hypotension
    ▪ Direct myocardial depression (cardiac Na⁺ channel blockade)
    ▪ Smooth muscle relaxation, inhibits autonomic NS
- Depressant effect on cardiac contractility parallels the anesthetic potency
  - Arrhythmia
    - Impaired automaticity and conduction
    - Prolongs P-R, widens QRS → bradycardia/heart block
  - Bupivacaine → multiform VT/VF
    - ↑risk in pregnancy, hypoxia, acidosis
    - Pregnancy associated with lower concentrations of albumin and α-1-glycoprotein, which bind bupivacaine
    - Highly lipid soluble and protein bound = slow dissociation and prolonged effect

- Local Anesthetic Mixtures
  - Galindo 1980: chloroprocaine + bupivacaine for rat sciatic nerve blocks
    - Unpredictable onset and duration
    - May be related to drug solutions and pH
  - Seow 1982: lidocaine + bupivacaine for epidural in different ratios
    - Similar onset in all 5 groups, but duration of mixtures intermediate between each drug used alone
    - Pharmacokinetics of individual drugs unaltered
  - Toxic doses are additive

- Treatment
  - ABC’s
  - CNS
    - Stop seizure: benzodiazepines, thiopental, propofol
  - CV
    - Supportive: ACLS
    - Antiarrhythmics: amiodarone, bretylium
    - Cardiopulmonary Bypass
    - Intralipid (20% Fat Emulsion): 1mL/kg, 0.5ml/kg/min
  - Propofol is NOT a substitute for intralipid

- Toxic Doses

<table>
<thead>
<tr>
<th>Drug</th>
<th>Plain (mg/kg)</th>
<th>With Epinephrine (mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bupivacaine</td>
<td>3</td>
<td>n/a</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>4.5</td>
<td>7</td>
</tr>
<tr>
<td>Mepivacaine</td>
<td>4.5</td>
<td>7</td>
</tr>
<tr>
<td>Ropivacaine</td>
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<td>n/a</td>
</tr>
<tr>
<td>Chloroprocaine</td>
<td>10</td>
<td>15</td>
</tr>
<tr>
<td>Tetracaine</td>
<td>3</td>
<td>n/a</td>
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Local anesthetics are widely and commonly used throughout medical and dental practice. Although it is rare for patients to manifest serious adverse effects or experience complications secondary to local anesthetic administration, adverse events do occur. These range from the mild symptoms that may follow systemic absorption of local anesthetic from a correctly sited and appropriately dosed regional anesthetic procedure to major central nervous system (CNS) and/or cardiac toxicity (most often from unintentional intravascular injection) that can result in disability or death. A variety of factors influence the likelihood and severity of local anesthetic systemic toxicity (LAST), including individual patient risk factors, concurrent medications, location and technique of block, specific local anesthetic compound, total local anesthetic dose (the product of concentration × volume), timeliness of detection, and adequacy of treatment.

Interest in local anesthetic toxicity has had several peaks, including one that coincided with the initial awareness of local anesthetic toxicities after the introduction of cocaine in 1884, another that followed the linking of fatalities to the use of bupivacaine and etidocaine in the 1970s, and another after the introduction of ropivacaine and levobupivacaine in the late 1980s that continues through the present.1,2 There is suspicion (but scant evidence) that patients undergoing regional anesthesia are now less likely to have LAST than in earlier decades. On the other hand, improved understanding of LAST pathophysiology and new treatment modalities have emerged in the 2000s. Consequently, the American Society of Regional Anesthesia and Pain Medicine (ASRA) commissioned a panel of experts to update recommendations that came from the 2001 ASRA Conference on Local Anesthetic Toxicity. The current Practice Advisory focuses on LAST, which includes cardiac and CNS toxicity consequent to unintended intravascular injection or delayed tissue uptake. The advisory does not address tissue-related local anesthetic neurotoxicity, allergy, or the production of methemoglobinemia by local anesthetics.

A 2006 survey of US academic anesthesiology departments found no uniform, well-designed, rational approach for management of local anesthetic toxicity.3 The ASRA Practice Advisory Panel was also formed to correct this deficiency by identifying key practice modifications targeted specifically at improving prevention, diagnosis, and treatment of LAST. Our recommendations reflect our view of the primacy of prevention of LAST as the most effective intervention for enhancing patient safety.

**METHODOLOGY**

This practice advisory is derived from human and animal experimental studies related to the prevention, diagnosis, and treatment of LAST in adults and children. All available English-, German-, and French-language reports of human and animal scientific inquiry were considered, including randomized controlled trials (RCTs), observational studies, case series, and case reports. Key word literature searches were undertaken using major literature search engines such as the National Library of Medicine's PubMed, Ovid, and Google Search. Article bibliographies were cross-checked for references not identified by search engines.

The ASRA Board of Directors appointed the Panel at their Fall 2007 meeting. The Panel consists of recognized experts on local anesthetic toxicity and/or guideline development and includes all authors of this article. This group was responsible for the content of these guidelines.
for the initial literature search, assimilation of materials, expert opinion, development of recommendations, and writing the accompanying supporting articles. Individuals neither received direct financial support for their participation nor did any participants other than Drs. Weinberg and Butterworth declare a potential conflict of interest (see appended declaration). The ASRA received no direct financial support from industry or other grants to underwrite expenses (travel support for the panel) related to this initiative.

As suggested by recognized instruments for guideline development such as the Appraisal of Guidelines for Research & Evaluation, every effort was made to ensure the integrity and validity of the process leading to the recommendations made herein. External input, appraisal, and validity were sought using the following mechanisms. The Panel's recommendations were circulated to a separate group of experts selected on the basis of their demonstrated interest and/or expertise in local anesthetic toxicity (Appendix 1). General input was also sought by contacting the Editors-in-Chief of major journals for medical and dental specialties that commonly use local anesthetics (Appendix 2). Comments from these 2 groups were considered and incorporated when appropriate, and particularly as they related to content, interpretation, and clarity of the recommendations. One week before presentation in open forum at the May 3, 2008, ASRA meeting in Cancun, Mexico, meeting registrants were e-mailed a copy of the recommendations. Open comment was solicited primarily with regard to clarity and soundness of the recommendations. After finalizing recommendations, the Practice Advisory summary document and accompanying review articles were submitted to Regional Anesthesia and Pain Medicine for publication, where they were subjected to the journal's standard peer-review process. Readers are encouraged to read the accompanying reviews, which provide the details that led to recommendations contained within this summary article.

Grading the Strength of Recommendations

There are no RCTs evaluating serious human LAST; future RCTs are unlikely because of the rarity of these complications and the associated difficulty of obtaining informed consent for medical interventions in critical illness. Common strength-of-evidence schemas that are based on RCT-level evidence are therefore inappropriate for the topic of human LAST but are appropriate for animal studies. Hence, the Practice Advisory's recommendations are based on a modification of a Classification of Recommendations and Levels of Evidence schema that was developed by the American Heart Association (Table 1). The panel wishes to emphasize that assigning a Level of Evidence B or C should not be construed as implying that the associated recommendation is supported by conflicting data or is limited by conflicting interpretations of the available data. Rather, such recommendations reflect our recognition of the importance of the particular question as it relates to LAST, and to the reality that the specific question is either yet to be addressed by a RCT or does not lend itself to experimental inquiry in humans.

Limitations

As with previous ASRA-sponsored practice advisories, our recommendations should be viewed as guidelines that are based on existing literature and expert opinion. The scientific literature that provided the basis for these guidelines and recommendations is imperfect and always evolving. Animal studies should be interpreted with knowledge of species differences, variations in laboratory systems, and differing experimental models. The hypothesis being tested may limit the conclusions one can make, along with extrapolations to the clinical setting. Literature comprising case reports may be biased toward positive outcomes because clinicians are reluctant to present their cases that have poor outcome, and case reports without a "teaching point" will almost never be accepted for publication. Therefore, some local anesthetics, for example, ropivacaine or levobupivacaine, might seem safer than is the case, and specific treatments, for example, lipid emulsion, might fail more often than the literature indicates. Some of our recommendations are based on expert opinion alone. The nature of practice advisories is that they address issues of controversy and uncertainty. We strive to acknowledge these controversies, but then to offer our best advice within the setting of uncertainty. Particularly when addressing more controversial issues, our recommendations tend to err toward conservative management.

Our recommendations are intended to promote quality patient care; nevertheless, rigid observance of our recommendations may not guarantee a specific patient outcome. Our recommendations are not meant to be interpreted as standard of care and they should never supersede sound medical judgment. Those who apply these recommendations will determine their value. As with all practice advisories, these recommendations will be subject to timely revision as warranted by the evolution of technology, scientific evidence, and clinical experience.

HISTORY

Local anesthetic systemic toxicity has been recognized and reported since shortly after the introduction of cocaine into clinical practice in the 1880s. From the outset, systemic toxicity was associated with seizures and respiratory failure. It is unclear when direct cardiac toxicity was recognized as a major component of systemic toxicity, rather than an associated adverse effect. The systemic toxic effects of cocaine and cocaine's propensity to cause local tissue toxicity in part led to Einhorn's development of procaine in 1904. Unfortunately, LAST continued to be a major

<table>
<thead>
<tr>
<th>TABLE 1. Definitions for Classification of Recommendations and Levels of Evidence</th>
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<tbody>
<tr>
<td>Classification of Recommendations</td>
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<td>Class I. Conditions for which there is evidence and/or general agreement that a given procedure or treatment is useful and effective</td>
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<td>Class II. Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment</td>
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<tr>
<td>IIa. Weight of evidence/opinion is in favor of usefulness/efficacy</td>
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<tr>
<td>IIb. Usefulness/efficacy is less well established by evidence/opinion</td>
</tr>
<tr>
<td>Class III. Conditions for which there is evidence and/or general agreement that the procedure/treatment is not useful/effective, and in some cases may be harmful</td>
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</tbody>
</table>

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<thead>
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<th>Level of Evidence</th>
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<tbody>
<tr>
<td>Level A</td>
<td>Data derived from randomized clinical trials</td>
</tr>
<tr>
<td>Level B</td>
<td>Data derived from nonrandomized or laboratory, eg, animal studies; supported by multiple case reports or case series</td>
</tr>
<tr>
<td>Level C</td>
<td>Consensus opinion of experts</td>
</tr>
</tbody>
</table>

The above schema is modified from an American Heart Association schema for developing and grading guidelines.
patient safety concern, so much so that the American Medical Association (AMA) established the Committee for the Study of Toxic Effects of Local Anesthetics in the early 1920s. It became clear that local anesthetics were not only capable of causing death but that cardiac arrest could precede seizures or even occur in the absence of seizures. The AMA Committee stopped short of suggesting a ban on cocaine, but emphasized the primacy of a clear airway to optimize oxygenation and ventilation, a theme that Daniel Moore and Donald Bridenthal would continue to stress throughout the mid and late 20th century. The potent lipid-soluble local anesthetics bupivacaine and etidocaine were introduced into clinical practice in the 1960s and 1970s, respectively. By 1969, bupivacaine had been linked to fatal death in 1:900 women who received a paracervical block, admittedly without a clear understanding as to whether bupivacaine itself, the paracervical block technique, or some combination thereof was the responsible etiologic factor. Not until the late 1970s was bupivacaine linked to fatal cardiac arrest in otherwise healthy adult patients. The report of Prentice and Albright’s oft-cited editorial set in motion the events that would lead the US Food and Drug Administration and the 3 manufacturers of bupivacaine issuing a “Dear Doctor” letter withdrawing obstetric analgesia as an indication for 0.75% bupivacaine and warning against its further use in paracervical block and intravenous regional anesthesia. Despite the clinical release of the apparently less cardiotoxic single enantiomers ropivacaine and levobupivacaine in the late 1980s, serious morbidity and mortality from cardiac toxicity continued. In the 1990s, animal research gave hope that lipid emulsions might prove to be an antidote for LAST. The first case reports of successful rescue of humans experiencing refractory cardiac toxicity came in the mid 2000s. Today, research is ongoing to refine issues related to lipid emulsion therapy for severe LAST and its prodromes.

FREQUENCY, MODELS, AND MECHANISMS

What is known regarding LAST is derived primarily from 3 sources—epidemiologic studies that attempt to define incidence in specific patient populations, case series and case reports that describe clinical manifestations of toxicity and/or treatment, and animal studies that aim to establish relative toxicity, elucidate mechanisms, and identify cofactors that promote or attenuate their occurrence. Epidemiologic studies report statistics that vary widely depending on how toxicity is defined, the clinical scenario in which it occurs, and how the data were collected. For example, death from the application of cocaine or tetracaine to mucous membranes to facilitate otolaryngological procedures was reported in 1951 to occur in 7 of 39,278 patients (1.8;10,000). Seizures associated with brachial plexus blockade, particularly the interscalene and supraclavicular approaches (where local anesthetics may be unintentionally injected into an artery feeding the brain), have been reported in up to 79 in 10,000 patients from a single institutional database. Yet a large surveillance study of French anesthesiologists determined the overall frequency of seizures to be 0 to 25 in 10,000, depending on the type of block performed. Interestingly, there were no cardiac arrests secondary to LAST reported in this series. Information from case reports and series offers insights into clinical scenarios of LAST but is unable to define mechanisms. Human RCTs of local anesthetic toxicity will likely never be performed because of ethical and logistical concerns. Thus, most of what is understood regarding the mechanisms of LAST and its treatment comes from animal studies, yet there is limited consensus among investigations as to which animal model best reflects human toxicity. Even basic mechanistic information is controversial with regard to which anesthetic binding site, ion channel, signaling pathway, or enzyme is most important in CNS or cardiac toxicity or their treatment.

When one interprets animal studies of LAST, it is important to consider the model chosen by the investigators to study their hypothesis and what specific clinical circumstance the model is intended to mimic. Variables include in vivo whole animal models versus in vitro isolated heart versus tissue culture; whole cell, ion channel, or subcellular organelle models; large animal versus small animal; awake versus anesthetized; and bolus dosing versus infusion models. Other important features will influence the interpretation of the findings, including the chosen metrics and parameters of interest, the timing of such measures, or the presence of confounders such as hypoxia. Although each of these approaches provides specific advantage, there is no consensus that any model truly mimics clinical toxicity. For instance, many cases of toxicity occur in patients with underlying ischemic or other cardiac disease, which is not readily modeled in standard experimental animals or preparations. Given that summarizing the mechanisms of LAST assuredly represents an oversimplification, in general, it seems that cardiac toxicity results predominantly from the binding and inhibition of Na channels by local anesthetics. Notably, inhibition of cardiac conduction follows a rank order similar to local anesthetic potency for generating neural blockade. When compared with lidocaine, cardiac conduction channels are bound more rapidly and for longer duration by the more potent local anesthetics bupivacaine, etidocaine, and ropivacaine, albeit less avidly by their (S) isomers. Such evidence notwithstanding, a vast array of other inotropic and metabotropic cell signaling systems are affected by local anesthetics and have been implicated in mediating symptoms and signs of LAST. Furthermore, virtually every component of oxidative phosphorylation is inhibited by potent local anesthetics; this observation provides support for mitochondrial metabolism as an important, potential target of local anesthetics and could help explain why symptoms of LAST include predominantly the organs least tolerant of anaerobic metabolism (heart and brain).

Local anesthetics also differ with regard to their CNS toxicity. The cardiovascular (CV)/CNS ratio describes the dose required to produce CV arrhythmias versus that required to produce seizures. This ratio tends to be lower with bupivacaine compared with lidocaine, which implies a reduced safety margin for the potent compounds when detecting impending cardiac toxicity based on premonitory CNS signs. These more potent local anesthetics indeed generate arrhythmias at lower concentrations compared with lidocaine and mepivacaine. At comparable doses in dogs, bupivacaine and etidocaine caused severe arrhythmias without decreased contractility, while lidocaine caused the opposite, that is, depressed myocardial contractility without arrhythmia. However, once plasma concentrations reach higher levels, local anesthetics of all potencies are capable of producing severe myocardial depression.

PREVENTION

This Practice Advisory emphasizes the primacy of prevention in reducing the frequency and severity of LAST, yet no single intervention has been identified that can reliably eliminate risk. Central to prevention is limiting the opportunity for intravascular injection or tissue uptake of local anesthetic, which is best accomplished by early detection of intravascular needle or catheter placement. If an intravascular injection does occur, it should ideally contain the lowest possible dose of local anesthetic. To these ends, specific intravascular identification methods have been proposed since the description of the epinephrine test dose by Moore and Batra in 1981. Literature review
suggests that the frequency of LAST associated with epidural anesthesia may have decreased subsequently by 10- to 100-fold. Conversely, actual published reports of LAST have increased recently, most likely because of renewed interest and new information related to the introduction of the less cardiotoxic stereoisomers ropivacaine and levobupivacaine and to clinical experience with successful lipid emulsion rescue.

Local anesthetic dose can be limited by several methods. Total dose (the product of volume \( \times \) concentration) should be tailored to the minimum mass of local anesthetic molecules necessary to achieve the desired clinical effect. Evidence suggests that most peripheral nerve blocks are performed with significantly larger doses than are necessary to achieve desired clinical end points; these data are further supported by ultrasound-guided regional anesthesia (UGRA) and continuous perineural catheter studies that document adequate blockade using exceedingly small doses of properly placed local anesthetic. Dose reduction may be particularly important for those patients thought to be at greater risk of LAST, for example, those patients at extremes of age (<4 months or >70 years) or those with cardiac conduction defect or a history of ischemic heart disease. Neither body weight nor body mass index correlates with local anesthetic plasma levels after a specific dose in adults; the correlation is more accurate in children. Block site, intrinsic vasoactivity of the local anesthetic, use of epinephrine, and patient-related factors such as cardiac, renal, or hepatic dysfunction are more important predictors of local anesthetic plasma levels than either body weight or body mass index.

When the above noted factors that may predispose to LAST are present, reduction of local anesthetic dose is intuitively logical, yet there are no established parameters to guide actual dose reduction. Incremental injection of 3 to 5 mL of local anesthetic with a concomitant pause for at least one circulation time before further injection is a time-honored recommendation with intuitive appeal, but with no objective efficacy data. Practical considerations suggest that the potential benefit from this approach could be outweighed by prolonging overall injection time with an attendant risk of needle movement. Of note, circulation times are increased with lower extremity injection compared with upper extremity injection. Aspiration of needles and catheters, although recommended, may fail to identify intravascular placement in at least 2% of patients. Substituting the less potent levoenantiomers ropivacaine or levobupivacaine might reduce the potential for systemic toxicity. Nonetheless, these drugs are potentially toxic and the theoretical benefit of chirality becomes less important with increasing doses, particularly among patients at greater than normal risk for local anesthetic toxicity. It is possible that risk inherent to comorbidities such as ischemic heart disease, conduction defects or low output states far outweighs the potential risk reduction of using levoenantiomers.

How can a clinician reduce the risk of LAST? Although imperfect, intravascular test dosing remains the most reliable marker of intravascular injection. Of the various options described, only fentanyl and epinephrine meet suggested standards for reliability and applicability. Intravenous fentanyl 100 \( \mu \)g has been shown to reliably produce drowsiness or sedation in laboring patients. With regard to epinephrine, 10 to 15 \( \mu \)g/mL epinephrine has a positive predictive value and 80% sensitivity in detecting intravascular injection in adults if heart rate increases by 10 beats per minute or higher or systolic blood pressure increases by 15 mm Hg or higher. For children, intravascular epinephrine 0.5 \( \mu \)g/kg is associated with a 15-mm Hg increase or higher in systolic blood pressure. Nevertheless, epinephrine test doses are unreliable in the elderly, or in patients who are sedated, taking \( \beta \)-blockers, or anesthetized with general or neuraxial anesthesia. Epinephrine is also controversial with regard to its role in nerve injury. Although epinephrine has been shown in animal models to worsen local anesthetic-induced neurotoxicity, it is unclear if the additive injury in humans is clinically relevant over and above that caused primarily by the local anesthetic itself. The frequency of seizures during performance of peripheral nerve block was similar to the frequency of permanent nerve injury in one major study (1.2 versus 2.4 in 10,000, respectively). Notably, severe LAST, but not nerve injury, has the potential to cause death.

Ultrasound guidance may reduce the frequency of vascular puncture, but there are no RCTs that confirm or refute an actual reduction of LAST. Two large case series present conflicting results—one found a statistically significant (\( P = 0.001 \)) reduction in the number of vascular punctures occurring under UGRA versus peripheral nerve stimulation, but no difference in LAST. The other series reported a significant (\( P = 0.044 \)) reduction in seizures with ultrasound-assisted nerve localization versus peripheral nerve stimulation. Although intravascular injection can be observed during UGRA, case reports describe symptomatic intravascular injection despite its use. Whether generation of a hypoechoic region consequent to injected local anesthetic is a sufficient monitor of intravascular injection to warrant omission of epinephrine is the subject of considerable debate, particularly when one considers the frequent needle movements inherent to UGRA techniques versus the generally fixed needle techniques associated with nonultrasound blocks. Thus, prevention of intravascular injection is perhaps best accomplished with a combination of UGRA and epinephrine test dosing. Because the literature offers no firm guidance and no method of detection is perfect, meticulous attention to detail remains the most important asset for prevention. Recommendations for preventing LAST are given in Table 2.

**CLINICAL DIAGNOSIS OF SYSTEMIC TOXICITY**

The classic description of LAST includes subjective symptoms of CNS excitement such as auditory changes, circumoral numbness, metallic taste, and agitation that then progress to seizures and/or CNS depression (coma, respiratory arrest). In classic descriptions of LAST, cardiac toxicity does not occur without preceding CNS toxicity. When LAST occurs secondary to direct intravascular injection (particularly with injection into the carotid or vertebral arteries), premonitory symptoms can be bypassed and the patient can rapidly develop seizure activity that may progress to cardiac excitation (hypertension, tachycardia, ventricular arrhythmias). With greatly increased blood concentrations, cardiac excitation may be followed by cardiac depression (bradycardia, asystole, decreased contractility, and hypotension). Particularly with the most potent local anesthetics, cardiac toxicity may occur simultaneously with seizure activity or even precede it. Despite this classic description, case reports of LAST emphasize the extreme variability of its presentation, including timing of onset, initial manifestations, and duration. We found an atypical presentation was reported in approximately 40% of published cases of LAST. In these instances, symptoms were delayed by 5 mins or more or occurred with only CV signs of toxicity. The practitioner's vigilance is of critical importance in recognizing these early signs of LAST, appreciating their variable presentation, and having a low threshold for considering LAST in patients that have received potentially toxic doses of local anesthetics and manifest atypical or unexpected signs and symptoms.
but it is likely that most of these cases involve Fentanyl 100
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Recommendations for Preventing LAST
Recommendations for Ultrasound guidance may reduce the frequency of intravascular injection, but actual reduction of LAST remains unproven in clinical practice. Recent American Society of Anesthesiologists Closed Claims data note that LAST accounted for one-third of claims associated with regional anesthesia.42 Conversely, physicians tend to report and publish their successes rather than their failures—in our review of 93 separate LAST events contained within 74 reports, there was only 1 death. Our review spanned 30 years, yet 65% of the reports were published in the last 10 years. From this review, several patterns emerge. First, two-thirds of patients were female and nearly half the cases were in patients at the extremes of age—16% were younger than 16 years and 30% were older than 60 years. More than 90% of cases involved the most potent local anesthetics, that is, bupivacaine, ropivacaine, and levobupivacaine. Less than 1 in 5 cases involved continuous infusion techniques and half of these were in children. Although analysis of case reports only establishes association rather than cause-and-effect, it is interesting to note that more than one-third of reports of cardiac and CNS toxicity involved patients with underlying cardiac, neurologic, or metabolic disease, for example, diabetes, renal failure, isotropic failure.

In our reviewed single injection cases, the median time from injection to first symptom was 52.5 seconds (interquartile range, 30–180 seconds), which suggests direct injection into an artery supplying the brain or a large intravascular bolus containing sufficient local anesthetic dose to cause CNS symptoms even after first pass clearance through the lungs. For this same group of cases, the mean time to first symptom was 89 seconds (95% confidence interval, 67–120 seconds). Most other reports noted first symptoms between 1 and 5 mins of injection, suggesting partial intravascular injection, lower extremity injection, and/or tissue uptake. Importantly, approximately 25% of cases described symptoms first appearing more than 5 mins after injection (one report described a 60-min delay), which emphasizes the importance of prolonged observation of patients receiving potentially toxic doses of local anesthetic. Local anesthetic systemic toxicity may occur as frequently as 1:1000 peripheral nerve blocks,43 but it is likely that most of these cases involve minor subjective symptoms that do not progress to frank CNS or cardiac toxicity. Of those cases serious enough to report and publish, 45% involved only CNS signs and symptoms, whereas 44% involved both CNS and cardiac manifestations. Reported cases rarely presented with only cardiac signs and symptoms.24

Our overall analysis of case reports suggests that although LAST tends to follow classic presentations, variations are common. Although seizure was the most common presenting symptom, less than 20% of cases involved any of the classic prodromal symptoms such as auditory changes, metallic taste, or disinhibition. Thus, practitioners are advised to be ever-vigilant of potential LAST, particularly in patients at the extremes of age who may have underlying cardiac, pulmonary, renal, hepatic, metabolic, or neurologic disease. Importantly, LAST does not always manifest itself as obvious seizure or cardiac arrhythmias in close temporal relationship to local anesthetic injection. Practitioners should consider the diagnosis of impending LAST in patients that develop unexplained agitation or CNS depression, or unexplained signs of CV compromise, for example, progressive hypotension, bradycardia, or ventricular arrhythmia, even if more than 15 mins after last local anesthetic injection.2 Recommendations for diagnosing LAST are contained in Table 3.

**TREATMENT**

Local anesthetic systemic toxicity continues to be a major source of morbidity and mortality in regional anesthesia practice. Recent American Society of Anesthesiologists Closed Claims data note that LAST accounted for one-third of claims for death or brain damage associated with regional anesthesia.42 Conversely, physicians tend to report and publish their successes rather than their failures—in our review of 93 separate LAST events contained within 74 reports, there was only 1 death. Our review spanned 30 years, yet 65% of the reports were published in the last 10 years. From this review, several patterns emerge. First, two-thirds of patients were female and nearly half the cases were in patients at the extremes of age—16% were younger than 16 years and 30% were older than 60 years. More than 90% of cases involved the most potent local anesthetics, that is, bupivacaine, ropivacaine, and levobupivacaine. Less than 1 in 5 cases involved continuous infusion techniques and half of these were in children. Although analysis of case reports only establishes association rather than cause-and-effect, it is interesting to note that more than one-third of reports of cardiac and CNS toxicity involved patients with underlying cardiac, neurologic, or metabolic disease, for example, diabetes, renal failure, isovolemic academia.

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Our overall analysis of case reports suggests that although LAST tends to follow classic presentations, variations are common. Although seizure was the most common presenting symptom, less than 20% of cases involved any of the classic prodromal symptoms such as auditory changes, metallic taste, or disinhibition. Thus, practitioners are advised to be ever-vigilant of potential LAST, particularly in patients at the extremes of age who may have underlying cardiac, pulmonary, renal, hepatic, metabolic, or neurologic disease. Importantly, LAST does not always manifest itself as obvious seizure or cardiac arrhythmias in close temporal relationship to local anesthetic injection. Practitioners should consider the diagnosis of impending LAST in patients that develop unexplained agitation or CNS depression, or unexplained signs of CV compromise, for example, progressive hypotension, bradycardia, or ventricular arrhythmia, even if more than 15 mins after last local anesthetic injection.2 Recommendations for diagnosing LAST are contained in Table 3.

**TREATMENT**

Treatment priorities for LAST include airway management, circulatory support, and promoting the diminution of the systemic effects of local anesthetics. Unlike the case for treatment of “conventional” cardiac arrest, the key to successful care of LAST patients is recognizing the primacy of airway management. As reported by Moore and colleagues a half century ago, prevention of hypoxia and acidosis by immediate restoration of oxygenation and ventilation can either halt progression to CV collapse and seizure or facilitate resuscitation. Subsequent laboratory investigations confirm this concept.5 If seizures occur, they should be rapidly controlled to prevent injury to the patient and acidosis. The Panel recommends that benzodiazepines are the ideal drugs to treat seizures because they have limited potential for cardiac depression. In the absence of readily available benzodiazepine, propofol or thiopental are acceptable alternatives; however, their potential for worsening existing hypotension or cardiac depression requires using the lowest effective dose. The Panel recognizes that further experience with lipid infusion could lead to its use in preference

**TABLE 2. Recommendations for Preventing LAST**

- There is no single measure that can prevent LAST in clinical practice.
- Use the lowest effective dose of local anesthetic (dose = product of volume × concentration) (I; C)
- Use incremental injection of local anesthetics—administer 3- to 5-mL aliquots, pausing 15–30 s between each injection. When using a fixed needle approach, eg, landmark, paraesthesia-seeking, or electrical stimulation, time between injections should encompass one circulation time (~30–45 s); however, this ideal may be balanced against the risk of needle movement between injections. Circulation time may be increased with lower extremity blocks. Use of larger dosing increments would dictate the need for longer intervals to reduce the cumulative dose from stacked injections before an event of LAST. Incremental injection may be less important with ultrasound guidance, given that frequent needle movement is often used with the technique (I; C).
- Aspire the needle or catheter before each injection, recognizing that there is an ~2% false-negative rate for this diagnostic intervention (I; C).
- When injecting potentially toxic doses of local anesthetic, use of an intravascular marker is recommended. Although epinephrine is an imperfect maker and its use is open to physician judgment, its benefits likely outweigh its risks in the majority of patients (IIa; B):
  - Intravascular injection of epinephrine 10–15 μg/mL in adults produces a ≥10 beat heart rate increase or a ≥15-mm Hg systolic blood pressure increase in the absence of β-blockade, active labor, advanced age, or general/neuraxial anesthesia.
  - Intravascular injection of epinephrine 0.5 μg/kg in children produces a ≥15-mm Hg increase in systolic blood pressure.
- Appropriate subtoxic doses of local anesthetic can produce subjective symptoms of mild systemic toxicity (auditory changes, excitation, metallic taste, etc.) in unpremedicated patients.
- Fentanyl 100 μg produces sedation if injected intravascularly in laboring patients.
- Ultrasound guidance may reduce the frequency of intravascular injection, but actual reduction of LAST remains unproven in humans. Individual reports describe LAST despite the use of UGRA. The overall effectiveness of ultrasound guidance in reducing the frequency of LAST remains to be determined (IIa; C).

The class of recommendation and level of evidence for each intervention are given in parenthesis (Table 1).
TABLE 3. Recommendations for Diagnosing LAST

- Classic descriptions of LAST depict a progression of subjective symptoms of CNS excitement (agitation, auditory changes, metallic taste or abrupt onset of psychiatric symptoms), followed by seizures then CNS depression (drowsiness, coma, or respiratory arrest). Near the end of this continuum, initial signs of cardiac toxicity (hypertension, tachycardia, or ventricular arrhythmias) are supplanted by cardiac depression (bradycardia, conduction block, asystole, decreased contractility). However, there is substantial variation in this classic description, including:
  - Simultaneous presentation of CNS and cardiac toxicity
  - Cardiac toxicity without prodromal signs and symptoms of CNS toxicity
  - Thus, the practitioner must be vigilant for atypical or unexpected presentation of LAST (I; B).
- The timing of LAST presentation is variable. Immediate (<60 s) presentation suggests intravascular injection of local anesthetic with direct access to the brain, whereas presentation that is delayed 1–5 mins suggests intermittent intravascular injection, lower extremity injection, or delayed tissue absorption. Because LAST can present >15 mins after injection, patients that receive potentially toxic doses of local anesthetic should be closely monitored for at least 30 mins after injection (I; B).
- Case reports associate LAST with underlying cardiac, neurologic, pulmonary, renal, hepatic, or metabolic disease. Heightened vigilance may be warranted in these patients, particularly if they are at the extremes of age (IIa; B).
- The overall variability of LAST signs and symptoms, timing of onset, and association with various disease states suggests that practitioners should maintain a low threshold for considering the diagnosis of LAST in patients with atypical or unexpected presentation of CNS or cardiac signs and symptoms after receiving more than a minimal dose of local anesthetic (IIa; B).

The class of recommendation and level of evidence for each intervention are given in parenthesis (Table 1).

to benzodiazepines. If tonic-clonic movements persist despite these measures, small doses of succinylcholine may be considered as a bridging therapy until tissue levels of local anesthetic have cleared.

Lipid emulsion therapy can be instrumental in facilitating resuscitation, most probably by acting as a “lipid sink” that draws down the content of lipid-soluble local anesthetics from within cardiac tissue, thereby improving cardiac conduction, contractility, and coronary perfusion. We recommend an initial bolus of 1.5 mL/kg (lean body mass) 20% lipid emulsion, followed by an infusion of 0.25 mL/kg per minute continued for 10 mins after hemodynamic stability is attained. Failure to achieve stability should prompt an additional bolus and increase of infusion rate to 0.5 mL/kg per minute. Approximately 10 mL/kg lipid emulsion for 30 mins is recommended as an upper limit for initial administration.

There are several as yet unanswered questions regarding lipid emulsion therapy. Initial recommendations conservatively suggested that it be used only after standard resuscitative efforts have failed.

TABLE 4. Recommendations for Treatment of LAST

- If signs and symptoms of LAST occur, prompt and effective airway management is crucial to preventing hypoxia and acidosis, which are known to potentiate LAST (I; B).
- If seizures occur, they should be rapidly halted with benzodiazepines. If benzodiazepines are not readily available, small doses of propofol or thiopental are acceptable. Future data may support the early use of lipid emulsion for treating seizures (I; B).
- Although propofol can stop seizures, large doses further depress cardiac function; propofol should be avoided when there are signs of CV compromise (III; B). If seizures persist despite benzodiazepines, small doses of succinylcholine or similar neuromuscular blocker should be considered to minimize acidosis and hypoxemia (I; C).
- If cardiac arrest occurs, we recommend standard Advanced Cardiac Life Support with the following modifications:
  - If epinephrine is used, small initial doses (10–100 μg boluses in the adult) are preferred (IIa; C)
  - Vasopressin is not recommended (IIIC; B)
  - Avoid calcium channel blockers and β-adrenergic receptor blockers (III; C)
  - If ventricular arrhythmias develop, amiodarone is preferred (IIa; B); treatment with local anesthetics (lidocaine or procainamide) is not recommended (III; C)
- Lipid emulsion therapy (IIa; B):
  - Consider administering at the first signs of LAST, after airway management
  - Dosing:
    - 1.5 mL/kg 20% lipid emulsion bolus
    - 0.25 mL/kg per minute of infusion, continued for at least 10 mins after circulatory stability is attained
    - If circulatory stability is not attained, consider rebolus and increasing infusion to 0.5 mL/kg per minute
    - Approximately 10 mL/kg lipid emulsion for 30 mins is recommended as the upper limit for initial dosing
  - Propofol is not a substitute for lipid emulsion (III; C).
- Failure to respond to lipid emulsion and vasopressor therapy should prompt institution of cardiopulmonary bypass (CPB) (IIa; B). Because there can be considerable lag in beginning CPB, it is reasonable to notify the closest facility capable of providing it when CV compromise is first identified during an episode of LAST.

The class of recommendation and level of evidence for each intervention are given in parenthesis (Table 1).
attempts had failed, but recent case reports\(^6\),\(^5\)\(^0\)–\(^5\)\(^2\) support the early use of lipid emulsion at the first sign of arrhythmia from suspected LAST, prolonged seizure activity, or rapid progression of the toxic event. Because tissue depots of local anesthetic can redistribute to the circulation over time and delayed recurrence of severe toxicity has been reported, we recommend that any patient with significant LAST be observed for at least 12 hrs. There is no evidence that one formulation of lipid emulsion is superior to another for the treatment of LAST. However, it is important to note that propofol is not a substitute for lipid emulsion therapy because of its low lipid content (10%), the large volumes required for the benefit of lipid in resuscitation (hundreds of milliliters) and the direct cardiac depressant effects of propofol. Our recommendations for the treatment of LAST are presented in Table 4. Those recommendations are summarized in Appendix 3, which is available online in two sizes and can be printed and laminated for display in areas where potentially toxic doses of local anesthetics are used. (See Supplemental Digital Content 1, http://links.lww.com/AAP/A17, for a condensed version of Appendix 3, and Supplemental Digital Content 2, http://links.lww.com/AAP/A18, for a full-size version).

**FUTURE DIRECTIONS**

It is apparent that continued investigation is needed to guide future methods for preventing and treating LAST. Improved, less toxic, longer-acting local anesthetics are desired. Novel delivery methods may reduce the dose required to achieve clinical anesthesia and analgesia. Examples include both current technology (UGRA) and delivery methods in development, such as capsaicin coinjection\(^5\)\(^3\) and sustained release microspheres or liposomes.\(^5\)\(^4\) We hope that continued laboratory investigation will lead to improved resuscitation methods. Alternative formulations of lipid emulsion or new agents designed to increase partitioning, binding, capture, or otherwise neutralizing local anesthetic molecules hold the promise of a rapid, effective antidote to LAST. Further refinement is needed with regard to the ideal timing of lipid emulsion therapy, along with identification of potential toxicities or adverse effects.

Our understanding of the mechanisms of LAST, although incomplete, has increased significantly since local anesthesia was introduced more than a century ago. Stepwise improvements in our knowledge regarding prevention, diagnosis, and treatment have likely led to a reduction in fatalities associated with LAST; it is less certain whether the frequency of nonfatal seizures and cardiac events has also declined, particularly those events associated with peripheral nerve block (as opposed to epidural techniques). Although probably linked to the recent development of UGRA and lipid emulsion therapy, the resurgence of published reports of LAST, (particularly involving successful resuscitation) suggests that LAST remains a significant clinical problem. Considering (1) the extensive use of local anesthetics, (2) the frequent use of doses sufficient to cause significant morbidity or mortality, and (3) the imperfect nature of our ability to prevent, detect, and treat these complications, it remains the responsibility of all clinicians using local anesthetics to understand their potential for severe systemic toxicity and to be prepared to respond immediately to these events when they occur.

**REFERENCES**

24. Groban L, Deal DD, Vernon JC, James RL, Butterworth J. Ventricular
Regional Anesthesia and Pain Medicine • Volume 35, Number 2, March-April 2010

Local Anesthetic Toxicity Practice Advisory


APPENDIX 1

External Expert Appraisers

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APPENDIX 2

Professional Societies Invited to Comment on Draft Guidelines

American Academy of Family Medicine
American Academy of Orthopedic Surgeons
American College of Emergency Physicians
American College of Surgeons
American Dental Association
American Academy of Orthopedic Surgeons
American Academy of Family Medicine
American Anesthesia Patient Safety Foundation

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APPENDIX 3

AMERICAN SOCIETY OF REGIONAL ANESTHESIA AND PAIN MEDICINE

Practice Advisory on Treatment of Local Anesthetic Systemic Toxicity

For Patients Experiencing Signs or Symptoms of Local Anesthetic Systemic Toxicity (LAST)

- Get Help
- Initial Focus
  - Airway management: ventilate with 100% oxygen
  - Seizure suppression: benzodiazepines are preferred
  - Basic and Advanced Cardiac Life Support (BLS/ACLS) may require prolonged effort
- Infuse 20% Lipid Emulsion (values in parenthesis are for a 70 kg patient)
  - Bolus 1.5 mL/kg (lean body mass) intravenously over 1 min (~100 mL)
  - Continuous infusion at 0.25 mL/kg/min (~18 mL/min; adjust by roller clamp)
  - Repeat bolus once or twice for persistent cardiovascular collapse
  - Double the infusion rate to 0.5 mL/kg per minute if blood pressure remains low
  - Continue infusion for at least 10 mins after attaining circulatory stability
  - Recommended upper limit: approximately 10 mL/kg lipid emulsion over the first 30 mins
- Avoid vasopressin, calcium channel blockers, β-blockers, or local anesthetic
- Alert the nearest facility having cardiopulmonary bypass capability
- Avoid propofol in patients having signs of cardiovascular instability
- Post LAST events at www.lipidrescue.org and report use of lipid to www.lipidregistry.org
BE PREPARED
• We strongly advise that those using local anesthetics (LAs) in doses sufficient to produce systemic toxicity (LAST) establish a plan for managing this complication. Making a local anesthetic toxicity kit and posting instructions for its use are encouraged.

RISK REDUCTION (BE SENSIBLE)
• Use the least dose of LA necessary to achieve the desired extent and duration of block.
• Local anesthetic blood levels are influenced by site of injection and dose. Factors that can increase the likelihood of LAST include: advanced age, heart failure, ischemic heart disease, conduction abnormalities, metabolic (eg, mitochondrial) disease, liver disease, low plasma protein concentration, metabolic or respiratory acidosis, and medications that inhibit sodium channels. Patients with severe cardiac dysfunction, particularly very low ejection fraction, are more sensitive to LAST and also more prone to receive ‘stacked’ injections (with resulting elevated LA tissue concentrations) because of slowed circulation time.
• Consider using a pharmacologic marker and/or test dose, for example, epinephrine 5 μg/mL of LA. Know the expected response, onset, duration, and limitations of a “test dose” in identifying intravascular injection.
• Aspirate the syringe prior to each injection while observing for blood.
• Inject incrementally, observing for signs and querying frequently for symptoms of toxicity between each injection.

DETECTION (BE VIGILANT)
• Use standard American Society of Anesthesiologists (ASA) monitors.
• Monitor the patient during and after completing the injection, as clinical toxicity can be delayed up to 30 mins (or longer after tumescent procedures).
• Consider LAST in any patient with altered mental status, neurologic symptoms, or cardiovascular instability following a regional anesthetic.
• Central nervous system signs (may be subtle or absent)
  o Excitation (agitation, confusion, muscle twitching, seizure)
  o Depression (drowsiness, obtundation, coma, apnea)
  o Nonspecific (metallic taste, circumoral numbness, diplopia, tinnitus, dizziness)
• Cardiovascular signs (often the only manifestation of severe LAST)
  • Initially may be hyperdynamic (hypertension, tachycardia, ventricular arrhythmias), then
    o Progressive hypotension
    o Conduction block, bradycardia, or asystole
    o Ventricular arrhythmia (ventricular tachycardia, torsades de pointes, ventricular fibrillation)
  • Sedative hypnotic drugs reduce seizure risk, but even light sedation may abolish the patient’s ability to recognize or report symptoms of rising LA concentrations.

TREATMENT
• Timing of lipid infusion in LAST is controversial. The most conservative approach, waiting until after ACLS has proven unsuccessful, is unreasonable because early treatment can prevent cardiovascular collapse. Infusing lipid at the earliest sign of LAST can result in unnecessary treatment because only a fraction of patients will progress to severe toxicity. The most reasonable approach is to implement lipid therapy on the basis of clinical severity and rate of progression of LAST.
• There is laboratory evidence that epinephrine can impair resuscitation from LAST and reduce the efficacy of lipid rescue. Therefore it is recommended to avoid high doses of epinephrine and use smaller doses, for example, 1 μg/kg, for treating hypotension.
• Propofol should not be used when there are signs of cardiovascular instability. Propofol is a cardiovascular depressant with lipid content too low to provide benefit. Its use is discouraged when there is a risk of progression to cardiovascular collapse.
• Prolonged monitoring (>12 hrs) is recommended after any signs of cardiac toxicity because cardiovascular depression due to LAs can persist or recur after treatment.

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The ASRA Practice Advisory on Local Anesthetic Toxicity is published in the society’s official publication Regional Anesthesia and Pain Medicine, and can be downloaded from the journal Web site at www.rapm.org.

OVERVIEW OF ULTRASOUND PRINCIPLES
Ed Mariano, M.D., M.S.

Potential Advantages of Ultrasound\textsuperscript{1-3}
- Direct visualization of relevant anatomy
- Real-time confirmation of local anesthetic spread
- Improved operator performance and outcomes
- Improved quality and patient safety

Basic Ultrasound Principles
- Transducer sends and receives high-frequency sound waves
- Body tissues have different acoustic impedances
- Sound waves can be absorbed, reflected, and refracted
- “Echoes” are digitally processed into images

General Rules
- Higher frequency emitted (10-15 MHz) = more resolution but less penetration (depth)
  - Superficial: IS, SC, Ax, Fem, Pop
- Lower frequency emitted (2-8 MHz) = less resolution but more penetration (depth)
  - Deep: Sciatic, PVB, Lumbar Plexus, IC

Basic Ultrasound Imaging
- Blood vessels: hypo-echoic (dark)
- Muscles: intermediate (shades of gray)
- Periosteum: hyper-echoic (white)
- Nerves: hyper, hypo, or both
**Imaging Techniques**
- In-plane: needle is visualized in its entirety
- Out-of-plane: needle is not parallel with ultrasound beam

**Importance of Needle Angle**
- Use curvilinear probe for greater depth or steeper needle angles
- Linear probe: needle should be at 90°
- Larger needles may be easier to visualize

**Image Optimization**
- "PART"
  - P=Pressure
  - A=Alignment
  - R=Rotation
  - T=Tilting

**Traditional vs. Ultrasound-Guided Blocks**
- Traditional "Blind" Techniques
  - Paresthesia-seeking or nerve stimulation
  - Trial and error
  - Using the "Force" (left to experts)
- Ultrasound-Guided
**Detecting Intraneural Injection**

- Visualize tissue expansion with hypoechoic fluid
- Stimulating current not always reliable
- 45% intraneural with >0.5 mA current
- Significance of intraneural injection?

**Ultrasound vs. Nerve Stimulation: Which one is Better?**

- 188 axillary blocks: NS, US, or USNS
  - Complete sensory block (3/3): NS (63%), US (83%, p=0.01), USNS (81%, p=0.03)
  - *Successful surgical anesthesia: NS (86%), US (95%, NS), USNS (92%, NS)*
- 59 axillary blocks (20 ml ropiv): NS vs US
  - Faster onset of sensory block in US group (5 min)
  - *No difference in onset of motor block, successful surgical anesthesia, satisfaction, or sequelae*

**Summary**

- **Know your anatomy** and match regional technique to surgery
- Ultrasound improves our understanding of peripheral nerve anatomy
- Ultrasound may be used as “scout” to confirm landmarks or for real-time image-guidance
- Ultrasound may have advantages over traditional techniques

“Regional anesthesia is an art. Remembering that even experts may fail, we should try often and again, observing scrupulously its principles, until we succeed.”


Ultrasound-guided Regional Anesthesia

Current State of the Art
Andrew T. Gray, M.D., Ph.D.*

HIGH-RESOLUTION ultrasound can provide direct real-time imaging of peripheral nerves and identify tissue planes that permit favorable local anesthetic distribution for conduction block and catheter placement. To be successful at ultrasound-guided neural blockade, one must be familiar with the relevant cross-sectional anatomy and the coordination of the imaging probe with the block needle. Ultrasound has many roles in pain management interventions, both peripheral and neuraxial.

Relation of Ultrasound with Other Techniques for Regional Block

With imaging playing an increasing role in vascular access, transesophageal echocardiography, and regional blockade, the ultrasound machine may become an important component of the anesthesia machine of the future. Other fields of medicine in which practitioners are familiar with ultrasound imaging, such as emergency medicine, also may use ultrasound to guide regional blockade. Ultrasound guidance can be combined with alternative techniques for regional block, including nerve stimulation.

Ultrasound guidance can be used for neuraxial blocks. Ultrasound imaging may improve success with epidural placement.1 Paramedian longitudinal imaging planes provide the best acoustic window around bony structures. Of neuraxial structures, the dura mater is well visualized with ultrasound imaging. However, formal review of ultrasound guidance for neuraxial anesthesia is beyond the scope of this article.

Nerve Imaging with Ultrasound

Additional information regarding this is available on the ANESTHESIOLOGY Web site at http://www.anesthesiology.org.†

Because peripheral nerves can be difficult to identify from adjacent background structures, it is important to know all of their distinguishing features. The smallest peripheral nerves that have been imaged with ultrasound are the digital nerves.2 These nerves are 2 mm in diameter and have been examined for the purpose of assessing nerve repair. While the limits of resolution continue to improve, most of the nerves for regional blockade can be imaged with ultrasound technology today. Nerves can have a round, oval, or triangular shape.3 Interestingly, a single nerve can have all three shapes along its nerve path as it travels between adjacent structures.4

Nerves are not static structures. Nerve position within the subarachnoid space is influenced by gravity and body position.5 Extremity movement causes sciatic nerve rotation in the popliteal fossa.6 Light pressure with the ultrasound probe can displace nerves to the side of the axillary artery.7 Peripheral nerves also can be displaced by the advancing block needle or local anesthetic injection, and this may be an underlying safety factor for peripheral block.

Cervical nerve roots (ventral rami) have a monofascicular appearance on ultrasound scans,8 whereas more peripheral nerves have an internal fascicular pattern characterized by hypoechoic (dark) fascicles surrounded by...
hyperechoic (bright) connective tissue. This fascicular echotexture results in the “honeycomb” appearance of nerves on short axis (transverse) scan. Although the genesis of the fascicular echotexture pattern is not completely understood, approximately one third the number of fascicles visible on light microscopy is visible on ultrasound at 15 MHz.9

Nerve identity can be confirmed by scanning along the known course of the nerve. Ultrasound can easily follow the oblique course of the nerve, and this is difficult to accomplish with other imaging modalities such as magnetic resonance imaging.10 Short axis (transverse) scanning is preferred to follow a nerve along its course.

Although nerve vasculature can be demonstrated with color Doppler in some healthy subjects,11 this imaging mode is useful for distinguishing smaller nerves from vessels. Specifically, a robust Doppler signal distinguishes a blood vessel from a small nerve. Unlike vessels, nerves are not compressible structures.

Tendons have similar ultrasound appearance to nerves. The tendon echotexture consists of a fibrillar pattern: fine linear echoes resembling fibrils, with hypoechoic areas that are not as prominent (like the fine hairs of a violin’s bow). A 10-MHz transducer can differentiate the fascicular and fibrillar echotexture patterns. In addition, tendons only form at the ends of muscle, whereas nerve area is relatively uniform along the nerve path. Furthermore, most blocks are performed where tendons are not in the scan plane. Tendons are more anisotropic than nerves, meaning the echo intensity will vary more substantially with the angle of insonation.

Advances in ultrasound technology will allow imaging of smaller and deeper nerves. Today, high-frequency broadband linear probes provide the best nerve imaging.12 Display of nerve sonograms is commonly performed with grayscale postprocessing maps, although there is recent evidence that color encoding received echoes improves musculoskeletal imaging.12

**Needle Visibility**

The primary factors that determine the ultrasound visibility of the needle are the insertion angle and gauge.13 At steep angles, backscatter from the needle rather than specular reflections is received by the ultrasound transducer.14 This results in marked reductions in needle tip visibility. Many authors have emphasized the critical importance of establishing needle tip visibility before advancing the needle when the in plane approach is used (see section entitled The In-plane Needle Approach). However, needle tip visibility is inherently reduced at steep angles and may present problems. Entering the skin with the needle close to the transducer disturbs the surface contact and forces steep angles to the target.

Large-bore needles are easier to visualize for two reasons. First, the larger cross-sectional area makes the needle easier to locate. Second, larger needles are less flexible and therefore less likely to bend out of the plane of imaging. One strategy has been to use large-bore (17-gauge) needles to promote needle tip visibility for deeper blocks.15

The role of acoustic background is substantial: The needle tip is best visualized within dark (anechoic) vessels or local anesthetic. A dark background, which can be created by low receiver gain, can improve needle tip visibility. Commercial modifications (coating or dimpling) to improve echogenicity of regional block needles are technically possible but have not been specifically marketed at this time.

Vascular punctures have been reported despite use of the in plane technique, emphasizing the importance of needle tip visibility in clinical practice.15,16 These inadvertent vascular punctures have occurred despite the fact that vessels are the easiest anatomical structures to identify with ultrasound. However, the vascular puncture rates with ultrasound guidance are probably lower than with other approaches to regional block.17

**Local Anesthetic Solutions and Injection**

Injection of quiescent (unagitated) solution can serve as reverse contrast, outlining the borders of the anesthetized nerve. Nerves will often be easier to identify after injection of undisturbed local anesthetic and sometimes can be seen to float freely within the injected solution. Injection of small amounts of air (0.3–0.5 ml) into the tissue through a needle can be used to identify the location of the tip.18 Although bubbles are easy to identify sonographically and can serve as a useful marker of the needle tip, bubbles also can disperse in tissue and cause acoustic shadowing distally, becoming problematic. Therefore, all air bubbles are removed from the local anesthetic solution before injection. Most practitioners elect not to use bicarbonate containing solutions of local anesthetic because these solutions evolve carbon dioxide, which obscures imaging.

One of the most important advantages of ultrasound imaging is the ability to reposition the needle after initial injection of local anesthetic. Test injections to visualize local anesthetic distribution should be small (1–2 ml). If the local anesthetic distribution is not seen on the monitoring screen immediately stop, aspirate, and move the transducer or needle (do not continue to inject because inadvertent intravascular injection is one of the possibilities). If the local anesthetic distribution does not adequately surround the nerves, the block needle can be repositioned, and the process of test injections can be continued. It is not necessary to contact nerves with the block needle to surround them with local anesthetic if

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the correct fascial planes are identified. After injection, the local anesthetic distribution can be assessed by sliding the transducer along the nerve path with the nerve viewed in short axis.

**Imaging Planes and Approaches to Regional Block**

**Imaging Planes for Nerves**

Nerves can be imaged in short axis or long axis (fig. 1). This nomenclature is familiar to many anesthesiologists because it is used in the field of transesophageal echocardiography. Similarly, the terms transverse and longitudinal have been used in the radiology literature. Ultrasound-guided blocks are generally performed with short axis imaging of nerves for several reasons. First, identification of peripheral nerves is relatively easy. Second, there is good resolution of the fascial barriers that surround nerves. Third, dynamic assessment and verification of circumferential distribution of local anesthetic with injection is possible. Finally, if the transducer moves slightly, the image is still workable (an oblique view of the nerve). For these reasons, short axis views of peripheral nerves for regional blocks have dominated practice at many institutions.

**The Out-of-plane Needle Approach**

The out-of-plane (OOP) technique involves inserting the needle so that it crosses the plane of imaging near the target. With this approach, the target is typically centered within the field of view and the depth noted. If the needle tip is not visualized, the endpoint for injection is not so clear and may require more dependence on small-volume test injections for visualization of adequate local anesthetic distribution. The OOP technique can be made similar to the in-plane (IP) technique (see section entitled The In-plane Needle Approach) with sliding and tilting of the transducer so as to follow the needle tip.

**The In-plane Needle Approach**

The needle can be inserted within the plane of imaging to visualize the entire shaft and tip (IP technique). For the IP approach, the imaged needle path should be maximized by placing the target on the side of the imaging field of view away from the approaching needle. The transducer can be manipulated as necessary to bring the needle into the plane of imaging. If the needle tip is not clearly identified within the plane of imaging, do not advance the needle. When the needle is in plane (longitudinal scan), the in vivo sonographic appearance will be hyperechoic, with parallel hyperechoic traces displayed away from the transducer. These hyperechoic traces result from reverberations inside the needle itself.

**General Comments**

Both the IP and OOP approaches are currently in clinical use, and the merits of each have been debated. Critics of the OOP approach are concerned that lack of needle tip visibility during the procedure can lead to complications. Finding an echogenic dot for the OOP approach within a bright background can be difficult (but IP needle tip identification also can be difficult in this circumstance). Critics of the IP approach are concerned that this approach is time-consuming and that partial lineups of the needle and probe create a false sense of security. If the transducer tilt is critical to nerve visibility, then with the IP approach, which usually requires transducer manipulation, it can be difficult to visualize the block needle and nerve simultaneously. The IP approach requires longer needle insertion paths than the OOP approach and can therefore cause more patient discomfort.

For either the OOP or the IP approach, the author’s institution prefers a freehand technique to the use of needle guides. A flat angle of approach improves needle visualization (place the needle entry point away from the transducer to achieve a flatter angle and produce less problems with probe contact). Optimal visualization of the needle occurs when the needle is parallel to the active face of the transducer. The needle should be inserted with the bevel directly facing (or avverting) the active face of the transducer to improve visibility of the needle tip.

The long axis in plane approach may be suitable for vascular access procedures. However, alignment on nerves can be difficult because nerves do not always have a straight path and slight movement of the transducer can result in loss of the nerve image. Furthermore, with the long axis IP approach, the needle is constrained to come down directly on the nerve and therefore may increase the chance of injecting into the targeted structure.

**Clinical Studies**

A number of clinical trials have examined block characteristics with ultrasound guidance (table 1). Several types of clinical blocks at different anatomical locations have been studied. All studies found improved block characteristics with ultrasound guidance (or a trend toward such a difference). This includes block performance time, an issue of interest today because of the focus on operating room efficiency. The lack of statistical difference in success rates is not surprising given the high overall success rates (the studies were underpowered to find a small increase in success rate). No study has found that nerve stimulation improves block characteristics compared with ultrasound. Although one cannot exclude the possibility of reporting bias, favorable block outcomes with ultrasound guidance are strongly suggested.

The reported incidence of nerve injury after peripheral nerve block is low and highly depends on the method of
Fig. 1. (A) Approaches to regional block with ultrasound (SAX OOP, SAX IP, LAX OOP, and LAX IP). For the OOP approach, the needle crosses the plane of imaging as an echogenic dot with the target centered in the field of view. For the IP technique, the entire tip and shaft of the needle are seen while the needle approaches the target on the opposite side of the field. IP = in-plane approach of the needle; LAX = long axis view of the target; OOP = out-of-plane approach of the needle; SAX = short axis view of the target. (B) Short axis (transverse cross-sectional) ultrasound scan of the musculocutaneous nerve in the axilla. The needle tip and local anesthetic injection (arrowheads) are identified within the plane of imaging (SAX IP approach). After the initial injection the needle tip is substantially displaced from the nerve. Large tick marks are spaced 10 mm. (C) Short axis (transverse cross-sectional) ultrasound scan of the musculocutaneous nerve in the axilla. The needle tip crosses the plane of imaging to facilitate local anesthetic injections (SAX OOP approach). Multiple test injections and needle repositioning were performed based on feedback using the observed images. Large tick marks are spaced 10 mm.
follow-up. Therefore, large controlled studies are needed to look at approaches to peripheral nerve block and their complications. These safety issues have yet to be addressed in a prospective fashion.

As this new field develops, we must appreciate that we are studying an evolving technology. Therefore, published results may not accurately reflect current practice. An effect of training during a clinical trial has been shown for ultrasound guidance but not for the control nerve stimulation group.26 While clinical trials will continue to compare effort and operator dependent techniques, this result suggests that performance of ultrasound guidance will improve.

Recent Developments in Ultrasound Imaging

In this issue of Anesthesiology, Dr. Chan et al.30 convincingly demonstrate that it is possible to image the largest peripheral nerve in the body (the sciatic nerve, which is approximately 17 mm in its mediolateral dimension) with low-frequency (2- to 5-MHz) ultrasound and curved array transducers. Previous investigators have stated that frequencies of 10 MHz or higher are necessary to discriminate peripheral nerves from tendons or background. This advance will appear subtle to some readers, but the implications for the future of anesthetic practice may be enormous.

The study dispels the belief that ultrasound frequencies of 10 MHz or higher are necessary to image peripheral nerves. Attenuation of ultrasound waves relates to frequency via the attenuation constant (approximately 0.75 dB/(cm-MHz) in soft tissue), indicating larger attenuation of high frequencies. Because sound waves are longitudinal waves, the frequency only relates to one component of resolution (the axial resolution along the path of the sound beam). Other components of resolution (lateral resolution and elevational resolution) are typically worse and therefore potentially more important.

Now that we are aiming at lower frequencies for nerve imaging with ultrasound, new issues arise. There is some suggestion from the sonograms provided that nerve fascicles can be identified at 2–5 MHz. However, adjacent structures may have similar sonographic appearance to the sciatic nerve in the thigh (specifically, the tendon of

Table 1. Clinical studies measuring characteristics of ultrasound guided peripheral nerve blocks

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Block</th>
<th>Ultrasound</th>
<th>Nerve Stimulation</th>
<th>P Value</th>
<th>Study Design</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Performance</td>
<td>Supravacicular</td>
<td>5.0 ± 2.4 (40)</td>
<td>9.8 ± 7.5 (40)</td>
<td>&lt; 0.001</td>
<td>Randomized</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>Infracocicular</td>
<td>10.0 ± 4.4 (114)</td>
<td>NA</td>
<td>NA</td>
<td>Prospective</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>Muscularcutaneous</td>
<td>1.9 ± 0.7 (10)</td>
<td>NA</td>
<td>NA</td>
<td>Prospective</td>
<td>27</td>
</tr>
<tr>
<td>Success (%)</td>
<td>Supravacicular</td>
<td>85% (40)</td>
<td>78% (40)</td>
<td>NS</td>
<td>Randomized</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>Infracocicular</td>
<td>95% (40)</td>
<td>NA</td>
<td>NA</td>
<td>Prospective</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>Muscularcutaneous</td>
<td>100% (20)</td>
<td>100% (20)</td>
<td>NS</td>
<td>Randomized</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>Three-in-one</td>
<td>95% (20)</td>
<td>85% (20)</td>
<td>NS</td>
<td>Randomized</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>Three-in-one</td>
<td>95% (20)</td>
<td>80% (20)</td>
<td>NS</td>
<td>Randomized</td>
<td>17</td>
</tr>
<tr>
<td>Onset (min)</td>
<td>Infracocicular</td>
<td>6.7 ± 3.2 (114)</td>
<td>NA</td>
<td>NA</td>
<td>Prospective</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>Supravacicular</td>
<td>9 [5-11] (20)</td>
<td>15 [5-25] (20)</td>
<td>&lt; 0.001</td>
<td>Randomized</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>Muscularcutaneous</td>
<td>3.4 ± 0.9 (10)</td>
<td>NA</td>
<td>NA</td>
<td>Prospective</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>Three-in-one</td>
<td>14 ± 14 (20)</td>
<td>27 ± 14 (20)</td>
<td>&lt; 0.05</td>
<td>Randomized</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>Three-in-one</td>
<td>13 ± 16 (20)</td>
<td>27 ± 12 (20)</td>
<td>&lt; 0.01</td>
<td>Randomized</td>
<td>17</td>
</tr>
<tr>
<td>Duration (min)</td>
<td>Supravacicular</td>
<td>846 ± 531 (40)</td>
<td>652 ± 473 (40)</td>
<td>NS</td>
<td>Randomized</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>Supravacicular</td>
<td>364 [280-480] (20)</td>
<td>310 [210-420] (20)</td>
<td>&lt; 0.001</td>
<td>Randomized</td>
<td>28</td>
</tr>
</tbody>
</table>

Unless otherwise stated, data are expressed as mean ± SD (N value). Mrozek et al. 2004 expressed data as median (range).34 Chan et al. 2003 confirmed all ultrasound guided blocks with nerve stimulation.46 Spence et al. 2005 confirmed some ultrasound guided blocks with nerve stimulation.47 NA = not applicable. NS = not statistically significant (P ≥ 0.05). Ref. = reference.
the long head of the biceps femoris). At these low frequencies, nerves and tendons must be distinguished using different criteria than fascicular or fibrillar echotexture. Tendons and nerves must be discriminated based on position and change in size and shape along their course.

These investigators used a curved array that provides a broad view useful for imaging the approaching block needle. However, in this study, block needle visibility was not demonstrated, so the critical issue with the use of curved arrays and low frequencies may actually relate more to needle visibility than to nerve visibility. Controlled studies of needle visibility comparing linear and curved arrays are needed to address this issue specifically. If needle visibility at these frequencies with a curved probe is problematic, nerve stimulation is probably still essential. Sciatric nerve stimulation was consistent with sonographic evidence of needle–nerve contact (unlike previous studies of the brachial plexus by this same research group).

Most observed nerve depths ranged between 3 and 7 cm, depths that can be reached with high-frequency ultrasound and better image quality. The biggest advance of this study might be for obese subjects, who were not formally included. In this set of 15 volunteers, these authors did not detect proximal sciatric nerve division by the piriformis muscle (an anatomical variant with estimated incidence between 1.5 and 21%),31 a suggested benefit of ultrasound imaging to prevent incomplete block.22

Conclusions

Clinical studies suggest that ultrasound guidance has advantages over more traditional nerve stimulation–based techniques for regional block. If desired, ultrasound guidance can be combined with nerve stimulation to confirm proximity to neural structures. However, it is not necessary to use electrical stimulation or obtain paresthesias to achieve reliable conduction block of peripheral nerves. Given clinical experience, practitioners will become confident in assigning nerve identity based on ultrasound appearance alone. Because ultrasound imaging is especially useful in patients with difficult external anatomy, many clinicians have now integrated its use into their routine clinical practice to gain expertise with this important technology.

References


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Ultrasound guidance in regional anesthesia has grown in popularity over the past 5 years. Its attractiveness stems from the unprecedented ability to visualize the target nerve, approaching needle, and the real-time spread of local anesthetic. As ultrasound experience grows within the regional anesthesia community, the limitations and challenges begin to declare themselves. Chief among these limitations are ultrasound-generated artifacts. Recognition of such optical events combined with an appreciation of the mechanisms involved supports a high quality ultrasound-guided regional anesthesia practice. The objective of this article (Part I) is to describe the physical properties of ultrasound most relevant to the regional anesthesiologist so that clinical sonographic imaging can be optimized and common ultrasound-generated artifacts (discussed in more detail in Part II) can be recognized.

**Ultrasound Generation, Frequency, and Wavelength**

An ultrasound wave is a form of acoustic energy and is generated when multiple piezoelectric crystals inside a transducer (i.e., the probe) vibrate at high frequency in response to an alternating current. The rapid vibration, which is transmitted to the patient through a conductive gel, propagates longitudinally into the body as a short, brief series of compressions (high pressure) and rarefactions (low pressure). Each ultrasound wave is characterized by a specific wavelength (distance between pressure peaks) and frequency (number of pressure peaks per second). The propagation velocity of a sound wave (i.e., acoustic velocity) is fairly constant in the human body (c) and is approximately 1,540 meters per second. Therefore, in the human body, we can use the following equation:

\[ c = \lambda \cdot f \]

where \( \lambda \) = wavelength, \( f \) = frequency, and \( c = 1,540 \) meters per second. In order to generate a clinically useful image, the ultrasound waves must bounce off of tissues and return to the probe. The probe, after emitting the wave, switches to a receive mode. When ultrasound waves return to the probe, the piezoelectric crystals will vibrate once again, this time transforming the sound energy into electrical energy. This process of transmission and reception can be repeated over 7,000 times a second and, when coupled to computer processing, will result in the generation of a real-time 2-dimensional image that appears seamless.

The degree to which the ultrasound waves reflect off of a structure and return to the probe will de-
Ultrasound Interactions with Tissues

As the ultrasound waves travel through the body (Fig 1), they are influenced by reflection, refraction, and attenuation. When an ultrasound wave encounters a boundary between 2 different types of tissues, part of the acoustic energy is reflected and part is transmitted. A large and smooth reflector (e.g., the needle) acts like a mirror and is hence called a specular reflector. An irregular surface randomly scatters ultrasound and is referred to as a scattering reflector. Most neural images are generated based on scattering rather than specular reflection. The amount of ultrasound that is reflected is proportional to the difference in acoustic impedance (tendency to resist the passage of ultrasound) between adjacent tissues. The greater the mismatch in acoustic impedance between 2 tissue interfaces, the more energy is reflected back towards the probe, resulting in 2 distinct images on the ultrasound screen. A bone/soft tissue interface, for example, reflects 43% of the incoming ultrasound waves. In contrast, a muscle/blood interface reflects 0.1% of the ultrasound waves.

Clinical pearls: The regional anesthesiologist is at a distinct advantage when the target nerve is surrounded by tissue that has a different acoustic impedance. For example, the sciatic nerve in the popliteal fossa is surrounded by adipose tissue. The large difference in acoustic impedance between the sciatic nerve and the adipose tissue causes the nerve to appear clearly hyperechoic relative to the hypoechoic surrounding adipose tissue (Figs 2 and 3). The reverse is true for the roots of the brachial plexus in the interscalene region. Here, there is a large difference in acoustic impedance between the fascial layers that envelop the plexus and the nerves themselves thereby causing the nerves to appear unmistakably hypoechoic relative to their surroundings (Fig 4).

When ultrasound passes through a tissue interface (nonreflected), it will likely change its direction of travel. This is a process known as refraction and occurs when the wave reaches a boundary that separates 2 tissues with different, however slight, acoustic velocities. Light also is refracted (Snell’s law) and is the reason a fork appears bent when it is inserted into a glass of water. Refracted ultrasound may not contribute to successful imaging of the target structure if a significant amount of the ultrasound does not return to the probe. Refraction (as well as reflection away from the probe) occurs

![Fig 1](image1.png)

**Fig 1.** The many responses that an ultrasound wave produces when traveling through tissue. (a) Scatter reflection: the ultrasound wave is deflected in several random directions both to and away from the probe. Scattering occurs with small or irregular objects. (b) Transmission: the ultrasound wave continues through the tissue away from the probe. (c) Refraction: when an ultrasound wave contacts the interface between 2 media with different propagation velocities, the ultrasound wave is refracted (bent) depending upon the difference in velocities. (d) Specular reflection: reflection from a large, smooth object (such as the needle) which returns the ultrasound wave toward the probe when it is perpendicular to the ultrasound beam.

![Fig 2](image2.png)

**Fig 2.** The short axis view of the sciatic nerve in the popliteal fossa. The large arrow indicates the nerve. The adipose tissue creates a distinct interface with the sciatic nerve which allows for an easy visual distinction between nerve and surrounding muscle. The nerve is hyperechoic (white) and the fat is hypoechoic (dark).
to a larger extent when the angle of incidence between the ultrasound beam and the structure is other than perpendicular.3

Clinical pearls: With respect to needle visualization, the goal of the anesthesiologist is to simultaneously minimize refraction and maximize reflection back toward the probe by keeping the needle perpendicular to the ultrasound beam as indicated in Figure 5A. With deeper nerve targets, the angle of incidence between the beam and needle becomes more parallel such that more ultrasound waves are redirected (by refraction and reflection) and fewer waves successfully return to the probe. The end result is that the needle becomes less visible (Fig 5B). For this reason, many providers prefer the out-of-plane needle approach for deeper target nerves (Fig 6).

Attenuation is the progressive loss of acoustic energy as a wave passes through tissue.4 This results in a progressive decrease in the returning signal intensity as the ultrasound travels deeper into a tissue bed. The major source of ultrasound attenuation is the conversion of some of the acoustic (i.e., mechanical) energy into heat by a process known as absorption. Attenuation is directly related to the depth of beam penetration, the type of tissue being imaged, and varies indirectly with the frequency of the ultrasound waves. Different tissues will result in different degrees of attenuation. Attenuation is measured in decibels per centimeter of tissue (dB cm⁻¹) and is represented by the attenuation coefficient of the specific tissue. The higher the attenuation coefficient, the more attenuated the ultrasound waves are by the specified tissue. Examples of attenuation coefficients of different physiologic tissues are listed in Table 1. Figure 7 shows the impact of frequency and depth on the attenuation of ultrasound.

Clinical pearls: While attenuation can have a profound negative impact on image quality, there are 2 important adjustments that can be made on the ultrasound machine that help to overcome some of the effects of attenuation. First, most machines allow the operator to artificially increase (or decrease) the signal intensity of the returning echoes from all points in the displayed field. This is accomplished by adjusting the gain control higher to increase the overall brightness. Second, most machines offer the operator the ability to control gain independently at specified depth intervals. This is known as time gain compensation. The time gain compensation should be progressively increased as the depth of penetration increases in order to compensate for the corresponding loss of signal intensity (Fig 8).

Resolution

Resolution refers to the ultrasound machine’s ability to distinguish one object from another.5 The most important types of resolution for the regional anesthesiologist are axial, lateral, and temporal resolution.

Axial resolution refers to the machine’s ability to separate 2 structures lying at different depths, parallel to the direction of the ultrasound beam. Axial resolution is roughly equal to one half of the pulse length. If the distance between 2 objects is greater than one half of the length of the ultrasound pulse, then the structures will appear as 2 separate objects (Fig 9). It follows then that higher frequency probes (shorter pulse lengths) produce the best axial reso-
solution. However, as described above, higher frequency ultrasound waves are more readily attenuated than lower frequency sound waves, resulting in poor tissue penetration.

Clinical pearls: High frequency transducer probes (e.g., 8-12 MHz) afford high axial resolution of superficial structures (e.g., axillary region) but have low tissue penetration. Low frequency probes (e.g. 4-7 MHz) allow for...
deeper tissue penetration (e.g., subgluteal region) at the expense of fine axial resolution. Therefore, probe selection is always a trade-off between axial resolution and depth of penetration. When performing a peripheral nerve block, choose the probe and settings with the highest possible frequency that will still afford adequate depth penetration for imaging of the target nerve. See Figure 8 for an example of an ultrasound interface that allows the operator to control the frequency (wavelength) of the ultrasound. Most ultrasound systems allow the operator to change through multiple frequencies for a given probe.

Lateral resolution (Fig 10) refers to the machine’s ability to distinguish 2 objects lying beside one another, perpendicular to the ultrasound beam. Lateral resolution is always worse than axial resolution, thus contributing to more clinical challenges. Despite the generated 2-dimensional image, modern ultrasound machines emit a 3-dimensional ultrasound beam that diverges as it propagates through the body (Fig 11). When electronically launched in various sequences and patterns, the collective beams generated from the multiple piezoelectric elements in the transducer will produce the 3-dimensional beam. The shorter the distance between 2 adjacent element beams, the better the lateral resolution. High frequency and focused ultrasound beams generate the narrowest beams, thus maximizing lateral resolution.

Clinical pearls: The focal zone of the ultrasound beam, indicated on most screen displays, represents the narrowest part of the beam and should be positioned at the exact level of the target nerve. See Figure 8 for an example of the focus button on an ultrasound machine. The focus icon that is displayed on the ultrasound screen is shown in Figures 4 and 5 of Part II.

Table 1. Attenuation Coefficients (at 1 MHz)

<table>
<thead>
<tr>
<th>Material</th>
<th>dB cm⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone</td>
<td>20</td>
</tr>
<tr>
<td>Air</td>
<td>12</td>
</tr>
<tr>
<td>Muscle</td>
<td>1.2</td>
</tr>
<tr>
<td>Brain</td>
<td>0.9</td>
</tr>
<tr>
<td>Fat</td>
<td>0.6</td>
</tr>
<tr>
<td>Blood</td>
<td>0.2</td>
</tr>
<tr>
<td>Water</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Fig 7. Attenuation. Attenuation is estimated as \( \alpha \times f \times \text{path length} \), where \( f \) is the frequency of the ultrasound wave and \( \alpha \) is the attenuation coefficient. Notice the lower frequency wave (2.5 MHz) has less attenuation at a given distance when compared with the 10 MHz wave. Thus, the 2.5 MHz wave is able to penetrate the tissue more effectively than the 10 MHz wave.

Fig 8. An image of a typical ultrasound interface. (1) Probe frequency control. In the depicted system and probe, the frequency can be adjusted from 3 MHz to 12 MHz. The wavelength can not be adjusted independently; however, manual adjustments to frequency result in corresponding changes in wavelength. (2) Overall gain button. This dial changes how bright or dark the entire image appears. (3) Depth control. The objective is to set the depth to just below the target of interest, thereby optimizing temporal resolution. (4) Focus button. It is important to position the focus of the ultrasound beam at the same level as the target of interest. This will optimize both lateral and axial resolution. (5) Time gain compensation. These toggle dials control the gain at consecutive depth intervals. The top dials control the superficial gain and the bottom dials control deeper gain. Because attenuation occurs more with deeper imaging, the typical pattern of the time gain compensation dials is a progressive increase in gain as indicated in this figure.
ultrasound because of the rapid motion of the heart. As the frame rate decreases, motion-related events become progressively blurred. During nerve blocks, motion occurs with probe movement, needle insertion, and injection of local anesthesia. Therefore, during these critical moments, a low frame rate could result in an ambiguous image. The temporal resolution (frame rate) is limited by the sweep speed of the ultrasound beam. In turn, the sweep speed of the ultrasound beam is limited by the speed of sound in tissue, as the ultrasound from the deepest aspects of the image must return to the probe before the next pulse is generated in the neighboring beam. The sweep speed can be increased by reducing the number of individual piezoelectric elements that make up the larger global beam sector or by decreasing the sector scanning angle (for phased array probes). The first option decreases the lateral resolution and the second decreases the image field width, underscoring the fundamental concept that temporal resolution cannot be increased without a compromise secondary to principles of physics.

Clinical pearls: The main maneuver the anesthesiologist can perform to improve the temporal resolution is to decrease the imaging depth to just below the target(s) of interest (Fig 8). Additionally, the injection of local anesthetic should be slow, so as to minimize high velocity tissue movement which can blur the real-time image.

Color Doppler

Doppler technology allows for the identification and quantification of blood flow. In essence, the Doppler principle states that if an ultrasound pulse is sent out and strikes moving red blood cells, the ultrasound that is reflected back to the probe will...
have a frequency that is different from the original emitted frequency (Fig 12). This change in frequency is known as the Doppler shift.\(^6\) It is this frequency change that can be used in cardiac and vascular applications to calculate both blood flow velocity and blood flow direction.\(^7\) The Doppler equation states that:

\[
\text{Frequency shift} = \frac{2 \cdot V \cdot F_i \cdot \cos(\Phi)}{c}
\]

Where \(V\) is the velocity of the moving object, \(F_i\) is the transmitted frequency, \(\Phi\) is the angle of incidence of the ultrasound beam and the direction of blood flow, and \(c\) is speed of ultrasound in the media.

Clinical pearls: The most important application of Doppler technology for the regional anesthesiologist is to confirm the absence of blood flow in anticipated trajectory of the needle, rather than the quantification of the actual velocity or direction of this flow. Doppler information is complicated by the frequent occurrence of artifact generation.\(^2\)

Summary

In summary, in order to optimize clinical imaging and to appreciate ultrasound-related pitfall errors and artifacts, a solid understanding of the physics of ultrasound is extremely helpful. A 3-dimensional ultrasound beam is generated when many multiple tiny piezoelectric crystals rapidly vibrate in response to an electrical current. This ultrasound energy is transmitted through tissue where it is transmitted, reflected, scattered, refracted, and attenuated. Fortunately, some of the reflected ultrasound returns to the probe to be converted back to electrical energy. This electrical information is processed by the system’s computer to ultimately generate the 2-dimensional image. The anesthesiologist has the ability to control image quality and appearance by interfacing with the system to change the characteristics of the ultrasound that is being sent out such as the frequency, focus, wavelength, and frame rate. In a similar fashion, the anesthesiologist has the ability to control how the returning image is processed by adjusting such variables as the gain and various proprietary post processing technologies.

References

Artifacts and Pitfall Errors Associated With Ultrasound-Guided Regional Anesthesia

Part II: A Pictorial Approach to Understanding and Avoidance

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The use of real-time ultrasound guidance in regional anesthesia is growing in popularity. Paramount to the successful and safe use of ultrasound is the appreciation and accurate interpretation of common ultrasound-generated artifacts. An artifact is any perceived distortion, error, or addition caused by the instrument of observation (signal processor). Imaging artifacts can be considered display phenomena, and, therefore, can potentially complicate the planned procedure. There are 4 generic categories of imaging artifacts: (1) Acoustic: error in presentation of ultrasound information; (2) Anatomic: error in interpretation (often called “pitfall” error); (3) Optical illusion: error in perception; and (4) Other: electrical noise.

This article builds on the fundamental principles of ultrasound physics that are discussed in Part I of this article. The objective of this article is to describe and illustrate many of the acoustic and anatomic artifacts commonly encountered by the regional anesthesiologist. In the process, we will offer underlying physical explanations and describe practical tips on how to negotiate these often misleading phenomena.

ACOUSTIC ARTIFACTS

Acoustic artifacts associated with performing regional anesthesia can be further subdivided into 2 major categories: (1) Missing or falsely perceived structures; and (2) degraded images. The reader should note that different imaging artifacts may have the same underlying physical mechanism.

Missing Structures or Falsely Perceived Objects

Inappropriately low gain settings may result in the apparent absence of an existing structure (ie, “missing structure” artifact), whereas inappropriate high gain settings can easily obscure existing structures.

Overgain and Undergain Artifacts

Inappropriate gain settings are fraught with potential artifact generation. Take advantage of the ability to control overall gain levels and TGC. Adjust the gain settings to optimally define the structure of interest. The usual pattern of the TGC dials is depicted in Figure 3B, with a gradual increase in signal intensity; the near field gain is turned down and the far field gain is increased in a progressive fashion.

Lateral Resolution Artifacts

Lateral resolution refers to the system’s ability to distinguish 2 objects from one another when they exist in a lateral to medial relationship.

Example 1: Figure 1 represents two identical images of the interscalene brachial plexus with the overall gain set too high (Fig. 1A) and too low (Fig. 1B).

Example 2: The incorrect use of the time gain compensation (TGC) dials can create an image wherein existing structures appear absent. In Figure 2, the fourth TGC button was turned down too low, effectively abolishing the image of the nerve roots. When the TGC was set correctly (Fig. 3), the C5 through C7 nerve roots can easily be seen.

Clinical pearls: Gain adjustments are fraught with potential artifact generation. Take advantage of the ability to control overall gain levels and TGC. Adjust the gain settings to optimally define the structure of interest. The usual pattern of the TGC dials is depicted in Figure 3B, with a gradual increase in signal intensity; the near field gain is turned down and the far field gain is increased in a progressive fashion.

Acoustic Shadowing

Acoustic shadowing occurs when a structure has a larger attenuation coefficient than the tissue that lies deep to it, causing the deeper tissue to appear far less echogenic than normal. Acoustic shadowing occurs most notably when seeking a target that lies deep to bone. The appreciation of acoustic shadowing is critical to the performance of safe and effective...
ultrasound-guided regional anesthesia. We will therefore present 5 examples spanning the spectrum of regional anesthesia.

Example 1: This is a case of acoustic shadowing caused by bone during spinal imaging in preparation for a neuraxial blockade. The acoustic shadow generated by the adult spinous process impedes the penetration of the ultrasound waves, resulting in the inability to reliably visualize the ligamentum flavum, epidural space, and dura (Fig. 6). The larger intervertebral spaces combined with less densely ossified childhood bone cause less acoustic shadowing and enable visualization of these important structures.

Clinical pearls: The acoustic shadows produced by the spinous processes and lamina can help the operator identify the midline when performing neuraxial blockade, especially in obese patients. The operator may opt for needle insertion either above or below the level of any spinous process. Traditional endpoints for confirmation of correct needle location into the epidural or intrathecal space should always be employed.

Example 2: Acoustic shadowing created by the first rib in the supraclavicular region. Acoustic shadowing can lead to the erroneous assumption that there exist no structures of interest in an anechoic (black) region. In the performance of a supraclavicular nerve block, the goal of the ultrasound exam is to visualize the subclavian artery, the first rib, and the trunks or divisions of the brachial plexus. The important structure to avoid contact with is the pleura which should exist immediately below the first rib. However, because the rib shields the pleura from the ultrasound beam, no anatomical information is provided (Fig. 7).

Clinical pearls: Never insert the needle into the anechoic region deep to the first rib because the location of the pleura cannot be identified.

Example 3: Acoustic shadowing created by air during local anesthetic injection. In this dramatic case of acoustic shadowing, a popliteal sciatic nerve block was aborted secondary to the presumed damage to the sciatic nerve. Figure 8 shows the sciatic nerve before the injection. Figure 9 shows the nerve after 10 mL of local anesthetic was injected. The sciatic nerve appears to have been physically dissected in half. The most likely explanation for this acoustic shadow is an air bubble located at the tip of the needle. In the video loop of this block, when the needle is removed from the patient, the nerve appears to suddenly reform (Appendix, Video 1) A small amount of air serves as the perfect medium to generate a dropout shadow, as air does not conduct ultrasound.

Clinical pearls: When you suspect that the anatomy is erroneous secondary to needle or air-induced acoustic shadowing, simply move the needle or reposition the probe slightly to allow the ultrasound waves to bypass the obstruction from air or metal. Further, the operator should pay careful attention to remove all air from the injection syringes.

Example 4: This is an example of acoustic shadowing created by a 19-gauge needle during an out-of-plane approach to place a continuous femoral nerve catheter. In this example, the needle crossed the ultrasound beam in a perpendicular manner creating a linear acoustic shadow transecting the nerve (Fig. 10). This acoustic shadow is helpful because it tells the operator that the needle is correctly aligned in the lateral-medial plane. However, because the exact location of the needle tip is unknown (in the anterior-posterior plane), an alternative endpoint for injection or catheter threading is necessary (such as nerve stimulation).

Clinical pearls: Search for an acoustic shadow (transecting the target nerve) when inserting a needle using the out-of-plane technique. This will help to confirm the correct lateral-medial location of the needle relative to the target nerve. The operator should appreciate the limitations of the out-of-plane technique, primarily, the inability to confirm the real-time exact location of the needle tip. See Figure 6 of Part I for the comparison of in-plane versus out-of-plane techniques.
Example 5: Acoustic shadowing may not only hide important structures or distort normal anatomy (as in examples 1–4), it may also be a sign of serious patient pathology. For example, calcified arterial plaques act as strong specular reflectors that generate distinct acoustic shadows deep to the affected artery. Because most ultrasound-guided nerve blocks make use of the intimate association of nerves and blood vessels as an important reference point, the regional anesthesiologist will inevitably be confronted with the primary discovery of vascular pathology. In addition, if a transarterial technique is contemplated, one may wish to choose another approach if acoustic shadowing is identified related to a blood vessel of interest. Figure 11 shows an acoustic shadow associated with an atherosclerotic plaque of the right femoral artery discovered during the placement of a single injection femoral nerve block. Figure 12 shows another acoustic shadow associated with an atherosclerotic lesion of the right carotid artery discovered during the placement of an interscalene catheter. The hyperchoic plaque is also well visualized.

Clinical pearls: If an acoustic shadow is identified related to a blood vessel, further clinical evaluation may be needed to assess for significant vascular disease. This may be most important for patients in whom the regional anesthesiologist may traumatize the blood vessel during the performance of the nerve block.

Acoustic Enhancement

Acoustic enhancement occurs when a region behind a weakly attenuating structure produces stronger echoes than those observed from adjacent tissues. Enhancement artifacts commonly occur when ultrasound waves pass relatively unattenuated through blood vessels (weak attenuators), resulting in false enhancement of the adjacent deeper tissue. Because many peripheral nerves are associated with large blood vessels, acoustic enhancement is a common finding.

Examples 1 and 2: Enhancement artifact in the region of the infraclavicular and axillary brachial plexus can be most misleading as the tissue immediately behind the posterior wall of the axillary artery often appears very hyperechoic and is easily mistaken for either the radial nerve (axillary block; Fig. 13) or the posterior cord (infraclavicular block; Fig. 14). Clinical pearls: Because acoustic enhancement can make it difficult to definitively visualize either the radial nerve or the...
posterior cord of the brachial plexus, it may be important to use an additional confirmation technique such as nerve stimulation.

Absent Blood Flow When Blood Flow Actually Exists

Doppler is an important technology in screening for vascularity of a region. However, as is true for 2-dimensional imaging, the assessment of blood flow has the potential for artifact generation. The major concern for the regional anesthesiologist is to falsely conclude that a structure is not a blood vessel when no flow is seen. As explained in Part I, Doppler technology allows for the assessment of both velocity and directionality of blood flow. The complicating factor is that for accurate analysis, blood flow should be parallel to the ultrasound beam. This is based on the Doppler equation (Part I, Fig. 6). In most cases, the regional anesthesiologist is imaging blood vessels on short axis, and, therefore, the blood flow is completely perpendicular to the ultrasound beam. As the angle of incidence of the beam and the blood flow approaches 90 degrees, the cosine of this angle approaches zero (Doppler equation), thereby creating an artifact of no flow.

Clinical pearls and example: Figure 9 shows an acoustic shadow, most likely generated by an air bubble at the needle tip. This acoustic shadow is easy to see passing right through the nerve and into the anterior tissues.
scales and higher color gain will tend to increase the sensitivity to detect flow.

**Degraded Images**

Image degradation may be the result of user interface issues, but can often be the result of a phenomenon known as reverberation. Reverberations occur as the result of ultrasound waves bouncing back and forth between two strong specular reflectors. The result is usually multiple linear and hyperechoic areas emanating distal to the reflecting structures. When multiple reverberation artifacts are merged, this has been referred to as the comet tail sign.\(^6\)

**Needle Reverberation Artifact**

Example 1: Although there are many reverberation artifacts described in the cardiac literature\(^7\), the most relevant reverberation artifact for the regional anesthesiologist involves 2 specular reflectors: the probe itself and the block needle. A depiction of an 18-gauge needle inserted in-plane with the ultrasound beam is elsewhere in this issue (Part I, Fig. 5A).\(^3\)

Under the needle are seen multiple and equally spaced linear densities that represent ultrasound waves bouncing back and forth within the lumen of the needle. When the ultrasound energy finally returns to the probe to be processed, a duplicate image of the needle will be displayed on the screen. This duplicate image will appear deeper than the primary (actual) needle because more time has elapsed for the ultrasound energy to return to the probe. The mechanism of the reverberation artifact is depicted in Figure 16.

Example 2: Figure 17 illustrates the in-plane approach for a musculocutaneous nerve block. The needle is inserted through the biceps muscle. Due to a reverberation artifact involving the needle, the 22-gauge b-bevel needle appears larger than it

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**FIGURE 11.** Ultrasound image of the femoral artery in short axis showing an atherosclerotic lesion. This pathology was identified during the performance of a femoral nerve block. Note the hyperechoic plaque and the characteristic acoustic shadow. FA, femoral artery.

**FIGURE 12.** Ultrasound image of the carotid artery in long axis showing an atherosclerotic lesion. This pathology was identified during the performance of an interscalene catheter. Note the hyperechoic plaque and the characteristic acoustic shadow.

**FIGURE 13.** Ultrasound image of the structures in short axis as seen in the axillary fossa. Acoustic enhancement of the tissue immediately posterior to the blood vessel is indicated by the arrow. This hyperechoic area can easily be mistaken for the radial nerve (R) which is actually lying adjacent to the artery. A, axillary artery; M, median nerve; MCN, musculocutaneous nerve; U, ulnar artery.

**FIGURE 14.** Ultrasound image of the structures in short axis as seen in the infraclavicular fossa. Acoustic enhancement of the tissue posterior to the blood vessel can be seen. This generates confusion as to the exact location of the posterior cord (P) of the brachial plexus. A, axillary artery; L, lateral cord; M, medial cord; PMa, pectoralis major muscle; PMi, pectoralis minor muscle; V, axillary vein.
Clinical pearls: Reverberation artifacts occur to a larger degree when the needle is completely perpendicular to the ultrasound beam. Therefore, if the angle of incidence is adjusted to less than 90 degrees, there will be less artifact (illustrated in Fig. 5B of Part I). The operator should keep in mind that as the needle becomes less perpendicular to the ultrasound beam, the needle shaft will also become more difficult to visualize. The other helpful tactic is to reduce the far gain in an effort to darken the duplicate images of the needle.

Tissue Reverberation Artifact

Example 1: Multiple reverberations generated by the pleura in the infraclavicular region can produce a comet tail sign (Fig. 18A). Hyperechoic streaks (“comets”) emanating from a strong specular reflector such as the pleura should alert the provider that the planned point of entry is too medial or that the plane of imaging is too oblique, thereby prompting the repositioning of the probe prior to needle insertion. Figure 18B is an example of the comet tail sign associated with the subclavian artery identified during a supraclavicular block.

Example 2: A linear artifact is generated when a linear tissue plane participates in a reverberation process which generates a reproduction of the image deep to its actual location. Figure 19 represents the performance of an interscalene nerve block. The C5 nerve root can be easily visualized prior to injection (Fig. 19A). Postinjection (needle not present), there appears to be a physical structure now present within the center of the C5 nerve root (Fig. 19B). This artifact most likely resulted...
from a reverberation process associated with the relative echogenicity of a fascial layer above the brachial plexus. Following the injection of local anesthesia, the ultrasound waves are now reflected back and forth between this fascial layer and another specular reflector (most likely the probe itself). The end result is the depiction of the fascial layer at an erroneous position through the C5 nerve root.

Clinical pearls: The comet tail sign (example 1) can be helpful as an alert to the provider that a strong specular reflector (eg, bone or pleura) exists in the region of the proposed needle trajectory. To help confirm that a suspicious structure is a reverberation artifact, increase the pressure applied to the probe against the skin. This pressure application should move (or eliminate) a linear artifact to a more superficial location (because the distance to the primary specular reflector has been decreased). Following probe pressure in example 2, the artifact disappeared. If there truly were a lesion within the C5 nerve root, then it would still appear at the original location within the C5 nerve root.

Example 3: “Double-barreled subclavian artery.” A similar artifact has been reported in the cardiac ultrasound literature for the aorta. Ultrasound may bounce back and forth within the lumen of an artery, generating a duplication of the 2-dimensional image of the subclavian artery with the artifact existing deep to the actual structure. This duplication will also occur with Doppler flow. Figure 20 shows a mirror image artifact involving the subclavian artery seen during the performance of a supraclavicular block.

Clinical pearls: When performing a supraclavicular block, neural structures should be found adjacent to the more superficial (nonartifact) artery. If a needle is inserted towards the deeper (artifact), a pneumothorax will likely ensue.

Bayonet Artifact

The term Bayonet artifact was coined by Gray et al. and first reported with respect to a transarterial axillary plexus block.
An example of a Bayonet artifact is illustrated in Figure 12 captured during a popliteal sciatic block performed with the patient in the supine position. The needle is inserted in-plane and almost completely perpendicular to the ultrasound beam. The ultrasound image suggests that the needle itself appears broken or bent. This degraded image artifact is generated due to the subtle differences in the speed of ultrasound in various biological tissues. Although we generally assume that ultrasound travels at 1,540 meters per second inside the human body, the reality is that ultrasound wave velocity varies slightly with different tissues. In Figure 21, the needle travels through muscle and into the adipose tissue surrounding the sciatic nerve. The apparent bend in the needle occurs because the speed of ultrasound in adipose tissue is slower than that in the surrounding muscle. Therefore, the needle appears to bend away (anterior) from the probe. When ultrasound velocity is reduced, it takes longer for the waves to return to the probe. Based on the basic formula of distance equals velocity multiplied by time, the machine will register the part of the needle in the adipose tissue as deeper than the part of the needle in the muscle. This creates the bending appearance. The direction of the bend in the needle is opposite to that presented by Gray in which the needle bends toward the probe, because the speed of ultrasound in blood is faster than in the surrounding nerve sheath.

**Probe-Skin Artifact**

Because air does not conduct ultrasound, the probe faceplate must fully contact the skin without any interfacing air. This is the reason that a conductive gel is often placed between the probe faceplate and the skin. Two situations can arise that generate significant dropout. The first case can occur when only a portion of the probe footprint is able to make contact with the skin due to size mismatch between the breadth of the footprint and the anatomical region to be imaged, as commonly occurs during tibial nerve block at the ankle or ulnar nerve block at the wrist. The latter is illustrated in Figure 22. This may preclude the ability to image the progress of the needle if it is inserted from the side of the dropout shadow. When complete contact is made between the entire probe footprint and the skin (Fig. 23), the dropout shadow is eliminated. The second case of dropout can occur when air pockets are contained between the plastic probe cover and the probe footprint.

**Clinical pearls:** Careful probe positioning, appropriate probe selection, and placement of generous amounts of ultrasound transmission gel should eliminate most of the skin-to-probe dropout artifacts.

![Figure 22](image-url)  
**FIGURE 22.** The incorrect position of the probe on the skin (A) can generate a large dropout shadow (B) which could complicate the performance of an ulnar nerve (UN) block in the mid forearm. UA, ulnar artery.

![Figure 23](image-url)  
**FIGURE 23.** The correct way to place the probe on the skin (A) to generate a complete image without dropout (B). The is important because the needle is commonly inserted in-plane from the ulnar (i.e., medial) side of the probe. In situations similar to Figure 23, the approaching needle may not be visualized. UA, ulnar artery; UN, ulnar nerve.

![Figure 24](image-url)  
**FIGURE 24.** Ultrasound image of the median nerve (N) imaged in short axis in the distal forearm. Note the similarity in echogenicity of the tendons and nerve. The triangles indicate the tendons. The nerve becomes rounder and separates from the tendons as the probe is moved more proximally in the arm.

![Figure 25](image-url)  
**FIGURE 25.** Short axis ultrasound images of the structures found in the popliteal fossa including the common peroneal (CPN) and the tibial (TN) nerves. Note the similarity of the nerves to the surrounding muscle. The only aspect of this image that supports the ability to identify the nerves is the small layer of adipose tissue that separates muscles from nerves. BFM, biceps femoris muscle; STM, semitendinosus muscle.
Anatomic Artifacts

Anatomic artifacts are tissue structures—either normal or aberrant—that may resemble the target nerve and thus mislead the operator into pursuing the wrong target. These errors in interpretation are often referred to as “pitfall errors.” The common solutions to all pitfall errors are to: (1) trace the target nerve along its expected anatomic course; and (2) use a peripheral nerve stimulator as an adjunct to confirm the target’s identity.

Tendons and Muscles

Chief among the pitfall errors is mistaking a tendon for the target nerve. The ultrasound appearance of nerves and tendons can appear indistinguishably similar. With experience, the ultrasonographer will appreciate the subtle hyperechoic continuous fibrils that comprise a tendon compared with the hypoechoic fascicles inside a nerve. Flexor tendons can be easily mistaken for the median nerve when performing a distal forearm median nerve block as depicted in Figure 24. In the forearm, the tendons appear more irregular and less oval in comparison with the median nerve.

Muscles can confuse the performance of an ultrasound-guided nerve block as well. This commonly occurs in the popliteal fossa. The common peroneal, tibial, and sciatic nerves have very similar ultrasound appearances when compared with the surrounding biceps femoris, semitendinosus, and semimembranosus muscles. One can appreciate this similarity in Figure 25, depicting an image of the popliteal fossa after the division of the sciatic nerve. The operator can easily distinguish the nerve from the surrounding muscle by appreciating the interpositioned adipose tissue (indicated in Fig. 25). Adipose tissue is more hypoechoic than either the nerve or the muscle, and, therefore, creates a discernable interface. In our experience, the most challenging popliteal blocks to perform are in athletes.
with well developed muscles and little adipose tissue. The sciatic nerve of an athlete as imaged proximally in the popliteal fossa is shown elsewhere in Figure 3 of Part I. The difficulty in distinguishing the sciatic nerve from the surrounding muscle is due to the paucity of surrounding adipose tissue. Muscles can actually be confused for major blood vessels. Figure 26 shows the anatomy commonly encountered during a supraclavicular approach to the brachial plexus. In this patient, a structure appears in long axis situated anterior to the brachial plexus. Due to the tubular and anechoic appearance, this structure appears virtually identical to a large caliber blood vessel. This structure is the inferior belly of the omohyoid muscle and Doppler interrogation will reveal no blood flow. The inferior belly of the omohyoid muscle is a helpful landmark in localizing the nerves which usually lie just posterior to the muscle.

**Blood Vessels**

Blood vessels are not usually mistaken for nerves because there are several key identifying features that differentiate one from the other. In general, nerves are echogenic, whether hypoechoic or hyperechoic relative to the surrounding tissue, while blood vessels are uniformly anechoic structures. Second, arteries can be seen to pulsate and resist compression. Conversely, veins do not pulsate and are easily compressible. Importantly, nerves appear nonpulsatile and are not compressible. Finally, color Doppler can detect blood flow within an imaged structure, thereby positively identifying it as a blood vessel. Color Doppler may be especially important to help differentiate artery from nerve when performing an ultrasound-guided interscalene brachial plexus blockade. Unlike most other nerves in the body, the roots of the brachial plexus can appear perfectly round and anechoic. A small caliber non-compressible artery in the neck may be dangerously mistaken for a nerve root, as evidenced in Figure 29, which depicts a thrombosed internal jugular vein. A thrombosed vein is non-compressible with internal hypoechoic shadows, not dissimilar from the appearance of a nerve. Whenever basic maneuvers (compression), defining features (internal echogenicity), and color Doppler fail to identify a structure of interest, the operator must remember to trace the structure proximally and distally as well as use a nerve stimulator for definitive confirmation. In...

**FIGURE 30.** Ultrasound appearance of lymphadenopathy found in the inguinal region during the performance of a femoral nerve block. Lymph nodes (LN) often have a heterogeneous ultrasound appearance. They may be round, oval, and have septi (as in this case). They can easily be confused for neural tissue or occluded veins (fig. 31).

**FIGURE 31.** Ultrasound appearance of an inguinal lymph node discovered during the performance of a continuous femoral nerve catheter. We originally believed this structure to be an occluded saphenous vein. However, patency of the saphenous vein was later confirmed. The anechoic outer ring of the lymph node (indicated by the arrows) represents perinodal edema, whereas the more echogenic interior represents the soft tissue aspects of the node. FA, femoral artery.
addition, it is useful to scan the anticipated path of the needle with color Doppler prior to needle insertion. This will help (as in Fig. 28) to identify any unnamed and unsuspected vascular structures.

**Lymph Nodes**

For the regional anesthesiologist, inflamed lymph nodes may complicate ultrasound-guided peripheral nerve blockade in the cervical, axillary, and inguinal regions. There are several sonographic features that can help to differentiate lymph nodes from nerves. Inflamed lymph nodes are generally large noncompressible, well circumscribed, round anechoic structures with small internal hypoechoic oval-shaped opacities, which are representative of intranodal necrosis. Figure 30 depicts inguinal lymphadenopathy incidentally encountered upon performing a femoral nerve block in a patient presenting for a total knee arthroplasty. Upon recognition of the lymphadenopathy, the operators decided to perform a single injection procedure instead of the originally planned continuous femoral nerve catheter. Figure 31 shows a lymph node that was initially mistaken for a venous thrombosis involving the saphenous vein in the infrainguinal region. Finally, lymph nodes have a very similar appearance to nerves in the axilla and as such can confound the performance of an ultrasound-guided axillary block. In these situations a nerve stimulator may be indispensable to physiologically distinguish a lymph node from nerve.

**Nerves**

How can we be fooled by the target nerve itself? Commonly, the operator can easily identify the target nerve in a particular location, but while manipulating the probe to optimize the image quality, the nerve suddenly disappears. There are 2 explanations for this apparent vanishing act.

First, peripheral nerves are highly mobile structures that can change position with even small amounts of pressure routinely applied to administer a peripheral nerve block. This phenomenon was aptly described by Retzl and colleagues who demonstrated the varying location of the median nerve relative to the axillary artery with gentle pressure applied by the ultrasound probe. Further, textbooks traditionally designate the area posterior to the axillary artery as the location of the median nerve.
radial nerve, but ongoing experience with ultrasound is teaching us that the location of the radial nerve is highly variable. Further, as Figure 32 shows, the ulnar nerve is often located at a significant distance from the axillary artery. In this patient, the ulnar nerve was 3.5 cm away from the axillary artery during the performance of an axillary block. Nerve stimulation was used to confirm that this was truly the ulnar nerve.

Secondly, there is the issue of reflection and refraction of ultrasound energy. The only way an image can be displayed on the ultrasound screen is if ultrasound reflects off of a nerve and successfully returns to the probe. If a significant portion of the ultrasound energy bounces off of the nerve and is transmitted away from the probe, then the image of the nerve will either be degraded or completely missing. Figure 33 shows how subtle angulations of the probe can either degrade or optimize the neural image. The amount of ultrasound reflected or refracted depends on the angle at which the ultrasound beam hits the interface between different objects (media). As the angle of incidence nears 90 degrees (perpendicular to the structure of interest), a higher percentage of reflected ultrasound successfully returns to the probe. Therefore, the operator should sweep the beam through an arc to try to generate a situation which optimizes the image.

Edema

The regional anesthesiologist performing extremity blocks will inevitably encounter patients with significant peripheral edema. This edema may physically distort the neural anatomy (depth change), mask hypoechoic structures, dilute the local anesthetic injection, and possibly alter nerve stimulation thresholds. Figure 34 shows mid calf edema in a patient having a mid calf saphenous nerve block. In this case the operators were unable to find the saphenous nerve or saphenous vein due to the severity of the edema.

Alternatively, edema may sometimes facilitate the image localization of a nerve. That is, a nerve that appears primarily hyperechoic (eg, sciatic), may become prominently outlined by the hypo-echoic edema fluid. This is analogous to the injection of ultrasound contrast media to facilitate nerve localization or cardiac imaging.11

FIGURE 34. Ultrasound appearance of the soft tissues of the mid calf during the performance of a saphenous nerve block. Because the ultrasonic approach to the saphenous nerve block relies in the visualization of the greater saphenous vein, edema (indicated by arrows) can compound this block by obscuring the landmark vein. Edema has the same anechoic appearance as any vein. This procedure was aborted.

CONCLUSION

Knowledge of ultrasound related artifacts is an exciting educational opportunity for the regional anesthesiologist. At the very least, these artifacts are nuisances and provoke intellectual curiosity. At the very worst, a misinterpretation of an ultrasound generated artifact may result in a negative patient outcome. It should be emphasized that as our community’s experience grows with these relatively new techniques, there will undoubtedly be additions to this preliminary database of artifacts.

Our anecdotal and collective experiences are that the appreciation of the existence, the understanding of the mechanisms, and the recognition of the appearances of the aforementioned artifacts supports the efficient and safe conduct of ultrasound-guided regional anesthesia.

REFERENCES


APPENDIX: SUPPLEMENTARY MATERIAL

(VIDEO FILES)

Supplementary videos can be found at http://links.lww.com/AAP/A6 and http://links.lww.com/AAP/A7.
Ultrasound-Guided Perineural Catheter Insertion

Three Approaches but Few Illuminating Data

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A

s ultrasound-guided regional anesthesia becomes more popular and practiced, a plethora of research involving this relatively new modality is being published—to the degree that Regional Anesthesia and Pain Medicine recently added an entire ultrasound-related section to every issue.1 However, most of these reports involve single-injection peripheral nerve blocks, to the exclusion of perineural catheter insertion.2 Unfortunately, data from many of these publications cannot be automatically inferred to perineural catheter placement for multiple reasons. First, although the angle between the long axis of the placement needle and nerve is relatively unimportant for single-injection blocks, it is critical for perineural catheter insertion because catheters tend to exit the needle and traverse past any nerve that is perpendicular to the needle itself.3 Second, a major advantage of ultrasound guidance for single-injection nerve blocks lies in the real-time repositioning of the needle tip to maximize local anesthetic spread, whereas perineural catheter bolus and/or infusion is analogous to a single-point injection.4 Third, unlike needles, flexible perineural catheters rarely remain within a 2-dimensional ultrasound view, making it difficult to observe catheter tip placement relative to the target nerve.5 Although it is impossible to include all ultrasound-guided techniques and respective equipment, the purpose of this editorial is to briefly review the major ultrasound-guided catheter insertion approaches along with their relative potential strengths and weaknesses.

ULTRASOUND ORIENTATION

Before engaging in any discussion involving ultrasound, commonly accepted vocabulary must be understood. A needle inserted with its length within a 2-dimensional ultrasound beam is described as “in plane,” whereas a needle inserted across a 2-dimensional ultrasound beam is “out of plane.”6 A nerve with its long axis within the ultrasound beam is viewed in “long axis,” compared with “short axis” when viewed in cross section.6

NEEDLE IN-PLANE, NERVE IN SHORT-AXIS APPROACH

For single-injection peripheral nerve blocks, most reports describe a short-axis view of the nerve because this view allows for easier identification and differentiation from surrounding structures (Fig. 1, left).6 When the long axis of the needle is inserted within the ultrasound plane, the needle tip location can be more easily identified relative to the target nerve. If the initial local anesthetic bolus is placed through the needle, the spread may be observed and adjustment of the needle tip can be made if desired. Unfortunately, when the perineural catheter is inserted past the needle tip, it has the tendency to bypass the nerve given the perpendicular orientation of the block needle and target nerve,3 although there are certain anatomic locations that will often allow a catheter to be passed and remain perineural.7,8 Some practitioners have advocated either passing the catheter a minimal distance past the needle tip (although others have suggested this may result in a dislodged catheter tip as the needle is withdrawn over the catheter, especially by trainees),9 or advancing the catheter further initially and then, after needle removal, retracting the catheter such that its orifice(s) lie a minimal distance (<2 cm)
past the original needle tip position. Some advocate using an extremely flexible perineural catheter in an attempt to keep the catheter tip near the target nerve if the catheter is inserted more than a minimal distance.\textsuperscript{10-12} Still others describe reorienting the needle from an in-plane to a more parallel trajectory and inserting a stimulating catheter to better monitor catheter tip location.\textsuperscript{13}

Proposed benefits include using the same basic technique for both single-injection and perineural catheter placement, simply adding the insertion of a catheter via the placement needle/angiocatheter, and its application in nearly all anatomic catheter locations, even for deeper target nerves.\textsuperscript{12} If a 17- or 18-gauge needle is used, the needle tip may be more easily identified and remain within the ultrasound plane owing to its rigidity compared with smaller gauge needles (Fig. 2).\textsuperscript{14} Although some have speculated that the use of a large needle is more painful, 7 prospective studies reported a median catheter insertion pain score of 0 to 2 on a 0 to 10 numeric rating scale (10, most pain imaginable) when the needle track was first anesthetized with lidocaine via a 25- to 27-gauge needle.\textsuperscript{9,11,12,15-18} In addition, the potential benefits of using a larger needle gauge (fewer needle passes given the relative ease of keeping a rigid, larger-gauge needle in plane and less risk of undesired tissue contact owing to misinterpretation of the needle shaft for the needle tip) must be weighed against the potential risks (increased patient discomfort, increased tissue trauma, and increased injury if a vessel is punctured).

Disadvantages of this approach include the following: new needle entry sites relative to the nerve compared with more traditional nerve stimulation modalities that typically use a parallel needle-to-nerve insertion, challenges keeping the needle shaft in-plane,\textsuperscript{19} difficult needle tip visualization for relatively deep nerves,\textsuperscript{20,21} and, as noted above, the catheter tip may bypass the target nerve given the perpendicular orientation of the needle and nerve.\textsuperscript{3} If an extremely flexible catheter is used in an attempt to minimize this issue, it is sometimes difficult to thread past the tip of the placement needle.

**NEEDLE OUT-OF-PLANE, NERVE IN SHORT-AXIS APPROACH**

One benefit of this approach is a generally familiar parallel needle-to-nerve trajectory used with traditional nerve stimulation techniques (and also vascular access; Fig. 1, middle). In addition, because the needle is parallel to the target nerve, the

![FIGURE 1. Various ultrasound-guided perineural catheter insertion approaches: needle within the ultrasound plane and target nerve in cross section or short axis (left), needle out-of-plane and target nerve in short axis (middle), and both the needle and target nerve within the ultrasound plane (right).](image1)

![FIGURE 2. Placement needle visualization under ultrasound. A 17-gauge uninsulated Tuohy-type needle (left; FlexTip; Arrow International, Reading, PA) and a 21-gauge insulated B-bevel needle (right; Stimuplex; B. Braun Medical, Bethlehem, PA).](image2)
catheter theoretically may remain nearer the nerve, even when threaded more than a centimeter past the needle tip.\(^9,25\) The main disadvantage of this technique is the relative inability to visualize the advancing needle tip, which, some speculate, increases the likelihood of unwanted contact with nerves, vessels, peritoneum, pleura, or even meninges\(^9,24\) (however, others have suggested that the consequent orientation of needle more along the long axis of the target nerve—as opposed to perpendicular—makes nerve penetration very unlikely, especially with a 17- or 18-gauge Tuohy needle). Practitioners often use a combination of tissue movement and hydrolocation in which fluid is injected and the resulting expansion infers the needle tip location (either with or without color Doppler flow).\(^22,28\) Some have suggested that for superficial catheters (eg, interscalene and femoral), the consequent longitudinal orientation of needle with nerve makes precise visualization of needle tip less critical because the needle tip tends to remain relatively close to the nerve if the needle tip is advanced beyond the ultrasound beam. However, for deeper nerves, this technique is not as straightforward as guiding the needle tip to a target nerve as in the in-plane technique described above and may be more difficult to master (and, at times, nearly impossible).\(^20,21\)

**NEEDLE IN-PLANE AND NERVE IN LONG-AXIS APPROACH**

Theoretically, this technique takes the benefits of both previously described approaches and harbors few of the limitations (Fig. 1, right). The nerve can be viewed along with the needle shaft/tip, and the catheter can be monitored as it exits the needle parallel to the target nerve. The problem is in the execution: keeping 3 structures—the needle, nerve, and catheter—in the ultrasound plane is not only very difficult to learn but also difficult to execute even after mastery.\(^25\) Until now, evidence of this technique’s difficulties could be found only indirectly in the scarcity of published reports.\(^22,26\) However, in this issue of *Regional Anesthesia and Pain Medicine*, Wang et al\(^27\) provide data from a well-designed randomized, observer-masked study demonstrating the difficulties of this approach. Fifty patients had a femoral perineural catheter placed using ultrasound guidance with an in-plane needle shaft. Half of the subjects had the nerve imaged in-plane as well (long-axis view; Fig. 1, right), whereas the remainder had the nerve imaged in cross section (short-axis view; Fig. 1, left). For the long-axis view group, catheters were advanced approximately 7 cm along the femoral nerve; for the short-axis view group, catheters were advanced 2 cm past the needle tip, but then withdrawn 2 cm after needle removal, theoretically leaving the catheter tip at the original needle tip perineural position.

For the long-axis treatment group, the investigators had great difficulty in keeping the nerve, needle, and catheter all within the ultrasound plane and “could not advance the catheters with real-time ultrasonographic visualization in the majority of the patients.”\(^27\) They “had to resort to some maneuvers including changing the position and direction of the ultrasound probe, tilting the probe, shaking and mild withdrawal of the catheter, and injecting 2 to 5 mL saline to find the tip of the catheter.”\(^27\) Even with these maneuvers, 10% of catheters could not be placed within 30 mins, and the mean (SD) time for all insertions was 21 (8) versus 12 (3) mins for the comparison group ($P < 0.01$). A difference of 9 mins for placement was not only statistically significant but also clinically significant in many—if not most—anesthesiology practices and, combined with the increased variability (SD of 8 versus 3 mins), would often prevent perineural catheter insertion based simply on time constraints. There are additional limitations of the long-axis approach that preclude its use in multiple circumstances. To view the nerve in long axis, the nerve itself must be relatively straight; and there can be only 1 target nerve as opposed to multiple branches as found within the brachial plexus. All of these issues combine to make the needle in-plane, nerve in long-axis technique the most challenging of the 3 approaches discussed above. However, this balance may change with advances in catheter and/or ultrasound technology in the future.\(^28\)

The limited length of an editorial precludes a discussion of multiple additional ultrasound-related issues, such as transducer selection, the concomitant use of nerve stimulation (an important tool in a subset of patients),\(^2\) and various methods for catheter tip localization.\(^2\) Although many proponents voice firm opinions based on their personal experience, few clinical data exist comparing aspects of any 1 placement technique with another. This editorial may likely trigger a plethora of letters from practitioners sharing their approaches and experiences, and we believe that sharing of information can only benefit the evolution of perineural catheter insertion techniques. However, only by prospectively comparing various approaches will their relative benefits and drawbacks be truly revealed and the science of perineural infusion advanced. To this end, we applaud the recent publication by Wang et al\(^27\) and eagerly await the results of additional well-designed, randomized, controlled clinical trials, allowing the transition from an editorial highlighting a lack of answers, to practice guidelines based on prospectively collected data.

**REFERENCES**


12. Mariano ER, Loland VJ, Bellars RH, et al. Ultrasound guidance...


**Review of Upper Extremity Anatomy**

Sarah Madison, M.D.

### Nerves of the Brachial Plexus

#### Roots: C5-T1 ventral rami (+C4 or T2)
- Exit between anterior and middle scalene muscles and travel with subclavian artery
- **Dorsal Scapular Nerve** (C3,4,5):
  - pierces middle scalene, deep to levator scapulae
  - **S**: NONE
  - **M**: Levator scapulae, Rhomboid major and minor
- **Long Thoracic Nerve** (C5,6,7):
  - anterior surface of serratus anterior, runs with lateral thoracic artery
  - **S**: NONE
  - **M**: Serratus anterior

#### Trunks: Superior, middle, inferior
- **Suprascapular Nerve** (C5,6):
  - emerges from upper trunk through scapular notch, under ligament
  - **S**: Shoulder joint
  - **M**: Supraspinatus, infraspinatus
- **Nerve to subclavius** (C5,6):
  - from upper trunk, descends anterior to plexus, posterior to clavicle
  - **S**: NONE
  - **M**: Subclavius

#### Divisions: 3 anterior, 3 posterior

#### Cords: Lateral, posterior, medial

**Lateral Cord**
- **Lateral root to median nerve**
- **Lateral pectoral Nerve** (C5,6,7):
  - runs with pectoral artery
  - **S**: NONE
  - **M**: Pectoralis major, minor
- **Musculocutaneous Nerve** (C5,6,7):
  - pierces coracobrachialis between bicep and brachialis
  - **S**: Elbow, Proximal radioulnar joint, Lateral forearm (lateral cutaneous n. of forearm)
  - **M**: Coracobrachialis, Biceps brachii, Brachialis (anterior compartment of arm)

**Medial Cord**
- **Medial root to median nerve**
- **Medial pectoral Nerve** (C8,T1)
  - **S**: NONE
  - **M**: Pectoralis minor, major
  - **M**: Flexor carpi ulnaris, Flexor digitorum profundus (digits 4,5), Palmaris brevis (Superficial branch), Adductor pollicis, Flexor pollicis brevis, Abductor digitii minimi, Flexor digitii minimi brevis, Opponens digitii minimi, Dorsal interossei, Volar interossei, Lumbricals (3,4)

**Ulnar Nerve** (C8,T1):
- travels through cubital tunnel, behind medial epicondyle
  - **S**: Ulnocarpal joint, Joints of the hand except IP joint of the thumb, Medial palm and 1 ½ digits, Medial dorsal hand and 1 ½ digits

**Medial Cutaneous nerve of forearm** (C8,T1):
- runs with basilic vein
  - **S**: Medial forearm and anterior arm
  - **M**: NONE

**Medial Cutaneous nerve of arm** (T1)

**Posterior Cord**
- **Upper Subscapular** (C5,6)
- **Lower Subscapular** (C5,6)
- **Thoracodorsal Nerve** (C7,8):
  - runs with thoracodorsal artery
  - **S**: NONE
  - **M**: Subscapularis, Teres major
  - **M**: Latissimus dorsi
• **Axillary Nerve** (C5,6): can be injured in proximal humerus fractures
  
  S: AC joint, Glenohumeral joint, Lateral upper arm (superior lateral cutaneous n. of arm)
  
  M: Deltoid (deep branch), Teres minor (superficial branch)

• **Radial Nerve** (C5,6,7,8,T1): runs in spiral groove of humerus, divides at the elbow into PIN (motor) and superficial radial nerve (sensory)
  
  S: Elbow, Radioulnar joints, Radiocarpal joint, Lateral arm (Inferior Lateral cutaneous n. of arm), Posterior arm (Posterior cutaneous n. of arm), Posterior forearm (Posterior cutaneous n. of forearm), Dorsal 3 ½ digits and hand, Dorsal wrist capsule
  
  M: Triceps, Anconeus (posterior compartment of arm), Brachioradialis, Extensor carpi radialis longus, Extensor carpi radialis brevis, Extensor carpi ulnaris, Extensor digiti minimi, Extensor digitorum communis, Supinator, Abductor pollicis longus, Extensor pollicis longus, Extensor pollicis brevis, Extensor indicis proprius

**BRANCHES**

• **Median Nerve** (C6,7,8,T1)
  
  S: Elbow, radioulnar joints, Wrist and hand joints, Dorsal distal phalanges of lateral 3 ½ digits, Volar wrist capsule, Volar 3 ½ digits and lateral palm (Palmar cutaneous branch)
  
  M: Pronator Teres, Flexor Carpi Radialis, Palmaris Longus, Flexor digitorum superficialis, Flexor digitorum profundus (digits 2,3), Flexor pollicis longus, Pronator quadratus (Anterior compartment of forearm), Adductor pollicis brevis, Opponens pollicis, Flexor pollicis brevis, lateral 2 lumbricals (Motor recurrent branch)
OVERVIEW OF UPPER EXTREMITY NERVE BLOCKS
Vanessa Loland, M.D.

Advantages and Disadvantages of Regional Anesthesia

• Benefits of Regional Anesthesia\(^1\)
  o Superior pain relief
  o Avoids GA
  o Opioid-sparing
  o Less PONV
  o Bypass PACU
  o Avoid hospitalization

• Risks of Regional Anesthesia\(^2\)
  o Local anesthetic toxicity
  o Site infection
  o Hematoma
  o Nerve injury
  o Site-specific risks

Nerve Localization Techniques

• Anatomic landmarks
• Electrical nerve stimulation
• Sustained “twitch” at < 0.5 mA current suggests appropriate needle position
• Ultrasound
• Combination

Infraclavicular Block

• Optimal CPNB site for distal upper extremity surgery
• Performed at the level of the brachial plexus cords
• Coracoid approach may be performed with arm at side or abducted 90°
• Spares T2 (intercostobrachial nerve)
• Ultrasound may improve outcomes and minimize risks
• Site-specific risks:
  o Intravascular injection
  o Pneumothorax (Coracoid < Raj)
- **Surface Anatomy**
  - Position: supine with arm at side or abducted 90°
  - Palpate coracoid process between AC joint and deltopectoral groove
  - The brachial plexus runs under the coracoid process

- **Stimulator Technique**
  - Insert the block needle 2 cm medial and 2 cm caudad to the coracoid process
  - Needle is inserted plumb-bob (toward the floor)
  - Average depth 4.24±1.49 cm in men, 4.01±1.29 cm in women
  - Elicit a distal twitch at <0.5 mA
  - Musculocutaneous nerve is the most cephalad branch (off Lateral cord)
  - Use double-stim technique for better success
  - Multiple injections may or may not improve block quality3,4
• Ultrasound Technique
  o Small curvilinear (C11) probe placed infra-coracoid for a cross sectional image of axillary artery
  o Needle inserted cephalad to probe and directed in-plane toward artery
  o Deposit local anesthetic at each cord or posterior to artery
  o For CPNB, leave catheter posterior to artery

  o Use curvilinear probe for greater depth and steeper needle angles
  o Larger needles may be easier to visualize in-plane
**Interscalene Block**

- Indicated for shoulder and upper arm surgery
- Frequently spares lower trunk (C8 and T1)
- Site-specific risks:
  - 100% incidence of phrenic nerve block
  - Side effects: Horner’s syndrome, hoarseness, decreased chest wall sensation
  - Rare complications: pneumothorax, spinal, epidural, or vertebral artery injection

**Surface Anatomy**
- Position: supine with head turned away
- SCM clavicular head
- Interscalene groove posterior to SCM at cricoid level (C6)
- External jugular vein
- Subclavian artery
**Stimulator Technique**
- Needle inserted in IS groove above C6
- Antero-lateral approach
- Needle angle 30-45º
- Elicit motor response (deltoid, biceps, triceps, pectoralis)
- Stay superficial (1-1.5 cm)
- Identify subclavian pulse (for direction)
- Phrenic stim = too anterior
- Scapular elevation = too posterior
- EJV often overlies ISG

**Ultrasound Technique**
- Place linear probe posterior to SCM to visualize plexus
- Insert needle in-plane between levator scapulae and trapezius
- Advance needle through middle scalene
- Place catheter between superior and middle trunks
- Lateral position helpful for catheter
- Set ultrasound depth 2-3 cm
- Visualize IJ vein first then move posteriorly until hypoechoic nerves in interscalene groove seen clearly
- Optimize transverse XS view before inserting needle in-plane
Testing the Block: the 5 “P’s”

- Push
  - Extend arm: radial nerve
- Pull
  - Flex arm: musculocutaneous nerve
- Pinch
  - Fifth finger: ulnar nerve
- Pinch
  - Index finger: median nerve
- Pinch
  - Medial forearm: medial antebrachial cutaneous nerve

Upper Extremity Regional Anesthesia
Essentials of Our Current Understanding, 2008

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Abstract: Brachial plexus blockade is the cornerstone of the peripheral nerve regional anesthesia practice of most anesthesiologists. As part of the American Society of Regional Anesthesia and Pain Medicine’s commitment to providing intensive evidence-based education related to regional anesthesia and analgesia, this article is a complete update of our 2002 comprehensive review of upper extremity anesthesia. The text of the review focuses on (1) pertinent anatomy, (2) approaches to the brachial plexus and techniques that optimize block quality, (3) local anesthetic and adjuvant pharmacology, (4) complications, (5) perioperative issues, and (6) challenges for future research.

(Reg Anesth Pain Med 2009;34: 134–170)

Upper extremity regional anesthesia has been a mainstay of the anesthesiologist’s armamentarium since Hall1 first reported the use of cocaine to block the brachial plexus in 1884. Recognizing that upper extremity neural blockade represents the most frequent use of peripheral nerve blocks in most anesthesiologists’ practice,2 in 2001, the American Society of Regional Anesthesia and Pain Medicine (ASRA) undertook a critical review of all available English-language publications pertinent to this topic. The resulting extensive source document was synthesized into a comprehensive review article3 that was published in 2002; both the source and the review documents will be updated approximately every 5 years.

Rather than publishing only new material that has become available since 2002, the original review article has been completely revised so that readers may continue to view the subject matter in its entirety. New topics in this review include ultrasound-guided brachial plexus block, continuous catheter-based analgesia, and a collection of new images* by medical illustrator, Jennifer Gentry (www.gentryvisualization.com). This review summarizes the essential scholarly work available from the source document, which can be viewed at www.asra.com.

This review article strives (1) to serve as a review of pertinent anatomy, (2) to compare the effectiveness of brachial plexus approaches and techniques, (3) to present available evidence to guide selection of pharmacological agents, (4) to describe the complications inherent to upper extremity anesthesia, (5) to consider pertinent perioperative issues, and (6) to identify informational gaps and emphasize where we believe further study is warranted.

BRACHIAL PLEXUS ANATOMY

Neural Elements

Performing upper extremity regional anesthesia requires a thorough knowledge of brachial plexus anatomy to facilitate the technical aspects of block placement and to optimize patient-specific block selection. Gray’s Anatomy describes the brachial plexus as that network of nerves that begin as spinal nerve roots and continue to the terminal branches that supply the upper extremity. The brachial plexus starts as the union of the ventral primary rami of cervical nerves 5 through 8 (C5–C8), including a greater part of the first thoracic nerve (T1). Variable contributions may also come from the fourth cervical (C4) and the second thoracic (T2) nerves.4 The ventral rami are the roots of the brachial plexus. The C5 and C6 rami typically unite near the medial border of the middle scalene muscle to form the superior trunk of the plexus; the C7 ramus becomes the middle trunk; and the C8 and T1 rami unite to form the inferior trunk (Fig. 1). The C7 transverse process lacks an anterior tubercle, which facilitates the ultrasonographic identification of the C7 nerve root.5 The roots and trunks pass through the interscalene groove, a palpable surface anatomic landmark between the anterior and middle scalene muscles (Figs. 1–3). The 3 trunks undergo primary anatomic separation into anterior (flexor) and posterior (extensor) divisions at the lateral border of the first rib. Divisions undergo yet another level of reorganization into cords, which are defined by their spatial relationship to the second part of the axillary artery. The anterior divisions of the superior and middle trunks form the lateral cord of the plexus, the posterior divisions of all 3 trunks form the posterior cord; and the anterior division of the inferior trunk forms the medial cord. The 3 cords divide and give rise to the terminal branches of the plexus, with each cord possessing 2 major terminal branches and a variable number of minor intermediary branches.6 The lateral cord contributes the musculocutaneous nerve and the lateral component of the median nerve. The posterior cord generally supplies the dorsal aspect of the upper extremity via the radial and axillary

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nerves. The medial cord contributes the ulnar nerve and the medial component of the median nerve. Important intermediary branches of the medial cord include the medial antebrachial cutaneous nerve and the medial cutaneous nerve, which joins with the smaller intercostobrachial nerve (T2) to innervate the skin over the medial aspect of the arm. Figure 4 illustrates an idealized brachial plexus.

Despite the aforementioned “classic” schema, 7 major configurations of the brachial plexus have been described, with none having more than a 57% representation; indeed, 61% of individuals exhibit right/left asymmetry. These normal anatomic variations take on particular importance during ultrasonic examination of the upper extremity neural components, which makes it easier to directly visualize normal variants such as a solitary trunk, a postfixed plexus wherein contribution from T2 leads to a lesser or absent C5 nerve root, or C5 and C6 nerve roots that penetrate the anterior scalene muscle rather than reside within the interscalene groove. Whether these anatomic variations significantly impact the successful provision of upper extremity regional anesthesia is unknown.

The architecture of the brachial plexus and the structure of peripheral nerves contribute to understanding the pathophysiology of perioperative nerve injury (Fig. 5). Peripheral nerves are constructed of a varying number of fascicles that consist of individual nerve fibers (axons) that are contained within endoneurium. Fascicles are contained within perineurium, while groups of fascicles are contained within epineurium. As the nerve travels away from the spinal cord, the density of the epineurium (stroma and connective tissue) diminishes, but its total volume increases. The amount of neural tissue remains constant. Thus, the ratio of nonneural to neural tissue contained within the epineurium increases from 1:1 in the proximal plexus to 2:1 in the distal plexus, where the cross-sectional area of a peripheral nerve may consist of up to 70% loose connective tissue. The possible clinical significance of this observation is that when a needle unintentionally enters a peripheral nerve, it does not invariably come to rest within a fascicle but may instead lie within connective tissue.

Peripheral nerve anatomy also determines patterns of local anesthetic blockade and clearance. Local anesthetic is first
absorbed by the mantle fibers on the nerve’s periphery, resulting in blockade that manifests itself proximal to distal. Conversely, block resolution follows a distal-to-proximal pattern, suggesting that local anesthetic is preferentially cleared from the core fibers by the core’s vascularity (Fig. 5).

The increased ratio of nonneural to neural tissue as one moves away from the spinal cord may also explain the relatively longer block onset times with distal as opposed to more proximal approaches.

Other Pertinent Neuroanatomy

Several nerves that are either significant branches of, or not an actual part of, the brachial plexus are clinically important with regard to upper extremity surgery because they may require separate blockade or indicate needle malposition. The supraclavicular nerves, which are branches of the superficial cervical plexus (C3-C4), provide sensory innervation to the “cape” of the shoulder, from the anterior second rib over the shoulder and down to the top of the scapula. The phrenic nerve (C3-C4, occasionally C5) overlies the anterior scalene muscle, where it can be unintentionally stimulated if the block needle is directed too far anterior during interscalene block (ISB). The C5 anterior rami and the phrenic nerve are separated only by 2 mm; the distance between these 2 structures increases as one moves caudad. Stimulation of the dorsal scapular nerve (C5) causes rhomboid and levator scapulae motor responses and indicates that the block needle is directed too far posterior. The suprascapular nerve (C5-C6) branches from the upper trunk and sends sensory fibers to the shoulder capsule and the acromioclavicular joint. The intercostobrachial nerve originates from the second intercostal nerve (T2) and, with the medial cutaneous nerve, innervates the upper half of the posterior and medial skin of the arm.

Sensory and Motor Innervation of the Arm

The sensory and motor innervation of the upper extremity is clinically important, determining which cutaneous nerve distributions within a surgical field require conduction blockade, which terminal nerve branches require supplementation for an incomplete block, and determining the existence and distribution of preoperative and postoperative neurological deficit. The cutaneous nerves of the upper extremity are a collection of neural fibers that originate from a variety of spinal cord segments. Assigning cutaneous territory to a specific peripheral nerve is inconsistent, if not impossible (Fig. 6). Indeed, this situation significantly compromises rigorous evaluation of sensory blockade in most research studies. Motor innervation is clinically relevant as a means of matching a peripheral nerve stimulator (PNS)–induced motor response to the major nerve(s) that has been stimulated. For example, superior trunk stimulation results in a deltoid motor response. Musculocutaneous nerve stimulation causes the arm to flex at the elbow. Median nerve stimulation results in forearm pronation, wrist flexion, and thumb opposition. Ulnar nerve motor responses include ulnar deviation of the wrist, little-finger flexion, thumb adduction, and flaring of the fingers. Wrist and finger extensions are the hallmark of radial nerve stimulation.

Assessing the Extent of Brachial Plexus Blockade

Because innervation of the arm comes from different nerves, the extent of blockade is best assessed by evaluating functions unique to each terminal nerve. A method of performing such an assessment is the 4 P’s. The patient is asked to push the arm by extending the forearm at the elbow against resistance (radial nerve), followed by resisting the pull of the forearm at the elbow (musculocutaneous nerve). The median nerve is assessed by the ability to distinguish a pinch at the

palmar base of the index finger, whereas another pinch at the palmar base of the little finger assesses the ulnar nerve. Movement of the little finger during infraclavicular block (ICB) helps to identify which cord is being stimulated. With the arm adducted, movement of the little finger medially toward the body indicates medial cord stimulation, whereas lateral movement away from the body indicates lateral cord stimulation. The posterior cord is identified when the little finger moves posteriorly.

Vascular Elements

In addition to the neural elements, several vascular structures have profound clinical importance as anatomic landmarks or structures to avoid. The vertebral artery travels cephalad from its origin in the subclavian artery; at the C6 level, it enters the vertebral foramen located in each of the cervical vertebral transverse processes. As the cervical roots of the brachial plexus leave the intervertebral foramina, they course immediately posterior to the vertebral artery, thereby offering an interposed portal for potential intravascular injection, particularly if the anesthetizing needle courses anterior and medial to the anterior scalene muscle (Fig. 1). The external jugular vein often overlies the interscalene groove at the level of C6 but is not a reliable anatomic marker. The subclavian artery lies alongside the brachial plexus as they course over the first rib (Figs. 1, 2, 7). Here, the trunks/divisions of the brachial plexus lie posterior, cephalad, and eventually lateral to the subclavian artery, which presents a valuable anatomic relationship during placement of supraclavicular block. The cords are defined by their lateral, posterior, or medial relationship to the second part of the axillary artery, although their actual position varies significantly between individuals. In the base of the axilla, the axillary artery occupies its characteristic location relative to the terminal branches of the plexus—anterior to the radial nerve, posteromedial to the median nerve, and posterolateral to the ulnar nerve. However, significant individual variation occurs (Fig. 8). Of practical importance, nerve-vascular relationships are affected by changes in the arm position and/or applied external pressure during block performance.

FIGURE 5. Peripheral nerve anatomy. Nerves are a collection of individual axons, which are surrounded by loose endoneurium and freely interdigitate along their course (12-o’clock). Axons receive nutrition from intrinsic vessels. Extrinsic vessels supply the intrinsic system and are under adrenergic control. Fascicles are collections of axons contained within perineurium. Fascicles are separated by connective tissue and surrounded by epineurium. Illustration by Jennifer Gentry. ©American Society of Regional Anesthesia and Pain Medicine.

FIGURE 6. Cutaneous sensory distribution of the upper extremity. Terminal nerves of the brachial plexus provide sensory innervation to the arm. The sensory distribution of these nerves is variable and overlapping—as depicted by blended colors as the zones converge. Illustration by Jennifer Gentry. ©American Society of Regional Anesthesia and Pain Medicine.

FIGURE 7. Cryomicrotome section of the right supraclavicular area. The brachial plexus (arrows) lies posterior and lateral to the subclavian artery (SA). Note the proximity of the lung. There is no evidence of a defined brachial plexus sheath in this section. Cryomicrotome courtesy of Quinn H. Hogan, MD.
The precise architecture of those tissues surrounding the brachial plexus is incompletely understood and highly debated. Recent research with opposing viewpoints has reignited interest in this long-standing controversy, which centers on the structural integrity and function of a connective tissue sheath versus a more rigid axillary tunnel defined by surrounding muscle and bone. The divergent views on this topic are partially explainable by the difficulties encountered in correlating cadaveric studies with fresh tissue observations and with reconciling imaged-based findings with clinical observations.

Similar to other neurovascular bundles throughout the body, portions of the brachial plexus are embedded within connective tissues of varying density (Figs. 2, 7, and 9). Some investigators described the connective tissues as forming a multicompartamental structure comprising thin layers of fibrous tissue, which in cadavers are permeable to dye or latex. Earlier investigators proposed the concept of a tubular sheath of high structural integrity, which contains only nerves and vessels. These concepts have been subsequently refined over nearly a half-century, in part to reconcile clinical observations of actual local anesthetic blockade with observations related to the surrounding tissue architecture. The presence of a well-defined sheath varies along the course of the brachial plexus; for example, there is no evidence of a substantial sheath on cryomicrotome sections of the supravacuicular region (Fig. 7). Yet, other cadaveric studies note a distinct fibrous structure filled with loose connective tissue. Between the epineurium and the connective tissue lies a potential space that may offer a pathway of less resistance that promotes longitudinal, rather than circumferential, spread of local anesthetic. This often made clinical observation that local anesthetic is less likely to spread circumferentially may also reflect where it is injected. For example, some investigators interpret the terminal nerves at the base of the axilla as traveling independently of each other in their own connective tissue envelopes, which potentially limit

FIGURE 8. Axillary block. Top left insert depicts the expected distribution of anesthesia consequent to AXB. The 4 terminal nerves are drawn in their classic relationship to the axillary artery, which in turn is correlated to ultrasonic anatomy that shows the hyperechoic nerves. Note: To correlate with the illustration, the ultrasound inset is rotated 90 degrees clockwise from the way it is normally viewed in a patient. There is significant variation in how the terminal nerves relate to the axillary artery. The upper right inset depicts these variations as color-coded nerves in various positions around the artery (radial nerve = orange, ulnar nerve = blue, median nerve = green). The color saturation correlates with the expected frequency of the nerve residing in a specific location—the deeper the saturation, the more frequently the nerve is found in that position. The musculocutaneous nerve (MC) lies in the fascial plane between the coracobrachialis and biceps muscles. Illustration by Jennifer Gentry. © American Society of Regional Anesthesia and Pain Medicine.

FIGURE 9. Dissection of the right axilla. The brachial plexus is contained within connective tissue of the axillary sheath and lies inferior to the biceps and coracobrachialis muscles. At this level, the musculocutaneous nerve is likely within the belly of the coracobrachialis muscle or the fascial plane between it and the biceps. Note that the intercostobrachial nerve is not part of the plexus. Photo courtesy of Quinn H. Hogan, MD.
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*(AXB versus SCB and ISB).*

![Brachial plexus blocks: AXB, axillary; SCB, supraclavicular; ISB, interscalene; ICB, infraclavicular; ISCM, intrasternocleidomastoid; PCN, proximal cranial needle SCB; TCB, transcoracobraclial; PNS, peripheral nerve stimulation. Criteria for successful block: N, evaluation of individual nerve function; A, need for anesthesia supplementation. NR, not reported; NS, not significant.]

circumferential diffusion but facilitate longitudinal spread of local anesthetic. Others suggest that the interlinking of trunks, divisions, and cords potentially creates interconnecting channels that promote wider spread of local anesthetics injected near the apex of the axilla.²⁵ Yet another viewpoint is that rather than connective tissue structures, it is the rigid anatomy comprising the surrounding bony and muscular structures (the “axillary tunnel”) that plays a vital role in directing the flow of injected solutions. This concept likewise is consistent with clinical observation of longitudinal local anesthetic spread.²⁵,²⁶

Despite ongoing debate regarding the structural components of the tissues surrounding the brachial plexus, it is clear that the nerves are embedded in connective tissue. The functional interactions of connective tissues with individual nerves, of the brachial plexus with rigid elements of the axillary tunnel, and the level at which the local anesthetic is injected may all influence distribution. That these factors seemingly promote either longitudinal or circumferential spread of local anesthetic correlates functionally with the clinical observation that anesthetic success at the more distal blocks is improved by multiple, rather than single, injections.²⁵,²⁶

**APPROACHES TO THE BRACHIAL PLEXUS**

Throughout this review, we define approach as the level along the brachial plexus that the block needle is placed, for example, the interscalene or the axillary approach. We define technique as that technical aspect of how the block is actually performed, for example, how the nerve is localized or how many injections are made around the nerve.

Clinicians have approached the nerves of the upper extremity at every anatomic division of the brachial plexus, from the nerve roots to individual terminal branches (Fig. 4). Despite the existence of a myriad of techniques for each of these approaches, there are few clinical comparisons of block success rate, and less still of latency or duration as a function of the chosen anesthetic approach and/or technique (Table 1). Indeed, the very definition of success varies widely. Some studies compare successful blockade of all nerves as the criteria for success, whereas others compare adequacy for the intended surgical procedure (ie, need for general anesthesia). This section summarizes the relatively sparse data pertaining to brachial plexus approaches. No attempt was made to describe the actual performance of individual blocks; instead, the reader is encouraged to seek this information in the source document at www.asra.com or refer to the cited original descriptions.

**Interscalene Block**

The principal indication for an ISB is surgery of the shoulder (Fig. 10). Three primary variations of this approach exist—the classic approach of Winnie et al,⁶³ a modified lateral approach,⁶² and the transmidscale ultrasound-guided approach.⁶⁴ Local anesthetic spread after interscalene administration extends from the distal roots/proximal trunks and follows a distribution to the upper dermatoes of the brachial plexus⁶⁵ that consistently includes the (nonbrachial plexus) supravacular nerve (C3-C4), which supplies sensory innervation to the cape of the shoulder.⁶⁶ An ISB using paresthesia or PNS localization technique often functionally spares the lower trunk (primarily the ulnar nerve), which remains unanesthetized in 30% to 50% of blocks.⁶⁷ More inclusive anesthetization of the lower trunk is possible with ultrasound-guided techniques.⁶⁸ Several technical caveats pertain to ISB. First, paresthesia or motor response to the arm or anterior shoulder is appropriate for shoulder surgery.⁶⁹,⁷⁰ Second, the observation of unintended evoked motor responses may help refine needle placement. Contraction of the diaphragm indicates phrenic nerve stimulation and too anterior placement of the needle tip. Rhomboid muscle movement indicates stimulation of the dorsal scapular nerve (C5) and needle placement that is too posterior.⁷¹ Third, the roots and trunks normally appear as hypoechoic structures within the interscalene groove when visualized with
ultrasound, but roots sometimes pass through the scalene muscles.\(^8,9\) Finally, PNS- or paresthesia-guided ISB is typically a single-injection technique, whereas ultrasound-guided ISB uses multiple injections to ensure local anesthetic spread around the plexus.\(^62,64,72\)

**Cervical Paravertebral Blocks**

Posterior approaches to the brachial plexus were popularized by Pippa et al\(^73\) and more recently refined by Boezaart et al.\(^74\) Cervical paravertebral block is primarily used for shoulder surgery.\(^57,74,75\) Observational studies have shown 98% overall success with this approach.\(^76\) The posterior approach of Boezaart et al\(^74\) is comparable to the lateral approach of Winnie et al in terms of block success and side effects.\(^69\) The cervical paravertebral block causes less motor block\(^74\) and greater ease of perineural catheter placement\(^75\) as compared with traditional interscalene approaches. Several ultrasound-guided posterior approaches to the brachial plexus have been described.\(^77,78\)

**Interscalene Block**

The interscalene block (ISB) is a variation of the supraclavicular approach and is indicated for hand and arm surgery. The ISB involves significant modifications from other supraclavicular approaches, including directing the needle laterally between the heads of the sternocleidomastoid muscle.\(^72\) This technique has been advocated for its ease of catheter insertion and theoretically lowers the risk of pneumothorax, although the latter claim is unsubstantiated. The needle, by passing behind the clavicular head of the sternocleidomastoid muscle, passes near the apex of the pleura as it progresses toward the brachial plexus. Interscalene block using a catheter technique fails to achieve ulnar anesthesia in 15% of patients.\(^79\)

**Supraclavicular Block**

The usual indications for supraclavicular plexus block are surgery of the hand and arm (Fig. 11). It can also be used for shoulder surgery but may require supplementation of the supraclavicular nerve (C3-C4) to ensure anesthesia of the cape of the shoulder. Three primary variations of this block have been described—the subclavian perivascular approach,\(^23\) the “plumbbob” approach,\(^80\) and an ultrasound-guided approach.\(^81\) This block is performed where the brachial plexus is presented most compactly—at the distal trunk/proximal division level. This compactness may explain the block’s historical reputation for providing short latency and complete, reliable anesthesia for upper extremity surgery,\(^80\) although confirmatory data do not exist. Several technical caveats apply to supraclavicular plexus block. First, the risk of pneumothorax may be substantially reduced by technical modifications of the block, which are discussed in the section on pneumothorax. Second, stimulation of the middle trunk (hand contraction or paresthesia) has been associated with higher success rates for hand surgery.\(^82,83\) Third, if ultrasound-guided regional anesthesia (UGRA) is used, concomitant PNS is redundant for improving block success.\(^84\) Finally, in contrast to the contention that UGRA facilitates blockade with smaller volumes of local anesthetic, the minimum volume required for UGRA supraclavicular blockade in 50% of patients is 23 mL, which is similar to recommended volumes for traditional nerve localization techniques.\(^85\)

**Infraclavicular Block**

Surgeries of the hand and arm are indications for ICB, which is performed at the level of the cords (Fig. 12). As compared with the supraclavicular approaches, ICB has less impact on pulmonary function but is more likely to spare the radial nerve distribution if a single injection is used.\(^22\) The
FIGURE 11. Supraclavicular block. Inset depicts the expected distribution of anesthesia consequent to supraclavicular block. The trunks begin to diverge into the anterior and posterior divisions as the brachial plexus courses below the clavicle and over the first rib. The plexus is posterior and lateral to the subclavian artery, and both overlie the first rib in close approximation to the pleura and lung. The classic ultrasound view depicts the hypoechoic trunks bundled together lateral to the subclavian artery and over the first rib, which casts an acoustic shadow as the ultrasound beam is attenuated by bone. Note that the pleura does not impede the passage of the ultrasound beam to the same extent. Illustration by Jennifer Gentry. ©American Society of Regional Anesthesia and Pain Medicine.

FIGURE 12. Infraclavicular block. Inset depicts the expected distribution of anesthesia consequent to ICB. The cords take on their characteristic position lateral, posterior, and medial to the second part of the axillary artery in this illustration of the coracoid approach. The medial cord frequently lies between the axillary artery and vein (4-o’clock). There is considerable variation in the relationship of the artery to the cords, as depicted by the color-coded cords in the upper right inset (lateral cord = green, medial cord = blue, posterior cord = orange). The color saturation correlates with the expected frequency of the cord residing in a specific location—the deeper the saturation, the more frequently the cord is found in that position. Illustration by Jennifer Gentry. ©American Society of Regional Anesthesia and Pain Medicine.
The infraclavicular approach provides more consistent anesthesia of the axillary and musculocutaneous nerves than the axillary approach, although often at the expense of longer latency.15,16 There are 3 primary variations of the ICB (from most lateral to medial)—the coracoid approach,17,18 the lateral sagittal approach,19 and the vertical approach.20 The coracoid approach seems to be the most popular North American variation, perhaps because the anatomic landmarks are straightforward and the block’s lateral entry point most reduces the possibility of pneumothorax and hemidiaphragmatic paresis (HDP).16 Technical caveats for the ICB include the following: first, although the lateral, posterior, and medial cords are named by their relationship with the second part of the axillary artery, the cords are likely to be anterior to the artery at the more medial approaches to the block. At the coracoid level, substantial variation exists in where the cords actually reside in relation to the artery.16 Second, when using a PNS, a double-injection technique increases success as compared with a single-injection technique, particularly when one of the injections is near the posterior cord.27,30,102 Third, acceptance of a musculocutaneous motor response in lieu of a more distal lateral cord response is associated with less successful ICB, because the musculocutaneous nerve frequently branches from the lateral cord more proximally (Fig. 4). Finally, when using UGRA, achieving local anesthetic spread around the axillary artery,96,97 particularly posterior to the artery,95 improves success.

Axillary Block

The axillary block (AXB) is indicated for hand and arm surgery and remains a widely used, studied, and modified approach to the brachial plexus (Fig. 8). All techniques—paresthesia-seeking,98 nerve-stimulating,54 perivascular,99 transarterial,100 and ultrasound-guided101—work at the level of the terminal nerves. Successful blockade of individual nerves varies from 60% to nearly 100%, depending on the technique. Several technical caveats apply to AXB. First, all AXB techniques rely on the relationship of the terminal nerves to the axillary artery, which is the primary surface landmark for this block. Significant variation exists regarding the position of the nerves relative to the axillary artery (Fig. 8).17,18 Second, multiple injections are superior to single injection for the axillary approach.27,30,102 Radial nerve identification seems to be most important for successful block, whereas ulnar nerve identification is least important and unnecessary if the other nerves have been localized.102–104 With regard to the midaxillary approach, obtaining 4 nerve stimulations significantly increased overall success rate (91% vs 76%) and reduced time for readiness for surgery when compared with eliciting 3 separate paresthesias and blindly supplementing the musculocutaneous nerve. However, in this study, only blockades of the radial nerve and the musculocutaneous nerve (blocked separately) were statistically different, suggesting that the techniques may be more similar than dissimilar.105 When using a 4-nerve-stimulation, midhumeral approach, blocking the radial nerve before the ulnar nerve improves subsequent nerve localization.106 Third, the relationship of the musculocutaneous nerve to the brachial plexus deserves special consideration, because it courses away from the axillary artery early and resides within the body of the coracobrachialis muscle or the fascial layers between the coracobrachialis and the biceps muscles. Anesthesia of the musculocutaneous nerve is best ensured by a separate injection into the belly of the coracobrachialis muscle96,107 or by using direct ultrasound guidance.108

Accessory Upper Extremity Nerve Blocks

Block of the Supraclavicular Nerves of the Superficial Cervical Plexus

The supraclavicular nerves are branches of the superficial cervical plexus (C3–C4) and provide cutaneous innervation of the cape of the shoulder (Fig. 13). Although not part of the brachial plexus, they are consistently blocked with the
interscalene approach. However, they may require separate blockade if shoulder surgery is contemplated using more distal approaches to the brachial plexus.

**Suprascapular Nerve Block**

The suprascapular nerve (C5-C6) provides sensory innervation to the posterior/superior 70% of the shoulder joint, the acromioclavicular joint, and to the anterior axilla in ~10% of patients (Fig. 14) This nerve branches from the upper trunk (Figs. 1 and 4) and is typically anesthetized during an ISB. Suprascapular block is most useful as an adjunct to general anesthesia or as a rescue block for posterior shoulder pain or anterior arthroscopic port pain in the setting of an incomplete ISB. Approaching the suprascapular spine from a cephalad-to-caudad direction, rather than posterior-to-anterior, likely reduces the risk of pneumothorax by avoiding needle translocation through the suprascapular notch and into the pleura.

**Intercostobrachial Nerve Block**

Because it is not part of the brachial plexus but rather is a branch of the second intercostal nerve (Fig. 9), it is not anesthetized by plexus techniques. The intercostobrachial nerve (T2) requires separate blockade for surgeries of the medial upper arm or axilla. Placement of intercostobrachial nerve block may prevent tourniquet sensation within the T2 distribution, but its importance in reducing tourniquet pain is controversial because tourniquet pain is likely mediated by ischemia and distal tissue compression in addition to local sensation.

**Lateral and Medial Antebrachial Cutaneous Nerve Blocks**

The medial antebrachial cutaneous nerve is a branch of the medial cord; it innervates the ulnar volar forearm. The lateral antebrachial cutaneous nerve is the sensory terminus of the musculocutaneous nerve that provides sensation to the radial volar forearm. These blocks are useful as a primary anesthetic for superficial forearm surgery or for safely rescuing an incomplete proximal plexus block because they do not seek needle-to-nerve proximity.

**Selective Nerve Blocks at the Elbow, Forearm, or Wrist**

Blockade of individual nerves at the elbow or wrist is limited by the need to block several nerves for most hand and forearm surgical indications, by tourniquet considerations, and by limited evidence that suggests blocking partially anesthetized nerves to rescue failed proximal plexus blockade may increase the risk of nerve injury. Ultrasound-guided techniques for selective terminal nerve blockade in the upper arm or forearm have been described. Although comparative data are limited, recent studies have shown ultrasound-guided wrist blocks to be as efficient as PNS-guided ones.

**Comparative Effectiveness of Brachial Plexus Approaches**

Four major randomized controlled trials (RCTs) comparing intraoperative brachial plexus blockade to fast-track general anesthesia have shown superior analgesia with the regional technique but no further outcome benefits after 24 hrs. Likewise, 8 of 9 comparisons of continuous perineural techniques to single-shot upper extremity regional anesthetic techniques have supported the positive role of continuous blocks in routine and advanced patient management (Table 2). The beneficial effects of...
continuous blocks are improved by the preemptive use of multimodal analgesic pathways. The following subsections examine ideal regional anesthesia and analgesia approaches for specific surgical indications.

**Analgesia for Shoulder Surgery**

Single-shot ISB is generally considered the standard to which other methods for analgesia after shoulder surgery are compared. A suprascapular nerve block (SSNB) decreased pain and hospital stay after shoulder arthroscopy performed under general anesthesia but did not improve outcomes in patients undergoing open shoulder surgery with combined general/interscalene analgesia plus supplemental SSNB. An SSNB is superior to intra-articular injection after shoulder arthroscopy but is inferior to ISB. When directly compared in another study, ISB gave better early analgesia than intra-articular injection but similar analgesia at 24 hrs. The combination of SSNB and an axillary nerve block has also received preliminary study for analgesia after shoulder surgery. Interscalene block is superior to subacromial bursa block. Perhaps most important, continuous brachial plexus blocks consistently provide superior analgesia with fewer side effects than either continuous subacromial infusion or single-shot ISB, while needle localization by either paresthesia or nerve localization. As single-injection infraclavicular and AXBs sum up comparative studies consistently show it equal or superior to the axillary approach. Axillary block typically has a shorter latency than the midhumeral block, but the comparative success rates between them vary greatly—showing higher success with the axillary, or the midhumeral, or no difference between the 2 blocks.

**Technique Aspects of Brachial Plexus Block**

**Methods of Nerve Localization**

Key to regional anesthesia is localizing the block needle sufficiently close to the nerve to accomplish successful neural blockade but not so close as to injure the nerve. This section summarizes information that compares various methods of nerve localization. As single-injection infraclavicular and AXBs fall into disfavor, so does reliance on the perception of fascial clicks, which are poor indicators of needle-to-nerve proximity. Novel use of surface localization techniques such as skin nerve stimulation has emerged. In particularly challenging patients, such as those with tumor near or within the brachial plexus, computed tomography is useful for nerve localization.

**Paresthesia Versus Peripheral Nerve Stimulation**

Although paresthesia seems to be a more sensitive indicator of needle-to-nerve proximity than is a PNS-generated motor response, the explanation for this phenomenon is unclear. Needle localization by either paresthesia or nerve localization is considered the gold standard by many anesthesiologists, although the differences between the 2 methods appear to be small and not statistically significant.

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**Table 2. Comparison of Single-Shot and Continuous Techniques**

<table>
<thead>
<tr>
<th>Author</th>
<th>No. Subjects</th>
<th>Comparison</th>
<th>Outcome Improvement With Continuous Technique</th>
</tr>
</thead>
<tbody>
<tr>
<td>Klein et al</td>
<td>40</td>
<td>ISB (0.5% ropi+epi) ISB+cISB (0.2% ropi)</td>
<td>Less pain and opioid use; more frequent need for no opioids</td>
</tr>
<tr>
<td>Salonen et al</td>
<td>60</td>
<td>AXB (0.75% ropi) AXB+cAXB (0.1% ropi) AXB+cAXB (0.2% ropi)</td>
<td>No differences in pain or opioid use; however, subjects had minimally painful surgery</td>
</tr>
<tr>
<td>Ilfeld et al</td>
<td>30</td>
<td>ICB (1.5% mepi+epi) ICB = cICB (0.2% ropi)</td>
<td>Less pain, opioid use, and nausea/pruritus; better patient satisfaction and sleep</td>
</tr>
<tr>
<td>Ilfeld et al</td>
<td>20</td>
<td>ISB (1.5% mepi+epi) ISB+cISB (0.2% ropi)</td>
<td>Less pain, opioid use, and nausea/pruritus; better patient satisfaction and sleep</td>
</tr>
<tr>
<td>Delaunay et al</td>
<td>30</td>
<td>ISB+subacromial wound infusion ISB+cISB</td>
<td>Less pain, opioid use, and less local anesthetic use; more mild respiratory complaints</td>
</tr>
<tr>
<td>Ilfeld et al</td>
<td>30</td>
<td>cISB overnight cISB until POD 4</td>
<td>Less pain and opioid use; earlier achievement of discharge criteria</td>
</tr>
<tr>
<td>Capdevila et al</td>
<td>40</td>
<td>ISB (0.5% ropi) ISB+cISB (0.2% ropi)</td>
<td>Less pain, opioid use, nausea and vomiting, sleep disturbance, dizziness; earlier ambulation and increased daily activity</td>
</tr>
<tr>
<td>Kean et al</td>
<td>8</td>
<td>ISB (0.5% levobupi) ISB+cISB (0.25% levobupi)</td>
<td>Less pain and opioid use; higher satisfaction</td>
</tr>
<tr>
<td>Hofmann-Kiefer et al</td>
<td>87</td>
<td>ISB (0.75% ropiva) ISB+cISB</td>
<td>Less pain, opioid use, nausea and vomiting; no difference in joint mobility or rehabilitation</td>
</tr>
</tbody>
</table>

AXB indicates axillary; ISB, interscalene; ICB, infracaular; cISB, continuous interscalene; GETA, general endotracheal anesthesia. Agents: LIDO, lidocaine; CP, chloroprocaine; BUPI, bupivacaine; ropi, ropivacaine; ISO, isoflurane; DES, desflurane. LMA, laryngeal mask airway; POD, postoperative day.
PNS seems to be equally efficacious—studies that directly compare these 2 modalities note similar success rates (70%–90%), albeit these rates are generally lower than reported by others in noncomparative studies. When using a PNS, obtaining an appropriate motor response at 0.5 to 0.8 mA or less has been associated with a greater likelihood of successful blockade.  

Transarterial Injection Versus Paresthesia or Peripheral Nerve Stimulation

When compared with a 4-nerve stimulation technique, the 2-injection transarterial technique for AXB was less successful (90% vs 62%, respectively). A noncomparative study of a single large-volume (50 mL) transarterial injection technique reported 99% success, although 2 injections were actually made “in the same location posterior to the axillary artery.”

Transarterial Versus Perivascular Techniques

Whether by “fanning” local anesthetic on either side of the axillary artery or by stable-needle transarterial injection(s), perivascular AXB techniques are associated with reasonable (88%–99%) success and low complication rates. Although a noncomparative study reported 99% success with 2 injections posterior to the artery, a comparative study reported faster and more complete block by splitting the injection anterior and posterior to the artery, rather than using a single injection.

Peripheral Nerve Stimulation Versus Ultrasound Guidance

Ultrasound studies have consistently demonstrated that the block needle tip can be in close proximity to a nerve without accompanying paresthesia or motor response even at high current. Because motor response to PNS can be variable when the needle tip is observed to be on the surface of or even within the nerve, ultrasound guidance is theorized to provide a more definitive end point of needle-to-nerve proximity. Indeed, recent studies of ICB have demonstrated excellent anesthesia based on ultrasound guidance that was independent of the evoked motor response. In an AXB model, paresthesia was only 38% sensitive, and motor response was 75% sensitive even when ultrasound confirmed needle-to-nerve contact. Yet, despite these differences in localizing the neural end point, ultrasound guidance has resulted in either similar or marginally higher success rates as compared with PNS or perivascular techniques (Table 3).

Ultrasound-Guided Brachial Plexus Blockade

Ultrasound-guided regional anesthesia may facilitate brachial plexus blockade in several ways, including enhanced visualization of the neural target and its surrounding structures, assessment of proper needle-tip position, visualization of local anesthetic spread around the neural target, identification of anomalous anatomy or pathology, optimizing nerve localization when PNS is problematic, such as in patients with amputations or in patients with vascular anomalies, and possibly enhanced block quality. Ultrasound may also improve resident learning of techniques pertinent to the safe and effective provision of brachial plexus anesthesia. With regard to the practice of commingling PNS and UGRA, 2 studies imply that combining the 2 techniques does not add value to ultrasound guidance alone. Block success was not improved when a motor response was present rather than unobtainable during needle placement for supraclavicular block. Similarly, block success was independent of the presence of a motor.

**TABLE 3. Randomized Double-Blind Studies of Ultrasound Guidance for Brachial Plexus Blockade**

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Approach</th>
<th>Design</th>
<th>Main Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Williams et al</td>
<td>2003</td>
<td>Supraclavicular</td>
<td>US+PNS vs PNS R, DB</td>
<td>Decreased block performance time with US</td>
</tr>
<tr>
<td>Marhofer et al</td>
<td>2004</td>
<td>Infraclavicular; pediatric population</td>
<td>US vs PNS R, DB</td>
<td>Decreased sensory onset time and prolonged duration with US; less discomfort during block</td>
</tr>
<tr>
<td>Soeding et al</td>
<td>2005</td>
<td>Interscalene and axillary</td>
<td>US vs surface landmarks, R, DB</td>
<td>Decreased sensory onset time and greater success with US; less paresthesias during block</td>
</tr>
<tr>
<td>Arcand et al</td>
<td>2005</td>
<td>Infraclavicular vs supraclavicular</td>
<td>US/PNS vs US/PNS R, DB</td>
<td>Greater radial nerve block failure in infraclavicular group</td>
</tr>
<tr>
<td>Bigeleisen and Wilson</td>
<td>2006</td>
<td>Infraclavicular: medial vs lateral US approach</td>
<td>US vs US, R, open label</td>
<td>Medial approach faster performance time and more effective; less vascular puncture</td>
</tr>
<tr>
<td>Sites et al</td>
<td>2006</td>
<td>Axillary</td>
<td>Transarterial vs US perivascular, R, SB</td>
<td>Greater success in US group (less conversion to GA)</td>
</tr>
<tr>
<td>Casati et al</td>
<td>2007</td>
<td>Axillary</td>
<td>PNS vs US R, DB</td>
<td>No difference in block success; faster sensory onset and less procedure-related pain in US group</td>
</tr>
<tr>
<td>Kapral et al</td>
<td>2008</td>
<td>Interscalene</td>
<td>PNS vs US R, SB</td>
<td>Greater block success in US group; better sensory, motor, and extent of blockade better in US group</td>
</tr>
<tr>
<td>Sauter et al</td>
<td>2008</td>
<td>Infraclavicular</td>
<td>PNS vs US R, DB</td>
<td>Equal success, performance time, onset, and patient comfort</td>
</tr>
<tr>
<td>Macaire et al</td>
<td>2008</td>
<td>Wrist</td>
<td>PNS vs US R, SB</td>
<td>Time to perform median and ulnar nerve blocks faster with US; total time (performance plus onset) and success were equivalent</td>
</tr>
</tbody>
</table>

Abbreviations: US, ultrasound; PNS, peripheral nerve stimulation; R, randomized; DB, double-blind; SB, single-blind.
response greater or less than 0.5 mA during ISB. To date, no studies attest to enhanced safety with UGRA; indeed, recent case reports note that complications such as nerve injury and intravascular injection can still occur despite the use of ultrasound. Although clearly useful, there are also limitations to UGRA such as technical difficulty in nerve visualization from subcutaneous air or edema and technical challenges in maintaining needle visualization.

The feasibility of ultrasound guidance for brachial plexus blockade has been demonstrated for most of the major approaches to the plexus, including interscalene, posterior cervical, supraclavicular, infraclavicular, and axillary blocks. Similar feasibility studies have been performed for selective blockade of the musculocutaneous, median, ulnar, and radial nerves in the forearm. These feasibility studies have been followed by RCTs that compare various measures of anesthetic success with UGRA to success with PNS. The results of these trials are notable for their inconsistent findings, which are in part related to approach, operator experience, whether ultrasound machine setup is included in time comparisons, and end point definition (Table 3). For instance, performance time for supraclavicular and infraclavicular blocks is 4 to 5 mins faster when ultrasound guidance alone is compared with ultrasound guidance plus peripheral nerve stimulation. In most ultrasound studies, the onset of sensory and motor blockade of individual nerves is faster and duration is longer than expected infusion rates initially and lower-than-expected basal rates initially and just before reservoir exhaustion; and spring-powered pumps tend to provide higher-than-expected basal rates initially and just before reservoir exhaustion.

Whether these inaccuracies and inconsistencies are relevant to daily clinical practice is unclear.

**LOCAL ANESTHETIC AND ADJUVANT PHARMACOLOGY**

### Local Anesthetics

Few large controlled studies compare the various local anesthetics for brachial plexus blockade. Analysis of these studies is difficult by virtue of the many possible variations during a brachial plexus block procedure—which block technique is chosen, which adjuvant is added, pH of the injected solution, how duration is defined and measured, the surgical model, and individual patient characteristics. Despite these limitations, available literature provides insight into how local anesthetic agent selection, dose, concentration and volume, and physical modifications can affect onset, spread, quality, and duration of anesthesia.

#### Local Anesthetic Selection

Selecting a specific local anesthetic should be tailored to specific goals. In general, the intermediate-acting agents lidocaine and mepivacaine demonstrate faster onset and lower failure rates than bupivacaine or ropivacaine but at the expense of shorter analgesic duration. However, 1 study of ISB found ~8-min faster onset and 2-times longer analgesic duration with plain 1% ropivacaine as compared with plain 2% mepivacaine. Whether prolonged analgesia is desirable depends on how much the patient desires a numb extremity, the ability to protect the insensate arm from injury, and the surgeon’s need to assess neurovascular function.

Contemporary studies mostly compare ropivacaine and levobupivacaine to racemic bupivacaine. Although 0.5% ropivacaine and 0.25% bupivacaine provide excellent analgesia, neither consistently provides surgical anesthesia.

For surgical anesthesia, sensory and motor block onset and duration were not different with plain 0.75% ropivacaine compared with plain 0.5% bupivacaine. Increasing plain ropivacaine concentrations up to 1% did not improve sensory and motor block success or analgesic duration as compared with plain 0.5% bupivacaine. Thus, 0.75% ropivacaine and 0.5% bupivacaine seem to be equivalent for brachial plexus anesthesia. Limited and somewhat conflicting studies have found levobupivacaine to have similar block characteristics as racemic bupivacaine and equal-concentration ropivacaine.

Similar to single-shot applications, there is no evidence to support the superiority of one local anesthetic over another when used for continuous techniques. Direct comparison of

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Ropivacaine and bupivacaine is difficult because their precise equipotency is unknown. Equivalent analgesia has been reported using 0.125% bupivacaine and 0.125% ropivacaine for AXB.218,219 or 0.2% ropivacaine and 0.125% levobupivacaine for ISB.217 Preservation of motor function during continuous ISB seems to be minimally better with 0.2% ropivacaine than with 0.15% bupivacaine.219

**Dose, Concentration, and Volume**

Whether increasing local anesthetic mass (mass = concentration × volume) results in a higher success rate is controversial in clinical settings. Laboratory studies clearly indicate that neural blockade requires very little local anesthetic. A variety of animal models have shown that neural blockade can be successfully accomplished with extremely small amounts of local anesthetic. For example, neural blockade occurs with only 1.6% of the total injected volume of local anesthetic,220 with only 0.02% lidocaine concentration within the nerve,220,221 or with local anesthetic deposited along only 3 cm of nerve length.222 Although these animal data represent an idealized state wherein local anesthetic is deposited directly on nerves, they suggest that anesthesiologists may well overdose local anesthetic in their clinical practice. Studies using ultrasonography vary in their findings on the ability to reduce local anesthetic volume without sacrificing block quality.85

In a series of studies involving continuous AXB using 1% mepivacaine with epinephrine, Vester-Andersen et al223–227 systematically evaluated the role of volume, concentration, and dose on block efficacy. When dose was held constant, increasing volume from 20 to 40 to 80 mL had little effect on sensory blockade of most nerves,224 although motor block was superior at lower volumes, probably reflecting a concentration effect.225 When volume was held constant, sensory blockade was 70% to 100% successful in all nerve groups, regardless of increasing concentration (0.5% to 1% to 1.5%).225 Increasing the dose from 400 to 500 to 600 mg resulted in no difference in sensory or motor anesthesia.226 Ultimately, isolated changes in volume, concentration, or dose had minimal effect on sensory nerve blockade. Minor improvements in block quality were achievable only with the combination of increasing volume and drug mass. More recent studies corroborate these findings. Equivalent clinical axillary blockade occurs with 20-, 28-, or 38-mL volumes of 1% mepivacaine,228 whereas 5 or 10 mL of 0.5% ropivacaine manifests equivalent analgesia after ultrasound-guided ISB.229 Similarly, 30, 40, or 60 mL of ropivacaine does not affect the onset of axillary sensory block.229 Purely analgesic block has been reported with as little as 10 mL of 0.25% bupivacaine or 0.5% ropivacaine.66,67 Increasing ropivacaine concentration does not significantly alter ISB characteristics.214 In summary, onset, quality, and duration of brachial plexus local anesthetic blockade are not improved by arbitrarily increasing drug mass or its determinants, volume and concentration. Indeed, doing so may worsen local anesthetic systemic toxicity and neurotoxicity in the event of accident.

The onset and duration of brachial plexus block can also be linked to patient-related conditions. Block onset and duration are unaffected by altitude.231 Anesthetic duration is not prolonged in patients with chronic renal failure.232 The pharmacokinetic profile of levobupivacaine does not vary between patients with or without uremia.232 whereas ropivacaine plasma concentrations 24 hrs after AXB are higher in patients with renal failure.215 Block onset is delayed in areas of local infection as compared with noninfected areas within the distribution of the same nerve.234

**Local Anesthetic Mixtures**

Mixtures of local anesthetics are intended to provide faster block onset than long-acting agents and to extend the duration typically seen with intermediate- or short-acting agents. Overall, mixtures provide few clinically significant advantages, but instead result in a profile similar to a pure intermediate-acting agent.236 Furthermore, combined administration of local anesthetics produces epinephrogenic effects that are additive.237 A more elegant approach to tailoring local anesthetic profile involves selective application of different local anesthetic agents or clonidine238 to individual nerves. By injecting lidocaine on the musculocutaneous and radial nerves, and bupivacaine on the median and ulnar nerves, one can achieve faster recovery from motor block but longer analgesic duration when compared with injecting a mixture of lidocaine and bupivacaine on all 4 nerves.239

**Physical Manipulations**

Certain physical manipulations of local anesthetic solutions have been evaluated as methods to improve brachial plexus block onset or spread. Alteration of local anesthetic temperature has contradictory effects. Injecting ice-cold lidocaine hastens block onset and increases duration but is painful.240 Warming local anesthetic to 37°C may,241 or may not quicken onset time.242 Because local anesthetic blockade of sodium channels is use-dependent, exercising the arm after block placement significantly speeds up anesthesia onset but does not improve success or prolong duration.243 Conversely, the use of transcutaneous nerve stimulation to “exercise the arm” is of no benefit.244 Rapid injection of local anesthetic reduces anesthetic spread and increases failure rate.245 Firm digital pressure applied during the time of injection neither reduces the incidence of HDP,246 nor improves block spread with the interscalene22 or axillary approach.223 Finally, abduction of the arm to 0 degrees increases local anesthetic spread centrally with AXB but does not affect sensory blockade.244 Conversely, maintaining the arm in 90-degree abduction after AXB has been reported to improve onset and duration.248

**Alkalization of Local Anesthetics**

Clinical studies are inconclusive regarding alkalization of local anesthetics as a means of hastening block onset. The presence or absence of epinephrine is a central dividing point for analyzing this topic.249–251 Alkalization seems most effective with commercially prepared epinephrine-containing local anesthetics, probably because these solutions are formulated at a lower pH and the relative effects of raising pH are greater than with plain local anesthetic solutions. However, when fresh epinephrine is added to plain lidocaine, onset times of brachial plexus anesthesia with alkalization are similar to those seen without alkalization.252 The clinical significance of faster onset is questionable. For instance, adding sodium bicarbonate to mepivacaine with epinephrine significantly decreased sensory block onset time from 1.8 ± 0.2 to 1.0 ± 0.2 mins.244 Effects on other block characteristics are similarly unconvincing. For example, alkalization does not improve sensory block success rate,251,252 nor does it affect plasma mepivacaine levels in the absence of epinephrine.251 There are no well-controlled clinical observations of the impact of alkalization on peripheral nerve block intensity and duration in humans, but in rats, alkalization of plain 1% lidocaine decreased block intensity by 25% and decreased block duration by more than 50%. Similar effects were not observed.
with 1% lidocaine with epinephrine. In summary, clinical data do not support the alkalization of local anesthetics used for brachial plexus blockade.

Adjuvants

Significant prolongation of brachial plexus analgesia is ideally accomplished with placement of continuous catheters. For moderate prolongation of analgesia (~24 hrs), various adjuvant drugs can be admixed with local anesthetic. There are no ultralong-acting local anesthetics or slow-release formulations clinically available.

Epinephrine

Epinephrine prolongs duration and intensity of most local anesthetics used for peripheral nerve block. For example, a 1,200,000 dilution (5 µg/mL) significantly increases the mean duration of lidocaine (264 with vs 186 mins without epinephrine). These effects are due to vasoconstriction, which prolongs the nerve's exposure to local anesthetic drug by limiting clearance. Other benefits of epinephrine include acting as a marker of intravascular injection and potentially limiting systemic local anesthetic toxicity by reducing time-to-peak concentration and peak plasma concentration, although the latter effect is not seen with ropivacaine. Adjuvant epinephrine is most effective with lipophobic local anesthetics such as mepivacaine or lidocaine, where it prolongs anesthetic duration in a dose-dependent manner up to a 1:200,000 dilution. Stronger concentrations are associated with hemodynamic side effects—increased heart rate and cardiac output and decreased peripheral vascular resistance. A 1:400,000 dilution (2.5 µg/mL) slightly decreases block duration as compared with 1:200,000 dilution (240 vs 264 mins, respectively) but is associated with minimal hemodynamic alteration and does not decrease nerve blood flow.

Routine use of adjunctive epinephrine clearly prolongs brachial plexus block duration with little, if any, risk. However, on a theoretical basis with some supporting animal data, anesthesiologists may prefer to use weaker concentrations (1:400,000) or avoid epinephrine altogether in patients at risk for cardiac ischemia or potentially prone to nerve injury as a consequence of decreased blood flow secondary to chemotherapy, diabetes, or atherosclerotic disease. Safety and efficacy data for adjunctive epinephrine in continuous perineural infusions are limited. For digital nerve blocks, there is no convincing evidence that epinephrine-containing local anesthetics are causally linked to digital ischemia.

Clonidine

Clonidine is a useful adjuvant for brachial plexus blockade, particularly when admixed with intermediate-acting local anesthetics for AXB. Clinical evidence generally supports its use and has been extensively reviewed. Clonidine does not serve as an intravascular marker, nor does it significantly affect local anesthetic plasma levels. Prolongation of anesthesia and analgesia with brachial plexus clonidine is most likely peripherally mediated and, like its side effect profile, dose-dependent. Brachial plexus clonidine 150 µg delays the onset of pain by 2-fold when compared with systemic control, and 0.1 µg/kg prolongs analgesia by 50% compared with placebo (492 vs 260 mins). When added to mepivacaine, the minimum dose required to prolong analgesia is 0.1 µg/kg, whereas that needed to prolong anesthesia is 0.5 µg/kg (hypotension, bradycardia, sedation) do not occur up to a dose of 1.5 µg/kg or a maximum dose of 150 µg or less.

The choice of local anesthetic affects the effectiveness of clonidine. Dose-dependent prolongation of clonidine admixed with mepivacaine or lidocaine is well established, but its ability to increase analgesic duration after brachial plexus blocks with long-acting local anesthetics is less pronounced. Clonidine accelerates block onset in areas of localized infection. Clonidine has no beneficial effects when used with continuous perineural infusions. Once pain occurs, the presence of clonidine does not alter its intensity. Clonidine does not affect tourniquet pain. Whether clonidine is better than, or adds value to, epinephrine-containing mixtures is uncertain, but human studies that independently assessed the effects of epinephrine and clonidine using the same experimental model demonstrated greater lidocaine block prolongation with epinephrine.

Opioids

Peripheral opioid effects have been demonstrated with intra-articular injection and with wound infiltration, but the clinical relevance of peripheral opioid receptors is uncertain. This lack of basic science clarity extends to the clinical effects of adjunctive opioids used with brachial plexus blockade. Interpretation of clinical studies is difficult because many lack a control group from which to separate the possibility of systemic opioid effect. Indeed, as the quality of study improves, the evidence for a clinically significant peripheral opioid effect at the brachial plexus diminishes. Brachial plexus studies that include a systemic control group mostly fail to demonstrate compelling reasons to add opioids to anesthetizing solutions, most often finding no significant differences in the onset, duration, block quality, or pain scores. Systematic reviews of the role of opioids in peripheral nerve block conclude that their anesthetic and analgesic effects are not clinically relevant. If there is a role for additive opioid, it may be the addition of buprenorphine 0.3 mg as a means of prolonging analgesic duration.

Other Adjuvant Drugs

A variety of other adjuvants for prolonging brachial plexus blockade have been reported but either are ineffective, are associated with side effects, or have unresolved issues related to neurotoxicity. Adenosine does not improve brachial plexus block quality. Tramadol, an analgesic with peripheral effects similar to local anesthetics and clonidine, moderately increases sensory block duration (approximately to the same degree as epinephrine or clonidine) in a dose-dependent manner up to 200 mg when compared with placebo and systemic control. The neurotoxicity of tramadol is unknown; however, it causes skin rash when administered subcutaneously. Brachial plexus verapamil offers little advantage over epinephrine if expected surgical duration is less than 3.5 hrs. Neostigmine does not improve sensory or motor block qualities but is associated with a 30% incidence of gastrointestinal side effects. Dexmethasone has been shown to prolong analgesia, based on an underpowered study without benefit of systemic control. There are theoretical concerns that dexmethasone may adversely affect peripheral nerve blood flow in diabetic patients and/or cause hyperglycemia. Ketamine does not improve ropivacaine blockade but is associated with side effects. Magnesium prolongs prilocaine AXB to the same extent as epinephrine; its peripheral neurotoxicity profile has not been studied. Midazolam has been shown to prolong bupivacaine block by 2 hrs, but concerns have been raised regarding its neurotoxicity. Hyaluronidase does not hasten block onset.
reduce the incidence of failed block, or affect local anesthetic blood concentration, but it does shorten block duration. To date, there have been no studies evaluating nonsteroidal anti-inflammatory drugs as adjuvants for brachial plexus blockade.  

In summary, local anesthetic and adjuvant selection, as well as dosing, clearly affects brachial plexus block characteristics. Yet, despite our ability to modify local anesthetic solutions, it is unclear to what extent block spread and quality are more a function of technical intervention than pharmacological adjustment. Whereas no studies evaluate the pharmacological contributions of local anesthetic and adjuvant selection versus the technical issues of block selection and performance, anesthesiologists should be aware that both profoundly affect the success of brachial plexus anesthesia.

COMPLICATIONS
As with any medical procedure, brachial plexus anesthesia is associated with risks. Large outcome studies of major complications after brachial plexus block are limited. The incidence of various complications ranges from the extremely rare to the relatively common. For instance, a large study in France included 21,278 peripheral nerve blocks, in which the incidence of cardiac arrest (0.01%), death (0.005%), seizures (0.08%), and radiculopathy (0.02%) was extremely small. In a follow-up study, the same group reported that the overall risk of a serious adverse event after peripheral nerve block was 0.04% (Table 4). In its 1999 report, the American Society of Anesthesiologists (ASA) database of closed malpractice claims concerning anesthesia-related nerve injury (ARNI) noted that 28% involved the ulnar nerve (only 15% of these were associated with regional anesthesia) and 20% involved the brachial plexus (only 16% of which were directly attributable to regional anesthesia). Subsequent reports noted that 10% of brachial plexus injuries were for pneumothorax, whereas claims for death and brain damage were most commonly linked to local anesthetic systemic toxicity. Overall, the incidence of severe short- and long-term complications after ISB (catheter and single-shot techniques) is quite low (0.4%). Less serious complaints are common—for instance, 50% of patients undergoing AXB report at least 1 side effect such as soreness (40%), transient numbness (11%), or bruising (23%).

**Peripheral Nerve Injury**
Perioperative nerve injury is a rare complication of regional anesthesia and can present as residual paresthesia, hypoesthesia, or rarely as permanent paresis. The overall incidence of long-term nerve injury ranges between less than 0.02% and 0.4%, depending on the definition of injury and the length of follow-up. The timing of first presentation of neurological injury varies, with a substantial portion becoming apparent in the early postoperative period—ranging from 21% presenting immediately after surgery to 100% within 48 hrs of surgery. Those deficits arising within the first 24 hrs most likely represent extraneural or intraneural hematoma, intraneural edema, or a lesion involving a sufficient number of axons to allow immediate diagnosis. Other subsets of ARNI present 1 to 28 days postoperatively. In the ASA Closed Claims Study, median presentation was 3 days after surgery. Although most injuries are evident by 3 weeks, delayed symptoms can develop weeks after surgery. Such late presentation of neuropathy suggests an alternate mechanism, such as a tissue reaction or scar formation leading to neural fiber degeneration, or patient distraction by perioperative circumstances such as pain or immobility. Over time, the incidence of persistent ARNI decreases. In summary, evidence of neurological abnormality occurs within the first 24 hrs in up to 19% of patients, but will decrease to 3% to 8% by 4 to 6 weeks and will be well less than 0.4% by 1 year.

**Peripheral Nerve Injury and Brachial Plexus Blockade**
Perioperative nerve injuries after upper extremity surgery may be the result of several contributing factors either unrelated or directly related to the regional anesthetic technique (Table 4). Unrelated risk factors include patient and surgical issues, with the latter being responsible for 89% of perioperative neurological complications in a report of 1614 blocks for upper extremity surgery. Regional anesthetic factors that may contribute directly to ARNI include mechanical trauma, ischemic injury, or chemical injury. Whether patients with pre-existing clinical or subclinical injury that involves the brachial plexus are at increased risk for injury from a secondary insult during block placement (the “double-crush” phenomenon) is a concern that is neither confirmed nor refuted by current literature. One large investigation did not link the risk of postoperative paresthesia to pre-existing paresthesia. Similarly, the risk of new or exacerbated injury after ulnar nerve transposition did not vary with general or regional anesthesia, although injuries in the regional group were associated with ulnar nerve paresthesia during block placement. Brachial plexopathy has been reported after block placement in a patient who had received cisplatin and in another patient with multiple sclerosis. Whether such cases reflect isolated instances of injury or are indicative of heightened risk is unknown; thus,
practitioners are advised to weigh risk-to-benefit ratios and alternative anesthesia and analgesia techniques in patients with pre-existing neurological injury to the brachial plexus.305

Mechanical Trauma: The Role of Needle or Catheter Injury

Mechanical trauma, needle type, elicitation of paresthesias, and high injection pressure have all been investigated as contributors to peripheral nerve injury.114,115,301,302,307–309 Animal models have been used to examine needle type (long [14 degrees] vs short [45 degrees] bevel) and bevel configuration.307,310 Selander et al310 examined the immediate (2 hrs) histological implications of needle trauma in isolated or in situ rabbit sciatic nerves. Neuronal injury occurred more frequently with long-beveled needles as compared with short-beveled ones. Whereas the overall frequency of nerve injury was less with short-beveled needles, injury severity was greater. Injury also varied in this study with bevel orientation, particularly with long-beveled needles, where transverse insertion caused more severe injury as compared with insertion parallel to nerve fibers. Rice and McMahon307 also noted that long-beveled needles in the parallel configuration produced less neuronal damage than transverse long- or short-beveled needles, both immediately after injury and at 7 days. Importantly, by 28 days, all injuries caused by long-beveled needles were resolving and overall nerve injury scores were significantly lower, whereas those induced by short-beveled needles continued to display evidence of severe injury (Fig. 16). They further demonstrated that neural repair may be accelerated and more organized with long-beveled injuries, making long-term consequences less concerning. The approach of Rice and McMahon307 of evaluating long-term histological and functional manifestations of injury may be more clinically relevant than the method of Selander et al.310 Moreover, because multifasciculated rabbit nerve tends to slide away from needle tips, the model of Selander et al310 may overstate the “protective effect” of short-beveled needles.

When fascicular implant does occur, both studies agree that nerve injury is more severe with short-beveled needles. There are no RCTs to support or refute the ability of various needle types and bevel configurations to impale human nerves. Further clinical study is necessary before definitive recommendations can be made regarding the use of differently configured needles during peripheral nerve block. There is no evidence that larger-gauge needles used to place perineural catheters increase the risk of nerve injury.63

Mechanical Trauma: The Role of Paresthesias

Whether the elicitation of a paresthesia represents direct needle trauma, thereby increasing the risk of nerve injury, is unknown. Clinical studies of paresthesia and ARNI have thus far been unable to definitively answer this question.114,115,148,301,309,310 Selander et al311 reported a higher incidence of ARNI in patients where a paresthesia was intentionally sought during AXB compared with those undergoing a pervascular technique (2.8% vs 0.8%, respectively; not significant). Because unintentional paresthesias were elicited and injected upon in patients within the pervascular group who then experienced ARNI, Winnie311 has argued that these results do in fact become statistically significant. Forty percent of patients within the pervascular group reported unintentional paresthesias, demonstrating the difficulty with standardization of technique, analysis of nerve injury, and, perhaps most importantly, the futility of completely avoiding a paresthesia when a needle is placed in proximity of a nerve. Auroy et al292 noted that all cases of radiculopathy after peripheral nerve block were associated with either a paresthesia during needle insertion or pain on injection (paresthesia or discomfort coincident with local anesthetic injection) and that the neuropathy had the same topography as the associated paresthesia. In contrast to the above observations, the ASA Closed Claims Study305 found that only 31% of patients with persistent injury experienced paresthesia during needle placement or with local anesthetic injection, and a recent RCT noted no correlation between the location of a paresthesia or motor response and subsequent persistent paresthesia.309 A prospective investigation301 using a variety of regional anesthetic techniques—transarterial, paresthesia, and nerve stimulator—failed to associate complication rates with technique, an observation that has been confirmed by others.148,306 Winchell and Wolfe309 reported a 0.36% incidence of ARNI, despite 98% of patients experiencing a paresthesia. Although this incidence is at the higher end of reported ARNI, resolution occurred in all patients within 7 months. These studies would seem to support Moore’s312 contention that mechanical paresthesias are not, per se, an indication of nerve injury. In contrast, a recent study of ISB noted a 13-fold higher risk of developing neurological sequelae if a paresthesia was experienced during PNS-guided block placement.294 Finally, there is some evidence that neurological injury may vary by approach to the brachial plexus—the incidence of ARNI after PNS techniques was higher with ISBs than with AXBs (4% vs 1%, respectively).71 Although elicitation of paresthesia during regional techniques is not definitively linked to ARNi, pain on injection does seem to be more consistently linked to injury.305,313

Does nonintrafascicular injection of local anesthetic after a paresthesia, or supplemental injection after a failed block, increase the risk of nerve injury? Injury did not occur when local anesthetic was injected through an axillary catheter, although unintentional paresthesias were obtained during catheter placement in 39% of patients.308 Similarly, there was no ARNI in patients who experienced a paresthesia during transarterial AXB.

FIGURE 16. Percent of maximal rat sciatic nerve injury as a function of time, and needle bevel type and orientation. Nerve injury is determined by the cumulative score of 3 graded components: intraneuronal disruption (graded 0 to 5), axonal degeneration (graded yes/no), and disorganized fiber regeneration (graded yes/no). Nerve lesions induced by short-bevel needles are more severe and take longer to repair than those induced by long-bevel needles. Nerve injury induced by short-bevel needle was often associated with persisting signs of injury 28 days after the injury. LB(p) indicates long-bevel needle in parallel configuration to nerve fibers; LB(t), long-bevel needle in transverse configuration to nerve fibers; SB(p), short-bevel needle in parallel configuration to nerve fibers; SB(t), short-bevel needle in transverse configuration to nerve fibers. Reproduced by permission of Oxford University Press/British Journal of Anaesthesia.307

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when the needle was redirected before local anesthetic injection.\textsuperscript{301} Yet, others have noted increased nerve injury associated with paresthesia despite redirection of the needle before injection.\textsuperscript{284} Because the intensity of paresthesias may be attenuated, probing near a partially anesthetized nerve for the purpose of supplementing incomplete anesthesia may theoretically increase the risk of neural injury. Two studies support this concern.\textsuperscript{67} Sixty-seven percent of patients with deficits lasting more than 1 year\textsuperscript{114} and 100% of patients with injury after transarterial AXB had received a supplemental injection.\textsuperscript{115} Techniques using multiple stimulations or paresthesia elicitation after partial injection of local anesthetic dose may also theoretically increase the risk of nerve injury, but this question has received limited study.\textsuperscript{21} There are no data to support or refute the safety of using ultrasound guidance during injection of supplemental local anesthetic around partially anesthetized nerves.

Mechanical Trauma: The Role of High Injection Pressures

Preliminary data from dogs have questioned if intrafascicular injection is consistently associated with higher injection pressures and if monitoring these pressures can predict and/or prevent nerve injury. Hadzic et al\textsuperscript{314} have demonstrated that needles placed at the subperineurium (ie, into the nerve fascicle) required higher injection pressures 57% of the time as compared with subepineurium injections, which were always associated with low injection pressures. Dogs having intrafascicular injections that were concurrently associated with higher injection pressures developed severe, persistent motor deficits and histological pathology that was still present when the animals were euthanized a week later. Although these results are intriguing, there is no clinical correlation in humans. Furthermore, anesthesiologists are unable to discern injection pressures accurately based on “syringe feel.”\textsuperscript{315} An alternative method to prevent the development of high syringe pressure involves not compressing an air column within an injection syringe by more than 50% of its volume,\textsuperscript{316} but this method is also limited by the absence of clinical data.

Ischemic Injury: The Role of Epinephrine and Neural Edema

The functional integrity of a peripheral nerve is highly dependent on its microcirculation,\textsuperscript{317} which consists of an intrinsic supply of exchange vessels within the endoneurium and an extrinsic supply of larger, nonnutritive vessels (Fig. 5).\textsuperscript{118} Extrinsic circulation is under adrenergic control and therefore highly responsive to epinephrine-containing solutions. For example, the topical application of plain 2% lidocaine reduces rat sciatic neural blood flow (NBF) by 39%, and adding epinephrine (5 \textmu g/kg) results in an even greater (78%) reduction.\textsuperscript{318} Although plain ropivacaine causes the greatest reduction in NBF (65%), this decrease is not worsened by the addition of epinephrine; nor are histopathologic changes apparent 48 hrs after administration.\textsuperscript{319} Whether such dramatic experimental reduction in NBF is relevant in humans is unclear. Epinephrine is likely safe when applied to nerve fascicles with intact tissue barriers but may accentuate injury in the event of barrier disruption, such as may occur after an intraneural injection\textsuperscript{229} or in individuals with chemotheraphy-related neurotoxicity, diabetic neuropathies,\textsuperscript{320} or atherosclerosis. Vast human experience suggests that even these risks are decidedly remote, but there are no human RCTs that specifically evaluate adjuvant epinephrine as a factor contributing to ARNI.\textsuperscript{234}

Ischemic nerve injury may also occur after the intrafascicular injection of local anesthetic.\textsuperscript{320,322} Intrrafascicular injection can result in compressive nerve sheath pressures that exceed 600 mm Hg for up to 15 mins. Elevated pressure interferes with endoneural microcirculation\textsuperscript{322} and may alter the permeability of the blood-nerve barrier, resulting in axonal degeneration and axonal dystrophy. Subsequent fibroblast proliferation at the site of injury contributes to late-occurring changes in perineural thickness and endoneural fibrosis.\textsuperscript{323} These changes may result in delayed tissue reaction or scar formation, accounting for symptoms that develop days or even weeks after peripheral nerve blockade.\textsuperscript{114,291,292,295,302}

Chemical Injury: The Role of Local Anesthetic Neurotoxicity

Clinical experience suggests that local anesthetic drugs are overwhelmingly safe when administered correctly and in the recommended concentrations. However, when inappropriately high concentrations, prolonged exposure times (eg, continuous infusions or epinephrine), or intraneuronal injections are encountered, severe degenerative changes may occur leading to neurological sequelae.\textsuperscript{154,320} The persistent neurotoxic effects of local anesthetics are concentration-dependent and seem to parallel anesthetic potency.\textsuperscript{324} Acute-phase (48 hrs) histopathologic and functional effects completely resolve 10 to 14 days later—observations that apply to histological changes\textsuperscript{225} as well as changes to compound action potentials.\textsuperscript{323} These changes happen with both long- and short-acting agents, with and without epinephrine. Continuous catheter techniques raise concern about potential neurotoxicity from repeated perineural injection of local anesthetic. Kron et al\textsuperscript{254} examined the neurotoxic effects of perisclerotic injection of equipotent lidocaine doses repeated 3 times a day for 3 days in rats. Severe neurotoxicity occurred with 4% lidocaine only when rapid dilution of the drug was prohibited, but lidocaine 1% and 2% was innocuous regardless of dilutional factors. Similarly, Kyatta et al\textsuperscript{327} noted myelin sheath injury after repeated injection of 0.5% bupivacaine around rat sciatic nerve over 3 days but no nerve damage after a 3-hr infusion of bupivacaine. Limited clinical evidence has not found continuous perineural local anesthetic infusion to increase the risk of nerve injury over that seen with single-shot techniques.\textsuperscript{293}

Regional anesthesia–induced nerve injury may require a combined mechanical and chemical insult (Fig. 17).\textsuperscript{134,320,325} Selander et al\textsuperscript{329} demonstrated that topical application of bupivacaine, with or without epinephrine, was innocuous in rabbits, whereas intraneuronal injection resulted in severe neural injury. Saline and plain 0.5% bupivacaine resulted in a similar degree of nerve injury, suggesting that injury was not from the injected test solution but rather was the result of injection trauma alone. However, higher concentrations of bupivacaine (1%) or the addition of epinephrine (1:200,000) to 0.5% bupivacaine resulted in significantly more severe axonal injury than saline or 0.5% bupivacaine alone. In contrast, Rice et al\textsuperscript{307} failed to document significant injury after saline injection alone. Although intraneuronal injection of 0.2% or 0.75% plain ropivacaine does not have a deleterious effect on rat sciatic nerve motor function,\textsuperscript{325} this single study does not establish ropivacaine as being less neurotoxic than other local anesthetics used clinically.

THE ROLE OF LOCALIZATION TECHNIQUE

Peripheral Nerve Stimulation

The use of electrical stimulation to locate peripheral nerves was introduced in 1962.\textsuperscript{330} Several advantages have been claimed with this technique, including a higher success
rate, the avoidance of vascular injury, and the avoidance of paresthesias and associated neurological injury.

There is evidence that PNS can reduce the frequency of unintended paresthesia to $\leq 15\%$. However, there are no human RCTs that clearly support the assertion that PNS improves patient safety. Neurological complication rates associated with PNS range from 0% to more than 10%, but within each of these investigations, there were no statistically significant differences between techniques (nerve stimulator, paresthesia, transarterial). Some advocates of the PNS approach argue that it provides exact needle localization without actually contacting nerve tissue. However, investigations have examined the relationship between a subjective paresthesia and an objective motor response elicited by a PNS in patients undergoing interscalene or axillary blockade. Nearly 25% of patients initially reporting paresthesia required a current of more than 0.5 mA to manifest a motor response, suggesting an inconsistency of elicited motor responses despite the needle presumably being near a nerve. Concerns were therefore raised that awareness of a paresthesia subsequent to needle advancement could be compromised in sedated or anesthetized patients, thus potentially subjecting them to unrecognized intraneural injection. These clinical data are further strengthened by recent animal studies in which stimulating needles were inserted into the nerves under direct vision, yet the electrical current required to achieve a motor response could exceed 1 mA. Therefore, the assertion that nerve stimulation allows clinicians to approach neural structures without the risk of mechanical trauma does not seem to be valid. In part because of the above concerns, the ASRA Practice Advisory on Neurologic Complications of Regional Anesthesia and Pain Medicine suggests that brachial plexus blockade, particularly the interscalene approach, not be undertaken routinely in anesthetized patients.

**Ultrasound Guidance**

Similar to peripheral nerve stimulation, UGRA holds the potential for reducing ARNI. Using ultrasound guidance, it is possible to observe a block needle penetrating a peripheral nerve in both animals and humans. Studies in animals also demonstrate the variability of motor response to nerve stimulation even when the needle is observed by ultrasound to be within or touching the nerve. These findings suggest that ultrasound guidance might facilitate avoidance of unwanted needle-to-nerve contact. However, no clinical studies exist to confirm or refute these potential advantages of ultrasound guidance, and nerve injury has occurred despite its use.

**Diagnosis and Evaluation of Neurological Complications**

Patient, surgical, and anesthetic risk factors may all contribute to perioperative nerve injury (Table 5). Although most neurological complications completely resolve within several days or weeks, significant injuries necessitate neurological consultation to locate the lesion, document the degree of injury,
and coordinate further evaluation and rehabilitation. Although some recommend waiting until evidence of denervation has appeared before performing neurophysiological testing (typically 2–3 weeks after injury), a baseline study (including evaluation of the contralateral extremity) is often helpful in ruling out underlying pathology or a pre-existing condition. Furthermore, persistent symptoms may occur secondary to other readily treatable disease processes such as carpal tunnel syndrome or complex regional pain syndrome. When faced with a complete or progressive postoperative nerve deficit, anesthesiologists are urged to seek immediate neurosurgical consultation for evaluation of possible reversible causes of injury. Conversely, improving or stable injuries can be observed or require less urgent neurological consultation.

In summary, ARNI remains a rare but poorly understood complication of brachial plexus anesthesia that is likely multifactorial in nature (Fig. 17). Our lack of knowledge is underscored by the absence of human RCTs of sufficient statistical power to confidently link risk to outcome. Furthermore, anesthesiologists seem to both underestimate the true risk of nerve injury and then fail to fully disclose this risk to their patients. Most admonitions for eschewing ARNI—such as short-beveled needles, avoidance of paresthesia, injection pressure monitoring, or the use of PNS or ultrasound for nerve localization—have no clinical evidence upon which to base their acceptance. Nevertheless, certain risk factors for ARNI emerge from analysis of accumulated evidence. These include damage to axonal protective coverings perpetrated by intraneurium injection, the likely worsening of injury by local anesthetics or epinephrine when the structural integrity of the fascicle has been compromised, and the potentially increased risk of performing brachial plexus blockade, especially via the interscalene approach, in anesthetized or heavily sedated patients.

**Hemidiaphragmatic Paresis**

The proximity of the phrenic nerve and its originating cervical nerve roots (C3–C5) to the brachial plexus frequently leads to unintended local anesthetic blockade and resultant diaphragmatic dysfunction (Fig. 18). The frequency and clinical relevance of this side effect vary with block site but should be carefully considered when providing above the clavicle techniques in patients with underlying pulmonary disease. The incidence of HDP is 100% after ISB. Some patients will report mild dyspnea or altered respiratory sensations and may experience 25% to 32% reduction in spirometric measures of pulmonary function. The development of HDP and pulmonary function changes is not altered by the application of digital pressure during block injection, reducing local anesthetic volume to 20 mL using PNS techniques, or both. Single injection of 10 mL 0.25% bupivacaine has been shown to attenuate HDP and accompanying spirometric changes as compared with 0.5% bupivacaine. A recent study has shown that decreasing the volume of local anesthetic from 20 to 5 mL using an ultrasound-guided technique can decrease both the incidence and severity of HDP. Conversely, a preliminary report that used 10 mL local anesthetic administered via ultrasound guidance was unable to demonstrate a difference in HDP compared with that observed with 20 mL. Abnormal diaphragmatic function persists in 50% of patients after 24 hrs of dilute bupivacaine continuous infusion. Ropivacaine’s purported ability to preserve motor function was not protective in one study, whereas another showed minimally better spirometric values after nonequipotent concentrations of ropivacaine and bupivacaine. Acute respiratory failure and lobar collapse have been reported after continuous interscalene infusion of local anesthetic in patients with marginal pulmonary function. Of note, a continuous catheter study in healthy patients using 0.2% ropivacaine showed diaphragmatic and pulmonary functions similar to a patient-controlled intravenous opioid group.

Supraclavicular block has a lower incidence of HDP as compared with the interscalene approach (50%; 95% confidence interval, 14%–86%) and is not associated with respiratory symptoms or change in pulmonary function. The presence or absence of pulmonary function changes after supraclavicular block may reflect the degree of diaphragmatic paresis. In contrast to the more medially placed vertical infraclavicular approach, the lateral infraclavicular approaches, that is, coracoid and Raj, are not associated with pulmonary function changes. Because HDP occurs in all patients administered ISB with local anesthetic 20 mL or greater and happens unpredictably after supraclavicular and medial ICBs, none of these approaches are recommended in patients unable to tolerate a 30% reduction in pulmonary function. Although ultrasound guidance may or may not reduce the incidence of HDP,
neither does ultrasound guidance eliminate it, nor have the relatively less severe changes in spirometric values been clinically linked to less respiratory compromise in at-risk patients. Although HDP is usually transient, rare cases of permanent phrenic nerve paresis have been reported after ISB and may reflect trauma to the phrenic nerve or an unknown etiology. There are anecdotal reports of phrenic nerve injury after the intersternocleidomastoid approach. Persistent hiccups, presumably a reflection of phrenic nerve irritation, have been reported after ISB.

Pneumothorax

Pneumothorax is a serious complication associated with supravclavicular approaches, including the ISCMB. It has also been reported following interscalene,\(^\text{295}\) coracoid and vertical infraclavicular,\(^\text{359,360}\) and suprascapular blocks. The historical incidence of pneumothorax after supravclavicular block was 0.5% to 6.1%, which reflected experience with classic supravclavicular approaches, wherein the anesthetizing needle was guided toward the apical pleura.\(^\text{361}\) The plumb-bob and subclavian perivascular approaches were designed in part to lessen the risk of pneumothorax.\(^\text{362}\) The risk of pneumothorax in tall, thin patients may be further reduced by initially directing the needle 45 degrees cephalad during the supine plumb-bob technique, rather than directly toward the floor; this magnetic resonance imaging finding has not been confirmed clinically.\(^\text{362}\) Experience with more than 3000 nonobese\(^\text{356}\) and obese\(^\text{357}\) patients suggests that the risk of pneumothorax is 0.1% or less (upper limit of 95% confidence interval) using the subclavian perivascular approach. Because the pleura and first rib are often easy to visualize, UGRA may theoretically reduce the risk of pneumothorax. Although existing studies are too small to confirm these purported advantages,\(^\text{170}\) ultrasound-guided approaches do replace the traditional cephalad-to-caudad\(^\text{364}\) or anterior-to-posterior\(^\text{360}\) needle approach with either lateral-to-medial\(^\text{81}\) or medial-to-lateral\(^\text{364}\) approach whose trajectories are less in-line with the lung.

Patients who develop pneumothorax are not likely to report symptoms for 6 to 12 hrs (in the absence of positive pressure ventilation). This implies futility of early chest radiographs and raises concerns about performing these blocks on outpatients with problematic medical follow-up. Many patients report only mild symptoms, primarily pleuritic chest discomfort.\(^\text{366}\) A chest radiograph taken during full exhalation confirms the diagnosis of pneumothorax.

Local Anesthetics—Unintended Destinations

Intravascular Injection

The proximity of the brachial plexus to major vascular structures invites intravascular injection of local anesthetic. This complication occurred in 0.2% of patients receiving transarterial AXB in one study, despite test dosing and aspiration.\(^\text{115}\) The incidence of systemic signs of local anesthetic injection through perineural catheters is also 0.2%.\(^\text{63}\) Even with ultrasound guidance, placement of perineural catheters results in vascular puncture in 0% to 11% of patients, with the range most likely reflecting differences in anatomic approach and needle/catheter characteristics.\(^\text{15,132,195,196,270,347}\) The use of ultrasound per se does not eliminate intravascular injection of local anesthetic.\(^\text{109,362}\) Intra-arterial injection can be dramatic during interscalene or supravclavicular block, because local anesthetic injected directly into the vertebral or carotid artery, or retrograde flow via the subclavian artery, proceeds directly to the brain. The estimated convulsant doses after unintended carotid or vertebral artery injection are lidocaine 14.4 mg and bupivacaine 3.6 mg; symptomatic toxicity has been reported at similar doses.\(^\text{364}\) Intravenous injection may allow larger volumes to be injected before toxicity. The tissue absorption rate of local anesthetic does not vary as a function of brachial plexus block approach.\(^\text{359}\) Gradual absorption of local anesthetic from tissue deposits results in slowly rising local anesthetic concentrations, which cause systemic toxicity less frequently as compared with relatively lower concentrations that rise quickly as a result of intravascular injection.\(^\text{370}\) Local anesthetic concentrations should peak 10 to 30 mins after single injection or up to 1 hr if epinephrine has been added. Up to 48 hrs of 9-mL/hr infusion of 0.2% ropivacaine results in plasma levels well below those associated with central nervous system toxicity,\(^\text{371}\) as does 5 days of continuous bupivacaine infusion.\(^\text{372}\)

What constitutes the maximum safe recommended local anesthetic dose for brachial plexus anesthesia is controversial and poorly grounded in evidence. Peak arterial plasma levels of local anesthetic do not correlate with body surface area or patient weight.\(^\text{373,374}\) Despite manufacturers’ recommended doses, there are multiple published reports of significantly higher doses delivered to the brachial plexus without adverse sequelae, although the safety of this practice is not well studied.\(^\text{67,100}\) Importantly, local anesthetic toxicity may become problematic in patients with compromised pharmacokinetics secondary to congestive heart failure, advanced age, or hepatic failure or those undergoing continuous techniques.\(^\text{375}\) Total doses in these patients should be reduced, but to what extent is poorly defined.

The incidence of seizure after peripheral nerve block is 5 times more likely as compared with epidural injection.\(^\text{376,377}\) This scenario is best avoided by meticulous test dosing, aspiration, and fractionated dosing with continuous observation for signs and symptoms of local anesthetic toxicity, understanding that these maneuvers are not totally reliable.\(^\text{115}\) No data attest to the value of using ultrasound to reduce the frequency of intravascular injection, but there are reports of intravascular injection despite its use.\(^\text{389,367}\) The seizure rate per 1000 patients varies according to the brachial plexus approach selected—1.2 to 1.3 for axillary (equally likely to occur with a transarterial, PNS, or midhumeral technique),\(^\text{158}\) 3 to 7.6 for interscalene,\(^\text{294}\) 1 to 7.9 for supravclavicular,\(^\text{263,376}\) and up to 10 for vertical infraclavicular approaches.\(^\text{377}\) Continuous axillary catheters are associated with seizures in up to 8 per 1000 blocks.\(^\text{347}\) Compared with seizures, the risk of cardiovascular collapse after unintentional intravascular injection is less certain. Animal studies suggest a margin of safety afforded by lidocaine over longer-acting agents (safety ratio of 1:2.9 representing bupivacaine–levobupivacaine/ropivacaine–lidocaine, respectively). The safety profile of levobupivacaine as compared with ropivacaine is less clear,\(^\text{378,379}\) but cardiovascular collapse does occur with bupivacaine and ropivacaine.\(^\text{380,381}\) Most importantly, anesthesiologists should understand that the risk of intravascular injection with subsequent seizure is very high with brachial plexus anesthesia, perhaps exceeded only by caudal anesthesia.\(^\text{292,376}\) Should cardiac systemic toxicity occur with ropivacaine or bupivacaine, advanced cardiac life support protocols should be instituted immediately and consideration given to early administration of lipid emulsion.\(^\text{†}\)

Subarachnoid or Epidural Injection

Local anesthetics intended for the brachial plexus may spread to the neuraxis. Single-shot and continuous interscalene

†The ASRA Practice Advisory on Local Anesthetic Toxicity is expected to be published in Regional Anesthesia and Pain Medicine in 2009.
and posterior paravertebral blocks have been linked to unintended subarachnoid and cervical or thoracic epidural blocks.\textsuperscript{75,382,383} Spinally mediated bradycardia, hypotension, apnea, and/or cardiac arrest can follow and may require timely and definitive resuscitation, including epinephrine.\textsuperscript{382} Needle or catheter entry into the subarachnoid space can occur directly, or uncommonly via the dural cuff or injection into the nerve or ganglion (Fig. 19). These complications are best avoided by using shorter needles, directing the needle slightly caudad to avoid the intervertebral foramen, by slow/fractionated injection, and perhaps by lower volumes. Cadaver studies emphasize the nearness of the central neuraxis to an ISB needle. The minimum distances from skin to the C6 foramen and vertebral column are 23 and 35 mm, respectively.\textsuperscript{383,384} Imaging studies suggest that the risk of needle entry into the spinal canal, using the Winnie approach, can be reduced by using a more proximal entry point and a more steeply angled needle (≥50 degrees caudad).\textsuperscript{384} There are no clinical studies to verify these image-based findings, although neuraxial injection has not been linked to the modified lateral\textsuperscript{63} or middle\textsuperscript{385} interscalene approach.

Cervical Sympathetic Chain

Excessive local anesthetic spread can also affect the cervical sympathetic chain (Fig. 20), causing the patient to manifest Horner syndrome. This side effect occurs with interscalene,\textsuperscript{386} vertical infraclavicular, and especially supraclavicular (20%–90%)\textsuperscript{382,386} and cervical paravertebral (40%) blocks.\textsuperscript{75} Although lower injectate volume may logically decrease the likelihood of Horner syndrome, this association is unproven.\textsuperscript{389} Cervical sympathetic chain anesthesia has been associated with continuous blocks via the lateral interscalene approach.\textsuperscript{63} Other than educating patients regarding the temporary nature of this phenomenon, there is generally no harm from its occurrence. Rarely, continuous techniques have been linked to prolonged\textsuperscript{387} and delayed Horner syndrome.\textsuperscript{388}

Recurrent Laryngeal Nerve

Hoarseness may transpire after ISB\textsuperscript{386} and after 1.3% of supraclavicular blocks\textsuperscript{82} but has not been reported with the infraclavicular approaches. Continuous techniques have been associated with this side effect in 0.8% to 0.9% of interscalene\textsuperscript{53,347} and 10% of cervical paravertebral approaches.\textsuperscript{75} Hoarseness presumably occurs as a consequence of excessive local anesthetic spread to the recurrent laryngeal nerve (arrow) and cause Horner syndrome. Illustration by Gary J. Nelson. Reproduced with permission from Neal and Rathmell. Complications in Regional Anesthesia and Pain Medicine (Elsevier Saunders).\textsuperscript{328}

Infection

Serious infections associated with continuous or single-shot brachial plexus blocks are extremely rare. Whereas catheter tip colonization is frequent (29%), 2 large series reported inflammation in 0.8% to 3% of patients and abscess formation in only a single diabetic patient.\textsuperscript{53,347} A third series of 3491 patients noted inflammation in 4.2%, infection in 2.4%, and infection requiring incision and drainage in 0.8% of patients, despite the routine use of hair covering, face mask, and sterile gown.\textsuperscript{389} Risk factors for catheter-related inflammation include intensive care unit admission, catheter duration of more than 48 hrs, male sex, the absence of prophylactic antibiotic at the time of insertion, and operator experience.\textsuperscript{347,389} The 2004

FIGURE 19. Mechanisms of unintended neuraxial block during interscalene brachial plexus anesthesia. The spinal canal and its contents are within 35 mm of the skin in most patients and can be accessed by unintentionally deep needle placement. Needles can also enter long dural root cuffs, thereby accessing cerebrospinal fluid (inset). Illustration by Gary J. Nelson. Reproduced with permission from Neal and Rathmell. Complications in Regional Anesthesia and Pain Medicine (Elsevier Saunders).\textsuperscript{328}

FIGURE 20. Mechanisms of cervical sympathetic trunk anesthesia. The stellate ganglia is quite close to the brachial plexus. Diffusion of local anesthetic from properly placed needles near the brachial plexus can unintentionally anesthetize the stellate ganglia (arrow) and cause Horner syndrome. Illustration by Gary J. Nelson. Reproduced with permission from Neal and Rathmell. Complications in Regional Anesthesia and Pain Medicine (Elsevier Saunders).\textsuperscript{328}
Hypotensive/Bradycardic Events

Severe, sudden hypotensive and/or bradycardic events (HBE) have been reported in 13% to 24% of awake sitting patients undergoing shoulder arthroscopy with interscalene brachial plexus anesthesia. Possible etiologies of HBE included β1-agonist effects of exogenous epinephrine and activation of the Bezold-Jarisch reflex. This reflex occurs when the combination of decreased venous return and heightened sympathetic tone leads to forceful contraction of a near-empty left ventricle, with consequent parasympathetically mediated arterial vasodilation and bradycardia (Fig. 22). The incidence of HBE is decreased when prophylactic metoprolol (but not glycopyrrolate) is administered after block placement in 2.5-mg increments to an end point of either heart rate of less than 60 beats/min or maximal dose of 10 mg. Clinically, HBE is unpredictable, typically occurring 61 ± 18 mins after block placement and often heralded by light-headedness or nausea. The vast majority of these events are reported in minimally to moderately sedated patients. Whether the incidence is different in patients under general anesthesia or a combined technique is unknown.

Vascular Injury

Vascular complications are rare but potentially devastating events that are reported with varying frequencies during upper extremity regional anesthesia. Unlike the risks of anticoagulation and neuraxial blockade, the risk for brachial plexus vascular injury in anticoagulated patients is less well defined. The ASRA Guidelines on Anticoagulation and Regional Anesthesia suggest that performing brachial plexus blocks in patients who are mildly to moderately anticoagulated is not contraindicated, provided risk-to-benefit is considered. Increased caution...
is prudent in those blocks where an expanding hematoma could compress the airway or be difficult to access.

Transient vascular insufficiency is a reported complication of brachial plexus blocks, occurring in up to 1% of patients. Vasospasm may follow arterial puncture or be a consequence of local anesthetic-induced vasoconstriction. Treatment includes intra-articular lidocaine (being mindful of total local anesthetic dose to avoid high plasma levels), topical warming, or nitroglycerin paste. The risk of hematoma immediately after brachial plexus techniques is small (0.001%--0.02%). The incidence of hematoma may increase at 1-month follow-up, although the incidence may vary for different techniques. Hematomas occur at a slightly higher rate with continuous catheter techniques compared with single-shot techniques. Although most are inconsequential, hematomas have been associated with postoperative paresthesia or transient nerve injury. Pseudoaneurysm formation is another rare complication of brachial plexus blocks. Pressure-induced neural ischemia with subsequent neurological impairment may occur because of the close proximity of neurovascular structures within the axilla. Risk factors include the extent of the injury (number of needle punctures), impaired vascular elasticity, diabetes mellitus, hypertension, and anticoagulation. Axillary artery dissection can result from intramural injection of local anesthetic. In summary, vascular complications are rare after brachial plexus blockade but must be considered in patients with postoperative neurological impairment. Early recognition and prompt surgical intervention are critical to avoid long-lasting neurological sequelae.

**Muscle Injury**

Local anesthetics can cause myonecrosis, with bupivacaine producing the most intense effect. Because damage is dose related, continuous local anesthetic administration may worsen injury. Epinephrine and steroid also intensify this effect, which produces immediate and complete destruction of adult myocytes. Local anesthetic myotoxicity is dependent on a nonspecific increase in sarcoplasmic reticulum permeability to calcium. Immature myocytes are spared because they lack an internal calcium reservoir; consequently, new muscle regenerates over 3 to 4 weeks. Short-term continuous perineural infusion models in animals confirm myotoxicity with bupivacaine and, to a lesser extent, ropivacaine.

**Perineural Catheter Complications**

Large prospective studies involving more than 5500 patients suggest that the incidence of complications with continuous catheter techniques is very low and perhaps even lower than incidences reported with single-shot techniques. Several complications are unique to continuous catheter techniques. For instance, the most common complication is unintentional dislodgement, which can occur in 0% to 30% of patients. However, the combination of liquid adhesive, subcutaneous tunneling of the catheter, and securing the catheter-hub connection with tape or specifically designed devices can reduce catheter dislodgement to less than 5% over 6 to 9 days. Catheters may also knot and shear. Although knotting is distinctly uncommon, any catheter that is difficult to remove or causes pain or paresthesia during initial traction should prompt discontinuation of removal efforts and evaluation for minimally invasive or surgical removal.

**Tourniquet Effects**

Oclusive tourniquets are applied to the upper extremity to improve the surgical field. Ischemic nerve or muscle damage is unlikely in the noncompressed area if flow is re-established within 6 hrs, but damage may occur under the cuff within 2 to 4 hrs. Tourniquet pressures in excess of 400 mm Hg have been linked to nerve injury. Up to 40 mins is necessary to return to normal metabolic status after 3 hrs of tourniquet inflation. Tourniquets produce pain by a complex mechanism, most likely involving neural ischemia. Reperfusion almost immediately relieves tourniquet pain, although a transient second phase (not usually seen with regional techniques) may ensue.

**PERIOPERATIVE ISSUES**

**Informed Consent and Documentation**

Informed consent and its proper documentation are essential elements in the practice of medicine, yet evidence suggests that regional anesthesiologists both inaccurately estimate the risk of major complications and frequently fail to discuss these risks with their patients. Both medical and legal experts decry this practice. Accurate documentation of brachial plexus blockade has become more complicated as a result of perineural catheter placement, ultrasound guidance, and reimbursement and regulatory requirements for documentation. Consequently, forms to facilitate documentation have been developed.

**Avoiding Wrong-Side Block**

The Joint Commission on Accreditation of Healthcare Organizations has focused attention on eliminating wrong-sided surgeries and other procedures such as regional blocks. A method to prevent wrong-sided block incorporates a “pause” just before placing the block needle at the injection site. Elements of a pause include (1) confirming the patient’s identity, (2) confirming the intended procedure, (3) verifying agreement of the anesthesiologist and patient regarding the correct side of the intended procedure, and (4) visually confirming that the proper surgical site has been clearly marked on the patient’s skin. Nonetheless, wrong-side blocks have been reported despite the methods created to prevent them.

**Limb Protection and Discharge Criteria**

Studies have addressed the issue of limb protection after block placement, particularly when continuous techniques are used. It is generally safe to discharge patients, including children, with partial sensory block or continuous infusions. Patients with residual or continuous upper extremity sensory and/or motor block should be properly fitted with a sling or similar protective device. Instructions should include a warning to protect the insensate limb from pressure or thermal injury and advice as to when to expect sensory block resolution. Especially with continuous ambulatory techniques, patients should be provided with detailed written instructions and physician contact information. Indeed, when this is provided, 97% of patients report feeling safe and are accepting ambulatory analgesic techniques. As an alternative to prolonged motor blockade, the midhumeral approach allows for selectively anesthetizing individual nerves to achieve faster motor block resolution while maintaining prolonged analgesia of nerves within the surgical site. Selective application of clonidine also prolongs analgesia while limiting motor block.

**FUTURE RESEARCH DIRECTIONS**

On the occasion of our 2002 review of brachial plexus anesthesia, we suggested future directions for research to fill gaps in existing knowledge. It is heartening that the ensuing
6 years have indeed made great, and at times amazing, strides toward these goals. New imaging modalities, particularly UGRA, have resulted in an exponential proliferation of scientific literature that is rapidly moving from pure description of techniques to meaningful comparison of ultrasound guidance to existing standards such as PNS. An exciting spin-off of this work is an increased understanding of needle-to-nerve proximity. In 2002, few would have guessed, much less admitted, that block needles are frequently touching or within nerves (when viewed by ultrasound), yet this needle-to-nerve proximity is not invariably associated with the expected paresthesia or motor response. So important has ultrasound become that Regional Anesthesia and Pain Medicine created a new section in the journal devoted to UGRA and its related topics.420 The intervening years have also witnessed an unprecedented proliferation of adequately powered studies that compare meaningful outcomes of upper extremity blockade to fast-track general anesthesia and do so based on relevant definitions of success (ie, surgical block of all major terminal nerves within 30 mins) and in geriatric populations of patients (ie, those undergoing moderately to severely painful surgeries). In this same vein, continuous perineural catheter techniques have been subjected to increasingly sophisticated evaluations in terms of their ability to improve immediate outcomes such as analgesia and reduction of opioid-related side effects, and investigators have also begun to assess the ability of perineural techniques to affect longer-term outcomes such as hospital discharge or improved rehabilitation. We previously noted the need for further understanding of 2 serious complications of brachial plexus anesthesia—peripheral nerve injury and systemic local anesthetic toxicity. Although ultrasound guidance, improvements in peripheral nerve stimulation technology,427 and injection pressure monitoring have yet to be proven clinically effective in reducing the frequency of nerve injury, it is reasonable to speculate that these new technologies will improve our understanding of basic pathophysiology of nerve injury, which should in turn improve outcomes. Contemporaneously, advances in lipid emulsion rescue of systemic local anesthetic toxicity428 hold promise for improving our ability to treat this potentially fatal complication. Indeed, ASRA will publish the proceedings of its 2008 Practice Advisory on Local Anesthetic Toxicity in 2009. Finally, we noted the challenges of training physicians in old techniques and new technologies. Recent studies have introduced or validated new tools used to assess resident learning,429,430 provided insight into the education of regional anesthesia fellows,431 and suggested guidelines for regional anesthesia fellowship training.432 Moreover, ASRA and the European Society of Regional Anesthesia and Pain Therapy have published their suggested curriculum for learning ultrasound, which addresses both resident and postgraduate physician learners.432

Despite great progress, challenges remain and acquisition of knowledge serves only to expand the list of questions. The largest gap in contemporary knowledge of upper extremity regional anesthesia is the need for further high-quality data, including well-designed RCTs, concerning the effectiveness of ultrasound guidance for improving block quality and efficiency as compared with existing nerve localization techniques.433 Enhanced safety with UGRA remains unproven; indeed, recent case reports of complications demonstrate that the technique will not completely eliminate serious complications. Yet, more than any other recent technology in regional anesthesia, UGRA has the potential to improve efficiency and safety—the challenge is to prove it so. Two other barriers to the universal adoption of UGRA as the standard of care for nerve localization are the high cost of equipment and the issue of anesthesiologist training.72,432 With regard to continuous perineural catheter techniques, will their proven short-term benefits be extended to show improvement in health-related quality of life? Which patients most benefit from perineural infusions? What are the best delivery, dosing strategy, and drug combinations? Finally, regional anesthesia, just as the entire specialty of anesthesiology,434 is challenged by the need to train a sufficient number of academicians and researchers to continue to improve and advance our specialty into the future.435

REFERENCES

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184. Sinha SK, Abrams JH, Weller RS. Ultrasound-guided interscalene needle placement produces successful anesthesia regardless of motor stimulation above or below 0.5 mA. Anesth Analg. 2007;105:848-852.


222. Vester-Andersen T, Eriksen C, Christiansen C. Perivascular axillary block III: blockade following 40 mL of 0.5%, 1% or 1.5% mepivacaine with adrenaline. Acta Anaesthesiol Scand. 1984;28:95–98.


278. Murphy DB, McCartney CJI, Chan VWS. Novel analgesic...


304. Winneke AP. Does the transarterial technique of axillary block provide a higher success rate and lower complication rate than a paresthesia technique? Reg Anesth. 1995;20:482–485.


308. Claudio R, Hadzic A, Shih H, Vloka JD, Castro J,


353. Dullenkopf A, Blumenthal S, Theodorou P, Roos J, Perschak H, Borgeat A. Diaphragmatic excursion and respiratory function after...


Ultrasound-guided infraclavicular brachial plexus block

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Background. Peripheral nerve blocks are almost always performed as blind procedures. The purpose of this study was to test the feasibility of seeing individual nerves of the brachial plexus and directing the block needle to these nerves with real time imaging.

Methods. Using ultrasound guidance, infraclavicular brachial plexus block was performed in 126 patients. Important aspects of this standardized technique included (i) imaging the axillary artery and the three cords of the brachial plexus posterior to the pectoralis minor muscle, (ii) marking the position of the ultrasound probe before introducing a Tuohy needle, (iii) maintaining the image of the entire length of the needle at all times during its advancement, (iv) depositing local anaesthetic around each of the three cords and (v) placing a catheter anterior to the posterior cord when indicated.

Results. In 114 (90.4%) patients, an excellent block permitted surgery without a need for any supplemental anaesthetic or conversion to general anaesthesia. In nine (7.2%) patients local or perineural administration of local anaesthetic, and in three (2.4%) conversion to general anaesthesia, was required. Mean times to administer the block, onset of block and complete block were 10.0 (SD 4.4), 3.0 (1.3) and 6.7 (3.2) min, respectively. Mean lidocaine dose was 695 (107) mg. In one patient, vascular puncture occurred. In 53 (42.6%) patients, an indwelling catheter was placed, but only three required repeat injections, which successfully prolonged the block.

Conclusion. The use of ultrasound appears to permit accurate deposition of the local anaesthetic perineurally, and has the potential to improve the success and decrease the complications of infraclavicular brachial plexus block.

Br J Anaesth 2002; 89: 254–9

Keywords: anaesthesia regional, brachial plexus; anaesthetics local, lidocaine; measurement techniques, ultrasound; surgery, pectoral

Accepted for publication: March 6, 2002

During infraclavicular approach to the brachial plexus block, electrical stimulation is employed to ensure close proximity of the needle to the nerves. The success of this method depends on a good understanding of anatomy and strong reliance on landmarks which may be obscured by obesity or anatomical variations. In addition, this technique requires eliciting twitches of muscles distal to the wrist; a proximal response may be obtained in as many as 21% of patients in whom the failure rate may be as high as 66%. Because of the blind nature of this technique, unintentional puncture of blood vessels or nerve injury may also occur. By providing precise control of needle placement, ultrasound may improve the success rate of the block and minimize vascular and neurological complications. However, previous studies using ultrasound with different techniques in various approaches to the brachial plexus reported mixed results regarding the success rate, onset time and complications of this method. We have developed a standardized, ultrasound-guided infraclavicular brachial plexus block technique that involves injections of local anaesthetic around each cord. In this report we describe the technique and present its performance characteristics.

Methods

After obtaining Institutional Review Board approval, 126 consecutive consenting patients were included in this prospective study. Children aged below 18 yr, adults over 80 yr and patients with pre-existing neurological disorders were excluded. Routine monitors, including pulse oximeter,
electrocardiogram and blood pressure cuff were used, and an i.v. line was inserted. Each patient, except one who weighed 225 kg and had obstructive sleep apnea, received midazolam 2 mg and fentanyl 50 µg prior to the procedure.

**Technique**

With a patient in the supine position, the arm was abducted to 90°. The deltopectoral region was scanned with a 2.5 MHz probe of a Hewlett-Packard 77020A ultrasound monitor (Andover, MA, USA). A transverse image of the second part of the axillary artery and vein, and of the three cords of the brachial plexus, was obtained posterior to the pectoralis minor muscle. The outline of the ultrasound probe was marked on the skin. The area was prepared with betadine and draped. Figure 1 depicts the location of the probe and a diagrammatical representation of the sonographic image. The probe was covered with a sterile sheath (Microtech Medical Inc., Columbus, MS, USA) after applying a liberal amount of gel (Aquasonic, Parker Laboratories, Fairfield, NJ, USA), and placed over the previously marked area which was covered with another layer of sterile gel. Depending on availability, a 17- or 18-gauge Tuohy needle without a stylet was connected to sterile extension tubing attached to a stopcock and two 20-ml syringes, and flushed with local anaesthetic until the air in the system was completely removed. An 18-gauge needle was used to puncture the previously anaesthetized skin. The Tuohy needle was then introduced and advanced until it was imaged. The needle tip was first directed to the medial cord between the axillary artery and vein (Fig. 2). One or 2 ml of 2% lidocaine, with epinephrine 1:200 000, and sodium bicarbonate (0.9 mEq/10 ml), was injected to ensure that the needle tip was within the neurovascular bundle, behind the posterior fascia of the pectoralis minor muscle; local anaesthetic would distribute within the muscle if the needle bevel did not completely penetrate the fascia. After confirming satisfactory spread of lidocaine, an additional 7–11 ml of local anaesthetic was injected around the medial cord. The needle was partially withdrawn and redirected between the lateral cord and the superior aspect of the axillary artery (Fig. 3). Again, after 1–2 ml lidocaine injection to ensure satisfactory spread, 7–11 ml of anaesthetic solution was injected. The needle was then advanced slightly deeper than the posterior aspect of the artery, and its shaft was brought into a more horizontal position to place its tip between the artery and the posterior cord. Then an additional 7–11 ml of lidocaine was deposited (Fig. 4). The spread of lidocaine around the cords was observed sonographically during each injection. During all manoeuvres the image of the entire needle was kept in view. When the image was lost because of misalignment between the probe and the needle, further manipulation or injection was carried out only after obtaining the image of the entire needle by realignment. Gentle in-and-out jiggling of the needle was also used to help regain the image.

![Diagram](image)

Fig 1 Sagittal section of the right deltopectoral region with corresponding diagrammatical representation of the ultrasound image obtained by an anteriorly placed transducer. Location of the ultrasound probe and the needle entry point are depicted on the left chest. Note that the block needle reaches the neurovascular region after traversing the pectoralis major and minor muscles. US, ultrasound probe; A, axillary artery; V, axillary vein; L, P and M are lateral, posterior and medial cords, respectively.

![Diagram](image)

Fig 2 Diagram representing infraclavicular region and advancement of block needle towards the medial cord of the brachial plexus with ultrasound guidance. A, axillary artery; V, axillary vein. 1 is the initial direction of needle advancement and 2 is the final direction.

In 53 patients in whom surgery was expected to last longer than 2 h, a single-hole, 19-gauge Flexitip (Arrow International, Reading, PA, USA) or 20-gauge epidural
The needle is withdrawn into pectoralis minor muscle from its final position shown in Figure 2, and redirected towards the antero-superior aspect of the axillary artery (position 3). Then the needle is advanced further in a more vertical direction to place its tip between axillary artery and the lateral cord (position 4). A, axillary artery; V, axillary vein.

The block needle is advanced further posteriorly just beyond the axillary artery (position 5). Then the needle tip is redirected in a more horizontal manner to bring up its tip between the posterior wall of the axillary artery and the posterior cord (position 6). A, axillary artery; V, axillary vein.

catheter (Sims Portex Inc., Keene, NH, USA) was passed through the needle and placed 4–5 cm beyond the needle tip between the posterior cord and the axillary artery (Fig. 5). Multiorifice catheters were avoided to prevent escape of local anaesthetic into unintended areas. The position of the catheter tip was confirmed by injecting 1–2 ml of air and observing its echogenic spread around the posterior cord. The catheter was secured with a transparent adhesive dressing.

Assessment of block

Sensory block was initially tested by pinching the skin of the hand and arm at the following areas innervated by individual nerves: the thenar eminence, the hypothenar region, the dorsum of the hand, the lateral aspect of the forearm and the area overlying the insertion of the deltoid muscle, for median, ulnar, radial, musculocutaneous and axillary nerves, respectively. When a decreased response to pinch was noted, a 22-gauge needle was used to evaluate the sensory block in the tested area. The motor block was evaluated by asking the patient to flex the arm (musculocutaneous), extend the flexed arm and wrist (radial), abduct the shoulder (axillary), sustain elevation of the arm (axillary), and adduct the arm (medial and lateral pectoral nerves and thoracodorsal nerve). Onset of the block was defined as the time from the last injection to diminished response to pinch and motor weakness. Anaesthesia was considered to be at surgical level when the patient could not feel pain from the needle in tested areas of the upper extremity and was unable to move the shoulder, elbow and/or wrist. Time to perform the block included the time needed to image and mark the area, prepare and drape the field, insert the needle, inject the local anaesthetic, and in 53 patients, place the catheter.

Results

Patients’ characteristics are shown in Table 1. One patient weighed 225 kg and had obstructive sleep apnea, hypertension, and diabetes mellitus. All patients with end-stage renal disease received the block for the creation of an arteriovenous fistula or for the placement of a graft for haemodialysis. In the remaining patients, the block was given for surgery of the hand, including tendon, vessel and nerve repair, and external fixation or open reduction of fractures of the digits, hand or forearm. The insertion and manipulations of the needle were well tolerated by all patients. The neurovascular structures were easily imaged in all patients. In three patients (2.4%) the block was incomplete, necessitating conversion to general anaesthesia with tracheal intubation. Nine patients (7.2%) required augmentation of the block; two patients each received local infiltration, median nerve or ulnar nerve block at the wrist,
Table 1 Patient characteristics (n=126). Many patients had more than one pre-existing condition

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<td>Mean age (range) (yr)</td>
<td>42.9 (18-79)</td>
<td>–</td>
</tr>
<tr>
<td>Mean weight (SD) (kg)</td>
<td>76.5 (24.3)</td>
<td>–</td>
</tr>
<tr>
<td>Male/female</td>
<td>93/33</td>
<td>–</td>
</tr>
<tr>
<td>Mean ASA status (SD)</td>
<td>1.8 (0.8)</td>
<td>–</td>
</tr>
<tr>
<td>Patients without history of pre-existing conditions</td>
<td>69</td>
<td>54.7</td>
</tr>
<tr>
<td>Patients with history of pre-existing conditions</td>
<td>57</td>
<td>45.2</td>
</tr>
<tr>
<td>Hypertension</td>
<td>25</td>
<td>19.8</td>
</tr>
<tr>
<td>End-stage renal disease</td>
<td>18</td>
<td>14.2</td>
</tr>
<tr>
<td>Bronchospastic disease</td>
<td>9</td>
<td>7.2</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>7</td>
<td>5.5</td>
</tr>
<tr>
<td>Cardiac valvular disease</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>Dysrhythmias</td>
<td>4</td>
<td>3.1</td>
</tr>
<tr>
<td>Morbid obesity</td>
<td>4</td>
<td>3.1</td>
</tr>
<tr>
<td>Sleep apnoea</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td>2</td>
<td>1.6</td>
</tr>
<tr>
<td>Chronic alcoholism</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>7</td>
<td>5.5</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>2</td>
<td>1.6</td>
</tr>
<tr>
<td>Hepatitis</td>
<td>4</td>
<td>3.1</td>
</tr>
<tr>
<td>Human immunodeficiency virus</td>
<td>2</td>
<td>1.6</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>1</td>
<td>0.8</td>
</tr>
</tbody>
</table>

One was given a radial nerve block at the wrist and two received digital nerve blocks. One of the patients who required local infiltration had a complete block of the upper extremity, but surgery involved a region of the axilla and torso that is innervated by the brachial plexus. Patients with incomplete blocks also received additional doses of fentanyl (50–150 μg). Despite excellent sensory and motor block in six patients, additional doses of midazolam 2–4 mg and/or propofol, either a bolus 20–70 mg or infusion 10–25 μg kg\(^{-1}\) min\(^{-1}\), were administered because of anxiety in two, agitation in one, back pain secondary to prolonged surgery in two, and frequent movement of the torso causing an unstable field under the microscope in one. Mean surgical duration was 117 (SD 58) min; the longest operation was 300 min. Mean time to administer the block was 10 (4.4) min. The onset of anaesthesia was 3.0 (1.3) min. Complete block occurred in 6.7 (3.2) min in 114 (90.5%) patients who did not require general anaesthesia or additional augmentation with local anaesthetic. An upper arm tourniquet was used in 96 patients, none of whom developed tourniquet pain. Mean lidocaine dose was 695 (107) mg. An indwelling catheter was placed in 53 patients, but it was used in only three patients for prolonging the anaesthesia because the initial injection provided a sufficiently long duration of anaesthesia for completion of surgery in the rest of the patients. In all three instances, these repeat injections relieved the surgical pain and discomfort caused by dissipation of the initial dose.

In one patient (0.8%) blood was aspirated prior to injection, necessitating withdrawal of the needle and application of pressure to the area. Ultrasound examination prior to removal of the needle in this patient did not suggest puncture of the axillary artery or vein, nor was haematoma seen around these vessels with ultrasound examination. A successful block was subsequently administered. Paraesthesias occurred in three patients during manipulation of the block needle from the lateral to the posterior cord, probably as a result of stretching of the lateral cord with the shaft of the needle rather than by direct contact of either cord with the needle tip. Patients were followed for 24 h after surgery, either by visiting them in the hospital or by telephoning them at home. No immediate complications related to the block occurred. We did not follow these patients thereafter. However, their surgeons saw them in their offices and did not report any neurological complications. Blood lidocaine concentrations were not monitored, but no patient developed signs or symptoms of local anaesthetic toxicity.

**Discussion**

The present work is the largest prospective series published on ultrasound-guided brachial plexus block. The results of our study suggest that this technique has the potential to improve success rate, time of onset and of performance of the block, and to decrease complications such as vascular puncture. The original study by Raj and colleagues reported a success rate of 95% and an onset time of 20 min for infraclavicular block. The time required to perform the procedure and the complication rate were not addressed. Coracoid block, a variant of the infraclavicular block developed by Whiffler had a success rate of 92.5%, onset time of 10–20 min and axillary artery puncture rate of 50%. With the recently reported modified Raj technique, the success rate was improved to 97% when a twitch response could be obtained at the wrist or fingers. However, the rate was only 44% when a proximal response was obtained. Their overall success rate was 86%. Indeed, in practice it is not uncommon to obtain a proximal response and to experience difficulty in stimulating the hand in a timely manner. This leads to reduced success and/or prolonged time to perform the block. Our results with ultrasound guidance compare favourably with those mentioned above. Nevertheless, a rigorously performed randomized prospective comparative study will be needed to establish the superiority of our technique.

To our knowledge, only two previous studies used ultrasound imaging as a guide for infraclavicular brachial plexus block. Wu and colleagues reported eight successful blocks in nine patients, but three were complicated by subclavian artery puncture. (Based on their landmarks they were probably describing the axillary artery; the subclavian becomes the axillary artery at the lateral border of the first rib.) These authors did not attempt to identify the echogenic cords; instead they deposited the local anaesthetic at the lateral border of the subclavian artery. Furthermore, they used a thin (23-gauge) spinal needle that we find difficult to see sonographically. To reach the
target, they calculated the maximum allowable depth of penetration at the angle at which the needle was introduced. The needle then was advanced based on this calculation rather than by following it with real time imaging. In addition to testing the technique in a substantially greater number of patients, we directed our block needle to each of the cords individually. The entire length of the needle was seen at all times. We believe this simple measure was a major factor in obtaining the higher success rate and substantially lowering the rate of vascular puncture (0.8% vs 33%) in our study. Several investigators have already emphasized the importance of depositing local anaesthetic around each nerve in the brachial plexus as a factor in improving success rate.\textsuperscript{11,12} Using a 17- or 18-gauge Tuohy needle and aligning it with the probe enabled us to follow its image and to direct it to each cord. In addition, the rigidity of a large bore needle provides better control of its tip during manipulations than a thinner needle that bends easily. We believe that use of a Tuohy needle with its blunt tip also helped avoid vascular puncture by pushing away vessels and nerves, although we recognize that vascular puncture with this type of needle may produce greater damage than with a smaller gauge needle. Finally, a large bore Tuohy needle permits easy placement of a catheter for continuous use.

A recent study by Ootaki and colleagues,\textsuperscript{8} reported 100% success rate with the use of ultrasound guidance in infraclavicular block. Of their 60 patients, in whom blocks were performed by the principal author, 57 did not require any additional local anaesthetic or opioid supplementation. Two patients were given additional infiltration of local anaesthetic and one received analgesia with fentanyl. Although not recorded, the time to perform the block was estimated as 5 min. While they claimed an overall success rate of 100%, the ulnar, radial and median nerves were spared in 10%, 6.7% and 3.3% of patients, respectively, 30 min after injection. Thus we believe their actual success rate is comparable to ours. The onset time in their study appears to be 30 min; it was 6.7 (3.2) min in our series. This delay can be attributed to the fact that no attempt was made to observe the nerve trunks or cords. Consequently, the anaesthetic was deposited on all sides of the subclavian artery to surround it like a doughnut with the expectation that it would spread around the nerves. Incidentally, it appears from their diagram and sonographic image that, like Wu and colleagues,\textsuperscript{5} they also called the axillary artery the subclavian. More importantly, at their midclavicular needle entry point the divisions of the brachial plexus are all closely apposed posterosuperiorly to the axillary artery.\textsuperscript{13} Depositing local anaesthetic in a doughnut-like fashion around the artery at this level limits the quantity that diffuses into the nerves, which are located only on one side of the vessel.\textsuperscript{13} With our technique, the needle entry point is more lateral, at the level of the coracoid process, where the cords of the plexus are not close together, but lie on three sides of the axillary artery. Thus, the anaesthetic can easily be deposited around each cord. We strongly believe that the rapid onset and reliability of the block depends on perineural rather than perivascular spread. Another reason for the slow onset in the study of Ootaki and colleagues\textsuperscript{8} may be related to the use of a slightly lower concentration of lidocaine (1.5%) without sodium bicarbonate. Sodium bicarbonate is used routinely in our institution to hasten the onset of block irrespective of the technique used for nerve blocks.

The approximately 9.3 mg kg\textsuperscript{-1} dose of lidocaine (average 700 mg) used in our study (similarly to Wu and colleagues\textsuperscript{5}) may appear large as compared with that used by Ootaki and colleagues\textsuperscript{8} (7.3 mg kg\textsuperscript{-1}). Previous studies using 900 mg and up to 18 mg kg\textsuperscript{-1} have demonstrated the safety of larger doses of lidocaine.\textsuperscript{14,15} Nevertheless, we have recently been able to produce successful infraclavicular blocks with comparable onset time using ultrasound guidance at substantially reduced doses (4.3 mg kg\textsuperscript{-1}) and low volume (13–15 ml) of 2% lidocaine.\textsuperscript{16}

We used a 2.5 MHz transthoracic echocardiography probe which gives a grainy image. This was the only probe available for this study. At present we use a 3.5–7 MHz probe that provides substantially better imaging. Ootaki and colleagues\textsuperscript{8} used a 7 MHz probe, whereas Wu and colleagues\textsuperscript{5} did not specify the frequency of their probe.

An advantage of ultrasound guidance is that the block may be repeated at the same site when it begins to dissipate; this is not feasible with the nerve stimulator technique. Similarly, a successful block can be administered with this technique in patients with amputated distal upper extremities. Ultrasound guidance also provides an excellent educational tool; more than 90% of the blocks in this study were performed by approximately 20 residents at different levels of training, with no prior experience of peripheral nerve blocks. They were all supervised by an attendant who also held the ultrasound probe in place. It is highly probable that our success rate could have reached 100% if all the blocks had been performed by the authors, as in the study of Ootaki and colleagues.\textsuperscript{8} Although we did not specifically focus our study to determine the learning curve for this procedure, we feel that approximately 20 procedures under direct supervision of an expert may enable an operator to be proficient.

In conclusion, ultrasound-guided infraclavicular block appears to be associated with a high success rate, short onset time, easy placement of catheter, low complication rate, and excellent analgesia even when a tourniquet is used. It is well tolerated by patients. The cost of the ultrasound device may be considered a limiting factor. However, it represents a one-time capital expense that, if prorated over a large number of patients, may become cost effective, especially when the time saved for each procedure is taken into account.

Acknowledgements
The authors are indebted to Sanford Miller, M.D. for his invaluable advice and editing of the manuscript. They also express sincere gratitude to
References

7 Yang WT, Chui PT, Metreweli C. Anatomy of the normal brachial plexus revealed by sonography and the role of sonographic guidance in anesthesia of brachial plexus. AJR Am J Roentgenol 1998; 171: 1631-6
16 Sandhu NS, Bahnwal CS, Capan LM. Ultrasound guidance reduces local anesthetic requirements for infraclavicular block. Anesthesiology 2001; 95: A851
Ultrasound-Guided Posterior Approach for the Placement of a Continuous Interscalene Catheter

John G. Antonakakis, MD, Brian D. Sites, MD, and Jeffrey Shiffrin, MD

Background and Objectives: The posterior approach to performing a continuous brachial plexus block at the level of the nerve roots has been described using traditional superficial landmarks. We describe an ultrasound-guided approach for the placement of a continuous interscalene brachial plexus catheter at the level of the nerve roots using a posterior approach. In addition, we provide the clinical characteristics of the first 16 catheters placed at our institution utilizing this approach.

Methods: Sixteen patients having major shoulder surgery underwent ultrasound-guided placement of a posterior interscalene catheter at the level of the nerve roots. After generation of an optimized short axis image of the neural and vascular structures in the midneck, a 17-gauge Tuohy needle was directed into the skin between the levator scapulae and middle scalene muscles. Using the in plane approach, the needle was advanced until the tip was located between C5 and C6 nerve roots. Following a bolus injection of local anesthetic, a catheter was threaded 2 to 4 cm and secured. Visualization of the spread of local anesthetic through the catheter was used to dynamically confirm correct perineural catheter location. The characteristics of these catheters were assessed including dislodgment, postoperative opioid consumption, complications, and patient satisfaction.

Results: All 16 catheters were successfully placed. There were no unintended catheter dislodgments. Patient satisfaction was high and postoperative opioid consumption was minimal.

Conclusions: Results suggest the use of ultrasound for placing a continuous interscalene nerve catheter via the posterior approach is a viable technique that offers an alternative to the more conventional non-image-guided superficial landmark techniques.

Key Words: ultrasound, nerve block, continuous catheter, posterior approach

(Reg Anesth Pain Med 2009;34: 64–68)

The posterior approach to the brachial plexus at the level of the nerve roots was first described by Kappis in 1912 and subsequently reintroduced by Pippa et al. in 1990. This block has never gained widespread popularity, partially due to the discomfort generated by needle insertion through the extensor muscles of the neck. Boczaart et al. introduced a less stimulating posterior approach by having the needle enter between the levator scapulae and trapezius muscles. Using the landmarks described by Pippa et al., van Geffen et al. recently described an ultrasound-guided approach for performing a posterior single injection interscalene brachial plexus block.

The posterior approach has the advantage of secure catheter placement because it courses through multiple muscle layers. This is analogous to the continuous infraclavicular brachial plexus block where the catheter is secured within pectoralis major and minor muscles. A possible reason that the posterior approach to the interscalene block still has not gained widespread popularity is because of the need to rely on non-image-guided bony landmarks that have proximity to the spinal cord and vertebral artery. In the following technical report, we describe a stepwise approach to placing a continuous interscalene catheter, using ultrasound and a posterior approach. We also provide our experience with the first 16 catheters placed at our institution using this approach.

METHODS

Technique

The patient is placed in the lateral decubitus position with the operative side up and the head supported by a pillow. Following standard skin sterilization and draping techniques, a high frequency (10–13 MHz) linear ultrasound transducer is placed in a transducer stabilization device (ultraStand™; Wellan Medical Inc., Lebanon, NH) and covered with a sterile sheath. The ultrasound transducer is positioned on the neck in order to generate a standard short axis view of the brachial plexus (Fig. 1). The roots of the brachial plexus appear as distinct round to oval hypoechoic structures (Fig. 2). Needle entry point will occur approximately 2 to 3 cm from the edge of the transducer (Fig. 1). The subcutaneous tissue is then anesthetized and a 17-gauge Tuohy needle (Arrow International, Reading, PA) is advanced using the in plane needle insertion technique (Fig. 2). The entire length of the needle should remain perpendicular to the direction of the ultrasound beam, thus facilitating clear needle visualization. The needle is advanced until it enters the interscalene groove and is between the C5 and C6 nerve roots of the brachial plexus (Fig. 3). After a negative aspiration is confirmed, a 1 to 3 mL test dose of local anesthetic or D5W is injected slowly to confirm that the Tuohy needle has penetrated the appropriate fascial layers. A total of 10 to 15 mL of the same solution is then injected, with the primary objective to visualize the hypoechoic local anesthetic spreading around the C5 and C6 nerve roots (Fig. 4 and Supplementary Video 1, http://links.lww.com/A641). If intramuscular spread of local anesthetic is suspected, the needle should be repositioned and retested. Following a successful test injection, the catheter is advanced 2 to 4 cm past the tip of the needle. When the catheter exits the needle tip, it should be transiently visualized as it defines its course either proximally or distally within the brachial plexus sheath (Fig. 5). However, the catheter may or may not be visualized in its entirety depending on its orientation to the ultrasound beam. Figure 5 shows the bevel of the needle perpendicular to the ultrasound beam, thereby
capturing the catheter threading under the C5 nerve root. The catheter should thread with ease. If there is resistance to catheter threading, then the catheter should be withdrawn back into the needle shaft. Minor adjustments of the Tuohy needle can be made including turning it clockwise or counterclockwise, or withdrawing or advancing slightly before readvancing the catheter. The Tuohy needle is then removed. To confirm that the catheter tip is correctly positioned in the interscalene groove, further test solution should be injected through the catheter. The spread of local anesthetic should have similar intrasheath characteristics as for the needle injection (Supplementary Video 1, http://links.lww.com/A641). Depending on the location of the catheter tip, the transducer may need to be slightly repositioned proximally or distally in the neck in order to visualize the spread of the injectate. If the spread of local anesthetic is not clearly visualized around the C5 and C6 nerve roots, then the catheter should be pulled back or repositioned as one cannot be certain that the catheter has been correctly placed. Figure 6 demonstrates an image of the catheter within the brachial plexus sheath. The catheter is subsequently secured to the skin with an adhesive sterile transparent dressing.

Case Series

As a supplement to this technical report, we present our experience with the first 16 ultrasound-guided continuous nerve catheters that we have placed at the root level of the brachial plexus using a posterior approach. Data was acquired through the Dartmouth-Hitchcock Medical Center’s Regional Anesthesia Database and chart reviews. Both the maintenance and querying of the regional anesthesia database were approved by the Dartmouth College Committee for the Protection of Human

FIGURE 1. Patient positioning and transducer location in order to develop the short axis view of the brachial plexus at the cervical root level. The ultrasound transducer is secured in a mechanical stabilizing device. The needle enters using the in plane insertion technique.

FIGURE 2. A 17-gauge Tuohy needle as it courses through the middle scalene muscle and approaches the sheath of the brachial plexus using the in plane technique. The roots of C5, C6, and C7 are seen as hypoechoic (dark) circles. The triangle indicates the bevel of the needle facing towards the skin. The large arrows outline the needle shaft. AS, anterior scalene muscle; MS, middle scalene muscle; PS, posterior scalene muscle.

FIGURE 3. The bevel of the needle (arrowhead) is clearly visualized as it enters the sheath of the brachial plexus and lies now between the C5 and C6 nerve roots. The roots of C5, C6, and C7 are seen as hypoechoic (dark) circles. The triangle indicates the tip of the needle facing towards the skin. The large arrows outline the needle shaft. AS, anterior scalene muscle; MS, middle scalene muscle; PS, posterior scalene muscle.

FIGURE 4. Local anesthetic is visualized as it is spreading around the C5 nerve root. Notice that visualization of the C6 and C7 nerve roots has been lost due to acoustic shadowing (drop out) created by the needle. The local anesthetic is outlined by the white line. The needle tip is indicated by the large arrow.
8 mL/h of 0.2% ropivacaine provided effective analgesia without started at a lower rate (7 mL/h). In all 3 of these patients, 7 to of the infusion for 4 hours; the infusion was subsequently re-scribed. To our knowledge, our report is the first description of approach using superficial surface landmarks has been de-

*b*

64 ± 7 years. The mean height was 163 ± 9 cm. The mean body mass index was 32 ± 5.

Table 1 presents the average pain and satisfaction as-

**Table 1.** Pain and Satisfaction as- sessment of All 16 Patients

<table>
<thead>
<tr>
<th>Item</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain score</td>
<td>3.2 ± 1.7</td>
</tr>
<tr>
<td>Satisfaction score</td>
<td>7.5 ± 1.2</td>
</tr>
</tbody>
</table>

Subjects. There were 11 females and 5 males. The mean age was 64 ± 7 years. The mean height was 163 ± 9 cm. The mean body mass index was 32 ± 5.

Table 1 presents the average pain and satisfaction as-

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<table>
<thead>
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</tr>
</tbody>
</table>

**RESULTS**

The performance of a nonultrasound-guided continuous brachial plexus nerve block at the root level using a posterior approach has previously been described by Boezaart and colleagues. Further, an ultrasound-guided single injection posterior approach using superficial surface landmarks has been de-

**DISCUSSION**

Boezaart’s technique involves a 17- or 18-gauge Tuohy needle inserted in the “V” groove formed by the levator scapulae and trapezius muscles. The needle is aimed in a caudad and slightly medial direction toward the suprasternal notch. The initial goal is to make contact with the pars intervertebralis of the sixth cervical vertebrae. A nerve stimulator is then attached and an air-filled syringe connected to the needle. The needle is ad-

**FIGURE 5.** The triangle indicates the catheter exiting the needle in a direction towards the C5 nerve root. The large arrow indicates the needle tip.

**FIGURE 6.** After the needle is removed the catheter is clearly visualized (arrows) as it is embedded in the muscles of the neck. Notice how the catheter lies in the brachial plexus sheath. One can appreciate the amount of muscle in which the catheter is embedded. The C6 and C7 nerve roots are once again visualized as the acoustic shadowing from the needle no longer exists.
Chronic opioid users (n = 7) 0.79
Nonopioid users (n = 9) 0.08

NOTE. All values are mean ± standard error.

Abbreviation: VAS, verbal analog scale.

‡This value was calculated by dividing the total mg of consumed morphine equivalent by the total number of hours the catheter was in place.
†Patients were asked prior to catheter removal: “How was your overall experience with the nerve block” on a satisfaction scale of 1 = poor, 2 = satisfactory, and 3 = outstanding.
‡‡VAS score of 0 to 10, from 0 = no pain, to 10 = worst pain ever experienced, obtained via floor nursing charts 3 times daily.

Contrary to the paravertebral technique described by Boezaart et al., we believe that the approach we describe is further away from the neuraxial structures including the pars intervertebralis, vertebral artery, and neural foramina. Although we insert the needle in the posterior aspect of the neck, the final destination is the interscalene groove where the nerve roots are a significant distance from deeper and more central structures (Fig. 7).

We believe that this block is being performed at the root level of the brachial plexus, but this is subject to debate. At what point the roots become the trunks of the brachial plexus is difficult to distinguish by ultrasound alone. What we call the nerve roots of C5, C6, and C7 may indeed be upper, middle, and lower trunks. The more caudal the transducer is in the neck, the more likely the trunks of the brachial plexus are being imaged. The further cephalad the transducer is from the subclavian artery, the more likely the roots of the brachial plexus are being imaged. Our clinical experience suggests that we are blocking at a root level because we consistently block the superficial cervical plexus, C5, and C6 dermatomes; we consistently spare the C8 and T1 dermatomes.

We believe that a major advantage of the posterior approach to the brachial plexus is secure catheter placement. Due to the superficial nature of the brachial plexus, continuous interscalene catheters placed via traditional approaches are only sited a few centimeters subcutaneously and therefore have a high incidence of dislodging. This lack of catheter stability may contribute to a failure rate of up to 25% with traditional approaches,8 which has been consistent with our experience. With the technique we describe, the distance between the posterior aspect of the levator scapulae muscle and the fifth cervical root of the brachial plexus is approximately 4 to 6 cm. If the catheter is advanced 2 to 4 cm out of the needle tip, then a total of 6 to 10 cm of catheter is threaded into the neck. This length of catheter traveling through the levator scapulae, posterior, and middle scalene muscles may provide the stability.

Conclusions about the safety of our ultrasound-guided approach compared with traditional superficial landmark techniques cannot be drawn from this technical report. Intracord injections have been reported using the posterior approach with traditional landmark techniques.9 It is our hope that, because the needle is farther away from the neuraxis (contact with the pars intervertebralis of C6 is not necessary during the ultrasound technique), there may be a reduction in the likelihood of an epidural or intrathecal spread of local anesthetic.10,11 Finally, the need to contact a bony landmark with the nonultrasound-guided approach also represents an opportunity to generate patient dis-

**TABLE 1. Pain and Satisfaction Assessment During Catheter Infusion**

<table>
<thead>
<tr>
<th></th>
<th>Morphine Equivalent Consumption (mg/h)*</th>
<th>Satisfaction Score†</th>
<th>VAS Score During Catheter Infusion‡</th>
<th>Preoperative Bolus (mL) Through Tuohy Needle and Catheter (0.5% Bupivacaine)</th>
<th>Total Postoperative Bolus (mL) Through Catheter (0.25% Bupivacaine or 0.02% Ropivacaine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic opioid users (n = 7)</td>
<td>0.79 ± 0.13</td>
<td>2.9 ± 0.1</td>
<td>1.9 ± 0.2</td>
<td>18.0 ± 0.4</td>
<td>8.3 ± 3.1</td>
</tr>
<tr>
<td>Nonopioid users (n = 9)</td>
<td>0.08 ± 0.02</td>
<td>2.8 ± 0.1</td>
<td>1.5 ± 0.2</td>
<td>18.5 ± 0.4</td>
<td>6.6 ± 1.8</td>
</tr>
</tbody>
</table>

FIGURE 7. Demonstration of the C5 and C6 cervical nerve roots in relation to the deeper central neuraxial structures including the pars intervertebralis and vertebral artery. AS, anterior scalene muscle; MS, middle scalene muscle; SCM, sternocleidomastoid muscle.
physically holds the transducer and thereby frees up 1 of the operator’s hands. In our 1 case where the stabilizing device was not used, a second operator was needed. The transducer stabilizing device has its own inherent set of limitations. The stabilizing device has a rigid arm to prevent unintentional movement of the transducer, thereby limiting some of the fine and subtle real time adjustments often made by the operator as the needle approaches the target. The transducer stabilizing device also represents more steps in the procedure including physical positioning, cleaning, and storage.

In summary, based on the clinical characteristics of the 16 catheters placed, we conclude that the use of ultrasound for placing a continuous interscalene nerve catheter via the posterior approach is a viable technique that offers an alternative to the more conventional nonimage-guided superficial landmark techniques. Whether or not our technique offers any safety or effectiveness advantage over traditional techniques will require further investigation.

APPENDIX: SUPPLEMENTARY MATERIAL

A supplementary video can be found at http://links.lww.com/A641. This is a video of the technique of placing a continuous interscalene nerve catheter using ultrasound and the posterior approach. Key clinical points of the video are: (1) the needle can be seen entering into the brachial plexus sheath; (2) the bolus of local anesthetic through the needle confirms intrasheath location; (3) the catheter can be seen entering into the sheath next to the C5 nerve root; and (4) the bolus of local anesthetic through the catheter can be seen spreading around the C5 and C6 nerve roots, confirming correct placement.

REFERENCES


A Trainee-Based Randomized Comparison of Stimulating Interscalene Perineural Catheters With a New Technique Using Ultrasound Guidance Alone

Edward R. Mariano, MD, MAS, Vanessa J. Loland, MD, NavParkash S. Sandhu, MS, MD, Michael L. Bishop, MD, Matthew J. Meunier, MD, Robert Afra, MD, Eliza J. Ferguson, BS, Brian M. Ilfeld, MD, MS

Objective. Compared to the well-established stimulating catheter technique, the use of ultrasound guidance alone for interscalene perineural catheter insertion is a recent development and has not yet been examined in a randomized fashion. We hypothesized that an ultrasound-guided technique would require less time and produce equivalent results compared to electrical stimulation (ES) when trainees attempt interscalene perineural catheter placement.

Methods. Preoperatively, patients receiving an interscalene perineural catheter for shoulder surgery were randomly assigned to an insertion protocol using either ultrasound guidance with a nonstimulating catheter or ES with a stimulating catheter. The primary outcome was the procedural duration (in minutes), starting when the ultrasound probe (ultrasound group) or catheter insertion needle (ES group) first touched the patient and ending when the catheter insertion needle was removed after catheter insertion.

Results. All ultrasound-guided catheters (n = 20) were placed successfully and resulted in surgical anesthesia versus 85% of ES-guided catheters (n = 20; P = .231). Perineural catheters placed by ultrasound (n = 20) took a median (10th–90th percentiles) of 8.0 (5.0–15.5) minutes compared to 14.0 (5.0–30.0) minutes for ES (n = 20; P = .022). All catheters placed according to the protocol in both treatment groups resulted in a successful nerve block; however, 1 patient in the ES group had local anesthetic spread to the epidural space. There was 1 vascular puncture using ultrasound guidance compared to 5 in the ES-guided catheter group (P = .182).

Conclusions. Trainees using a new ultrasound-guided technique can place interscalene perineural catheters in less time compared to a well-documented technique using ES with a stimulating catheter and can produce equivalent results.

Key Words: continuous interscalene block; electrical stimulation; perineural infusion; ultrasound-guided regional anesthesia.

Interscalene perineural catheters with continuous postoperative local anesthetic infusion have shown efficacy in reducing pain, decreasing supplemental opioid requirements and side effects, improving sleep quality and range of motion, and shortening the time until discharge readiness after moderately to severely painful shoulder surgery. Techniques using electrical stimulation (ES)
Interscalene Catheters: Ultrasound Versus Stimulation

for inserting perineural catheters have been validated in clinical trials,\textsuperscript{1–4} and there is evidence suggesting that the use of stimulating catheters to confirm the catheter tip position may have benefits over nonstimulating catheters, such as a faster surgical block onset,\textsuperscript{5} improved analgesia,\textsuperscript{6} decreased supplemental opioid requirements,\textsuperscript{6–8} and a reduced consumption of local anesthetics during patient-controlled perineural analgesia.\textsuperscript{8}

Despite the high success rates reported with stimulating catheter insertion,\textsuperscript{3,5,9} procedural times can be prolonged, occasionally in excess of 30 minutes.\textsuperscript{9,10} With growing pressure to improve operating room efficiency, the time requirement for stimulating perineural catheter placement may limit its application by anesthesiologists, limit the teaching of these techniques to trainees, and discourage surgeons from recommending continuous nerve blocks to their patients.\textsuperscript{11}

Techniques using ultrasound guidance alone for interscalene perineural catheter insertion are relatively new.\textsuperscript{12–15} Although studies comparing ES to ultrasound for single-injection nerve blocks show potential advantages of the ultrasound technique (eg, less time for block placement, increased success rate, and faster onset),\textsuperscript{16–21} to our knowledge, no randomized comparison has been performed for interscalene perineural catheter insertion.\textsuperscript{22}

We therefore tested the hypothesis that nonstimulating interscalene perineural catheters placed by trainees using ultrasound guidance alone require less time for placement and produce equivalent results compared to stimulating catheters placed using ES.

Materials and Methods

The Institutional Review Board of the University of California San Diego School of Medicine approved the protocol and oversaw the study through data analysis. Patients offered enrollment included adults (≥18 years) scheduled for at least moderately painful orthopedic surgery of the shoulder who desired and were approved for a continuous interscalene nerve block for postoperative analgesia. Exclusion criteria included known neuropathy of any etiology in the surgical extremity, pregnancy, incarceration, and the inability to communicate with the investigators and hospital staff.

Protocol

After written informed consent, patients were randomized to 1 of 2 treatment groups, ES or ultrasound guidance, using a computer-generated randomization table based in a secure, password-protected, encrypted central server (www.PAINfRE.com; General Clinical Research Center, Gainesville, FL). All catheter insertion procedures were performed by an attending physician with extensive experience in both placement techniques or a regional anesthesia fellow/resident supervised one-on-one by the attending physician.

All patients had a peripheral intravenous (IV) catheter inserted and were placed in either the supine (ES group) or lateral (ultrasound group, surgical side up) position. Standard noninvasive monitors were applied, and oxygen was administered via a cannula face mask. Intravenous midazolam and fentanyl were titrated for patient comfort while ensuring that patients remained responsive to verbal cues. The area that would be subsequently covered by the catheter dressing was shaved if necessary. Landmarks were drawn for all patients; the area was cleansed with chlorhexidine gluconate and isopropyl alcohol (ChloraPrep One-Step; Medi-Flex Hospital Products, Inc, Overland Park, KS); and a clear sterile fenestrated drape was applied. The nerve stimulator (ES group) or ultrasound (ultrasound group) was readied for use. All catheters were inserted by an anesthesiology resident in the final year of residency or a regional anesthesia fellow with direct guidance and oversight provided by an attending anesthesiologist with experience in both ES- and ultrasound-guided techniques.

Electrical Stimulation Technique

Patients randomized to the ES technique had the brachial plexus located with a nerve stimulator attached to an insulated needle using a slightly modified technique of a method described previously.\textsuperscript{9} After sterile preparation and draping, a local anesthetic skin wheal was raised over the groove between the anterior and middle scalene muscles at the cephalad-caudad level of the cricoid cartilage. With the bevel directed anterolaterally, an 8.89-cm 17-gauge insulated needle (StimuCath; Arrow International, Reading, PA) was inserted with the long axis of the needle 45°
to the parasagittal, transverse, and coronal planes. This was connected to a nerve stimulator (Stimuplex-DIG; B. Braun Medical, Bethlehem, PA) initially set at 1.2 mA and 2 Hz. Once the needle tip was through the skin and immediate underlying fascia, the stylet was removed to allow for identification of a penetrated vessel. The needle was redirected as needed until deltoid or biceps motion was elicited with a current between 0.30 and 0.70 mA.

The 19-gauge stimulating catheter was then placed through the length of the needle, and the nerve stimulator was transferred from the needle to the catheter, which has a conducting wire through its length delivering current to its tip. The stimulating current was allowed to be increased up to 0.80 mA while advancing the catheter 4 cm beyond the needle tip. If biceps or deltoid motion decreased as the stimulating catheter was advanced, the catheter was withdrawn into the needle, the needle redirected or rotated, and the catheter readvanced. If there was resistance during catheter withdrawal, the needle was withdrawn until the catheter resistance resolved.

Once a catheter had been successfully advanced 5 cm past the needle tip, the needle itself was withdrawn over the catheter, the catheter stylet removed, and the catheter tunneled subcutaneously laterally toward the sternal notch using the included needle stylet and 17-gauge insulated needle. The injection port was attached to the end of the catheter, the nerve stimulator attached to the injection port, and the minimum current resulting in muscle contraction noted. The catheter was secured with sterile liquid adhesive, an occlusive dressing, and an anchoring device (StatLock; Venetec International, San Diego, CA) to affix the catheter hub to the patient. After negative aspiration, 40 mL of an anesthetic solution (mepivacaine, 1.5%, with epinephrine, 2.5–5.0 µg/mL) was injected in divided doses circumferentially around the target nerve via the needle.

A 19-gauge flexible epidural-type nonstimulating catheter (FlexTip; Arrow International) was then placed through the length of the needle and advanced 5 cm beyond the needle tip. Once a catheter had been inserted, the needle itself was withdrawn over the catheter. Because the in-

**Ultrasound Technique**

Patients randomized to the ultrasound technique had their target nerve group located using ultrasound guidance alone.13 Using a 6- to 13-MHz linear ultrasound probe (HFL38 MicroMaxx; SonoSite, Inc, Bothell, WA), the brachial plexus was identified between the left anterior and middle scalene muscles at the cephalad-caudal level of the cricothyroid membrane (Figure 1). At the junction of the levator scapulae and trapezius muscles, a local anesthetic skin wheal was injected to anesthetize skin and the track into the middle scalene muscle under ultrasound guidance. With the bevel directed caudad and lateral, an uninsulated 8.9-cm 17-gauge Tuohy-tip needle (FlexTip; Arrow International) was inserted through the local anesthetic skin wheal. Under continuous in-plane ultrasound guidance23 (probe held in the operator’s nondominant hand), the needle (in the operator’s dominant hand) was directed anteriorly toward the brachial plexus, passing lateral to the posterior scalene and through the middle scalene muscles to the brachial plexus. A local anesthetic solution (40 mL; mepivacaine, 1.5%, with epinephrine, 2.5–5.0 µg/mL) was injected in divided doses circumferentially around the target nerve via the needle.

A 19-gauge flexible epidural-type nonstimulating catheter (FlexTip; Arrow International) was then placed through the length of the needle and advanced 5 cm beyond the needle tip. Once a catheter had been inserted, the needle itself was withdrawn over the catheter. Because the in-

**Figure 1.** Transverse (short-axis) image of the brachial plexus (BP). At the cephalad-caudal level of the cricothyroid cartilage, the hypoechoic trunks of the brachial plexus can be visualized posterior and deep to the sternocleidomastoid muscle (SCM) and anterior to the transverse process of the cervical vertebra (CTP) between the anterior scalene muscle (ASM) and middle scalene muscle (MSM).
plane ultrasound-guided needle placement technique effectively “tunneled” the catheter through the middle scalene muscle, the catheter was not tunneled further but was otherwise dressed and secured in a manner similar to that for the ES technique.

**Outcome Measurements**

The time for catheter placement, the primary outcome, started when the ultrasound probe (ultrasound group) or catheter placement needle (ES group) first touched the patient and ended when the catheter placement needle was removed after catheter placement. A research coordinator with no other concurrent responsibilities measured and recorded all times. If a catheter could not be placed according to the protocol within 30 minutes, the placement was considered a failure and the primary outcome recorded as 30 minutes. In such cases, the attending physician had the option of attempting catheter placement using the alternate method. Patients who did not have a catheter placed according to their randomized group protocol were not included in further data collection, although they were followed on a daily basis until catheter removal and nerve block resolution according to our routine clinical practice.

Patients were asked to rate their discomfort with catheter placement on a numeric rating scale of 0 to 10 (0, no discomfort; 10, worst discomfort imaginable). Fifteen minutes after injection, block onset was evaluated and scored in the affirmative if patients were unable to abduct the shoulder and had decreased sensory perception to a light touch over the deltoid muscle compared to the contralateral limb. Patients with a successful surgical block were retained in the study; those with a failed surgical block had their catheters discontinued and were removed from the study.

In the recovery room, or before if the duration of the initial surgical block required extension, a 20-mL secondary anesthetic bolus of ropivacaine, 0.2%, with epinephrine, 2.5 to 5.0 µg/mL, was administered via the catheter after negative aspiration. The time of this bolus was recorded.

**Assessing Catheter Placement Success**

Using the ultrasound protocol, it is theoretically possible to inject mepivacaine via the needle to produce a successful surgical block yet have an inaccurately placed catheter. Therefore, to assess the accurate positioning of perineural catheters placed with ultrasound, the ropivacaine bolus described above was delivered via the catheter for all patients. Patients were contacted the following day and asked to report the time that the dense surgical block resolved (as well as fluid leakage occurrence and average and worst pain since surgery on the 0–10 numeric ranking scale). Because the durations of interscalene blocks are greater than 5 hours for ropivacaine and less than 5 hours for mepivacaine,1,24 the catheter was considered accurately placed if the time from the initial surgical block until the time of block resolution was greater than 5 hours.

**Statistical Analysis**

The sample size estimate was centered around the primary hypothesis that inserting an interscalene perineural catheter with ultrasound guidance alone would be associated with a faster time to placement compared to ES guidance alone. We considered a 5-minute difference in placement time to be clinically relevant. On the basis of an SD for each group of 5 minutes and assuming a 2-sided type I error protection of 0.05 and a power of 0.80, approximately 17 patients in each group were required (StatMate 2.0; GraphPad Software, San Diego, CA). To allow for variability in the SD of each group and patient dropouts, we enrolled a total of 40 patients.

Normality of distribution was determined using the Kolmogorov-Smirnov test (NCSS Statistical Software, Kaysville, UT). For normally distributed data, comparisons of independent samples were performed using the Student t test. For continuous data in distributions other than normal, the Mann-Whitney U test was used.
The Fisher exact test was used for comparisons of categorical variables. Two-sided \( P < .05 \) was considered statistically significant for the primary outcome. Statistically significant findings in secondary outcomes should be interpreted as suggestive, requiring confirmation in a prospective trial before being considered definitive.\(^2\)

**Results**

Forty patients were enrolled, and all were randomly assigned to one of the two treatment groups. Demographic and morphometric characteristics were similar between groups (Table 1). Of patients randomized to ultrasound (\( n = 20 \)), all had a successful catheter placement, and all had a successful nerve block as defined by the study protocol. However, 1 patient in the ultrasound group required greater than 30 minutes for catheter placement and was therefore considered to have had a placement failure according to the protocol (Figure 2). Of the patients randomized to ES (\( n = 20 \)), 3 (15\%) had failed catheter placement according to the ES protocol (\( P = .231 \) compared with the ultrasound group; 2 catheters were subsequently successfully placed using the ultrasound protocol); 1 (5\%) had a catheter placed according to the protocol, resulting in appropriate brachial plexus anesthesia, but went on to have signs of epidural local anesthetic spread (Figure 2). One of the 3 ES catheter placement failures resulted from an inability to elicit a motor response via the stimulating needle at a current of less than 0.7 mA, as specified in the protocol, and 2 failures resulted from an inability to maintain the proper motor response via the stimulating catheter with a current of less than 0.8 mA as the catheter was advanced past the needle tip, as specified in the protocol.

**Primary Outcome**

Nonstimulating perineural catheters placed by ultrasound (\( n = 20 \)) took a median (10th–90th percentiles) of 8.0 (5.0–15.5) minutes compared to 14.0 (5.0–30.0) minutes for stimulating catheters placed with ES (\( n = 20; P = .022 \); Figure 2).

**Secondary Outcomes**

Patients in the ultrasound group scored their pain during catheter placement as a median of 2.0 (0.0–6.0) compared to 4.0 (0.0–5.2) for the ES group (\( P = .303 \)). There was 1 vascular puncture using ultrasound guidance versus 5 in the ES group (\( P = .182 \)). There were no statistically significant differences in other secondary outcomes (Table 2).

**Discussion**

For the placement of interscalene perineural catheters by trainees, a technique using ultrasound guidance alone with a nonstimulating catheter shows a statistically significant time advantage compared to a stimulating catheter technique without compromising placement success or analgesic benefits. To our knowledge, a randomized investigation documenting and quantifying the benefits of a pure ultrasound-guided technique for continuous interscalene nerve blocks has not been reported previously.

**Catheter Placement Time**

The median time savings of 6 minutes per procedure gained by ultrasound over ES may be clinically important in practice environments with a high surgical volume and rapid turnover between cases. Even more compelling is the fact that 9 stimulating catheters required more than 15 minutes to place (including 3 failures), where-

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**Table 1. Population Data and Procedural Information**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Ultrasound (( n = 20 ))</th>
<th>ES (( n = 20 ))</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>51 (44–60)</td>
<td>50 (41–59)</td>
<td>.900</td>
</tr>
<tr>
<td>Sex, female/male</td>
<td>12/8</td>
<td>6/14</td>
<td>.111</td>
</tr>
<tr>
<td>Height, cm</td>
<td>174 (165–179)</td>
<td>174 (167–180)</td>
<td>.605</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>84 (69–99)</td>
<td>80 (74–97)</td>
<td>.685</td>
</tr>
<tr>
<td>Minimum current via needle, mA</td>
<td>NA</td>
<td>0.5 (0.4–0.6)</td>
<td>NA</td>
</tr>
<tr>
<td>Minimum current via catheter, mA</td>
<td>NA</td>
<td>0.6 (0.4–0.6)</td>
<td>NA</td>
</tr>
</tbody>
</table>

Values are median (25th–75th percentiles) or number of patients, as indicated. NA indicates not applicable.
as all but 2 ultrasound-guided nonstimulating catheters were placed in 15 minutes or less. We believe that the time advantage reported by this study may actually be an underestimation for 2 reasons: (1) our protocol for measuring the placement time did not include the time necessary for subcutaneous tunneling of the catheter or the injection of the local anesthetic (ES group only) via the catheter after placement; and (2) given that the local anesthetic bolus in the ultrasound-guided technique is administered via the needle before catheter placement, anesthetic block onset was most likely more rapid, further decreasing the interval from the start of block performance to the anesthesia-ready time. The latter point is based on our clinical observations and requires further investigation.

Equipment setup was not included in our procedural time measurement because of our practice environment. In our regional anesthesia induction area (“block room”), ultrasound equipment remains on throughout the day, and nerve stimulators are readily available. The difference in equipment preparation times between ultrasound and ES techniques in this setting is negligible and unlikely to affect the results of this study given its measurement precision. However, we acknowledge that the setup time for either technique will differ in other practice environments and may greatly influence the total procedure time. Practitioners must consider the availability of equipment and logistics of their own practices when applying the results of this study.

Failed Catheter Placements
Deserving comment is the failure to place 3 of the 20 stimulating catheters (15%) by ES. According to the study protocol, if the electrical current via the needle could not be reduced to less than 0.7 mA while maintaining a motor response within 15 minutes, catheter placement was deemed a “failure.” Thus, the decreased ES success rate reported in our study may have been a result of overly restrictive protocol criteria. However, there is evidence that strict catheter placement criteria provide high ultimate catheter placement and surgical block success rates.3,5 The absolute time limitation of 30 minutes for catheter placement in this study may explain the difference in the success rate compared to previous investigations that used a nearly identical catheter placement protocol without similar time limits.3,26 Another possible explanation is that nearly all catheters in this study were placed by trainees (38 of 40 [95%]), whereas previous investigations relied exclusively on experienced attending physicians. Alternatively, differences in patient populations affect study samples and may have influenced the success rate.

Combined Ultrasound With ES
Although we elected to compare ultrasound guidance alone to ES alone for interscalene catheter placement for the purpose of this study,
we by no means suggest that these techniques are mutually exclusive. Although case reports have described interscalene catheter placement techniques using ultrasound alone,\textsuperscript{12,13} to our knowledge, no previous study has directly compared the ultrasound-guided technique to the validated stimulating catheter technique; therefore, the potential advantages and disadvantages of either technique, including the procedural time, have remained unknown. It is possible that using a combination of both approaches may offer additional benefits over either technique alone.\textsuperscript{27,28} However, the need for both modalities remains controversial and deserves further investigation.\textsuperscript{14,29,30}

**Study Limitations**

The lack of masking is one limitation of this investigation but was accepted because it was deemed impossible to mask investigators to the treatment group. In addition, the two methods for perineural catheter placement compared in this study were somewhat different in equipment and technique (eg, local anesthetic injected via the needle in the ultrasound group and via the catheter in the ES group). We use the StimuCath for ES-guided perineural catheter placements because of its demonstrated efficacy when used as designed and approved by the US Food and Drug Administration.\textsuperscript{31,32} In clinical practice, using the stylited and insulated StimuCath for an ultrasound-guided in-plane technique frequently results in a misplaced catheter tip that bypasses the nerve because of the perpendicular orientation of the in-plane needle and short-axis view of the nerve. Therefore, for this ultrasound technique, a more flexible catheter is preferred to greatly reduce the risk of catheter tip misplacement (FlexTip).\textsuperscript{33,34} The results of this study pertain specifically to the techniques and equipment used in this investigation; the optimal perineural catheter technique and equipment are currently unknown, and other approaches and catheter designs would most likely have altered our findings.\textsuperscript{1,2,4} Last, the results of this study should not be inferred for other perineural catheter insertion sites because perineural anatomy directly affects catheter insertion and infusion characteristics.\textsuperscript{35,36}

In summary, this randomized controlled study suggests that nonstimulating interscalene perineural catheters placed by trainees using ultrasound guidance alone take less time for insertion than those placed using a more traditional ES technique with a stimulating catheter.

**References**

Interscalene Catheters: Ultrasound Versus Stimulation


OVERVIEW OF LOWER EXTREMITY ANATOMY AND NERVE BLOCKS
Sarah Jane Madison, M.D.

Femoral Nerve Block: Indications and Considerations
• Procedures on anterior thigh and knee
• Continuous infusion may decrease time to discharge readiness following TKA\textsuperscript{1,2}
• May reduce opioid consumption, improve mobility, and shorten hospital length of stay after TKA\textsuperscript{3}
• Obturator nerve is not reliably blocked using an anterior approach\textsuperscript{4,5}

Lumbar Plexus Functional Anatomy
• Anterior rami of T12-L4
• Branches emerge from psoas muscle anteriorly, laterally, and medially
  o Ilioinguinal: T12-L1
  o Iliohypogastric: L1
  o Genitofemoral: L1-L2
  o Lateral Femoral Cutaneous: L2-L3
  o Femoral: L2-L4
  o Obturator: L2-L4
• Femoral, LFC, and obturator are targeted in lower extremity blocks

Femoral Nerve Anatomy
• Anterior Division
  o Anterior rami of L2-L4
  o Motor: sartorius, pectineus (medial thigh)
  o Sensory: anterior medial skin of thigh
• Posterior Division
  o Anterior rami of L2-L4
  o Motor: quadriceps (knee extension, patellar ascension)
  o Sensory: anterior thigh, \textit{hip}, and \textit{knee}; medial aspect of leg (saphenous)

Obturator Nerve
• Anterior Division
  o Anterior rami of L2-L4
  o Motor: gracilis, adductor brevis/longus, pectineus (thigh adductors)
  o Sensory: variable; posterior medial thigh, medial knee, \textit{hip}
• Posterior Division
  o Anterior rami of L2-L4
  o Motor: obturator externus, adductor magnus (adduction, lateral rotation)
  o Sensory: articular branches to \textit{knee}

Lateral Femoral Cutaneous Nerve
• Anterior rami of L2-L3
• Motor: none
• Sensory: anterior lateral and posterior aspects of thigh terminating in prepatellar plexus

**Femoral Nerve Block Technique**

• Position patient supine, with leg to be blocked out straight
• Clear away obstructions: retract pannus with foam tape, remove or retract undergarments
• Surface landmarks: Inguinal crease or ligament (ASIS → pubic tubercle)
  - Femoral nerve is widest and most superficial at the crease
• Femoral pulse: artery is *medial* to nerve
• Stimulator Technique
  - After cleansing and anesthetizing skin, insert block needle just lateral to femoral artery at a 45° angle
  - Stimulation of the femoral nerve (patellar elevation) should be elicited immediately with proper placement
  - Sartorius contraction indicates insertion too lateral (direct stimulation) or too medial (nerve to sartorius)
  - Vascular puncture indicates insertion too medial
  - If patellar elevation elicited between 0.2 and 0.4 mA, accept and inject
• “Fascia Iliaca” Technique
  - Blind technique
  - Identify the junction of the lateral third and medial two-thirds of the inguinal ligament
  - Insert block needle 1-2 cm inferior to inguinal ligament at 75°
  - Feel for two “pops” indicating passage through the fascia lata and fascia iliaca
  - Change needle angle to 30°, advance 1 cm, and inject
• Ultrasound Technique
  - High-frequency linear probe
  - Image femoral nerve and vessels in cross-section
  - Nerve lies lateral to artery just below fascia iliaca
  - Choose insertion site based on observed depth of nerve
  - Insert block needle just lateral to lateral edge of probe (in-plane technique)
  - Dissect nerve away from fascia iliaca using local anesthetic
  - Place catheter deep to femoral nerve
**Femoral Nerve Block: Complications**

- Infection
  - 28% of perineural catheters colonized
  - 1/1416 infected
  - Diabetics may be at higher risk for infection
- Hematoma (compressible)
- Nerve Injury
- Local anesthetic toxicity

**Saphenous Nerve Block: Indications and Considerations**

- Generally used in conjunction with Sciatic block for procedures below the knee
- Covers medial aspect of leg, may extend to medial aspect of foot

**Saphenous Nerve Block Technique**

- Paravenous approach
  - Saphenous nerve lies posteromedial to saphenous vein at the level of the tibial tuberosity
  - Local anesthetic infiltration can be ultrasound-guided or landmark-based
    - Saphenous nerve is generally not visible by ultrasound guidance
    - Extensive branching at this level may lead to an incomplete block
- Transsartorial approach
  - Linear probe placed on the medial thigh, perpendicular to the long axis of the leg
  - Start scanning 7 cm proximal to popliteal crease
  - Identify descending genicular artery
  - Inject 5-10 mL of local
• Saphenous block in the adductor canal
  o Place linear transducer on medial thigh
  o Trace the femoral artery as it courses through the adductor canal
  o Identify the saphenous nerve in the fascial plane between sartorius, vastus medialis, and adductor longus
  o 77% effective in one case series

• Comparison of Techniques
  o 10 healthy volunteers
  o Perifemoral, transartorial, medial femoral condyle approach, below-the-knee field block (paravenous), and medial malleolus field block compared
  o Best approach for sensory anesthesia to the medial leg: transartorial, perifemoral, and below-the-knee field block
  o Best approach for sensory anesthesia to the medial foot: transartorial

Sciatic Nerve Block: Indications and Considerations
• Foot and ankle surgery (with saphenous)
• Below-knee amputations (with femoral)
• Supplement to femoral block for TKA
• Proximal approaches block posterior femoral cutaneous nerve

Sciatic Nerve Anatomy
• Tibial
  - Motor: plantar flexion and inversion
  - Sensory: heel and sole of foot

• Common Peroneal
  - Motor: dorsiflexion and eversion
  - Sensory: lateral leg and dorsum of foot

**Sciatic Nerve Block: Classic Approach**

- Sims position: lateral with affected side up, crossing dependent leg
- Greater trochanter
- Posterior superior iliac spine (PSIS)
- Sacral Hiatus
- 4” needle inserted perpendicular to skin 5 cm below midpoint of line from GT to PSIS
- Elicit motor response of the foot/ankle (tibial response preferred)\(^\text{10}\)
- If bone is contacted, redirect medially or laterally along the line between GT and sacral hiatus
**Sciatic Nerve Block: Popliteal Approach**

- **Position:** prone with knee slightly flexed
- **Surface Anatomy**
  - Popliteal crease
  - Biceps femoris laterally
  - Semimembranosus medially
  - Intertendinous junction
- **Stimulator Technique: Posterior Approach**
  - Insertion site: 8-10 cm cephalad to midpoint of popliteal crease or at intertendinous junction
  - 4 inch needle angled 45° cephalad
- **Stimulator Technique: Lateral Approach**
  - When pt unable to assume prone position
  - Identify groove between biceps femoris and vastus lateralis muscles
  - 4” needle perpendicular to skin
  - Contact femur then redirect 20-30° posterior
- **Ultrasound Technique**
  - Image sciatic nerve anterior and medial to biceps femoris
  - Insert needle laterally and advance in-plane through biceps femoris
  - Inject local anesthetic around nerve
  - Place flexible catheter anterior to nerve

**Sciatic Nerve Block: Complications**

- Infection
- Hematoma (compressible)
- Nerve Injury
- Local anesthetic toxicity

**Ankle Block: Indications and Considerations**

- Indicated for procedures on the foot
- Five nerves of the foot (posterior tibial, sural, deep peroneal, superficial peroneal, and saphenous)
- Motor function is spared so patients may ambulate with assistance
Ankle Block Technique

- Surface Anatomy
  - Medial malleolus (MM)
  - Anterior border of Achilles tendon
  - Posterior tibial artery
  - Tibial nerve typically runs posterior to artery
  - Tibialis anterior (TA)
  - Extensor hallucis longus (EHL)
  - Lateral malleolus (LM)
  - Anterior Tibial/Dorsalis Pedis artery

- Post tibial: posterior to posterior tibial artery
- Sural: between lateral malleolus and Achilles
- Deep Peroneal: deep to anterior tibial artery between EHL and TA tendons
- Superficial Peroneal and Saphenous: infiltration along dorsum of foot between malleoli


Lower-Extremity Peripheral Nerve Blockade: Essentials of Our Current Understanding

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The American Society of Regional Anesthesia and Pain Medicine introduced an intensive workshop focused on lower-extremity peripheral nerve blockade in 2002. This review is the compilation of that work. Details concerning the techniques described in this text are available at the website ASRA.com, including video demonstrations of the blocks. Lower-extremity peripheral nerve blocks (PNBs) have never been as widely taught or used as other forms of regional anesthesia. Unlike the upper extremity, the entire lower extremity cannot be anesthetized with a single injection, and injections are generally deeper than those required for upper extremity block. In addition, neuraxial techniques are widely taught and use alternative methods for providing reliable lower-extremity anesthesia. Over the past decade, several developments have led to an increased interest in lower extremity PNBs, including transient neurologic symptoms associated with spinal anesthesia, increased risk of epidural hematoma with the introduction of antithromboembolic prophylaxis regimens, and evidence of improved rehabilitation outcome with continuous lower-extremity PNBs. This review will focus on the anatomy of the lumbosacral plexus and its terminal nerves, followed by a discussion of techniques and applications. In addition, we will review neural localization techniques and potential complications.

Lower-Extremity Peripheral Nerve Anatomy

Lower-extremity PNB requires a thorough understanding of the neuroanatomy of the lumbosacral plexus. Anatomically, the lumbosacral plexus consists of 2 distinct entities: the lumbar plexus and the sacral plexus. There is some communication between these plexi via the lumbosacral trunk, but for functional purposes these are distinct entities.1 Details of the motor and sensory branches of the lumbosacral plexus are summarized in Tables 1 and 2 and Figures 1 and 2. The lumbosacral plexus arises from at least 8 spinal nerve roots, each of which contains anterior and posterior divisions that innervate the embryologic ventral or dorsal portions of the limb. With the exception of a small cutaneous portion of the buttock (which is supplied by upper lumbar and sacral segmental nerves), the innervation of the lower extremity is entirely through branches of the lumbosacral plexus. The nerves to the muscles of the anterior and medial thigh are from the lumbar plexus. The muscles of the buttocks, the posterior muscles in the thigh, and all the muscles below the knee are supplied by the sacral plexus. There are a multitude of approaches to each peripheral nerve block described for the lower extremity. Thus, a detailed review of the course of each of the relevant terminal peripheral nerves of the lower extremity is warranted in this review.

Lumbar Plexus Anatomy

The lumbar plexus is formed within the psoas muscle from the anterior rami of T12-L4.1-4 The branches of this plexus, the iliohypogastric, ilioinguinal, genitofemoral, lateral femoral cutaneous,
and femoral and obturator nerves emerge from the psoas laterally, medially, and anteriorly (Figs 2 and 3). Of these, the femoral, lateral femoral cutaneous, and obturator nerves are most important for lower-extremity surgery.  

**Femoral Nerve.** The femoral nerve is formed by the dorsal divisions of the anterior rami of the second, third, and fourth lumbar nerves. The femoral nerve emerges from the psoas muscle in a fascial compartment between the psoas and iliacus

<table>
<thead>
<tr>
<th>Nerve</th>
<th>Spinal Segment</th>
<th>Motor Innervation</th>
<th>Motion Observed*</th>
<th>Sensory Innervation</th>
<th>Articular Branches</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iliohypogastric</td>
<td>T2-L1</td>
<td>Int/ext oblique</td>
<td>Ant abdominal wall</td>
<td>Inferior abd wall</td>
<td>None</td>
</tr>
<tr>
<td>Iliinguinal</td>
<td>L1</td>
<td>Transverse abdominis</td>
<td>Ant abdominal wall</td>
<td>Upper lat quadrant of buttock</td>
<td>None</td>
</tr>
<tr>
<td>Genitofemoral</td>
<td>L1-L2</td>
<td>Cremaster</td>
<td>Testicular</td>
<td>Inferior to mid portion of inguinal ligament</td>
<td>None</td>
</tr>
<tr>
<td>Lateral Femoral Cutaneous</td>
<td>L2-L3</td>
<td>None</td>
<td>None</td>
<td>Anterior lateral and posterior aspects of thigh terminating in prepatellar plexus</td>
<td>None</td>
</tr>
<tr>
<td>Femoral</td>
<td>L2-L4</td>
<td>Sartorius</td>
<td>Medial aspect of the lower thigh</td>
<td>Anterior medial skin of the thigh</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pectineus</td>
<td>Adductor of thigh</td>
<td>Ant thigh</td>
<td>Hip and knee</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Quadriceps</td>
<td>Knee extension, patellar ascension</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Obturator</td>
<td>L2-L4</td>
<td>Gracilus, adductor brevis &amp; longus pectineus</td>
<td>Thigh adduction</td>
<td>Variable, posterior medial thigh, medial knee</td>
<td>Hip</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Obturator externus, adductor magnus</td>
<td>Thigh adduction with lateral hip rotation</td>
<td>None</td>
<td></td>
</tr>
</tbody>
</table>

**Table 1. Lumbar Plexus Anatomy**

<table>
<thead>
<tr>
<th>Nerve</th>
<th>Spinal Segment</th>
<th>Motor Innervation</th>
<th>Motion Observed*</th>
<th>Sensory Innervation</th>
<th>Articular Branches</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gluteal nerves</td>
<td>L4-S2</td>
<td>Piriformis, sup/inf gemellus obturator internus, quadratus femoris</td>
<td>Buttocks with lat hip rotation</td>
<td>Upper medial aspect of buttock</td>
<td>Hip</td>
</tr>
<tr>
<td>Sciatic, tibial</td>
<td>L4-S3</td>
<td>Biceps femoris, semitendinosus, adductor magnus Popliteus</td>
<td>Hamstrings with knee extension</td>
<td>Medial and lat heel sole of foot</td>
<td>Hip knee, and ankle</td>
</tr>
<tr>
<td>Sciatic, peroneal Superficial</td>
<td>L4-S3</td>
<td>Gastrocnemius, soleus, flexors of foot, brevis</td>
<td>Knee flexion, Plantar flexion Toe flexion</td>
<td>Distal anterior leg, dorsum of foot</td>
<td>Knee and ankle</td>
</tr>
<tr>
<td>Deep</td>
<td>L4-S3</td>
<td>Short head of biceps femoris peroneus longus, brevis</td>
<td>Knee flexion, Foot inversion</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Sural Components from peroneal &amp; tibial</td>
<td>None</td>
<td>Extensors of foot, toes</td>
<td>None</td>
<td>None</td>
<td>Ankle</td>
</tr>
<tr>
<td>Post cut nerve of thigh</td>
<td>S1-S3</td>
<td>None</td>
<td>None</td>
<td>Post calf, lat border of foot and 5th toe</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
<td>None</td>
<td>None</td>
<td>Distal medial quadrant of buttock perineum, post thigh including popliteal fossa</td>
<td>None</td>
</tr>
</tbody>
</table>

Abbreviations: Int, internal; Ext, external; Ant, anterior; Abd, abdominal; Lat, lateral.  
*Motion observed refers to the observed motor response with electrical stimulation of that nerve.

**Table 2. Sacral Plexus Anatomy**

<table>
<thead>
<tr>
<th>Nerve</th>
<th>Spinal Segment</th>
<th>Motor Innervation</th>
<th>Motion Observed*</th>
<th>Sensory Innervation</th>
<th>Articular Branches</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gluteal nerves</td>
<td>L4-S2</td>
<td>Piriformis, sup/inf gemellus obturator internus, quadratus femoris</td>
<td>Buttocks with lat hip rotation</td>
<td>Upper medial aspect of buttock</td>
<td>Hip</td>
</tr>
<tr>
<td>Sciatic, tibial</td>
<td>L4-S3</td>
<td>Biceps femoris, semitendinosus, adductor magnus Popliteus</td>
<td>Hamstrings with knee extension</td>
<td>Medial and lat heel sole of foot</td>
<td>Hip knee, and ankle</td>
</tr>
<tr>
<td>Sciatic, peroneal Superficial</td>
<td>L4-S3</td>
<td>Gastrocnemius, soleus, flexors of foot, brevis</td>
<td>Knee flexion, Plantar flexion Toe flexion</td>
<td>Distal anterior leg, dorsum of foot</td>
<td>Knee and ankle</td>
</tr>
<tr>
<td>Deep</td>
<td>L4-S3</td>
<td>Short head of biceps femoris peroneus longus, brevis</td>
<td>Knee flexion, Foot inversion</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Sural Components from peroneal &amp; tibial</td>
<td>None</td>
<td>Extensors of foot, toes</td>
<td>None</td>
<td>None</td>
<td>Ankle</td>
</tr>
<tr>
<td>Post cut nerve of thigh</td>
<td>S1-S3</td>
<td>None</td>
<td>None</td>
<td>Post calf, lat border of foot and 5th toe</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
<td>None</td>
<td>None</td>
<td>Distal medial quadrant of buttock perineum, post thigh including popliteal fossa</td>
<td>None</td>
</tr>
</tbody>
</table>

Abbreviations: Sup, superior; Inf, inferior; Lat, lateral; Post, posterior; Cut, cutaneous.  
*Motion observed refers to the observed motor response with electrical stimulation of that nerve.
muscles, in which it gives off articular branches to the hip. It enters the thigh posterior to the inguinal ligament. There it lies lateral and posterior to the femoral artery. This relationship to the femoral artery exists near the inguinal ligament, but not after the nerve enters the thigh. As the nerve passes into the thigh, it divides into an anterior and a posterior division and quickly arborizes (Fig 4). At the level of the inguinal ligament, there are dense fascial planes, the fascia lata, and fascia iliaca. The femoral nerve is situated deep to these fascial planes. The femoral artery, vein, and lymphatics reside in a separate fascial compartment medial to the nerve.

The anterior division of the femoral nerve gives off the medial and intermediate cutaneous nerves that supply the skin of the medial and anterior surfaces of the thigh. The muscular branches of the anterior division of the femoral nerve supply the sartorius muscle and the pectineus muscle and articular branches to the hip. The posterior division of the femoral nerve gives off the saphenous nerve, which is the largest cutaneous branch of the femoral nerve, and the muscular branches to the quadriceps muscle and articular branches to the knee.

The terminal nerves of the posterior division of the femoral nerve, the saphenous and the vastus medialis nerves, continue distally through the adductor canal. After leaving the adductor canal, the saphenous nerve emerges from behind the sartorius muscle, in which it gives off an infrapatellar branch and then continues distally to supply the cutaneous innervation of the anteromedial lower leg down to the medial aspect of the foot.

**ObturatoR Nerve.** The obturator nerve is a branch of the lumbar plexus formed within the substance of the psoas muscle from the anterior division of the second, third, and fourth lumbar nerves. It is the nerve of the adductor compartment of the thigh, which it reaches by piercing the medial border of the psoas and passing straight along the sidewall of the pelvis to the obturator foramen. After entering the thigh through the obturator
groove, the nerve divides into an anterior and posterior division. The anterior division has three branches including the muscular branches to the adductor muscles, an articular branch to the hip joint, and a cutaneous branch to the medial side of the thigh. The extent of this cutaneous sensory innervation has been investigated by Bouaziz et al. These investigators performed an isolated obturator nerve block on patients before a femoral nerve block. All the obturator nerve blocks were successful as shown by adductor paresis. In 57% of the patients, there was no cutaneous sensory loss demonstrable. In 23% of patients, a zone of hypoesthesia was present on the superior medial aspect of the popliteal fossae. Only 20% of the patients showed a sensory deficit on the inferior aspect of the medial thigh. The inconsistency of the sensory distribution of the obturator nerve must be considered when evaluating reports of obturator nerve block success rates based on sensory findings only.

The posterior division of the obturator nerve descends with the femoral and popliteal artery to the knee joint, and forms 2 branches: a muscular branch to the external obturator and adductor magnus muscles and an articular branch to the knee. The divergence of the obturator nerve from the femoral nerve begins as they emerge from the substance of the psoas muscle. At the level of the inguinal ligament, the obturator nerve lies deep and medial relative to the femoral nerve and is separated from it by several fascial compartments. This separation at the level of the inguinal ligament is obvious in anatomic dissections (Fig 5) and has also been shown both radiographically with contrast and by magnetic resonance image.

**Lateral Femoral Cutaneous Nerve.** The lateral femoral cutaneous nerve is formed by union of

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**Fig 4.** Anatomy of the femoral nerve in the inguinal area: 1, femoral nerve; 2, lateral femoral cutaneous nerve; 3, branches of the femoral nerve to the sartorius muscle; 4, inguinal ligament; 5, femoral artery; 6, femoral vein.

**Fig 5.** Organization of the lumbar plexus components at the level of the inguinal ligament: 1, femoral nerve; 2, obturator nerve; 3, genitofemoral nerve; 4, lateral femoral cutaneous nerve; 5, psoas muscle; 6, ureter; 7, iliacus nerve and vein; 8, rectum.
fibers from the posterior division of the anterior primary rami of L2 and L3. It emerges from the lateral border of psoas major below the iliolumbar ligament, passing around the iliac fossa on the surface of the iliacus muscle deep to the iliac fascia. Above the inguinal ligament, it slopes forward and lies inside the fibrous tissue of the iliac fascia. It perforates the inguinal ligament approximately 1 cm from the anterior superior iliac spine from where it enters the thigh. The lateral femoral cutaneous nerve supplies the parietal peritoneum of the iliac fascia and the skin over a widely variable aspect of the lateral and anterior thigh. It has no motor innervation.

Sacral Plexus Anatomy

The sacral plexus is formed within the pelvis by the merger of the ventral rami of the fourth and fifth lumbar and the first 3 or 4 sacral nerves. The fourth and fifth lumbar ventral rami are common to both the lumbar and the sacral plexus and the lumbosacral trunk. Of the 12 branches of the sacral plexus, 5 are distributed within the pelvis and the other 7 emerge from the pelvis to distribute to the buttock and the lower extremity. The sacral plexus provides motor and sensory innervation to portions of the entire lower extremity including the hip, knee, and ankle. The most important components of the sacral plexus for lower-extremity surgery are the sciatic and the posterior cutaneous nerves and their terminal branches.

Sciatic Nerve. The lumbosacral trunk (L4-L5) and anterior divisions of the sacral plexus (S1-S3) merge to form the tibial nerve, whereas the posterior divisions merge to form the common peroneal nerve. These 2 large mixed nerves of the sacral plexus are initially bound together by connective tissue to form the sciatic nerve. At this level, the tibial component is medial and anterior, whereas the common peroneal component is lateral and slightly posterior (Fig 6). The superior gluteal artery is immediately superior and medial to the sciatic nerve at the level of the piriformis. Doppler identification of the superior gluteal artery has been used to help identify appropriate needle insertion site during sciatic nerve block. The sciatic nerve exits the pelvis via the greater sciatic notch below the piriformis muscle. At this level, it lies lateral and posterior to the ischial spine. As it enters the thigh and descends toward the popliteal fossa, it is posterior to the lesser trochanter of the femur, on the posterior surface of the adductor magnus muscle within the posterior medial thigh compartment deep to biceps femoris. There is no artery after a

similar course because the chief blood supply to the thigh is through the anterior femoral artery. The popliteal artery and vein, the continuation of the femoral artery and vein, reach the popliteal fossa by passing through the adductor hiatus and continue downward with the artery anterior to the vein. In the upper part of the popliteal fossa, the sciatic nerve lies posterolateral to the popliteal vessels. Specifically, the popliteal vein is medial to the nerve, whereas the popliteal artery is anterior, lying on the popliteal surface of the femur (Fig 7). The sciatic nerve usually divides into its component nerves, the tibial and common peroneal nerves, at the upper aspect of the popliteal fossa. In a cadaveric evaluation, Vloka et al. reported that the division of the sciatic nerve into its components occurs at a mean distance of 6 ± 3 cm above the popliteal crease. However, in this small sampling, the range was quite large (0-11.5 cm).

Tibial Nerve. In the popliteal fossa, the tibial nerve lies posterior and lateral to the popliteal vessels (Fig 8). In the lower part of the fossa, it sends branches to the major ankle plantar flexors, the
gastrocnemius, and soleus muscles. The tibial nerve then courses on the posterior surface of the tibialis posterior muscle, along with the posterior tibial vessels. At the ankle, the nerve and vessels enter a compartment beneath the flexor retinaculum (Fig 9). As it passes to the plantar aspect of the foot, it gives off the lateral and medial plantar nerves. Of the digital nerves, those to the medial 3½ toes are supplied by the medial plantar nerve, whereas those of the lateral 1½ toes are supplied by the lateral plantar nerve; a distribution similar to the median and ulnar nerves in the hand.

Peroneal Nerve. The common peroneal nerve diverges laterally leaving the popliteal fossa by crossing the lateral head of the gastrocnemius. It lies subcutaneously just behind the fibular head, in which it can be easily traumatized. As it rounds the neck of the fibula, the common peroneal nerve divides into its terminal branches, the deep peroneal nerve and the superficial peroneal nerve. The deep peroneal nerve continues distally, accompanied by the anterior tibial artery, on the interosseous membrane. Nerve and artery emerge on the dorsum of the foot between the extensor hallucis longus and tibialis anterior. At this level, the deep peroneal nerve is lateral to the dorsalis pedis artery. The deep peroneal nerve innervates the extensor (dorsiflexor) muscles of the foot and the first web-space. The superficial peroneal nerve descends in the lateral compartment, between the peroneus longus and brevis muscles. After supplying these ankle evertors innervates, it emerges between them to innervate the skin of the lower leg and foot.
Posterior Femoral Cutaneous Nerve. The posterior femoral cutaneous nerve is a purely sensory nerve derived from the anterior rami of S1-S3.14 It travels with the sciatic nerve out of the pelvis and into the upper thigh. While deep to the gluteus maximus, it gives off the inferior clunial nerves (sensory nerves to the lower buttock) and perineal branches (sensory to the external genitalia). It emerges from the lower edge of the gluteus maximus to lie in subcutaneous tissue and continues down the posterior aspect of the thigh and the leg giving off, in succession, femoral and sural branches (sensory branches to the back of the thigh and the calf). It becomes superficial near the popliteal fossa where its terminal branches often anastomose with the sural nerve.

Sural Nerve. The medial and lateral sural nerves are pure sensory nerves derived from the tibial and common peroneal nerves, respectively, at the level of the knee joint. Together, they supply the posterolateral aspect of the leg and ankle and the dorsal surface of the foot.

Approaches to the Lower Extremity

Nerve Blocks of the Lumbar Plexus

Psoas Compartment Block. The psoas compartment block was first described by Chayen et al.15 in 1976. It can be performed as a single-injection technique or with a catheter placed for prolonged analgesia. It has been used to provide anesthesia for thigh surgery. In combination with parasacral nerve block, it has been used for hip fracture repair.16 It is successfully used for analgesia after total hip arthroplasty (THA) or total knee arthroplasty (TKA).2,3,17,18 It has also been used in the treatment of chronic hip pain.19 The distribution of the psoas compartment block is shown in Figure 10A.

The psoas compartment block is a deep block of the lumbar plexus from a posterior approach. Traversing from posterior to anterior at the level of L4-L5, the following structures would be encountered: posterior lumbar fascia, paraspinous muscles, anterior lumbar fascia, quadratus lumborum, and the psoas muscle (Fig 10D). The common iliac artery and vein are situated anterior to the psoas muscle, which is inside a fascial sheath, the psoas compartment (Fig 3). Because the final positioning of the needle is within the body of the psoas muscle through which the lumbar plexus traverses, it is thought to be the most consistent approach to block the entire lumbar plexus with a single injection. It is useful for providing consistent anesthesia in the distributions of the femoral, lateral femoral cutaneous, and the obturator nerves (Fig 10A).

Several descriptions of the needle entry site for the psoas compartment blocks have been described.2,3,21-24 All rely on bony contact with the transverse process as a guide to depth of needle placement. Capedevila et al.2 described a slightly modified entry point based on computed tomography (CT) scans of the lumbar plexus of patients undergoing THA. They estimated the distance from the skin to the lumbar plexus to be 8.35 cm in men (range 6.1-10.1 cm) and 7.1 cm in women (range 5.7-9.3 cm). The depth of the lumbar plexus correlated with gender and body mass index. Importantly, the distance from the transverse process to the lumbar plexus was extremely consistent at a distance of less than 2 cm. This relationship of transverse process to the lumbar plexus was independent of body mass index or gender. Thus, contact with the transverse process provides a consistent landmark to avoid excessive needle penetration during psoas compartment block2 (Fig 10B-D).

The depth of needle insertion is emphasized because of the complications associated with excessive needle depth including renal hematoma, pneumocele, total spinal anesthesia, and unintended intra-abdominal, and intervertebral disk catheter placement.2,25-27 To ensure the proper position of the needle during psoas compartment block and avoid excessive needle insertion, it is highly recommended that the transverse process be intentionally sought. Epidural spread of local anesthetic is another common side effect of psoas compartment block, occurring in 9% to 16% of adult patients3,28 (Table 3). In children, Dalens et al.29 reported a >90% incidence of epidural spread when using the original landmarks of Chayen et al.15 compared with no epidural spread when using the landmarks as modified by Winnie.29 This side effect is usually attributed to retrograde diffusion of the local anesthetic to the epidural space when large volumes of local anesthetic are used (greater than 20 mL). In most cases, there is residual lumbar plexus blockade apparent after the resolution of the contralateral block. However, there are case reports of total spinal anesthesia occurring during lumbar plexus blockade and vigilance must be maintained during the management of this block.26,30 (see complications).

Continuous Psoas Compartment Blocks. Continuous techniques have been described to provide analgesia after a variety of operations including THA, TKA, open reduction and internal fixation of acetabular fractures, open reduction and internal fixation of femur fractures, and anterior cruciate ligament reconstruction.2,17,18,31,32 Interest in this block developed as practitioners sought alternatives to neuraxial techniques that could provide consistent analgesia after hip, femur, and knee surgery. One theoretical advantage of psoas compartment block...
Fig 10. Psoas compartment block. (A) The sensory distribution of a psoas compartment block is shown on the right. The osteotomes blocked by the psoas compartment block are shown on the left. (B) Landmarks for the psoas compartment block. Needle entry is marked 1 cm cephalad to the intercristal line, two thirds the distance from the midline to the PSIS line. (C) Psoas compartment deep landmarks observed from above. Post, posterior; Ant, anterior. (D) Psoas compartment block, final needle placement. Note the structures deep to the lumbar plexus including major vascular structures, kidneys, and abdominal contents. (Courtesy of Mayo Foundation.)
over other continuous approaches to the lumbar plexus is the decreased likelihood of catheter dislodgement because of the large muscle mass that must be traversed to reach the lumbar plexus. The muscle mass anchors the catheter.

Pandin and colleagues described a slightly more medial puncture site for placement of continuous lumbar plexus blocks for postoperative analgesia. They believed the more medial puncture site improved the likelihood of obtaining an obturator nerve block and optimized catheter insertion with an insertion angle of 20° to 30°. They failed to place a catheter in only 3% of their patients and reported a high success rate (100% femoral, 93% obturator, 91% lateral femoral cutaneous) bolusing through a nonstimulating catheter.

**Femoral Nerve Block.** Indications for single-injection femoral nerve block include anesthesia for knee arthroscopy in combination with intra-articular local anesthesia and analgesia for femoral shaft fractures, anterior cruciate ligament reconstruction (ACL), and TKA as a part of multimodal regimens. Their use in complex knee operations is associated with lower pain scores and fewer hospital admissions after same-day surgery. The femoral nerve divides into the posterior and anterior divisions shortly after it emerges from under the inguinal ligament and undergoes extensive arborization. Commonly, the anterior branch of the femoral nerve will be identified first. Vloka et al. reported this to be the first motor response elicited 97% of the time. Stimulation of this branch leads to contraction of the sartorius muscle on the medial aspect of the thigh and should not be accepted, as the articular and muscular branches derive from the posterior branch of the femoral nerve. The needle should be redirected slightly laterally and with a deeper direction to encounter the posterior branch of the femoral nerve. Stimulation of this branch is identified by patellar ascension as the quadriceps contract.

**Defining the 3-in-1 Block.** During femoral nerve block, it has been advocated to use a higher volume of local anesthetic and apply firm pressure just distal to the needle during and a few minutes after injection to block the femoral, lateral femoral cutaneous, and obturator nerves, the so-called “3-in-1 block.” However, despite many efforts to consistently produce a 3-in-1 block, the effectiveness of these maneuvers has not been shown. In most reports, the femoral nerve is the only nerve consistently blocked with this approach. Blockade of the lateral femoral cutaneous nerve occurs through lateral diffusion of local anesthetic and not through proximal spread to the lumbar plexus. The obturator nerve is less frequently anesthetized during 3-in-1 block than the lateral femoral cutaneous (LFC), which is not surprising given the number of fascial barriers between these structures at the level of the inguinal ligament. Despite the lack of scientific support for the term 3-in-1, many authors still continue to refer to the anterior femoral nerve block as a 3-in-1 block. Within this text, we will refer to this approach as a femoral nerve block.

**Continuous Femoral Nerve Block.** Continuous femoral nerve block has been shown to improve outcome

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**Table 3. Success Rate of Lumbar Plexus Block With Different Techniques**

<table>
<thead>
<tr>
<th>Reference</th>
<th>N</th>
<th>Technique</th>
<th>Sensory Block</th>
<th>Motor Block</th>
<th>Number of Failures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Fem</td>
<td>LFC</td>
<td>OBT</td>
</tr>
<tr>
<td>Parkinson</td>
<td>28*</td>
<td>Psoas @ L3, n.s.</td>
<td>95%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parkinson</td>
<td>23</td>
<td>Psoas @ L4-5</td>
<td>95%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parkinson</td>
<td>20</td>
<td>Femoral paresthesia</td>
<td>95%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parkinson</td>
<td>20</td>
<td>Femoral, n.s.</td>
<td>85%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seeberger</td>
<td>39</td>
<td>Femoral, n.s. 20 mL</td>
<td>41%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seeberger</td>
<td>41</td>
<td>Femoral, n.s. 40 mL</td>
<td>44%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lang</td>
<td>32</td>
<td>Femoral paresthesia 30 mL</td>
<td>96%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Farny</td>
<td>45</td>
<td>Psoas, n.s. 1.0-0.5 mA</td>
<td>100%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morau</td>
<td>20</td>
<td>Femoral, n.s. 0.5 mL bolus via catheter</td>
<td>100%</td>
<td>70%</td>
<td>88%</td>
</tr>
<tr>
<td>Lang</td>
<td>30</td>
<td>Femoral, n.s. 30 mL</td>
<td>93%</td>
<td>63%</td>
<td>47%</td>
</tr>
<tr>
<td>Tokat</td>
<td>132</td>
<td>Psoas n.s. 0.3 mA bolus via catheter</td>
<td>100%</td>
<td>93%</td>
<td>91%</td>
</tr>
<tr>
<td>Capdevila</td>
<td>50</td>
<td>Femoral n.s. 0.5 mL 30 mL</td>
<td>90%</td>
<td>62%</td>
<td>52%</td>
</tr>
<tr>
<td>Kaloul</td>
<td>20</td>
<td>Femoral n.s. 0.5 mA bolus via catheter</td>
<td>95%</td>
<td>97%</td>
<td>97%</td>
</tr>
</tbody>
</table>

Abbreviations: Fem, femoral; LFC, Lateral femoral cutaneous; OBT, obturator; n.s., nerve stimulator.

*Use of uninsulated needles; no mA given.

†These studies reported rate of success for blocking the components of the lumbar plexus using a variety of nerve localization techniques and approaches to the nerves.
after major knee and vascular surgery of the lower extremity compared with intravenous narcotic therapy or continuous infusion or injection of analgesics. Chelly et al. showed a 20% reduction in hospital length of stay in patients receiving continuous femoral nerve block analgesia compared with patients receiving intravenous patient-controlled analgesia narcotics after major knee surgery. Two prospective randomized studies examined 3 different modes of analgesia: continuous femoral nerve block, epidural analgesia, and intravenous narcotic therapy after TKA. These studies showed improvement in perioperative rehabilitation scores and a decreased duration of stay in a rehabilitation center for patients receiving the regional anesthesia techniques. Continuous femoral nerve block was shown to have equivalent analgesia with fewer side effects than epidural analgesia in both of these studies. However, not all investigators have been able to show these improvements in outcome with continuous femoral nerve blocks. Hirst et al. found no differences in narcotic consumption or pain scores between patients receiving a single-injection femoral nerve block and patients receiving a continuous femoral nerve block after TKA. The accuracy of catheter placement may play a role in these conflicting findings. Continuous femoral nerve blocks have been associated with a high rate of inaccurate catheter placement. In a prospective study, Capdevila et al. showed that continuous femoral nerve block using a standard approach led to unpredictable catheter placement. Their technique was to elicit a vastus intermedius muscle response at 0.5 mA and then insert a catheter 16 to 20 cm after distending the sheath with 5 mL saline and bolusing local anesthetic through the catheter. Catheter placement was evaluated radiographically, and only 25% of the catheters were lying near the lumbar plexus. Most of the catheters tended to course medially in the direction of the psoas muscle or laterally in the direction of the iliacus muscle. The accuracy of final catheter placement correlated with the degree of analgesia after proximal lower limb surgery, although visual analog scale values were generally low in all groups. Comparing a stimulating catheter to a nonstimulating catheter, Salinas and colleagues were able to increase the success rate of continuous femoral nerve block in volunteers from 85% to 100%. The role of stimulating versus nonstimulating catheters for continuous peripheral nerve blocks to improve success rate is an active area of research at this time.

**Fascia Iliacus Block.** Dalens et al. originally described the fascia iliaca block in children. The indications for its use are the same as those for single-injection femoral nerve block. Advocates believe its utility lies in the double pop technique for applying this block. The double pop refers to the sensation felt as the needle traverses the fascia lata then the fascia iliaca, is traversed. (Courtesy of Mayo Foundation.)

![Fig 11. Approach to the fascia iliaca block. The needle gives a discernible pop as the fascia lata, then the fascia iliaca, is traversed. (Courtesy of Mayo Foundation.)](image)
Continuous Fascia Iliacus Blocks. Continuous fascia iliacus blocks have been described for analgesia after femur fracture and repair, femoral elongation procedures, skin graft harvesting, ligamentous knee reconstruction, and TKA.\textsuperscript{57,58} Much like femoral continuous catheters, the degree of analgesia seems to be highly correlated with the final position of the catheter. Ganapathy et al.,\textsuperscript{57} using a modified approach to the fascia iliaca block with a nerve stimulator, showed a high degree of catheter malpositioning. In this study, CT scans found only 40% of catheters placed were ideally positioned (superior to the upper third of the sacroiliac joint in the psoas sheath). Another variable examined in this study was the infusate, saline, 0.1% bupivacaine, or 0.2% bupivacaine. All the patients in the study had excellent pain relief regardless of the catheter position or infusate. This was attributed to the multimodal analgesic regimen the patients received. However, the best analgesia was highly correlated with ideal catheter tip position and the use of 0.2% bupivacaine.

Obturator Nerve Block. Indications for a single-injection obturator nerve block are generally limited to diagnostic indications or therapeutic relaxation of the adductor muscles of the thigh.\textsuperscript{59} Despite the significant amount of literature that has been devoted to anesthetic sparing of this nerve with many approaches to the lumbar plexus, only 2 studies have examined the effect of the addition of an obturator nerve block to improve analgesia after major knee surgery.\textsuperscript{60,61} Both studies reported a decrease in opioid consumption and pain scores in patients undergoing TKA receiving obturator nerve block in addition to a femoral or femoral and sciatic nerve block.

LFC Nerve Block. The LFC nerve of the thigh is a purely sensory nerve that supplies a large but variable area from the inguinal ligament to the knee on the lateral aspect of the thigh.\textsuperscript{9} LFC nerve block is most commonly used as the sole anesthetic during diagnostic muscle biopsy and harvesting of split thickness skin grafts.\textsuperscript{62,63} It has also been used to provide analgesia in elderly patients undergoing hip fracture repair.\textsuperscript{64} However, in a study comparing LFC nerve block, femoral nerve block, and patients receiving no block following femoral neck repair, LFC nerve block was not as effective at controlling postoperative pain as femoral nerve block.\textsuperscript{65}

Typically, this block is done as a fan technique with variable success. Whether this is because of variability in the distribution of innervation or to poorly localizing the nerve is not known. Shannon and colleagues\textsuperscript{66} compared the traditional fan technique for LFC nerve block to the use of a nerve stimulator technique seeking tingling in the distribution of the nerve. They reported a 40% success rate with the fanning technique compared with 100% with the nerve stimulating technique. There was no difference in the extent of the blockade in successful blocks. Femoral nerve block has been reported after LFC block.\textsuperscript{67} This is not surprising given the bulk of data reporting spread to the LFC nerve during femoral nerve block.

Saphenous Nerve Block. The saphenous nerve follows the saphenous vein to the medial malleolus and supplies the cutaneous area of the medial aspect of the calf and foot to the level of the midfoot. The saphenous nerve block is often combined with a sciatic block to provide anesthesia and analgesia for surgery involving the medial aspect of the lower leg and foot. The saphenous nerve is a purely sensory nerve and does not contribute to the bony innervation of the foot. Approaches to the saphenous nerve along its entire course, from the adductor canal to the ankle, have been described. Success rates vary widely between techniques. For example, successful block is reported in 33% to 65% of cases with a field infiltration performed medially at the level of the tibial plateau,\textsuperscript{68,69} 70% to 80% of cases with the trans sartorial approach,\textsuperscript{68,70} 95% to 100% of cases with femoral paracapsular approach,\textsuperscript{70} and near 100% of cases with the paravenous approach.\textsuperscript{69} The saphenous nerve has been reported to be selectively blocked, sparing of the quadriceps musculature, in the adductor canal.\textsuperscript{71} However, this has not been confirmed in a large series of patients receiving this approach to the saphenous nerve.

Comparisons of Approaches to the Lumbar Plexus

Psoas Compartment Block Versus Femoral Nerve Block

Parkinson et al.,\textsuperscript{28} were the first to compare the extent of blockade after single-injection femoral nerve block and psoas compartment block. They compared the extent of blockade of the lumbar plexus with 5 different methods: posterior approach at L3 and L4-5 with a nerve stimulator using non-insulated needles and anterior femoral nerve block approaches with a paresthesia technique and nerve stimulating technique.\textsuperscript{28} They reported a 100% success rate of femoral nerve blockade with all techniques. The lateral femoral cutaneous nerve success rate was 85% to 95%. The obturator nerve, as assessed by thigh adduction, was blocked 100% of the time with the posterior approaches and never with the anterior approaches. Limitations of this report include lack of details regarding the type of nerve stimulation, the small sample size, and exclusion of patients in whom femoral nerve block failed.
to develop. A more recent comparison has been made between psoas compartment blocks and femoral nerve blocks. In this study, patients receiving a psoas compartment block developed a sensory block of the femoral, lateral femoral cutaneous, and obturator nerves in 100%, 97%, and 77% of patients versus 93%, 63%, and 47% of the patients receiving a femoral nerve block.

**Femoral Nerve Block Versus Fascia Iliacus Block**

Direct comparisons of the extent of blockade between the fascia iliaca block and femoral nerve block has been done in both adults and children. In adults, the fascia iliaca block, performed with the double-pop technique, provided faster onset and a higher rate of lateral femoral cutaneous nerve block compared with femoral nerve blocks performed with a nerve stimulator. Both techniques provide adequate postoperative analgesia. In children, the fascia iliaca block is more likely to block the lateral femoral cutaneous nerve compared with a femoral nerve block. However, the duration of analgesia from these single-injection techniques was somewhat shorter in the fascia iliaca group. The authors speculated this was related to greater spread of the local anesthetic.

A single study directly comparing continuous fascia iliaca blocks to continuous femoral nerve blocks has been reported. Again, the degree of analgesia was highly correlated with catheter positioning. Overall, there was a greater degree of blockade of the lateral femoral cutaneous nerve in the fascia iliaca group and a greater likelihood of blocking the obturator nerve in the femoral group.

**Continuous Psoas Compartment Blocks Versus Epidural Analgesia**

Advantages of continuous psoas compartment block compared with epidural block include unilateral analgesia and motor block, lack of impairment of bladder function, and improved risk/benefit ratio in patients anticoagulated after surgery. These advantages must be weighed against the disadvantages of incomplete blockade for anesthesia and the need for supplementation in a balanced analgesic regimen for effective analgesia.

Turker and coworkers compared continuous psoas compartment block with epidural block for analgesia after THA under combined general/regional technique. They showed that continuous psoas compartment block provided excellent intra- and postoperative analgesia with a low incidence of complications. Epidural block took longer to perform and had a significantly higher incidence of hypotension, whereas analgesia and patient satisfaction provided by the 2 blocks was similar. Epidural block also provided more motor blockade, longer time to ambulation, and significantly more complications.

**Continuous Psoas Compartment Blocks Versus Continuous Femoral Blocks.** After TKA, continuous femoral nerve block and continuous psoas compartment block reduce narcotic consumption and pain scores compared to intravenous morphine usage alone. However, no differences in outcome were observed between the 2 peripheral nerve block groups despite a more consistent presence of obturator nerve block in the psoas compartment group.

**Nerve Blocks of the Sacral Plexus**

**Parasacral Block**

The parasacral nerve block (PSNB) described by Mansour in 1993 has been described as more than an isolated sciatic nerve block. It has been used to provide analgesia following major foot and ankle reconstruction. Parasacral block will consistently block both components of the sciatic nerve and the posterior cutaneous nerve of the thigh. Spread of local anesthetic may also anesthetize other branches of the sacral plexus including the superior and inferior gluteal and pudendal nerves. The pelvic splanchnic nerves (S2-S4), the terminal portion of the sympathetic trunk, the inferior hypogastric plexus, and the obturator nerve all lie in close proximity to the elements of the sacral plexus and may all be anesthetized with this approach. For procedures below the knee, the adductor weakness from the obturator and superior gluteal nerve block may actually be disadvantageous for mobilization of the patient. The sympathetic nerve supply to the bladder is also in close proximity but problems with voiding and the need for bladder catheterization after PSNB have not been reported. A notable difference from other approaches to the sciatic nerve is the type of muscle response deemed acceptable as an endpoint for injection. Mansour described contraction of the hamstring muscles (biceps femoris, semitendinous) above the knee as the endpoint for PSNB with most consistent success.

**Continuous Parasacral Blocks**

Continuous parasacral blocks have been used in combination with lumbar plexus block to provide lower extremity anesthesia for TKA, above the knee amputation, ACL repair, and a variety of other lower-extremity procedures. Gaertner reported successful
catheter placement, as confirmed by radiographic contrast dye in 86 of 87 consecutive patients undergoing lower-extremity surgery, using a nonstimulating catheter. All patients developed analgesia in the distribution of the tibial, peroneal, and posterior cutaneous nerve of thigh.

Sciatic Nerve Block: At the Level of the Gluteus Maximus

The sciatic nerve, the largest nerve derived from the sacral plexus, innervates the posterior thigh and almost the entire leg below the knee. The most common indications for sciatic nerve block are anesthesia and analgesia for foot and ankle surgery. There are a variety of approaches to the sciatic nerve block and their success rate is widely variable, ranging from 33% to 95%,79-82

Gaston Labat53 first described, at the beginning of the 20th century, the sciatic nerve block that is now referred to as the Classic Approach of Labat. This approach is based on the bony relationship of the posterior superior iliac spine and the greater trochanter with the patient positioned in a modified Sims position. Winnie79 was the first to modify the original description, adding in an additional landmark, the sacral hiatus to greater trochanter distance, to more precisely account for varying body habitus (Table 4). Difficulty identifying these landmarks led Chang and colleagues84 to describe a transrectal method of identifying the ischial spine.

Franco85 described a simple approach to the sciatic nerve block in the prone position. The needle entry site is perpendicular to the floor 10-cm lateral from the middle of the intragluteal sulcus regardless of the patient’s gender or body mass index. The sciatic nerve was found by trainees in 2/3 passes in 85% of the cases reported. Whether the success of this simple approach will be replicated in a larger sample size remains to be seen.

Subgluteal Approaches to the Sciatic Nerve

Raj et al.80 described a supine approach to the sciatic nerve in the flexed hip position, initiating the block at the midpoint between the greater trochanter of the femur and the ischial tuberosity. The positioning of the patient was thought to be advantageous compared to the classic approach of Labat by “thinning the gluteus maximus muscles, making the sciatic nerve more superficial.” However, identifying these bony landmarks in very obese patients is sometimes difficult and the patient position requires additional personnel to maintain.

A lateral subgluteal approach to the sciatic nerve using the greater trochanter of the femur as a landmark was first described by Ichniyanagi in 1959.86 Other investigators have described a high success rate using this high lateral approach with a slightly more caudal entry point.82 Notably, when using this approach the success rate of the blockade of the posterior cutaneous nerve of the thigh was 83%. Although theoretically the posterior cutaneous nerve should reliably be blocked in most proximal approaches to the sciatic nerve, the success rate of blockade is not usually reported.

The anterior approach to the sciatic nerve has the appeal of supine positioning and a single prep of the patient for combined femoral and sciatic nerve blocks. Its popularity had long been limited by its low success rate and relatively painful use of the femur as a deep landmark.87,88 Chelly and Delaunay89 described a nerve stimulating technique positioning the needle at the level of the lesser trochanter as originally described by Beck. Vloka et al.90 described the importance of internal rotation of the leg if the path to the sciatic nerve is obstructed by the lesser trochanter. A magnetic resonance imaging study of the anatomy of this area found that in 65% of patients the sciatic nerve is inaccessible from the anterior approach at the level

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**Table 4. Sciatic Nerve Block Approaches, Nerve Stimulating Current And Block Success**

<table>
<thead>
<tr>
<th>Approach, Author</th>
<th>Number of Patients</th>
<th>Recommended Minimal Stimulating Current and Its Pulse Width</th>
<th>Success Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>At the level of the sciatic notch Posterior, Morris77</td>
<td>30</td>
<td>≤ 0.2 mA; 100 μsec pulse width</td>
<td>97%</td>
</tr>
<tr>
<td>At the level of the ischial spine Labat, di Benedetto84</td>
<td>135</td>
<td>&lt; 0.5 mA; 100 μsec pulse width</td>
<td>98%</td>
</tr>
<tr>
<td>Trans-rectal, Chang84</td>
<td>40</td>
<td>≤ 0.4 mA; 200 μsec pulse width</td>
<td>92.5% (cross-over design)*</td>
</tr>
<tr>
<td>At the level of the ischial tuberosity Lithotomy</td>
<td></td>
<td>Not reported</td>
<td></td>
</tr>
<tr>
<td>Posterior, Sutherland115</td>
<td>76</td>
<td>0.3-0.5 mA; 100 μsec pulse width</td>
<td>95%</td>
</tr>
<tr>
<td>At the level of the upper thigh Posterior Subgluteal, di Benedetto113</td>
<td>64</td>
<td>&lt; 0.5 mA; 100 μsec pulse width</td>
<td>94%</td>
</tr>
<tr>
<td>Anterior, Chelly89</td>
<td>22</td>
<td>&lt; 0.7 mA; 100 μsec pulse width</td>
<td>100%</td>
</tr>
<tr>
<td>Lateral, Guardini82</td>
<td>&gt; 100</td>
<td>Not reported</td>
<td>≈ 94%</td>
</tr>
</tbody>
</table>

*Failures in this study were due to the inability to obtain this endpoint or to technical factors (e.g., patient movement and abandonment of the block [12%]) rather than to the failure of the endpoint itself.
of the lesser trochanter.\textsuperscript{91} These authors suggested needle placement 4 centimeters lower where obstruction to the sciatic nerve occurred in only 5\% of the patients.

Dalens et al.\textsuperscript{92} has compared the success rate of the posterior, lateral, and anterior approaches to the sciatic nerve in children. Although they had a success rate of 90\% with all approaches, the authors reported fewer manipulations were required to perform either a lateral or posterior approach compared with the anterior approach. Recently, Chowdary and Splinter\textsuperscript{93} reported on a medial approach to the sciatic nerve at the level of the lesser trochanter in only 10 children. Advantages of this approach are the lack of obstruction from the femur and no muscle mass to transverse. The authors reported a 70\% rate of blockade of the posterior cutaneous nerve of the thigh with this medial approach.

di Benedetto et al.\textsuperscript{94} described their experience in 135 consecutive patients using a posterior subgluteal approach to the sciatic nerve. The time to perform the block was 41 ± 25 seconds (mean ± SD), with an average of 2 needle redirections. The degree of discomfort reported was very low and only 16 patients (12\%) reported severe pain during placement of the block. In contrast to this, Fanelli et al.\textsuperscript{95} reported patient discomfort in 88\% of patients receiving a classic Labat approach to the sciatic nerve.

Sciatic Nerve Block at the Level of the Popliteal Fossa

Popliteal fossa block is chiefly used for foot and ankle surgery.\textsuperscript{96-98} Short saphenous vein stripping may also be performed under combined popliteal and posterior cutaneous nerve block.\textsuperscript{99} The block has also been successfully used in the pediatric population.\textsuperscript{100} Popliteal fossa block anesthetizes the entire leg below the tibial plateau save the skin of medial aspect of the calf and foot (i.e., saphenous nerve distribution). Potential advantages of popliteal block over ankle block are improved calf tourniquet tolerance and immobile foot. The components of the sciatic nerve may be blocked at the level of the popliteal fossa via posterior or lateral approaches. Patient positioning—prone, lateral (operative side nondependent), or supine (with leg flexed at the hip and knee)—may determine the optimal approach for an individual patient.\textsuperscript{101} Continuous techniques have been described using both the posterior\textsuperscript{102-104} and lateral\textsuperscript{105} approaches.

The classic posterior approach to the popliteal fossa is accomplished with the patient positioned prone (Fig 7). Traditionally, the sciatic nerve is located 5 cm above the popliteal crease.\textsuperscript{96} However, to block the sciatic nerve before its division, a 7- to 10-cm distance has been recommended.\textsuperscript{97,98,106-108} With a large-volume single-injection technique, inversion is the motor response that best predicts complete neural block of the foot.\textsuperscript{109} A lateral approach to blockade of the sciatic nerve in the popliteal fossa has been described.\textsuperscript{110-112} Because the common peroneal nerve is located more superficially than the tibial nerve, the stimulating needle encounters it first (Fig 8).

Success rate with all approaches is typically 90\% to 95\%, with approximately 5\% of patients requiring supplemental general anesthesia. It is believed that incomplete block is the result of poor diffusion (because of the size of the sciatic nerve), the separate fascial coverings of the tibial and peroneal nerves, or blockade of only a single component of the sciatic nerve. This has led some practitioners to endorse the practice of dual stimulation to improve success rate\textsuperscript{110} (see Multistimulation versus single-stimulation techniques).

Continuous Sciatic Nerve Blocks

Continuous sciatic nerve blockade can theoretically be achieved at any place along the course of the sciatic nerve. These blocks have been used for analgesia after major foot and ankle reconstruction, ankle fracture fixation, and below the knee amputation.\textsuperscript{102,103,113-115} Several studies have been published on the use of continuous popliteal blocks for analgesia after extensive foot and ankle surgery.\textsuperscript{102-104} All studies reported excellent analgesia with few side effects. Compared with intravenous analgesia or placebo infusion, a continuous infusion of local anesthetic via a popliteal catheter reduces pain scores and opioid consumption, and decreases sleep disturbances.\textsuperscript{102,103} Successful catheter placement has been reported with both lateral and posterior approaches. The only consistent problem reported with popliteal catheters is a high incidence (15\%-25\%) of kinking or dislodgement.\textsuperscript{102,103}

di Benedetto et al.\textsuperscript{113} compared the subgluteal approach to the posterior popliteal approach for continuous infusions in a prospective study. In the 24-hour observation period after surgery, 13.3\% of the catheters in the popliteal group were either occluded or dislodged compared with 6.6\% of the catheters in the subgluteal group. This difference did not reach statistical difference.

Ankle and Foot Block

Indications for blockade of the terminal nerves of the lumbosacral plexus distally, at the ankle and
midtarsal levels, include anesthesia for surgery to the foot.116,117 Diagnostic block has also been described.118 The peripheral nerves blocked at these levels are terminal branches of both the sciatic (posterior tibial, superficial peroneal, deep peroneal, and sural) and femoral (saphenous) nerves.

The 5 peripheral nerves that supply the foot are relatively easy to block at the ankle (Fig 9). There are no important variants in the innervation of the distal musculature. However, there is considerable variation in the branching and distribution of the sensory nerves of the foot. For this reason, blockade of all 5 nerves has been advocated.119 Neural blockade of the posterior tibial nerve has been described at the supramalleolar,119-121 midmalleolar,116 subcalcaneal,122,123 and midtarsal124 levels with no evidence of superiority of any technique.

Few studies evaluating perioperative outcomes with ankle block exist,125 although the technique has been performed for decades.83 Rather, most publications describe variations to improve success rate. Peak blood levels of local anesthetic occur around 90 minutes after blockade and are very low even after bilateral ankle block.126

Intravenous Regional Anesthesia of the Lower Extremity

Intravenous regional anesthesia (IVRA) may be used for foot, ankle, and knee surgery lasting up to 1 hour.127 It may also be used for treatment of complex regional pain syndrome in the lower limb.128 In a questionnaire survey,129 most responding anesthesiologists (>80%) acknowledge that lower limb IVRA is seldom performed for surgical anesthesia because of a lack of clinical experience. Other reasons for its lack of popularity include difficulty in locating veins in the foot or ankle, thigh tourniquet pain, and perceived requirement of a larger, potentially unsafe, local anesthetic dose than for upper limb IVRA.

The technique for lower limb IVRA involves application of a double pneumatic thigh cuff after proper padding and establishment of a venous access on the dorsum of the foot or around the ankle with a 20- to 22-G cannula. The greater saphenous vein is often the most suitable vein. After limb elevation for several minutes and exsanguination with an Esmarch bandage, the proximal tourniquet is inflated to 100 mm Hg above the limb occlusion pressure (min 300 mm Hg). Most commonly, lidocaine 0.25% is injected to a maximum of 3 mg/kg over several minutes. This yields a large injected volume of up to 1.2 mL/kg (e.g., 84 mL for a 70-kg subject).127,130 The recommended inflation time is 20 minutes minimum and 90 minutes maximum.

Alternatively, a calf tourniquet can be used for foot and ankle surgery.131 In this case, a single cuff is applied at least 3 inches below the head of fibula to avoid common peroneal nerve injury. A proximal “back up” cuff is placed on the thigh in case of drug leakage. A double cuff in the calf is generally not advisable because tapering calf curvature prevents a firm fit and risks accidental cuff slippage. Clinical experience suggests that lidocaine 0.5% up to 3 mg/kg and 0.6 mL/kg provides consistent surgical anesthesia within 10 minutes.

An intercuff IVRA technique has been described for knee arthroscopy achieved successfully with 40 mL lidocaine 0.5%.132 This technique involves inflation of a double-cuffed tourniquet in the thigh after exsanguination, injection of local anesthetic through a foot cannula, then application of a single cuff in the calf, and re-exsanguination of the foot before inflation of the calf tourniquet. This technique allows surgical anesthesia to be most concentrated around the knee joint. At the end of surgery, the calf cuff is deflated first, allowing residual local anesthetic to empty into the foot before release of the proximal thigh cuff.

Comparisons Between Approaches to the Sacral Plexus

PSNB Versus Classic Sciatic Nerve Block

Cuvillon et al.133 reported on 150 patients presenting for lower-extremity surgery using PNB. For the sciatic component of their anesthetic, the patients were randomized to receive a PSNB, a single-injection sciatic nerve block as described by Winnie, or a double-injection sciatic nerve block as described by Winnie. The onset time and success rate were similar in the PSNB and double-injection groups and were superior to the single-injection group in this report (Fig 12). The authors attributed this high rate of success with the PSNB to its proximal location with the potential for blockade of additional branches of the sacral plexus, although this was not evaluated in the study design.

Sciatic Block at the Gluteus Maximus Versus Sciatic Block at the Popliteal Fossa

Kilpatrick et al.134 compared the classic sciatic block with popliteal fossa block in patients undergoing foot surgery. All blocks were performed using a nerve stimulator technique. Popliteal fossa blocks were less painful because the sciatic nerve is no longer covered by thick musculature at this level. However, the success rate was lower with the popliteal approach (45%) than with the classic (95%). Using more modern techniques, a comparison of
classical, subgluteal, and lateral popliteal approaches showed similar success rates (96%, 92%, and 96% respectively) but slower onset time for the lateral popliteal group compared with the more proximal approaches. This difference was attributed to the greater distance separating the components of the sciatic nerve as it traverses through the popliteal fossa.

**Posterior Versus Lateral Approaches to the Sciatic Nerve Block at the Popliteal Fossa**

Hadzic and Vloka evaluated the ease of performance and efficacy of the lateral and posterior approaches to the sciatic nerve in the popliteal fossa. All blocks were performed using a single-stimulation nerve stimulator technique. Either a tibial or common peroneal response was accepted. Onset and quality of block was comparable; there was no difference in the success rate between the 2 groups. However, time to complete the block was slightly longer with the lateral approach (mean, 8 minutes; range, 1-17 minutes) compared with the posterior approach (mean, 6 minutes; range, 1-16 minutes).

**Popliteal Fossa Block Versus Subcutaneous Infiltration After Foot Surgery**

McLeod et al. prospectively evaluated the use of popliteal fossa block using the lateral approach and subcutaneous wound infiltration in providing postoperative analgesia for ambulatory foot surgery. All blocks were performed after induction of general anesthesia. In both groups, the local anesthetic consisted of 20 mL 0.5% bupivacaine. There was no difference in the pain scores in the recovery room or at the time of hospital dismissal. However, during the first 24 hours postoperatively, only 14% of patients in the popliteal fossa block rated their pain as severe, whereas 60% of patients with subcutaneous infiltration complained of severe pain. The duration of analgesia was also significantly longer in the popliteal fossa group, 18 hours compared with 6 hours. The authors concluded that popliteal fossa block provided effective analgesia and was associated with a high level of patient satisfaction. A recent review also recommended popliteal fossa block as the technique of choice in patients undergoing major foot or ankle surgery.

**Comparisons of Nerve Localization Techniques**

**Nerve Stimulation Versus Paresthesia Techniques for Lower-Extremity PNB**

There are few studies directly comparing success rate with paresthesia techniques versus peripheral nerve stimulation (PNS) techniques in lower-extremity PNBs. However, PNS provides a success rate comparable to earlier reports of paresthesia techniques. In addition, it may improve patient comfort during block performance. However, its biggest advantage may be the redirection cues that are provided to the operator.

**Redirection Cues**

Lower-extremity PNBs generally tend to be deeper blocks than most approaches to the brachial plexus. Perhaps one of the most compelling reasons for using PNS during lower-extremity PNB is the valuable "redirection cues" obtained during initial unsuccessful passes of the needle. For example, when performing a sciatic nerve block in the gluteal region, one may observe knee flexion as a result of stimulation of the superior gluteal nerve. This likely indicates that the needle is posterior, lateral, and
Multistimulation Versus Single-Stimulation Techniques

Multiple-stimulation techniques by definition require individual stimulation of each component of a peripheral nerve with deposition of a small volume of local anesthetic at each site. For instance, during performance of a sciatic block a peroneal motor response is elicited first and a small volume of local anesthetic is deposited. The needle is then redirected medially to obtain a tibial nerve motor response with subsequent deposition of additional local anesthetic. Whether the search for individual components of a PNB versus identification of a single component will become the norm for PNB is not clear. Advocates of multiple-stimulation techniques believe the technique increases the success rate and allows an injection of a smaller volume of local anesthetic. Advocates of single injection techniques believe multistimulation and injection techniques may add risk of nerve injury during redirection of the needle through partially anesthetized nerves.

Several studies have supported the clinical utility of multiple-stimulation technique. Paqueron et al. compared the block characteristics in patients undergoing popliteal fossa block with the lateral approach using either a single injection (inversion response) or a double injection (both common peroneal and tibial components identified). A total of 20 mL local anesthetic was injected. Double stimulation was associated with a higher success rate than single stimulation, 88% versus 54%, respectively. The onset time of complete sensory block was also reduced with the double-stimulation technique. Similar results were reported for multiple-stimulation sciatic nerve blocks by other investigators. No neurologic complications have been reported in any of these studies.

Casati et al. showed that a lower volume of local anesthetic could be used for femoral nerve block when comparing multi-injection technique to single injection in a prospective randomized and blinded study. In this study, multiple stimulation of the femoral nerve involved injecting on each of 3 stimulations, the vastus medialis, vastus intermedius, and vastus lateralis, compared with a single injection on a vastus intermedius stimulation. Using a staircase method to determine the volume of local anesthetic required to produce a sensory and motor block within 20 minutes, the authors found a 27% reduction in volume in the multistimulation group. Whether this difference in volume (total of 9 mL) will improve safety is unknown.

In each of these reports the issue of safety, specifically the risk of nerve injury, when using a multistimulation injection technique has been raised. There were no reported nerve injuries in these studies performed by experienced regional anesthesiologists. This is in agreement with the large cohort of patients studied by Fanelli et al. using multistimulation techniques in over 2,000 patients with no nerve injury attributed to nerve block. However, nerve injury is a rare event after PNB and even in a study of this size may not have a large enough sample size to determine the relative risk of multiple versus single injection techniques.

Imaging Aids

Several investigators have examined the use of imaging technology to improve localization of both the lumbar plexus and the femoral nerve. Kirchmair and colleagues showed the usefulness of ultrasound in localizing the psoas major using a curved array transducer at low (4-5 MHz) frequency. The location of the lumbar plexus is then inferred. It is not possible to distinguish peripheral nerves from tendon fibers with the ultrasound technology currently commercially available. The main limitations to visualization in this volunteer study were obesity and occasional high riding iliac crests in male patients. In a follow-up study, ultrasound guidance was used to place needles in the lumbar plexus of cadaveric specimens. CT scan verified the accuracy of needle placement in all cases. Of the 60 attempts the psoas major was visualized in 48 specimens and the needle successfully placed in 47. Again obesity, spinal deformities, and conditions related to embalming of the cadavers were the main limitations for use of this technique.

Marhofer et al. compared the use of ultrasound guidance to nerve stimulation during femoral nerve blocks. These investigators found that ultrasound guidance was superior to nerve stimulation because it allowed the use of a smaller volume of local anesthetic and shorter latency period. The authors attributed this difference to the ability to visualize the administration of the local anesthetic during injection. They used ultrasound to reposition the needle when the local anesthetic spread out of the fascial plane and away from the nerve. It should be noted that ultrasound failed to identify the femoral nerve in a small number of patients in each of these studies.
Local Anesthetic Choices and Dosing of Lower-Extremity PNB

Pharmacologic Considerations

Selection of a local anesthetic solution for lower-extremity blocks differs somewhat from that of upper-extremity approaches because of the indications and applications of each. For example, upper-extremity blocks are commonly performed as the intraoperative anesthetic. In addition, pain after surgery to the upper extremity may not be as severe or protracted. As a result, intermediate-acting local anesthetics and local anesthetic mixtures are frequently selected for surgery to the arm. These principles may not apply to lower-extremity surgery in which peripheral blockade is often supplemented with a neuraxial or general anesthetic intraoperatively, and the need for sustained postoperative analgesia is achieved with long-acting amides administered either as single injections or continuous infusions. Finally, although the use of adjuvants such as clonidine, opioids, and ketorolac is common during lower-extremity peripheral techniques, their efficacy in improving the quality or duration of blockade has not been consistently shown.

Local Anesthetic Selection. Few randomized studies have compared local anesthetics for lower-extremity block. Fanelli et al. evaluated the onset and duration of combined femoral-sciatic block performed with 0.75% ropivacaine, 0.5% bupivacaine, or 2% mepivacaine. Ropivacaine had an onset similar to that of mepivacaine but with a duration of analgesia between that of bupivacaine and mepivacaine. Connelly et al. reported no significant clinical differences between 0.75% ropivacaine and 0.5% bupivacaine for sciatic nerve blockade. When equipotent (rather than equivalent) concentrations were compared, onset times for the 2 local anesthetics showed no differences in onset times for sensory and motor block. However, the times to block regression and first analgesia were slightly longer with bupivacaine. In a single comparative study of sciatic block, levobupivacaine has block characteristics similar to ropivacaine.

Epinephrine. Epinephrine prolongs the duration and quality of most local anesthetics used for lower-extremity peripheral block. The effects are the result of vasoconstriction of the perineural vessels, which decreases uptake and thereby increases the neural exposure to the local anesthetic. However, the difference is only somewhat dose dependent. The addition of epinephrine 5 μg/mL (1:200,000 dilution) significantly increases the duration of lidocaine from 186 minutes to 264 minutes. Although epinephrine 2.5 μg/mL (1:400,000 dilution) prolongs the block to nearly the same extent (240 minutes), it has no effect on nerve blood flow. The addition of epinephrine to local anesthetics with vasoconstrictive properties, such as ropivacaine, may not increase block duration but would still facilitate detection of intravascular injection. The decision to add epinephrine (and the dose of epinephrine) is based on the concerns related to cardiac or neural ischemia versus the ability to discern an intravascular injection. In general, because seizures related to intravascular injection were highest in patients undergoing peripheral nerve block, the benefits of adding epinephrine outweigh the risks. However, the nearly equivalent effects on block quality and duration reported with epinephrine 2.5 versus 5.0 μg/mL suggest that the lower concentration is optimal, particularly in patients theoretically at risk for nerve injury (diabetics, patients with chemotherapy-induced neuropathy).

Bicarbonate. The addition of bicarbonate has been recommended to increase the speed of onset of peripheral and plexus blockade. However, most studies that have shown statistically significant differences used commercially prepared epinephrine-containing solutions of local anesthetics (which have a much lower pH due to the addition of antioxidants) compared with plain local anesthetic solutions. A recent review of the literature involving brachial plexus block concluded that there was little reason to add sodium bicarbonate with plain local anesthetics or those with freshly added epinephrine. These results were substantiated in a study by Candido et al., which reported no difference in the onset or duration of combined lumbar plexus-sciatic block in patients that received 0.5% bupivacaine with alkalinization compared with those who received a non-alkalinized solution.

Clonidine. Clonidine has been extensively investigated as an adjuvant for brachial plexus block. Prolongation of analgesia after the addition of clonidine is most likely peripherally mediated and dose dependent. During intravenous regional anesthesia, clonidine 150 μg may improve tourniquet tolerance. Side effects such as hypotension, bradycardia, and sedation do not occur with a dose less than 1.5 μg/kg or a maximum dose of 150 μg. Clonidine as an adjuvant for lower-extremity block is much less defined. The limited data for lower-extremity techniques validates those of previous upper-extremity reviews. The results are most notable with intermediate-acting agents. A single study has compared the effect of lower-extremity peripheral block with/without clonidine. Casati et al. reported the addition of clonidine 1 μg/kg to 0.75% ropivacaine for patients undergoing foot surgery under sciatic-femoral block prolonged the time to first analgesia from 13.5 to 16.8 hours. Clonidine is often a component of lumbar plexus or
sciatric continuous infusions after hip, knee, or foot surgery. However, the efficacy has not been established. A single study involving a continuous brachial plexus infusion of ropivacaine with or without clonidine failed to show a clinically significant effect.

Opioids

To date, there are no comparative studies evaluating the effect of opioids as adjuvants to lower-extremity single-dose or continuous techniques. Despite this lack of data, opioids, including morphine, sufentanil, and fentanyl, are often added to lumbar plexus infusions. Investigations involving the brachial plexus report no difference in block onset, quality, or duration when opioids are added to the local anesthetic solution. A recent review concluded that the role of opioids in peripheral nerve block is not clinically relevant.

Other Adjuvants

Most studies investigating adjuvants such as neostigmine, hyaluronidase, and tramadol involve upper-extremity blocks. A single study evaluating the efficacy of nonsteroidal antiinflammatory drugs as adjuvants reported that the addition of ketorolac to lidocaine for ankle block resulted in longer duration and improved analgesia after foot surgery compared with intravenously administered ketorolac.

In summary, selection of a local anesthetic solution for lower-extremity peripheral blockade requires thoughtful consideration and is based on the duration of surgery, analgesic requirements, and anticipated rehabilitative efforts. The lowest effective dose and concentration should be used to minimize local anesthetic systemic and neural toxicity. Likewise, the addition of 1:200,000 or 1:400,000 epinephrine is recommended to facilitate detection of intravascular injection, as well as decrease local anesthetic levels. The role of other adjuvants is less defined; additional studies are required to determine the efficacy of clonidine, opioids, tramadol, and nonsteroidal antiinflammatory drugs in single-dose or continuous lower-extremity techniques.

Complications of Lower-Extremity Peripheral Nerve Blocks

Complications associated with peripheral nerve blockade are not common. Auroy and colleagues prospectively evaluated serious complications after 21,278 PNBs in a 5-month period in France. Using a 95% confidence interval, they estimated the potential for serious complications per 10,000 PNBs to be 0 to 2.6 deaths, 0.3 to 4.1 cardiac arrests, 0.5 to 4.8 neurologic injuries, and 3.9 to 11.2 seizures. There is a paucity of reports of complications specifically associated with lower-extremity PNBs as compared with upper-extremity PNBs. This is most likely related to their less common application rather than to inherent safety of the techniques.

Local Anesthetic Systemic Toxicity. The potential for systemic local anesthetic toxicity would seem to be very high for lower-extremity PNBs. Relatively large doses of local anesthetic are used for combined femoral and sciatic nerve blocks to anesthetize the entire lower extremity. However, there are only a few case reports of local anesthetic toxicity associated with lower-extremity PNBs. For instance, in Fanelli and colleagues’ series of 2,175 patients undergoing femoral sciatic combined blocks, there were no systemic adverse local anesthetic reactions reported. The apparent margin of safety seems to vary with individual block techniques. For instance, there are no case reports of toxicity after popliteal sciatic blockade, whereas there are several case reports of severe toxicity following lumbar plexus and proximal sciatic blocks. Anatomic differences in the anatomy, primarily in the vascularity and presence of deep muscle beds in the area of blockade, are the most likely explanation for this discrepancy. Severe toxic reactions typically occur during the injection or immediately thereafter. This suggests that the mechanism of these events is commonly an unintentional intravascular injection of local anesthetic into the circulation, rather than absorption. A forceful injection of local anesthetic carries a much higher risk of local anesthetic toxicity than a slow, gentle injection. This is because the mean dose of local anesthetic that elicits the signs of central nervous system toxicity is much less during rapid intravascular injection as compared with that associated with slower absorption after appropriate deposition. After a lower-extremity peripheral nerve block, local anesthetic levels peak at approximately 60 minutes after deposition (Fig 13). Perhaps this slow time to peak blood levels offers an explanation for the low incidence of toxic complications associated with absorption. Important measures to decrease the risk of severe toxicity include the use of epinephrine as an intravascular marker, slow methodical injection while avoiding high-injection pressure, frequent aspiration, constant assessment of the patient and vital signs, and prudent selection of local anesthetic concentration and volume.

Proximal Spread (Neuraxial Block). A potential needle misadventure of proximal peripheral nerve blocks is infrasacular spread of the local anesthetic proximally toward the spinal cord, resulting in neuraxial blockade. This is a...
particular concern with block techniques that involve needle placement at the level of the nerve roots or spinal nerves, such as paravertebral, and psoas compartment block. Forceful, fast injections within the dural cuffs or perineurium can result in unintentional spinal or epidural anesthesia. In their large series of severe complications associated with regional anesthesia, Auroy and colleagues found the posterior approach to the lumbar plexus to have the highest incidence of complications of the lower extremity PNBs. With only 394 posterior lumbar plexus blocks reported, there were 5 serious complications in this cohort. Three of these complications, 1 cardiac arrest and 2 respiratory arrests, were directly attributed to central placement or diffusion of the local anesthetic to the epidural or intrathecal space. Their recommendation was to manage this block with the same degree of vigilance as for a neuraxial block.

**Hemorrhagic Complications.** Several approaches for PNBs of the lower extremity involve deep needle penetration. These approaches include the psoas compartment approach to the lumbar plexus, the obturator nerve block, and the parasacral and classical approaches to the sciatic nerve. Despite the proximity of these deep nerves to vascular and hollow viscous structures, there are relatively few reports of needle misadventures. Vascular puncture during femoral nerve block placement has been reported to be as frequent as 5.6%. However, few complications were reported after unintentional vascular puncture during femoral nerve block. Kent et al. reported a 0.2% (20/9,585) incidence of neuropathy after cardiac catheterization. Sixteen of these patients developed neuropathies from large retroperitoneal hematomas. Twenty percent of these patients had persistent, mild sensory, or motor neuropathy at long-term follow-up. The other 4 patients had groin hematomas. In all of these patients, the neuropathy resolved.

Retroperitoneal hematoma formation after psoas compartment block has been reported by several investigators. To reach the lumbar plexus, the needle must transverse multiple muscle and other tissue layers. The combination of its deep location and inability to apply pressure after an inadvertent puncture of deeply situated blood vessels supplying the local muscles and other structures may make this block less suitable in the setting of anticoagulation as compared with other more superficial lower extremity nerve blocks. Conservative management of retroperitoneal hematoma is recommended unless the patient develops hypotension unresponsive to volume resuscitation.

**Infectious Complications.** There are no case reports of infection after single-injection, lower-extremity PNBs. Cuvillon et al. reported on the incidence of bacterial complications associated with the use of continuous femoral nerve blocks. In their cohort of 208 patients, 57% had positive bacterial colonization of the catheter at 48 hours postoperatively. Three patients had transitory symptoms of bacteremia that resolved with removal of the catheter. There were no long-term sequelae related to these positive catheter cultures. Two case reports of psoas abscess requiring drainage and intravenous antibiotic therapy has been reported in patients who received a continuous femoral nerve block.

**Neurologic Complications**

Although there are relatively few published reports of anesthesia-related nerve injury associated with the use of PNBs, it is likely that the incidence is underestimated. The less frequent clinical application of lower-extremity nerve blocks may be the main reason that there are even fewer reports of anesthesia-related nerve injury associated with lower-extremity PNBs as compared with upper-extremity PNBs.

Neurologic complications after lower-extremity PNB can be related to a variety of factors related to the block including needle trauma, intraneuronal injection, and neuronal ischemia. However, a search for other causes should include surgical factors such as positioning, retractor injury, and hematoma formation. In many instances, the neurologic injury may be a result of a combination of these factors.
Peripheral Nerves: Functional Anatomy and Mechanisms of Nerve Injury. The functional anatomy of the peripheral nerve is important for understanding the mechanisms of peripheral nerve injury. A peripheral nerve is a complex structure consisting of fascicles held together by the epineurium, an enveloping, external connective sheath (Fig 14). Each fascicle contains many nerve fibers and capillary blood vessels embedded in a loose connective tissue, the endoneurium. The perineurium is a multilayered epithelial sheath that surrounds individual fascicles. Nerve fibers depend on a specific endoneurial environment for their function. This is different than the extraneural interstitium. Peripheral nerves are richly supplied by an extensive vascular network in which the endoneurial capillaries have endothelial “tight junctions,” a peripheral analogy to the “blood-brain barrier.” The entire neurovascular bed is regulated by the sympathetic nervous system and its blood flow can be as high as 30 to 40 mL/100 g per minute.188 In addition to conducting nerve impulses, nerve fibers also maintain axonal transport of various functionally important substances, such as proteins and precursors for receptors and transmitters. This process is highly dependent on oxidative metabolism. Any of these structures and functions can be deranged during a traumatic nerve injury, with the possible result of temporary or permanent impairment or loss of neural function.

Direct Needle Trauma. Most needles available for PNBs are manufactured as short-bevel needles (i.e., angles 30°-45°). The needle designs are largely based on the work of Selander and colleagues, who showed that the risk of perforating a nerve fascicle was significantly lower when a short-bevel (45°) needle was used compared with a standard long-bevel (12°-15°) needle. In contrast, the work of Rice and McMahon suggested that the short-beveled needles might cause more mechanical damage than the long-beveled needles when purposefully advanced through a nerve in vitro. In their experiment, after deliberately penetrating the largest fascicle of rat sciatic nerves with 12° to 27° beveled injection needles, the degree of neural trauma on histologic examination was greater with short-beveled needles. The sharp needles produced clean cuts and the blunt needles produced noncongruent cuts on the microscopic images. In addition, the cuts produced by the sharper needles recovered faster and more completely than the irregular, more traumatic injuries caused by the blunter short-beveled needles. Despite the lack of consistent data and no randomized controlled trials in humans, the theoretical advantage of short-beveled needles in reducing the risk of nerve penetration has had an influence on manufacturers and practitioners. Most needles manufactured for PNB placement are, today, short-beveled needles.

The clinical significance of isolated, direct needle trauma, however, remains unclear. For instance, during femoral arterial cannulation, it is likely that the needle is often inserted into the femoral nerve, yet injuries to the nerve are rare, and are usually attributed to hematoma formation.184 It is possible that a needle-related trauma without injection results in injury of a lesser magnitude, which readily heals and may go undetected. In contrast, needle trauma coupled with injection of local anesthetic into the nerve may carry a risk for much more severe injury.

Intraneural Injection. Little is known about how to avoid or recognize insertion of a needle into a nerve or how to avoid an intraneuronal injection. Pain with injection has long been cited as the cardinal sign of intraneuronal injection. However, multiple case reports of neurologic injury suggest that pain may not be reliable as a sole warning sign of impending nerve injury.191-194 Experimental evidence suggests that intraneuronal injection may be associated with pain on injection but also with a resistance to needle advancement or an increased pressure on injection of local anesthetic.195 In a model of nerve injury by Selander et al., a pressure of at least 19 psi was required to inject solution into a nerve fascicle of a rabbit sciatic nerve. Injec-
Neuronal Ischemia. The perineurium is a tough and resistant tissue layer. An injection into this compartment or a fascicle can cause a prolonged increase in endoneural pressure, exceeding the capillary perfusion pressure. This pressure, in turn, can result in endoneural ischemia. The addition of vasoconstricting agents theoretically can enhance ischemia because of the resultant vasoconstriction and reduction in blood flow. The addition of epinephrine was shown in vitro to decrease the blood supply to intact nerves in the rabbit. However, in patients undergoing lower-extremity surgery, the addition of epinephrine to the local anesthetic solution used in combined femoral and sciatic nerve blocks was not shown to be a risk factor for the development of post-block nerve dysfunction.

Risk Factors for Neuropathy After PNB

Few investigations exist regarding neurologic complications associated with lower-extremity PNB. The American Society of Anesthesiologists’ closed-claims analysis of nerve injury associated with anesthesia showed a consistently low report of sciatic (5% of nerve injury claims) or femoral (2% of nerve injury claims) injuries. Postoperative neurologic complications were more frequently reported after general anesthesia, 61% of the claims, and neuraxial anesthesia than after PNB. In this analysis, there was no specific discussion of lower-extremity neuropathy associated with PNB.

In the report by Auroy and colleagues, there were 4 neurologic injuries reported after PNB. The type of block performed and the nature of the injury are not reported. All of the neurologic injuries were reported within the first 48 hours postoperatively. All of these patients reported paresthesias during block placement or pain with injection. In all cases, the injury had the same topography as the associated paresthesia or pain. Fanelli et al. reported on 2,175 combined sciatic-femoral nerve blocks performed using a nerve stimulator and a technique of multiple injections. Consistent with the report of Auroy and coworkers, they reported an incidence of transient neurologic dysfunction in 1.7% of patients. There were no permanent neurologic injuries reported in this large cohort of patients. The only variable correlated with the development of postoperative neurologic dysfunction was tourniquet inflation pressure of >400 mm Hg. Unintended paresthesia was reported in 14% of patients in the Fanelli et al. study. By study protocol, no local anesthetic was injected if a paresthesia occurred. Univariate analysis of potential risk factors for postoperative neurologic dysfunction did not demonstrate paresthesia as a risk factor. Indeed, in a more recent study from France, a nerve stimulator was used in 9 of 12 documented nerve injuries. This suggests that the mechanism of nerve injury may be related to some events during and after the injection (e.g., intraneural injection), rather than to the method of nerve localization.

Blocks Performed in Anesthetized Patients. There are a several individual case reports of neuropathy after femoral or fascia iliacus block performed with a nerve stimulator or using a fascial click technique in anesthetized patients. Although proper sedation and analgesia are essential ingredients for block success, maintenance of meaningful patient contact allows the patient to report pain or paresthesia on injection and may provide an additional margin of safety.

Other Etiologies of Perioperative Lower-Extremity Neurologic Complications. Nerve injuries are frequently attributed to the use of PNBs. However, neuropathy after abdominal or lower-extremity surgery is relatively common. There are a number of factors that have been implicated in the development of lower-extremity neuropathy. These factors include positioning, surgical factors, hematoma formation, compartment syndrome, and tourniquet palsy.

Positioning. Positioning injuries are thought to be caused mostly by compression or stretching of the nerve(s) or plexi as a result of patient positioning. Of the sciatic nerve injury claims in the closed-claims analysis of nerve injury associated with anesthesia, half were associated with the lithotomy or frog-leg operative positions. In a prospective study of lower extremity neuropahties associated with the lithotomy position, nerve injury to the obturator, lateral femoral cutaneous, and sciatic nerves were observed. Femoral nerve palsy is associated with deep hip flexion and extension associated with THA and repair of acetabular fractures. Positioning nerve injuries are consistently correlated with the length of surgery.
Surgical Factors Leading to Neuropathy. Some surgical procedures are associated with a high rate of nerve injury. For instance, femoral neuropathy is associated with operations that require deep pelvic exposure including acetabular fracture repair, in which the femoral nerve is relatively superficial and vulnerable to compression by retractors. An incidence of nerve injury as high as 17% after ankle arthroscopy has been reported. Tourniquet-induced neuropathy is well documented in the orthopedic literature and ranges from mild neuropraxia to permanent neurologic injury. The incidence of tourniquet paralysis has been reported as 1 in 8,000 operations. A prospective study of lower-extremity nerve blockade suggested that higher tourniquet inflation pressure (>400 mm Hg) was associated with an increased risk of transient nerve injury. Current recommendations for appropriate use of the tourniquet include the maintenance of a pressure of no more than 150 mm Hg greater than the systolic blood pressure and deflation of the tourniquet every 90 to 120 minutes. Even with these recommendations, posttourniquet application neuropathy may occur, particularly in the setting of preexisting neuropathy.

Compartment Syndrome. A single case of compartment syndrome after revised forefoot arthroplasty under ankle block has been reported. The diagnosis was delayed secondary to residual local anesthetic effects. However, prompt surgical intervention prevented long-term sequelae. This report emphasizes the need for vigilance in monitoring block resolution and patient positioning in the postoperative period. Consultation with the surgical team is of utmost importance when making a decision on the use of nerve blocks and their duration in patients with a risk of developing compartment syndrome.

Tourniquet Neuropathy. Tourniquet-induced neuropathy is associated with both needle misadventures during performance of lower extremity PNB and anticoagulation. As opposed to spinal or epidural hematoma, in all cases, neuropathy from this etiology has resolved completely. Little data exist regarding the safety of peripheral nerve block in anticoagulated patients. The American Society of Regional Anesthesia and Pain Medicine has published guidelines regarding this issue. However, these reports emphasize the important differences in the risk-benefit ratio of peripheral nerve blocks compared with neuraxial blocks in patients receiving anticoagulant therapy.

Evaluating the Patient After Lower-Extremity Peripheral Nerve Block

Assessment of Lower-Extremity PNBs

Neal has proposed a simple and effective system for assessing the adequacy of lower-extremity PNBs (Fig 15A-D). Based on a well-known system for assessing the upper extremity, the lower-extremity evaluation uses 4 Ps: push, pull, pinch, and punt. Push evaluates the adequacy of sciatic nerve block by asking the patient to push against the examiner’s hand or “to step on the gas” with their foot. Pull checks the strength of the adductors of the thigh to assess obturator nerve blockade. The examiner abducts the thigh and asks the patient to pull their thigh to the midline. Pinch refers to the evaluation of the lateral femoral cutaneous nerve. A pinch on the lateral proximal thigh will check the adequacy of blockade of the lateral femoral cutaneous nerve. Finally, punt assesses the degree of motor blockade in the femoral nerve distribution. The examiner supports the patient’s knee lifting it off the bed and asks the patient to punt an imaginary football. This maneuver requires quadriceps contraction to extend the leg and will be limited by femoral nerve blockade.

Discharge Criteria

The ability to ambulate independently is an important consideration for patients receiving lower extremity PNBs. Klein et al. have examined the controversy of long-lasting analgesia versus potential complications from insensitive extremities after PNB in ambulatory surgery patients. They prospectively studied 1,791 patients receiving either upper- or lower-extremity nerve block with ropivacaine 0.5% and being discharged home the same day. There was a single complication related to a fall after combined femoral and sciatic nerve blocks. The authors attributed the low rate of complications to the immobilization related to the surgical procedure and generally cautious nature of postsurgical patients. Sample discharge instructions for patients with single injection and continuous lower-extremity peripheral nerve blocks can be found in Table 5.

Future Directions

Lower-extremity peripheral nerve blocks provide unquestioned superiority of analgesia after lower-
Lower-extremity surgery compared with traditional intravenous narcotic therapy for the duration of the block. Research efforts directed toward extending the duration of analgesia that these techniques can provide should be supported. The current application of continuous infusion therapy with indwelling perineural catheters is probably just a first step toward this goal. Much work is needed to complete our understanding of the ideal delivery devices and infusates. Further efforts to prolong analgesia may include improved drug design, such as controlled release local anesthetics, or innovative additives.

Clearly, these techniques have a wider application for postoperative analgesia than is currently used. Further research efforts should be directed toward improving the ease of performing these techniques. Imagining devices that improve visualization of the structures to be anesthetized may decrease the failure rate, thereby increasing their use in many anesthesia practices.

Finally, although there is a paucity of reported complications following lower-extremity PNBs, they are not without risks. Further efforts to delineate the role of injection pressure and needle design on nerve injury should be supported. Local anesthetic toxicity still complicates the use of PNBs. Efforts to improve the early detection of intravascular local anesthetic injection would be welcomed by all practitioners. An antidote to local anesthetic overdose would be added to every formulary. We envision a future in which the use of lower-extremity PNBs is widely taught and applied by all anesthesiologists not just for regional anesthesia enthusiasts.

Fig 15. Assessment of lower-extremity nerve block by the Four P’s acronym. (A) Push; inability to plantar flex the foot against resistance indicates sciatic nerve blockade. (B) Pull: the anesthesiologist resists the patient’s attempt to adduct the leg toward the midline. Weakness signals conduction block of the obturator nerve. (C) Pinch: inability to detect a pinch on the proximal lateral thigh shows anesthesia within the lateral femoral cutaneous nerve distribution. (D) Punt: the anesthesiologist raises the knee and asks the patient to extend the knee against resistance. Inability to perform this task signals successful femoral nerve block. (Reprinted with permission.220 Copyright 2002 by the American Society of Regional Anesthesia and Pain Medicine.)
Table 5. Patient Instructions After Lower-Extremity Nerve Block

You have received an injection near one of your nerves in your leg to help you with your pain after surgery. Precautions that you should take are:

1. **DO NOT DRIVE** while your leg is numb.
2. You must use your walker, crutches, or wheelchair until the nerve block has worn off.
3. Keep your leg elevated as much as possible for the first 24 hours after surgery to help prevent swelling.
4. Keep your leg in the brace at all times except when doing physical therapy until your surgeon tells you to take it off.
5. Do not use heating pads on your leg while it is numb.
6. The numbness in your leg will wear off completely about an hour after you notice that you can feel tingling in the numb part. Please take your pain medications when the numbness begins to wear off and you feel the tingling.
7. If you are ready for bed and the numbness has not worn off, please take your pain medication before you go to bed.

Instructions for Patients Receiving Continuous Lower-Extremity Blocks

Your anesthesia doctor has placed a small tube near the nerve to your leg to decrease the pain you feel after surgery. This is a very effective way to control pain when it is added to the other pain medications your surgeon has given you.

Precautions you should use during this treatment are:

1. **DO NOT DRIVE** while you have the catheter in place.
2. You must use your walker, crutches, or wheelchair until the nerve block has worn off and the catheter has been removed.
3. Keep your leg elevated as much as possible for the first 24 hours after surgery to help prevent swelling.
4. Keep your leg in the brace at all times except when doing physical therapy until your surgeon tells you to take it off.
5. Do not use heating pads on your leg while it is numb.
6. The medication you are getting through the pump device is not as strong as the first medicine that you got. When the numbness begins to wear off, please push the extra medication button. Wait 15 minutes and then take your pain pills if you need more pain relief. Once the initial block wears off you should be able to wiggle your toes and make a muscle in your thigh.
7. If you have questions about the pump or your pain medications call the pager number given to you.

Acknowledgment

The authors would like to thank Anita Yeager, BS, Coordinator of Information/Publications Services in the Department of Anesthesiology at the University of Florida, for her calm aplomb in editing this beast of a manuscript. The authors also thank Dr Joseph M. Neal, Editor-in-Chief of *Regional Anesthesia and Pain Medicine*, for his patience with and guidance of this project. The authors thank you both wholeheartedly.

References


35. Mulroy MF, Larkin KL, Batra MS, Hodgson PS, Owens BD. Femoral nerve block with 0.25% or 0.5% bupivacaine improves postoperative analgesia following outpatient arthroscopic anterior cruciate ligament repair. *Reg Anesth Pain Med* 2001;26:24-29.


112. Vloka JD, Hadžić A, Kitain E, Lesser JB, Kuroda M, April EW, Thys DM. Anatomic considerations for

...


proach, with single- and double-injection techniques, to block the sciatic nerve. Anesthesiology 2003;98: 1436-1441.


171. Elmas C, Atanassoff PG. Combined inguinal para-
vascular (3-in-1) and sciatic nerve blocks for lower
172. Misra U, Pridie AK, McClymont C, Bower S. Plasma
centrations of bupivacaine following combined
sciatic and femoral 3 in 1 nerve blocks in open knee
Plasma concentrations after high doses of mepivacaine
with epinephrine in the combined psoas com-
partment/sciatic nerve block. Reg Anesth 1990;15:
256-260.
174. Scott DB. Evaluation of the toxicity of local anesthes-
175. Selander D, Sjostrand J. Longitudinal spread of intra-
neurally injected local anesthetics. An experimental
study of the initial distribution following intraneural
176. Singelyn FJ, Conterras V, Gouverneur JM. Epidural
anesthesia complicating continuous 3-in-1 lumbar
177. Gentili M, Aveline C, Bonnet F. Total spinal anes-
thesia complicating posterior lumbar plexus block.
178. Cuvillon P, Ripart J, Lalourcey L, Veyrat E,
L’Hemite J, Boisson C, Thouabtia E, Eledjam JJ. The
continuous femoral nerve block catheter for post-
operative analgesia: Bacteria colonization, infe-
tious rate and adverse effects. Anesth Analg 2001;93:
1045-1049.
179. Jörh M. [A complication of continuous femoral
180. Kent KC, Moscucci M, Gallagher SG, DiMattia ST,
Skillman JJ. Neuropathy after cardiac catheterization:
Incidence, clinical patterns, and long-term
Enoxaparin associated with psoas hematoma and
lumbar plexopathy after lumbar plexus block. Anes-
thesiology 1997;87:1576-1579.
182. Weller RS, Gerancher JC, Crews JC, Wade KL. Ex-
tensive retroperitoneal hematoma without neuro-
logic deficit in two patients who underwent lumbar
plexus block and were later anticoagulated. Anesthe-
184. Kent KC, Moscucci M, Mansour KA, DiMattia S,
Gallagher S, Kuntz R, Skillman JJ. Retroperitoneal
hematoma after cardiac catheterization: Prevalence,
risk factors, and optimal management. J Vasc Surg
185. Adam F, Jaziri S, Chauvin M. Psoas abscess compli-
cating femoral nerve block catheter. Anesthesiology
186. Bernstein IT, Hansen BJ. Iatrogenic psoas abscess.
187. Hadzić A, Vloka JD, Kuroda MM, Koonr D, Birnbach
Dj. The practice of peripheral nerve blocks in the
188. Selander D. Nerve toxicity of local anesthetics. In:
Lofstrom JB, Sjostrand U, eds. Local Anesthesia and
Regional Blockade. Amsterdam: Elsevier Science;
1988;77.
189. Selander D, Dhuner KG, Lundborg G. Peripheral
nerve injury due to injection needles used for re-
182-189.
190. Rice ASC, McMahon SB. Peripheral nerve injury
caused by injection needles used in regional anes-
thesia: Influence of bevel configuration, studied in a
191. Lim EK, Pereira R. Brachial plexus injury following
192. Bashein G, Robertson TH, Kennedy WF. Persistent
phrenic nerve paresis following interscalene bra-
193. Gillespie JH, Menk EJ, Middaugh RE. Reflex symp-
thetic dystrophy: A complication of interscalene
194. Fremling MA, Mackinnon SE. Injection injury to the
195. Selander D, Mansson GL, Karlsson L, Svanvik J.
Adrenergic vasoconstriction in peripheral nerves of
196. Hadzic A, Dilberovic F, Shah S, Mornjakovic Z,
Divanovic Kucuk-Alijia, Zulic I, Selak I, Kulenovic A.
Combination of intraneural injection and high
injection pressure leads to severe fascicular injury
and neurologic deficits in dogs. Reg Anesth Pain Med
197. Selander D. Peripheral nerve injury after regional
anesthesia. In: Finucane BT, ed. Complications of Re-
gional Anesthesia. Philadelphia: Churchill Living-
stone; 1999:105-115.
198. Cheney FW, Domino KB, Caplan RA, Posner KL.
Nerve injury associated with anesthesia: A closed
199. Bradshaw E, McHale S. Bupivacaine and femoral
200. Frerk CM. Palsy after femoral nerve block. Anaes-
201. McNichol LR. Palsy after femoral nerve block (let-
DR, Maxson PM. Lower extremity neuropathies as-
soiated with lithotomy positions. Br J Anaesth
203. Gruson KI, Moed BR. Injury of the femoral nerve
during total hip replacement: An explanation for iat-
204. Slater N, Singh R, Senasinghe N, Gore R, Goroszeniuk
T, James D. Pressure monitoring of the femoral nerve
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Relationship Between Ultrasound Imaging and Eliciting Motor Response During Femoral Nerve Stimulation

Antoun Nader, MD, Khalid Malik, MD, Mark C. Kendall, MD, Hubert Benzon, MD, Robert J. McCarthy, PharmD

Objective. Nerve stimulator-assisted localization of the femoral nerve is well described; however, direct ultrasound imaging of the femoral nerve branches may be challenging. The purpose of this study was to correlate the evoked motor responses obtained by femoral nerve stimulation and the topographic orientation of the femoral nerve branches during ultrasound examinations of the infringuinal region. Methods. Eighty-two patients undergoing total knee replacement were enrolled in this study. A 25-mm, 5- to 10-MHz broadband linear array transducer was used to identify the femoral nerve at the inguinal crease. The medial and lateral aspects of the femoral nerve were stimulated under ultrasound imaging. Twenty cadavers were dissected to support our clinical findings. Results. A quadriceps contraction was elicited in 1.2% and 96% of the patients when stimulating the medial and lateral aspects of the femoral nerve, respectively. In contrast, a sartorius muscle contraction was elicited in 94% and 0% when stimulating the medial and lateral aspects of the femoral nerve. Our findings during anatomic dissection revealed that the femoral nerve branch to the quadriceps muscle, when compared with the branch to the sartorius muscle, originated laterally in 95% and medially in 5% of the specimens. Conclusions. When using out-of-plane ultrasound imaging at the inguinal crease, directing the stimulating needle to the lateral half of the femoral nerve may be associated with a higher probability of encountering the motor branch to the quadriceps muscle. Key words: cadaver; femoral nerve; quadriceps; ultrasound.

Ultrasound imaging of the femoral nerve can be best achieved at the level of the inguinal region, where the nerve is found lateral to the femoral artery, ventromedial to the iliopsoas muscle, and lateral to the iliopectineal arch. Identification of the branches of the femoral nerve innervating the quadriceps and sartorius muscles on ultrasound imaging may be challenging at this location. Needle localization for local medication deposition near either branch of the femoral nerve is frequently performed by elicitation of their corresponding muscle contractions. The purpose of this study was to investigate the relative orientation of the motor branches of the femoral nerve visualized during ultrasound imaging and anatomic dissections.
Materials and Methods

After obtaining institutional approval and written informed consent, 82 American Society of Anesthesiologists physical status 1 to 3 adult (>18 years) patients scheduled for total knee replacement were included in this study. Exclusion criteria were contraindications to the use of regional anesthesia, pregnancy, infection or previous surgery in the inguinal region, hemostatic abnormality, and a preexisting neuropathy or neuromuscular disease that could interfere with data collection.

An ultrasound examination of the infrainguinal region was performed with a 25-mm, 5- to 10-MHz broadband linear array transducer (Titan; SonoSite, Inc, Bothell, WA) with the imaging preset to NRV and the optimization set to RES. The ultrasound probe was initially positioned just below the inguinal ligament at the level of the inguinal crease in a transverse plane. The probe was manipulated to optimally visualize the femoral artery and then moved laterally to identify the femoral nerve.

The skin at the needle entry site was infiltrated with 2 mL of 1% lidocaine via a 25-gauge, 1.5-in hypodermic needle. An 18-gauge, 4-cm stimulating needle connected to the negative lead of a constant voltage nerve stimulator (Stimuplex DIG; B. Braun McGaw Medical, Inc, Bethlehem, PA) was inserted out of plane toward the medial part of the nerve (Figure 1). The stimulation frequency was set at 2 Hz; the pulse width was set at 100 microseconds, and the intensity of the stimulating current was set to deliver 1 mA. The tip of the needle was maintained under the center of the probe to allow optimal visualization of tissue displacement during needle advancement. The stimulating needle was advanced toward the medial half of the nerve in an anteroposterior direction until a brisk elicited motor response was observed (Figure 2). Ultrasound imaging was performed by a single investigator (A.N.), and the evoked motor response, or twitch, was monitored and recorded by an independent observer (M.C.K.). The needle was redirected first laterally (toward the lateral half of the nerve, away from the artery) and then medially to seek optimal quadriceps muscle stimulation, and the elicited response was recorded. The depth at which the motor response was observed was also recorded.

Dissections of the inguinal area were performed on 20 cadaver limbs (10 right and 10 left) to determine the anatomic relationship between the branches to the quadriceps as well as the sartorius muscle. The anatomic dissections were performed in the anatomy laboratory at Northwestern University, Feinberg School of Medicine, with the approval and cooperation of...
the Department of Anatomy. Dissections were performed by a single investigator (A.N.) and independently verified by a second investigator (M.C.K. or H.B.), who was unaware of the orientation classified by the other raters (Figures 3 and 4).

The sample for the clinical study was based on the following assumption: a lateral relationship would exist between the femoral nerve branches to the quadriceps muscle and the branch to the sartorius muscle in 90% of the dissections.

Results

Ultrasound examinations of the infrainguinal region were performed on 58 female and 24 male adult patients (37 left and 45 right legs). The characteristics of the study sample were a median age of 65 years (range, 46–86 years), mean height ± SD of 167 ± 11 cm, and mean weight of 84 ± 22 kg. The median number of skin punctures and mean needle depth to obtain a quadriceps contraction were 1 (range, 1–3) and 34 ± 1 mm, respectively.

An evoked motor response was elicited in 79 of 82 patients after stimulation of the medial half of the femoral nerve, whereas stimulation of the lateral half of the nerve elicited an evoked motor response in all patients. Stimulation of the medial aspect of the femoral nerve produced a sartorius contraction in 77 patients (94%), a combined sartorius and quadriceps contraction in 1 patient (1.2%), an iliacus muscle contraction in 1 patient (1.2%), and a quadriceps contraction in 1 patient (1.2%). When the motor response was a sartorius stimulation (77 patients), a redirection toward the lateral half of the femoral nerve resulted in a quadriceps contraction in 75 patients (91.5%) and a combined quadriceps and sartorius contraction in 2 patients (2.4%). When the initial motor response was either a combination of a quadriceps and sartorius contractions or an iliacus muscle stimulation or when no evoked motor response was obtained, stimulation of the lateral half of the femoral nerve produced a quadriceps contraction. When the initial response was a quadriceps contraction, lateral redirection resulted in a combined sartorius and quadriceps contrac-

Figure 2. Ultrasound imaging of the infrainguinal region at the level of the crease. The stimulating needle was advanced out of plane in an anteroposterior direction toward the medial half (asterisk) and the lateral half (double asterisks) of the femoral nerve. A indicates femoral artery, and V, femoral vein.

Figure 3. Anatomic dissection of the infrainguinal region of a left lower extremity showing the relationship between the femoral nerve branches to the sartorius and quadriceps muscles.
Ultrasound Imaging and Femoral Nerve Stimulation

Figure 4. Anatomic dissection of the infrainguinal region of a left lower extremity showing the branches to the sartorius and quadriceps muscles.

Table 1. Association of Needle Direction With Elicited Motor Response (N = 82)

<table>
<thead>
<tr>
<th>Response Type</th>
<th>Lateral Part of the Femoral Nerve</th>
<th>Medial Part of the Femoral Nerve</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quadriceps contraction, n (%)</td>
<td>79 (96)</td>
<td>1 (1.2)</td>
<td></td>
</tr>
<tr>
<td>Sartorius contraction, n (%)</td>
<td>0 (0)</td>
<td>77 (94)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Other</td>
<td>3 (4)</td>
<td>4 (4.8)</td>
<td></td>
</tr>
</tbody>
</table>

*Both sartorius and quadriceps contraction.

Two with no evoked motor response, 1 with both sartorius and quadriceps contraction, and 1 with iliacus contraction.

Discussion

The important finding of our study is that at the inguinal crease, when combining an out-of-plane ultrasound examination and needle-assisted stimulation, the motor branch of the femoral nerve innervating the quadriceps muscle is located in a lateral position relative to the branch to the sartorius muscle. This finding is supported by our anatomic dissections, which identified a similar relationship among the branches of the femoral nerve that innervate the quadriceps and sartorius muscles. Traditionally, in cadaver dissections, the relationship between the divisions of the femoral nerve has been described as the branch innervating the sartorius muscle arising from the anterior division and the branch of the quadriceps muscle arising from the posterior division. In this study, we combine ultrasound imaging, a nerve stimulation technique, and anatomic dissections to describe the mediolateral relationship between the motor branches of the femoral nerve.

Ultrasound needle localization for peripheral nerve blocks relies on the knowledge of the surrounding anatomy and echogenic tissue characteristics. Direct identification of the femoral nerve branches on ultrasound imaging may be complicated by the phenomenon of anisotropy of the nerve and fascia covering the iliacus. This may obscure the nerve within the hypoechoic background or make it difficult to differentiate the branches that supply the corresponding muscles. In addition, factors such as the depth of the nerve, the fat content of the femoral triangle, and the presence of the lateral femoral circumflex artery may increase the difficulty in identification of the branches of the femoral nerve. Other studies have investigated the ultrasound identification of the femoral nerve below the

After the femoral triangle was identified, the skin, subcutaneous tissue, fascia lata, and fascia iliacus were removed to expose the femoral vessels. The femoral nerve and femoral vessels were isolated and dissected from the inguinal ligament to the knee. Our findings during anatomic dissection revealed that the nerve to the quadriceps muscle originated laterally in 95% of the specimens in comparison with the branch to the sartorius muscle.
inguinal crease; however, to our knowledge, an attempt to describe the topographic relationship among the branches of the femoral nerve using ultrasound at this level has not been reported previously. Gruber et al performed panoramic scans of the infrainguinal region and concluded that delineation of the femoral nerve beyond 5 cm below the inguinal ligament after it has branched was insufficient because of the surrounding low-contrast hyperechoic tissues. Tsui et al suggested that although the femoral artery and fascia lata were easily identifiable, the fascia iliaca separating the femoral nerve and vessels was difficult to visualize, therefore making it more challenging to identify the separate branches of the nerve.

We used a fixed stimulating current of 1 mA for eliciting motor responses during needle redirections to generate a brisk motor response. We chose this current to create a primarily binary result of either a quadriceps or sartorius contraction when evaluating the effect of needle redirection. Several authors have suggested that current intensities of 0.5 to 1 mA are sufficient for needle localization during block placement. Although in clinical practice we seek minimal threshold currents of less than 1 mA, we did not attempt to minimize the threshold current because our intent was not to optimize the needle distance but rather to record the elicited motor response. It is unlikely that the current used in this study affected the directional relationship between the needle and the branches of the femoral nerve. One case showed a combination of both evoked motor responses, which could have been affected by a lower current intensity.

There were limitations to our study. We used a short-axis transverse imaging out-of-plane ultrasound imaging technique to access needle redirections while maintaining visualization of the femoral nerve. Both in-plane and out-of-plane techniques have been described, and there are advantages to each method. In-plane imaging allows visualization of the needle tip as it approaches structures, whereas with an out-of-plane technique, only tissue displacement can be determined. In addition, using in-plane imaging would have likely required anteroposterior redirections of the needle, necessitating adjustments of the probe position to locate the needle tip. The use of the out-of-plane technique allowed us to minimize movement of the probe without changing the appearance of our image. We used an 18-gauge needle in an attempt to improve visualization of tissue displacement and more accurately assess needle redirections. Although it is possible to injure the femoral nerve while attempting to localize it, the risk of injury has not been shown to be decreased with the use of ultrasound regardless of the plane of imaging. The risk of intraneural needle placement may be potentially minimized with the use of a 1-mA current. In our study, only 2 cases did not evoke a motor response when the needle passed beyond the medial part of the femoral nerve. In these 2 cases, a quadriceps contraction was elicited after lateral needle redirection.

An additional limitation was our lack of assessment to correlate sensory and motor responses, such as injecting a local anesthetic after stimulation of the branches of the femoral nerve. We think, while providing analgesia for total knee replacements, that it is undesirable to inject a local anesthetic while eliciting a sartorius motor response; therefore, we would not have been able to correlate the results with the needle redirections. All patients enrolled in this study underwent total knee replacement, in which localization of the motor branch of the femoral nerve to the quadriceps muscle is an important determinant of successful analgesia after a nerve block. Therefore, we chose to correlate the elicited motor response with the anatomic findings as a surrogate measure of the effect of needle redirection under ultrasound visualization of the inguinal region.

In conclusion, when using out-of-plane ultrasound imaging at the inguinal crease, directing the stimulating needle to the lateral part of the femoral nerve may be associated with a higher probability of encountering the motor branch to the quadriceps muscle. We think that this relationship may be useful for needle localization when a blockade of either of the motor branches of the femoral nerve is desired.

References

Ultrasound Imaging and Femoral Nerve Stimulation


Electrical Stimulation Versus Ultrasound Guidance for Popliteal-Sciatic Perineural Catheter Insertion

A Randomized Controlled Trial

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Background: Sciatic perineural catheters via a popliteal fossa approach and subsequent local anesthetic infusion provide potent analgesia and other benefits after foot and ankle surgery. Electrical stimulation (ES) and, more recently, ultrasound (US)-guided placement techniques have been described. However, because these techniques have not been compared in a randomized fashion, the optimal method remains undetermined. Therefore, we tested the hypotheses that popliteal-sciatic perineural catheters placed via US guidance require less time for placement and produce equivalent results, as compared with catheters placed using ES.

Methods: Preoperatively, subjects receiving a popliteal-sciatic perineural catheter for foot and/or ankle surgery were randomly assigned to either the ES with a stimulating catheter or US-guided technique with a nonstimulating catheter. The primary end point was catheter insertion duration (in minutes) starting when the US transducer (US group) or catheter-placement needle (ES group) first touched the patient and ending when the catheter-placement needle was removed after catheter insertion.

Results: All US-guided catheters were placed per protocol (n = 20), whereas only 80% of stimulation-guided catheters could be placed per protocol (n = 20; P = 0.106). All catheters placed per protocol in both groups resulted in a successful surgical block. Perineural catheters placed by US took a median (10th-90th percentile) of 5.0 min (3.9–11.1 min) compared with 10.0 min (2.0–15.0 min) for stimulation (P = 0.034). Subjects in the US group experienced less pain during catheter placement, scoring discomfort a median of 0 (0.0–2.1) compared with 2.0 (0.0–5.0) for the stimulation group (P = 0.005) on a numeric rating scale of 0 to 10.

Conclusions: Placement of popliteal-sciatic perineural catheters takes less time and produces less procedure-related discomfort when using US guidance compared with ES.

(Reg Anesth Pain Med 2009;34: 480–485)

Popliteal-sciatic continuous peripheral nerve blocks (CPNBs) provide potent analgesia and other benefits after foot and ankle surgery, as documented by previous randomized controlled investigations.1,2 Most perineural catheter reports from the previous 2 decades have used electrical stimulation (ES) to locate the target nerve via an insulated needle, followed by insertion of either a nonstimulating or stimulating catheter. More recently, ultrasound (US)–guided perineural catheter placement has been described.3–5 While ES- and US-guided techniques have been directly compared for single-injection peripheral nerve block placement (and suggest possible advantages with US in block placement time, success rates, and patient comfort),6 no comparison for perineural catheter placement is available. As such, the optimal catheter-placement method and any possible benefits of one technique over the other remain undetermined.

We therefore tested the hypotheses that popliteal-sciatic perineural catheters placed via US guidance require less time for placement and produce equivalent results, as compared with catheters placed using ES. The primary outcome was catheter insertion duration (in minutes) starting when the US probe (US group) or catheter-placement needle (ES group) first touched the patient and ending when the catheter-placement needle was removed after perineural catheter insertion.

METHODS

The institutional review board (University of California, San Diego School of Medicine, San Diego, Calif) approved the protocol and oversaw the study through data analysis. Patients offered enrollment included adults (≥18 years) scheduled for at least moderately painful orthopedic surgery of the foot and/or ankle who desired, and were approved for, a popliteal-sciatic CPNB for postoperative analgesia. Exclusion criteria included known neuropathy of any etiology in the surgical extremity; pregnancy; incarceration; and inability to communicate with the investigators and hospital staff.

Protocol

After written, informed consent, subjects were randomized to 1 of 2 treatment groups—ES or US guidance—using a computergenerated randomization table based in a secure, password-protected, encrypted central server (www.PAINRE.com; General
Clinical Research Center, Gainesville, Fla). All catheters were placed by an attending physician with extensive experience in both placement techniques or a regional anesthesia fellow/resident under the direct supervision and guidance of the attending physician.

All subjects had a peripheral intravenous catheter inserted and were placed in the prone position. Standard noninvasive monitors were applied, and oxygen was administered via a face mask. Midazolam and fentanyl (intravenous) were titrated for patient comfort, while ensuring that patients remained responsive to verbal cues. The area that would be subsequently covered by the catheter dressing was shaved, if necessary. Landmarks were drawn for all subjects; the area was cleansed with chlorhexidine gluconate and isopropyl alcohol (Chloraprep One-Step; Medi-Flex Hospital Products, Inc, Overland Park, Kan); and a clear, sterile, fenestrated drape was applied. The nerve stimulator (ES group) or US (US group) was readied for use.

**ES Technique**

Subjects randomized to the ES technique had the sciatic nerve located with a nerve stimulator attached to an insulated needle using a slightly modified technique of a method described previously. A local anesthetic skin wheal was raised 1 cm directly caudal to the apex of the popliteal fossa (bounded by the semimembranosus muscle medially and the biceps femoris muscle laterally), but not more than 10 cm cephalad to the popliteal fossa skin crease. An 8.9-cm, 17-gauge, insulated needle (StimuCath; Arrow International, Reading, Pa) was inserted through the skin wheal, with the long axis of the needle at a 45-degree angle to the skin/nerve and the bevel directed cephalad. The needle was connected to a nerve stimulator (Stimuplex-DIG; B. Braun Medical, Bethlehem, Pa) initially set at 1.2 mA, 2 Hz, and an impulse duration of 0.1 millisecond. If the sciatic nerve was not identified after 5 to 8 cm of insertion, depending on patient body habitus, the needle was withdrawn and redirected laterally, then medially, until discrete, stimulatable foot/toe plantar flexion occurred with a current amplitude between 0.30 and 0.60 mA.

The 19-gauge catheter was then placed through the length of the needle and the nerve stimulator connecting wire transferred from the needle to the catheter, which has a conducting wire through its length to deliver current to its tip. The stimulating current was allowed to be increased up to 0.80 mA, and the catheter was advanced 5 cm beyond the needle tip. If plantar flexion decreased as the stimulating catheter was advanced, the catheter was withdrawn into the needle, the needle redirected or rotated, and the catheter readvanced.

Once a catheter had been successfully advanced 5 cm past the needle tip, the needle itself was withdrawn over the catheter, and the catheter stylet was removed. The catheter was tunneled subcutaneously 5 to 7 cm in a lateral direction using the included needle stylet and 17-gauge insulated needle. The injection port was attached to the end of the catheter, the nerve stimulator attached to the injection port, and the minimum current resulting in muscle contraction noted. The catheter was secured with sterile liquid adhesive, an occlusive dressing, and an anchoring device (StatLock; Venetec International, San Diego, Calif) to affix the catheter hub to the patient. After negative aspiration, 40 mL of anesthetic solution was injected via the catheter with gentle aspiration between divided doses. The injectate contained mepivacaine 1.5% and epinephrine 2.5 to 5.0 μg/mL.

**US-Guided Technique**

Subjects randomized to the US-guided technique had their target nerve located using US guidance alone. With a high-frequency linear array transducer (HFL38; SonoSite MicroMaxx, Bothell, Wash) in a sterile sleeve, the sciatic nerve was identified in a transverse cross-sectional view at the apex of the popliteal fossa. Once the optimal image of the sciatic nerve was obtained, a local anesthetic skin wheal was raised lateral to the US transducer. An 8.9-cm, 17-gauge, Tuohy-tip needle (FlexTip; Arrow International) was inserted through the skin wheal in plane beneath the US transducer and directed medially toward the sciatic nerve, with the bevel directed posteriorly. Local anesthetic solution (40 mL, mepivacaine 1.5% with epinephrine 2.5–5.0 μg/mL) was injected in divided doses circumferentially around the target nerve via the needle.

A 19-gauge, flexible, epidural-type catheter (FlexTip; Arrow International) was then placed through the length of the needle and advanced 5 cm beyond the needle tip. Once a catheter had been inserted, the needle itself was withdrawn over the catheter. The injection port was attached to the end of the catheter, and catheter tip position was inferred by injecting 1 mL of air via the catheter under US, slightly withdrawn when necessary, and another 1 mL of air injected—this process was repeated, as necessary (the positive and negative predictive values of this test are currently unknown, and whether it influenced accurate catheter placement in this study similarly remains unknown). The catheter was not tunneled further but was dressed and secured in a similar manner as in the ES technique.

**Outcome Measurements**

Time for catheter placement was the primary outcome and began when the US probe (US group) or catheter-placement needle (ES group) first touched the patient and ended when the catheter-placement needle was removed after catheter placement. Therefore, the time required for tunneling ES-guided catheters was not included in this measurement. A research coordinator with no other concurrent responsibilities recorded all times. If no evoked motor response (ES group) or visual identification of the target nerve (US group) could be achieved within 15 mins, the placement was considered a failure, and the primary end point was recorded as 15 mins. If a catheter could not be placed per protocol within 30 mins, the placement was considered a failure, and the primary end point was recorded as 30 mins. In such cases, the subject had a catheter-placement attempt using the alternative method. Subjects who did not have a catheter placed as per their randomized group protocol were removed from further study.

**Secondary Outcomes**

Immediately after the procedure, patients were asked to rate their discomfort with catheter placement on a numeric rating scale of 0 to 10 (0 = no pain, 10 = the worst pain imaginable). Fifteen minutes after local anesthetic injection, block onset was evaluated and scored in the affirmative if motor control was nearly abolished during either plantar or dorsiflexion, and there was decreased sensory perception on the plantar aspect of the foot as compared with the contralateral limb. Subjects with a successful surgical block were retained in the study; those with a failed surgical block had their catheters removed and were removed from the study. Given that the primary outcome of this study was the time for catheter insertion—completed before entering the operating room—the subsequent surgical anesthesia was not standardized among subjects.

In the recovery room—or before admission to the recovery room if the initial surgical block duration required extension—the perineural catheter was filled with a bolus of 20 mL of 0.5% ropivacaine with epinephrine 2.5 to 5.0 μg/mL, after negative aspiration. The time of this bolus was recorded.

**References**

Perineural catheters were attached to portable infusion pumps (Pain Pump 2 BlockAid; Stryker Instruments, Kalamazoo, Mich) set to deliver an infusion of 0.2% ropivacaine (basal rate of 8 mL/hr; patient-controlled bolus of 4 mL; 30-min lockout interval). Patients used an oral opioid (oxycodeone, 5-mg tablets) for breakthrough postoperative pain inadequately treated with the perineural ropivacaine infusion/bolus. Although study-related procedures ended on postoperative day 1, all patients received daily telephone follow-up from a health care provider throughout the duration of their perineural infusions through the day after catheter removal as is standard practice at our institution.

**Assessment of Catheter Placement Success**

With the use of the US-guided protocol, it is theoretically possible to inject ropivacaine via the needle and produce a successful surgical block but has the perineural catheter inaccurately placed. Therefore, to help document the accurate positioning of perineural catheters placed with US, the ropivacaine bolus described above was delivered via the catheter. Subjects were contacted the following day and asked for the time that their dense surgical block resolved. Because the durations of anesthetic action for lower-extremity blocks are less than 7 hrs for mepivacaine and more than 7 hrs for ropivacaine, the catheter was considered accurately placed if the time from the initial surgical block until the time of block resolution was greater than 7 hrs.

In addition to procedure-related pain scores, subjects were also surveyed on the day after surgery regarding fluid leakage occurrence and average and worst pain since surgery on a 0- to 10-point numeric rating scale.

**Statistical Analysis**

Sample size calculations were centered around the hypothesis that when inserting a popliteal-sciatic perineural catheter, the use of US guidance is associated with a decreased time of placement compared with ES guidance. To this end, we chose the time for catheter placement as the outcome measure to estimate a probable sample size. We considered a 5-min difference in placement time to be clinically relevant. Based on an SD of each group of 5 mins and assuming a 2-sided type I error protection of 0.05 and a power of 0.80, approximately 17 patients in each group were required (StatMate 2.0; GraphPad Software, San Diego, Calif). To allow for variability in the SD of each group and subject dropouts, we enrolled a total of 40 subjects.

**TABLE 1.** Population Data and Procedural Information

<table>
<thead>
<tr>
<th></th>
<th>US (n = 20)</th>
<th>ES (n = 20)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>46 (39–55)</td>
<td>47 (26–56)</td>
<td>0.62</td>
</tr>
<tr>
<td>Sex, no.</td>
<td>9/11</td>
<td>8/12</td>
<td>0.79</td>
</tr>
<tr>
<td>female/no. male</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Height, cm</td>
<td>175 (169–178)</td>
<td>174 (166–178)</td>
<td>0.20</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>100 (80–120)</td>
<td>79 (67–93)</td>
<td>0.02</td>
</tr>
<tr>
<td>Minimum current via needle, mA</td>
<td>NA</td>
<td>0.5 (0.5–0.6)</td>
<td>NA</td>
</tr>
<tr>
<td>Minimum current via catheter, mA</td>
<td>NA</td>
<td>0.5 (0.4–0.7)</td>
<td>NA</td>
</tr>
</tbody>
</table>

Values are reported as median (25th–75th percentiles) or number of subjects, as indicated. NA indicates not applicable.

**RESULTS**

Forty patients enrolled, and all were randomized to 1 of the 2 treatment groups. The demographic, morphometric, and surgical characteristics of each group are presented in Tables 1 and 2. All perineural catheters in the US group were placed by trainees compared with 19 (95%) of 20 in the ES group. Of subjects randomized to ES (n = 20), 4 (20%) failed to have a catheter placed as per the ES protocol (all were subsequently successfully placed using the US-guided protocol), and the remaining 16 (80%) had both successful catheter placement and surgical block onset, as defined by the study protocol. Of the 4 ES catheter-placement failures, 3 resulted when no evoked motor response could be elicited with the stimulating needle within 15 mins, and 1 resulted when the catheter could not be advanced 5 cm past the needle tip while retaining an evoked motor response within 30 mins. Of subjects randomized to US (n = 20), all had surgical block onset and a successful catheter placement, as defined by the study protocol (P = 0.106 compared with ES group).

Normality of distribution was determined using the Kolmogorov-Smirnov test (InStat 3.6; GraphPad Software). Continuous, normally distributed data are reported as mean (SD). Categorical data are reported as median (percentiles) or percentages, when appropriate. For normally distributed data, single comparisons were performed using the t test. For continuous data in distributions other than normal, the Mann-Whitney U test was used. The Fisher exact test was used for comparisons of categorical data. A 2-sided P < 0.05 was considered statistically significant for the primary outcome. Significant findings in secondary outcomes should be interpreted as suggestive, requiring confirmation in a future trial before considering them as definitive.

**FIGURE 1.** Time required for catheter placement according to method. Four catheters of the nerve stimulation group could not be placed per protocol and were subsequently placed successfully using the US technique (marked by t).
Table 3. Secondary Outcomes

<table>
<thead>
<tr>
<th></th>
<th>US (n = 20)</th>
<th>ES (n = 20)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venous puncture, n</td>
<td>0</td>
<td>2</td>
<td>0.487</td>
</tr>
<tr>
<td>Fluid leakage at site, n</td>
<td>6</td>
<td>1</td>
<td>0.104</td>
</tr>
<tr>
<td>Worst pain, POD 1 (0–10)</td>
<td>7.5 (1.8–10.0)</td>
<td>6.0 (9.0–0)</td>
<td>0.300</td>
</tr>
<tr>
<td>Average pain, POD 1 (0–10)</td>
<td>4.5 (0.7–1)</td>
<td>3.5 (5.0–5.0)</td>
<td>0.232</td>
</tr>
</tbody>
</table>

Values are reported as median (10th–90th percentiles) or number of subjects, as indicated.

POD indicates postoperative day.

Primary Outcome
Perineural catheters placed by US took a median (10th–90th percentile) of 5.0 mins (3.9–11.1 mins) compared with 10.0 mins (2.0–15.0 mins) for ES (n = 20, P = 0.034; Fig. 1).

Secondary Outcomes
Subjects in the US group experienced less pain during catheter placement, scoring discomfort a median of 0.0 (0.0–2.1) compared with 2.0 (0.0–5.0) for the ES group (P = 0.005). There were no statistically significant differences in the number of venous punctures, degree of fluid leakage, or postoperative pain scores between the 2 treatment groups (Table 3).

Adverse Events
There were no adverse events related to study procedures, perineural catheter placement, or outpatient perineural local anesthetic infusion.

Discussion
This randomized controlled study provides evidence that popliteal-sciatic perineural catheters may be placed more quickly, on average, with US guidance compared with ES (with stimulating catheters) with similar analgesic results. In addition, procedure-related patient discomfort is lower when using US compared with ES. Although investigators have previously suggested possible benefits of placing perineural catheters using US, in the data of the current study are the first to document and quantify these previously theoretical advantages.

Catheter Placement Time
The median difference of 5 mins gained by US is clinically relevant in the present era of operating room efficiency. This difference is likely an underestimate for 2 reasons: (1) our protocol for determining placement time for the ES group did not include the time required for tunneling or the bolus injection of local anesthetic via the catheter after placement needle removal; and (2) given that the local anesthetic bolus (mepivacaine) in the US-guided technique is administered via the needle before catheter placement, we speculate that the anesthetic block onset may be more rapid, further decreasing the interval from the start of block performance to anesthesia-ready time. The latter point is based on our subjective perception and clinical experience and requires further investigation.

Additional procedures that affect placement time were excluded from the primary outcome measurement as well. For example, the times to retrieve and set up the US and nerve stimulator were not included for this study. At our institution, all peripheral nerve blocks and perineural catheters are placed in a regional anesthesia induction area (“block room”), with both of these pieces of equipment at each bedside. Given that the US remains turned on throughout the day and the nerve stimulator requires fewer than 5 secs to turn on, the difference in equipment preparation between US and ES at our institution is less than 10 secs—irrelevant, given the primary outcome precision of the current study. However, the 5-min time advantage of the US-guided technique could easily be negated by preparation time if a nerve stimulator was continuously available, while a US machine had to be retrieved, set up, and powered on for each procedure. It is obviously impossible in a single clinical study to account for the nearly-limitless number of scenarios at all institutions, and practitioners need to be cognizant of this fact when applying the results of our study to their own practices.

Placement Success Rate
Deserving comment is the failure to place 4 (20%) of the 20 catheters in the ES group, which were subsequently all successfully placed by US. Catheter placement was deemed a “failure” when a motor response could not be evoked within 15 mins, the electrical current via the needle could not be reduced to less than 0.6 mA with an evoked motor response within 15 mins, or the stimulating current via the catheter could not be reduced to less than 0.8 mA while retaining an evoked motor response with the catheter inserted 5 cm beyond the needle tip within 30 mins even after adequate needle stimulation was achieved. These criteria may be unnecessarily restrictive and therefore may have directly affected the ES group success rate. However, there is evidence that strict catheter-placement criteria provide definitive benefits, and the protocol used in the current study is nearly identical to one used previously, which resulted in high success rates.

We can only speculate on why the present study had an 80% success rate for ES-guided catheter placement, whereas previous investigations with nearly-identical protocols reported success rates of 93% and 96%. One possible explanation is that nearly all catheters for the present study were placed by trainees (residents and fellows), whereas previous investigations exclusively relied on experienced attending physicians. Alternatively, differences in patient populations between previous studies and the present study may have influenced the success rate. Lastly, the time limitation of 15 to 30 mins for needle/catheter placement of the current study may explain the difference compared with previous investigations without similar time limitations.

Combined US Guidance–Nerve Stimulation
For the purpose of this study, we elected to compare CPNB placement using ES alone to US guidance alone to clearly define the advantages and disadvantages of each technique and estimate the difference in procedural time between techniques. It is worth mentioning the possibility that using a combination of both approaches may offer additional benefits over either technique alone. However, to date, this supposition remains controversial and uninvestigated for perineural catheter placement.

Study Limitations
One limitation of our study is that subjects and investigators were not masked to treatment group assignment. Our results pertain specifically to the techniques and equipment used in this study—using other approaches and/or catheter designs would undoubtedly alter the findings. We can speculate that using a combination of stimulating/insulated needle and non-stimulating catheter alone may have taken less time than using a stimulating catheter as in our study, possibly producing a similar procedural time to US guidance alone. Procedural times for US-guided and stimulation-guided, single-injection, popliteal-sciatic nerve blocks, without perineural catheter placement, have not demonstrated a statistically significant difference. For
this study on perineural catheters, we elected to use stimulating catheters as there is evidence that for sciatic catheters placed in the popliteal fossa without US, stimulating catheters result in superior postoperative analgesia and decreased opioid requirements. At the time of this writing, we are not aware of any randomized studies comparing the insulated needle and non-stimulating catheter technique to US guidance.

Importantly, the 2 methods of perineural catheter placement compared in this study were different in multiple ways and clearly distinguish one method versus the other (eg, local anesthetic was injected via the needle in the US group and via the catheter for the ES group). Such differences were accepted before study initiation as we used our current clinical protocols for both US- and ES-guided perineural catheter placement. However, the optimal insertion techniques for both US and ES are currently undefined, and undoubtedly, our choices affected the study results.

Another limitation is the use of trainees to place all but one of the perineural catheters included in this study. This theoretically may have led to prolonged procedural times. However, each of the trainees involved in the placement of perineural catheters for this study was supervised one-on-one by an attending physician who was facile with both placement techniques to minimize the training effect. In fact, the use of trainees to perform the procedures may have actually been an advantage in retrospect, demonstrating the relative ease of acquiring US-guided regional anesthesia skills while still performing CPNB in a timely fashion. Of interest, subjects randomized to the US group were heavier to a statistically significant degree compared with those in the ES group (median of 100 vs 79 kg, \( P = 0.02 \)). Our past experience suggests that this difference should have biased the results in favor of the ES group, and therefore, the finding that US resulted in a 5-min time savings may be an underestimation when comparing the 2 techniques. Lastly, the results of this study should not be inferred to other perineural catheter insertion sites as perineural anatomy directly affects catheter insertion and infusion characteristics.

In summary, placement of popliteal-sciatic perineural catheters takes less time and is less painful for patients when performed under US guidance rather than ES. Although differences in postoperative analgesia between the 2 techniques were not detected, the risk of a type II error is high, given that these were secondary end points, and these results require confirmation with a future study.

ACKNOWLEDGMENTS

The authors thank the entire operating and recovery room staff at the University of California, San Diego Hillcrest (San Diego, Calif), and Thornton hospitals (La Jolla, Calif) for their invaluable assistance.

REFERENCES


Ultrasound Guidance Versus Electrical Stimulation for Femoral Perineural Catheter Insertion

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Objective. Continuous femoral nerve blocks provide potent analgesia and other benefits after knee surgery. Perineural catheter placement techniques using ultrasound guidance and electrical stimulation (ES) have been described, but the optimal method remains undetermined. We tested the hypothesis that ultrasound guidance alone requires less time for femoral perineural catheter insertion and produces equivalent results compared with ES alone. Methods. Preoperatively, patients receiving a femoral perineural catheter for knee surgery were randomly assigned to either ultrasound guidance with a nonstimulating catheter or ES with a stimulating catheter. The primary outcome was the catheter placement procedure time (minutes) starting when the ultrasound transducer (ultrasound group) or catheter insertion needle (ES group) first touched the patient and ending when the catheter insertion needle was removed after catheter insertion. Results. Perineural catheters placed with ultrasound guidance (n = 20) took a median (10th–90th percentiles) of 5.0 (3.9–10.0) minutes compared with 8.5 (4.8–30.0) minutes for ES (n = 20; P = .012). All ultrasound-guided catheters were placed according to the protocol (n = 20) versus 85% of ES-guided catheters (n = 20; P = .086). Patients in the ultrasound group had a median procedure-related discomfort score of 0.5 (0.0–3.1) compared with 2.5 (0.0–7.6) for the ES group (P = .015). There were no vascular punctures with ultrasound guidance versus 4 in the ES group (P = .039). Conclusions. Placement of femoral perineural catheters takes less time with ultrasound guidance compared with ES. In addition, ultrasound guidance produces less procedure-related pain and prevents inadvertent vascular puncture. Key words: continuous femoral nerve block; electrical stimulation; perineural infusion; ultrasound-guided regional anesthesia.
Although studies have been performed comparing single-injection nerve blocks using ES versus ultrasound with possible advantages attributed to the ultrasound-guided technique (eg, increased success rate and faster onset),9–12 these modalities have not been directly compared in a randomized fashion for femoral perineural catheter insertion to date. We therefore tested the hypothesis that femoral perineural catheters placed via ultrasound guidance require less time for placement and produce equivalent results compared with catheters placed via ES.

Materials and Methods

The Institutional Review Board of the University of California San Diego School of Medicine approved the protocol and oversaw the study through data analysis. We included adults (≥18 years old) scheduled for at least moderately painful (anticipated postoperative pain scores ≥4 of a possible 10) orthopedic surgery of the knee or thigh with a continuous femoral nerve block for postoperative analgesia. Exclusion criteria were as follows: neuropathy of any etiology in the surgical extremity, pregnancy, incarceration, and inability to communicate with the investigators and hospital staff.

Protocol

After written informed consent, patients were randomized to 1 of 2 treatment groups, ES or ultrasound guidance, by a computer-generated randomization table based in a secure, password-protected, encrypted central server (General Clinical Research Center, Gainesville, FL; www.PAINfRE.com). All procedures were performed by an attending physician with extensive experience in both placement techniques or a regional anesthesia fellow/resident under direct one-on-one supervision by the attending physician.

All patients had a peripheral intravenous catheter inserted and were placed in the supine position. Standard noninvasive monitors were applied, and oxygen was administered via a face mask. Intravenous midazolam and fentanyl were titrated for patient comfort while ensuring that patients remained responsive to verbal cues. The area that would be subsequently covered by the catheter dressing was shaved, if necessary. Landmarks were drawn for all patients; the area was cleansed with chlorhexidine gluconate and isopropyl alcohol (ChloraPrep One-Step; MedFlex Hospital Products Inc, Overland Park, KS); and a clear, sterile, fenestrated drape was applied. The nerve stimulator (ES group) and ultrasound system (ultrasound group) were readied for use.

Electrical Stimulation Technique

Patients randomized to the ES technique had the femoral nerve located with a nerve stimulator attached to an insulated needle using a slightly modified technique of a method described previously.1 A local anesthetic skin wheal was raised 1 cm lateral to the palpated femoral pulse within the femoral crease. An 8.9-cm, 17-gauge, insulated needle (StimuCath; Arrow International Inc, Reading, PA) was inserted through the skin wheal in the parasagittal plane with the long axis of the needle at a 45° angle to the skin/gurney and the bevel directed cephalad. The needle was connected to a nerve stimulator (Stimuplex-DIG; B. Braun Medical Inc, Bethlehem, PA) initially set at 1.2 mA, 2 Hz, and an impulse duration of 0.1 millisecond. If the femoral nerve was not identified after 5 to 8 cm of insertion, depending on patient habitus, the needle was withdrawn and redirected laterally and then medially until discrete stimulated quadriceps muscle contractions with a patellar rise occurred with a current amplitude between 0.30 and 0.60 mA.

The 19-gauge catheter was then placed through the length of the needle, and the nerve stimulator connecting wire was transferred from the needle to the catheter, which had a conducting wire through its length to deliver current to its tip. The stimulating current was increased up to 0.80 mA if necessary while advancing the catheter 5 cm beyond the needle tip. If the quadriceps contraction amplitude decreased as the stimulating catheter was advanced, the catheter was withdrawn into the needle; the needle was redirected or rotated; and the catheter was readvanced.

Once a catheter was successfully advanced 5 cm past the needle tip, the needle itself was withdrawn over the catheter, and the catheter stylet was removed. The catheter was tunneled subcutaneously 5 to 7 cm in a lateral direction using the included needle stylet and a 17-gauge insulated
needle. The injection port was attached to the end of the catheter; the nerve stimulator was attached to the injection port; and the minimum current resulting in muscle contractions was noted. The catheter was secured with sterile liquid adhesive, a clear occlusive dressing, and an anchoring device (StatLock; Venetec International Inc, San Diego, CA) to affix the catheter hub to the patient. After negative aspiration, 40 mL of an anesthetic solution (mepivacaine, 1.5%, with epinephrine, 2.5–5.0 μg/mL) was injected via the catheter with gentle aspiration between divided doses.

**Ultrasound Technique**

Patients randomized to the ultrasound technique had their target nerve located by ultrasound guidance alone. With a 13–6 MHz linear array transducer (HFL38, MicroMaxx; SonoSite Inc, Bothell, WA) in a sterile sleeve, the femoral nerve was identified in a transverse (short-axis) view at the inguinal crease. In a transverse view, the internal appearance of the peripheral nerve bundle is a mixture of hypoechoic neural tissue (fascicles) and hyperechoic connective tissue (perineurium and epineurium).13 Once the optimal image of the femoral nerve was obtained, a local anesthetic skin wheal was raised lateral to the ultrasound transducer. An uninsulated 8.9-cm, 17-gauge, Tuohy-tip needle (FlexTip; Arrow International Inc) was inserted through the skin wheal and directed medially in plane beneath the ultrasound transducer toward the femoral nerve (Figure 1).14 The local anesthetic solution described above (40 mL) was injected in divided doses circumferentially around the target nerve via the needle.

A 19-gauge flexible epidural-type catheter (FlexTip) was then placed through the length of the needle and advanced 5 cm beyond the needle tip posterior to the nerve by the primary provider while an assistant stabilized the ultrasound transducer. Once the catheter had been inserted, the needle itself was withdrawn over the catheter. The catheter tip position was assessed by injecting 1 mL of air via the catheter under ultrasound guidance with the appearance of hyperechoic air bubbles posterior to the femoral nerve confirming proper catheter placement.15 Because the in-plane ultrasound-guided needle placement technique effectively “tunneled” the catheter in a lateral-to-medial direction under the transducer, the catheter was not tunneled further but was otherwise dressed and secured in a manner similar to the ES technique.

**Outcome Measurements**

The time for catheter placement was the primary outcome and began when the ultrasound transducer (ultrasound group) or catheter placement needle (ES group) first touched the patient and ended when the catheter placement needle was removed after catheter placement. For the purpose of this study, the time required for catheter tunneling and administration of the local bolus (ES group) was not included in the catheter placement time. A research coordinator with no other concurrent responsibilities recorded all times. If a catheter could not be placed according to the protocol within 30 minutes, the placement was considered a failure, and the primary outcome was recorded as 30 minutes. In such cases, the patient had a catheter placement attempt using the alternative method. Patients who did not have a catheter placed according to their randomized group protocol were removed from further study.

![Figure 1. Transverse (short-axis) image of the femoral nerve at the inguinal crease with in-plane needle guidance. FN indicates femoral nerve; IM, iliacus muscle; LA, local anesthetic; and N, needle. The internal appearance of the femoral nerve shown here is a mixture of hypoechoic neural tissue (fascicles) and hyperechoic connective tissue (perineurium and epineurium).13](image-url)
Secondary Outcomes
During the procedure, vascular puncture was determined by the presence of frank blood in the hub of the needle or aspiration of blood when the needle was attached to tubing and a syringe. Immediately after the nerve block procedure, patients were asked to rate their discomfort with catheter placement on a numeric rating scale of 0 to 10 (0, no discomfort; 10, worst discomfort imaginable). Fifteen minutes after the injection, block onset was evaluated and scored in the affirmative if patients were unable to extend the knee and experienced decreased sensory perception to a light touch at the femoral nerve distribution compared to the contralateral limb. Patients with a successful surgical block were retained in the study; those with a failed surgical block had their catheters discontinued and were removed from the study.

In the recovery room or before if the duration of the initial surgical block required extension, a bolus of 20 mL of ropivacaine, 0.5%, and epinephrine, 2.5 to 5.0 μg/mL, was administered via the perineural catheter after negative aspiration. The time of this bolus was recorded. Perineural catheters were attached to portable infusion pumps (Pain Pump 2 BlockAid; Stryker Instruments, Kalamazoo, MI) set to deliver an infusion of ropivacaine, 0.2% (basal rate, 8 mL/h; patient-controlled bolus, 4 mL; lockout interval, 30 minutes). Patients used an oral opioid (oxycode, 5-mg tablets) for breakthrough postoperative pain inadequately treated with the perineural ropivacaine infusion and bolus.

Assessing Catheter Placement Success
With the ultrasound protocol, it is theoretically possible to inject mepivacaine via the needle and produce a successful surgical block yet have an inaccurately placed catheter. Therefore, to assess the accurate positioning of perineural catheters placed with ultrasound guidance, the ropivacaine bolus described above was delivered via the catheter for all patients. Patients were contacted the following day and asked for the time that their dense surgical anesthetic block resolved. Because the anesthetic duration of action for lower extremity blocks is reported to be less than 7 hours for mepivacaine and greater than 7 hours for ropivacaine,16 the catheter was considered accurately placed if the time from the initial surgical block until the time of block resolution was greater than 7 hours.

In addition to procedure-related pain scores, patients were also surveyed the day after surgery regarding fluid leakage occurrence and the average and worst pain since surgery on the 0 to 10 numeric rating scale.

Statistical Analysis
The sample size estimate was centered around the primary hypothesis that femoral perineural catheter insertion with ultrasound guidance would result in a decreased time to placement compared with ES. We considered a 5-minute difference in the placement time to be clinically relevant. On the basis of an SD for each group of 5 minutes and assuming a 2-sided type I error protection of .05 and power of .80, approximately 17 patients in each group were required (StatMate 2.0; GraphPad Software Inc, San Diego, CA). To allow for variability in the SD of each group and dropout, we enrolled a total of 40 patients.

The normality of the distribution was determined by the Kolmogorov-Smirnov test (NCSS-PASS statistical software; NCSS, Kaysville, UT). For normally distributed data, comparisons of independent samples were performed with a Student t test. For continuous data in distributions other than normal, the Mann-Whitney U test was used. The Fisher exact test was used for comparisons of categorical variables. Two-sided $P < .05$ was considered statistically significant for the primary outcome. Statistically significant findings for secondary outcomes should be interpreted as suggestive, requiring confirmation in a prospective trial before being considered definitive.17

Results
Forty patients were enrolled, and all were randomly assigned to 1 of the 2 treatment groups. Demographic and morphometric characteristics were similar between groups (Table 1). In the ultrasound group ($n = 20$), all patients had successful catheter placement according to the study protocol, and all had a successful nerve block as defined by the protocol. Of the patients randomized to ES ($n = 20$), 3 (15%) had failed catheter placement according to the protocol (all were subsequently successfully placed by the ultra-
sound protocol), and the remaining 17 (85%) had both successful catheter placement and surgical block onset ($P = .086$ compared with the ultrasound group). Two of the ES catheter placement failures resulted from an inability to elicit a motor response via the stimulating needle, and 1 failure resulted from an inability to maintain a motor response via the stimulating needle of less than 0.6 mA, as specified in the protocol.

**Primary Outcome**
Perineural catheters placed by ultrasound guidance ($n = 20$) took a median (10th–90th percentiles) of 5.0 (3.9–10.0) minutes compared with 8.5 (4.8–30.0) minutes for ES ($n = 20$; $P = .012$; Figure 2).

**Secondary Outcomes**
Patients in the ultrasound group had less pain during catheter placement, with a median discomfort score of 0.5 (0.0–3.1) compared with 2.5 (0.0–7.6) for the ES group ($P = .015$). No ultrasound-guided catheters resulted in vascular puncture compared with 4 in the ES group ($P = .039$). There were no statistically significant differences in other secondary outcomes (Table 2).

**Discussion**
For femoral perineural catheter placement, an ultrasound-guided technique decreases the procedure time compared with nerve ES alone while maintaining a similar success rate. Furthermore, patients in the ultrasound group reported less procedure-related pain during perineural catheter placement and had fewer inadvertent vascular punctures. To our knowledge, a randomized investigation to document and quantify the benefits of ultrasound guidance for continuous femoral nerve blocks has not been reported previously.

**Catheter Placement Time**
Although the median time savings gained by ultrasound was 3.5 minutes and less than the 5-minute threshold we selected in our sample size calculation, the result was still statistically significant. On the basis of clinical observation, 5 minutes was chosen as the expected difference for calculation purposes, taking into account practice environments with high surgical volumes and rapid turnover between cases. In terms of clinical importance, it is noteworthy that all ultrasound-guided placements were performed successfully in 11 minutes or less, whereas 35% of the ES-guided placements took more than 13 minutes, and 15% failed according to the protocol. In a survey of orthopaedic surgeons’ attitudes toward regional anesthesia, the primary reason for surgeons’ not favoring regional anesthesia for their patients is fear of case delays despite the known beneficial effects on postoperative pain.\(^\text{18}\) The results of this study show a technique that reliably places perineural catheters in...

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**Table 1. Morphometric Data and Procedural Information**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Ultrasound (n = 20)</th>
<th>ES (n = 20)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>55 (26–76)</td>
<td>62 (24–78)</td>
<td>.588</td>
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<td>Sex, female/male</td>
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<td>9/11</td>
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<tr>
<td>Height, cm</td>
<td>168 (157–183)</td>
<td>170 (160–183)</td>
<td>.595</td>
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<td>Weight, kg</td>
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<td>82 (68–105)</td>
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</tr>
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<td>Body mass index, kg/m(^2)</td>
<td>31 (23–35)</td>
<td>28 (24–35)</td>
<td>.378</td>
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<tr>
<td>Minimum current via needle, mA</td>
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</tr>
<tr>
<td>Minimum current via catheter, mA</td>
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<td>Placement by resident/fellow</td>
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<td>5/14</td>
<td>&gt;.900</td>
</tr>
</tbody>
</table>

Values are median (10th–90th percentiles) or number of patients. NA indicates not applicable.

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*J Ultrasound Med 2009; 28:1453–1460*
an efficient manner, potentially increasing the use of this analgesic modality to benefit a larger patient population.

We think that the time savings may actually be an underestimation for 2 reasons: (1) our protocol for determining the placement time did not include subcutaneous tunneling or the injection of a local anesthetic via the catheter for the ES group; and (2) local anesthetic administration via the needle before catheter placement in the ultrasound group likely resulted in faster anesthetic onset, further decreasing the interval from the start of block performance to the anesthesia-ready time. The latter point is based on our subjective perception and requires further investigation.

On the basis of our practice model, the setup time was not included in our procedure time measurement. In our regional anesthesia induction area (“block room”), ultrasound equipment remains powered on throughout the day, and nerve stimulators are readily available. The difference in equipment preparation between the ultrasound- and ES-guided techniques in this setting was negligible and unlikely to have affected the results of this study given its measurement precision. However, the setup time for either technique may greatly influence the total procedure time in different practice environments. Practitioners must consider the availability of equipment and logistics of their own practices when applying the results of this study.

**Placement Success Rate**

Deserving comment is the failure to place 3 of the 20 catheters (15%) in the ES group, which were subsequently all successfully placed by ultrasound guidance. When the electrical current via the needle could not be reduced to less than 0.6 mA while maintaining a motor response within 15 minutes, catheter placement was deemed a failure. The decreased ES success rate reported in our study may have been a result of overly restrictive protocol criteria. However, there is evidence that strict catheter placement criteria in clinical research studies provide definitive benefits.

The absolute time limit of 30 minutes for needle and catheter placement in this study may explain the difference in success rates compared with previous investigations without similar time limits but nearly identical catheter placement protocols. Alternately, differences in patient populations affect study samples and may have influenced the success rate.

**Combined Ultrasound and Nerve ES**

For the purpose of this study, we elected to compare femoral perineural catheter placement using ES alone with ultrasound guidance alone to clearly define the advantages and disadvantages of each technique and estimate the difference in the procedure time between techniques. It is possible that using a combination of both approaches may offer additional benefits over either technique alone for brachial plexus perineural catheters. To date, however, the need for ES in addition to ultrasound guidance remains controversial, especially for lower extremity perineural catheter placement.

Combining ultrasound with ES does negate any cost advantages attributed to ultrasound guidance alone. At our institution, where ultrasound and ES equipment is readily available, the cost of supplies for the techniques presented in our study is approximately US $40 less per patient when an ultrasound-guided nonstimulating perineural catheter is placed rather than a stimulating catheter.

**Vascular Puncture**

Four patients (20%) in the ES group had inadvertent vascular punctures compared with none in the ultrasound group. Although incidental vascular punctures rarely result in clinically relevant complications, we can speculate that the presence of...
blood in the vicinity of the peripheral nerve may impair subsequent direct nerve stimulation and contribute to failed catheter placement.

**Study Limitations**

The lack of participant masking was one limitation of this investigation. In addition, the methods for perineural catheter placement compared in this study were different in equipment and techniques (eg, local anesthetic injected via the needle in the ultrasound group and via the catheter in the ES group). We use the StimuCath for ES-guided perineural catheter placements because of its demonstrated efficacy when used as designed and approved by the US Food and Drug Administration. In clinical practice, using the styleted and insulated StimuCath for an ultrasound-guided in-plane technique frequently results in a misplaced catheter tip that bypasses the nerve because of the perpendicular orientation of the in-plane needle while maintaining nerve visualization in the short-axis view. Therefore, for this ultrasound-guided technique, a more flexible catheter (FlexTip) is preferred. The results of this investigation pertain specifically to the techniques and equipment used in the investigation; the optimal perineural catheter technique and equipment are currently unknown, and other approaches and catheter designs would most likely have altered our findings. Furthermore, ultrasound and ES guidance for femoral nerve blocks are not mutually exclusive and combined ultrasound and ES guidance for perineural catheter placement deserves investigation.

Another limitation to applying our results to all practices is the use of trainees to place all but 1 of the perineural catheters included in this study. Although this situation may have led to artificially prolonged procedure times, this factor may be viewed as an advantage of the study by showing the relative ease of performing advanced ultrasound-guided regional anesthesia procedures while maintaining operating room efficiency. We can only speculate on the time and training necessary to achieve competency in performing ultrasound-guided perineural catheter placement. On the basis of data from residency training in epidural catheter placement and other traditional regional anesthesia techniques, we can estimate that 60 or more of the same procedures may be necessary. Last, the results of this study should not be extrapolated to other perineural catheter insertion sites because perineural anatomy directly affects catheter insertion and infusion characteristics.

In summary, placement of femoral perineural catheters takes less time when using ultrasound guidance compared with ES. In addition, procedure-related pain scores and the incidence of vascular puncture are lower when ultrasound is used.

**References**

Ultrasound Versus Stimulation for Femoral Catheters


Anatomic Basis to the Ultrasound-Guided Approach for Saphenous Nerve Blockade

Jean-Louis Horn, MD, Trevor Pitsch, MD, Francis Salinas, MD, and Brion Benninger, MD

Background and Objectives: Successful blockade of the saphenous nerve using surface landmarks can be challenging. We evaluated the anatomic basis of performing a saphenous nerve block with ultrasound (US) using its relationship to the saphenous branch of descending genicular artery, sartorius muscle, and the adductor hiatus as defined by cadaveric measurements.

Methods: Using a total of 9 cadaveric knee dissections, the saphenous nerve and its relationship to the saphenous branch of the descending genicular artery (SBDGA) were examined. The distances from the patella to the distal end of the adductor canal and the bifurcation of the saphenous nerve were recorded. US images of an above-the-knee, subsartorial saphenous nerve block were reviewed.

Results: The saphenous nerve coursed with the SBDGA. It exited the adductor canal at a median of 10.25 cm (range, 7.0–11.5 cm) cephalad to the proximal patellar border and traveled closely with the SBDGA. At its bifurcation into the infrapatellar branch and sartorial branch, the saphenous nerve was at its closest approximation to the SBDGA. This point was found to be at a median of 2.7 cm (range, 2.1–3.4 cm) cephalad and a median of 6.6 cm (range, 5.0–9.0 cm) posterior to the proximal and posterior patellar border, respectively.

Conclusions: The US-guided approach for saphenous nerve blockade using its close anatomic relationship to the SBDGA is a feasible alternative to previously described surface landmark–based or US-guided paravenous approaches.

(Reg Anesth Pain Med 2009;34: 486–489)

Sciatic nerve blockade in the popliteal fossa with an associated saphenous nerve block is a well-established regional anesthesia technique for surgeries distal to the knee. Several techniques have been described to block the saphenous nerve. Traditionally, a subcutaneous wheal of local anesthetic is injected from the medial aspect of the tibial tuberosity to the anterior border of the medial head of the gastrocnemius muscle; however, this has been associated with a high failure rate. Improved success has been reported with surface landmark approaches such as the transsartorial, the paravenous, and peripheral nerve stimulation techniques. Gray and Collins published a letter to the editor in 2003 describing the use of ultrasound (US) to identify the saphenous vein below the knee to aid in performing the block. Using its close anatomic relationship to the SBDGA is a feasible alternative to previously described surface landmark or US-guided paravenous approaches.

METHODS

Cadaver Study

Our institutional review board approved the research on cadavers procured in this study. Nine knees from embalmed whole cadavers were dissected. All the specimens were supine and in full extension. The skin and subcutaneous tissues of the anterior and medial thigh from the level of the femoral triangle to the level of the medial condyle were carefully removed to reveal the relationship of the sartorius muscle to the vastus medialis muscle. The sartorius muscle was reflected anteriorly, to reveal the adductor canal and subsartorial compartment at the proximal patellar border.

METHODS

Cadaver Study

Our institutional review board approved the research on cadavers procured in this study. Nine knees from embalmed whole cadavers were dissected. All the specimens were supine and in full extension. The skin and subcutaneous tissues of the anterior and medial thigh from the level of the femoral triangle to the level of the medial condyle were carefully removed to reveal the relationship of the sartorius muscle to the vastus medialis muscle.
the distal end of the adductor canal. The course of the saphenous nerve was followed from within the adductor canal to the point where it emerged from the distal end of the adductor canal and then further distally to its bifurcation into the infrapatellar and sartorial branches (Fig. 2).

Careful measurements were taken from reproducible landmarks by 2 independent examiners. The surface landmark of the proximal and medial patella was used because it is easily palpable in most patients. The longitudinal distance from the proximal border of the patella and the anteroposterior distance from the medial border of the patella to the bifurcation of the saphenous nerve into the infrapatellar and sartorial branches were recorded. Also, the distance from the distal aspect of the adductor canal to the proximal border of the patella was measured. Measurements were rounded to the nearest millimeter and recorded as median with ranges.

**US Imaging**

Our institutional review board was contacted for this case report and waived their requirement for a formal approval as it involves retrospective data review of a routine anesthetic technique. The block was performed in prone position on a 43-year-old man, 173-cm, 77-kg, American Society of Anesthesiologists physical status I, scheduled for ankle surgery. Conscious sedation was provided with fentanyl and midazolam. Ultrasound imaging for the saphenous nerve blockade was accomplished with an L12-3 probe connected to an HD11XE (Philips Ultrasound, Bothell, Wash). A mark was made approximately 2.7 cm cephalad to the proximal patellar border to aid in preliminary scanning (middle lateral line). The probe was then covered with a sterile transparent dressing (Tegaderm; 3M Health Care, Borken, Germany), and sterile ultrasonic gel (Aquasonic 100, Fairfield, NJ) was used. The leg was prepared in sterile fashion using chlorhexidine/alcohol (Chloraprep with tint; Enturia Inc, Leawood, Kan) (Fig. 3).

The saphenous nerve was blocked after a US-guided popliteal approach for the sciatic nerve blockade. The US probe was repositioned on the medial surface of the knee, with the probe placed in transverse orientation relative to the sartorius muscle (Fig. 3A). The goal was to obtain short-axis views of the muscles, saphenous nerve, and SBDGA. The vastus medialis was identified anteriorly, and the sartorius muscle was located superficially (medial) and posterior to the vastus medialis. The gracilis muscle was located directly posterior to the sartorius muscle (Fig. 3B), and the saphenous nerve and SBDGA lay deep to the sartorius muscle within a subsartorial fascial plane. The saphenous nerve appeared as a hyperechoic, round to oval structure, which is often surrounded by a rim of hypoechoic perineural fat (so-called subsartorial fat-pad). The SBDGA typically appears as a small pulsatile anechoic circular structure directly adjacent to the saphenous nerve. Color flow Doppler was used to identify the artery that is often too small to visualize without Doppler. The color flow Doppler was set at 3.8 MHz, 65% gain with a scale ranging from −5 to +5 cm/sec. After the transducer was positioned to identify the SBDGA, a short-bevel, 22-gauge, 50-mm needle (Stimuplex; B. Braun Medical Inc, Bethlehem, Pa) was advanced vertically from posterior to anterior using an in-plane technique (to the US beam) for needle advancement toward either the saphenous nerve (when visible) or the SBDGA from the posterior insertion point in this

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**FIGURE 1.** Anatomic drawing. Used with permission from Netter; Atlas of Human Anatomy, 2006, © Elsevier.

**FIGURE 2.** Medial view of a dissected knee. The sartorius muscle is reflected to expose the anatomic structures. Cau indicates caudate; Ceph cephalad; Ant, anterior; Post, posterior; A, artery of the descending genicular; N, saphenous nerve; G, gracilis muscle and tendon; AC, adductor canal; P, patella; VM, vastus medialis; AM, tendon of the adductor magnus.
achieved the best success rate but used a nerve

We chose to block

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A, Block performance. The posterior aspect of the knee is prepared for the sciatic nerve block and saphenous nerve block, with the patient in prone position. The probe is positioned on the medial aspect of the knee. The middle lateral line marks the proximal border of the patella. The needle was advanced in-plane with the probe under direct US visualization. B, Ultrasound image. Color Doppler displays the SBDGA, deep to the sartorius muscle. Med, medial; Lat, lateral; Post, posterior; Ant, anterior. A, saphenous branch of the descending branch of the genicular artery; N, saphenous nerve; G, gracilis muscle; V, vastus medialis; S, sartorius muscle.

case. Once the needle tip was located in close proximity to the target structures, gentle aspiration was performed followed by incremental injection of 8 mL of ropivacaine 0.5% (Naropin, Novaplus; AstraZeneca, Wilmington, Del) within the subsartorial compartment around the SBDGA. The block was assessed with cold spray in the sartorial and infrapatellar branch distributions first and then with pinprick before surgical incision in the sartorial branch distribution.

RESULTS

Anatomic Findings From Dissections

The saphenous nerve runs with the SBDGA as it exits the adductor canal. The sartorius muscle is reflected to expose the subsartorial compartment. The median distance from the proximal patella to the distal end of the adductor canal is 10.25 cm, with a range of 7 to 11.5 cm. The bifurcation of the saphenous nerve was measured in 2 dimensions: anterior-posterior and caudad-cephalad with respect to the proximal and medial borders of the patella, respectively. The infrapatellar branch of the saphenous nerve is reflected downward. The median distance from the medial border of the patella to the bifurcation of the infrapatellar and sartorial branches of the saphenous nerve was 6.6 cm (range, 5.0–9.0 cm) in the anterior-posterior dimension. The median distance from the proximal border of the patella to the same point was 2.7 cm (range, 2.1–3.4 cm) in the caudad-cephalad dimension. Left-to-right variability on the cadaver specimens ranged from 0 to 0.9 cm (anterior-posterior) and 0 to 0.8 cm (caudad-cephalad). Interobserver variability was 0 to 0.2 cm. At its bifurcation into the infrapatellar branch and sartorial branch, we found that the saphenous nerve was at its closest approximation to the SBDGA (Fig. 2). A typical US image with color flow Doppler (Fig. 3B) of the subsartorial compartment was captured before injection of local anesthetic for the saphenous nerve block. The sartorial branch of the saphenous nerve was successfully anesthetized, and the patient underwent ankle surgery with light sedation (Fig. 2).

DISCUSSION

We describe the anatomic basis for a US-guided subsartorial saphenous nerve block that offers advantages over previously reported techniques. Using US to identify the SBDGA and its relationship to the saphenous nerve, we have shown an important vascular landmark to block the saphenous nerve.

Based on our cadaveric studies, the saphenous nerve reliably traverses the distal thigh with the SBDGA. We have found that at the point where the infrapatellar branch divides from the sartorial branch at approximately 2.7 cm proximal to the patellar border, the saphenous nerve is within its closest proximity to the artery. Because the saphenous nerve may be challenging to identify in some patients with only 2-dimensional US imaging, we take advantage of US imaging and the close anatomic relationship of the SBDGA via use of color flow Doppler to guide the injection.

Several approaches to block the saphenous nerve have been described with and without US guidance with variable success. Benzon et al8 achieved the best success rate but used a nerve stimulator to elicit paresthesias with their transsartorial approach, which may be uncomfortable for the patient. Also, landmark-based approaches can become challenging in the obese population. Even with US, the sartorius muscle may be very thin and hard to identify in some populations. With technological advancements and improved economy, ultrasonographic guidance is increasingly used successfully to perform high-quality peripheral nerve blocks.

The identification of the saphenous nerve was greatly facilitated with color Doppler visualization of the SBDGA running with the nerve. The artery is usually easy to identify. More proximally, the sonographer can identify the femoral artery within the adductor canal, but caution should be used here because it is a tight compartment where nerve entrapment has been responsible for saphenous neuropathy.16 We chose to block the nerve several centimeters after it exits the adductor canal when it is in close proximity to the SBDGA, approximately 2.7 cm above the proximal patellar border based on the cadaver study. More distally, the saphenous nerve divides into the infrapatellar and sartorial branches, and the anatomic relationships may be less predictable, yielding inconsistent or less dense blocks with more distal approaches.

While we described the saphenous nerve block performed in the prone position, it is also important to note that we have used the described US-guided landmark technique in the supine position when indicated. In the supine position, the approach is from anterior to posterior, with the needle tip directed toward the SBDGA within the subsartorial fat-pad.
Correlating our dissections with clinical anatomy from US imaging, we have found a reliable blockade of the saphenous nerve when using US by exploiting its intimate anatomic relationship with the SBDGA artery and sartorius muscle just proximal to the patella.

Disadvantages of the US-guided approach to the saphenous nerve block include the need for a high-quality US machine with a high-frequency probe (8–12 mHz) and color flow Doppler capability and proficiency in US-guided nerve block techniques. Knowledge of the pertinent anatomic structures is essential with any peripheral nerve block under US visualization. This study demonstrates the feasibility of the US-guided approach and was not designed to prove efficacy or safety, which will require a rigorous prospective clinical study.

In conclusion, the saphenous nerve can be precisely located, taking advantage of its close anatomic relationship to the SBDGA within the subsartorial compartment just proximal to the knee joint line and deep to the sartorius muscle using US guidance. This relationship can be used to facilitate a successful saphenous nerve blockade.

REFERENCES


Continuous Peripheral Nerve Blocks at Home: A Review

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From the Departments of Anesthesiology and Orthopaedics and Rehabilitation, University of Florida, Gainesville, Florida

Postoperative analgesia is generally limited to 12–16 h or less after single-injection regional nerve blocks. Postoperative analgesia may be provided with a local anesthetic infusion via a perineural catheter after initial regional block resolution. This technique may now be used in the outpatient setting with the relatively recent introduction of reliable, portable infusion pumps. In this review article, we summarize the available published data related to this new analgesic technique and highlight important issues related specifically to perineural infusion provided in patients’ own homes. Topics include infusion benefits and risks, indications and patient selection criteria, catheter, infusion pump, dosing regimen, and infusate selection, and issues related specifically to home-care.

(Anesth Analg 2005;100:1822–33)

In the past decade, there has been an increasing interest in “continuous peripheral nerve blocks,” also called “perineural local anesthetic infusions.” This technique involves the percutaneous insertion of a catheter directly adjacent to the peripheral nerves supplying an affected surgical site (as opposed to a “wound” catheter placed directly at a surgical site). Local anesthetic is then infused via the catheter providing potent, site-specific analgesia. Combining a perineural catheter with a portable infusion pump, outpatients may theoretically experience the same level of analgesia previously afforded only to those remaining hospitalized. A previous review article (1) of perineural infusion for inpatient analgesia concluded, “whether this technique is effective for ambulatory patients remains to be determined.” Subsequently, a plethora of data regarding continuous peripheral nerve blocks in outpatients has been published. In this review, we summarize this new evidence, and highlight important issues related specifically to perineural local anesthetic infusion provided at home.

Infusion Benefits

Although continuous regional blockade was first described more than 50 yr ago (2), it was not until 1998 that the introduction of lightweight, portable infusion pumps made home infusion possible (3). Subsequently, case reports or series of ambulatory perineural infusion were described via peripheral nerve catheters in various locations including paravertebral (4), interscalene (5–7), intersternocleidomastoid (8), infraclavicular (6), axillary (9), psoas compartment (9,10), femoral (9,11), fascia iliaca (5), sciatic/Labat (9,10), sciatic/popliteal (6,12), and tibial nerve placement (6). Ambulatory continuous peripheral nerve blocks in pediatric patients have also been reported in patients as young as 8 yr of age (13). However, the first prospective evidence of infusion benefits was not reported until a randomized, double-masked, placebo-controlled investigation was published in 2000 (14).

This study by Klein et al. involved 40 subjects undergoing open rotator cuff repair who received an interscalene block and perineural catheter preoperatively and were randomized to receive either perineural ropivacaine 0.2% or normal saline postoperatively (10 mL/h). Patients receiving perineural ropivacaine averaged a score of 1 on a visual analog pain scale of 0–10 compared with a 3 for subjects receiving placebo. Although a pump designed for ambulatory infusion was used, patients remained hospitalized during local anesthetic infusion, and health care providers removed all catheters before home discharge. Because patients remained hospitalized, the investigators “felt compelled to provide more than oral analgesics,” and patients had access to IV morphine via patient-controlled analgesia (PCA) (14). Therefore, patients
receiving placebo theoretically receive a greater degree of analgesia than that available to ambulatory patients who must rely on oral instead of IV opioids. Consequently, although these data suggested perineur- al infusion might improve postoperative analgesia after hospital discharge, the extent of improvement for patients actually at home remained unknown.

Subsequently, four randomized, double-masked, placebo-controlled studies provided data involving patients discharged home with a catheter in situ (15–18). All of these investigations involved patients scheduled for moderately painful procedures who had an infraclavicular (15), interscalene (17), or posterior popliteal (16,18) perineural catheter placed (Table 1). Patients receiving perineural local anesthetic achieved both clinically and statistically significant lower resting and breakthrough pain scores and required dramatically fewer oral analgesics.

Patients who received perineural local anesthetic also experienced additional benefits related to improved analgesia. Zero to 30% of patients receiving perineural ropivacaine reported insomnia as a result of pain, compared with 60%–70% of patients using only oral opioids (15–17). Patients receiving perineural ropivacaine awoke from sleep because of pain an average of 0.0–0.2 times on the first postoperative night, compared with 2.0–2.3 times for patients receiving perineural saline (15–17). Dramatically less opioid consumption in patients receiving perineural local anesthetic resulted in fewer opioid-related side effects, including less nausea, vomiting, pruritus, and sedation (15–18). Furthermore, patients receiving perineu- ral local anesthetic reported satisfaction with their postoperative analgesia (0–10, 10 = highest) of 8.8–9.8 compared with 5.5–7.7 for patients receiving placebo (15–18). Finally, patients with popliteal local anesthetic infusion rated their “quality of recovery” (0–100, 100 = highest) an average of 96 compared with 83 for patients receiving placebo (18). Whether these demonstrated benefits result in an improvement in patients’ health-related quality of life remains unexplored (19).

Indications and Selection Criteria

Because there are inherent risks with an outpatient infusion, most published series limit this technique to patients expected to have moderate postoperative pain of a duration more than 24 h that is not easily managed with oral opioids (20,21). However, outpatient infusion may be used after mildly painful procedures—defined here as those usually well managed with oral opioids—to decrease opioid requirements and opioid-related side effects (3,22). Because not all patients desire, or are capable of accepting, the extra responsibility that comes with the catheter and pump system, appropriate patient selection is crucial for safe ambulatory local anesthetic infusion. As some degree of postoperative cognitive dysfunction is common after surgery (23), investigators often require patients to have a caretaker at least through the first postoperative night (15–17,24–27). Whether a caretaker is necessary for one night or for the entire duration of infusion remains unresolved (28). If catheter removal at home is expected, then a caretaker willing to perform this procedure must be available at the infusion conclusion if the patient is unwilling or unable to do this themselves (e.g., psoas compartment catheter).

Complications that could be managed routinely within the hospital may take longer to identify or be more difficult to manage in medically unsupervised patients at home. Investigators often exclude patients with known hepatic or renal insufficiency in an effort to avoid local anesthetic toxicity (29). For infusions that may affect the phrenic nerve and ipsilateral diaphragm function (e.g., interscalene or cervical para-vertebral catheters), patients with heart or lung disease are often excluded because continuous interscalene local anesthetic infusions have been shown to cause frequent ipsilateral diaphragm paralysis (30). Although the effect on overall pulmonary function may be minimal for relatively healthy patients (31), conservative application of this technique is warranted until additional investiga- tion of hospitalized and medically supervised patients documents its safety (32,33).

Catheter Placement

Inaccurate catheter placement occurs in a substantial number of cases (17,34,35); it is reported to be as frequent as 40% in some reports (36). Although this is a significant issue for all patients, it is of vital importance for ambulatory patients because catheter placement is not an option once the patient has left the medical facility. There are multiple techniques and equipment types available for catheter insertion. One common technique involves giving a bolus of local anesthetic via an insulated needle to provide a surgical block, followed by the introduction of a catheter (14). However, using this technique, it is possible to provide a successful surgical block with inaccurate catheter placement (17). Reported catheter failure rates are as much as 40% (36). For outpatients, the inadequate perineural infusion often will not be detected until after surgical block resolution after home discharge (17). Some investigators first insert the catheter and then administer a bolus of local anesthetic via the catheter in an effort to avoid this problem, with a reported failure rate of 1%–8% (37,38). Alternatively, catheters that deliver current to their tips have been developed in an attempt to improve initial placement success rates (39). These catheters provide feedback on

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Table 1. Randomized, Controlled Studies of Continuous Peripheral Nerve Blocks Involving Patients Discharged Home with a Catheter *In Situ*

<table>
<thead>
<tr>
<th>Author</th>
<th>Catheter location</th>
<th>Total subjects</th>
<th>Infusate</th>
<th>Basal (mL/h)</th>
<th>Bolus (mL)</th>
<th>Lockout (min)</th>
<th>Primary outcome</th>
<th>Secondary outcomes</th>
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<td>Local anesthetic versus placebo</td>
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<td>White et al. (18)</td>
<td>Popliteal (posterior, traditional approach)</td>
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<td>Ilfled et al. (16)</td>
<td>Popliteal (posterior, intertendinous technique)</td>
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<td>Ilfled et al. (15)</td>
<td>Infraclavicular (coracoid technique)</td>
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<td>Ilfled et al. (17)</td>
<td>Interscalene (lateral approach)</td>
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<td>Ropivacaine versus bupivacaine</td>
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<td>Rawal et al. (22)</td>
<td>Axillary (paresthesia or nerve stimulator)</td>
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<td>Dosing regimens (e.g. bolus-only versus basal-only)</td>
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<td>Ilfled et al. (27)</td>
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<td>Local anesthetic with clonidine versus local anesthetic without clonidine</td>
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<td>Ilfled et al. (26)</td>
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<td>Ilfled et al. (59)</td>
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<td>Three infusion pump models (Group A: elastomeric device with bolus administered with syringe (74); Groups B &amp; C: electronic pumps with bolus control)</td>
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<td>Capdevila et al. (73)</td>
<td>Interscalene, femoral, and tibial (at ankle level)</td>
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| NA = not applicable (an elastomeric pump without bolus capability was used). One additional randomized, controlled investigation was published but not included above since it was aborted prior to completion (28). |
the positional relationship of the catheter tip to the target nerve before local anesthetic dosing (24,25). Although there is evidence that passing current via the catheter may improve the accuracy of catheter placement (40), there are no investigations directly comparing stimulating and nonstimulating catheters (36). Further study is required to identify the optimal placement techniques and equipment for ambulatory perineural infusion (41). Regardless of the equipment/technique used, a test dose of local anesthetic with epinephrine should be administered via the catheter in an effort to identify intrathecal (42), epidural (43), or intravascular (44) placement before infusion.

One major difference between inpatient and ambulatory infusion is that an experienced medical professional will not observe the catheter site daily and reinforce the dressing with ambulatory infusion. Therefore, every effort to optimally secure the catheter must be made for outpatients. These have included the use of sterile liquid adhesive (e.g., benzoin), sterile tape (e.g., Steri-Strips), securing of the catheter-hub connection with either tape or specifically designed devices (e.g., Statlock), subcutaneous tunneling of the catheter (39,45), and the use of 2-octyl cyanoacrylate glue (46). Using a combination of these maneuvers (24,25,27), investigators have reported a catheter retention rate of 95%–100% for more than 60 h in ambulatory patients (Fig. 1).

Infusate Selection

Most publications regarding perineural infusion have involved bupivacaine or ropivacaine, although levobupivacaine (47) and shorter acting drugs have been reported (48–50). As these local anesthetics have varying durations of action (51), investigations involving one may not be applied to another. One trial involving inpatient interscalene infusion found that ropivacaine 0.2% and bupivacaine 0.15% provide similar analgesia but that ropivacaine was associated with better preservation of strength in the hand and less paresthesia in the fingers (51). However, another study of interscalene infusion found ropivacaine 0.2% and levobupivacaine 0.125% equivalent after shoulder surgery, with patients receiving levobupivacaine consuming a smaller volume of anesthetic (47). Similarly, a third investigation found no difference between 0.125% bupivacaine and ropivacaine provided as self-administered bolus doses via an axillary catheter after mildly painful surgery of the upper extremity (22). Unfortunately, the precise equipotent local anesthetic concentrations within the peripheral nervous system remain undetermined, making the evaluation of comparisons problematic. Currently, there is insufficient information to determine if there is an optimal local anesthetic for ambulatory infusions. When deciding on an infusate, providers should consider the risk of local anesthetic toxicity as the concentration of local anesthetic increases (50).

Investigators have added clonidine to long-acting local anesthetic (1–2 μg/mL) for continuous perineural femoral (52), anterior lumbar plexus (53–55), interscalene (56), and popliteal (57) infusions for inpatients.
Unfortunately, although clonidine increases the duration of single-injection nerve blocks (58), the only controlled investigations of adding clonidine to a continuous ropivacaine infusion (1 or 2 μg/mL) failed to reveal any clinically relevant benefits in outpatients (26,59). Additionally, opioids and epinephrine have been added to local anesthetic infusions, but there are currently insufficient published data to draw any conclusions regarding these adjuvants.

**Dosing Regimen**

Investigations of inpatient interscalene (56), axillary (60), fascia iliaca (61), extended femoral (53,55), and subgluteal (62) catheters suggest that the optimal local anesthetic dosing regimen varies with anatomic location. Therefore, data from studies involving one catheter location cannot necessarily be applied to another anatomic location. Three publications specifically investigated the optimal dosing regimen for ambulatory perineural infusions (24,25,27). All involved moderately painful surgical procedures, ropivacaine local anesthetic, stimulating catheters, electronic infusion pumps, and a randomized, double-masked study design. The first two, involving infraclavicular and popliteal infusions, demonstrated that providing PCA bolus doses without a basal infusion results in a longer duration until local anesthetic exhaustion but less potent analgesia, increased sleep disturbances, and less satisfaction compared with a regimen including both a basal infusion and bolus capability (25,27). For both types of infusions, adding PCA bolus doses allowed for a slower continuous basal rate and decreased local anesthetic consumption compared with a basal-only regimen, thereby increasing the duration of infusion benefits when in an ambulatory environment with a limited local anesthetic reservoir. Furthermore, for infraclavicular catheters, providing only continuous basal infusion results in larger oral analgesic consumption (25) and increased opiate-related side effects (15).

For interscalene catheters after shoulder surgery, decreasing the basal rate from 8 to 4 mL/h lengthens infusion duration and provides similar baseline analgesia when patients supplement their block with large bolus doses (24). However, patients experience an increase in breakthrough pain incidence and intensity and sleep disturbances and a decrease in satisfaction with their analgesia. Therefore, if ambulatory patients do not return for additional local anesthetic, practitioners are left with the dilemma of superior analgesia for a shorter duration versus a lesser degree of analgesia for a longer period of time. It should be noted that with a reprogrammable infusion pump, the basal infusion rate may be decreased as surgical pain resolves, thus lengthening the infusion duration and theoretically maximizing postoperative analgesia (7).

There are limited data available on which to base recommendations on the optimal basal rate, bolus volume, and lockout period. Although additional investigations of dosing regimen optimization involving hospitalized patients are available (53,55,56,60–62), data derived from inpatient infusion cannot necessarily be applied to outpatients. Furthermore, in all probability, other confounding variables may affect the optimal regimen, including the surgical procedure, catheter location, physical therapy regimen, and specific local anesthetic infused. Available published data related to dosing regimen optimization for outpatients involved surgical procedures producing moderate postoperative pain. It is possible—even probable—that adequate analgesia for procedures inducing mild postoperative pain would be adequately treated with a bolus-only dosing regimen (22). Additionally, there is a theoretical possibility that stimulating catheters may be placed, on average, closer to the target nerve/plexus compared with nonstimulating devices (40). If this proves to be true, then potentially different dosing regimens, basal rates, and bolus doses would be optimal for different types of catheters. However, currently published data are insufficient to draw any conclusions.

Available inpatient and outpatient data suggest that after procedures producing moderate-to-severe pain, providing patients with the ability to self-administer local anesthetic doses increases perioperative benefits or decreases local anesthetic consumption (24,25,27). Unfortunately, other than for interscalene infusions (24), no information is available to base recommendations on the optimal basal rate, bolus volume, or lockout period. In all probability, these factors will also be influenced by the variables noted above. Until recommendations based on prospectively collected data are published, practitioners should be aware that investigators have reported successful analgesia using the following with long-acting local anesthetics: basal rate of 5–10 mL/h, bolus volume of 2–5 mL, and lockout duration of 20–60 min. Additionally, the maximum safe doses for the long-acting local anesthetics remain unknown. However, multiple investigations involving patients free of renal or hepatic disease have reported blood concentrations within acceptable limits after up to 5 days of perineural infusion with similar dosing schedules (29,63–65).

**Infusion Pump Selection**

Many factors must be considered to determine the optimal device for a given clinical application (66). Such factors include—but are not limited to—the acceptable infusion rate accuracy, PCA bolus capability, and total local anesthetic volume requirement. The infusion devices reviewed in this article include those...
for which performance data are available from independent sources (Table 2 and Appendix).

**Accuracy, Consistency, Reliability**

For the purposes of this review, accuracy is defined as infusing at the set or expected rate and consistency is infusing at the same rate for most of the infusion (Fig. 2). In general, electronic infusion pumps provide highly accurate (90%–100% expected) and consistent (+5% baseline) basal rates over the entire infusion duration (67–70). Elastomeric devices provide a more rapid than expected basal rate initially (110%–150% expected), return to their expected rate within 2–12 h, and again increase to a higher rate before reservoir exhaustion (67–71). Similarly, spring-powered pumps initially provide a more rapid than expected basal rate (115%–135% expected) which steadily decreases to a less rapid than expected rate (70%–75% expected) by reservoir exhaustion (67,69,71). There are insufficient published data to determine the clinical situations in which the typical basal rate variation of nonelectronic pumps would be clinically relevant. Although investigators have used elastomeric pumps for multiple catheter locations and surgical procedures (6,14,17), it

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**Table 2. Infusion Pump Attributes**

<table>
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<tr>
<th>Pump model (References)</th>
<th>Wt. (g)</th>
<th>Reservoir volume (max mL)</th>
<th>Basal infusion (mL/h)</th>
<th>Bolus dose (mL)</th>
<th>Bolus lockout (min–h)</th>
<th>Retail price (US $)</th>
<th>Power source</th>
</tr>
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<tbody>
<tr>
<td><strong>Programmable, reusable models</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6060 MT (70)</td>
<td>525</td>
<td>IV bag*</td>
<td>0.1–50.0</td>
<td>0–50</td>
<td>0–60</td>
<td>3995</td>
<td>Electronic</td>
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<td>ambIT PCA (70)</td>
<td>133</td>
<td>IV bag*</td>
<td>0–20</td>
<td>0–20</td>
<td>5–24</td>
<td>500–800†</td>
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</tr>
<tr>
<td>AutoMed 3400</td>
<td>325</td>
<td>IV bag*</td>
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<td>0–50</td>
<td>0–60</td>
<td>675</td>
<td>Electronic</td>
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<td>323</td>
<td>IV bag*</td>
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<td>0–30</td>
<td>0–24</td>
<td>1750–2300</td>
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<td>CADD-Legacy PCA (68)</td>
<td>372</td>
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<td>0–50</td>
<td>0–9.9</td>
<td>5–24</td>
<td>3595</td>
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<tr>
<td>CADD-Prism PCS (68)</td>
<td>547</td>
<td>IV bag*</td>
<td>0–30</td>
<td>0–9.9</td>
<td>5–24</td>
<td>4125</td>
<td>Electronic</td>
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<tr>
<td>Ipump PMS (70)</td>
<td>415</td>
<td>IV bag*</td>
<td>0–19.9‡</td>
<td>0–9.9</td>
<td>1–6</td>
<td>4295</td>
<td>Electronic</td>
</tr>
<tr>
<td>Microject PCA (67,68)§</td>
<td>198</td>
<td>IV bag*</td>
<td>0–9.9</td>
<td>0–2</td>
<td>6–1</td>
<td>N/A§</td>
<td>Electronic</td>
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<tr>
<td>Microject PCEA (69)§</td>
<td>198</td>
<td>IV bag*</td>
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<td>10–120</td>
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<td>Electronic</td>
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<td><strong>Programmable, Disposable Models</strong></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>ambIT LPM (70)</td>
<td>133</td>
<td>IV bag*</td>
<td>0–20</td>
<td>0–20</td>
<td>5–24</td>
<td>250–350†</td>
<td>Electronic</td>
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<td>AutoMed 3200 (70)</td>
<td>350</td>
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<td>0–10</td>
<td>0–5</td>
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<td>255</td>
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<td>Pain Pump II (69)</td>
<td>408</td>
<td>400</td>
<td>0.5–15</td>
<td>0–15</td>
<td>10–2</td>
<td>250‡</td>
<td>Electronic</td>
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<tr>
<td><strong>Nonprogrammable, disposable, basal- and bolus-capable models</strong></td>
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<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Accufuser Plus XL (68–70)</td>
<td>109</td>
<td>550</td>
<td>5, 8, or 10</td>
<td></td>
<td>2</td>
<td></td>
<td>15, 60 min</td>
</tr>
<tr>
<td>Pain Care 3200 (69)</td>
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<td>200</td>
<td>5.7 –2.9</td>
<td></td>
<td>4–6</td>
<td></td>
<td>40–1.3</td>
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<tr>
<td>On-Q C-Bloc with OnDemand (70)</td>
<td>135</td>
<td>400**</td>
<td>5</td>
<td></td>
<td>5</td>
<td></td>
<td>60 min</td>
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<tr>
<td><strong>Nonprogrammable, disposable, basal- or bolus-only models</strong></td>
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<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Accufuser (67)</td>
<td>95</td>
<td>275</td>
<td>2, 4, 5, 8, 10</td>
<td></td>
<td>N/A</td>
<td>N/A</td>
<td>150–225</td>
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<tr>
<td>C-Bloc (67)</td>
<td>65</td>
<td>400</td>
<td>5 or 10</td>
<td></td>
<td>N/A</td>
<td>N/A</td>
<td>395‡</td>
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<tr>
<td>Infusor LV5 (69)</td>
<td>65</td>
<td>275</td>
<td>2, 5, 7, 10</td>
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<td>N/A</td>
<td>55</td>
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<tr>
<td>Pain Pump I (67)</td>
<td>104</td>
<td>120</td>
<td>0.8, 2.1, 4.2</td>
<td></td>
<td>N/A</td>
<td>N/A</td>
<td>150‡</td>
</tr>
<tr>
<td>Sgarlato (67)</td>
<td>225</td>
<td>200</td>
<td>0.5, 1, 2, 4</td>
<td></td>
<td>N/A</td>
<td>N/A</td>
<td>225‡</td>
</tr>
</tbody>
</table>

N/A = not applicable.

Weight includes batteries and disposable cassette in electronic pumps and excludes infusate for all pumps.

* Local anesthetic reservoir is an external syringe or IV-style bag of any size; † approx. price for Florida (USA); other regions may vary; ‡ if a bolus dose is not provided, the maximum basal rate is 90 mL/h; § the Microject pumps may be reused as disposable cassettes are used with the mechanical pump, but the pumps themselves are less expensive than some disposable pumps, and may thus be considered disposable, if desired. No longer available in the US; ¶ fixed during manufacture.

¶ Basal infusion rate described as “4 mL/h continuous flow” on product packaging and marketing materials. However, product information contained within the instruction manual specifies that the rate is 5.7 mL/h at the beginning of the infusion, and steadily declines to 2.9 mL/h by reservoir exhaustion. Bolus dose is variable and lockout increases as infusion progresses (69).

** On-Q C-Bloc with OnDemand may be overfilled to 500 mL, decreasing the basal rate for a portion of the infusion, but allowing for a longer infusion duration (70).
is not known whether providing a less variable basal rate would have affected outcomes. Additionally, there are few published data regarding the failure rates—or reliability—of the various pump models (72). Of note, the Microject patient-controlled epidural analgesia (PCEA) pump has been noted to have a frequent rate of false alarm activation (73). However, redesigned models are replacing both the Microject PCA and PCEA. There are electronic pumps that have been noted to infuse without an erroneous alarm for more than 10,000 cumulative hours of clinical use (24,25,27). Although the nonelectronic pumps cannot trigger alarms which are an irritant to both patients and health care providers (73), there is also no warning if a catheter occlusion or pump malfunction occurs (16).

**Bolus-Dose Capability**

Various pumps allow for both patient-controlled local anesthetic boluses and a basal infusion (Table 2), whereas others allow for only one of these (67–70,74). Without the option for a bolus dose (74), larger doses of oral opiates are often required for breakthrough pain (25). Patient-controlled local anesthetic administration, also called patient-controlled regional analgesia (PCRA), provides equivalent or superior analgesia with less local anesthetic consumption compared with continuous infusions alone with a variety of perineural techniques (25,53,55,56). PCRA is often important for ambulatory patients because the infusion may be tailored to provide a minimum basal rate allowing maximum infusion duration and minimal motor block (7) yet allow bolus dosing for breakthrough pain (25) and before physical therapy (24,27,75). Finally, for patients with difficulty applying force to a bolus button (e.g., patients with arthritis), electronic pumps offer easily depressed buttons compared with the manual bolus injection systems of nonelectronic units (Fig. 2).

Some investigators have used elastomeric pumps that provide bolus-only dosing when the patient releases a clamp on the tubing connecting the pump and catheter (3,5,22). The patient is instructed to reclamp the tubing after a specified period of time (3,22). If a patient forgets to reclamp the tubing it is possible for the entire contents of the local anesthetic reservoir to be administered in less than an hour. This potentially devastating scenario has been reported, although no apparent morbidity has yet occurred (5). Although the safety of this method may be demonstrated in the future, practitioners should consider the relative risks and benefits now that multiple pumps are available providing controlled bolus dosing (Table 2).

**Programmability**

If various rates of infusion, bolus volumes, and lockout times are desired, an electronic pump will be required. However, most of the nonelectronic pumps may be ordered at various infusion rates, although this aspect is usually fixed during manufacturing and cannot be adjusted; Baxter Healthcare International manufactures an elastomeric pump with an adjustable basal rate that is currently unavailable in the United States (personal communication, Mary Kingsbury, 2004). Just as with epidural infusions, the optimal basal infusion rate for perineural catheters is highly variable among patients (15,26). Allowing patients to vary their basal rate (with instructions from a health care provider via the telephone) has allowed analgesia optimization (7,26).

**Disposability and Unit Price**

It may be cost-effective for practitioners who use these devices repeatedly to use a more-expensive, reusable, electronic pump that uses relatively inexpensive disposable cassettes for each new patient (Table 2). This scenario requires the patient to either be provided
with a padded envelope for infusion pump return (41) or revisit the surgical center (76).

Miscellaneous Factors

Most elastomeric pumps regulate their infusion rate using a temperature-dependent device (67–70). Although older pump models demonstrated a basal rate increase up to 35% with a 4°C increase in ambient temperature (67), current units are more resistant to temperature variations (68–70). Under hypobaric conditions, such as those occurring at high altitude, elastomeric pump infusion rates are reduced (77). Finally, the required local anesthetic reservoir volume is determined by the infusion rate, PCA bolus doses, and anticipated infusion duration (Table 2). Spring and electronic pumps are refillable, but elastomeric pumps may not function properly if simply refilled (unpublished data).

Discharge and Home Care

Patient Education

Because most patients have some degree of postoperative cognitive dysfunction, most investigators educate both patient and caretaker at the same time before discharge. Although currently uninvestigated, there is consensus among practitioners that both verbal and written instructions should be provided, along with contact numbers for health care providers who are available throughout the infusion duration (6,15,22,78). Along with standard postoperative outpatient instructions, topics reviewed usually include infusion pump instructions, expectations regarding surgical block resolution, breakthrough pain treatment, specific instruction to not drive or operate machinery, catheter site care (sponge bath instead of shower), limb protection, what to do if local anesthetic leaks from under the protective dressing, signs and symptoms of possible catheter-related and local anesthetic-related complications, and catheter removal plan.

Patients being discharged home must be able to ambulate. Therefore, discharge with a lower extremity peripheral nerve block remains controversial (79). Although there is evidence that discharge with an insensate extremity after a single-injection nerve block can result in minimal complications (80), whether patients should weight-bear with a continuous peripheral nerve block remains unexamined. Therefore, conservative management may be optional; some investigators have recommended that patients avoid using their surgical limb for weight bearing (8,16,27). This is usually accomplished with the use of crutches, and the patient’s ability to use these aids without syncope or difficulty must be confirmed before discharge. The importance of protecting the surgical extremity must be emphasized as well. Any removable brace or splint should remain in place except during physical therapy sessions.

If the initial surgical block has not resolved before home discharge, postoperative analgesic requirements cannot be assessed. Although perineural infusions of local anesthetic usually decrease postoperative pain dramatically, many patients still require oral analgesics. The percentage of patients who will use supplemental oral opioids is dependent on a multitude of factors, including the type of surgery, other analgesic adjuvants such as cryotherapy, the local anesthetic used for infusion, and the infusion dosing regimen provided. Furthermore, the possibility of catheter misplacement during initial insertion or subsequent dislodgement will usually require the use of oral analgesics. However, it is currently impossible to accurately predict which patients will require oral opioids. Therefore, a prescription for oral analgesics should be provided to all patients, and the importance of filling the prescription immediately after leaving the surgical center should be emphasized. A period of inadequate analgesia may result if patients wait to fill the prescription until after they have determined if oral analgesics are required.

Patient Contact and Catheter Removal

Although not systematically investigated, practitioners may want to consider documenting each patient contact, as is standard of care for inpatients (Fig. 3). The optimal frequency of contact with ambulatory patients is currently unknown and is probably dependent on multiple factors, such as patient comorbidities and surgical procedure. Multiple investigators have suggested that patients be contacted daily by telephone (15–17,22,81); others have provided twice-daily home nursing visits in addition to telephone calls (6,73). Issues deserving attention consist of signs and symptoms of potential complications including, but not limited to, site infection (82), nerve injury (83), pulmonary compromise (32,33), and local anesthetic toxicity (44). There are case reports of initially misplaced catheters (42–44,84,85), but migration after a documented correct placement has not been described (but remains a theoretical risk). Possible complications of an unidentified initially misplaced catheter or of a catheter migration include intravascular or interpleural placement/migration resulting in local anesthetic toxicity, IM placement/migration resulting in myonecrosis, and epidural/intrathecal placement/migration when using interscalene, intersternocleidomastoid, paravertebral, or psoas compartment catheters.

Investigators have reported catheter removal by various techniques: some discharge patients with written instructions (12), others have insisted on a health care provider performing this procedure (76),
Progress Note for Ambulatory Perineural Local Anesthetic Infusion

Surgery Date / /200  

Home phone: ( ) - 

Procedure:  

Other phone: ( ) - 

Post-op in PACU

☐ Catheter w/ neg. aspiration & cc of w/ mcg epi/cc to catheter w/ neg aspiration q2 cc
☐ No heart rate or sensory changes within 5 minutes
☐ Instructions and local anesthetic toxicity symptoms explained to pt & all questions answered, MD phone #s provided
☐ Pump tubing secured to catheter, pump programmed & infusion begun

Notes:

Physician Signature

POD #0:

☐ Patient or patient’s caretaker contacted by phone
☐ Symptoms of local anesthetic toxicity, catheter migration and infection denied
☐ Appropriate sensory/motor function of affected extremity acknowledged
☐ Surgical pain under control
☐ Patient would like to have catheter remain in situ at this time
☐ All questions answered

Notes:

Physician Signature

POD #1:

☐ Patient or patient’s caretaker contacted by phone
☐ Symptoms of local anesthetic toxicity, catheter migration and infection denied
☐ Appropriate sensory/motor function of affected extremity acknowledged
☐ Surgical pain under control
☐ Patient would like to have catheter remain in situ at this time
☐ All questions answered

Notes:

Physician Signature

POD #2:

☐ Patient or patient’s caretaker contacted by phone
☐ Symptoms of local anesthetic toxicity, catheter migration and infection denied
☐ Appropriate sensory/motor function of affected extremity acknowledged
☐ Surgical pain under control
☐ Patient would like to have catheter remain in situ at this time
☐ Catheter removed by patient’s caretaker with MD on phone, tip reported to be blue/silver
☐ All questions answered

Notes:

Physician Signature

POD #3:

☐ Patient or patient’s caretaker contacted by phone
☐ Symptoms of local anesthetic toxicity, catheter migration and infection denied
☐ Appropriate sensory/motor function of affected extremity acknowledged
☐ Surgical pain under control
☐ Patient would like to have catheter remain in situ at this time
☐ Catheter removed by patient’s caretaker with MD on phone, tip reported to be blue/silver
☐ All questions answered

Notes:

Physician Signature

POD #4:

☐ Patient or patient’s caretaker contacted by phone
☐ Symptoms of local anesthetic toxicity, catheter migration and infection denied
☐ Appropriate sensory/motor function of affected extremity acknowledged
☐ Surgical pain under control
☐ Patient would like to have catheter remain in situ at this time
☐ Catheter removed by patient’s caretaker with MD on phone, tip reported to be blue/silver
☐ All questions answered

Notes:

Physician Signature

Figure 3. An example of a progress note that may be used to record telephone contacts with ambulatory patients.
although others have patients’ caretakers (or occasionally the patients themselves) remove the catheters with instructions given by a provider over the telephone (15–17,24,25,27). Although there are no data documenting the superiority of any one technique, one survey revealed that with instructions given by phone, 98% of patients felt comfortable removing their catheter at home (86). Of note, only 4% would have preferred to return for a health care provider to remove the catheter, and 43% responded that they would have felt comfortable with exclusively written instructions (86). Practitioners may consider providing nonsterile gloves for patients having their catheters removed at home (15–17). The presence of a blue/silver catheter tip identified by the person removing the catheter confirms complete removal (depending on catheter design) and should be documented in the medical record.

Conclusions
In keeping with evidence-based medical practice, we believe the optimal techniques, equipment and patient oversight should be determined by prospective, controlled trials and not merely by institutional preference. We have noted the available relevant data and information. There is strong evidence suggesting that continuous peripheral nerve blocks provided at home improve postoperative analgesia, sleep quality, and patient satisfaction while decreasing supplemental opioid requirements and opioid-related side effects. In addition, a basal infusion after moderately painful surgery maximizes infusion benefits, whereas adding PCA bolus doses allows for a decreased basal rate and increased infusion duration. However, because of the relatively recent evolution of outpatient perineural infusion, illuminating data on many aspects of this analgesic technique are unavailable. Future investigation should include determining which patients and procedures benefit most from perineural infusion, the optimal local anesthetic, concentration, and adjuvants, the most advantageous delivery regimen and dosing structure, the optimal catheters (e.g., stimulating versus nonstimulating catheters), placement techniques, and infusion pumps, the safest frequency of patient contact and method of catheter removal, and, finally, whether additional outcomes are affected with ambulatory perineural local anesthetic infusion (e.g., health-related quality of life).

Appendix: Infusion Pump Distributors

<table>
<thead>
<tr>
<th>Pump (reference)</th>
<th>Distributor</th>
<th>City</th>
<th>State</th>
</tr>
</thead>
<tbody>
<tr>
<td>6060 MT (70)</td>
<td>Baxter Healthcare</td>
<td>Deerfield</td>
<td>IL</td>
</tr>
<tr>
<td>Accufuser (67)</td>
<td>McKinley Medical</td>
<td>Wheat Ridge</td>
<td>CO</td>
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<tr>
<td>Accufuser Plus XL (68–70)</td>
<td>McKinley Medical</td>
<td>West Jordan</td>
<td>UT</td>
</tr>
<tr>
<td>ambIT LPM (70)</td>
<td>Sorenson Medical</td>
<td>West Jordan</td>
<td>UT</td>
</tr>
<tr>
<td>ambIT PCA (70)</td>
<td>Sorenson Medical</td>
<td>Salt Lake City</td>
<td>UT</td>
</tr>
<tr>
<td>AutoMed 3200 (70)</td>
<td>Algos, LC</td>
<td>Salt Lake City</td>
<td>UT</td>
</tr>
<tr>
<td>AutoMed 3400 (69)</td>
<td>Algos, LC</td>
<td>Salt Lake City</td>
<td>UT</td>
</tr>
<tr>
<td>BlockIt (WalkMed) (68)</td>
<td>McKinley Medical</td>
<td>Wheat Ridge</td>
<td>CO</td>
</tr>
<tr>
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<td>Smiths Medical</td>
<td>St. Paul</td>
<td>MN</td>
</tr>
<tr>
<td>CADD-Prism PCS (68)</td>
<td>Smiths Medical</td>
<td>St. Paul</td>
<td>MN</td>
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<td>C-Bloc (67)</td>
<td>I-Flow Corporation</td>
<td>Lake Forest</td>
<td>CA</td>
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<tr>
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<td>Baxter Healthcare</td>
<td>Deerfield</td>
<td>IL</td>
</tr>
<tr>
<td>Ipump (70)</td>
<td>Baxter Healthcare</td>
<td>Deerfield</td>
<td>IL</td>
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<tr>
<td>Microject PCA (67,68)</td>
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<td>West Jordan</td>
<td>UT</td>
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<td>Microject PCEA (69)</td>
<td>Sorenson Medical</td>
<td>West Jordan</td>
<td>UT</td>
</tr>
<tr>
<td>On-Q C-Bloc with OnDemand (70)</td>
<td>I-Flow Corporation</td>
<td>Lake Forest</td>
<td>CA</td>
</tr>
<tr>
<td>Pain Care 3200 (69)</td>
<td>Breg, Inc.</td>
<td>Vista</td>
<td>CA</td>
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<td>Pain Pump I (67)</td>
<td>Stryker Instruments</td>
<td>Kalamazoo</td>
<td>MI</td>
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<tr>
<td>Pain Pump II (69)</td>
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<td>Kalamazoo</td>
<td>MI</td>
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<tr>
<td>Sgarlato (67)</td>
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<td>Los Gatos</td>
<td>CA</td>
</tr>
</tbody>
</table>

References


NERVE INJURY AFTER PERIPHERAL NERVE BLOCK
Michael Bishop, M.D.

Magnitude of the Problem
• Brul et al., 2007¹
  o Retrospective study
  o Reviewed all English language studies from January 1995-December 2005 found on MEDLINE search
  o Total of > 65,000 peripheral nerve blocks
  o Overall incidence of nerve injury < 3%

<table>
<thead>
<tr>
<th>Block</th>
<th># Studies</th>
<th># Blocks</th>
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<tr>
<td>Interscalene</td>
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<td>6017</td>
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<tr>
<td>Supraclavicular</td>
<td>1</td>
<td>1899</td>
<td>0.03</td>
</tr>
<tr>
<td>Axillary</td>
<td>10</td>
<td>17395</td>
<td>1.48</td>
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<tr>
<td>Midhumeral</td>
<td>2</td>
<td>8870</td>
<td>0.02</td>
</tr>
<tr>
<td>Lumbar Plexus</td>
<td>3</td>
<td>4733</td>
<td>0.19</td>
</tr>
<tr>
<td>Femoral Nerve</td>
<td>4</td>
<td>13378</td>
<td>0.34</td>
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<tr>
<td>Sciatic Nerve</td>
<td>3</td>
<td>10714</td>
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</tr>
<tr>
<td>Popliteal</td>
<td>4</td>
<td>2086</td>
<td>0.24</td>
</tr>
<tr>
<td>TOTAL</td>
<td>65092</td>
<td></td>
<td>&lt;3%</td>
</tr>
</tbody>
</table>

  o Permanent nerve injury defined as an injury with symptoms lasting >12 months after the block
  o Studies that followed patients for that period of time demonstrated only one permanent injury in a patient who had a femoral nerve block
  o Self reported data may have underestimated true incidence of injury

• Review by Sorenson, 2008²
  o Incidence of nerve injury of 10-15% in prospective studies
  o 95% of deficits resolve in 4-6 weeks
  o 99% of deficits resolve within 1 year

• In Summary:
  o Nerve injury after peripheral regional block is uncommon
  o Permanent injury is rare

Nerve Anatomy³
Classification and Pathophysiology of Nerve Injury

- The Seddon Classification published in 1943 describes three grades of nerve injury that are clinically useful in predicting functional outcome.

  o **Neuropraxia**
    - Mildest grade of injury
    - Defined as a reduction or complete block of conduction across a nerve segment without disruption of axonal continuity
    - The symptoms are thought to be due to ion-induced conduction block and in some cases damage to myelin in the injured segment
    - No Wallerian degeneration occurs
    - Functional loss is transient and full recovery is the rule
    - Symptoms may last from hours to weeks

  ![Diagram of Neuropraxia](image)

  - **Neuropraxia**

  o **Axonotmesis**
    - Results from more severe injury and causing interruption of the axon and myelin sheath
    - The neural connective tissue, including endoneurium, perineurium, epineurium and other supporting tissues, remains intact and provides a conduit to guide regrowing axons to the target tissues
    - Distal Wallerian degeneration occurs
    - Prognosis for functional recovery is good
    - Duration of symptoms depends on the location of the lesion; proximal lesions require a longer time period for regrowth of the axons to the target tissues
    - Axon regrowth occurs at approximately 1 inch per month and there is a period of maturation preceding functional recovery. Thus, resolution of symptoms typically can require months.
    - Return of function is not dependent on perfect recovery of preinjury nerve structure.
    - With very proximal lesions recovery of function may not be complete
    - This occurs if atrophy of motor end plates or sensory receptors occurs before the axon can regrow to reinnervate these structures

  ![Diagram of Axonotmesis](image)

  - **Axonotmesis**

  o **Neurotmesis**
    - Most severe grade of injury
    - Occurs when there is complete transection of the axon and all supporting neural connective tissue or when, in addition to axonal...
interruption, the neural connective tissue is so damaged that severe internal fibrosis occurs within the nerve

- Without surgical intervention functional recovery is poor because resulting scar tissue prevents axonal regrowth to the target tissues

- Wallerian Degeneration
  - Follows neural injury with axonal interruption
  - The nerve fiber distal to the site of injury undergoes a predictable anterograde degenerative process known as Wallerian Degeneration
  - This calcium-mediated process begins within hours of injury and results in fragmentation and phagocytosis of the axon and myelin sheath
  - The process typically is completed within 5-8 weeks and results in an endoneurial sheath containing only Schwann cells
  - The nerve fiber proximal to the site of injury may show no or only mild degeneration, however in severe trauma the degenerative process may proceed in the retrograde fashion to include the nerve cell body.

Causes of Nerve Injury

- Mechanical Trauma due to puncture of the nerve by the nerve block needle has long been thought to be a primary cause of nerve injury.
  - Bigeleisen(2006) investigated this possibility
    - Twenty six patients underwent axillary block with ultrasound assistance using a 22 ga B bevel needle
- Musculocutaneous, median, ulnar and radial nerves identified using ultrasound
- Each nerve localized by elicitation of a paresthesia or feeling a "pop" as the needle pierced the fascia surrounding the nerve
- 2-3 ml of the local anesthetic solution was injected
- If the injection appeared intraneural, the needle was withdrawn and an additional 2-3 ml was injected around the nerve
- If a halo appeared on initial injection an additional 2-3 ml was injected around the nerve
- All blocks were successful and no patients required analgesia in the PACU
- Twenty two of 26 patients (72 of 104 nerves) had puncture of at least one nerve as determined by ultrasound
- Puncture of a nerve did not always result in paresthesia or dysesthesia
- If paresthesia or dysesthesia did occur on nerve puncture, it variably increased or decreased during injection
- No patients had residual neural injury following the blocks as determined by 6 month follow up
- This suggested that "neral puncture and or injection per se are not the immediate or most likely cause of nerve injury after nerve block using the techniques described in this study"
  - Baciarello et al. (2007) suggested that, while intraneural injections may not necessarily cause nerve injury, intrafascicular injections almost invariably do cause nerve injury
  - Kapur et al. (2007) found that epineural injections of dog sciatic nerve in vivo with 4 ml of 2% lidocaine resulted in nerve injury only when the injection pressure exceeded 12 psi
    - This suggests that the intraneural pressure may be the causative factor in nerve injury following intraneural puncture and injection.
  - There is no clear evidence that technique of nerve block (paresthesia, nerve stimulator, ultrasound guided) has a better safety profile with respect to nerve injury.

- Ischemia can occur with high intraneural pressure due to intraneural injection, or vascular compromise due to tourniquet use or patient positioning
  - Large myelinated fibers appear to be more sensitive to ischemia than smaller nonmyelinated fibers
  - Greensmith and Murray cite an investigation into the effect of epinephrine containing injectate in resulting nerve injury
    - Rabbit sciatic nerves in vivo were subjected to topical endoneurial or intrafascicular injections with various concentrations of bupivacaine with or without 5 mcg/ml epinephrine
    - Intrafascicular injections were always associated with nerve injury while the endoneurial applications were associated with nerve injury only in the presence of epinephrine
    - This suggests that epinephrine may play a contributing role in the development of nerve injury after nerve block

- Compression may result in injury independent of ischemia
  - Studies with pressure cuffs demonstrated conduction block associated with focal demyelization after displacement of axoplasm and myelin internodes
  - Associated with obliteration of nodes of Ranvier
• **Nerve Stretch**
  - Normal nerves can stretch up to 10-20% before injury occurs
  - One study found 17 nerve injuries attributed to traction in 417 total shoulder arthroplasties performed under general anesthesia
  - Traction using greater than 7 kg has also been associated with a higher risk of nerve injury

• **Patient Positioning**
  - The effect of wrist extension for intra-arterial puncture on nerve injury was studied in awake healthy volunteers
  - All were found to have conduction block involving the median nerve after 30-60 minutes of wrist extension

• **Local Anesthetic Toxicity** is of uncertain significance in the etiology of injury after nerve block
  - High concentrations of local anesthetic applied directly to nerve fibers may result in irreversible conduction loss in experimental preparations
  - The significance of this factor in daily practice is less clear

• **Unknown Factors** also account for some clinical postoperative nerve injuries
  - The incidence of nerve injury following general anesthesia, in the absence of nerve block, is said to be 1/300 for the ulnar nerve and 1/1000 for all other peripheral nerves

---

**Diagnosis of Nerve Injury**

• **Careful Physical Examination** with specific neurological focus would appear to be the first and foremost activity to be undertaken when a patient presents with potential nerve injury after nerve block
  - Motor and sensory deficits should be carefully documented

• **Electromyography (EMG)** involves the direct examination of skeletal muscles by placement of a small needle electrode
  - Normal muscle at rest is electrically silent
  - Axonotmesis/Neurotmesis injury patterns include:
    - fibrillation, positive sharp wave discharge at rest
    - abnormal recruitment pattern
  - Changes are best seen 2-3 weeks after initial injury
    - use of the EMG in the acute injury phase may show complete loss of recruitment suggestive of acute injury
    - may show evidence of an old pre-existing injury

• **Nerve Conduction Study (NCS)** involves the measurement of the ability of peripheral nerves to conduct electrical activity after stimulation
  - Latency, distance travelled and nerve conduction velocity are all measured
  - The hallmark of Neuropraxia is slowed or blocked conduction across a nerve segment
  - In the immediate post injury phase, NCS may show decreased recruitment pattern in either Neuropraxia or Axonotmesis.
  - EMG/NCS studies can:
    - Help localize a nerve injury to a specific root, trunk, cord or peripheral nerve
    - Determine if the lesion involves motor, sensory or both types of nerve fibers
    - Help determine if there is preexisting nerve pathology

• **Imaging Studies** such as MRI and CT scan may also be helpful in the evaluation of a nerve injury
Both MRI and CT have limitations in distinguishing nerves from the surrounding soft tissues.

MRI and especially MRN (magnetic resonance neurography) is superior to CT.

MRI of muscles can reveal signal changes in denervated (Axonotmesis/Neurotmesis) muscle as early as 4 days post injury.

Normal STIR/T2 weighted images are consistent with Neuropraxia.

Careful examination with documentation of motor and sensory deficits

Neurological Consultation

If compression by hematoma or other external influence is suspected, perform MRI/CT

EMG in 1-3 days. If normal repeat in 3-4 weeks. If abnormal repeat in 6 months.

NCS in 1-3 days. If normal follow clinically. If abnormal repeat in 6 months.

Complete or progressive neural deficits should prompt urgent evaluation by a neurologist or neurosurgeon.

Incomplete lesions with evidence of moderate or severe defect are an indication for early neurological consultation and consideration of neurophysiologic testing.

Mild and/or resolving symptoms without objective evidence of neural deficit require only patient reassurance.

Have team in place before it is needed

Anesthesiologist

Surgeon

Neurologist/Neurophysiologist

Physical Therapist

Involve members early after suspected injury

Make sure everyone is telling the patient the same thing to avoid confusion.

Treatment of Nerve Injury

Dictated by the results of the work up

Rarely is surgical intervention warranted

Detailed discussion with patient as to:

Nature of injury

Expected prognosis including low likelihood of permanence of symptoms

Time course of expected recovery

Physical therapy to maintain mobility

Careful follow up

Prevention of Nerve Injury

Patient should be awake or lightly sedated

Pain on needle placement or injection is not absolutely predictive of nerve injury, it seems prudent to utilize this important feedback

Special care with interscalene blocks

Use care with Needle Placement

It seems obvious that careful needle placement and use of a B bevel needle should help to minimize the likelihood of injury

Cautious use of Epinephrine

Use volume over concentration with respect to local anesthetic.
Nerve Stimulation Technique Criteria
- Obtain loss of twitch at or above 0.2 MA (if using a stimulator with 0.1ms pulse width)
- Instant loss of twitch with initial 0.5ml injected
- Low resistance to injection
- Painless injection

Ultrasound guided needle placement
- A somewhat controversial editorial appeared in the British Journal of Anesthesia
  - Suggested that ultrasound may be the new gold standard for regional anesthesia
- Ultrasound guidance certainly seems to have "face validity " if nothing else. What can compare to actually seeing your needle and injection in real time?

Use caution in patients with known or suspected preexisting neurological disease
- Diabetes mellitus
- Chemotherapy induced
- Scheduled surgery on a nerve in the distribution of the planned block

Careful positioning during and after the block
- Document the block carefully including any untoward occurrences

References
Background: Several previous surveys have estimated the rate of major complications that occur after regional anesthesia. However, because of the increase in the use of regional anesthesia in recent years and because of the introduction of new techniques, reappraisal of the incidence and the characteristics of major complications is useful.

Methods: All French anesthesiologists were invited to participate in this 10-month prospective survey based on (1) voluntary reporting of major complications related to regional anesthesia occurring during the study period using a telephone hotline service available 24 h a day and managed by three experts, and (2) voluntary reporting of the number and type of regional anesthesia procedures performed using pocket booklets. The service was free of charge for participants.

Results: The participants (n = 487) reported 56 major complications in 158,085 regional anesthesia procedures performed (3.5/10,000). Four deaths were reported. Cardiac arrest occurred after spinal anesthesia (n = 10; 2.7/10,000) and posterior lumbar plexus block (n = 1; 80/10,000). Systemic local anesthetic toxicity consisted of seizures only, without cardiac toxicity. Lidocaine spinal anesthesia was associated with more neurologic complications than bupivacaine spinal anesthesia (14.4/10,000 vs. 2.2/10,000). Most neurologic complications were transient. Among 12 that occurred after peripheral nerve blocks, 9 occurred in patients in whom a nerve stimulator had been used.

Conclusion: This prospective survey based on a free hotline permanent telephone service allowed us to estimate the incidence of major complications related to regional anesthesia and to provide a detailed analysis of these complications.

IN France, the number of regional anesthetic procedures has increased 12-fold between 1980 and 1996.¹ This tremendous increase can be linked to the perception that regional anesthesia is associated with numerous advantages and with very few severe complications.² This increase has been seen not only in obstetrics but also for other surgical procedures. Numerous new techniques have been described during these two decades, and their use also explains the large development of regional anesthesia. Because major complications related to traditional techniques are rare, their exact incidence is known only approximately.³ A previous prospective survey assessed the complication rate of 103,730 regional anesthetics and was based on the voluntary participation of 736 anesthesiologists.³ However, in this study, complications were reported in detail on a written form, and the detailed numbers of each type of block performed were not recorded. Moreover, the incidence of major complications associated with the more recently introduced techniques could not be assessed at that time. Thus, we created a hotline service (SOS Regional Anesthesia Service) that had three main goals: (1) to provide online clinical help for the practitioner facing a severe complication, (2) to obtain immediately relevant clinical information for every complication reported, and (3) to estimate the incidence of complications from a prospective declaration of all regional techniques performed by practitioners who had subscribed to the service.

Methods

Three weeks before the beginning of the study period, a letter was mailed to 8,150 French anesthesiologists introducing the concept of the hotline service and inviting them to participate in a survey of complications of regional anesthesia from August 1, 1998, to May 31, 1999. The service was free of charge. A 2-month period (June and July 1998) was used as a test period, and data collected during this initial phase were not entered into the database. The survey was divided into five periods of 2 months each. The participants were informed of the cellular phone number where they could reach one of three experts (D.B., C.E., K.S.) 24 h a day and 7 days a week for any question related to regional anesthesia (complication or advice). The participants were asked to report immediately any serious adverse event they encountered after regional anesthesia by calling the hotline. Nine severe complications were tallied: (1) cardiac...
arrest requiring cardiac massage and/or epinephrine; (2) acute respiratory failure requiring tracheal intubation and/or assisted ventilation; (3) seizures; (4) peripheral nerve injury, defined as a sensory and/or motor deficit with clinical and/or electrophysiologic abnormalities suggesting a peripheral site of injury and no evidence of spinal cord lesion; (5) cauda equina syndrome; (6) paraplegia; (7) cerebral complication; (8) meningeal syndrome; and (9) death. The complications described during each telephone call were recorded using a preprinted form. Postdeclaration follow-up of each case was performed by the expert who received the initial call.

Each expert remained “on call” during a 1-week period, at the end of which the cases were sent by electronic mail to the other experts for reading. During the week on call, each expert was autonomous for the responses given. However, because a given individual’s expertise cannot be complete for every topic, the experts could communicate within the group to discuss difficult questions, ask for advice from experts outside of the group, or even delay nonurgent responses to improve their own knowledge by reading pertinent literature or consulting medical databases.

The events reported were later reviewed by the three experts to decide whether they should be included in the “serious complications” list. Then, serious complications were classified into three groups: (1) unrelated to regional anesthesia and entirely explained by nonanesthetic factors, (2) related to regional anesthesia, and (3) unclassified. Causal inference was decided by consensus among the experts and was based on the following factors: complication temporally related to regional anesthesia occurring in an anatomic area corresponding to the lesion (except for systemic complications) and no other obvious cause found. Three other experts (F. Bonnet, M.D., J. Hamza, M.D., and L-J Duprè, M.D., listed in the Acknowledgments) not involved in the overall process of the study were asked to provide their own conclusions on 20 randomly selected cases using the same classification.

To precisely calculate the incidence of complications after each type of block, the following system was organized to record all blocks performed. A 17-page pocket booklet was prepared, in which each page was dedicated to a specific regional block. Obstetric and pediatric cases were also specifically recorded. For spinal anesthesia, the drug used (bupivacaine or lidocaine) had to be recorded. After each anesthesiologist had agreed to participate, he or she was sent a booklet covering a 2-month period. At the end of this period, the booklets were returned, and a new one was sent by regular mail. The booklets were used only to report the number of blocks performed, whereas complications were reported via telephone calls.

Since, in the present study, one observation corresponds to one anesthetic procedure, and because each anesthesiologist reported several procedures, the observations are not independent from a statistical point of view. This phenomenon corresponds to a “cluster effect,” which leads to a bias in the calculation of the SD and the P value. To correct this bias, we used a bootstrap procedure designed specifically for the present study through a routine in S-PLUS 2000 (MathSoft, Seattle, WA). The exact variance of the incidence of complications was computed in this way. The naive variance was also computed, and the ratio of both variances (design effect) was systematically between 2.2 and 2.4. Thus, all confidence intervals or statistical tests were computed using naive variance increased by a factor of 2.4.

In the tables and in the text, data that approximately follow a normal distribution are presented as mean ± SD, whereas non–normally distributed data that are widely skewed are presented as median with 25th and 75th corresponding percentiles. Pearson chi-square test was used for dichotomous categorical data. To compare continuous variables, the Student t test was used, except when the distribution was not normal, in which case the Mann–Whitney U test was used. Formulae based on the normal distribution were used to calculate 95% confidence intervals. When the distribution was not normal, tables of the Poisson distribution were used.

Table 1. Characteristics of Anesthesiologists Who Reported No or at Least One Complication

<table>
<thead>
<tr>
<th>Anesthesiologists Who Reported at Least One Complication (n = 67)</th>
<th>Anesthesiologists Who Did Not Report Any Complications (n = 420)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)*</td>
<td>45 ± 5 (43–50)</td>
<td>47 ± 6 (39–47)</td>
</tr>
<tr>
<td>Nonprivate practice (%)</td>
<td>57</td>
<td>48</td>
</tr>
<tr>
<td>Previous experience performing regional anesthesia (yr)*</td>
<td>16 ± 6 (11–22)</td>
<td>16 ± 6 (12–20)</td>
</tr>
<tr>
<td>Episodes of regional anesthesia reported per participant for the study period (n)†</td>
<td>314 (202–555)</td>
<td>254 (138–450)</td>
</tr>
</tbody>
</table>

*Values are mean ± SD (range). †Median values (25th and 75th percentiles).
Table 2. Complications Reported and Their Relation to Regional Anesthesia

<table>
<thead>
<tr>
<th></th>
<th>Related</th>
<th>Unrelated*</th>
<th>Unclassified</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac arrest†</td>
<td>11</td>
<td>1</td>
<td>0</td>
<td>12</td>
</tr>
<tr>
<td>Respiratory failure‡</td>
<td>7</td>
<td>2</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>Seizures§</td>
<td>8</td>
<td>1</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>Peripheral neuropathy∥</td>
<td>26</td>
<td>7</td>
<td>6</td>
<td>39</td>
</tr>
<tr>
<td>Cauda equina syndrome#</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Meningitis</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>56</td>
<td>14</td>
<td>7</td>
<td>77</td>
</tr>
</tbody>
</table>

*Complications not related to regional anesthesia and their cause. † Amniotic fluid embolism (n = 1). ‡ Amniotic fluid embolism (n = 2). §Epileptic fit occurring lately after regional anesthesia in a patient with known epilepsy (n = 1). ‖ Neurologic complication related to surgery, tourniquet, or patient positioning (n = 9); neurologic abnormalities existing before the block and modified by regional anesthesia (n = 2); neurologic complications occurring in an area unrelated to regional anesthesia (n = 1); neurologic complications occurring more than 1 week after regional anesthesia (n = 1). **Neurologic complications related to hypertension and occurring lately after regional anesthesia (n = 1); transurethral resection of the prostate syndrome (n = 1).

Results

During the five periods of 2 months each, 487 anesthesiologists out of 8,150 agreed to participate in the study. The participants who used the hotline service performed more blocks than the mean number of blocks performed by French anesthesiologists overall (table 1). Those who agreed to participate were allowed to subscribe at any time during the study and thus received 1–5 booklets. Overall, the participants reported performing 158,083 regional blocks, including 41,251 episodes of spinal anesthesia, 35,379 epidural blocks, 1,474 combined spinal–epidural blocks, 50,223 peripheral blocks, 4,448 episodes of intravenous regional anesthesia, and 17,071 peribulbar blocks. These blocks were performed for surgery in adults (74.3%), children (2.8%), or for obstetric purposes (22.9%). To ascertain that a valuable denominator had been obtained, 20 randomly chosen anesthesiologists (4.1%) who had participated in the study were asked to show their operating room records during the study period. Fifteen of them sent copies of their operating room lists within 1 month of request, allowing comparison between the numbers of blocks reported in the booklets during the study period and hospital records. Underestimation was found to be 4% (5% for spinal anesthesia, 3% for epidural anesthesia, and 2% for peripheral nerve blocks).

Sixty-eight anesthesiologists out of 487 reported 77 serious complications as defined previously. There was no significant difference for any characteristics between those who reported at least one complication and those who did not report any (table 1). Table 2 shows that only 56 complications were classified as being related to regional anesthesia. Tables 3 and 4 show the number of blocks and the incidence of each type of complication for each type of block performed for adult nonobstetric and obstetric patients, respectively. Among the 1,474 cases of combined spinal–epidural anesthesia, the 4,448 episodes of intravenous regional anesthesia, and the 17,071 peribulbar blocks performed, no severe complications were recorded. In addition, no severe complications were reported in the 4,435 blocks performed in children. Secondary analysis of the 20 selected cases showed that the three experts not involved in the hotline service were in complete agreement with the conclusions provided by the hotline experts for 19 cases, whereas only two experts agreed on the one remaining case.

Cardiac Arrest and Acute Respiratory Failure

Bradycardia was recorded before each cardiac arrest that occurred during spinal anesthesia. The three cardiac arrests followed by death were delayed (> 40 min after spinal injection) and occurred in elderly patients (> 80 yr) who had undergone hip surgery. One case of irreversible cardiac arrest occurred during a posterior lumbar plexus block. A sensory level higher than T2 and a bilateral mydriasis were noticed immediately before the arrest.

Respiratory failure occurred during the course of central blocks (spinal or epidural anesthesia) or posterior lumbar plexus blocks; none led to death. In all complications related to posterior lumbar plexus block, a high

Table 3. Number and Incidence of Serious Events Related to Central (Neuraxial) Blocks (Excluding Obstetric Cases)

<table>
<thead>
<tr>
<th></th>
<th>Cardiac Arrest</th>
<th>Respiratory Failure</th>
<th>Seizures</th>
<th>Peripheral Neuropathy</th>
<th>Cauda Equina Syndrome</th>
<th>Central Neurologic Event</th>
<th>Meningitis</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spinal (35,439 performed)</td>
<td>9 (2.5)</td>
<td>2 (0.6)</td>
<td>1 (0.3)</td>
<td>9 (2.5)</td>
<td>3 (0.8)</td>
<td>0 (0.0–0.8)</td>
<td>1 (0.3)</td>
<td>3 (0.8)</td>
</tr>
<tr>
<td></td>
<td>(0.0–5.1)</td>
<td>(0.0–2.0)</td>
<td>(0.0–1.4)</td>
<td>(0.0–5.1)</td>
<td>(0.0–2.3)</td>
<td>(0.0–1.4)</td>
<td>(0.0–2.3)</td>
<td></td>
</tr>
<tr>
<td>Epidural (5,561 performed)</td>
<td>0 (0.0)</td>
<td>1 (0.0–0.5)</td>
<td>1 (1.8)</td>
<td>0 (0.0–0.5)</td>
<td>0 (0.0–0.5)</td>
<td>0 (0.0–0.5)</td>
<td>0 (0.0–5.0)</td>
<td>0 (0.0–9.0)</td>
</tr>
</tbody>
</table>

Values are expressed as n (n/10,000) (95% CI).

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dermatomal level and a bilateral mydriasis were observed, suggesting intrathecal cephalad spread of the local anesthetic. In one case, the occurrence of respiratory failure was facilitated by preexisting morbid obesity. Finally, in one additional case, respiratory failure occurred after an erroneous dose was used during continuous spinal anesthesia.

**Seizures**
Seven cases of seizures occurred after epidural (n = 1) or peripheral injection (n = 6) and were related to systemic toxicity of local anesthetics. Arrhythmias were not noted in any of the cases. In one additional case, seizures occurred during spinal anesthesia at the time of cardiac arrest.

**Neurologic Complications**
Most neurologic complications completely resolved within 8 postoperative days. Twelve patients had a peripheral nerve injury (n = 9) or cauda equina syndrome (n = 3) after spinal anesthesia. In nine patients, neither pain nor paresthesia had been noted during puncture. All recovered completely within 3 weeks. Of those nine patients, five had received lidocaine, whereas the three patients who had paresthesia during the puncture had received bupivacaine. In the three patients in whom paresthesia occurred during the procedure, neurologic sequelae were still present 6 months later. Neurologic complications during spinal anesthesia occurred with a statistically different incidence regardless of whether lidocaine (5/3,459 or 14.4/10,000) or bupivacaine (7/31,980 or 2.2/10,000) had been used (P < 0.01).

Twelve other patients had a peripheral neuropathy after a peripheral block, and seven of them had sequelae still present after 6 months. Neurologic complications were observed in nine patients in whom a nerve stimulator had been used: two had described paresthesia during puncture, and in three cases a low intensity of stimulation (< 0.5 mA) had been used during the procedure.

**Discussion**
With this free-of-charge regional anesthesia service involving the voluntary participation of 487 anesthesiologists, 158,083 regional blocks were prospectively recorded in a 10-month period. The calculated incidences of severe complications related to regional block are lower than 5 in 10,000 patients in this series. This “low” incidence a posteriori validates the concept that a large-

### Table 4. Number and Incidence of Serious Events Related to Upper Limb Blocks (Excluding Obstetric Cases)

<table>
<thead>
<tr>
<th>Block Type</th>
<th>Cardiac Arrest</th>
<th>Respiratory Failure</th>
<th>Seizures</th>
<th>Peripheral Neuropathy</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interscalene block (3,459 perf.)</td>
<td>0 (0.0–8.7)</td>
<td>0 (0.0–8.7)</td>
<td>0 (0.0–8.7)</td>
<td>1 (2.9)</td>
<td>0 (0.0–8.7)</td>
</tr>
<tr>
<td>Supraclavicular block (1,899 perf.)</td>
<td>0 (0.0–15.9)</td>
<td>0 (0.0–15.9)</td>
<td>1 (5.3)</td>
<td>0 (0.0–15.9)</td>
<td>0 (0.0–15.9)</td>
</tr>
<tr>
<td>Axillary plexus block (11,024 perf.)</td>
<td>0 (0.0–2.7)</td>
<td>0 (0.0–2.7)</td>
<td>1 (0.9)</td>
<td>2 (1.8)</td>
<td>0 (0.0–2.7)</td>
</tr>
<tr>
<td>Midhumeral block (7,402 perf.)</td>
<td>0 (0.0–4.1)</td>
<td>0 (0.0–4.1)</td>
<td>1 (1.4)</td>
<td>1 (1.4)</td>
<td>0 (0.0–4.1)</td>
</tr>
</tbody>
</table>

Values are expressed as n (n/10,000) (95% CI).

### Table 5. Number and Incidence of Serious Events Related to Lower Limb Blocks (Excluding Obstetric Cases)

<table>
<thead>
<tr>
<th>Block Type</th>
<th>Cardiac Arrest</th>
<th>Respiratory Failure</th>
<th>Seizures</th>
<th>Peripheral Neuropathy</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posterior lumbar plexus block (394 perf.)</td>
<td>1 (25.4)</td>
<td>2 (50.8)</td>
<td>1 (25.4)</td>
<td>0 (0.0–76.1)</td>
<td>1 (25.4)</td>
</tr>
<tr>
<td>Femoral block (10,309 perf.)</td>
<td>0 (0.0–2.9)</td>
<td>0 (0.0–2.9)</td>
<td>0 (0.0–2.9)</td>
<td>3 (2.9)</td>
<td>0 (0.0–2.9)</td>
</tr>
<tr>
<td>Sciatic nerve block (8,507 perf.)</td>
<td>0 (0.0–3.5)</td>
<td>0 (0.0–3.5)</td>
<td>2 (4.5)</td>
<td>2 (2.4)</td>
<td>0 (0.0–3.5)</td>
</tr>
<tr>
<td>Popliteal sciatic nerve block (952 perf.)</td>
<td>0 (0.0–31.5)</td>
<td>0 (0.0–31.5)</td>
<td>0 (0.0–31.5)</td>
<td>3 (31.5)</td>
<td>0 (0.0–31.5)</td>
</tr>
</tbody>
</table>

Values are expressed as n (n/10,000) (95% CI).
Table 6. Number and Incidence of Serious Events Related to Regional Anesthesia in Obstetrics

<table>
<thead>
<tr>
<th>Cardiac Arrest</th>
<th>Respiratory Failure</th>
<th>Seizures</th>
<th>Peripheral Neuropathy</th>
<th>Cauda Equina Syndrome</th>
<th>Central Neurologic Event</th>
<th>Meningitis</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spinal (5,640 performed)</td>
<td>1 (1.8)</td>
<td>0 (0.0–5.3)</td>
<td>0 (0.0–5.3)</td>
<td>2 (3.5)</td>
<td>0 (0.0–5.3)</td>
<td>0 (0.0–5.3)</td>
<td>0 (0.0–5.3)</td>
</tr>
<tr>
<td>Epidural (29,732 performed)</td>
<td>0 (0.0–1.0)</td>
<td>3 (1.0)</td>
<td>2 (0.7)</td>
<td>0 (0.0–1.0)</td>
<td>0 (0.0–1.0)</td>
<td>0 (0.0–1.0)</td>
<td>0 (0.0–1.0)</td>
</tr>
</tbody>
</table>

Values are expressed as n (n/10,000) (95% CI).

scale study is necessary to assess this issue. The incidences observed are in the range of what has been observed in other studies, particularly in the recent French survey. However, the present study was implemented to overcome several weaknesses of the previous survey. First of all, within the past 5 yr, a significant number of new regional anesthesia techniques (posterior lumbar plexus block, humeral block, popliteal sciatic block) have entered the clinical scene, and the incidence and severity of complications that are associated with these techniques are largely unknown. Second, in France, the overall number of regional blocks has increased 12-fold in the last 16 yr. Third, because complications were immediately declared by using the hotline, a detailed description of clinical situations could be obtained prospectively using a systematic questionnaire. The decision to consider a causal relation with regional anesthesia was thus made easier. Moreover, follow-up could be more complete.

Compared with our previous study, another difference is noteworthy: since the experts were available 24 h a day, it can be speculated that, in several circumstances, they influenced patient care and possibly helped improve outcome. Unfortunately, because of the study design, one cannot definitively prove this hypothesis. In the previous study, we could not ascertain that all of the blocks performed were declared in the booklets (leaving some doubt regarding the absolute validity of the denominator). The audit performed retrospectively in randomly chosen participants showed a very low level of underestimation, thus validating our denominator. We also could not be sure that all complications were reported (uncertainty for the numerator). However, we believe that the current design contributed to better reporting, because the participants often expressed their interest during the study. For example, participants often called the hotline because they were worried that they would not receive their next booklet in time to start the new 2-month period. One could suspect that the rate of complications for procedures performed by nonparticipating anesthesiologists is different from what we observed in our study population consisting of anesthesiologists who volunteered to participate in an audit on complications of regional anesthesia. It is possible that participating anesthesiologists might actually encounter fewer complications than nonparticipating anesthesiologists. The former are, indeed, more skilled and perform more blocks than the average French anesthesiologist (32.5/month vs. 17.3/month). Incidentally, the participating anesthesiologists were more frequently employed in public hospitals (48% vs. 36%), but their mean age was not different (46 yr in both groups). Also, the causal link between a complication and regional anesthesia is sometimes difficult to establish. The risk of error was limited by immediate informal discussion among experts and formal analysis of all cases every 4 months in a joint meeting of experts. Moreover, external validation was obtained by comparing our conclusions on selected cases with those provided by three other experts. However, in a limited number of cases, the causal role of regional anesthesia could still not be determined. The main reasons for failure were (1) loss of follow-up and (2) electrophysiologic studies were not performed at all, were not performed on time, or were performed with a method not precise enough to make any valid conclusion.

The incidence of regional anesthesia-induced cardiac arrest may have been lower than what we found in our previous study. However, statistical tests were not applied because the data came from two different studies performed at different times with different anesthesiologists. Interestingly, however, the clinical situations in which cardiac arrests occurred were very similar and involved—in most cases, a central block performed during hip surgery in an elderly patient. We also recorded one case of cardiac arrest and two respiratory complications (not leading to cardiac arrest) that occurred during a lumbar plexus block performed via the posterior approach (incidence of severe complication, 80/10,000). These three complications were related to cephalad diffusion of the local anesthetic in the epidural or intrathecal space. The lumbar blocks leading to severe complications had been performed by anesthesiologists trained in this technique. It is thus unlikely that technical factors played a prominent role. Although it is still too early to draw any definite conclusion regarding this
block, anesthesiologists should be warned against the high rate of complications that was found with the posterior lumbar plexus block and should be advised to manage this block with at least the same vigilance as for a central block.

The incidence of systemic toxicity of local anesthetics and related seizures may also have been lower than in our previous report. Moreover, there were no cardiac arrests related to systemic toxicity. This low incidence of systemic complications may be related to better physician information and improved practice patterns (lower doses, slow injection, test dose, fractionated injection, and so forth). Although no local anesthetic-induced cardiac toxic event had been observed in our previous survey (at a time in which ropivacaine was not available in France), it is possible that the introduction of ropivacaine in clinical practice during this period has played a role, but this hypothesis cannot be verified using our methodology.

The incidence of neurologic complications after spinal anesthesia is higher with lidocaine than with bupivacaine. This supports the greater neurotoxicity of intrathecal lidocaine. Neurologic complications also occurred after peripheral nerve blocks. One main reason to support the use of a nerve stimulator is the perceived reduction in the risk of nerve trauma. The present study was not designed to address this issue, and the use of a nerve stimulator was not specifically mentioned for each peripheral block performed. The exact incidence of neurologic complications after nerve stimulation (vs. other techniques) thus cannot be calculated. However, several complications occurred despite the use of a nerve stimulator. Inadequate patient positioning and/or noncooperative patients, insufficient physician experience, insufficient patient information on the procedure, excessive sedation, or a nongentle technique are critical factors that increase the risk of neurologic complications, and this is certainly also true when a nerve stimulator is used. Moreover, several anesthesiologists continue to mobilize their needle until they have a distinct distal muscular movement with a very low electrical intensity (< 0.5 mA), because it is widely believed that the lower the intensity required, the closer the needle from the nerve and thus the higher the success rate. Although there are, indeed, data to support this view, this remains a controversial issue, and too small a distance between the needle and the nerve may in fact cause more harm than benefit. Further study is required to ascertain the role (or lack thereof) of these technical factors in the incidence of nerve injury during regional anesthesia.

In conclusion, this large-scale survey combining immediate declaration and analysis using a telephone hotline has allowed us to prospectively estimate the incidence of major complications after regional anesthesia. Several situations already known to be associated with an increased risk were identified (i.e., spinal anesthesia-induced cardiac arrest in the elderly or lidocaine toxicity after spinal injection). The major contribution is, however, the report of a high incidence of major complications after posterior lumbar plexus block and the occurrence of neurologic complications after the use of a nerve stimulator used for peripheral nerve blocks. A continuing survey will be useful because of the significant changes in practice that continue to occur.

The authors would like to thank Professor Francis Bonnet, M.D. (Chairman, Service d’Anesthésie-Réanimation Chirurgicale, Hôpital Tenon, Paris, France), Professor Jamal Hamza, M.D. (Chairman, Service d’Anesthésie et de Réanimation Chirurgicale, Hôpital Saint Vincent-de-Paul, Paris, France), and Louis-jean Dupré, M.D. (Clinique Cleret, Chambéry, France), who acted as external experts. They also would like to thank all of the French anesthesiologists who participated for their enthusiasm and their constant help in the study process.

References
5. Dripps RD, Vandam LD. Long-term follow-up of patients who received 10,098 spinal anesthetics, failure to discover major neurological sequelae. JAMA 1954; 156:1480–91

Anesthesiology, V 97, No 5, Nov 2002


Neurological Complications After Regional Anesthesia: Contemporary Estimates of Risk

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Hossam El-Beheiry, MBBCh, PhD, FRCPC

BACKGROUND: Regional anesthesia (RA) provides excellent analgesia and analgesia for many surgical procedures. Anesthesiologists must understand the risks in addition to the benefits of RA to make an informed choice of anesthetic technique. Many studies that have investigated neurological complications after RA are dated, and do not reflect the increasing indications and applications of RA nor the advances in training and techniques. In this brief narrative review we collate the contemporary investigations of neurological complications after the most common RA techniques.

METHODS: We reviewed all 32 studies published between January 1, 1995 and December 31, 2005 where the primary intent was to investigate neurological complications of RA.

RESULTS: The sample size of the studies that investigated neurological complications after central and peripheral (PNB) nerve blockade ranged from 4,185 to 1,260,000 and 20 to 10,309 blocks, respectively. The rate of neuropathy after spinal and epidural anesthesia was 3.78:10,000 (95% CI: 1.06–13.50:10,000) and 2.19:10,000 (95% CI: 0.88–5.44:10,000), respectively. For common PNB techniques, the rate of neuropathy after interscalene brachial plexus block, axillary brachial plexus block, and femoral nerve block was 2.84:100 (95% CI 1.33–5.98:100), 1.48:100 (95% CI: 0.52–4.11:100), and 0.34:100 (95% CI: 0.04–2.81:100), respectively. The rate of permanent neurological injury after spinal and epidural anesthesia ranged from 0–4.2:10,000 and 0–7.6:10,000, respectively. Only one case of permanent neuropathy was reported among 16 studies of neurological complications after PNB.

CONCLUSIONS: Our review suggests that the rate of neurological complications after central nerve blockade is /H110214:10,000, or 0.04%. The rate of neuropathy after PNB is /H110213:100, or 3%. However, permanent neurological injury after RA is rare in contemporary anesthetic practice.

Regional anesthesia (RA) is associated with multiple benefits compared to general anesthesia, including reduced morbidity and mortality (1–5), superior postoperative analgesia (6–11), and enhanced cost effectiveness (12). However rare, neurological injury after RA can be distressing to patients and their families. Many of the studies that have addressed the incidence of neurological injury after RA are decades old and focused on neuraxial blockade (13–21). These dated studies may not reflect technical advances in central (CNB) and peripheral (PNB) nerve blockade. Although formal postgraduate training programs (22), consensus conference recommendations (23), new block techniques (24–30), and new local anesthetics (31) may enhance the safety of RA, the increasing prevalence of risk factors for nerve injury [e.g., obesity (32), diabetes (33), potent anticoagulants (23)] and the increasing use of continuous catheter-based PNB may alter the rate of neurological complications. The American Society of Anesthesiologists Closed Claims Project provides the most contemporary and comprehensive collection of adverse events associated with RA practice in the United States (34); however, the lack of a denominator prevents the calculation of the incidence of complications. Because nerve injury after RA is uncommon, prohibitively large numbers of patients are required for study in cohort to capture the incidence of neurological complications. Much of the available literature is restricted to retrospective reviews and surveys of anesthesiologists, both of which may be limited by under-reporting of complications. The objective of this brief narrative review is to gather and consolidate recent studies of neurological complications after RA to assist anesthesiologists and patients alike to more accurately understand risks.

METHODS

A MEDLINE search was performed using the medical subject heading (MeSH) words “anesthesia, spinal,” “anesthesia, epidural,” and “nerve block,” each

Vol. 104, No. 4, April 2007
limited to the MeSH subheading “adverse effects.” Search results were then cross-referenced with each of the MeSH heading words “nervous system diseases” and “postoperative complications.” Final search results were limited to English language studies published within the past 10 yr (between January 1, 1995 and December 31, 2005). Only studies in which the stated objective was to investigate neurological complications of RA were considered for the present review. Studies focused on the pediatric population were excluded. The reference sections of all relevant publications were examined to capture any additional material suited for the present review. For CNB, only studies with a minimum sample of 1000 spinal or epidural anesthetics were included. The quality of evidence for each study was graded (highest to lowest: I–III) according to the criteria described by Harris et al. (Appendix) (35).

Only adverse neurological sequelae reportedly related to or associated with the regional anesthetic are addressed in this review. Local anesthetic toxicity (characterized by seizures), transient neurological symptoms (characterized by temporary severe radicular back pain upon resolution of spinal anesthesia) (36), and epidural hematoma and abscess are discussed in detail elsewhere (37–42) and are not addressed in this review.

The rate of neurological injury reported by cohort studies is herein expressed as “incidence,” and the rate of neurological injury described by case–control studies and surveys is expressed as “frequency.” Because the clinical presentation of neuropathic symptoms can vary after nerve blockade (21,43), and because the timing of assessment varied between and within each study reviewed, the highest reported rate for each complication is recorded below (henceforth termed “rate of occurrence”). The rate of each neurological complication after CNB is expressed as n:10,000, and the rate of neuropathy after PNB is expressed as n:100. For the purpose of this review, permanent nerve injury is defined as neurological deficit lasting more than 12 mo (henceforth termed “rate of permanent injury”).

Confidence intervals (CI) were calculated for each complication cited in the source studies according to the method described by Zar (44). We used a meta-analysis random effects general linear model to determine aggregate estimates of the rate of occurrence and corresponding 95% CI for each complication pooled from all applicable source studies. The statistical model used was Poisson regression with χ-distributed random effects. For each complication, the Cochran Q test was applied to determine the heterogeneity between the source studies. Significance was considered at P < 0.05. All statistical analyses were performed using Comprehensive Meta-Analysis Version 2.0 statistical software (Biostat, Englewood, NJ).

RESULTS

Our MEDLINE search method yielded 235 results, of which 32 studies met our inclusion criteria. The quality of evidence score (Appendix) (35) for all 32 studies included in this review was grade II-2. Tables 1 and 2 list the rates and 95% CI for neurological complications associated with the most common CNB and PNB techniques, respectively. To summarize the data listed in Tables 1 and 2, the aggregate estimated rate of occurrence and corresponding 95% CI for each complication calculated using a random effects model are presented in Tables 3 and 4. For most of the complications considered herein, we found significant heterogeneity among the source studies (Tables 3 and 4). Figures 1 and 2 demonstrate the disparity between the aggregate estimated rates of occurrence of neurological complications after the various CNB and PNB techniques, respectively.

Neuraxial Blockade

The largest contemporary comprehensive study of neurological complications after CNB was published by Moen et al. (51) in 2004. The large, albeit approximate, number of CNBs (1,260,000 spinal and 450,000 epidural anesthetics) captured reflects the long study period (1990–99) as well as the authors’ efforts to accumulate data from multiple sources, including a postal survey to anesthesiologists, the national Swedish database for mandatory reporting of adverse events, and that country’s predominant manufacturer of neuraxial local anesthetics. The next largest study was conducted by Aromaa et al. (46) in 1997. These authors collected all claims of neurological complications associated with CNB that were reported by patients to Finland’s legislated no-fault patient compensation insurance program between 1987 and 1993, and retrospectively estimated the total number of CNBs administered in that country (550,000 spinal and 170,000 epidural anesthetics) over the same time period. Scott and Tunstall (50) performed a prospective survey that captured 14,856 obstetrical spinal anesthetics and 108,133 obstetrical epidural anesthetics performed between 1990 and 1991 in 79 obstetrical units across the United Kingdom. The next two largest comprehensive studies of neurological complications after CNB were performed by Auroy et al. (45,47) These two widely cited studies prospectively surveyed hundreds of practicing anesthesiologists in France to determine the frequency of major complications associated with all RA techniques. In addition to gathering the most extensive data on complications after PNB, Auroy et al. included 40,640 spinal and 30,413 epidural anesthetics performed in 1994 (47) and 41,079 spinal and 35,293 epidural anesthetics performed in 1998–1999 (45).

Moen et al. (51) reported that the overall frequency of severe neurological complications after spinal anesthesia was approximately 0.4:10,000. Auroy et al.
<table>
<thead>
<tr>
<th>Neurological complication</th>
<th>Study design</th>
<th>Number of occurrences</th>
<th>Number of blocks performed</th>
<th>Rate of occurrence ( (n = 10,000) )</th>
<th>Number of permanent injuries</th>
<th>Rate of permanent injury ( (n = 10,000) )</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Spinal anesthesia</strong></td>
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<tr>
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<td></td>
<td></td>
</tr>
<tr>
<td>Aromaa 1997 (46)</td>
<td>R</td>
<td>25</td>
<td>550,000</td>
<td>0.45 (0.31–0.66)</td>
<td>7</td>
<td>0.13 (0.06–0.26)</td>
<td>4 cases resolved by 1 wk; 2 cases resolved by 24 mo.</td>
</tr>
<tr>
<td>Dahlgren 1995 (49)</td>
<td>P, R</td>
<td>3</td>
<td>8,501</td>
<td>3.53 (1.28–10.31)</td>
<td>3</td>
<td>3.53 (1.28–10.31)</td>
<td>Obstetrical population. All cases resolved by 12 wk.</td>
</tr>
<tr>
<td>Scott 1995 (50)</td>
<td>P</td>
<td>8</td>
<td>14,856</td>
<td>5.39 (2.77–10.61)</td>
<td>0</td>
<td>0 (0.02–2.48)</td>
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<td></td>
</tr>
<tr>
<td>Moen 2004 (51)</td>
<td>R</td>
<td>20</td>
<td>1,260,000(^{bc})</td>
<td>0.16 (0.10–0.24)</td>
<td>20</td>
<td>0.16 (0.10–0.24)</td>
<td>20 cases include 2 continuous catheters.</td>
</tr>
<tr>
<td>Aurowy 2002 (45)</td>
<td>P</td>
<td>3</td>
<td>41,079(^{a})</td>
<td>0.73 (0.27–2.13)</td>
<td>?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aromaa 1997 (46)</td>
<td>R</td>
<td>1</td>
<td>550,000(^{b})</td>
<td>0.02 (undef–0.10)</td>
<td>1</td>
<td>0.02 (undef–0.10)</td>
<td></td>
</tr>
<tr>
<td>Aurowy 1997 (47)</td>
<td>P</td>
<td>5</td>
<td>40,640</td>
<td>1.23 (0.54–2.87)</td>
<td>?</td>
<td></td>
<td></td>
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<tr>
<td><strong>Intracranial event</strong></td>
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</tr>
<tr>
<td>Moen 2004 (51)</td>
<td>R</td>
<td>2</td>
<td>1,260,000(^{bc})</td>
<td>0.02 (undef–0.06)</td>
<td>?</td>
<td></td>
<td>Intracranial subdural hematoma ( (n = 2) ).</td>
</tr>
<tr>
<td>Aurowy 2002 (45)</td>
<td>P</td>
<td>0</td>
<td>41,079(^{a})</td>
<td>0 (0–0.73)</td>
<td>0</td>
<td>0 (0–0.73)</td>
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<tr>
<td><strong>Paraplegia</strong></td>
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</tr>
<tr>
<td>Moen 2004 (51)</td>
<td>R</td>
<td>1</td>
<td>1,260,000(^{bc})</td>
<td>0.01 (undef–0.04)</td>
<td>1</td>
<td>0.01 (undef–0.04)</td>
<td></td>
</tr>
<tr>
<td>Aurowy 2002 (45)</td>
<td>P</td>
<td>0</td>
<td>41,079(^{a})</td>
<td>0 (undef–0.90)</td>
<td>0</td>
<td>0 (undef–0.90)</td>
<td></td>
</tr>
<tr>
<td>Aromaa 1997 (46)</td>
<td>R</td>
<td>5</td>
<td>550,000(^{b})</td>
<td>0.09 (0.04–0.21)</td>
<td>5</td>
<td>0.09 (0.04–0.21)</td>
<td></td>
</tr>
<tr>
<td>Aurowy 1997 (47)</td>
<td>P</td>
<td>0</td>
<td>40,640</td>
<td>0 (undef–0.91)</td>
<td>0</td>
<td>0 (undef–0.91)</td>
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<tr>
<td><strong>Epidural anesthesia</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Horlocker 2003 (52)</td>
<td>R</td>
<td>0</td>
<td>4,298</td>
<td>0 (0.06–8.58)</td>
<td>0</td>
<td>0 (0.06–8.58)</td>
<td>Denominator includes 4,298 epidurals placed under GA.</td>
</tr>
<tr>
<td>Aurowy 2002 (45)</td>
<td>P</td>
<td>0</td>
<td>35,293(^{d})</td>
<td>0 (undef–1.05)</td>
<td>0</td>
<td>0 (undef–1.05)</td>
<td>Obstetrical population.</td>
</tr>
<tr>
<td>Paech 1998 (53)</td>
<td>P</td>
<td>1</td>
<td>10,995</td>
<td>0.91 (0.22–5.07)</td>
<td>?</td>
<td></td>
<td>Obstetrical population.</td>
</tr>
<tr>
<td>Aromaa 1997 (46)</td>
<td>R</td>
<td>5</td>
<td>170,000(^{d})</td>
<td>0.29 (0.13–0.69)</td>
<td>1</td>
<td>0.06 (0.01–0.33)</td>
<td>Denominator includes 148 epidurals.</td>
</tr>
<tr>
<td>Giebler 1997 (54)</td>
<td>P, R</td>
<td>10</td>
<td>4,185</td>
<td>23.89 (13.12–43.89)</td>
<td>0</td>
<td>0 (0.06–8.81)</td>
<td>Obstetrical population.</td>
</tr>
<tr>
<td>Holdcroft 1995 (55)</td>
<td>P</td>
<td>1</td>
<td>13,007</td>
<td>0.77 (0.19–4.28)</td>
<td>?</td>
<td></td>
<td>Obstetrical population.</td>
</tr>
<tr>
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<td>P</td>
<td>38</td>
<td>108,133</td>
<td>3.51 (2.56–4.82)</td>
<td>0</td>
<td>0 (undef–0.34)</td>
<td>Obstetrical population.</td>
</tr>
<tr>
<td><strong>Cauda equina syndrome</strong></td>
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<td></td>
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</tr>
<tr>
<td>Moen 2004 (51)</td>
<td>R</td>
<td>12</td>
<td>450,000(^{bc})</td>
<td>0.27 (0.15–0.47)</td>
<td>12</td>
<td>0.27 (0.15–0.47)</td>
<td>12 cases include 4 CSEs.</td>
</tr>
<tr>
<td>Aurowy 2002 (45)</td>
<td>P</td>
<td>0</td>
<td>35,293(^{d})</td>
<td>0 (undef–1.05)</td>
<td>0</td>
<td>0 (undef–1.05)</td>
<td></td>
</tr>
<tr>
<td>Aromaa 1997 (46)</td>
<td>R</td>
<td>1</td>
<td>170,000(^{d})</td>
<td>0.06 (0.01–0.33)</td>
<td>1</td>
<td>0.06 (0.01–0.33)</td>
<td></td>
</tr>
<tr>
<td>Aurowy 1997 (47)</td>
<td>P</td>
<td>0</td>
<td>30,413</td>
<td>0 (undef–1.21)</td>
<td>0</td>
<td>0 (undef–1.21)</td>
<td></td>
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<tr>
<td><strong>Intracranial event</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Moen 2004 (51)</td>
<td>R</td>
<td>3</td>
<td>450,000(^{bc})</td>
<td>0.07 (0.02–0.19)</td>
<td>?</td>
<td></td>
<td>Intracranial subdural hematoma ( (n = 3) ).</td>
</tr>
<tr>
<td>Aurowy 2002 (45)</td>
<td>P</td>
<td>0</td>
<td>35,293(^{d})</td>
<td>0 (undef–1.05)</td>
<td>0</td>
<td>0 (undef–1.05)</td>
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<tr>
<td><strong>Paraplegia</strong></td>
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</tr>
<tr>
<td>Moen 2004 (51)</td>
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<td>3</td>
<td>450,000(^{bc})</td>
<td>0.07 (0.02–0.18)</td>
<td>3</td>
<td>0.07 (0.02–0.18)</td>
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<tr>
<td>Aurowy 2002 (45)</td>
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<td>35,293(^{d})</td>
<td>0 (undef–1.05)</td>
<td>0</td>
<td>0 (undef–1.05)</td>
<td></td>
</tr>
<tr>
<td>Aromaa 1997 (46)</td>
<td>R</td>
<td>1</td>
<td>170,000(^{d})</td>
<td>0.06 (0.01–0.33)</td>
<td>1</td>
<td>0.06 (0.01–0.33)</td>
<td></td>
</tr>
</tbody>
</table>

Continues
noted the overall incidence of serious or major neurological complications after spinal anesthesia to be considerably higher, specifically, 11.8:10,000 in 1994 (47) and in 3.7:10,000 in 1998–1999 (45). At least one reason for this difference is the authors’ definition of “severe” (51) and “serious” (47); or “major” (45); neurological complications, that is, Auroy et al. (45,47) included radiculopathy and peripheral neuropathy as complications, whereas Moen et al. (51) did not. After epidural anesthesia, Moen et al. (51) determined the frequency of “severe” neurological complications to be approximately 1.6:10,000, whereas Auroy et al. found the overall incidence of “serious” or “major” neurological complications to be 3.9:10,000 in 1994 (47) and 0.3:10,000 in 1998–1999 (45). For all CNB studies, the present review suggests that spinal anesthesia carries a higher risk of radiculopathy or peripheral neuropathy (3.78:10,000; 95% CI: 1.06–13.50:10,000) compared to epidural anesthesia (2.19:10,000; 95% CI: 0.88–5.44:10,000) (Table 3). The rate of permanent neurological injury ranged from 0–4.2:10,000 and 0–7.6:10,000 after spinal and epidural anesthesia, respectively (Table 1).

Peripheral Nerve Blockade

There are a limited number of contemporary prospective studies in the literature examining the risk of neurological injury after PNB. Most of the available data involves upper extremity, rather than lower extremity, PNB, which reflects the preference for brachial plexus blockade in contemporary RA practice (71). In the two large prospective studies performed by Auroy et al., eight cases of neurological injury were identified among 21,278 PNBS (3.8:10,000) in 1997 (47) and 12 cases among 43,946 PNBS (2.7:10,000) in 1998–1999 (45). In the latter study, neurological symptoms were still present 6 mo after the PNB in 7 of the 12 cases of reported peripheral neuropathy (45). Unfortunately, however, neither of these two studies provides sufficient detail to determine the overall frequency of permanent neurological deficit. For all PNB studies, the present review suggests that interscalene block carries the highest risk of transient neurological deficit, specifically, 2.84:100 (95% CI: 1.33–5.98:100) (Table 4). Among the 16 studies in which complications were sought 12 mo after PNB, only one case of permanent neuropathy was reported (69) (Table 2).

**DISCUSSION**

As the practice of RA continues to gain popularity both in Europe (72) and North America (71), knowledge of the risks of neurological injury associated with the most common RA techniques is imperative. Historically, nerve injury after CNB is rare. In the 1950–1960s, several large scale studies of neurological complications after CNB were published underscoring the safety of spinal and epidural anesthesia (13–21). In the classic prospective study examining complications of spinal anesthesia, Vandam and Dripps (17) found 71 cases of transient neurological deficit after 10,098 spinal anesthetics. All but 1 of the 71 of these cases resolved, whereas the single case of permanent nerve injury was subsequently deemed unrelated to the spinal anesthetic (14). Dawkins (18) published the classic review of neurological complications after 32,718 epidural anesthetics and reported the frequency of transient and permanent nerve injury to be 0.1% and 0.02%, respectively. It is noteworthy that the incidence of permanent neurological deficit after CNB reported by Dahlgren and Tornebrandt (49) is considerably higher compared to most other studies presently reviewed (Table 1). At least one reason for this discrepancy may be that Dahlgren and Tornebrandt reported all neurological complications (including very mild sensory deficit) suffered by patients of all age groups (including children) and both genders who underwent a wide variety of operations and were often administered continuous epidural infusions postoperatively (49). By contrast, most other studies reviewed included, in all (50,53,55) or in part (45,51,73), young healthy women undergoing obstetrical spinal or epidural anesthesia. In fact, Moen et al. (51) calculated the frequency of severe neurological

---

**Table 1. (continued)**

<table>
<thead>
<tr>
<th>Neurological complication</th>
<th>Study design</th>
<th>Number of occurrences</th>
<th>Number of blocks performed</th>
<th>Rate of occurrence (n = 10,000)</th>
<th>Number of permanent injuries</th>
<th>Rate of permanent injury (n = 10,000)</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paraplegia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moen 2004 (51)</td>
<td>R</td>
<td>3</td>
<td>450,000&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0.07 (0.02–0.18)</td>
<td>3</td>
<td>0.07 (0.02–0.18)</td>
<td></td>
</tr>
<tr>
<td>Auroy 2002 (45)</td>
<td>P</td>
<td>0</td>
<td>35,293&lt;sup&gt;d&lt;/sup&gt;</td>
<td>0 ( undef –1.05)</td>
<td>0</td>
<td>0 ( undef –1.05)</td>
<td></td>
</tr>
<tr>
<td>Aromaa 1997 (46)</td>
<td>R</td>
<td>1</td>
<td>170,000&lt;sup&gt;e&lt;/sup&gt;</td>
<td>0.06 (0.01–0.33)</td>
<td>1</td>
<td>0.06 (0.01–0.33)</td>
<td></td>
</tr>
<tr>
<td>Auroy 1997 (47)</td>
<td>P</td>
<td>1</td>
<td>30,413</td>
<td>0.33 (0.08–1.83)</td>
<td>1</td>
<td>0.33 (0.08–1.83)</td>
<td>Associated with prolonged hypotension</td>
</tr>
</tbody>
</table>

95% confidence intervals appear in parentheses.

<sup>P</sup> = Prospective; <sup>R</sup> = Retrospective; <sup>undef</sup> = undefined; <sup>CSE</sup> = combined spinal-epidural; <sup>GA</sup> = general anesthesia; <sup>?</sup> = Insufficient data.

<sup>a</sup> Denominator includes 5640 obstetrical spinal anesthetics.

<sup>b</sup> Denominator includes 50,000 obstetrical spinal anesthetics.

<sup>c</sup> Denominator includes 29,732 obstetrical epidural anesthetics.

<sup>d</sup> Denominator includes 205,000 obstetrical epidural anesthetics.

<sup>e</sup> Denominator includes 205,000 obstetrical epidural anesthetics.
<table>
<thead>
<tr>
<th>Author/Year</th>
<th>Study design</th>
<th>Number of blocks performed</th>
<th>Rate of occurrence ( (n = 100) )</th>
<th>Number of permanent injuries</th>
<th>Rate of permanent injury ( (n = 100) )</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Brachial plexus blockade</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Candido 2005 (56)</td>
<td>P</td>
<td>31</td>
<td>693</td>
<td>0.03 (3.17–6.28)</td>
<td>0 (0.00–0.53)</td>
<td>All cases resolved by 12 wk.</td>
</tr>
<tr>
<td>Capdevila 2005 (57)</td>
<td>P</td>
<td>0</td>
<td>256†</td>
<td>0 (0.01–1.42)</td>
<td>0 (0.01–1.42)</td>
<td>All cases resolved by 6 mo.</td>
</tr>
<tr>
<td>Borgeat 2003 (24)</td>
<td>P</td>
<td>56</td>
<td>700†</td>
<td>8.00 (6.14–10.16)</td>
<td>0 (0.00–0.52)</td>
<td></td>
</tr>
<tr>
<td>Auroy 2002 (45)</td>
<td>P</td>
<td>1</td>
<td>3,459</td>
<td>0.03 (0.01–0.16)</td>
<td>0 (0.01–1.42)</td>
<td>73 cases resolved by 9 mo. Denominator includes single-injections ( (n = 286) ) and continuous catheters ( (n = 234) ).</td>
</tr>
<tr>
<td>Weber 2002 (58)</td>
<td>R</td>
<td>2</td>
<td>218</td>
<td>0.92 (0.28–3.26)</td>
<td>0 (0.01–1.67)</td>
<td></td>
</tr>
<tr>
<td>Borgeat 2001 (59)</td>
<td>P</td>
<td>74</td>
<td>520</td>
<td>14.23 (11.49–17.50)</td>
<td>0 (0.01–2.12)</td>
<td></td>
</tr>
<tr>
<td><strong>Supraclavicular block</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Auroy 2002 (45)</td>
<td>P</td>
<td>7</td>
<td>171</td>
<td>4.09 (2.03–8.21)</td>
<td>0 (0.01–2.12)</td>
<td>All cases resolved by 12 wk.</td>
</tr>
<tr>
<td><strong>Axillary block</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Capdevila 2005 (57)</td>
<td>P</td>
<td>0</td>
<td>1,899</td>
<td>0 (0.00–0.19)</td>
<td>0 (0.00–0.19)</td>
<td></td>
</tr>
<tr>
<td>Bergman 2003 (61)</td>
<td>R</td>
<td>2</td>
<td>405†</td>
<td>0.49 (0.15–1.77)</td>
<td>?</td>
<td></td>
</tr>
<tr>
<td>Auroy 2002 (45)</td>
<td>P</td>
<td>2</td>
<td>11,024</td>
<td>0.02 (0.00–0.07)</td>
<td>?</td>
<td></td>
</tr>
<tr>
<td>Hebl 2001 (62)</td>
<td>R</td>
<td>6</td>
<td>100</td>
<td>6.00 (2.83–12.48)</td>
<td>?</td>
<td></td>
</tr>
<tr>
<td><strong>Lumbar plexus blockade</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Lumbar plexus block</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Capdevila 2005 (57)</td>
<td>P</td>
<td>0</td>
<td>20†</td>
<td>0 (12.12–16.11)</td>
<td>0 (0.12–16.11)</td>
<td></td>
</tr>
<tr>
<td>Auroy 2002 (45)</td>
<td>P</td>
<td>0</td>
<td>394</td>
<td>0 (0.01–0.93)</td>
<td>0 (0.01–1.93)</td>
<td></td>
</tr>
<tr>
<td>Macaire 2002 (68)</td>
<td>R</td>
<td>2</td>
<td>4,319</td>
<td>0.05 (0.01–0.17)</td>
<td>0 (0.00–0.09)</td>
<td></td>
</tr>
<tr>
<td><strong>Femoral nerve block</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Capdevila 2005 (57)</td>
<td>P</td>
<td>3</td>
<td>683†</td>
<td>0.44 (0.16–1.28)</td>
<td>0 (0.00–0.54)</td>
<td>All cases resolved by 10 wk.</td>
</tr>
<tr>
<td>Auroy 2002 (45)</td>
<td>P</td>
<td>3</td>
<td>10,309</td>
<td>0.03 (0.01–0.09)</td>
<td>?</td>
<td></td>
</tr>
<tr>
<td>Cuvilleon 2001 (69)</td>
<td>P</td>
<td>1</td>
<td>211†</td>
<td>0.47 (0.01–2.60)</td>
<td>1 (0.01–2.60)</td>
<td>1 case partial recovery by 12 mo.</td>
</tr>
</tbody>
</table>

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Continues
Table 2. (continued)

<table>
<thead>
<tr>
<th>Author/Year</th>
<th>Study design</th>
<th>Number of occurrences</th>
<th>Number of blocks performed</th>
<th>Rate of occurrence (n = 100)</th>
<th>Number of permanent injuries (n = 100)</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fanelli 1999 (60)</td>
<td>P</td>
<td>45</td>
<td>2,175</td>
<td>2.07 (1.55–2.76)</td>
<td>0</td>
<td>0 (0.00–0.17)</td>
</tr>
<tr>
<td>Sacral plexus blockade</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Capdevila 2005 (57)</td>
<td>P</td>
<td>0</td>
<td>32</td>
<td>0 (0.08–10.58)</td>
<td>0</td>
<td>0 (0.08–10.58)</td>
</tr>
<tr>
<td>Auroy 2002 (45)</td>
<td>P</td>
<td>2</td>
<td>8,507</td>
<td>0.02 (0.01–0.08)</td>
<td>?</td>
<td>—</td>
</tr>
<tr>
<td>Fanelli 1999 (60)</td>
<td>P</td>
<td>45</td>
<td>2,175</td>
<td>2.07 (1.55–2.76)</td>
<td>0</td>
<td>0 (0.00–0.17)</td>
</tr>
<tr>
<td>Popliteal nerve block</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Capdevila 2005 (57)</td>
<td>P</td>
<td>2</td>
<td>167</td>
<td>0 (0.02–2.17)</td>
<td>0</td>
<td>0 (0.02–2.17)</td>
</tr>
<tr>
<td>Borgeat 2004 (25)</td>
<td>P</td>
<td>0</td>
<td>500</td>
<td>0 (0.01–0.73)</td>
<td>0</td>
<td>0 (0.01–0.73)</td>
</tr>
<tr>
<td>Auroy 2002 (45)</td>
<td>P</td>
<td>3</td>
<td>952</td>
<td>0.32 (0.11–0.92)</td>
<td>?</td>
<td>—</td>
</tr>
<tr>
<td>Provenzano 2002 (70)</td>
<td>R</td>
<td>0</td>
<td>467</td>
<td>0 (0.01–0.79)</td>
<td>0</td>
<td>0 (0.01–0.79)</td>
</tr>
</tbody>
</table>

95% confidence intervals appear in parentheses.
P = Prospective; R = Retrospective; ? = Insufficient data.
* Continuous catheter technique.

Table 3. Aggregate Estimated Rate of Occurrence of Neurological Complications After Neuraxial Blockade

<table>
<thead>
<tr>
<th>Neurological Complication</th>
<th>Estimated rate of occurrence (n = 10,000)</th>
<th>Lower CI (n = 10,000)</th>
<th>Upper CI (n = 10,000)</th>
<th>Heterogeneity (Q value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spinal anesthesia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radiculopathy/neuropathy</td>
<td>3.78</td>
<td>1.06</td>
<td>13.50</td>
<td>168.70</td>
</tr>
<tr>
<td>Cauda equina syndrome</td>
<td>0.11</td>
<td>0.03</td>
<td>0.37</td>
<td>20.59</td>
</tr>
<tr>
<td>Intracranial event</td>
<td>0.03</td>
<td>0.00</td>
<td>0.20</td>
<td>1.66</td>
</tr>
<tr>
<td>Paraplegia (4 studies)</td>
<td>0.06</td>
<td>0.02</td>
<td>0.20</td>
<td>5.38</td>
</tr>
<tr>
<td>Epidural anesthesia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radiculopathy/neuropathy</td>
<td>2.19</td>
<td>0.88</td>
<td>5.44</td>
<td>142.30</td>
</tr>
<tr>
<td>Cauda equina syndrome</td>
<td>0.23</td>
<td>0.14</td>
<td>0.39</td>
<td>2.30</td>
</tr>
<tr>
<td>Intracranial event</td>
<td>0.07</td>
<td>0.03</td>
<td>0.21</td>
<td>0.24</td>
</tr>
<tr>
<td>Paraplegia (4 studies)</td>
<td>0.09</td>
<td>0.04</td>
<td>0.22</td>
<td>2.23</td>
</tr>
</tbody>
</table>

The estimated rate of occurrence was calculated using a random effects general linear model (see text).
CI = 95% confidence interval; NS = nonsignificant (nonsignificance indicates the absence of heterogeneity between studies).

Table 4. Aggregate Estimated Rate of Occurrence of Neuropathy After Peripheral Nerve Blockade

<table>
<thead>
<tr>
<th>Neurological Complication</th>
<th>Estimated rate of occurrence (n = 100)</th>
<th>Lower CI (n = 100)</th>
<th>Upper CI (n = 100)</th>
<th>Heterogeneity (Q value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brachial plexus blockade</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interscalene block</td>
<td>2.84</td>
<td>1.33</td>
<td>5.98</td>
<td>90.71</td>
</tr>
<tr>
<td>Supraclavicular block</td>
<td>0.03</td>
<td>0.00</td>
<td>0.42</td>
<td>NA</td>
</tr>
<tr>
<td>Axillary block (10 studies)</td>
<td>1.48</td>
<td>0.52</td>
<td>4.11</td>
<td>315.57</td>
</tr>
<tr>
<td>Midhumeral block (2 studies)</td>
<td>0.02</td>
<td>0.00</td>
<td>0.09</td>
<td>0.28</td>
</tr>
<tr>
<td>Lumbar plexus blockade</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lumbar plexus block</td>
<td>0.19</td>
<td>0.02</td>
<td>1.93</td>
<td>6.18</td>
</tr>
<tr>
<td>Femoral nerve block</td>
<td>0.34</td>
<td>0.04</td>
<td>2.81</td>
<td>57.51</td>
</tr>
<tr>
<td>Sacral plexus blockade</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sciatic nerve block</td>
<td>0.41</td>
<td>0.02</td>
<td>9.96</td>
<td>38.71</td>
</tr>
<tr>
<td>Popliteal nerve block</td>
<td>0.24</td>
<td>0.10</td>
<td>0.61</td>
<td>0.96</td>
</tr>
</tbody>
</table>

The estimated rate of occurrence was calculated using a random effects general linear model (see text).
CI = 95% confidence interval; NA = not applicable; NS = nonsignificant (nonsignificance indicates the absence of heterogeneity between studies).
complications after epidural anesthesia to be 2.8:10,000 when the obstetrical population is omitted, as opposed to 0.4:10,000 for obstetrical epidural anesthesia. Excluding obstetrics, Auroux et al. (45) similarly found the incidence of major neurological complications related to CNB to be 3.4:10,000 compared to 0.6:10,000 for the obstetric population. Another reason for the relatively high number of neurological complications reported by Dahlgren and Tornebrandt (49) may be the questionable association between the CNB and subsequent neurological symptoms as 1 of the 3 and each of the 7 cases of neuropathy after spinal and epidural blockade, respectively, may have been caused by surgery, patient positioning, or intercurrent disease (33,49).

Although there is a limited number of contemporary large scale studies examining neurological complications after PNB available for review, there are even fewer available for historical comparison with our present findings. In 1985, Winchell and Wolfe (74) prospectively followed 854 consecutive patients who underwent brachial plexus blockade for upper extremity surgery and found a 0.4% incidence of postoperative neuropathy and no cases of permanent neurological deficit. Weeks et al. (75) followed 834 patients who underwent axillary brachial plexus blockade and found that four patients (0.5%) suffered persistent pain unrelated to the surgical site when assessed at 2 yr postoperatively. Finally, in an observational study examining 242 consecutive axillary and 266 consecutive interscalene brachial plexus blocks for upper extremity surgery, Urban and Urquhart (76) determined the incidence of neurological deficit to be 5% and 3%, respectively, at 2 wk postoperatively, with only one patient in each group (0.4%) experiencing persistent deficit beyond 4 wk.

The heterogeneity and quality of the available source studies included in an article such as this calls for caution when interpreting the validity of our risk estimates. Differences in sample size, patient populations, comorbidities, and surgical procedures undermine faithful comparisons of neurological complications reported in each study. Moreover, the presentation, investigation, and diagnosis of anesthesia-related nerve injury is complex (77,78) and inconsistent among studies, likely resulting in underreporting in some studies and over-reporting in others. For example, identification of neurological complications likely varied depending on direct anesthesia follow-up (24,25,53,54,56,57,59,60,63,69), surgeon referral (49), voluntary reporting by anesthesiologists (45,47,50,51,55,68), retrospective chart review (48,52,58,62,64,70,73), or patient self-reporting (46,58,59), the latter associated with a relatively higher rate of neurological symptoms after nerve blockade.

The time at which assessment or follow-up occurred surely affected the incidence of complications as neurological symptoms after CNB and PNB diminish with time. In some studies, one or more anesthesiologists (24,45,47,49,53,55–57,59,67), neurologists (47,49,54,55), or surgeons (24,49,55,56) undertook diagnosis, whereas in most other studies it is unclear who, if anyone, was charged with diagnosing the etiology of nerve injury. Finally, none of the
studies presently reviewed were of prospective controlled design. Rather, the largest of the source studies reviewed relied, in all or in part, on self-reporting from anesthesia providers (45–47,50,51). The significant potential for under-reporting of anesthesia-related complications is the predominant limitation when self-reporting is sought from anesthesiologists (79). Although the tendency for under-reporting may be greater in voluntary self-reporting systems [e.g., Auroy et al. (45,47)] (80), mandatory self-reporting [e.g., Moen et al. (51)] does not guarantee that all adverse events will be reported either (79). Nonetheless, voluntary or mandatory self-reporting is one of the only practical means to capture rare (approximately incidence 1:10,000–1:100,000) occurrences (79). A more reliable and valid method to capture the true incidence of rare neurological complications would be an international, multicenter, prospective, standardized trial (79), the logistics of which can be highly impractical. For extremely rare events (approximate incidence 1:1,000,000), such as paraplegia after CNB, preemptive risk modeling would be ideal, but this strategy is still premature in our specialty (79). At present, collating and adjusting the reported rates of neurological complications and calculating CI (81) are likely our best means to quantify and estimate the incidence of such rare occurrences.

In summary, our review suggests that the rate of neurological complications after CNB is <4:10,000, or 0.04%. The rate of neuropathy after PNB is <3:100, or 0.3%. However, permanent neurological injury after RA is rare in contemporary anesthetic practice. The rate of neurological complications presented in this article may be under-estimated, because much of the source data relied on self-reporting from anesthesia providers rather than prospective controlled trials.

Appendix: Quality of Evidence (35)

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade I</td>
<td>Evidence obtained from at least one properly randomized controlled trial.</td>
</tr>
<tr>
<td>Grade II</td>
<td>Evidence obtained from well-designed controlled trials without randomization.</td>
</tr>
<tr>
<td>Grade II-1</td>
<td>Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group.</td>
</tr>
<tr>
<td>Grade II-2</td>
<td>Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.</td>
</tr>
<tr>
<td>Grade III</td>
<td>Opinions of respected authorities, based on clinical experience, descriptive studies and case reports, or reports of expert committees.</td>
</tr>
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REFERENCES


Ultrasound-Guided Regional Anesthesia and Patient Safety

An Evidence-Based Analysis

Joseph M. Neal, MD

Abstract: The role of ultrasound-guided regional anesthesia (UGRA) in reducing the frequency of regional anesthetic–related complications is difficult to ascertain from analyzing the limited literature on the topic. This evidence-based review critically evaluates the contributions of UGRA to improved patient safety, particularly as compared with standard nerve localization tools. Randomized controlled trials that compared UGRA with another form of neural localization and case series of more than 500 patients were used to compare safety parameters. The quality of studies and strength of evidence were graded. Of those randomized controlled trials identified by our search techniques, 22 compared the incidence of postoperative nerve symptoms, 17 assessed local anesthetic systemic toxicity parameters, and 3 studied hemidiaphragmatic paresis. Statistical proof for meaningful reduction in the frequency of extremely rare complications, such as permanent peripheral nerve injury, is likely unattainable. Although there is evidence for UGRA reducing the occurrence of vascular puncture and the frequency of hemidiaphragmatic paresis, as yet there is at best inconclusive scientific proof that these surrogate outcomes are linked to actual reduction of their associated complications, such as local anesthetic systemic toxicity or predictable diaphragmatic impairment in at-risk individuals. This evidence-based review thus strives to summarize both the power and the limitations of UGRA as a tool for improving patient safety.

METHODS

Randomized controlled trials (RCTs) were sought that compared UGRA with another form of neural localization, such as PNS or transarterial techniques (Table 1); subsequent comparative analysis of UGRA safety was based only on these RCTs. Case series (>500 patients) were used to provide supplemental information regarding the frequency of complications (Table 2). Some complications are so rare as to have been described only in case reports or correspondence. This form of reporting was used to document the existence of complications, but was not used to compare UGRA with other neural localization techniques. The relative quality of individual RCTs was graded using the Jadad score (0–5 points).

RESULTS

Twenty-two RCTs totaling 1863 subjects compared postoperative neurologic symptoms associated with UGRA (either UGRA alone or in combination with PNS) versus other techniques for nerve localization—PNS (18 studies), transarterial (2 studies), surface landmark (1 study), or fascial click (1 study). The median quality (Jadad score) of these studies was 3 (range, 2–5). These RCTs reported the incidence of immediate or transient paresthesia (<7 days) and/or the incidence of postoperative nerve injury (24 hrs to 2 months). Seven RCTs simply reported “none” for neurologic complications, whereas 15 RCTs reported actual incidence with or without statistical significance (Table 1). Four large case series reported incidences of postoperative neurologic symptoms from a combined total of 15,145 peripheral nerve blocks (Table 2).
<table>
<thead>
<tr>
<th>Reference (Year)</th>
<th>Jadad Score</th>
<th>Block</th>
<th>US, n</th>
<th>USNS, n</th>
<th>PNS, n</th>
<th>Vascular Puncture, n (%)</th>
<th>Paresthesia, n (%)</th>
<th>Nerve Injury, n (%)</th>
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<tbody>
<tr>
<td>Casati et al&lt;sup&gt;39&lt;/sup&gt; (2007)</td>
<td>4</td>
<td>Femoral</td>
<td>30</td>
<td>30</td>
<td>0 US</td>
<td>None</td>
<td>None</td>
<td>0 US at 24 hrs</td>
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<td>3</td>
<td>Axillary</td>
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<td>US 13 (20%)</td>
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<td>None</td>
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<tr>
<td>Chan et al&lt;sup&gt;28&lt;/sup&gt; (2007)</td>
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<td>Axillary</td>
<td>64</td>
<td>62</td>
<td>62</td>
<td>None</td>
<td>US 13 (15%)</td>
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<td>Danelli et al&lt;sup&gt;59&lt;/sup&gt; (2009)</td>
<td>3</td>
<td>Popliteal sciatic</td>
<td>22</td>
<td>22</td>
<td>None</td>
<td>US 0 (0%)</td>
<td>None</td>
<td>None at 24 hrs</td>
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<td>2</td>
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<td>36</td>
<td>36</td>
<td>None</td>
<td>US 2 (6%)</td>
<td>US 5 (22%)</td>
<td>None</td>
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<td>3</td>
<td>Midfemoral sciatic</td>
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<td>31</td>
<td>None</td>
<td>US 1 (3%)</td>
<td>None</td>
<td>None</td>
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<td>25</td>
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<td>None</td>
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<td>3</td>
<td>Continuous interscalene</td>
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<td>40</td>
<td>None</td>
<td>PNS 1 neuropathic pain</td>
<td>Resolved at 10 d</td>
<td>Resolved 8 wk (NS)</td>
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<td>40</td>
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<td>None</td>
<td>US 0 (0%)</td>
<td>PNS 3 (8%)</td>
<td>None</td>
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<td>Kapral et al&lt;sup&gt;65&lt;/sup&gt; (2008)</td>
<td>2</td>
<td>Interscalene</td>
<td>80</td>
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<td>None</td>
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<td>Liu et al&lt;sup&gt;66&lt;/sup&gt; (2005)</td>
<td>2</td>
<td>Axillary</td>
<td>60</td>
<td>30</td>
<td>US 0</td>
<td>US 0 (0%)</td>
<td>US 3 (10%)</td>
<td>None</td>
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<td>Interscalene</td>
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<td>None</td>
<td>None</td>
<td>None</td>
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<td>Macaire et al&lt;sup&gt;67&lt;/sup&gt; (2008)</td>
<td>2</td>
<td>Median and ulnar nerves</td>
<td>30</td>
<td>30</td>
<td>None</td>
<td>US 0 (0%)</td>
<td>None</td>
<td>None</td>
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<td>1</td>
<td>3-in-1</td>
<td>20</td>
<td>20</td>
<td>US 0</td>
<td>PNS 3 (15%)</td>
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<td>None</td>
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<tr>
<td>Study</td>
<td>N</td>
<td>Technique</td>
<td>Level</td>
<td>Incidence</td>
<td>US Incidence</td>
<td>PNS Incidence</td>
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<td>2</td>
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<td>20</td>
<td>40</td>
<td>US 0 (0%)</td>
<td>PNS 4 (10%)</td>
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<td>3</td>
<td>Continuous popliteal sciatic</td>
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<td>20</td>
<td>US 0 (0%)</td>
<td>PNS 2 (10%)</td>
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<td></td>
</tr>
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<td>Obemdofer et al (2007)</td>
<td>4</td>
<td>Femoral/sciatic</td>
<td>23</td>
<td>23</td>
<td>None</td>
<td>None</td>
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<td>Perlas et al (2008)</td>
<td>4</td>
<td>Popliteal sciatic</td>
<td>37</td>
<td>33</td>
<td>US 0 (0%)</td>
<td>PNS 0 (0%)</td>
<td></td>
<td></td>
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<td>Redborg et al (2009)</td>
<td>5</td>
<td>Tibial nerve ankle</td>
<td>18</td>
<td>18</td>
<td>None</td>
<td>None</td>
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<td>Sauter et al (2008)</td>
<td>3</td>
<td>Lateral sagittal infraclavicular</td>
<td>40</td>
<td>40</td>
<td>US 2 (5%)</td>
<td>PNS 13 (33%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sites et al (2006)</td>
<td>3</td>
<td>Axillary</td>
<td>28</td>
<td>28*</td>
<td>US 1 (5%)</td>
<td>Landmark 5 (25%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soeding et al (2005)</td>
<td>1</td>
<td>Axillary and interscalene</td>
<td>20</td>
<td>20†</td>
<td>No seizure</td>
<td>None</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Taboada et al (2009)</td>
<td>3</td>
<td>Conocoid infraclavicular</td>
<td>35</td>
<td>35</td>
<td>US 1 (3%)</td>
<td>PNS 1 (3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tedore et al (2009)</td>
<td>3</td>
<td>US-infraclavicular</td>
<td>111</td>
<td>109‡</td>
<td>US 29 (26%)</td>
<td>TA 44 (40%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Williams et al (2003)</td>
<td>2</td>
<td>Supraclavicular</td>
<td>40</td>
<td>40</td>
<td>None</td>
<td>None</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Willschke et al (2005)</td>
<td>3</td>
<td>Ilioinguinal/iliohypogastric</td>
<td>30</td>
<td>30§</td>
<td>US 0 (0%)</td>
<td>PNS 16 (40%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yu et al (2007)</td>
<td>3</td>
<td>Axillary</td>
<td>40</td>
<td>40</td>
<td>None</td>
<td>None</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Transarterial.
† Landmark based.
‡ Transarterial axillary.
§ Fascial click.

LE indicates lower extremity; NS, not statistically significant; PONS, postoperative neurologic symptoms; TA, transarterial; US, ultrasound; USNS, ultrasound + nerve stimulation.
TABLE 2. Large Case Series of Ultrasound-Guided Regional Anesthesia With or Without Other Localization Techniques

<table>
<thead>
<tr>
<th>Reference (Year)</th>
<th>Block</th>
<th>US, n (%)</th>
<th>USNS, n (%)</th>
<th>PNS, n (%)</th>
<th>Vascular Puncture, n (%)</th>
<th>LAST, n (%)</th>
<th>Nerve Injury, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barrington et al (2009)</td>
<td>Australasian collaboration 8189 Peripheral blocks (early complications) 7156 Peripheral blocks (late complications)</td>
<td>1065 (13%)</td>
<td>4095 (50%)</td>
<td>2457 (30%)</td>
<td>Overall: 7.2/1000 (95% CI, 5.1–10.0/1000)</td>
<td>Overall: 0.98/1000 (95% CI, 0.42–1.9/1000)</td>
<td>30/7156 (0.42%)</td>
</tr>
<tr>
<td>Fredrickson and Kilfoyle (2009)</td>
<td>1010 Single and continuous blocks Upper and lower extremity US +/- PNS</td>
<td></td>
<td></td>
<td></td>
<td>US 5.1/1000 PNS 13.9/1000 (P = 0.001)</td>
<td>US vs PNS (NS)</td>
<td>27/30 not block related 3/30 block related (&lt;6, &gt;6, &lt;12 mo duration—0.4/1000 (95% CI, 0.08–1.1/1000)</td>
</tr>
<tr>
<td>Orebaugh et al (2009)</td>
<td>Retrospective quality-assurance database (5436 blocks)</td>
<td>2146 (39%)</td>
<td>3290 (61%)</td>
<td></td>
<td></td>
<td></td>
<td>All documented with EMG and NCS; 2 of 3 improving</td>
</tr>
<tr>
<td>Perlas et al (2009)</td>
<td>Supraclavicular (510 blocks)</td>
<td>510</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

EMG indicates electromyogram; NCS, nerve conduction studies; LAST, local anesthetic systemic toxicity; UE, upper extremity; US, ultrasound; USNS, ultrasound + nerve stimulation.

Peripheral nerve injury (III)
- Proving statistical differences in nerve injury as a function of nerve localization technique is likely futile.
- Underpowered results from RCTs and large case series find no difference in surrogate markers of nerve injury, such as paresthesia during or immediately after block placement, or temporary postoperative neurologic symptoms.
- UGRA seems to be associated with perioperative nerve injury at an incidence similar to historical reports of nerve injury after PNS.

Local anesthetic systemic toxicity (Ia and III)
- Compared with PNS, UGRA lowers the risk of unintended vascular puncture, a surrogate outcome for LAST (Ia).
- The weight of conflicting evidence is that UGRA does not affect the incidence of local anesthetic–induced seizures (III).

HDP (Ia and IV)
- RCTs confirm the ability of low-volume UGRA to reduce (but not eliminate) the incidence and severity of HDP using the interscalene approach. The incidence of HDP is nearly 0% using the supraclavicular approach with ultrasound guidance (Ia).
- No RCTs or case reports address whether patients at risk for pulmonary compromise can undergo above-the-clavicle regional anesthetic block. Because HDP can still occur unpredictably, caution remains warranted in any patient unable to withstand a 30% diminution of pulmonary function (IV).

Pneumothorax (III)
- No adequately powered studies directly address the risk of pneumothorax with UGRA.
- Pneumothorax has occurred despite the use of UGRA (III).

HDP indicates hemidiaphragmatic paresis; LAST, local anesthetic systemic toxicity.

Seventeen RCTs totaling 1279 subjects recorded vascular puncture. Six of these studies simply reported vascular punctures as “none,” whereas 11 provided actual incidence figures, with or without statistical significance. One study (40 patients) reported “no seizure.” The median Jadad score of these studies was 3 (range, 1–5; Table 1). Two case series reported the frequency of vascular puncture and/or LAST in 13,625 peripheral nerve blocks (Table 2).

The effect of ultrasound guidance on the frequency and severity of HDP has been reported in 3 RCTs totaling 65 UGRA patients.5–7 Jadad scores for these 3 studies were 2, 3, and 5. The absence of pneumothorax was mentioned in 3 RCTs totaling 110 UGRA patients8 and 1 case series of 510 supraclavicular blocks.8

No RCTs were identified that directly addressed issues of patient safety using ultrasound-guided neuraxial techniques.

DISCUSSION

Peripheral Nerve Injury

Needle or catheter-induced disruption of a peripheral nerve’s structural integrity, particularly the fascicles and their protective perineurium, is thought to contribute to peripheral nerve injury.14 Ultrasoundography may impact this potential injury mechanism by facilitating direct visualization of needle-to-nerve proximity. Ironically, UGRA research has furthered our understanding of more traditional forms of nerve localization such as PNS and paresthesia-seeking techniques and has confirmed previous research that demonstrates their low sensitivity for accurately identifying needle-to-nerve contact. Indeed in human axillary nerve block, US visualization demonstrates that paresthesia is only 38% sensitive and motor response only 75% sensitive in confirming needle-to-nerve contact.10 This relatively low sensitivity of PNS has been confirmed in another study of human supraclavicular block, wherein a motor response at 0.2 mA or less was indicative of intraneural needle placement as confirmed by US, but a motor response of greater than 0.2 to 0.5 mA or less could not rule out intraneural needle placement.11 Monitoring injection pressures may also aid in preventing intrafascicular injection, but this modality has been studied only in animals and, like other tools, is neither completely sensitive nor predictive of injury.12,13 Conversely, ultrasound is a sensitive tool for demonstrating intraneural injection in porcine models, as manifested by consistent nerve expansion observed with 1-mL injectate or less.13–15 However, although nerve expansion was correlated with histologic injury, concomitant functional injury was not observed.13 Human correlation has been reported with axillary block, wherein no patient had a nerve injury despite clearly observed nerve expansion after the injection of 2 to 3 mL local anesthetic during UGRA.16 Although these results suggest that PNS- or paresthesia-guided needles are likely placed within nerves much more frequently than previously realized, and that the usual absence of injury is likely explainable by the relative ease of placing needles into connective tissue rather than into a fascicle, in vitro studies of human sciatic nerve nevertheless demonstrate that sharp needles, in fact, enter fascicles 3.2% of the time, thereby potentially causing injury.17 Moreover, as one proceeds proximal to distal, the amount of nonneural connective tissues present within the cross-sectional area of the brachial plexus increases,18 suggesting that the interscalene area may be less forgiving of subpneumature needle placement compared with the axillary or supraclavicular areas. Thus, US is a more sensitive indicator of needle-to-nerve contact than either paresthesia or PNS, but it is unknown if this advantage translates to actual reduction of nerve injury. Adding balance to this observation is that current acoustic resolution limits our ability to consistently discern nerve microanatomy and that there are differences in technical skills between operators.

Of the 22 RCTs (Table 1) that compared UGRA, alone or in combination with PNS, with other forms of nerve localization, two found a statistically different incidence of paresthesia during block placement in dissimilar patient groups—26% in a US-infraclavicular group versus 40% in a transarterial axillary group (P = 0.035, 220 patients)19 and 25% using landmarks versus 5% using UGRA in interscalene and axillary blocks (P = 0.012, 40 total patients).20 The remaining 20 RCTs reported no difference in terms of transient paresthesia or short-lived postoperative neurologic symptoms, which is in agreement with a meta-analysis21 and a qualitative systematic review.22 Several large case series (Table 2) confirm that serious nerve injury is rare. In the largest of these, Barrington et al23 report a prospective audit of more than 7000 peripheral nerve
blocks from the Australasian Regional Anaesthesia Collaboration. Unintended paresthesia during block placement (16.8/1000) and block-related late neurologic deficit (0.4/1000; 95% confidence interval [CI], 0.08–1.1 per 1000) did not differ between UGRA and PNS techniques. The incidence of late neurologic deficit (0.04%) was similar to that reported for PNS-guided peripheral nerve blocks by Auroy et al\textsuperscript{24} (0.02%) and for continuous catheter blocks by Capdevila et al\textsuperscript{25} (0.21%, all deficits resolved by 10 weeks). These comparisons suggest, but do not prove, that the incidence of late postoperative neurologic symptoms, that is, those lasting weeks to months after the block, has not been altered by the introduction of UGRA.\textsuperscript{26} In a retrospective quality assurance review of 5436 peripheral nerve blocks performed with PNS or US with PNS, Orebaugh et al\textsuperscript{27} noted 3 neurophysiologic study–documented nerve injuries, all in the PNS group (not statistically significant). Fredrickson and Kilfoil\textsuperscript{y} reported new neurologic symptoms (from any cause) in a cohort of 1010 patients undergoing single or continuous peripheral nerve blocks under UGRA with or without concomitant PNS. The incidences of neurologic symptoms were 8.2% at 10 days and 3.7% at 1 month, which are similar to those reported by Borgeat et al\textsuperscript{28} using PNS localization. The 0% to 1.0% (95% CI, 0.0%–0.56%) incidence of prolonged (>6 months) nerve injuries judged to be block related in the Fredrickson and Kilfoil\textsuperscript{y} study compared favorably with other reports of injury in continuous catheter patients.\textsuperscript{29} Perlas et al\textsuperscript{30} noted transient numbness (several weeks) after 510 UGRA supraventricular blocks (0.4%; 95% CI, 0.1%–1.4%). To date, there are 2 reported cases of prolonged nerve injury associated with UGRA—a permanent brachial plexopathy in a patient with underlying multiple sclerosis and potential surgical causes of injury,\textsuperscript{31} and a volunteer who had a dysesthesia of the tibial nerve, which was present but improving after 2 months (this subject is included in the RCTs).\textsuperscript{32} In summary, limited literature and small patient numbers suggest 3 findings concerning peripheral nerve injury and UGRA: (1) block-related paresthesia, a surrogacy outcome at best, was not reduced when similar block groups were compared; (2) RCTs and large case studies report no permanent neurologic injuries, nevertheless; and (3) peripheral nerve injury associated with, but arguably unrelated to, UGRA has been reported. Because the examined RCTs were not powered to assess nerve injury, the best data on this topic come from the large case series, thereby providing level III strength of evidence (Table 3).

It is important to understand that the relationship of nerve localization technique and peripheral nerve injury is unlikely to ever reach statistical resolution. For example, if one assumes a moderate incidence of early, nonpermanent peripheral nerve injury (3%), a study would require 3000 patients per group to have 80% power (B) to prove a 50% reduction to 1.5%.\textsuperscript{33} However, the number of subjects would expand exponentially if one intends to analyze long-term injury (6–12 months), which is estimated to occur in only 0 to 4 per 10,000 blocks.\textsuperscript{23,24,26} Furthermore, recent analysis of block–related permanent nerve injury (>12 months) noted only one such injury reported in 65,092 blocks\textsuperscript{22} (upper limit 95% CI, 0.05/10,000).

**Local Anesthetic Systemic Toxicity**

Local anesthetic systemic toxicity (LAST) ranges from mild subjective symptoms to seizure and cardiac arrest. Ultrasound guidance has the potential to limit LAST by at least 3 mechanisms—identifying the absence of injectate spread around the target, visualizing turbulence or other intravascular anomaly during local anesthetic injection,\textsuperscript{34} and facilitating reduced volume of injected local anesthetic. The 17 RCTs reviewed herein add credence to a meta-analysis that showed US can reduce the risk of aspiration-proven vascular puncture compared with other localization techniques (pooled risk ratio, 0.16; 95% CI, 0.05–0.47).\textsuperscript{35} Although recognition of unintended vascular puncture is a necessary step toward eliminating LAST, it is only a surrogate outcome for seizure or cardiac arrest. Indeed, various case reports and correspondence document loss of consciousness, agitation, and cardiac arrest despite UGRA.\textsuperscript{36–37} Barrington et al\textsuperscript{23} found that although US significantly lowered the incidence of unintended vascular puncture as compared with PNS, the incidence of actual LAST (0.98/1000; 95% CI, 0.42–1.9 per 1000) did not differ as a function of localization technique. This incidence is very similar to the 0.8–per-1000 figure reported by Auroy et al\textsuperscript{24} using PNS. Conversely, Orebaugh et al\textsuperscript{27} reported more seizures (P = 0.044) in their upper-extremity blocks that involved PNS rather than UGRA. Thus, UGRA consistently reduces the likelihood of unintended vascular puncture, but case reports and most case series fail to link this advantage to an actual reduction in LAST. The strength of evidence for UGRA reducing the rate of vascular puncture as compared with PNS is level Ia, but only level III for its effect on the incidence of seizure.

The literature does not answer whether using less local anesthetic volume will reduce the frequency of LAST. Although 1 study showed no significant reduction in the volume of local anesthetic used for ultrasound-guided supraclavicular block,\textsuperscript{38} several others have shown that UGRA reduces minimum effective local anesthetic volume (MEV) as compared with PNS. For instance, Casati et al\textsuperscript{22} were able to lower the MEV using PNS-guided femoral nerve block from 26 to 15 mL using UGRA. However, the US MEV (15 mL; 95% CI, 7–23 mL) remains capable of causing LAST, particularly if injected intravascularly. Importantly, UGRA has been linked to faster absorption and higher maximum plasma concentrations of local anesthetic,\textsuperscript{30} which suggests that lowering the local anesthetic volumes used during UGRA is not just possible, but perhaps well considered.

**Hemidiaphragmatic Paresis**

Hemidiaphragmatic paresis is a universal occurrence with landmark- and nerve stimulator-based interscalene blocks, becoming progressively less frequent as blocks are placed below the clavicle and farther distal along the brachial plexus. Particularly with the more proximal approaches, some patients may experience reduced spirometric measures of pulmonary function, and even fewer may suffer respiratory compromise. For these reasons, above the clavicle blocks are relatively contraindicated in patients unable to withstand a 25% decrease in pulmonary function.\textsuperscript{3} Reducing the volume of injected local anesthetic to 20 mL does not limit the occurrence of HDK using traditional approaches, but because UGRA facilitates the use of even smaller local anesthetic volumes, 2 investigatory teams have examined whether this attribute could lower the incidence and severity of HDK without compromising anesthetic quality. One study\textsuperscript{3} performed interscalene UGRA with 20 versus 5 mL ropivacaine 0.5% and lowered the incidence of HDK 1 hour after surgery to 90% and 33%, respectively, without compromising sleep or analgesia over the first 24 hrs. Another group\textsuperscript{3} compared UGRA with PNS-guided supraclavicular block with 10 mL ropivacaine 0.75%, similarly lowering the incidence of complete or partial HDK to 13% and 93%, respectively, without affecting block success or early morphine requirements. The same group\textsuperscript{2} then compared US-guided supraclavicular block using 20 mL ropivacaine 0.75%. The incidence of HDK was 0% (95% CI, 0.00–0.14) versus 53% (P < 0.0001), respectively. Spirometric measures of pulmonary function were reduced 20%
or greater in the PNS patients with complete HDP (level Ia strength of evidence; Table 3). Despite the relative success of these UGRA/low-dose local anesthetic techniques, HDP continued to occur unpredictably in both interscalene studies, suggesting that this approach remains relatively contraindicated in those patients most at risk for pulmonary compromise (level IV strength of evidence). Although the suprACLavicular study suggests that the risk of HDP is very low using ultrasound guidance and 20 mL ropivacaine, the study was too small to detect a true incidence of HDP using this approach. A large series of UGRA suprACLavicular blocks (n = 510) noted symptomatic HDP in 1% of patients (95% CI, 0.4%–2.3%) using 33 ± 8 mL local anesthetic.8

Pneumothorax

Ultrasonography enables the anesthesiologist to directly visualize the pleura and lung, which intuitively lessens the risk of pneumothorax. Three RCTs2-5 and 1 case series6 of patients undergoing the suprACLavicular or lateral sagittal infraACLavicular approaches report no pneumothorax in 575 patients (upper limit 95% CI, 0.5%). Nevertheless, a pneumothorax has been reported after UGRA lateral sagittal infraACLavicular block41 and an interscalene continuous catheter block,42 plus an unreported pneumothorax complicated an attempted UGRA supraACLavicular/infraACLavicular approach at the author’s institution (level III strength of evidence; Table 3).

Indirect Effects of UGRA on Patient Safety

If the incidence of a major complication can be reduced, the direct versus indirect association with UGRA might be seen as immaterial semantics. Yet, a critical review should attempt to differentiate between improved outcomes directly attributable to a unique trait of UGRA versus an indirect benefit that results from a change in technique facilitated by, but not unique to, UGRA. For instance, UGRA interscalene block changes the traditional needle-toward-midline technique of Winnie43 to a more shallow posterior/lateral-to-anterior/medial needle trajectory that is superficial to the deep borders of the scalene muscles and that theoretically lessens the potential for unintended neuraxis contact. This approach, which should reduce the risk of direct neuraxial spread of local anesthetic and/or needle injury to the spinal cord, is not unique to UGRA; a modified lateral PNS-based approach has been described also by Borget et al.28 Another example pertains to UGRA-facilitated reduction in local anesthetic volume, which may lessen the incidence of LAST. Whereas UGRA may instill the confidence to use smaller volumes of local anesthetic, the tendency for practitioners to use excessive local anesthetic doses for peripheral nerve blocks has been demonstrated by multiple studies, including the ability to substantially reduce median effective volumes by using stimu-

lation can be challenging.44 Another indirect (and unique) benefit of UGRA is preprocedural scan of the target area, which may reveal and thus avoid unanticipated findings such as vascular anomalies,45 neurofibromatosis, or ventriculoperitoneal shunts.46 Therefore, without diminishing the importance of improving patient safety by whatever tactic, future studies and critical assessments of UGRA should acknowledge both its direct and indirect benefits.

Limitations and Future Directions

Just as it may be important to differentiate direct from indirect benefits of UGRA, in the future it may be possible to link UGRA to patient safety issues that are not obvious from current data. For instance, several RCTs demonstrate fewer needle passes with UGRA versus PNS-guided techniques.35,47 Although perhaps intuitive to link reduced needle passes to less nerve injury and vascular puncture, current data obtained from normal subjects cannot support this linkage. However, US may particularly improve nerve localization and perhaps reduce nerve injury in patients with diabetes mellitus, in whom PNS—or paresthesia-guided localization is insensitive, and whose nerves have an altered response to local anesthetics.48,49 Fewer needle passes and vascular punctures may also limit hematoma formation in anticoagulated patients, in whom deeper peripheral nerve blocks are relatively contraindicated.50 Finally, UGRA-facilitated reduction in local anesthetic volume may have a much greater benefit for the pediatric patient than the adult patient. Thus, future UGRA studies, if performed in patients at risk for specific complications, might reveal benefits not currently apparent in normal patients.

As just as the literature offers no proof that UGRA successfully improves patient safety with regard to rare devastating injuries, there is also no proof that UGRA indeed does not increase the likelihood of injury. Balancing the positive effects of UGRA is the recognition that characteristics of ultrasound machines vary,51 acoustic resolution is limited, and that operator skill, training, and experience are an unquantifiable component of patient safety. Key to ultrasound safety is keeping the needle tip in view during advancement and injection, yet needle visualiza-

tion can be challenging.52 Furthermore, the most common mistakes made by novices include failure to identify the needle tip before injection and failure to recognize maldis-

tribution of injected local anesthetic,53,54 both of which negate the advantages of UGRA and conceivably lead to injury. Although difficult to quantify, it is likely that even the best ultrasound technology cannot improve safety without properly trained and skilled operators.55-57 As investigators and everyday operators become well trained in UGRA, data regarding the impact of UGRA on patient safety should become more plentiful and reliable.

CONCLUSION

After a decade of critical appraisal, the science of UGRA remains in its infancy, particularly with regard to how it impacts patient safety. There are no RCT data that unequivocally support superior safety outcomes consequent to the use of UGRA. Statistical proof of improved outcomes for extremely rare events such as peripheral nerve injury is likely unattainable. Data from inadequately powered comparative studies show no differences in surrogate outcomes such as paresthesia during block placement or temporary neurologic symptoms. Improved surrogate safety outcomes such as vascular puncture or less frequent HDP are apparent with the use of UGRA, but there are no definitive data that confirm an actual reduction in true outcomes such as LAST or predictable elimination of HDP in normal patients. Case reports emphasize that absolute elimination of these serious complications has not occurred. Further research is necessary, particularly in those patients at increased risk for specific complications and for whom UGRA may be more likely linked to improved safety profiles.

REFERENCES


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In the practice of anesthesiology, catastrophic perioperative outcomes are very uncommon. The occurrence of perioperative nerve injury from the practice of peripheral regional anesthesia is no different. However, perioperative nerve injuries may occur from many causes, including regional nerve blocks, direct injury from positioning and surgery, and tourniquet compression. The ultimate outcome of any perioperative nerve injury depends on 1) the preparation done before the procedure, and 2) the appropriate diagnosis and management after the injury occurs. This chapter specifically addresses useful efforts to prevent, correctly diagnose, and manage the issues related to nerve injuries from peripheral regional anesthesia. The goal is to provide 1) the necessary framework for delivering effective and safe peripheral regional anesthesia, and 2) a basic overview for the evaluation and management of peripheral nerve injury related to nerve block anesthesia. Diagnostic methods (such as clinical neurophysiological studies) are discussed, as well as necessary preemptive patient education and documentation issues, acquisition of necessary data (history and physical examination), correct documentation of meaningful events, appropriate patient follow up, and referral for expert help. Other diagnostic methods that are used much less commonly, including blood tests to identify various predisposing neurologic diseases, are deferred to textbooks of internal medicine and neurology.

- **Regional Anesthesia Program**

Setting up a regional anesthesia program in the appropriate way will lead to better patient care, earlier diagnosis and treatment of possible neurologic injuries, and possibly better patient outcomes should complications occur. Before any regional block is performed, several issues need
to be addressed. Having a specific process in place for immediate care, full documentation, early follow up, and appropriate referral is not only essential to good patient care, but may save the anesthesiologist from medicolegal torment.

Patient information sheets (Table 1) should 1) describe what patients should expect (both normally and possibly adversely), and 2) list 24/7 hospital contact information. This information should be given to patients at the time of preoperative evaluation when a block is anticipated, and again when leaving the recovery room for inpatients or when discharged home in the case of ambulatory patients. Identification and contact information of patients receiving regional blocks should be noted to facilitate easy follow up and postoperative documentation. Some training institutions have created a regional anesthesia logbook for residents performing blocks to document the patient, type of block, intraoperative problems, and postoperative follow up for every patient receiving a peripheral nerve block. This system promotes the valuable accumulation of important reference information should any problem arise. A similar system of reference data accumulation should be in place in every institution where regional anesthesia blocks are performed.

Nurses in charge of immediate postoperative care need to be informed of the special needs of patients receiving nerve blocks. Many anesthesia departments provide some form of nursing education describing the physiological effects and immediate postoperative concerns of regional anesthesia. Nurses should be well-trained to handle issues of extremity protection, postoperative pain management, and patient education related to regional anesthesia.

To complete the setup of the regional anesthesia program, it is important to know the referral services that are available in your institution, specifically the services that can address possible block-related nerve injuries. An institution with a multidisciplinary pain clinic is at an advantage; such a clinic commonly consists of anesthesiologists, neurologists, psychiatrists, and physical therapy personnel. Additional expertise is also useful, if available, specifically someone who can help in the diagnosis and treatment of peripheral nerve injury. One can start to establish this comprehensive referral network by contacting the chief of neurology to

Table 1. Patient Education Handout Sheet

<table>
<thead>
<tr>
<th>Key points to cover:</th>
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<tr>
<td>1. Brief explanation of regional anesthesia.</td>
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<tr>
<td>2. Warnings to protect numb and or weaken limb until anesthesia wears off.</td>
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<tr>
<td>3. Expected duration of typical block.</td>
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<tr>
<td>4. When to take oral pain medications.</td>
</tr>
<tr>
<td>5. Patient should expect a follow-up phone call.</td>
</tr>
<tr>
<td>6. The 24-hour contact information for questions or problems.</td>
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inquire of individuals who may have expertise or particular interest in peripheral nerve injuries. Establishing a good working relationship with this individual is integral to any regional anesthesia program.

Preblock Protocol

Like with any general anesthesia case, a thorough knowledge of the patient’s current medical problems and medical history is necessary for the administration of a regional anesthesia block (Table 2). Knowledge of the patient’s medical history and physical examination, including that related to the block site, is essential. This is important not only for follow up, but also to help determine whether a block is appropriate for the procedure and the patient’s medical condition. For example, performing an interscalene block (which nearly always blocks the ipsilateral phrenic nerve) in a patient who has contralateral phrenic nerve palsy could result in the need for immediate mechanical ventilation and, hopefully, only a short stay in an intensive care unit. One may only know about this preexisting condition by performing a thorough history and physical examination.

Patient education and consent are also vital to a successful program. Simple discussion with the patient before the block is placed is necessary to help him or her understand what to expect throughout the process. This

<table>
<thead>
<tr>
<th>Table 2. Regional Anesthesia Procedure Checklist</th>
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<tbody>
<tr>
<td>1. Equipment and patient monitors setup</td>
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<tr>
<td>2. Patient preprocedure physical examination, evaluation, and education</td>
</tr>
<tr>
<td>a. Careful review of patient medical history, and physical examination</td>
</tr>
<tr>
<td>b. Surgical procedure and site verification</td>
</tr>
<tr>
<td>c. Patient education</td>
</tr>
<tr>
<td>i. Block procedure using nerve stimulator or paresthesia technique</td>
</tr>
<tr>
<td>ii. Any common side effects and expected block duration</td>
</tr>
<tr>
<td>iii. Plan for postoperative pain medication</td>
</tr>
<tr>
<td>iv. Plan for appropriate patient follow up</td>
</tr>
<tr>
<td>3. Appropriate patient sedation</td>
</tr>
<tr>
<td>4. Detailed procedure documentation</td>
</tr>
<tr>
<td>a. Equipment, technique, and attempts</td>
</tr>
<tr>
<td>b. Nerve stimulated with minimum current or paresthesia elicited</td>
</tr>
<tr>
<td>c. Any immediate side effects or reactions</td>
</tr>
<tr>
<td>i. Blood aspiration</td>
</tr>
<tr>
<td>ii. Increased pressure on injection</td>
</tr>
<tr>
<td>iii. Pain on injection</td>
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educational step should include: how the block is performed with a nerve stimulator, the expected duration of the block, care of the extremity while the block is in effect, and analgesic options when the block wears off. All of these issues should be understood by patients, and even possibly family members, before sedation is administered. These issues can be addressed in the preoperative evaluation clinic and briefly reinforced just before the block procedure. Not knowing about the possibility of a temporary hoarse voice or Horner’s syndrome after an interscalene block, for example, can create unnecessary anxiety for patients and their families. Such anxiety places the anesthesiologist in the possibly uncomfortable position of explaining procedure side effects after they have already occurred.

Sedation for placement of the block is another key issue. Taking into consideration the patient’s prior experience, allergies, and so on, sedation is titrated to achieve a comfort level in which the patient is still awake and responsive. Prolonged or significant paresthesia, as well as signs of local anesthetic intravascular injection, can only be diagnosed in an awake patient. Many anesthesiologists experienced in regional anesthesia prefer fentanyl alone (or in combination with midazolam) for gentle sedation and comfort while keeping patients with an ability to provide important feedback during the block procedure.

Block Documentation

Documentation of the block procedure is the only way that one can assign possible causal implications to the appropriate procedural event should there be a residual postoperative nerve injury. Documentation should include technique/approach, paresthesia versus nerve stimulator, the lowest electrical current achieved with the nerve stimulator, the specific nerve stimulated, the types of local anesthetics and adjuvants used, and if there were any issues on injection such as pain, increased pressure, blood aspiration, or signs of local anesthetic toxicity. Although not always possible in a rapid-turnover operating room, the extent of block or partial block should be documented. Intraoperative documentation should contain information about the need for general anesthesia as a result of incomplete block, the injection of additional local anesthesia by the surgeons, any surgical issues that may arise including tourniquet time, and a detailed surgical procedure description. The goal for this documentation is to be able to retrieve this information and determine which factors may be involved in a nerve injury. If, for example, the lateral cord is stimulated for an infraclavicular block, and the patient ends up with an ulnar neuropathy, it is unlikely that the block was a major factor in injury.
Early Patient Follow Up

Patient contact information for follow up in 24 to 48 hours after the block should be included with the other accumulated documentation described. An early postoperative check after regional anesthesia is similar to the postoperative check for patients having received general anesthesia. Documentation of this postoperative check should include: the effectiveness of block for postoperative pain control, duration of the block, requirement of postoperative pain medication, and any residual numbness or motor deficit. These issues, although being vitally important to document, can also serve in one’s own education for improving patient care. In addition, patients uniformly welcome this call and are thankful for care provided by the anesthesia team. The decision to provide continued follow up, either by phone or in person, and/or referral to a neurologist or multidisciplinary pain clinic, can also be made at this time. However, most nerve injury issues arise some time after the early recovery phase and are occasionally discovered only after weeks of recovery.

Problem Identification and Management

Determining which patients need to be seen in follow up begins with the postoperative visit or phone interview. Any affirmative answers regarding questions of residual effects of a regional block require at least another follow-up phone call within 48 hours. Those patients who describe problems of infection, motor deficiency, or significant sensory deficiency should be seen in follow up as soon as possible. Before seeing the patient, it is prudent to review the documentation of the block. Specifically, surgical procedure, type of block, block technique, local anesthetic agent and adjuvants used, and any complications or difficulties with the block should be noted. The sequence and timing of the onset of symptoms related to nerve injury is critical information. Exceptions should be noted in which surgical interventions may prevent patients from moving. For example, a patient’s response to the question, “Can you move your arm?” may be “no, because my arm has been immobilized by a plaster cast.” In these instances, the follow up should include questions to ascertain if the patient has any unusual signs of motor or sensory deficit. As one can imagine, it is sometimes very difficult to know that “all is well” in the first few weeks postoperatively. However, all the effort and documentation at early follow up can be very useful if a problem arises later.

Seeing the Patient

Having reviewed the individual record beforehand, a review of the perioperative course with the patient and a new physical examination will
allow for a more complete picture of the current problem. Querying the patient’s perspective is vital in understanding the cause of any problem. Correlating the physical examination with the perioperative course and block documentation may provide some insight as to the cause of the problem. At the very least, this process will help the anesthesiologist with the decision to refer the patient to an expert in such injuries for more in-depth follow up, providing a possible diagnosis and treatment plan. The decision to refer is based on the extent of sensory deficit and/or motor involvement, any significant pain, and possible surgical-related issues. An understanding of the complete perioperative course and physical findings related to the nerve injury are vital for the anesthesiologist to know before referral to any other specialist. Communication of all this information to the specialist will help guide diagnostic decisions that must be made for proper evaluation and management.

- **Electrophysiological Testing**

  The predominant methods of electrophysiological testing include electromyography and nerve conduction studies. These tests are important in defining 1) the neurogenic basis of nerve damage, 2) localization of the site of injury, and 3) the severity of injury. Therefore, the results of these tests in combination with the knowledge of the patient’s history, perioperative events, and physical examination can guide treatment options and outcome expectations. Unfortunately, electrophysiological testing does not indicate the exact etiology of the nerve injury. Testing may confirm the existence of a lesion, localize the lesion, suggest whether it is a new or old lesion, and indicate its severity, but the cause of the lesion must be inferred by the perioperative record and clinical evaluation. This fact renders both clinical perioperative documentation and subsequent serial evaluations extremely important if the definitive cause for any neurologic deficit is to be discovered.4

  Electromyographic examination involves inserting a needle electrode into a muscle and recording the electrical activity. Analysis of the electrical activity is helpful in determining if a lesion has a neurogenic basis and in defining the extent of that injury. It is possible to distinguish among radiculopathies, plexopathies, and neuropathies in one or several different nerves. Electromyography results may also provide information on chronicity, or time of onset of the injury, which when correlated with the perioperative course documentation may have medicolegal implications.3

  Nerve conduction studies provide a means for evaluating the function of motor and sensory nerves. Recording nerve conduction velocity, individual action potentials, and nerve latency of response can evaluate the functional integrity of peripheral nerves. This evaluation
allows for a focal nerve lesion to the localized. Nerve conduction studies, combined with electromyography, can determine if a nerve injury is complete or incomplete, which will guide prognosis and the likely course of recovery.¹,⁴

### Timing

Determining the optimal time for electrodiagnostic examination is an important part of the process. Useful information may be discovered during electrophysiological testing as early as 2 to 3 days postoperatively. Tests can reveal the presence of a lesion as evidenced by a reduced recruitment of involved muscle motor units. A complete lack of motor unit recruitment can provide a less favorable prognosis compared with evidence of at least some voluntary motor control. A repeat of the study 4 to 6 weeks after the injury can provide more definitive information, because the lesion has had more time to fully evolve. Serial studies are not generally necessary because the healing process can be followed clinically. However, patients with complete transection of nerves requiring surgical intervention may benefit from serial electrophysiological testing to document continued improvement.⁴

Electrophysiological testing does have diagnostic limitations. Nerve conduction studies test the function of large sensory and motor nerves. Lesions confined to small fibers are not fully detected with these techniques. However, it is the large peripheral and brachial plexus nerves that are most commonly injured by regional anesthesia.² Therefore, electrophysiological testing is indicated for workup in all questions of nerve damage. Electrodiagnostic studies cannot indicate the cause of the injury but will help to distinguish between, and rule out, various possibilities.²

### Summary

Peripheral nerve block anesthesia is a widely accepted, safe alternative to general anesthesia and is an excellent method of postoperative pain control. Because of a lack of definitive published information on the exact mechanisms of neural injury after nerve blockade and methods to prevent them, much research is needed in this area. In the meantime, anesthesiologists performing regional anesthesia should understand the necessity for good preprocedure patient education, history, physical examination, and detailed perioperative documentation. In the unlikely event of a possible block-related injury, the clinical perioperative record, along with electrophysiological studies, can help define the lesion, suggest possible treatments, and help predict outcomes.
# References


Executive Summary: Regional Anesthesia in the Patient Receiving Antithrombotic or Thrombolytic Therapy

American Society of Regional Anesthesia and Pain Medicine
Evidence-Based Guidelines (Third Edition)

Terese T. Horlocker, MD,* Denise J. Wedel, MD,* John C. Rowlingson, MD,†
F. Kayser Enneking, MD,‡ and American College of Chest Physicians

(Reg Anesth Pain Med 2010;35: 102–105)

Numerous studies have documented the safety of neuraxial anesthesia and analgesia in the anticoagulated patient. Patient management is based on appropriate timing of needle placement and catheter removal relative to the timing of anticoagulant drug administration. Familiarity with the pharmacology of hemostasis-altering drugs, the clinical studies involving patients undergoing neuraxial blockade while receiving these medications, as well as the case reports of spinal hematoma will guide the clinician in management decisions.

New challenges in the management of the anticoagulated patient undergoing neuraxial blockade have arisen as medical standards for the prevention of perioperative venous thromboembolism were established. Likewise, as more efficacious anticoagulants and antiplatelet agents have been introduced, patient management has become more complex. In response to these patient safety issues, the American Society of Regional Anesthesia and Pain Medicine (ASRA) convened its Third Consensus Conference on Regional Anesthesia and Anticoagulation. Portions of the material presented here were published as the proceedings of the 1997 and 2002 ASRA Consensus Conferences.1–6 The information has been updated to incorporate additional data available since the time of its publication. Variances from recommendations contained in this document may be acceptable based on the judgment of the responsible anesthesiologist. The consensus statements are designed to encourage safe and quality patient care but cannot guarantee a specific outcome. They are also subject to timely revision as justified by evolution of information and practice.

These recommendations focus on patients receiving neuraxial and peripheral techniques. The practice settings include inpatient (eg, operating rooms, intensive care units, postoperative surgical floors, labor and delivery settings, or hospital wards) and ambulatory facilities such as pain clinics. The recommendations are intended for use by anesthesiologists and other physicians and health care providers performing neuraxial and peripheral regional anesthetic/analgesic blockade. However, these recommendations may also serve as a resource for other health care providers involved in the management of patients who have undergone similar procedures (eg, myelography, lumbar puncture).

The original article developed from the Consensus Conference held during the 32nd Annual Regional Anesthesia Meeting and Workshops held on April 19–22, 2007, in Vancouver, British Columbia, Canada, is published in this issue of Regional Anesthesia and Pain Medicine (Reg Anesth Pain Med 35: 64–101). The full-length document provides the necessary background to a more complete understanding of the clinical issues discussed at the Consensus Conference.

1.0 Administration of Antithrombotic Agents for the Prevention and Treatment of Venous Thromboembolism

1.1 In accordance with American College of Chest Physicians guidelines, for each of the antithrombotic agents, we recommend that clinicians follow the manufacturer-suggested dosing guidelines (Grade 1C).

2.0 Anesthetic Management of the Patient Receiving Thrombolytic Therapy

Patients receiving fibrinolytic/thrombolytic medications are at risk for serious hemorrhagic events, particularly those who have undergone an invasive procedure. Recommendations are based on the profound effect on hemostasis, the use of concomitant heparin and/or antiplatelet agents (which further increase the risk of bleeding), and the potential for spontaneous neuraxial bleeding with these medications.

2.1 In patients scheduled to receive thrombolytic therapy, we recommend that the patient be queried and medical record reviewed for a recent history of lumbar puncture, spinal or epidural anesthesia, or epidural steroid injection to allow appropriate monitoring. Guidelines detailing original contraindications for thrombolytic drugs suggest avoidance of these drugs for 10 days after puncture of noncompressible vessels (Grade 1A).

2.2 In patients who have received fibrinolytic and thrombolytic drugs, we recommend against performance of spinal or epidural anesthetics, or epidural steroid injection to allow appropriate monitoring. Guidelines detailing original contraindications for thrombolytic drugs suggest avoidance of these drugs for 10 days after puncture of noncompressible vessels (Grade 1A).

2.3 In those patients who have received neuraxial blocks at or near the time of fibrinolytic and thrombolytic therapy, we recommend that neurologic monitoring...
should be continued for an appropriate interval. It may be that the interval of monitoring should not be more than 2 hrs between neurologic checks. If neuraxial blocks have been combined with fibrinolytic and thrombolytic therapy and ongoing epidural catheter infusion, we recommend the infusion should be limited to drugs minimizing sensory and motor block to facilitate assessment of neurologic function (Grade 1C).

2.4 There is no definitive recommendation for removal of neuraxial catheters in patients who unexpectedly receive fibrinolytic and thrombolytic therapy during a neuraxial catheter infusion. We suggest the measurement of fibrinogen level (one of the last clotting factors to recover) to evaluate the presence of residual thrombolytic effect and appropriate timing of catheter removal (Grade 2C).

3.0 Anesthetic Management of the Patient Receiving Unfractionated Heparin (UFH)

Anesthetic management of the heparinized patient was established during 2 decades ago. Initial recommendations have been supported by in-depth reviews of case series, case reports of spinal hematoma, and the American Society of Anesthesiologists Closed Claims Project. Recent thromboprophylaxis guidelines identifying more patients as candidates for thrice-daily anticoagulation with heparin during vascular surgery has prompted a modification of the previous ASRA guidelines.

3.1 We recommend daily review of the patient’s medical record to determine the concurrent use of medications that affect other components of the clotting mechanisms. These medications include antiplatelet medications, low–molecular weight heparin (LMWH) and oral anticoagulants (Grade 1B).

3.2 In patients receiving prophylaxis with subcutaneous UFH with dosing regimens of 5000 U twice daily, there is no contraindication to the use of neuraxial techniques. The risk of neuraxial bleeding may be reduced by delay of the heparin injection until after the block and may be increased in debilitated patients after prolonged therapy (Grade 1C).

3.3 The safety of neuraxial blockade in patients receiving doses greater than 10,000 U of UFH daily or more than twice-daily dosing of UFH has not been established. Although the use of thrice-daily UFH may lead to an increased risk of surgical-related bleeding, it is unclear whether there is an increased risk of spinal hematoma. We suggest that the risk and benefits of thrice-daily UFH be assessed on an individual basis and that techniques to facilitate detection of new/progressive neurodeficits (eg, enhanced neurologic monitoring occur and neuraxial solutions to minimize sensory and motor block) be applied (Grade 2C).

3.4 Because heparin-induced thrombocytopenia may occur during heparin administration, we recommend that patients receiving heparin for greater than 4 days have a platelet count assessed before neuraxial block and catheter removal (Grade 1C).

3.5 Combining neuraxial techniques with intraoperative anticoagulation with heparin during vascular surgery is acceptable with the following recommendations (Grade 1A):

3.5.1 Avoid the technique in patients with other coagulopathies.

3.5.2 Delay heparin administration for 1 hr after needle placement.

3.5.3 Remove indwelling neuraxial catheters 2 to 4 hrs after the last heparin dose and assess the patient’s coagulation status; re-heparin 1 hr after catheter removal.

3.5.4 Monitor the patient postoperatively to provide early detection of motor blockade and consider use of minimal concentration of local anesthetics to enhance the early detection of a spinal hematoma.

3.5.5 Although the occurrence of a bloody or difficult neuraxial needle placement may increase risk, there are no data to support mandatory cancellation of a case. Direct communication with the surgeon and a specific risk-benefit decision about proceeding in each case is warranted.

3.6 Currently, insufficient data and experience are available to determine if the risk of neuraxial hematoma is increased when combining neuraxial techniques with the full anticoagulation of cardiac surgery. We suggest postoperative monitoring of neurologic function and selection of neuraxial solutions that minimize sensory and motor block to facilitate detection of new/progressive neurodeficits (Grade 2C).

4.0 Anesthetic Management of the Patient Receiving LMWH

Anesthesiologists in North America can draw on the extensive European experience to develop practice guidelines for the management of patients undergoing spinal and epidural blocks while receiving perioperative LMWH. All consensus statements contained herein respect the labeled dosing regimen of LMWH as established by the Food and Drug Administration. Although it is not possible to devise recommendations that will completely eliminate the risk of spinal hematoma, previous consensus recommendations have seemed to improve outcome. Concern remains for higher-dose applications, where sustained therapeutic levels of anticoagulation are present.

4.1 The anti-Xa level is not predictive of the risk of bleeding. We recommend against the routine use of monitoring of the anti-Xa level (Grade 1A).

4.2 Antiplatelet or oral anticoagulant medications administered in combination with LMWH increase the risk of spinal hematoma. Education of the entire patient care team is necessary to avoid potentiation of the anticoagulant effects. We recommend against concomitant administration of medications affecting hemostasis, such as antiplatelet drugs, standard heparin, or dextran, regardless of LMWH dosing regimen (Grade 1A).

4.3 The presence of blood during needle and catheter placement does not necessitate postponement of surgery. We suggest that initiation of LMWH therapy in this setting should be delayed for 24 hrs postoperatively and that this consideration be discussed with the surgeon (Grade 2C).

4.4 Preoperative LMWH

4.4.1 Patients on preoperative LMWH thromboprophylaxis can be assumed to have altered coagulation. In these patients, we recommend that needle placement should occur at least 10 to 12 hrs after the LMWH dose (Grade 1C).

4.4.2 In patients receiving higher (treatment) dosages of LMWH, such as enoxaparin 1 mg/kg every 12 hrs, enoxaparin 1.5 mg/kg daily, dalteparin 120 U/kg every 12 hrs, dalteparin 200 U/kg
daily, or tinzaparin 175 U/kg daily, we recommend delay of at least 24 hrs to ensure normal hemostasis at the time of needle insertion (Grade 1C).

4.4.3 In patients administered a dose of LMWH 2 hrs preoperatively (general surgery patients), we recommend against a neuraxial technique because needle placement would occur during peak anticoagulant activity (Grade 1A).

4.5 Postoperative LMWH

Patients with postoperative LMWH thromboprophylaxis may safely undergo single-injection and continuous catheter techniques. Management is based on total daily dose, timing of the first postoperative dose and dosing schedule (Grade 1C).

4.5.1 Twice-daily dosing. This dosage regimen is associated with an increased risk of spinal hematoma. The first dose of LMWH should be administered no earlier than 24 hrs postoperatively, regardless of anesthetic technique, and only in the presence of adequate (surgical) hemostasis. Indwelling catheters should be removed before initiation of LMWH thromboprophylaxis. If a continuous technique is selected, the epidural catheter may be left indwelling overnight but must be removed before the first dose of LMWH. Administration of LMWH should be delayed for 2 hrs after catheter removal.

4.5.2 Single-daily dosing. The first postoperative LMWH dose should be administered 6 to 8 hrs postoperatively. The second postoperative dose should occur no sooner than 24 hrs after the first dose. Indwelling neuraxial catheters may be safely maintained. However, the catheter should be removed a minimum of 10 to 12 hrs after the last dose of LMWH. Subsequent LMWH dosing should occur a minimum of 2 hrs after catheter removal. No additional hemostasis-altering medications should be administered owing to the additive effects.

5.0 Regional Anesthetic Management of the Patient on Oral Anticoagulants

The management of patients receiving warfarin perioperatively remains controversial. Recommendations are based on warfarin pharmacology, the clinical relevance of vitamin K coagulation factor levels/deficiencies, case series, and the case reports of spinal hematoma among these patients. Web sites are available to assist clinicians with warfarin dosing (www.WarfarinDosing.org).

5.1 Caution should be used when performing neuraxial techniques in patients recently discontinued from chronic warfarin therapy. In the first 1 to 3 days after discontinuation of warfarin therapy, the coagulation status (reflected primarily by factor II and X levels) may not be adequate for hemostasis despite a decrease in the international normalized ratio (INR; indicating a return of factor VII activity). Adequate levels of II, VII, IX, and X may not be present until the INR is within reference limits. We recommend that the anticoagulant therapy must be stopped (ideally 4–5 days before the planned procedure), and the INR measured before initiation of neuraxial block (Grade 1B).

5.2 We recommend against the concurrent use of medications that affect other components of the clotting mechanisms and may increase the risk of bleeding complications for patients receiving oral anticoagulants and do so without influencing the INR. These medications include aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs), ticlopidine and clopidogrel, UFH, and LMWH (Grade 1A).

5.3 In patients who are likely to have an enhanced response to the drug, we recommend that a reduced dose be administered. Algorithms have been developed to guide physicians in the appropriate dosing of warfarin based on desired indication, patient factors, and surgical factors. These algorithms may be extremely useful in patients at risk for an enhanced response to warfarin (Grade 1B).

5.4 In patients receiving an initial dose of warfarin before surgery, we suggest the INR should be checked before neuraxial block if the first dose was administered more than 24 hrs earlier if or a second dose of oral anticoagulant has been administered (Grade 2C).

5.5 In patients receiving low-dose warfarin therapy during epidural analgesia, we suggest that their INR be monitored on a daily basis (Grade 2C).

5.6 Neurologic testing of sensory and motor function should be performed routinely during epidural analgesia for patients on warfarin therapy. To facilitate neurologic evaluation, we recommend that the type of analgesic solution be tailored to minimize the degree of sensory and motor blockade (Grade 1C).

5.7 As thromboprophylaxis with warfarin is initiated, we suggest that neuraxial catheters should be removed when the INR is less than 1.5. This value was derived from studies correlating hemostasis with clotting factor activity levels greater than 40%. We suggest that neurologic checks be continued for at least 24 hrs after catheter removal for these patients (Grade 2C).

5.8 In patients with INR greater than 1.5 but less than 3, we recommend that removal of indwelling catheters should be done with caution and the medication record reviewed for other medications that may influence hemostasis that may not effect the INR (eg, NSAIDs, clopidogrel, ticlopidine, UFH, LMWH) (Grade 2C). We also recommend that neurologic status be assessed before catheter removal and continued until the INR has stabilized at the desired prophylaxis level. (Grade 1C).

5.9 In patients with an INR greater than 3, we recommend that the warfarin dose be held or reduced in patients with indwelling neuraxial catheters (Grade 1A). We can make no definitive recommendation regarding the management to facilitate removal of neuraxial catheters in patients with therapeutic levels of anticoagulation during neuraxial catheter infusion (Grade 2C).

6.0 Anesthetic Management of the Patient Receiving Antiplatelet Medications

Antiplatelet medications, including NSAIDs, thienopyridine derivatives (ticlopidine and clopidogrel) and platelet glycoprotein (GP) IIb/IIIa antagonists (abciximab, eptifibatide, tirofiban) exert diverse effects on platelet function. The pharmacologic differences make it impossible to extrapolate between the groups of drugs regarding the practice of neuraxial techniques. There is no wholly accepted test, including the bleeding time, which will guide antiplatelet therapy. Careful preoperative assessment of the patient to identify alterations of health that might contribute to bleeding is crucial. These conditions include a
history of easy bruising/excessive bleeding, female sex, and increased age.

6.1 Nonsteroidal anti-inflammatory drugs seem to represent no added significant risk for the development of spinal hematoma in patients having epidural or spinal anesthesia. NSAIDs (including aspirin) do not create a level of risk that will interfere with the performance of neuraxial blocks. In patients receiving these medications, we do not identify specific concerns as to the timing of single-shot or catheter techniques in relationship to the dosing of NSAIDs, postoperative monitoring, or the timing of neuraxial catheter removal (Grade 1A).

6.2 In patients receiving NSAIDS, we recommend against the performance of neuraxial techniques if the concurrent use of other medications affecting clotting mechanisms, such as oral anticoagulants, UFH, and LMWH, is anticipated in the early postoperative period because of the increased risk of bleeding complications. Cyclooxygenase-2 inhibitors have minimal effect on platelet function and should be considered in patients who require anti-inflammatory therapy in the presence of anticoagulation (Grade 2C).

6.3 The actual risk of spinal hematoma with ticlopidine and clopidogrel and the GP IIb/IIIa antagonists is unknown. Management is based on labeling precautions and the surgical, interventional cardiology/radiology experience (Grade 1C).

6.3.1 On the basis of labeling and surgical reviews, the suggested time interval between discontinuation of thienopyridine therapy and neuraxial blockade is 14 days for ticlopidine and 7 days for clopidogrel. If a neuraxial block is indicated between 5 and 7 days of discontinuation of clopidogrel, normalization of platelet function should be documented.

6.3.2 Platelet GP IIb/IIIa inhibitors exert a profound effect on platelet aggregation. After administration, the time to normal platelet aggregation is 24 to 48 hrs for abciximab and 4 to 8 hrs for eptifibatide and tirofiban. Neuraxial techniques should be avoided until platelet function has recovered. Although GP IIb/IIIa antagonists are contraindicated within 4 weeks of surgery, should one be administered in the postoperative period (after a neuraxial technique), we recommend that the patient be carefully monitored neurologically.

7.0 Anesthetic Management of the Patient Receiving Herbal Therapy

Herbal drugs, by themselves, seem to represent no added significant risk for the development of spinal hematoma or patients having epidural or spinal anesthesia. This is an important observation because it is likely that a significant number of our surgical patients use alternative medications preoperatively and perhaps during their postoperative course.

7.1 The use of herbal medications does not create a level of risk that will interfere with the performance of neuraxial block. We recommend against mandatory discontinuation of these medications or avoidance of regional anesthetic techniques in patients in whom these medications have been administered (Grade 1C).

8.0 Anesthetic Management of Patients Receiving Thrombin Inhibitors (Desirudin, Lepirudin, Bivalirudin, and Argatroban)

8.1 In patients receiving thrombin inhibitors, we recommend against the performance of neuraxial techniques (Grade 2C).

9.0 Anesthetic Management of the Patient Receiving Fondaparinux

The actual risk of spinal hematoma with fondaparinux is unknown. Consensus statements are based on the sustained and irreversible antithrombotic effect, early postoperative dosing, and the spinal hematoma reported during initial clinical trials. Close monitoring of the surgical literature for risk factors associated with surgical bleeding may be helpful in risk assessment and patient management.

9.1 Until further clinical experience is available, performance of neuraxial techniques should occur under conditions used in clinical trials (single-needle pass, atraumatic needle placement, avoidance of indwelling neuraxial catheters). If this is not feasible, an alternate method of prophylaxis should be considered.

10.0 Anesthetic Management of the Anticoagulated Parturient

10.1 In the absence of a large series of neuraxial techniques in the pregnant population receiving prophylaxis or treatment of venous thromboembolism, we suggest that the ASRA guidelines (derived from mainly from surgical patients) be applied to parturients (Grade 2C).

11.0 Anesthetic Management of the Patient Undergoing Plexus or Peripheral Block

11.1 For patients undergoing deep plexus or peripheral block, we recommend that recommendations regarding neuraxial techniques be similarly applied (Grade 1C).

REFERENCES


PHARMACOLOGIC TREATMENT OF PAIN: ORAL OPIOIDS
Tim Furnish, M.D.

Analgesia and the Pain Pathway
• Pain is mediated through both peripheral and central mechanisms. In an acute trauma, peripheral nociceptors are stimulated and transmit pain signals to the dorsal horn of the spinal cord and ultimately to the thalamus and the cortex. In the normal pain response, pain intensity increases as the stimulus intensity increases.\textsuperscript{1-2}
• There are various sites along the pain pathway where analgesics exert their activity. Thus, in theory, the use of two or more agents with differing mechanisms or multiple modes of analgesia (i.e., epidural analgesia and NSAIDs) increases the likelihood of interrupting pain signals and relieving pain.\textsuperscript{1-2}
• Evidence suggests that COX-2 is induced in both the peripheral and central nervous systems in response to pain, thus suggesting that COX-2 inhibitors and NSAIDs capable of CNS penetration may provide pain relief via inhibition of central COX-2 induction in addition to their peripheral actions at the site of injury.\textsuperscript{3}

\textbf{DEA Classification}
• Class I: Heroin, Marijuana, GHB, MDMA, Psylocybin, Mescaline, Peyote, LSD, methylqualone
• Class II: Morphine, oxycodone, hydromorphone, Marinol, Ritalin, Dexedrine, Tapendetol
• Class III: Hydrocodone w/ tylenol, codeine w/ tylenol, Buprenorphine, Ketamine
• Class IV: Benzo’s, Ambien, Propoxyphene, Pentazocine, Butorphanol, Phenobarbital, Provigil
• Class V: Lyrica, Robitussin
**Opioid Mechanisms of Activity**
- Act on peripheral and central μ, κ, and δ opioid receptors
- Inhibit the transmission of nociceptive input from the periphery to the spinal cord (presynaptic and postsynaptic)
- Activate descending inhibitory pathways that modulate transmission in the spinal cord
- Alter limbic system activity

**Dependence, Tolerance, and Addiction**
- Physical dependence: withdrawal syndrome arises if drug discontinued, dose substantially reduced, or antagonist administered
  - Dependence occurs in almost all patients on opioids, and does not connote addiction.
- Tolerance: greater amount of drug needed to maintain therapeutic effect, or loss of effect over time
  - The number of patients who develop clinically relevant tolerance is unknown
  - Tolerance may also occur to side effects, and thus may be beneficial
  - Some patients who develop tolerance can have their pain managed by judicious dose increases; others who develop inexorable tolerance cannot have their pain managed by opioids.
  - There is no evidence to support a role for analgesic tolerance in the development of drug addiction. Addiction is, however, often (though not always) associated with tolerance.
- Pseudoaddiction: behavior suggestive of addiction; caused by undertreatment of pain
- Addiction (psychological dependence): psychiatric disorder characterized by continued compulsive use of substance despite harm
  - Addiction is a psychiatric disorder consisting of continued, compulsive use of the substance despite harm. *The Diagnostic and Statistical Manual of Mental Disorders* provides nine categories of opioid use or opioid-induced disorders, including diagnostic criteria for opioid dependence or opioid abuse.
  - True addiction (patient loss of control) may become obvious only when the physician stops prescribing the medicine. There is, however, little evidence that addiction is common within the chronic pain population. In a study reviewing the available data, it was found that prevalence estimates for addiction in patients with chronic pain ranged from 3% to 19%.

**Dosing and Administration**
- Begin with short-acting weak opioid
- Commonly used first-line agents include
  - Propoxyphene
  - Hydrocodone
  - Codeine
- If the patient is requiring more than 3-4 short-acting weak opioid/day, consider converting to a long-acting opioid:
  - Controlled-release morphine (MSContin, Kadian, Oramorph, Avinza)
  - Controlled-release oxycodone (Oxycontin)
  - Methadone
  - Transdermal fentanyl (Duragesic)
  - Controlled-release hydromorphone (Exalgo)
  - Controlled-release oxymorphone (Opana)
- Limited access to a short-acting medication for breakthrough pain may be appropriate
Conversion from a short-acting to long-acting medication may require adjustment for 1-2 weeks.

Once the patient is on a stable dosage, 4 to 6 weeks are required to assess both pain and function.

Evaluation by a pain specialist may be considered when MS equianalgesic dosages exceed 90 mg/d.

The benefits of levels higher than 180 mg/d in patients with neuropathic pain have not been established.

**Opioid Adverse Effects**

- **Constipation:** dose dependent; tolerance to constipation does not develop
  - Monotherapy of constipation with stool softeners is not effective, and often requires laxative along with stool softener
- **Sedation:** 20-60%; often transient with initiation/dose escalation
- **Nausea:** 25%; usually transient
- **Pruritis:** 2-10%; worse with neuraxial administration
- **Neurotoxic effects**
  - Delirium
  - Hyperalgesia
- **Respiratory depression**
- **Other effects**
  - Hypogonadism
  - Decreased immunity

**Opioid-Induced Hyperalgesia**

- Hyperalgesia and/or allodynia as a consequence of opioid administration
- Distinct from tolerance
- Pharmacologically distinct from tolerance
- Controversial
- 3 Clinical Scenarios:
  - Maintenance therapy or withdrawal: animal and human studies
  - Ultra-high dose or dose escalation: mostly animal studies
  - Ultra-low dose: mostly animal studies

**Opioid Classification: Receptor Activity**

- **Agonists**
  - Morpine – prototypical
  - Oxycodone, hydrocodone, hydromorphone, codeine, fentanyl, propoxyphene, oxymorphone, methadone
- **Antagonists**
  - Naloxone, Naltrexone (oral)
- **Mixed Agonist/Antagonists**
  - Butorphanonl, buprenorphine, nalbuphine

**Tramadol**

- **Mechanism**
  - Weak μ opioid agonist
  - Norepinephrine and serotonin reuptake inhibitor
- **Dosing and Administration**
  - In RCTs the optimum dosage self-selected by patients was 250 mg/d
• Initiate at low dosages 50 mg/d or BID
• Titrate every 3 to 7 d by 50 to 100 mg/d in divided doses as tolerated
• An adequate trial requires 4 weeks at maximum dosage
• Initiate tramadol ER at 100 mg/d and increase every 5 days to maximum of 300 mg/d

• Adverse Effects
  o Nausea
  o In polypharmacy, increased risk with rapid dose escalation
    – Dizziness
    – Somnolence
    – Orthostatic hypotension
    – Serotonin syndrome with MAOIs or SSRIs
  o Dosage adjustment required for renal/hepatic disease
  o Lowers the seizure threshold
  o Increased risk of addiction in patients with history of substance abuse

**Morphine**
• Short Acting
  o Morphine IR
• Long Acting
  o MSContin
  o Kadian
  o Avinza
  o Oramorph

• Metabolism
  o 95% Phase 2 glucuronidation: M3G/M6G
  o M3G - no analgesia - exhibits neuroexcitatory effects, possibly hyperalgesia/allodynia
  o M6G - analgesia equal to or greater than morphine, longer half life
  o Excretion primarily as metabolites M6G/M3G via urine
  o 10% excreted in bile/feces, 10% excreted unchanged
  o Reduced clearance in elderly
  o Naloxone reverses M6G, but not M3G
  o Dosage adjustment for Hepatic / Renal insufficiency
    – Severe cirrhosis: bioavailability approaches 100%
    – Renal failure: M3G/M6G accumulate

• **MS Contin**
  o Indicated for moderate-to-severe chronic pain
  o Up to 12 hours of smooth, consistent pain relief
  o No bolus effect

• **Kadian**
  o Indicated for moderate-to-severe chronic pain
  o Up to 24 hours of smooth, consistent pain relief
  o No bolus effect
  o Three modes of administration
    – Oral
    – Sprinkle
    – G-tube

• Other Long-Acting Morphine
Avinza: Pharmacokinetic profile similar to Kadian
Oramorph: Pharmacokinetic profile similar to MS Contin

**Oxycodone**

- Short-acting
  - Combinations with acetaminophen: Percocet, Roxicet, Endocet
  - Combinations with aspirin: Percodan
  - Oxycodone, OxyIR, Roxicodone
- Long-acting
  - OxyContin: brand only; generic briefly available but now off the market
    - Indicated for moderate-to-severe chronic pain
    - Up to 12 hours of smooth, consistent pain relief
    - 10-20% bolus effect
    - Pharmacokinetics
      - 45% protein bound; 60% bioavailability
      - 12h controlled release
        - Peak pain relief 1hr
      - Biphasic absorption half-lives: Immediate release component absorption t1/2 in 35-40 min and slow release absorption t1/2 of 6.2hrs
      - Elimination ½ life: 4.5hrs
- Oxycodone Metabolism
  - Major metabolite is Noroxycodone
    - AUC 50% and analgesia 25% of parent drug
  - Minor metabolite: Oxymorphone
    - 14x more potent than parent drug, longer ½ life
  - Minor metabolite: Noroxymorphone – No analgesia.
  - Primarily excreted in urine as: Oxycodone and metabolites
  - Dosage adjustment for Hepatic / Renal Insufficiency
  - Peak concentration increased by 25% when administered with a high fat meal

**Methadone**

- Pharmacologically long acting
- PO 5mg, 10mg
- PO 40mg only available thru methadone clinics
- IV/IM/SC
- 10mg PO = 5-10mg IV/IM/SC
- Metabolism
  - Multiple CYP enzymes involved, increases variability in metabolism and risk of drug interactions; metabolites all inactive
  - Eliminated in urine as metabolite; urine excretion pH dependent
  - Eliminated in feces
  - Biphasic elimination
    - alpha elimination phase: 8-12 hours (analgesia)
    - beta elimination phase: 30-60 hours (withdrawal prevention)
- Pharmacokinetics
  - Racemic mixture: L and D isomers
  - Mu opioid receptor agonist; also MAO inhibition and NMDA antagonism
  - Lipophilic; 90% protein bound; redistribution to and accumulation in tissues which then act to maintain plasma concentrations
- Oral bioavailability of 80%
- Peak plasma in 4 hours
- Similar analgesic duration of action as morphine
- Half life is 15-40 hours
- Steady state achieved after 5 days

**Special Considerations**
- Dual mechanism of action - opioid and nonopioid effects
- Relatively inexpensive
- Long half-life - accumulates with repeat doses with limited analgesic effect
- Complex pharmacokinetics
  - Complicates conversion
- No known active metabolites
- Cardiac toxicity with high doses or with CYP3A4 inhibitors
  - QT prolongation especially at higher doses
- Most reported cases of torsades de pointes at doses >100mg/day
- Some have recommended pre and post tx ECG
- Adverse interaction with MAOIs

### Methadone Conversion

<table>
<thead>
<tr>
<th>Oral Morphine Equivalent</th>
<th>Morphine to Methadone Conversion Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;300 mg</td>
<td>6:1</td>
</tr>
<tr>
<td>301-600 mg</td>
<td>10:1</td>
</tr>
<tr>
<td>601-800 mg</td>
<td>12:1</td>
</tr>
<tr>
<td>801-1000 mg</td>
<td>15:1</td>
</tr>
</tbody>
</table>

### Duragesic

- Transdermal Fentanyl (patch)
- Mu opioid receptor agonist
- 80% protein bound/lipophilic
- Metabolism
  - Metabolized by CYP3A4 to norfentanyl
    - Nontoxic and inactive.
  - 75% excreted in urine as NF
  - 10% excreted in urine as unchanged
  - 10% excreted in feces (as metabolites)
- Contraindications
  - Opioid naive patients
  - < 3 years of age
  - Intermittent pain
  - Post operative pain/acute pain - expected short duration
  - Heat: tanning lamps, sauna, electric blankets

### Hydromorphone

- Short Acting:
  - PO 2mg, 4mg, 8mg
  - PR 3mg
  - IV/IM/SC
- Long Acting: Exalgo (new)
  - 8mg, 12mg, 16mg ER
  - 24 hour dosing
• Bioavailability 25%
• No histamine release
• Metabolism/Pharmacokinetics
  o Parent drug has high affinity for mu receptor
  o 95% - Phase 2 glucuronidation - H3G
    ▪  Primarily renal elimination
  o Metabolites without analgesic effects
  o H3G may have neuroexcitatory effects
  o Tmax: 40 min; T½: 2.6 hours
  o Extensive first pass metabolism
    ▪  25% oral bioavailability
    ▪  80% SQ bioavailability

Other Opioids
• Oxymorphone
  o Oxymorphone is a minor active metabolite of oxycodone
  o Unclear clinical advantage
  o Expensive
• Codeine
  o Natural alkaloid in opium
  o Metabolized to active metabolites: morphine (6-10%), C6G (70%), hydromorphone (1%)
  o Codeine to morphine via CYP2D6: 6-10% of Caucasians lacking
  o Antitussive and mild pain
  o Combo products: T3, T4, Soma Compound, etc.
• Propoxyphene
  o Weak Mu agonist; narrow therapeutic window
  o Propoxyphene and metabolite norpropoxyphene have local anesthetic properties. Block cardiac Na channels – arrhythmias and cardiodepressants more potent than lidocaine, quinidine or procaainamide. Decreased HR, contractility, conduction, and widened QRS – not reversed by naloxone.
  o Risk seizures and pulmonary edema
  o Darvone: propoxyphene napsylate
  o Darvocet: propoxyphene napsylane/APAP: 60/600 or 100/650
  o Avoid in: everyone, esp. children, elderly, renal/liver dz, pregnant
• Levorphanol
  o Opioid, NMDA, SNRI activity
  o 4mg oral levorphanol equivalent to 30mg morphine
  o Oral:Parenteral ratio 2:1
  o Duration of action 4-15 hrs
  o Available 2mg tabs
  o Dose q6-8 hrs
• Butorphanol
  o Agonist/antagonist at Mu, agonist at kappa
  o Kappa activity: dysphoria
• Buprenorphine
  o Partial agonist at Mu with very high binding affinity; naloxone may not fully reverse. Blocks activity of coadministered full agonists.
  o Triggers severe “precipitated withdrawal” in patients dependent on full agonists
    ▪  not reversible by full agonist opioids
- Antagonist at Kappa, agonist at Delta
- Suboxone and Subutex: high dose sublingual, for opioid dependence. Requires special DEA certification.
- Suboxone: 1 part naloxone: 4 parts buprenorphine

### PCA to Oral Conversion
- Determine total 24 hour IV opioid use pca and any prn IV push
- Convert to oral morphine equivalent (OME)
- Decrease by 25% for incomplete cross tolerance unless under 100mg OME and/or brief duration IV opioid use
- Divide into 2/3 long acting 1/3 short acting

### Opioid Conversions

<table>
<thead>
<tr>
<th>Opioid</th>
<th>Oral Dose (mg)</th>
<th>IV Dose (mg)</th>
<th>Conversion Factor to Morphine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>30</td>
<td>10</td>
<td>1x</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>6</td>
<td>1.5</td>
<td>5x</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>20</td>
<td>---</td>
<td>1.5x</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>30</td>
<td>---</td>
<td>1x</td>
</tr>
<tr>
<td>Codeine</td>
<td>200</td>
<td>130</td>
<td>0.15x</td>
</tr>
<tr>
<td>Oxymorphone</td>
<td>10</td>
<td>---</td>
<td>3x</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>---</td>
<td>0.1</td>
<td>300x (oral morphine)</td>
</tr>
<tr>
<td>Actiq</td>
<td>0.2</td>
<td>---</td>
<td>150x (oral morphine)</td>
</tr>
<tr>
<td>Meperidine</td>
<td>300</td>
<td>75</td>
<td>0.1x</td>
</tr>
<tr>
<td>Methadone</td>
<td>10</td>
<td>5-10</td>
<td>3x</td>
</tr>
</tbody>
</table>


PHARMACOLOGIC TREATMENT OF PAIN: NON-OPIOIDS
Tim Furnish, M.D.

Analgesic Options
• Acetaminophen
• NSAIDs/COX-2 inhibitors
• Local anesthetics
• Central analgesics (tramadol)
• Opioids
  o Codeine, hydrocodone, oxycodone, propoxyphene
  o Morphine, hydromorphone, methadone, fentanyl, oxymorphone
• TCAs
  o Amitriptyline, nortriptyline, desipramine, doxepin
• SNRIs
  o Duloxetine, venlafaxine, milnacipran
• Anticonvulsants
  o Gabapentin, pregabalin, carbamazepine, oxcarbazepine, topiramate
• Muscle relaxants
• NMDA antagonists
  o Ketamine
• Sedative/anxiolytics
• Topical therapy
  o Capsaicin, lidocaine, NSAIDs

Acetaminophen
• Mechanism of action unclear
• Inhibits COX-3, a cyclooxygenase-1 variant
• Cyclooxygenase isoenzymes are known to catalyze the rate-limiting step of prostaglandin synthesis and are targets of nonselective NSAIDs
• Severe liver toxicity with overdose
  o FDA recently recommended lowering the maximum daily dose to 2000 mg/day
  o Acetaminophen-opioid combination products may be removed from the market

NSAIDs
• Mechanism of Action

• Analgesic Properties
  o Target peripheral pain pathways (peripheral sensitization)
  o Anti-inflammatory and analgesic effects
  o Selectively inhibit C-fiber (“second pain”) and not A-δ fiber (“first pain”)
• Analgesic ceiling effect
  • Reversibly inactivate the COX enzyme (except aspirin)

• Benefits
  • No addiction
  • Decrease or eliminate opioid use
  • Lower side-effect profile than opioids

• Risks
  • Bleeding
  • PUD
  • Renal impairment
  • Wound/bone healing
  • Analgesic ceiling effect

• Peripheral and Central Prostaglandins and COX-2³

Gabapentin and Pregabalin
• Mechanism
  • Binds to α₂-δ subunit of voltage-gated calcium channels
    • Reduces Ca²⁺ influx during depolarization
    • Binding required for analgesic, anxiolytic, and anticonvulsant activity
  • Reduces release of neurotransmitters, e.g., glutamate, norepinephrine, substance P
  • Effective in trials of epilepsy, neuropathic pain, and generalized anxiety
• Dosing and Administration\textsuperscript{5,6}
  - The effective dose of gabapentin is 900 to 1800 mg/d and given in divided doses TID
  - The starting dose is 300 mg/d
  - Dosages up to 2400 mg/d have been well tolerated in long-term clinical studies
  - Doses of 3600 mg/d have also been administered to a small number of patients for a relatively short duration and have been well tolerated
  - Non-linear pharmacokinetics - decreasing bioavailability with increasing dose
  - Overdoses up to 35g reported with minimal toxicity

• Efficacy Timeline\textsuperscript{6-8}
  - Final dosage, usually 1800 mg/d, determined either by achieving targeted pain relief or by development of unacceptable AEs that do not resolve promptly
  - Should patient complain of AEs, dosage may be decreased, letting the effects dissipate, then resume titration
  - An adequate trial would include 3 to 8 weeks for titration to allow development of AEs, plus 1 to 2 weeks at the maximum tolerated dosage

• Adverse Effects
  - Somnolence and dizziness/ataxia
  - Mild peripheral edema
  - Weight gain
  - May cause or exacerbate gait and balance problems in the elderly
  - Dosage adjustment required in renal insufficiency
  - AEs usually subside within 10 days from initiation of treatment

• Opioid-Sparing Effect\textsuperscript{9-12}

<table>
<thead>
<tr>
<th>Study</th>
<th>Agent</th>
<th>N</th>
<th>Surgery</th>
<th>Outcome Measure</th>
<th>Significant Improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pandey et al (2005)</td>
<td>Gabapentin vs. Placebo</td>
<td>60</td>
<td>Spine surgery</td>
<td>46% reduction in PCA morphine</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Pregabalin
• Antiepileptic pharmacologically related to gabapentin
  - Modulates voltage gated Ca\textsuperscript{+} channels
• FDA approval for DPN, PHN and fibromyalgia
• Linear pharmacokinetics with high bioavailability
  - Faster and easier to titrate to effective dose
• Similar AE profile as gabapentin

Tricyclic Antidepressants\textsuperscript{13, 14}
• Relief of pain through serotonin and norepinephrine reuptake blockade
• Blockade of α-adrenergic receptors
• Sodium and potassium channel modulation
• Modulation of monoamine neurotransmitters
• NMDA-receptor antagonism
• AE Profile: Largely due to anticholinergic effects
• Sedation, dry mouth, constipation, dizziness, palpitations, confusion, urinary retention
• Risk of arrhythmias
• Desipramine and nortriptyline fewer AE
• Starting dose 10-20mg HS
• Titrate to analgesic effective dose 50-75mg/d - significantly lower than antidepressant effective dose

**SNRIs**
- Venlafaxine, duloxetine, milnacipran
- Inhibit norepinephrine and serotonin reuptake and increase synaptic availability
- Preliminary results suggest safety, tolerability, and effectiveness in patients with painful DPN and fibromyalgia
- Minimal anticholinergic AEs
  - Nausea
  - Serotonin syndrome, withdrawal syndrome
  - Duloxetine: caution with hepatic disease

**Lidocaine Patch**
- An amide-type local anesthetic
- Stabilizes neuronal membranes
- Inhibits ionic fluxes required for the initiation and conduction of impulses
- Penetration of lidocaine into the skin after application of the patch produces an analgesic effect
  - A topical, not transdermal, therapy
- A complete sensory block is not produced: analgesia, but not anesthesia, is produced
- Superior to both no treatment and vehicle patches in averaged category pain relief scores for PHN
- Reduces intensity of all common neuropathic pain qualities and may be of potential benefit in nonallodynic neuropathic pain states
- As add-on therapy, the patch was effective in:
  - Reducing ongoing pain
  - Reducing alldynia during the first 8 hours after application
  - Consistent pain relief over period of 7 days
- Efficacy also shown for:
  - Osteoarthritis knee
  - Post-op incisional pain (prostatectomy)
  - Low back pain
  - Myofascial pain
- Topical mechanism of action unclear
  - Blockade of Na channels on damaged/dysfunctional nociceptors underlying patch site without blockade of large myelinated A-beta fibers
- Adverse Effects
  - Excellent safety and tolerability
  - Only AEs are mild skin reactions, erythema, or rash
  - Studies to date have shown that patch use results in systemic concentrations of lidocaine far below any clinically meaningful level
  - Use up to 3 patches at a time. Package insert says 12 hours on, 12 hours off
**Centrally-Acting Muscle Relaxants**

- **Mechanisms**\(^{18,19}\):
  - Indirectly relax skeletal muscles by blocking polysynaptic neurons in the spinal cord
  - Block polysynaptic neurons in the descending reticular formation of the brain
  - Modest analgesic activity may be derived from suppression of nociceptive input
  - The antinociceptive mechanisms are unknown

- **The spasm-pain-spasm cycle**

- **Adverse Effects**\(^{18,20,21}\):
  - CNS side effects
    - Sedation
    - Dizziness
    - Confusion
    - Blurred vision
  - Potential for abuse with carisoprodol (Schedule IV in 10 states)
  - GI AEs
    - Nausea, epigastric distress, vomiting
  - Anticholinergic properties: dry mouth, urinary retention

- **Agents**
  - Baclofen: GABA-B agonist; first line for spasticity from cerebral palsy/MS; severe withdrawal syndrome mimics MH
  - Tizanidine (Zanaflex): alpha-2 adrenergic agonist
  - Diazepam: GABA-A agonist
  - Cyclobenzaprine (Flexeril): structure similar to TCA; anticholinergic
  - Carisoprodol (Soma): metabolized to meprobamate (controlled substance); barbiturate-like effects; strongest abuse potential; withdrawal if abruptly d/c
  - Metaxalone (Skelaxin): least sedating; unknown MOA

**Ketamine**

- Non-competitive NMDA receptor antagonist blocking glutamate excitatory action on Ca+ channel influx. Decreases central sensitization
- Inpatient infusion: analgesic and sedative with risk of hallucinations/unpleasant dreams - co-treat with benzodiazepine
- Infusion 0.2-0.5mg/kg/hr to start
- No effective oral NMDA antagonist
Perioperative Management of Acute Pain in the Opioid-dependent Patient

Sukanya Mitra, M.D.,* Raymond S. Sinatra, M.D., Ph.D.†

PAIN is “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.”1 In settings where pain is poorly controlled, patients suffer needlessly and may develop untoward emotional and cognitive responses that negatively affect behavior, rehabilitation, and quality of life. Providing rapid and effective relief of pain remains a humanitarian issue, whereas allowing patients to suffer as a result of analgesic undermedication may be considered a breach of fundamental human rights.2–4

Noticeable shifts in attitude have occurred in recent years regarding the use of opioids for the treatment of benign and malignancy-related pain. Primary care physicians and pain specialists prescribe opioids to a greater number of patients and in doses appropriate to needs.3–7 A variety of opioid analgesics and delivery systems have been introduced that have increased patient satisfaction, physician acceptance, and overall use. Concomitant with improvements in pain relief and quality of life, an increasing number of patients are affected by issues related to opioid tolerance and physical dependence. There have been only a small number of published reviews that address the treatment of acute pain in patients with substance abuse disorders,3–5 and fewer have focused specifically on perioperative pain management in opioid-dependent patients.6,7 This review outlines factors responsible for opioid tolerance, physical dependence, and addiction and provides perioperative analgesic dosing guidelines for this specialized subset of patients.

Many patients who present for surgery and anesthesia may be opioid dependent or at least moderately tolerant to the therapeutic effects of opioid analgesics.5–7 Causal factors underlying dependency include substance use disorder and, more commonly, legitimate use of opioid analgesics for treatment of chronic benign pain or malignancy-associated pain. Perioperative management of opioid-dependent patients poses a special challenge to primary caregivers, anesthesiologists, and pain specialists alike. This problem emanates from the often-conflicting needs to balance the rights of the patient on one hand and concerns of safety, diversion, and abuse on the other,6,7 thus raising important ethical issues.6–9

The percentage of patients to whom opioid analgesics for chronic pain are prescribed has increased dramatically in recent years. An Australian study found that in 83% of patients with chronic pain, including back pain, other forms of benign pain, and cancer pain, opioids were prescribed by the patients’ general practitioners at the time of referral to a multidisciplinary pain center.10 Moreover, 47% of these patients were treated with strong opioids, such as morphine, oxycodone, and methadone. In another study, long-term opioid use and dose escalation was noted in one third of patients with chronic noncancer pain.11 Factors responsible for the increased acceptance and prescription of opioid analgesics include physician education, concerns of analgesic undermedication and inadequate pain control, the favorable side effect profiles of newer semisynthetic and sustained-release opioids, and morbidity associated with nonsteroidal antiinflammatory drugs.5,4,10

Opioid-dependent patients, particularly substance abusers, may present with organ damage, infectious diseases such as human immunodeficiency virus, tuberculosis, hepatitis, associated psychological disorders, and drug-specific adaptations such as tolerance, physical dependence, and withdrawal.5,12 These variables alone or in combination may diminish opioid analgesic effectiveness in the perioperative setting. The following issues should be considered to provide a comprehensive pain management strategy: (1) key concepts and definitions including substance abuse, physical versus psychological dependence, and tolerance development; (2) clinical differentiation of opioid dependency; (3) preoperative assessment issues; and (4) postoperative management issues.
Table 1. Criteria for Substance Dependence

A maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by three (or more) of the following, occurring at any time in the same 12-month period:

1. Tolerance, as defined by either of the following:
   - A need for markedly increased amounts of the substance to achieve intoxication or desired effect
   - Markedly diminished effect with continued use of the same amount of the substance

2. Withdrawal, as manifested by either of the following:
   - The characteristic withdrawal syndrome for the substance (refer to criteria A and B of the criteria sets for withdrawal from the specific substances)
   - The same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms

3. The substance is often taken in larger amounts or over a longer period than was intended

4. There is a persistent desire or unsuccessful efforts to cut down or control substance use

5. A great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects

6. Important social, occupational, or recreational activities are given up or reduced because of substance use

7. The substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance

With physiologic dependence: evidence of tolerance or withdrawal (i.e., either item 1 or item 2 is present)

Without physiologic dependence: no evidence of tolerance or withdrawal (i.e., neither item 1 nor item 2 is present)

Criteria for opioid withdrawal:

A. Either of the following:
   1. Cessation of (or reduction in) opioid use that has been heavy and prolonged (several weeks or longer)
   2. Administration of an opioid antagonist after a period of opioid use

B. Three (or more) of the following, developing within minutes to several days after criterion A:
   1. Dysphoric mood
   2. Nausea or vomiting
   3. Muscle aches
   4. Lacrimation or rhinorrhea
   5. Pupillary dilation, piloerection, or sweating
   6. Diarrhea
   7. Yawning
   8. Fever
   9. Insomnia

Modified with permission from the DSM-IV.13

Basic Aspects of Substance Use Disorder

Criteria and Definitions

Substance use disorders have been classified according to clinical manifestations of psychological dependence with physical dependence or tolerance or both. Specific definitions can be found in table 1 and table 2.13,14 It may be noted that the terms and their distinctive boundaries are not always clear, especially terms such as addiction, dependence, abuse, and substance abuse. This is partly because these terms have evolved over time in varying historical and sociocultural contexts.12,13,15 They also reflect conflicts regarding appropriate terminology for the complex medical and psychosocial issues that underlie chronic and compulsive substance-using behavior. For example, the strict medical or biologic viewpoint that characterizes substance use disorder essentially as a disease or a disorder conflicts with the strictly sociocultural viewpoint that tends to “demedicalize” such behavior and explain it from a social and cultural context.14-16 For the purpose of this review, the terms addiction, substance use disorder, and psychological dependence will often be used interchangeably.

Physical Dependence

The term physical dependence describes alterations in physiologic response that result from opioid binding and receptor-mediated activity.15,16 Abrupt discontinuation of oral or parenterally administered opioids leads to opioid withdrawal or abstinence syndrome. This syndrome is characterized by increased sympathetic and parasympathetic responses mediated via the myenteric plexus, brainstem vagal and hypothalamic nuclei, resulting in hypertension, tachycardia, diaphoresis, abdominal cramping, and diarrhea, as well as physiologic and behavioral responses such as shaking (“wet dog shakes”), yawning, and leg jerking (“kicking the habit”).15-18 Opioid-dependent patients use the term “cold turkey” to describe the appearance of their cold, pale, goose-bumped skin when opioids are acutely discontinued.14,16 These symptoms, although very unpleasant, are rarely life threatening; however, they can often confuse clinical diagnosis and care.17 The time course of withdrawal is variable, depending on the opioid used.17 The onsets and peak intensities of withdrawal symptoms for different opioid analgesics are presented in table 3.

Opioid Tolerance

Opioid tolerance is a predictable pharmacologic adaptation. Continued opioid exposure results in a rightward shift in the dose-response curve, and patients require increasing amounts of drug to maintain the same pharmacologic effects. The phenomenon of tolerance develops to analgesic, euphoric, sedative, respiratory depres-
The degree or gradation of opioid tolerance is generally related to duration of exposure, daily dose requirement, and receptor association/dissociation kinetics. Opioid agonists binding to the same receptor may show asymmetric cross-tolerance depending on their intrinsic efficacy. For example, patients treated with sufentanil, an agonist having high intrinsic efficacy and requiring low receptor occupancy for a given analgesic effect, develop tolerance more slowly than to opioids having low intrinsic efficacy, such as morphine.

Although there are no clear gradation guidelines, individuals requiring the equivalent of 1 mg or more intravenous or 3 mg or more oral morphine per hour for a period greater than 1 month may be considered to have high-grade opioid tolerance.

Tolerance is observed in patients to whom opioids are legitimately prescribed for pain management as well as in those abusing this class of drug. In general, the higher the daily dose requirement, the greater is the degree of tolerance development. This is of importance for many patients and caregivers who perceive an increasing opioid dose requirement as reflecting harmful addiction rather than a normal adaptation to this class of analgesics.

Several types of opioid tolerance, including innate and acquired, have been characterized. Innate tolerance refers to preexisting insensitivity, which is genetically determined and hence is present before drug exposure. True tolerance is acquired after multiple exposures. This can be of three types: pharmacokinetic tolerance, learned tolerance, and pharmacodynamic tolerance. Pharmacokinetic tolerance refers to changes in distribution or metabolism of the drug, usually by enzyme induction and subsequent acceleration in metabolism. Opioids are biotransformed in the liver by two types of metabolic processes. Phase I reactions include oxidative and reductive reactions, such as those catalyzed by the cytochrome enzyme system (P-450), and hydrolytic reactions. Phase II reactions involve conjugation of a drug or its metabolite to an endogenous substrate, such as d-glucuronic acid, generating highly

### Table 2. Substance Use Disorder: Related Definitions

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Addiction</td>
<td>Commonly used term meaning the aberrant use of a specific psychoactive substance in a manner characterized by loss of control, compulsive use, preoccupation, and continued use despite harm; pejorative term, replaced in the DSM-IV in a nonpejorative way by the term substance use disorder (SUD) with psychological and physical dependence</td>
</tr>
</tbody>
</table>
| Dependence                  | 1. Psychological dependence: need for a specific psychoactive substance either for its positive effects or to avoid negative psychological or physical effects associated with its withdrawal  
2. Physical dependence: A physiologic state of adaptation to a specific psychoactive substance characterized by the emergence of a withdrawal syndrome during abstinence, which may be relieved in total or in part by readministration of the substance  
3. One category of psychoactive substance use disorder |
| Chemical dependence         | A generic term relating to psychological and/or physical dependence on one or more psychoactive substances |
| Substance use disorders     | Term of DSM-IV comprising two main groups:  
1. Substance dependence disorder and substance abuse disorder  
2. Substance-induced disorders (e.g., intoxication, withdrawal, delirium, psychotic disorders) |
| Tolerance                   | A state in which an increased dosage of a psychoactive substance is needed to produce a desired effect; cross-tolerance: induced by repeated administration of one psychoactive substance that is manifested toward another substance to which the individual has not been recently exposed |
| Withdrawal syndrome         | The onset of a predictable constellation of signs and symptoms after the abrupt discontinuation of or a rapid decrease in dosage of a psychoactive substance |
| Polydrug dependence         | Concomitant use of two or more psychoactive substances in quantities and frequencies that cause individually significant physiologic, psychological, and/or sociologic distress or impairment (polysubstance abuser) |
| Recovery                    | A process of overcoming both physical and psychological dependence on a psychoactive substance with a commitment to sobriety |
| Abstinence                  | Non-use of any psychoactive substance |
| Maintenance                 | Prevention of craving behavior and withdrawal symptoms of opioids by long-acting opioids (e.g., methadone, buprenorphine) |
| Substance abuse             | Use of a psychoactive substance in a manner outside of sociocultural conventions |

### Table 3. Time Course of Opioid Withdrawal

<table>
<thead>
<tr>
<th>Opioid</th>
<th>Onset</th>
<th>Peak Intensity</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meperidine</td>
<td>2–6 h</td>
<td>6–12 h</td>
<td>4–5 days</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>6–18 h</td>
<td>36–72 h</td>
<td>7–10 days</td>
</tr>
<tr>
<td>Morphine</td>
<td>6–18 h</td>
<td>36–72 h</td>
<td>7–10 days</td>
</tr>
<tr>
<td>Heroin</td>
<td>24–48 h</td>
<td>3–21 days</td>
<td>6–7 weeks</td>
</tr>
<tr>
<td>Methadone</td>
<td>24–48 h</td>
<td>3–21 days</td>
<td>6–7 weeks</td>
</tr>
</tbody>
</table>
hydrophilic molecules that are excreted primarily by the kidneys. With the exceptions of the N-dealkylated metabolite of meperidine and the 6- and possibly 3-glucuronides of morphine, opioid metabolites are generally inactive.16,17,22,23 Because P-450 is inducible by a host of compounds including opioids, barbiturates, and antiepileptics, patients exposed to these drugs for long terms can metabolize some opioids faster, thus producing pharmacokinetic tolerance.16,22 There is good evidence that drug metabolism by genetically variable P-450 can also influence the development of tolerance and dependence.22

A second type of tolerance, termed learned tolerance, refers to a reduction in the effects of a drug due to compensatory mechanisms that are learned. For example, an opioid abuser learns to behave normally (e.g., walking in a straight line) in spite of intoxication. Learned tolerance is also observed in methadone maintenance programs where abusers mask the effects of methadone so that a higher dose will be prescribed.21,25

Perhaps the most important form of tolerance relevant to opioids is pharmacodynamic tolerance. Pharmacodynamic tolerance has been related to neuroadaptive changes that take place after long-term exposure to the drug. These include changes in receptor density and alterations in receptor coupling to G proteins and signal transduction pathways.16,21,24 Basic research has provided a better understanding of the cellular and molecular mechanisms mediating pharmacodynamic opioid tolerance.16,21,25 These mechanisms occur at two distinct levels. The first occurs at the level of the opioid receptor and involves receptor desensitization on long-term or repeated exposure to opioids.25 The concept of receptor desensitization underlies the classic hypothesis of opioid tolerance.16,25 Opioid receptors on the cell surface become gradually desensitized by various mechanisms such as reduced transcription and subsequent decreases in the absolute number of opioid receptors (down-regulation), reduction in the number of opioid receptors on the cell surface by active endocytosis and receptor trafficking from cell surface to the interior of the cells (internalization), and the uncoupling of opioid receptors from underlying G proteins.16,21,25,26 However, this classic hypothesis that tolerance is primarily related to receptor desensitization has yet to be proven.

A second mechanism proposed to explain pharmacodynamic tolerance involves up-regulation of the cyclic adenosine monophosphate (cAMP).27 Acutely, opiates inhibit the functional activity of the cAMP pathway by blocking adenylyl cyclase, the enzyme that catalyzes the synthesis of cAMP. However, with long-term opiate exposure, the cAMP pathway gradually recovers, and tolerance develops. Increased synthesis of cAMP may be responsible for physical dependence and physiologic changes associated with withdrawal. In this regard, the activity of the cAMP pathway increases far above baseline levels after abrupt discontinuance of opioid bind-
anyl (Duragesic; Janssen Pharmaceutical Products, Titusville, NJ) dose escalation in 73 patients with pain related to terminal malignancy. They noted that the initial fentanyl dose of 75 μg/h increased approximately 25% to a final median dose of 100 μg/h. Thirty-two of 73 patients initially enrolled continued the drug until or nearly until death (median, 2.9 months; range, 1–23 months). One criticism of this study is that the relatively short lifespan of patients enrolled did not allow sufficient time for the full extent of tolerance and dose escalation to be observed. A careful review of the data indicates that the Duragesic dose range was very wide (25–700 μg/h) and that patients with longer survival required the highest doses and exhibited the greatest degree of dose escalation. Eight of 16 patients who received fentanyl for 3 months or longer required dose escalation, and 3 patients required dose increases to 300 μg/h or greater.

A second group exhibiting tolerance includes opioid abusers (opioid addicts). These patients are generally more problematic in terms of assessment and management. The exact prevalence of opioid addicted patients presenting for surgery is not known but may be expected to vary depending on setting, type of surgery, prevalence in the local and regional population, and the ability of the physician to screen or detect these patients.

Heroin is the most commonly abused opioid. Approximately one adult among three who tries heroin becomes addicted to this drug. Of patients entering treatment for heroin dependence in 1998 in the United States, 50% were non-Hispanic white, 25% were Hispanic, and 22% were non-Hispanic black. Heroin is readily available on the illicit market but has varying levels of purity. Each 100-mg bag of powder in early 1990 had only 4 mg (range, 0–8 mg) of heroin, and the rest was inert or sometimes contained toxic adulterants such as quinine. In the mid-1990s, street heroin reached 45–75% purity. In some large cities, 90% pure heroin was made available. Thus, heroin, which initially required intravenous injection, could be smoked or administered intranasally (snorted). Only 37% of new heroin abusers now inject the drug. Based on extrapolation of various data, including overdose deaths, applicants for treatment, and arrests, the number of heroin addicts in the United States is estimated to range from 800,000 to 1 million. Approximately 410,000 began using heroin between 1996 and 1998, underscoring a recent escalation in its incidence of abuse.

Heroin is a highly effective analgesic that is widely prescribed in the United Kingdom for control of acute and chronic pain. Nevertheless, heroin’s notoriety and perceived liability for abuse has prohibited its clinical use in the United States.

Prescribed opioids that provide a desirable “high,” that is, a rapid onset to peak effect and pleasurable feelings of sedation or euphoria, are also commonly abused. These include rapid-acting semisynthetics such as oxycodone, hydrocodone, oxymorphone, and hydromorphone and nonmorphinian synthetics including methadone and fentanyl. Only a small minority of abusers prefer drugs that produce dysphoria, such as meperidine and pentazocine. Reports of oxycodone and hydrocodone abuse increased 68% and 31%, respectively, from 1999 to 2000. The sustained-release opioid preparation OxyContin (Purdue-Pharma, Stamford, CT) has also gained notoriety for being abused. OxyContin was developed as a sustained-release opioid for moderate to severe pain that avoided peaks and troughs in analgesic plasma concentrations. OxyContin provides safe and effective pain relief; however, with tampering (i.e., crushing and powdering the preparation), it may be injected or used intranasally to provide a rapid and powerful opioid effect. Methadone (Dolophine [Eli Lilly, Indianapolis, IN]) is also abused. Oral methadone is not associated with euphoric or pleasurable effects but does provide effective analgesia in the setting of chronic pain and reliable maintenance for recovering addicts. Nevertheless, the oral tablet has high street value because after being crushed, placed into solution, and injected, addicts experience an intense and very prolonged “high.”

Drug addiction refers to a complex phenomenon with behavioral, cognitive, and physiologic components where the use of a particular drug assumes central importance in the user’s life, even in the face of obvious physical or psychological harm. Essentially, the life of the addicted patient centers on the repeated use of opioid and nonopioid narcotics to experience pleasure or to avoid displeasure (i.e., avoiding withdrawal). The matter, in actuality, is more complicated than classifying patients as abusers or legitimate users. For example, some patients to whom opioid analgesics are prescribed for chronic pain may actually become addicted to them. For user/abusers, pain control is only one of the motivations responsible for drug-seeking behavior and not the central theme, although it may superficially seem so. It is difficult to ascertain the prevalence of opioid addiction in chronic pain patients, but a study performed by Fishbain et al. found that 3–19% of chronic pain patients have an addictive disorder, which is comparable to the lifetime prevalence rate of addictive disorders in the general population. Savage and others have suggested that prevalence of addiction may

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be higher in chronic pain patients because of their background of emotional and psychological instability and conditioning behavior resulting from increasing pain intensity and relief resulting from opioid use.\(^1,2,15\) Therefore, there may be a subgroup of patients presenting in the perioperative period who are an amalgam of user/abuser, who may not be easily diagnosed and may be difficult to treat (table 4).

A unique subset of opioid-tolerant patients, who are neither abusers nor those to whom opioids are prescribed for chronic pain, are former addicts enrolled in long-term methadone maintenance programs. Many of these individuals have not been users for many years, are gainfully employed, and enjoy normal lifestyles. Nevertheless, they are exposed to relatively large doses of methadone, 25–100 mg/day, and, as might be expected, exhibit high-grade tolerance to the antinociceptive effects of opioids.\(^15,38\) There are no published research data on how to best address the concerns of this particular subclass. The anesthesiologist and pain specialist may devote time to allay patient apprehensions that they may lose control and possibly relapse or that their pain will be inadequately controlled. Patients may be reassured that despite a previous history of opioid dependency, effective pain control is an achievable goal and that the risk of relapse can be minimized.\(^5,15,37,39,40\) The patient, addictionologist, and rehabilitation counselor may meet before surgery and develop a management plan. Together, they may formulate and agree to follow a realistic protocol that would minimize but not eliminate pain perception, while avoiding excessive opioid doses that might lead to recurrence of addictive disorder\(^15,40,41\) (table 5). A practical approach might include the use of a medication agreement or contract, setting appropriate goals for pain intensity scores as well as daily dose of analgesic, and a method of analgesic administration. Patient monitoring may include drug screens, pill counts, and careful documentation of the postoperative course.\(^15,39,40\)

A final subset of opioid-dependent patients is those who have well documented chronic pain and who, superficially, resemble opioid abusers by virtue of their often obsessive drug-seeking behavior. These patients are usually found to have visited numerous physicians and have filled multiple prescriptions for opioids. In actuality, these individuals are not addicted but undermedicated and are only seeking adequate pain relief. This phenomenon was not recognized until recently, and has been termed pseudoaddiction by Weissman and Haddox.\(^42\) Its prevalence is unknown, but it may result in the treatment team becoming negatively biased against the patient and denying him or her adequate opioid coverage. Pseudoaddictive behavior generally reflects patients’ attempts to compensate for development of tolerance, progression of metastatic disease, or worsening of pain in settings where patients have become more functional. In general, pseudoaddictive patients can be differentiated from true drug abusers because increasing doses of opioids and improvement in pain control usually eliminate the drug-seeking behavior.\(^52\)

Finally, it is relevant to note that methadone-maintained and other opioid-tolerant patients are relatively pain intolerant and demonstrate significantly increased sensitivity during cold pressor and thermal testing.\(^38,43\) It has been hypothesized that continuous opioid receptor occupation produces hyperalgesia during less painful states; thus, these patients are unable to cope with sudden acute pain.\(^43,45\) Therefore, after surgery or other settings of acute pain, caregivers should not restrict medicating opioid-dependent patients, but rather treat the pain aggressively, while being aware of the altered pharmacokinetic–pharmacodynamic and behavioral issues involved.\(^38,40,46\) This necessitates a good assessment strategy and formulation of a perioperative management plan to provide adequate comfort to this particularly pain-sensitive population.

### Table 4. Difference between Chronic Pain and Opioid-abusing Patients

<table>
<thead>
<tr>
<th>Chronic Pain Patient</th>
<th>Opioid-abusing Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appropriate use of opioid</td>
<td>Out of control with opioids</td>
</tr>
<tr>
<td>Opioids improve quality of life</td>
<td>Opioid impair quality of life</td>
</tr>
<tr>
<td>Aware of side effects</td>
<td>Unconcerned</td>
</tr>
<tr>
<td>Follows treatment plan</td>
<td>Does not follow plan</td>
</tr>
<tr>
<td>Has medication saved from previous prescriptions</td>
<td>Out of medication, “loses” prescriptions, has a “story”</td>
</tr>
</tbody>
</table>

### Table 5. Suggested Guidelines for Administration of Methadone\(^14\)

<table>
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<tr>
<th>Methadone—daily dose at the same time as usual (oral, s.c./i.m.; relationship between oral and parenteral methadone 2:1)(^14)</th>
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4. There is a pattern of prescription problems for a variety of positive reasons that may include lost medications, spilled medications, problems associated with the opiate prescription. A patient may qualify with fewer visits if he or she creates a disturbance with the office staff.

3. The patient has a pattern of early refills (three or more) or escalating drug use in the absence of an acute change in his or her medical condition.

2. The patient displays an overwhelming focus on opiate issues during pain clinic visits that occupy a significant portion of the pain clinic visit and impedes progress with other issues regarding the patient’s pain. The behavior must persist beyond the third clinic treatment session.

1. The patient generates multiple telephone calls or visits to the administrative office to require more opiates, early refills, or problems associated with the opiate prescription. A patient may qualify with fewer visits if he or she creates a disturbance with the office staff.

4. There is a pattern of prescription problems for a variety of reasons that may include lost medications, spilled medications, problems associated with the opiate prescription. A patient may qualify with fewer visits if he or she creates a disturbance with the office staff.

5. The patient has supplemental sources of opiates obtained from multiple providers, emergency rooms, or illegal sources.

Table 6. Opiate Abuse Checklist

1. The patient displays an overwhelming focus on opiate issues during pain clinic visits that occupy a significant portion of the pain clinic visit and impedes progress with other issues regarding the patient’s pain. The behavior must persist beyond the third clinic treatment session.

2. The patient has a pattern of early refills (three or more) or escalating drug use in the absence of an acute change in his or her medical condition.

3. The patient generates multiple telephone calls or visits to the administrative office to require more opiates, early refills, or problems associated with the opiate prescription. A patient may qualify with fewer visits if he or she creates a disturbance with the office staff.

4. There is a pattern of prescription problems for a variety of reasons that may include lost medications, spilled medications, or stolen medications.

5. The patient has supplemental sources of opiates obtained from multiple providers, emergency rooms, or illegal sources.

Modifed with permission from Chabal et al.57

profoundly influence the postoperative course. The importance of patient assessment and early recognition cannot be overemphasized, because failing this essential first step, principles that follow become less relevant.3–7,41

The assessment strategy aims at correct identification of the opioid-abusing patient from dependent individuals with chronic pain conditions.15,47–49 The true abuser should be detected, whereas legitimate users are not to be falsely labeled as addicts. In other words, both “false-positive” as well as “false-negative” rates should be low.49–51 However, this is easier said than done because of drug-seeking behavior associated with pseudoadicction.52–54 Alternatively, patients who achieve effective pain control may take extraordinary steps to maintain an adequate supply of medication. Although indicative of addictive drug seeking, such behavior may in actuality reflect the efforts of an extremely anxious patient to maintain tolerable pain relief and prevent undermedication.57–49,52 Table 4 outlines the underlying principles that help clinicians to differentiate patients with chronic pain and opioid abusers.

Patients with substance use disorders to alcohol, marijuana, or nicotine show a higher incidence of dependence on other substances than the general population. This phenomenon has been termed cross-addiction or polydrug abuse.21,48,50,51 Nearly 70% of opioid addicts in the United States are dependent on either cocaine or other habituating substances.48,50 Opioid-dependent patients with superimposed cocaine dependence may present additional problems for acute caregivers, including hemodynamic instability and extreme emotional liability.21,55 Some opioid-dependent patients are also codependent on benzodiazepines and other anxiolytics.21 By simply focusing on opioid dependency issues and not accounting for or administering adequate doses of benzodiazepines, these individuals may experience severe withdrawal reactions, including anxiety, agitation, and confusion.46,47,52,53

Applying Diagnostic and Statistical Manual of Mental Disorders, 4th edition,15 criteria for drug abuse to patients taking prescribed opiates for a chronic pain problem is difficult.56,55,54 Therefore, special assessment criteria must be developed and applied.54–56 A retrospective case review identified some patient characteristics, such as recent polysubstance abuse, early prescription abuse, especially oxycodone, and aberrant drug-seeking behavior, as predictive of later opioid abuse.55 Two recently published studies addressed this assessment issue.57,58 Chabal et al.57 introduced a five-point prescription opiate abuse checklist that is easy to use, although it may lack sensitivity (table 6). Compton et al.58 developed a more detailed 42-item screening tool called the Prescription Drug Use Questionnaire that may help clinicians to uncover opioid abuse in chronic pain patients. These assessment tools are still in preliminary stages of development, and large-scale multicenter trials are warranted before their widespread application. A major problem with abuse checklists and questionnaires is that some of the criteria used for assessment necessitate prolonged physician contact with the patient and hence may be difficult to apply in acute perioperative settings.54,57,58

During patient assessment, the anesthesiologist should recognize that the terms opioid user or abuser may be considered highly sensitive labels.53,55,56 Patients are keenly aware of the significant social stigma surrounding opioid dependency and are entitled to privacy and the right to confidentiality. The anesthesiologist should develop a clear management strategy that maintains a balance: to gain patient trust with an understanding and caring approach while being prepared to overcome high-grade tolerance with liberal doses of opioid and nonopioid analgesics.3–5,7,41

The anesthesiologist should also be aware of the rapidly changing profile of opioid-based analgesia. Newly developed and marketed opioids often do not have names that are readily recognizable as opioids but represent potent or long-acting preparations that can confer a high degree of tolerance and dependence. Examples include (1) rapid-acting or novel-delivery preparations, Actiq (Cephalon Inc., West Chester, PA; fentanyl orlalet), Nasal Stadol (Bristol-Myers Squibb, New York, NY; butorphanol), and Oxy-IR (immediate-release oxycodone) (Purdue-Pharma, Stamford, CT); (2) sustained-release preparations containing fentanyl, Duragesic (fentanyl transdermal patch) or morphine (Kadian; [Elan Corporation, Dublin, Ireland], Avinza [Mayne Pharma (USA), Paramus, NJ], MS-Contin [Purdue-Pharma]); and (3) less often prescribed preparations containing codeine (Fioricet with codeine, Fiorinal with codeine [Sandoz Pharmaceuticals, East Hanover, NJ]), hydrocodone (Hy-
PAIN MANAGEMENT IN OPIOID-DEPENDENT PATIENTS

It should also be recognized that some patients presenting to the anesthesiologist or preadmission testing unit physicians may not realize that they are opioid dependent and may unintentionally deny the possibility. Patients may not know that opioids have been prescribed to them or may not recognize that escalations in their daily need for pain relievers reflects tolerance development. Although most patients are aware that morphine and Demerol (Sanofi-Synthelabs, New York, NY) are narcotics, many are not aware that they may have been given opioids of even greater potency for treatment of arthritis and low-back pain.

Other patients may consciously deny or underplay reporting opioid use or the amount of drug consumed. The latter scenario is likely to occur in patients highly addicted to opioids. In fact, these are the patients who must be identified before induction of anesthesia, to minimize postoperative risks of undermedication and inadequate analgesia. It should be understood that tolerance to any one opioid preparation results in clinically measurable insensitivity to most others. It does not matter whether individuals are using legally prescribed oxycodone or abusing street heroin—both exhibit a diminished response to intraoperative doses of fentanyl and postoperative doses of morphine.

In same-day surgical settings, not recognizing that a patient is highly opioid dependent may result in inadequate pain relief and an unscheduled hospital admission for pain management. In many cases, the onus of recognizing falls on the anesthesiologist, either in preadmission testing or, in the worst-case scenario, just minutes before the scheduled start of the procedure. An increased clinical index of suspicion is useful especially with patients who exhibit a chronic pain condition, those to whom opioids have been recently prescribed, and others whose lifestyle, general appearance, or general physical examination (e.g., multiple needle marks, thrombosed superficial veins, and skin abscesses) are suggestive of harboring an addictive disorder.

Finally, it is worth emphasizing that the immediate perioperative period is not the optimal time to attempt detoxification or rehabilitation management for any patient abusing opioids. Although obviously important, such issues should be dealt with later in the postoperative period, when the patient is stable and pain has declined in intensity.

**Patient Treatment**

**Preoperative Period.** There are few controlled studies or scientifically rigorous sources of data available to guide the anesthesiologist in optimizing anesthetic and analgesic care, despite the increasing prevalence of opioid dependency. Perioperative management of opioid-dependent patients is not discussed in any major anesthesiology textbook. The majority of scientific literature in this area is comprised of case reports that include recommendations for patient treatment, often based on the authors’ experience and expertise. We have summarized pertinent clinical findings from a number of case reports and, together with suggestions provided by pain management specialists at major medical centers and our experience caring for opioid-dependent patients, developed guidelines that may improve postoperative analgesia and patient satisfaction. These guidelines, although not tested scientifically, have been advocated in settings of opioid dependency and receptor down-regulation and serve as a backdrop against which future controlled clinical trials may be planned.

Perioperative management of opioid-dependent patients begins with preoperative administration of their daily maintenance or baseline opioid dose before induction of general, spinal, or regional anesthesia. Patients should be instructed to take their usual dose of oral opioid on the morning of surgery. Because most sustained-release opioids provide 12 h or more of analgesic effect, baseline requirements will generally be maintained during preoperative and intraoperative periods. Thereafter, baseline requirements may be provided orally, particularly after ambulatory surgery, or parenterally for those recovering in the hospital from more invasive procedures. Recovering addicts enrolled in a methadone maintenance program or receiving buprenorphine maintenance should continue taking those medications with one sip of water on the morning of surgery. The anesthesiologist usually need not be concerned about redosing baseline opioids during the intraoperative period because these preparations are also associated with prolonged durations of activity. Unless contraindicated, patients should also be instructed to take their morning dose of cyclooxygenase-2 inhibitor to reduce inflammatory responses to surgery and to augment opioid-mediated analgesia.

Patients who are instructed not to take or those who forget to take baseline opioids may be treated with an equivalent loading dose of morphine or hydromorphone, administered preoperatively as an oral elixir (if time permits) or intravenously, either at anesthetic induction or during the operative procedure. Patients should also be instructed to maintain their transdermal fentanyl patch into the operating room. If the preparation was removed, an intravenous fentanyl infusion may be initiated to maintain baseline plasma concentrations. A new patch may then be applied intraoperatively; however, it may take 6–12 h to reestablish baseline analgesic effects. The fentanyl infusion may be gradually decreased in rate and eventually discontinued during that time.

Baseline intravenous opioid infusions should also be maintained preoperatively and then converted to intravenous patient-controlled analgesia (PCA) after recovery.
from anesthesia. Epidural and intrathecal opioid infusions delivered by internally implanted devices are generally maintained throughout the perioperative period and are used to maintain baseline pain control. The only exception to this rule applies to patients receiving intrathecal infusions of the nonopioid relaxant Lioresal (baclofen) (Watson Laboratories, Corona, CA). It may be prudent to discontinue or reduce the intrathecal infusion rate of Lioresal during the immediate perioperative period because central effects and peripheral skeletal muscle relaxing effects of this agent may enhance neuromuscular blockade and increase the incidence of hypotension and excessive sedation.

Intravenous or oral doses of methadone and morphine may be used as baseline and intraoperative analgesics for patients abusing heroin. Baseline doses of intravenous methadone or morphine are also recommended for patients enrolled in a methadone maintenance program. Before administering an intravenous loading dose, heroin addicts may require placement of a central line because they typically present with poor peripheral venous access.

The importance of maintaining a baseline dose of methadone was underscored in a case described by de Leon-Casasola and Lema. An opioid-dependent patient who required 1,000 mg methadone daily did not have her methadone continued after pelvic surgery. She developed agitation, tachycardia, salivation, and lacrimation in addition to poor pain control. Her symptoms were diagnosed as acute opioid withdrawal, and she was given a morphine loading dose of 300 mg, followed by an intravenous infusion of 110 mg/h. Withdrawal symptoms disappeared, and she experienced good pain control. During the next several days, 30 mg methadone every 6 h was restarted, and her morphine infusion was decreased by 10 mg/h each day.

Recovering opioid abusers maintained on buprenorphine may continue on this partial opioid agonist for postoperative pain control. If the quality of analgesia provided by buprenorphine is inadequate, one may consider supplementation with methadone and morphine. Sublingual buprenorphine, 0.8 mg, is equianalgesic with 20 mg oral methadone. Opioid antagonists, including naloxone and naltrexone, should be avoided in opioid-dependent patients. Postoperative administration may precipitate withdrawal symptoms in patients who are dependent on potent opioids. In addition, mixed agonist-antagonist-type opioids that block μ receptors, such as nalbuphine, butorphanol, and pentazocine, may precipitate acute opioid withdrawal in these individuals. Similar abstinence symptoms have been reported in highly dependent patients who were treated with the weak μ-opioid α-adrenergic receptor agonist tramadol. Naltrexone, a long-acting oral opioid antagonist often used in recovering opioid abusers, should also be discontinued at least 24 h before surgery. After abrupt discontinuation, a selective up-regulation of μ receptors with enhanced opioid sensitivity may develop. Perioperative opioids must be titrated carefully to avoid excessive sedation or respiratory depression in this setting.

**Intraoperative and Postoperative Periods.** Patients recovering from ambulatory surgery should be initially treated with intravenous boluses of fentanyl or sufentanil. After stabilization in the postanesthesia care unit (PACU), they may be restarted on oral opioids in doses higher than baseline requirements, depending on the invasiveness of the procedure. In most nonambulatory surgeries, oral opioids are discontinued after anesthetic induction and converted to a parenteral equivalent. Judicious doses of morphine, hydromorphone, fentanyl, or methadone are used to augment intraoperative anesthesia and to provide effective postsurgical analgesia in addition to covering baseline requirements. Precise dosing guidelines have not been developed, but opioid doses required to meet intraoperative and postsurgical analgesic requirements are affected by receptor down-regulation and may need to be increased 30–100% in comparison with requirements in opioid-naive patients. (Refer to section on dosing guidelines.) Some anesthesiologists prefer to slowly “front load” relatively large amounts of morphine or methadone to cover baseline and estimated intraoperative opioid requirements after applying full monitoring and mask oxygen and while maintaining active communication with the patient. Others prefer administering one half of the estimated dose during preinduction and induction periods and titrate the remainder as the case progresses.

Differences in oral to intravenous dose equivalency need to be appreciated to estimate perioperative baseline and supplemental opioid dose requirements. Most intravenous or intramuscular doses of opioid can be adjusted downward from doses taken orally because parenteral administration bypasses gastrointestinal absorption variables and first-pass hepatic clearance and metabolism. This is particularly the case with intravenous morphine and hydromorphone which have three and two times, respectively, greater bioavailability and systemic potency than equivalent oral doses.

In contrast, oxycodone and sustained-release OxyContin have high oral bioavailability that approaches 83% of an intravenous dose, and the baseline oral dose can be approximated by nearly similar doses of intravenous morphine (1–1.5 mg oral oxycodone = 1 mg intravenous morphine). Patients treated with transdermal fentanyl (Duragesic) or receiving intravenous PCA morphine/hydromorphone at home or hospice are more straightforward because their baseline requirement may be supplied with an equivalent intravenous dose of opioid.

Because there may be significant interpatient variability in opioid dose requirements, intraoperative vital

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[Anesthesiology, V 101, No 1, Jul 2004]
signs, particularly heart rate, respiratory rate, and degree of pupil dilation, should be closely monitored. The optimal intraoperative dose avoids undermedication and overmedication, both associated with negative perioperative outcomes.\textsuperscript{6,7,41,72} One technique that may help to gauge the adequacy of intraoperative opioid dosing is to reverse neuromuscular blockade and allow patients to breath spontaneously at later stages of the general anesthetic. Patients with respiratory rates greater than 20 breaths/min and exhibiting slight to markedly dilated pupils generally require additional opioid dosing. Intra- venous boluses of morphine, fentanyl, or hydromorphone are titrated as needed to maintain a rate of 12-14 breaths/min and a slightly miotic pupil.

The surgeon may consider infiltrating the surgical site with a long-acting local anesthetic (0.5% bupivacaine or 0.75% levobupivacaine to further block pain perception during the immediate recovery period (refer to the section on regional analgesia). The patient may also be maintained in a mildly sedated state to avoid agitation and pain on emergence from anesthesia.\textsuperscript{7,72} This may be accomplished by administering additional opioid as needed before patient transport to the PACU.

**Parenteral Analgesia for Postoperative Pain.** A continuous parenteral opioid infusion or intravenous PCA provides useful options for effective postsurgical analgesia.\textsuperscript{7,41,79} Initiation of intravenous PCA in the PACU minimizes the risk of undermedication and breakthrough pain that may occur during patient transport to the surgical care unit. To compensate for opioid tolerance and receptor down-regulation, higher than normal doses of morphine or hydromorphone should be considered.\textsuperscript{41,72} A basal infusion equivalent either to the patient’s hourly oral dose requirement or one to two PCA boluses per hour may be added to maintain baseline opioid requirements.\textsuperscript{79} Basal infusions may not be required in patients receiving baseline analgesia via transdermal fentanyl patch.

Allowing substance abusers or recovering addicts to use intravenous PCA to control postoperative pain was initially considered controversial because caregivers worried that these individuals might self-administer excessive amounts of opioid or rekindle addictive behavior.\textsuperscript{7,41,72} It is now recognized that intravenous PCA may be offered to selected patients provided that pain intensity and opioid consumption are carefully assessed and that such therapy is supplemented with baseline doses of methadone, neural blockade, and nonopioid analgesics.\textsuperscript{7,41,80,81}

Boyle\textsuperscript{80} reported on the successful use of PCA in a 23-yr-old woman undergoing cesarean delivery who had been using intravenous heroin until the seventeenth week of her pregnancy, when she switched to 25 mg/ day oral methadone. At 32 weeks, it was decided to deliver the baby by cesarean delivery with general anesthesia. Postoperative analgesia was provided by patient-administered intravenous boluses of morphine (2 mg) with a background (basal) infusion of 3 mg/h. Intravenous PCA provided adequate pain relief for this patient, although initial morphine requirements (mg/h) at 2, 4, and 6 h were high (15, 16, and 10 mg, respectively).\textsuperscript{80} At 36 h after surgery, the basal morphine infusion was discontinued, and oral methadone was restarted. PCA boluses of morphine were continued for breakthrough pain until 48 h, whereupon oral morphine was substituted.\textsuperscript{80}

Oral methadone has been advocated for use in patients who experience ineffective postsurgical analgesia despite administration of relatively high doses of morphine or synthetic derivatives of morphine. Sartain and Mitchell\textsuperscript{82} recently described the case of a 25-yr-old man with a history of intravenous opioid abuse who was hospitalized with multiple fractures. The patient had dropped out of a methadone maintenance program and was being treated with a sustained-release morphine preparation, 100 mg twice daily. In the hospital, treatment with intravenous PCA morphine and supplemental doses of ketamine did not provide adequate pain relief. After receiving 100 mg oral morphine as well as 509 mg morphine and 769 mg ketamine by intravenous PCA over a 24-h period, his caregivers discontinued such therapy and initiated 50 mg oral methadone four times daily. This strategy was successful because the patient reported rapid and effective pain control. The improved analgesic efficacy observed in this case was probably related to the ability of methadone to activate a different spectra of \( \mu \) receptor subtypes to which morphine tolerance has not developed.\textsuperscript{83-86} In addition, the activity of methadone at \( \alpha \)-adrenergic receptors may provide useful analgesic effects that are not influenced by high-grade opioid tolerance.\textsuperscript{39,84} Finally, \( d \)-methadone has been shown to block morphine tolerance and opioid-induced hyperalgesia by virtue of its NMDA receptor antagonistic and \( \alpha \)-adrenergic agonist properties.\textsuperscript{38,84,85} For these reasons, some have advocated methadone as the intravenous PCA opioid of choice in opioid-dependent patients.\textsuperscript{4,80,81,86} Suggested guidelines for administration of methadone are presented in table 5.

Nonopioid analgesic adjuvants may also be used to reduce opioid dose requirements and provide multimodal analgesia, although relatively few evaluations have been performed in opioid-dependent patients. Nonopioid analgesics including nonselective nonsteroidal anti-inflammatory drugs and more specific cyclooxygenase-2 inhibitors to minimize inflammatory pain,\textsuperscript{62,87,88} low doses of ketamine (0.5 mg/kg) or similar agents to antagonize NMDA receptor activation,\textsuperscript{89,90} and clonidine patch (0.1 mg/h), which provides effective \( \alpha \)-adrenergic-mediated analgesia, have been studied.\textsuperscript{91}

Low-dose ketamine was used as an adjunct for parenteral opioids in highly tolerant patients with severe cancer pain\textsuperscript{90} and as balanced analgesia for the management of pain associated with multiple fractured ribs in an opioid addict.\textsuperscript{92} In the latter case, initial analgesic ther-
therapy consisting of epidural boluses of morphine (5 mg) and bupivacaine (0.25%) did not provide pain relief. Epidural analgesia was then supplemented with intravenous PCA fentanyl, 40-µg bolus dose with a 5-min lock-out time. Analgesia was still inadequate. The combination of a ketamine intravenous infusion at 10 mg/h plus 250 mg naproxen twice daily finally provided effective analgesia allowing active physiotherapy. The ketamine infusion was stopped, and the PCA fentanyl bolus was reduced to 20 µg on day 8. Thereafter, the patient was started on 40 mg methadone twice daily and made a good recovery.92

Finally, it may be worthwhile to consider the contribution of fear and anxiety to the overall pain syndrome.51,41,72 This is especially true for opioid-tolerant patients and polydrug abusers. Anxiety and fear should be discussed and treated with appropriate medication as required.

Neuraxial Analgesia for Postoperative Pain. Neuraxial administration of opioids offers a more efficient method of providing postsurgical analgesia than parenteral or oral opioids.93–96 Intrathecal and epidural doses of morphine are roughly 100 times and 10 times more efficacious, respectively, than the same dose of morphine given parenterally.94 Therefore, significantly greater levels of analgesia can be delivered to those patients recovering from more extensive procedures where postsurgical parenteral opioid doses would be expected to be very high.

There have been few evaluations of neuraxial analgesia in opioid-dependent patients.5,5.19,92,95,96 In contrast to local anesthetic blockade,94 neuraxial opioid analgesia is influenced by down-regulation of spinal opiate receptors,16,18 and epidural and intrathecal dose requirements are increased proportionally.18,95,96 Indirect scientific support for this comes from the landmark study of Wang et al.95 who noted that patients with terminal pelvic cancer and dependent on high doses of parenteral morphine (5–20 mg every 2 h) required relatively large amounts of intrathecal morphine (1 mg as often as every 4 h) to achieve effective pain relief. This dose of intrathecal morphine, although 2–3 times higher than amounts used for postoperative analgesia in opioid-naive patients, did not result in excessive sedation, nausea/vomiting, or delayed respiratory depression.

The opioid dose is generally a small fraction of the patient’s baseline oral requirement with intrathecal administration. Despite the fact that patients experience effective pain relief, plasma concentrations and superspinal receptor binding may decline to the point that acute withdrawal is precipitated, unless supplementary opioids are given.19,96 For this reason, it is important to maintain baseline opioid requirements either orally or by intravenous PCA. Monitoring for complications such as excessive sedation and respiratory depression is mandatory when administering opioids in higher dose and via different routes of administration. Caregivers on postsurgical units should be instructed about the high opioid dose requirements of highly tolerant patients, as well as the potential for overdose when parenteral and neuraxial opioids are administered concomitantly.

Increasing the concentration of epidurally administered opioids may compensate for spinal receptor down-regulation. An epidural opioid loading dose greater than that used in naïve patients, followed by a more concentrated infusion, may improve pain control in highly tolerant patients. Patient-controlled epidural boluses may be added to complement the basal epidural infusion. Local anesthetics such as 0.1% bupivacaine, 0.1% levobupivacaine, or 0.2% ropivacaine may be added to the epidural infusate to provide selective neural blockade and augment opioid-mediated analgesia.93,96 Rescue doses of parenteral and possibly oral opioids should be administered to gain supraspinal analgesic effects and to prevent withdrawal symptoms. In patients ordered to take nothing by mouth, epidural analgesia is used for postsurgical pain while baseline requirements are maintained with intravenous PCA, intravenous boluses of opioids, or “sip and swallow” doses of methadone.

Switching to an opioid that has high intrinsic potency has been previously advocated.18,19,96,97 de Leon-Casa-sola and Lema96 presented a case in which a patient with high-grade opioid tolerance recovering from pelvic surgery experienced ineffective pain control despite treatment with relatively high doses of epidural morphine (30 mg/h). After an epidural bolus of sufentanil (50 µg), her pain was substantially reduced. An epidural infusion containing 2 µg/ml sufentanil and 0.1% bupivacaine maintained excellent pain control for 19 days after surgery. After this interval, the medication was changed to oral methadone. Although this patient clearly benefited by switching to a more potent opioid agonist, it is conceivable that improved pain control could also have been achieved by increasing the dose of epidural morphine to 50–60 mg/h.

A final method that may be used to improve neuraxial analgesic efficacy is to administer opioids directly into the subarachnoid space.94,95 Subarachnoid dosing markedly increases the concentration of molecules available to bind spinal opioid receptors. Placement of subarachnoid catheters and administration of intrathecal opioids, although rarely used for acute pain management in opioid-naive patients, may provide effective analgesia in opioid-dependent patients (refer to intrathecal dosing guidelines outlined in appendix) although no scientific literature is available.

Regional Analgesia for Postoperative Pain. Expert opinion suggests that, whenever possible, opioid-tolerant patients should be offered regional anesthesia or analgesia, particularly for procedures performed on the extremities.5,7,41,72 Techniques that may be considered include tissue infiltration and nerve and plexus block-
ade. Advantages of a regional anesthetic/analgesic approach include reduction in parenteral/oral opioid requirements and improvement in distal perfusion as a result of sympathetic blockade. Regional blockade may offer a useful anesthetic alternative for most peripheral vascular and reimplantation surgeries and for other procedures requiring graft revision or replacement. Neural blockade may be initiated with bupivacaine or levobupivacaine in standard doses, and a continuous infusion may be continued postoperatively. Patients may be discharged home with indwelling brachial plexus catheters and local anesthetic infused for up to 48 h via disposable pumps. Other interventions include injection of local anesthetics and opioids into the knee and other articular joints and injections of local anesthetics into disc spaces or the iliac crest for spinal surgery. The goal is to minimize pain perception and reduce, although not completely eliminate, the use of oral or parenteral opioids for baseline requirements in dependent patients.

### Dose Tapering

Baseline requirements for oral opioids after ambulatory surgery generally must be supplemented with additional medication (generally 20–50% increases above baseline) to accommodate pain associated with surgical injury. Oral opioids should then be down-titrated slowly over 3–7 days to presurgical amounts as the intensity of acute pain diminishes.

Opioid analgesics should never be withheld from dependent patients, but some caregivers cautiously underestimate theoretical intravenous dose equivalencies in patients requiring extremely high baseline doses of oral or transdermal opioids. This is especially true in patients recovering from surgical procedures performed to reduce baseline chronic pain. For example, only 50% of an intravenous equivalent may be given to patients requiring oxycodone doses greater than 200 mg/day, morphine doses greater than 300 mg/day, or transdermal fentanyl doses greater than 150 μg/h. Opioid dosing may be increased as needed if patients do not experience adequate pain control. Baseline opioid dosing should be gradually tapered rather than abruptly stopped to avoid withdrawal when pain is markedly reduced after successful spine surgery, neurolysis, or cordotomy. In this setting, baseline dose may be reduced by 50% the day after surgery and then tapered 25% every 24–48 h, depending on the opioid administered. When the dose has been decreased to 10–15 mg morphine equivalent per 24 h, it may be discontinued.

Alternatively, patients can be switched to an equianalgesic dose of methadone, which can then be slowly tapered. Transdermal fentanyl patches are easily maintained and replaced. Surgical improvement in analgesia may allow fentanyl dose tapering of 25% within 24–48 h in patients recovering from back procedures. Further tapering may continue every 48–72 h as tolerated by the patient. Application of a 0.1–0.2 mg/h clonidine transdermal patch may help to minimize some of the autonomic aspects of opioid withdrawal if symptoms should become distressing.

After hospital discharge, opioid-dependent patients should be scheduled for a follow-up visit with a pain specialist, who can optimize pain management during rehabilitation and facilitate opioid dose tapering. Some patients may require the expertise of an addictionologist. Suggested guidelines for perioperative pain management in opioid-tolerant patients are provided in table 7 and the appendix.

### Future Directions in Management

Several newer agents have been shown to enhance postoperative analgesia or chronic pain control and may serve as useful analgesic adjuncts in opioid-dependent patients. These include the α2-adrenergic receptor agonist dexmedetomidine, the NMDA receptor antagonist dextromethorphan, the anticonvulsant gabapentin, and the second-generation parenteral cyclooxygenase inhibitors etoricoxib and parecoxib. Dextromethorphan, a common over-the-counter antitussive, has been shown to have a postoperative opioid-sparing effect in patients with bone malignancy and in patients under-

### Table 7. Guidelines for Perioperative Pain Management in Opioid-tolerant Patients

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<th>Preoperative</th>
<th>Intraoperative</th>
<th>Postoperative</th>
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<tr>
<td>1. Evaluation: Evaluation should include early recognition and high index of suspicion.</td>
<td>1. Maintain baseline opioids (oral, transdermal, intravenous).</td>
<td>1. Plan preoperatively for postoperative analgesia; formulate primary strategy as well as suitable alternatives.</td>
</tr>
<tr>
<td>2. Identification: Identify factors such as total opioid dose requirement and previous surgery/trauma resulting in undermedication, inadequate analgesia, or relapse episodes.</td>
<td>2. Increase intraoperative and postoperative opioid dose to compensate for tolerance.</td>
<td>2. Maintain baseline opioids.</td>
</tr>
<tr>
<td>3. Consultation: Meet with addiction specialists and pain specialists with regard to perioperative planning.</td>
<td>3. Provide peripheral neural or plexus blockade; consider neuraxial analgesic techniques when clinically indicated.</td>
<td>3. Use multimodal analgesic techniques.</td>
</tr>
<tr>
<td>4. Reassurance: Discuss patient concerns related to pain control, anxiety, and risk of relapse.</td>
<td>4. Use nonopioids as analgesic adjuncts.</td>
<td>4. Patient-controlled analgesia: Use as primary therapy or as supplementation for epidural or regional techniques.</td>
</tr>
<tr>
<td>5. Medication: Calculate opioid dose requirement and modes of administration; provide anxiolytics or other medications as clinically indicated.</td>
<td>5. Medication: Calculate opioid dose requirement and modes of administration; provide anxiolytics or other medications as clinically indicated.</td>
<td>5. Continue neuraxial opioids: intrathecal or epidural analgesia.</td>
</tr>
<tr>
<td>7. If surgery provides complete pain relief, opioids should be slowly tapered, rather than abruptly discontinued.</td>
<td>7. After discharge</td>
<td>7. After discharge</td>
</tr>
<tr>
<td>9. Arrange for a timely outpatient pain clinic follow-up or a visit with the patient’s addictionologist.</td>
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going general surgery during epidural or general anesthesia.\textsuperscript{103,104} Well-controlled phase III clinical evaluations of combined opioid agonist–dextromethorphan analgesics for postsurgical pain are in progress.\# 

Gabapentin has been shown to reduce postoperative morphine requirement in patients undergoing radical mastectomy\textsuperscript{101} and also to enhance morphine analgesia in healthy volunteers.\textsuperscript{105} There are no published reports of efficacy of this drug in opioid-dependent patient groups, but it may complement standard measures outlined above.

Another promising line of research and potential therapy concerns the development of agents targeted to reduce opioid tolerance and increase intrinsic efficacy, thus obviating the need for dose escalation. Production of nitric oxide, possibly influenced by NMDA receptor activation, has been implicated in tolerance development; however, its exact role remains unclear. Inhibition of nitric oxide synthase has been shown to reduce morphine tolerance.\textsuperscript{106} In contrast, Lauretti \textit{et al.}\textsuperscript{107} recently showed that transdermal nitroglycerine (which increases \textit{in vivo} concentrations of nitric oxide) provides a measurable opioid-sparing effect in patients with cancer pain. Dextromethorphan has been shown in animal studies to attenuate the development of and reverse established opioid tolerance.\textsuperscript{108} Finally, Basile \textit{et al.}\textsuperscript{109} recently demonstrated the role of M5 muscarinic acetylcholine receptors in mediating the reward and withdrawal-related properties of opioids. The analgesic efficacy of morphine and the development of tolerance remain unaltered by the lack of M5 receptors. One possible implication of this research is that if the M5 receptor is blocked, opioid analgesia might remain unimpaired, whereas opioid tolerance and addiction may not develop. This may eventually have significant clinical implications in treating opioid-dependent patients.

\section*{Conclusion}

Opioid-dependent patients have special needs in the perioperative period. There is lack of scientifically rigorous studies in this important area, and most of the information must be derived from anecdotal reports and personal experience of anesthesiologists working in this field. This review has highlighted the need to conduct such studies in the future.

The anesthesiologist plays the key role in maintaining baseline opioid requirements, administering supplemental intraoperative and postoperative opioids, and providing nonopioid analgesics and neural blockade. To prevent undermedication, the anesthesiologist and pain specialist may be required to titrate doses of opioid that would clearly result in overdose in opioid-naïve patients. Nevertheless, undermedicating these patients must be avoided. The dependent patient experiencing opioid overdosage is rare. However, delivering a patient to the PACU who has severe pain is an unacceptable practice and often results in an extremely difficult and time-consuming management issue. Awareness and administration of appropriate doses of analgesics as well as continuous clinical monitoring remain the keys to successful perioperative pain management in this special group of patients.

\section*{References}

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2002; 108:587–90
Nat Rev Neurosci 2001; 2:119 –28
27. Nestler EJ, Aghajanian GK: Molecular and cellular basis of addiction.
Science 1997; 278:58 – 63
201–17
opioid therapy. Pain 2002; 100:213–7
pain, morphine tolerance, and their interactions. Proc Natl Acad Sci U S A 1999;
96:7731– 6
31. Mao J, Sung B, Ji RR, Lim G: Chronic morphine induces downregulation of
spinal glutamate receptors: Implications in morphine tolerance and abnormal
32. Mao J, Sung B, Ji RR, Lim G: Neuronal apoptosis associated with morphine
tolerance: Evidence for an opioid-induced neurotoxic mechanism. J Neurosci
2002; 22:7650 – 61
33. Vanderah TW, Gardell LR, Burgess SE, Ibrahim M, Dogrul A, Zhang ET,
Malan TP, Ossipov MH, Porreca F: Dynorphin promotes abnormal pain and spinal
34. Basbaum AI: Insights into the development of tolerance. Pain 1995; 61:
349 –52
35. Nugent M, Davis C, Brooks D, Ahmedzai SH: Long-term observations of
patients receiving transdermal fentanyl after a randomized trial. J Pain Symptom
Manage 2001; 21:385–91
36. Fiellin DA, O’Connor PG: Office-based treatment of opioid-dependent
37. Fishbain DA, Rosomoff HL, Rosomoff RS: Drug abuse, dependence, and
38. Doverty M, Somogyi AA, White JM, Bochner F, Beare CH, Menelaou A, Ling
W: Methadone maintenance patients are cross-tolerant to the antinociceptive
39. Weaver M, Schnoll S: Abuse liability in opioid therapy in pain treatment in
Nursing 1997; 4:17–9
43. Compton P, Charuvastra VC, Kintaudi K, Ling W: Pain responses in
44. Rapp SE, Ready LB, Nessly ML: Acute pain management in patients with
prior opioid consumption: A case-controlled retrospective review. Pain 1995;
61:195–201
to daily heroin administration: An apparent phenomenon associated with enhanced pain sensitivity. Neuroscience 1999; 89:631– 6
46. Portenoy RK, Dole V, Joseph H, Lowinson J, Rice C, Segal S, Richman BL:
Pain management and chemical dependency: Evolving perspectives. JAMA 1997;
278:592–3
47. Heit HA: The truth about pain management: The difference between a
45:555– 88
50. Kosten TR, Rounsaville BJ, Kleber HD: Antecedents and consequences of
176:176 – 81
Manage 1993; 8:297–305
52. Aronoff GM: Opioids in chronic pain management: Is there a significant
53. Kirsh KL, Whitcomb LA, Donaghy K, Passik SD: Abuse and addiction issues
in medically ill patients with pain: Attempts at clarification of terms and empirical
2002; 18(suppl):S28 –38
55. Dunbar SA, Katz NP: Chronic opioid therapy for nonmalignant pain in
patients with a history of substance abuse: Report of 20 cases. J Pain Symptom
Manage 1996; 11:163–71
56. Portenoy RK: Opioid therapy for chronic non-malignant pain: Current
status, Progress in Pain Research and Management. Vol 1. Edited by Fields HL,
Liebeskind JC. Seattle, IASP, 1994, pp 247– 87
opiate abuse in chronic pain patients: Clinical criteria, incidence, and predictors.
58. Compton P, Darakjian J, Miotto K: Screening for addiction in patients with
chronic pain and “problematic” substance use: Evaluation of a pilot assessment

Anesthesiology, V 101, No 1, Jul 2004

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487–562
60. Rubenstein RB, Spira I, Wolff WI: Management of surgical problems in
61. Johnson RE, Jaffe JH, Fudala PJ: A controlled trial of buprenorphine
treatment for opioid dependence. JAMA 1992; 287:2750 –5
62. Reuben SS, Connelly NR: Postoperative analgesic effects of celecoxib or
63. Sevarino FB, Ning T: Transdermal fentanyl for acute pain management,
Acute Pain: Mechanisms and Management. Edited by Sinatra RS, Hord AH,
Ginsberg B, Preble LM. St. Louis, Missouri, Mosby Yearbook, 1992, pp 364 –9
Geriatrics 1992; 47:69 –72
66. Gomar C, Carrero EJ: Delayed arousal after general anesthesia associated
with baclofen. ANESTHESIOLOGY 1994; 81:1306 –7
67. Foley RM: Opioid analgesics in clinical pain management, Handbook of
EJ. New York, Springer Verlag, 1993, pp 697–743
68. Reisine T, Pasternak G: Opioid analgesics and antagonists, Goodman and
Gilman’s The Pharmacological Basis of Therapeutics, 9th edition. Edited by
Hardman JG, Limbird LE, Molinoff PB, Ruddon RW, Gilman AG. New York,
69. Manfredi PL, Ribeiro S, Cahndler SW, Payne R: Inappropriate use of
70. Thomas AN, Suresh M: Opiate withdrawal after tramadol and PCA (letter).
Anaesthesia 2000; 53:826 –7
and pharmacokinetic properties and therapeutic efficacy in the treatment of
72. Saberski L: Postoperative pain management for the patient with chronic
pain, Acute Pain: Mechanisms and Management. Edited by Sinatra RS, Hord AH,
Ginsberg B, Preble LM. St. Louis, Missouri, Mosby Yearbook, 1992, pp 422–31
Nursing 2001; 5:163–5
74. Pereira J, Lawlor P, Vigano A, Dorgan M, Bruera E: Equianalgesic dose
ratios for opioids: A critical review and proposals for long-term dosing. J Pain
Symptom Manage 2001; 22:672– 87
77. Ginsberg B, Sinatra RS, Adler LJ, Crews JC, Hord AH, Laurito CE, Ashburn
MA: Conversion to oral controlled-release oxycodone from intravenous opioid
Anaesth 2001; 87:36 – 46
79. Parker RK, Holtman B, White PF: Patient-controlled analgesia: Does a
concurrent opioid infusion improve pain management after surgery? JAMA 1992;
266:1947–52
80. Boyle RK: Intra- and postoperative anaesthetic management of an opioid
81. Fitzgibbon DR, Ready JB: Intravenous high dose methadone administered
by patient controlled analgesia and continuous infusion for the treatment of pain
refractory to high dose morphine. Pain 1997; 73:259 – 61
82. Sartain JB, Mitchell SJ: Successful use of oral methadone after failure of
84. Morley JS, Makin MK: The use of methadone in cancer pain poorly
responsive to other opioids. Pain Reviews 1998; 5:51– 8
289:1048 –53
86. Birnbach DJ, Stein DJ: The substance-abusing parturient: Implications for
12:443– 60
87. Katz WA: Cyclooxygenase-2-selective inhibitors in the management of
88. Mercadante S, Sapio M, Caligara M, Serrata R, Dardanoni G, Barresi L:
14:15–20
89. Trujillo KA, Akil H: Inhibition of morphine tolerance and dependence by
the NMDA receptor antagonist MK-801. Science 1991; 251:85–7
90. Clark JL, Kalan GE: Effective treatment of severe cancer pain of the head
using low-dose ketamine in an opioid-tolerant patient. J Pain Symptom Manage
1995; 10:310 – 4
91. Segal IS, Jarvis DJ, Duncan SR, White PF, Maze M: Clinical efficacy of
oral-transdermal clonidine combinations during the perioperative period. ANESTHESIOLOGY 1991; 74:220 –5


may be considered for heroin addicts and methadone-maintained patients. A methadone loading dose that approaches the patient’s daily baseline dose or a minimum of 0.5 mg/kg may be given either before or during induction of anesthesia.

### 3. Intraoperative Period

After induction of general anesthesia, supplemental intravenous doses of fentanyl, hydromorphone, or morphine are titrated as needed to augment intraoperative anesthesia and to treat surgical pain. The total intraoperative dose is liberal, generally 30–100% greater than that administered to naive patients. Patients treated with methadone may be given additional intraoperative doses (0.1 mg/kg) titrated in response to hemodynamic and pulmonary responses.

### 4. Intravenous PCA

Before initiating intravenous PCA, an additional loading dose of opioid may be required. Typical loading doses include morphine (5–20 mg), hydromorphone (2–5 mg), oxymorphone (1–2 mg), fentanyl (100–250 µg), or sufentanil (25–75 µg). The PCA device may be programmed to administer intermittent bolus doses of 3–5 mg morphine, 0.5–1 mg hydromorphone, 50–100 µg fentanyl, or 10–20 µg sufentanil with a lockout interval ranging from 6 to 10 min. A basal opioid infusion is added to cover baseline requirements in patients who cannot take their daily dose of oral opioid. A baseline oral opioid dose is converted to an equianalgesic intravenous dose, which is then administered as a basal infusion hourly over a 24-h period. For example, if the patient’s daily requirement for morphine is 60 mg, that dose is divided by 3 to compensate for the higher bioavailability of intravenous morphine, and the resulting 20 mg is administered as a basal morphine infusion of 0.8 mg/h.

### 5. Epidural Analgesia

Patients receiving epidural infusions or patient-controlled epidural analgesia may be given an opioid loading dose of 50–75 µg sufentanil, 100–200 µg fentanyl, 2–3 mg hydromorphone, or 8–12 mg morphine. In our practice, loading doses are mixed with local anesthetic (0.25–0.5% bupivacaine or 0.25–0.75% levobupivacaine) and generally administered before surgical incision. An epidural infusion is then initiated either in the operating room or in the PACU. Infusate concentrations for morphine range from 75 to 150 µg/ml or higher, depending on the magnitude of opioid tolerance. Concentrations for other opioids range as follows: hydromorphone, 20–60 µg/ml; fentanyl, 10–50 µg/ml; and sufentanil, 5–10 µg/ml. Epidural infusion rates, bolus dose, and lockout intervals for patient-controlled epidural analgesia vary at different institutions, however, the following settings may be considered: infusion rates ranging from 6 to 12 ml/h, and patient and controlled bolus doses ranging from 2 to 4 ml every 15 min for morphine, every 6–12 min for hydromorphone, and every 6–8 min for fentanyl and sufentanil. Unless contraindicated, local anesthetics, including 0.05–0.1% bupivacaine, 0.05–0.1% levobupivacaine, and 0.1–0.2% ropivacaine, may be added to the epidural infusate to augment opioid-based analgesia.

### 6. Intrathecal Analgesia

Single-dose intrathecal analgesia may be complicated by administering preservative-free morphine (0.5–2 mg Duromorp [Elkins-Sinn, Cherry Hill, NJ]) either alone or added to the spinal local anesthetic. Most patients experience 8–20 h of effective pain relief and are less likely than opioid-naive patients to experience clinically significant respiratory depression or severe itching or nausea and vomiting. For patients receiving continuous intrathecal analgesia, a standard 20-gauge epidural catheter or those developed for subarachnoid use is inserted 2 cm beyond the dura. A local anesthetic (0.1% bupivacaine) and an opioid analgesic (up to 10–30 µg/ml fentanyl or 50–100 µg/ml morphine) are infused intrathecally at a rate of 2–3 ml/h. Intravenous and oral

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Appendix: Dosing Recommendations for Perioperative Analgesia**

### 1. Day of Surgery

The patient should be instructed to take his or her morning dose of oral opioid before leaving for the hospital. The patient should not remove transdermal fentanyl patches but can replace them. Patients who are unable to take baseline opioids (heroin addicts, accident victims, or patients who forget to take prescribed analgesics) may be provided equianalgesic loading with intravenous doses of morphine, hydromorphone, or methadone.

### 2. Preinduction Period

After placement of a peripheral intravenous line, parenteral doses of fentanyl, morphine, or hydromorphone 25–50% higher than typically used in opioid-naive patients may be administered for sedation before induction of general or regional anesthesia. Intravenous methadone

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* Summarizing information gathered from case reports, reviews, suggestions provided by pain management specialists at major medical centers, and our experience caring for opioid-dependent patients.

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opioids are coadministered for breakthrough surgical pain and to maintain baseline plasma concentrations of opioid. It is preferable to tunnel all subarachnoid catheters to minimize the risk of infection. The potential for spinal headache exists; however, many such patients remain in bed for a longer period of time and are not troubled by this adverse effect.

8. Neural Blockade
For patients recovering from regional anesthesia with indwelling 20-gauge polyethylene catheters, a continuous neural infusion is initiated in the PACU with 0.125–0.25% bupivacaine. The initial anesthetic block is allowed to regress to the point that motor or position sense returns but never to the point that the patient experiences discomfort. Intravenous PCA is also initiated in the PACU for breakthrough pain. Again, PCA doses of morphine or hydromorphone are generally one to three times higher than amounts used for nondependent patients.

9. Adjunctive Analgesics
Nonopioid analgesics may be administered to augment postoperative analgesia and reduce opioid dose requirements. Intraoperative doses of 0.05 mg/kg ketamine provide NMDA receptor blockade and postoperative opioid sparing. Nonselective nonsteroidal antiinflammatory drugs and cyclooxgenase-2 inhibitors (50 mg oral rofecoxib solution daily or 400 mg celecoxib followed by 200 mg daily) offer safe antiinflammatory, analgesic, and opioid-sparing effects and may be used to supplement intravenous and epidural PCA and regional analgesia. Additional analgesic augmentation may be gained by applying transdermal clonidine patch (0.1 mg/h). Patients with neuropathic pain may experience a reduction in symptoms and opioid sparing after administration of 300–900 mg gabapentin three times daily and tricyclic antidepressants such as 25 mg desipramine or 25–50 mg trazodone taken at bedtime.
Recent Advances in Postoperative Pain Management

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Good pain control after surgery is important to prevent negative outcomes such as tachycardia, hypertension, myocardial ischemia, decrease in alveolar ventilation, and poor wound healing. Exacerbations of acute pain can lead to neural sensitization and release of mediators both peripherally and centrally. Clinical wind up occurs from the processes of N-Methyl D-Aspartate (NMDA\textsuperscript{†}) activation, wind up central sensitization, long-term potentiation of pain (LTP), and transcription-dependent sensitization. Advances in the knowledge of molecular mechanisms have led to the development of multimodal analgesia and new pharmaceutical products to treat postoperative pain. The new pharmacological products to treat postoperative pain include extended-release epidural morphine and analgesic adjuvants such as capsaicin, ketamine, gabapentin, pregabalin dexametomidine, and tapentadol. Newer postoperative patient-controlled analgesia (PCA) in modes such as intranasal, regional, transdermal, and pulmonary presents another interesting avenue of development.

Proper pain relief is a major concern and area of focus in the United States today. Pre-operatively, one of the most common questions asked by patients pertains to the amount of pain they will experience after the surgery. Pain is also one of the primary concerns of the surgeon because of its close ties with clinical outcome and acute postoperative patient well-being. Studies have indicated such negative clinical outcomes to include decreases in vital capacity and alveolar ventilation, pneumonia, tachycar-

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\textsuperscript{†}Abbreviations: NMDA, N-Methyl D-Aspartate; LTP, long-term potentiation; PCA, patient-controlled analgesia; BK, bradykinin; 5HT, 5 hydroxytryptamin; CGRP, calcitonin gene-related protein; AMPA, amino-3-hydroxyl-5-methyl-4-propionic acid; KAR, Kainate; EPSP, excitatory postsynaptic potentials; NO, nitric oxide; SO, superoxides; NK1, neurokinin receptor; COX-2, cyclooxygenase 2; EREM, extended-release epidural morphine; fentanyl ITS, fentanyl hydrochloride iontophoretic transdermal system; FDA, U.S. Food and Drug Administration; IV, intravenous; MAOI, monoamine oxidase inhibitors; PCRA, patient-controlled regional analgesia; RM, ropivacaine/morphine; RMK, ropivacaine/morphine/ketorolac; IN, intranasal; PCINA, patient-controlled intranasal analgesia; NNT, number-needed-to-treat; IA, intraarticular.

Keywords: opioids, acute pain, pain mechanisms, postoperative, patient-controlled analgesia

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dia, hypertension, myocardial ischemia, myocardial infarction, transition to chronic pain, poor wound healing, and insomnia [1,2,3].

Pain has been found to be one of the three most common medical causes of delayed discharge after ambulatory surgery, the other two being drowsiness and nausea/vomiting. Despite this overwhelming rationale for effective postoperative pain control, the clinical reality is, unfortunately, still far from satisfactory. As a recent editorial title suggests, we have a long way to go to achieve satisfactory postoperative pain control [3]. In an often-cited study [4] that assessed patients’ postoperative pain experience and the status of acute pain management in a random sample, approximately 80 percent of patients said they experienced acute pain after surgery. The authors concluded that despite an increased focus on pain management programs and the development of new standards for pain management, many patients continue to experience intense pain after surgery.

During the last couple of decades and especially the last few years, major technological breakthroughs that have the potential to significantly advance the field of postoperative analgesia have occurred and are still underway. This article discusses some of the more important of these recent advances. We focus on the developments particularly over the last five years.

There are several strands of development that overlap, and it is difficult to do justice to this burgeoning area within the scope and limits of this article. This review will outline the main directions of this development and dwell upon a few selected recent ones in some detail.

The recent advances in postoperative pain management can be loosely grouped in the following areas:

- Molecular Mechanisms
- Pharmaceutical products
- Routes and modes of delivery
- Other modes of analgesia
- Organizational and procedural aspects

MOLECULAR MECHANISMS

It is important to know about the recent advances in central sensitization since it plays an important role in post surgical and post traumatic pain [5,6]. Postoperative pain is mostly nociceptive, which is pain perception following surgical insult.

However, there can be exacerbation of acute nociceptive pain leading to neural sensitization when sensations that are not normally painful are perceived as painful, as in hyperalgesia and allodynia. Mechanical allodynia occurs due to the release of several primary and secondary noxious sensitizers such as PGEs, leukotrienes [7], bradykinin (BK), histamine, and 5 hydroxytryptamine (5HT). These conditions are commonly seen in those patients developing neuropathic pain. Primary hyperalgesia occurs when there is sensitization of peripheral nociceptors, while secondary hyperalgesia is associated with the sensitization of the spinal cord and the central nervous system.

In peripheral sensitization, there is a release of primary mediators such as prostaglandins, 5 hydroxytryptamine, leukotrienes, and bradykinins. These primary mediators stimulate the release of peptides such as calcitonin gene-related protein (CGRP) [8], substance P [9], and cholecystokinin [10] at the site of injury. Histamine-induced vasodilatation, nerve growth factor release, and reflex sympathetic efferent release of norepinephrine are other processes related with peripheral sensitization.

Impulses from the peripheral nociceptors travel via A delta and C fibers to synapse in the lamina II and lamina V of the spinal cord. C fibers also synapse in the lamina I of the spinal cord.

The second order neurons of the spinal cord are of two types: the first, in lamina I, responds to impulses from the C fibers; the second is the wide dynamic range neuron located in lamina V that responds to both noxious and non noxious stimuli. Neurotransmitters such as glutamate and aspartate present in lamina V produce fast synaptic transmission. They do so by binding and activating amino-3-hydroxyl-5-methyl-4-propionic acid (AMPA) and
Kainate (KAR) receptors that regulate Na+ and K+ ion influx. AMPA and KAR are almost impervious to Ca++ ions. Once the AMPA and KAR receptors are activated, they start the priming of NMDA, which is voltage mediated [11].

**NMDA receptor and central sensitization**

NMDA is a membrane protein that regulates the flow of Na+ and Ca++ into the cell and the outflow of K+ outside the cell by an ion channel present intrinsically. The NMDA receptor is made up of four subunits: two NR1, one NR2A, and one NR2B. Each of these has a cytoplasmic portion outside the cytoplasm that can be allosterically modified by zinc ions.

NMDA receptors require ligand binding with glutamate and aspartate and AMPA-induced membrane depolarization and a positive change in the voltage inside the cell. This makes NMDA receptors ligand dependent and voltage gated. Activated AMPA receptors produce a depolarization that dislodges a magnesium plug from the ion channel of the NMDA receptor. The removal of the magnesium plug initiates the entry of calcium ions into the neuronal. Direct action of glutamate at the glutamate binding site further sensitizes the channel [12].

As intracellular calcium accumulates, a chain of neurochemical and neurophysiologic changes leads to the rapid and independent firing of spinal neurons without stimulation. This process is termed as “wind up,” which is the excitation of the dorsal horn neurons not dependent on transcription of specific genes.

**Long-term potentiation of pain**

Clinical hyperalgesia occurs from the processes of NMDA activation, wind up, and central sensitization [13]. Central sensitization can occur in the spinal cord as well as in the supraspinal regions of the central nervous system, such as anterior cingulate gyrus, amygdale, and rostroventral medulla. Activation of the NMDA in the spinal cord and the supraspinal areas and increased neuronal calcium ion (Ca+++) influx lead to wind up and early LTP [14] of pain that is transcription independent in the induction phase. Long-term potentiation of pain increases the excitatory postsynaptic potentials (EPSP) involved in chronic pain.

**Transcription-independent and transcription-dependent central sensitization**

Central sensitization can be transcription dependent and transcription independent. Both activation of NMDA wind up and early LTP of pain are transcription-independent processes. There is increasing pain with each repetitive stimulation [15]. The transcription-independent process is heterosynaptic central sensitization, in which low threshold A Beta input elicit responses after C fiber conditioning. Wind up and early LTP are reversible processes.

Transcription-dependent sensitization occurs in prolonged noxious facilitation leading to the activation of genes, mRNA transcription, and subsequent translation into modified proteins. Excitotoxicity occurs from increased influx of Ca++ with resultant increase in prostaglandins PGE, nitric oxide (NO), and superoxides (SO). Transcription-dependent sensitization affects the spinal cord and other areas within the central nervous system. It is now thought that transcription-dependent sensitization is mediated by inflammation and related alterations in the dorsal root ganglion, the dorsal horn, and irreversible structural modifications in the central nervous system [16]. Transcription-dependent sensitization can take two forms: activity independent localized form, which includes the late phase of LTP, and the activity independent widespread form. Late phase LTP has been studied mainly in the hippocampus and other cortical areas [11].

**Common mechanisms of pain and memory**

It has been seen that the neurokinin receptor (NK1) and cyclooxygenase 2 (COX-2) are involved in central sensitization. The genes for Dynorphin and NK1 have been seen to be upregulated in the spinal cord, and widespread COX-2 has been seen to be upregulated in many areas of the central
nervous system by pain facilitation [11]. However, NK1 and COX2, which are involved in central sensitization, are not involved in hippocampal LTP. It is also known that NMDA receptors, essential for activity dependent central sensitization, also are necessary for the initiation of LTP, which has a role in the consolidation of memory. The common mechanisms in hippocampal early phase LTP and central sensitization are phosphorylation of synaptic receptors and the insertion of AMPA receptors into the post-synaptic membrane. There is only synaptic strengthening in hippocampal LTP, while central sensitization also can cause neuronal network changes and other cellular mechanisms. It is necessary then to avoid the interruption of memory formation and cortical function while treating central sensitization since the process of LTP is present in central sensitization as well as in memory mechanisms in the cortex [11].

Advances in knowledge of the molecular mechanisms of pain have led to development of multimodal analgesia and new pharmaceutical products to treat pain. We will highlight the important recent advances in pharmaceutical products and the routes through which they can be given, as well as important non-pharmacological advances in pain control that are useful for health care personnel treating postoperative pain. Non-pharmacological advances in analgesia are exemplified by application of acupuncture, and related therapies for postoperative pain control will be discussed. In addition, drug tolerance in patients with illicit drug use or a history of taking high doses of pain prescription medications prior to admission are making postoperative pain management a challenge and warrants discussion as well.

ADVANCES IN PHARMACEUTICAL PRODUCTS

The two most important new products are extended-action epidural morphine and iontophoretic transdermal fentanyl. Others include the use of various non-analgesic substances as adjuvants, major examples being ketamine and some anticonvulsants (notably gabapentin). There is also a renewed interest in judicious use of cyclooxygenase inhibitors (coxibs). Long-acting preparations of local anesthetics constitute another area of ongoing research.

Newer PCA in modes such as intranasal, regional, transdermal, and pulmonary presents an interesting avenue of development.

Multimodal analgesia

The concept of multimodal analgesia first proposed about 15 years ago is now quite well established in clinical practice. For example, non-steroidal anti-inflammatory medications combined with intravenous patient-controlled morphine administration may decrease nausea and sedation in patients when compared with those using patient-controlled morphine alone [17]. Different classes of analgesics using different routes of administration such as intravenous and epidural are used to produce fewer side effects of sedation, nausea, vomiting pruritis, constipation, and improved pain relief. Multimodal analgesia also can produce opioid sparing. Other studies have shown, however, that multimodal analgesia may not improve postoperative outcome significantly. Faster recovery, reduced hospital stay, and decreased length of convalescence can occur if multimodal analgesia is combined with a rehabilitation program that is multidisciplinary and multimodal [18]. The development of newer agents available for postoperative pain control opens up possibilities for newer combinations in multimodal analgesia.

Extended-release epidural morphine

The goal of current postoperative pain research and development is to find a medication that can work locally to give long-lasting pain relief at the site of surgical focus. The new drug, a single-dose, extended-release epidural morphine (EREM) called DepoDur™, may be a step toward this analgesic goal. When clinically applicable, the use of DepoDur™ has been found to have a duration of action up to 48 hours [19,20] with long-lasting analgesia in the absence of large systemic concentrations of opioids as well as better patient activity levels.
EREM is formulated for a one-time dose, given epidurally at the lumbar level. DepoDur™ has been evaluated in such surgeries as knee arthroplasty and cesarean section. Several studies have shown that EREM produces long-term pain relief [8-10].

Side effects of EREM have been treated with opioid antagonists. Twelve to 12.5 percent of patients who received EREM required opioid antagonists [19,20]. It has been stated that pruritis [19] and respiratory depression [20] were the primary causes for antagonist administration. The elderly are particularly sensitive to the effects of EREM and require close perioperative monitoring. It was shown that the elderly treated with 15 mg of EREM had equivalent fentanyl usage as younger patients treated with 20 mg of EREM [21]. Attentive perioperative monitoring is needed for elderly patients.

Fentanyl iontophoretic transdermal system

Although PCA has demonstrated efficacy and patient satisfaction, current techniques using intravenous (IV) administration present limitations, including the risk of programming errors and the potential to limit patient mobility due to pumps, lines, and tubing. The patient-controlled fentanyl hydrochloride iontophoretic transdermal system (fentanyl ITS) was designed to address these concerns [22]. Fentanyl ITS is an innovative, needle-free, self-contained, pre-programmed drug-delivery system that uses iontophoretic technology to deliver fentanyl through the skin by application of a low-intensity electrical field [23,24,25]. It has not been approved by the U.S. Food and Drug Administration (FDA) for current clinical use; however, clinical studies have been conducted on human subjects to evaluate it for efficacy, safety, and tolerability.

Efficacy of fentanyl ITS

The efficacy of fentanyl ITS in treating acute postoperative pain was first established in three phase 3 double-blind placebo-controlled clinical trials [26,27]. More importantly, fentanyl ITS now has been demonstrated to have efficacy and safety equivalent to morphine IV-PCA in four randomized controlled trials [28,18], a subgroup analysis [29], and a meta-analysis [30]. It is thought that 40 percent of the administered dose is absorbed in the first hour of treatment and the system reaches 100 percent efficacy in 100 hours.

Panchal et al. [31] evaluated the incidence of analgesic gaps resulting from system-related events (SREs) for patients using the fentanyl ITS vs. morphine IV PCA for postoperative pain management. Fentanyl ITS was associated with a significantly lower incidence of analgesic gaps than morphine IV PCA.

Safety and tolerability of fentanyl ITS

The safety and tolerability of fentanyl ITS have been found to be acceptable by several studies and pooled data analysis [32]. Adverse events associated with fentanyl ITS are similar to those reported with IV opioid administration, including nausea, vomiting, pruritis, headache, and mild-to-moderate dizziness. Nausea was the most common adverse event, with the incidence ranging between 26.6 percent and 67.5 percent [27,28,33].

Disadvantages

As with all transdermal systems, skin hypersensitivity, skin redness, and hyperpigmentation are potential problems. The system has not been adequately studied in children. It should be used with extreme caution for in-patients with severe hepatic dysfunction, head injuries, sleep apnea, and impending respiratory failure and in patients with increased intracranial pressure of any etiology.

The system lacks programmability and a basal infusion rate that may be important in opioid-dependent and opioid-tolerant patients. The number and timing of attempts by the patient also cannot be determined. The system has to be disposed only after disassembly by the pharmacist. The most important disadvantage at the current time is the availability of fentanyl ITS, since it is not currently being produced due to techni-
cal problems. Perhaps technological modifications, including recording the number and timing of the attempts and the addition of a basal rate, may make it more advantageous in the future.

**ANALGESIC ADJUVANTS**

Adjuvants are compounds, which by themselves have undesirable side effects or low potency but in combination with opioids allow a reduction of narcotic dosing for postoperative pain control. Adjuvants are needed for postoperative pain management due to side effects of opioid analgesics, which hinder recovery, especially in the increasingly utilized ambulatory surgical procedures [34]. Multiple adjuvants recently have been developed for the control of pain.

**Capsaicin**

Capsaicin (8-methyl-N-vanillyl-6-nonenamide) is a non narcotic and acts peripherally. It acts as a TRPV-1 agonist [35]. TRPV1 is a receptor that is markedly reduced in inflammatory conditions and is present on unmyelinated C fiber endings in the periphery. The activation of the TRPV receptors releases high intensity impulses and releases substance P, which results in the initial phase of burning. Continued release of substance P in the presence of capsaicin leads to the depletion of capsaicin and a subsequent decrease in C fiber activation. It is important to remember that capsaicin does not produce significant effects on the A delta and A alpha fibers and does not affect the temperature and touch sensations.

It can be used as a cream and also as an injectable analgesic. It is not an FDA approved product but is currently in Phase 3 trials for postoperative pain control, arthritis, musculoskeletal pain, and chronic neuropathic pain. Capsaicin is present in high concentration in the seeds and stem of chili peppers. It is an alkaloid.

Capsaicin cream contains capsaicin that is usually combined with narcotic analgesics and NSAIDS to relieve a variety of painful ailments such as back pain, arthritic joint pains, and strains and sprains. Capsaicin cream is also used in higher concentrations for the treatment of the neuropathic pain of post herpetic neuralgia. It can be used in the elderly as an adjuvant, as it is thought to have opioid sparing effects. This can be particularly beneficial for the elderly who are sensitive to respiratory depression that can occur with opioids.

Injectable capsaicin is used for the control of post operative pain, such as after total knee replacement, total hip replacement, hernia repair [36], shoulder arthroscopy, and bunionectomy. It also has uses in more long-term pain such as that due to interdigital neuromas, osteoarthritis of the knee, and neuropathic pain occurring after surgery or trauma. Pre-administration of neural blockade before injection of capsaicin may greatly decrease the burning discomfort.

Capsaicin appears to be a relatively safe drug with the only absolute contraindication being patient hypersensitivity. Relative contraindications include age less than 2 years, patients with elevated liver enzymes, patients on ACE inhibitors, and patients showing signs of septic arthritis and joint infections.

**Ketamine**

NMDA receptor antagonists, and specifically ketamine commonly used in clinical practice, have been used in perioperative pain management. Routes of administration include intravenous, subcutaneous, epidural, transdermal, and intra-articular. At low sub anesthetic doses (0.15–1 mg/kg), ketamine exerts a specific NMDA blockade and, hence, modulates central sensitization induced both by the incision and tissue damage and by perioperative analgesics such as opioids.

There has been a renewed interest in the use of sub-anesthetic doses of ketamine as an adjunct to provide postoperative pain relief in opioid-dependent patients [37]. There is a definite role of ketamine in preventing opioid-induced hyperalgesia in patients receiving high doses of opioid for their postoperative pain relief [38]. However, clinical use of ketamine can be limited due to psychotomimetic adverse effects such as hallucinations and bad dreams.
Other common adverse effects are dizziness, blurred vision, and nausea and vomiting [39].

**Gabapentin and pregabalin**

Gabapentin is an anti-epileptic drug that has demonstrated analgesic effect in diabetic neuropathy, post-herpetic neuralgia, and neuropathic pain. Gabapentin does not bind to GABA A or GABA B receptor but to the alpha-2 delta subunit of the presynaptic voltage gated-calcium channels responsible for the inhibition of the calcium influx. The inhibition of calcium release then prevents the release of excitatory neurotransmitters involved in the pain pathways. Most of the studies of gabapentin (and occasionally its structural analog pregabalin) in the perioperative setting have been published in the last three to four years, and several systematic reviews on the subject are available [31,39].

Most of the reviews and meta-analyses concur that perioperative gabapentin helps to produce a significant opioid-sparing effect and probably also improves postoperative pain score relative to the control group [40]. Tiippana et al. [41] found that the opioid-sparing effect during the first 24 hours after a single 300 to 1,200 mg dose of gabapentin, administered one to two hours preoperatively, ranged from 20 percent to 62 percent. Gabapentin and similar drugs seem to have a strong potential for perioperative use as an analgesic adjuvant and anti-hyperalgesic agent when used in conjunction with opioids.

**Pregabalin**

Recent years also have witnessed a heightened research interest in the analgesic, sedative, anxiolytic, and opioid-sparing effects of pregabalin (S+3-isobutyl GABA), a structural analog of GABA and a derivative of gabapentin, in various pain settings, including postoperative pain. Its mechanism of action is thought to be probably similar to that of gabapentin but has a superior pharmacokinetic profile [42]. Pregabalin has an established efficacy of varying degree in neuropathic pain conditions such as postherpetic neuralgia, painful diabetic neuropathy, central neuropathic pain, and fibromyalgia. While some studies do not demonstrate a significant analgesic effect in the acute, including postoperative, pain scenario [43], other studies suggest pregabalin to have effective sedative [44] and opioid-sparing effects [45,46], useful characteristics for the control of acute pain. Research on its established role as an analgesic adjuvant as a part of multimodal analgesia for acute pain control is ongoing. Opioid sparing effects and improved pain scores have been seen after abdominal and pelvic surgery. Its many potential actions such as reducing opioid requirements, prevention and reduction of opioid tolerance, improvement of the quality of opioid analgesia, decreased respiratory depression, relief of anxiety, and gastric sparing make it an attractive drug to consider for control of pain in the postoperative period [47].

**Dexmedetomidine**

Dexmedetomidine is a relatively new, highly selective central alpha2 agonist. Its sedative, pro-anesthetic, and pro-analgesic effects at 0.5-2 micrograms/kg given intravenously stem mainly from its ability to blunt the central sympathetic response by as yet unknown mechanism(s). It also minimizes opioid-induced muscle rigidity, lessens postoperative shivering, causes minimal respiratory depression, and has hemodynamic stabilizing effects. Dexmedetomidine, when used as an adjunct, can reduce postoperative morphine consumption in various surgical settings using various routes such as intravenous [48,49]. A recent study has shown the analgesic efficacy of dexmedetomidine in postoperative pain relief. The authors of this study found that the addition of dexmedetomidine to IV PCA morphine resulted in superior analgesia, significant morphine sparing, and less morphine-induced nausea, while it was devoid of additional sedation and untoward hemodynamic changes [49].

**OTHER RECENT ADVANCES IN PERIOPERATIVE PHARMACOTHERAPY**

**Local anesthetics**

To effectively respond to the issue of sending the ambulatory patient home in a pain-
freestate, one has to have methods to provide several days of effective and safe relief of moderate to severe pain for the unmonitored patients at home. It is clear that local anesthetic techniques, particularly peripheral nerve blockade, will be one of the cornerstones of postoperative pain management [50].

There are basically two overarching approaches for prolongation of local anesthetic action. One is the use of novel delivery techniques for existing drugs. In an endeavor to “make old drugs new” [51], liposome or polymer encapsulation of local anesthetics are being formulated. The second approach is the development of novel, extremely long-acting local anesthetics.

Liposomes are microscopic phospholipid-bilayered vesicles that are biocompatible, biodegradable, and non-immunogenic. Recently, substantial interest has been shown in developing drug delivery systems utilizing nanoparticles, micro-particles composed of biodegradable polymers. They have some advantages over liposomes in terms of stability both during storage and in vivo.

To date, many local anesthetics (most commonly bupivacaine, but also mepivacaine, ropivacaine, lidocaine, prilocaine, etc.) have been loaded in liposomes or polymer microspheres [52,36]. It is hoped that in the near future, some of these formulations will become a part of the pain clinician’s armamentarium. However, the road toward achieving this goal may be long and winding, due to problems of these drug delivery systems, such as shelf life, aggregation, leakage, and toxicity [53].

Renewed interest in NSAIDs and coxibs and acetaminophen

A recent review highlights current advances in our understanding of the role perioperative NSAIDs have on modulating nociception, their benefits when utilized as components of a multimodal analgesic regimen, and potential deleterious cardiovascular and estrogenic effects. Recent research indicates that, in addition to peripheral blockade of prostaglandin synthesis, central inhibition of cyclooxygenase-2 may play an important role in modulating nociception. Although nonspecific NSAIDs provide analgesic efficacy similar to coxibs, their use has been limited in the perioperative setting because of platelet dysfunction and gastrointestinal toxicity. Coxibs may be a safer alternative in that setting. Both coxibs and traditional NSAIDs may contribute to a dose-dependent increase in cardiovascular toxicity and impaired osteogenesis. When used short term at the lowest effective dose, however, NSAIDs may provide for analgesic benefit without significant toxicity.

The potential benefits of coxibs include [18] improved quality of analgesia; reduced incidence of GI side effects vs. conventional NSAIDs; and no platelet inhibition. Acetaminophen is antipyretic and analgesic but has little, if any, anti-inflammatory action. Its analgesic efficacy is not more than that of traditional analgesics; however, it has fewer side effects. The mechanism of action has been debated. In animal models, it has been seen to inhibit COX-3. At the spinal cord level, it has been shown to antagonize neurotransmission by NMDA, substance P, and nitric oxide pathways. Preparation of intravenous (IV) acetaminophen recently has been released in the United Kingdom and Europe (Perfalgan®, Bristol Meyers Squibb, New York). It is dissolved in mannitol and pH-buffered by disodium phosphate, with cysteine added as an anti-oxidant. A 100 ml solution is presented as 10 mg/ml for administration over a period of 15 minutes. The onset of action is within five to 10 minutes, with the peak at one to two hours. Optimal analgesia for moderate to severe postoperative pain cannot be achieved using a single agent alone, but a balanced approach in combination with non-steroidal agents can result in up to a 40 to 50 percent reduction in opioid requirements. IV propacetamol (1 g), a prodrug of acetaminophen, has been shown to be as efficacious as intramuscular morphine (10 mg) following dental extractions [54] and as effective as intramuscular ketorolac (30 mg) following lower limb arthroplasty [55]. With its inherent safety and demonstrated efficacy, IV acetaminophen can prove to be an asset in managing perioperative pain, especially of mild to moderate severity.
Other agents

Other non-opioid analgesic adjuvants include clonidine, neostigmine, tapentadol, and, recently, adenosine [56], though further research is necessary to establish their clinical efficacy. Of these, the use of low doses of clonidine proved to be a useful adjunct analgesic when given neuraxially and in combination with peripheral nerve blocks. Data about the systemic administration of clonidine could support the usefulness of low-dose IV administration [57].

Tapentadol

Combination analgesics that have moderate opioid efficacy and central adrenergic analgesic effects (e.g., tapentadol) have been found to provide analgesic effects similar to more potent opioids but with a lower adverse event profile. Recently, tapentadol has been approved in the United States as immediate release oral preparations of 50 mg, 75 mg, and 100 mg (Nucynta®, Johnson & Johnson) to be used every four to six hours, depending on pain intensity, with a maximum daily dose of 600 to 700 mg. Tapentadol was approved by the FDA in November 2008 for the treatment of moderate to severe pain in patients 18 years or older. Tapentadol is a centrally acting analgesic with a unique dual mode of action as an agonist at the μ-opioid receptor and as a norepinephrine reuptake inhibitor [58,59].

Tapentadol has an 18-fold affinity for the μ opioid receptor in humans as compared to morphine but is about two- to three-fold less potent than morphine, most likely because it is a norepinephrine reuptake inhibitor. It has improved gastrointestinal tolerability when compared to classical opioids. The dose of tapentadol does not have to be adjusted in the presence of renal impairment. Hepatotoxicity has not been reported.

The incidence of nausea and vomiting has been seen to be lower in patients taking tapentadol as compared to patients taking oxycodone immediate release [44,60]. Tapentadol has been useful for postoperative pain after bunionectomy. Significant pain relief was obtained 32 to 46 minutes after surgery [61].

Tapentadol’s two mechanisms of actions also may lend it opioid-sparing effects while maintaining adequate analgesia. Tapentadol is considered to have a potency between tramadol and morphine, with equivalent potency to that of opioids such as hydrocodone and oxycodone. The role of an oral preparation has inherent limitations in the acute postoperative period, but some recent data have shown its efficacy in dental surgery [62] and bunionectomy.

Tapentadol is contraindicated in patients with severe bronchial asthma, paralytic ileus, and in patients taking monoamine oxidase inhibitors (MAOI). Serotonin syndrome can develop with the use of tapentadol, and it should not be combined with serotonergic drugs such as selective serotonin reuptake inhibitor, selective norepinephrine reuptake inhibitor, tryptans, or tricyclic antidepressants, which can cause serotonin syndrome. Serotonin syndrome can include mental status changes such as hallucinations, coma, autonomic instability such as tachycardia, hyperthermia, and neuromuscular abnormalities such as hyperreflexia and incoordination.

ACUPUNCTURE FOR POSTOPERATIVE ANALGESIA

The term acupuncture describes a family of procedures involving the stimulation of anatomical points on the body using a variety of techniques. Acupuncture theory is based on two conditions: “yin,” which is considered feminine, passive, dark, and cold, and “yang,” which is masculine, aggressive, bright, and hot, as well as “qi,” which is considered the vital energy that flows and cycles throughout the body. The acupuncture theory is to harmonize any imbalance in yin-yang and qi in a human body to restore the body to a healthy condition. Acupuncture is thought to unblock any obstruction to the flow of qi and, thereby, relieves pain. The acupuncture technique that has been most often studied scientifically involves penetrating the skin with thin, solid, metallic needles that are manipulated by the hands or electrical stimulation.

Acupuncture has been used to treat a variety of conditions such as chronic lower
back pain, chronic neck and shoulder pain, osteoarthritis of the knee, migraine headache, dysmenorrhea, labor pains, and acute post operative pain.

Sun et al. [63] conducted a systematic review to quantitatively evaluate the efficacy of acupuncture and related techniques as adjunct analgesics for acute postoperative pain management. The authors concluded that perioperative acupuncture might be a useful adjunct for acute postoperative pain management. However, there are issues with applicability and generalizability of the procedure [64].

Further, acupuncture is an umbrella term that encompasses several often disparate procedures. This can create confusion in scientific studies and their interpretation. To reduce this confusion, Usichenko et al. [65] focused on randomized controlled trials of only auricular acupuncture (a popular method in which needles are placed in various parts of the earlobe) for postoperative pain control. They identified nine studies of acceptable quality (though none of the best quality), of which eight upheld the superiority of auricular acupuncture over the control conditions. The mechanism of pain relief by auricular acupuncture is not known. The authors concluded that the evidence that auricular acupuncture controls postoperative pain is promising but not compelling. More research of methodologically rigorous design (especially ensuring therapist blindness, which none of the published studies addressed) on larger samples from different centers are needed to reach a definitive conclusion in this regard.

**NEWER PATIENT-CONTROLLED ANALGESIC ROUTES**

**Patient-controlled regional analgesia**

One of the most significant changes in surgical practice during the last two decades has been the growth of ambulatory surgery [66]. Adequate postoperative analgesia is a prerequisite for successful ambulatory surgery. Sending patients home with perineural, incisional, and intra-articular catheters is a new and evolving area of postoperative pain management. Current evidence suggests that these techniques are effective, feasible, and safe in the home environment if appropriate patient selection routines and organization for follow-up are in place [25,66].

Patient-controlled regional analgesia (PCRA) encompasses a variety of techniques that provide effective postoperative pain relief without systemic exposure to opioids [25]. Using PCRA, patients control the application of pre-programmed doses of local anesthetics, most frequently ropivacaine or bupivacaine (occasionally in combination with an opioid), via an indwelling catheter, which can be placed in different regions of the body depending upon the type of surgery. Infusions are controlled either by a staff-programmed electronic pump (similar to that used for IV PCA) or a disposable elastomeric pump. An elastomeric pump is a device that has a distensible bulb inside a protective bulb with a built-in filling port, delivery tube, and bacterial filter [56]. Analgesia can be delivered directly into a surgical incision (incisional PCRA), intra-articular (IA) tissue (IA PCRA), or perineural site (perineural PCRA).

**Incisional PCRA**

Placebo-controlled trials have established the efficacy and safety of incisional PCRA [67]. In an active-comparator trial [68], incisional PCRA with ropivacaine 0.5 percent via an elastomeric PCRA pump provided superior analgesia without major side effects compared with bolus infusion in patients recovering from arthroscopic subacromial decompression.

**Intraarticular (IA) PCRA**

Although IA administration of opioids with or without local anesthetics is established practice for joint anesthesia, studies evaluating IA PCRA are limited, as published data focus primarily on single-dose and continuous modes of IA administration. Vintar et al. [69] conducted a randomized, placebo-controlled trial evaluating the efficacy of ropivacaine/morphine (RM), ropivacaine/morphine/ketorolac (RMK), and saline...
for postoperative pain management following anterior cruciate ligament construction. Patients self-initiated bolus doses of the analgesic mixture or saline solution via Microject PCA pump. While no significant differences in pain scores, side effects, and patient satisfaction were noted among the study groups, patients receiving RMK consumed significantly less rescue morphine per day compared with those receiving RM and placebo (RMK, 8 ± 8 mg; RM, 23 ± 20 mg; placebo, 46 ± 21 mg; p < 0.001).

**Perineural PCRA**

Perineural PCRA allows patients to self-titrate local anesthetic peripheral nerve blocks to achieve comfort. In a randomized, double-blind, placebo-controlled study (Ilfeld et al. [70]), perineural PCRA with ropivacaine 0.2 percent in the interscalene brachial plexus was shown to provide pain control superior to placebo in outpatients after moderately painful orthopedic surgery of the shoulder. On the first postoperative day, patients receiving perineural PCRA with ropivacaine reported significantly reduced pain (P < 0.001), less oral opioid use (P < 0.001), and lower sleep disturbance scores (P = 0.13) compared with patients receiving placebo infusions.

Rawal et al. [71] studied ambulatory patients receiving perineural PCRA into the brachial plexus at home. They have demonstrated that treatment with either ropivacaine 0.125 percent or bupivacaine 125 percent provides effective analgesia without signs and symptoms of local anesthetic toxicity. The incidence of side effects and technical problems was generally low with the most common complaint being numbness of the fingers (6.9 percent of ropivacaine patients and 29.0 percent of bupivacaine patients). On the day after surgery, the percentage of patients who were “satisfied or “very satisfied” was similar in the two groups (79 percent for ropivacaine and 83 percent for bupivacaine, respectively).

A number of studies have demonstrated that perineural PCRA results in equivalent or superior analgesic efficacy with lower total anesthetic consumption compared with continuous infusion in various settings and operations [72].

**Patient-controlled intranasal analgesia (PCINA)**

Intranasal (IN) opioids, either in the form of a dry powder or water or saline solution, are delivered using a syringe, nasal spray or dropper, or nebulized inhaler. In addition to needle-free administration, patient-controlled IN opioid administration (especially fentanyl) bypasses the hepatic first-pass effect and because of the excellent perfusion of the nasal mucosa, displays rapid absorption and rise in plasma concentration [73,74,75].

While evidence suggests that PCINA is efficacious, safe, noninvasive, and easy to administer, there have been only a limited number of small-sampled, randomized, placebo-controlled trials evaluating this route of analgesic administration in the postoperative period [75]. An acceptability study reported that 79 percent of patients receiving PCINA would want to use it again [76].

**Patient-controlled transpulmonary analgesia**

AeroLEF™ (aerosolized liposome-encapsulated Fentanyl; YM Biosciences Inc., Ontario, Canada) is a novel, proprietary inhalation formulation of free and liposome-encapsulated fentanyl intended to provide rapid, extended, and personalized analgesia for patients experiencing acute pain episodes. AeroLEF™ is in development for the treatment of moderate to severe pain, including cancer pain.

In contrast to fixed-dose approaches to opioid delivery, in which a significant titration period is often required to determine the suitable dose for the patient, AeroLEF™ is being developed to offer a simple and non-invasive route of administration, rapid onset of action, sustained effect, and self-titratable dosing for the treatment of acute and breakthrough pain. Using AeroLEF™, patients can identify and select a personalized dose for each pain episode, achieving both rapid onset and extended duration of analgesia. However, it is still a long way from being used in clinical practice.
ADVANCES IN ORGANIZATIONAL ASPECTS OF POSTOPERATIVE PAIN CONTROL

Procedure-specific analgesia

There is a need for the development of an evidence-based approach to reliable, comprehensive, individualized analgesic plans for specific surgical procedures. Although number-needed-to-treat (NNT) of a particular analgesic can give a valuable overview of efficacy, this concept is not necessarily applicable to all types of surgery. They proposed that procedure-specific acute pain management guidelines may be helpful because the pain intensity and its consequences may be procedure-related. Although the intensity of the acute pain state is expected to be related to the magnitude of the operation, this may not necessarily be so. When the size of the injury is considered, dental pain with a smaller injury may be relatively more painful compared with the pain observed in relation to the magnitude of tissue injury after hip replacement. However, the consequences of the injury and pain may be entirely different between these procedures because stress responses and organ dysfunctions resulting from the injury are different. The risk-benefit ratio of different analgesics also may vary according to the surgical procedure. Thus, the clinical effects of opioid sparing (which are variable between analgesics) also may depend on the effects of the surgical injury. Similarly, the risk and clinical implications of postoperative bleeding associated with certain analgesics are also procedure-specific. For example, the inhibition of platelet aggregation and, therefore, the risk of bleeding associated with NSAIDs are more relevant in operations that pose a risk of bleeding (e.g., a tonsillectomy). Therefore, analgesics with no effects on platelet function (e.g., acetaminophen and COX-2 specific inhibitors) may be preferable in these but not in other operations.

Kehlet et al. [77] argued that clinicians need information in which the choice of analgesic technique includes the consideration of the operation and is based on the available evidence from that particular surgical procedure. Such procedure specific guidelines are available from two sources: 1) the U.S. Veteran’s Health Administration, in collaboration with the U.S. Department of Defense and the University of Iowa (www.oqp.med.va.gov/cpg/cpg.htm) [78], and 2) the PROSPECT Working Group (www.postoppain.org), a group of European anesthesiologists and surgeons [79].

CONCLUSION

With the many advances in pain management for the surgical patient, surgeons and pain care providers have myriad choices of analgesic pharmacotherapy and analgesic techniques to choose from to provide adequate postoperative pain control for the surgical patient in the 21st century. However, many factors must be considered before deciding on the type of pain therapy to be provided to the surgical patient. These include the patients’ co-morbid conditions, psychological status, exposure to analgesic therapies, and the type of surgical procedure.

In the future, genetically informed “personalized medicine” may become a reality even for acute pain management. With the recent advent of studies documenting genetic polymorphisms with respect to pain response to morphine [80] and pressure pain sensitivity [81], this exciting possibility looks promising in the near future.

REFERENCES


56. Daniels S, Upmalis D, Okamoto A, Lange C, Häeussler J. A randomized, double-blind, phase III study comparing multiple doses of tapentadol IR, oxycodone IR, and placebo for...


Abstract: A continuous peripheral nerve block—also termed "perineural local anesthetic infusion"—involves the percutaneous insertion of a catheter adjacent to a peripheral nerve, followed by local anesthetic administration via the catheter, providing anesthesia/analgesia for multiple days or even months. Continuous peripheral nerve blocks may be provided in the hospital setting, but the use of portable infusion pumps permits ambulatory application as well. This technique's most common application is providing analgesia following surgical procedures. However, additional indications include treating intractable hiccups; inducing a sympathectomy and vasodilation to increase blood flow following a vascular accident, digit transfer/replantation, or limb salvage; alleviating vasospasm of Raynaud's disease; treating peripheral embolism and chronic pain such as complex regional pain syndrome, phantom limb pain, trigeminal neuralgia, and cancer-induced pain. Following trauma, perineural infusion can provide analgesia during transportation to a distant treatment center, or while simply awaiting surgical repair. Catheter insertion may be accomplished using multiple possible modalities, including nerve stimulation, ultrasound-guidance, paresthesia induction, fluoroscopic imaging, and simple tactile perceptions ("facial click"). Either a nonstimulating epidural-type catheter may be used, or a "stimulating catheter" that delivers electrical current to its tip. Infusates generally include exclusively long-acting, dilute, local anesthetic delivered as either a bolus-only, basal-only, or combination basal-bolus dosing. Documented benefits appear to be dependent upon successfully improving analgesia, and include decreasing baseline/breakthrough/dynamic pain, supplemental analgesic requirements, opioid-related side effects, and sleep disturbances. In some cases patient satisfaction and ambulation/functioning may be improved; an accelerated resumption of passive joint range-of-motion realized; and the time until discharge-readiness as well as actual discharge from the hospital or rehabilitation center realized. Lastly, postoperative joint inflammation and inflammatory markers may be decreased. Nearly all benefits occur during the infusion itself, but several randomized, controlled trials suggest that in several situations there are prolonged benefits following catheter removal as well. Minor complications easily rectified occur somewhat frequently; but major risks including clinically-relevant infection and nerve injury are very rare. This article is an evidence-based review of the published literature involving continuous peripheral nerve blocks.

Suggested Reviewers:
Continuous Peripheral Nerve Blocks: A Review of the Published Evidence

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• Attestation: Brian M. Ilfeld approved the final manuscript

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Short Title: Continuous Peripheral Nerve Blocks: A Review of the Published Evidence
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Parts of this report were previously presented continuously since 2003 when I started giving presentations--this is a review article and therefore covers material that I have presented previously.

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Abstract: A continuous peripheral nerve block—also termed “perineural local anesthetic infusion”—involves the percutaneous insertion of a catheter adjacent to a peripheral nerve, followed by local anesthetic administration via the catheter, providing anesthesia/analgesia for multiple days or even months. Continuous peripheral nerve blocks may be provided in the hospital setting, but the use of portable infusion pumps permits ambulatory application as well. This technique’s most-common application is providing analgesia following surgical procedures. However, additional indications include treating intractable hiccups; inducing a sympathectomy and vasodilation to increase blood flow following a vascular accident, digit transfer/replantation, or limb salvage; alleviating vasospasm of Raynaud’s disease; treating peripheral embolism and chronic pain such as complex regional pain syndrome, phantom limb pain, trigeminal neuralgia, and cancer-induced pain. Following trauma, perineural infusion can provide analgesia during transportation to a distant treatment center, or while simply awaiting surgical repair. Catheter insertion may be accomplished using multiple possible modalities, including nerve stimulation, ultrasound-guidance, paresthesia induction, fluoroscopic imaging, and simple tactile perceptions (“facial click”). Either a nonstimulating epidural-type catheter may be used, or a “stimulating catheter” that delivers electrical current to its
tip. Infusates generally include exclusively long-acting, dilute, local anesthetic delivered as either a bolus-only, basal-only, or combination basal-bolus dosing. Documented benefits appear to be dependent upon successfully improving analgesia, and include decreasing baseline/breakthrough/dynamic pain, supplemental analgesic requirements, opioid-related side effects, and sleep disturbances. In some cases patient satisfaction and ambulation/functioning may be improved; an accelerated resumption of passive joint range-of-motion realized; and the time until discharge-readiness as well as actual discharge from the hospital or rehabilitation center realized. Lastly, postoperative joint inflammation and inflammatory markers may be decreased. Nearly all benefits occur during the infusion itself, but several randomized, controlled trials suggest that in several situations there are prolonged benefits following catheter removal as well. Minor complications easily rectified occur somewhat frequently; but major risks including clinically-relevant infection and nerve injury are very rare. This article is an evidence-based review of the published literature involving continuous peripheral nerve blocks.

**Abstract Word Count:** 332
**Introduction.** Continuous peripheral nerve blocks (CPNB) are relatively simple in concept: a catheter is percutaneously inserted adjacent to a peripheral nerve, followed by local anesthetic administration *via* the catheter (Figure 1). Thus, the terms CPNB and “perineural local anesthetic infusion” are often used synonymously. Using currently-available long-acting local anesthetics, the maximum duration of a single-injection peripheral nerve block is 8-24 hours. Therefore, CPNB provides an alternative option when a prolonged perioperative neural blockade is desired.\textsuperscript{1,2} Since its first description in 1946,\textsuperscript{3} CPNB has evolved from an experimental case report involving a needle inserted through a cork taped to a patient’s chest, to a well-validated analgesic technique accepted by the medical community with products designed solely for its application. This article is an evidence-based review of the published CPNB literature.

**Indications.** The earliest reports of CPNB describe prolonging intraoperative surgical anesthesia\textsuperscript{3,4} and treating intractable hiccups.\textsuperscript{5} Later articles report using CPNB-induced sympathectomy and vasodilation to increase blood flow following a vascular accident,\textsuperscript{6} digit transfer/replantation,\textsuperscript{7,8} or limb salvage;\textsuperscript{9} alleviate the vasospasm of Raynaud's disease;\textsuperscript{10} and treat peripheral embolism.\textsuperscript{11} Following trauma,
CPNB can provide analgesia during transportation to a distant treatment center\textsuperscript{12} or while simply awaiting surgical repair.\textsuperscript{13} Although yet unvalidated, reports describe CPNB to treat chronic pain, such as complex regional pain syndrome,\textsuperscript{14} intractable phantom limb pain,\textsuperscript{15} as well as pain from terminal cancer\textsuperscript{16} and trigeminal neuralgia.\textsuperscript{17} However, the overwhelming majority of CPNB reports involve the perioperative period, and only this application of perineural local anesthetic infusion remains validated with randomized, controlled clinical trials (RCT).\textsuperscript{18}

Since there are intrinsic risks with CPNB, most providers restrict its use to surgical procedures that are expected to result in pain not easily controlled with less-invasive analgesic techniques (e.g., oral analgesics, cooling/heating pads, etc.)\textsuperscript{19} or in patients with an intolerance to alternative analgesics (e.g., opioids-induced nausea).\textsuperscript{20,21} The surgical site dictates the anatomic location of catheter insertion (Table 1). Although not as thoroughly validated as in adults, CPNB has been described in hundreds of pediatric patients.\textsuperscript{14,22-27}

**Catheter Insertion (Nerve Stimulation).** Historically, perineural catheters were inserted using induced paresthesia,\textsuperscript{3} a facial “click”,\textsuperscript{28} or fluoroscopic guidance.\textsuperscript{29} However, following the introduction of portable nerve
stimulators in the 1970s, the overwhelming majority of published CPNB
reports involve this modality. Originally, this technique involved using
electrical current to place an insulated needle adjacent to a peripheral nerve,
followed by injection of local anesthetic and subsequent perineural catheter
insertion. While multiple prospective studies document the possible high
success rate of this procedure, others have found an unacceptably-high
rate of “secondary block” failure, presumably when the catheter tip was
unknowingly misplaced during insertion. To help counter this risk, the
perineural catheter may be first inserted, followed by a local anesthetic bolus
via the catheter itself. However, remaining unknown is whether a
relatively large bolus of concentrated local anesthetic resulting in a
successful nerve block guarantees that the catheter tip is close enough to the
target nerve(s) to provide analgesia during the subsequent infusion with
relatively small volumes of dilute local anesthetic. Regardless, even if
prediction of successful perineural infusion is provided, the identification of
those failed catheters requires waiting at least 15 minutes for block
onset/failure, followed by removal of the catheter/dressing, re-preparation,
and catheter reinsertion—a process requiring a longer period of time than
many practices permit. In addition, a partial block is possible suggesting
the catheter tip is not optimally located, but often precluding replacement using electrical current.

An option is the use of a “stimulating catheter”: electrical current is used with an insulated needle to locate the target nerve(s), followed by the insertion of a perineural catheter that conducts current to its tip.\textsuperscript{19,41,42} If muscle contraction intensity decreases during catheter advancement, it is presumed that the catheter tip is moving away from the target nerve.\textsuperscript{43} This provides real-time evidence of catheter-nerve distance.\textsuperscript{44} There is data to suggest that in the area of the popliteal fossa, using stimulation during catheter advancement results in the catheter tip being placed closer to sciatic nerve.\textsuperscript{45-48} And while there is limited data suggesting a similar improvement for femoral and interscalene catheters,\textsuperscript{43,49,50} the clinical relevance is questionable for these anatomic locations.\textsuperscript{51-56}

Unfortunately, continuous muscle contraction guarantees neither surgical block nor postoperative infusion success.\textsuperscript{43,57-59} In addition, adequate muscle response cannot always be elicited with catheter advancement,\textsuperscript{43,59-64} stimulating catheters take—on average—more time for placement and cost more than their non-stimulating counterparts,\textsuperscript{48,65} leading some to question
their overall benefit.\textsuperscript{66} There is minimal,\textsuperscript{67} if any, benefit of injecting fluid via the needle prior to catheter insertion to “open” the perineural space,\textsuperscript{68} but D\textsubscript{5}W is recommended if a bolus is used.\textsuperscript{69,70} Lastly, few data exist to provide recommendations on the minimal acceptable current resulting in a muscle response.\textsuperscript{71}

The optimal distance to advance a perineural catheter past the needle tip remains unknown; but there is data to suggest that increasing the insertion distance is correlated with an increased the risk of catheter coiling, and possibly the final nerve-to-catheter tip distance.\textsuperscript{36,72-74} Considering the multiple catheter knots reported with insertion greater than 5 cm,\textsuperscript{75-78} and the lack of data suggesting insertion lengths more than 5 cm is beneficial, recommending a maximum insertion of 5 cm appears warranted.\textsuperscript{66} Recently-reported “self-coiling catheters” may render this issue mute in the future if they are found reliable and approved for human use.\textsuperscript{79} Similarly, the optimal minimum insertion distance remains unknown, with evidence that 0-1 cm results in a minimal risk of initial secondary block failure,\textsuperscript{33,80} but possibly an increased risk of subsequent dislodgement.\textsuperscript{81}
Catheter Insertion (Ultrasound). Unfortunately, data from controlled trials involving electrical-stimulation guided catheter insertion—or even ultrasound-guided single-injection blocks—is not automatically applicable to ultrasound-guided catheter insertion for multiple reasons. While the limited length of this review article precludes an in-depth discussion of these issues, the information is available elsewhere. Although multiple relatively large series demonstrate the feasibility of ultrasound-guided catheter insertion, there are currently few RCTs to help guide practice. One study suggests that for infraclavicular catheters, there is little difference in the surgical block resulting from a bolus of local anesthetic injected via the needle prior to catheter insertion compared with the catheter following needle removal. Another RCT demonstrates the difficulty and poorer success rate of inserting a catheter with the longitudinal plane of the needle parallel to the femoral nerve compared with a perpendicular orientation. Lastly, a recent publication suggests that for interscalene catheters, a needle with its long axis parallel to the nerve has distinct benefits compared with a perpendicular needle-to-nerve orientation.

Because of the multiple variables for various blocks/techniques (e.g., bolus via the catheter vs. needle, catheter insertion distance, catheter design, etc.),
applying the results of one study to various practices will most-likely prove
difficult.\textsuperscript{82} For example, the results of the above-mentioned infraclavicular
catheter study will probably not be replicated with a single catheter injection
of local anesthetic \textit{via} a popliteal-sciatic catheter due to differences in
perineural anatomy between the two sites.\textsuperscript{91} Similarly, in the RCT
comparing anterolateral and posterior approaches,\textsuperscript{90} a relatively rigid three-
orifice catheter was used, greatly increasing the chance that for the posterior
approach all three orifices would fail to reside within the narrow anterior-
posterior facial plane containing the brachial plexus.\textsuperscript{92} Evidence from other
investigations suggest that the posterior approach is highly reliable using a
relatively flexible single-orifice catheter;\textsuperscript{62,93} and that using a flexible
catheter for other needle in-plane approaches may help avoid the catheter tip
bypassing the target nerve during insertion.\textsuperscript{74,81}

While simply visualizing the catheter tip in close relation to the target nerve
intuitively appears to be an obvious solution, in practice identifying the tip is
often challenging since, unlike rigid needles, flexible catheters do not
usually remain within the ultrasound plane of view. While there are
exceptions,\textsuperscript{94,95} many investigators observe the location of fluid,\textsuperscript{96} an agitated
fluid/air mixture,\textsuperscript{97} or simply air\textsuperscript{98,99} through the catheter. Unfortunately, the
positive- and negative-predictive value of each of these methods remains unknown, and even what constitutes a “positive” or “negative” test has yet to be determined. Future technological developments in equipment such as 3-dimensional ultrasound may render this issue mute.100

**Nerve Stimulation vs. Ultrasound Guidance.** Multiple RCTs suggest that for most anatomic locations, catheters inserted with ultrasound guidance provide at least similar analgesia—and often decrease insertion-related discomfort and insertion time—when compared with an electrical technique using an insulated needle and nonstimulating101-103 or stimulating catheters.61,62,64,104,105 And while there are reports of combining nerve stimulation and ultrasound guidance for catheter insertion,43 the majority of these reports do not suggest much benefit93,97,104,106-108—and often increasing difficulties compared with using one technique alone104,109,110—leading some to question the utility of stimulating catheters,109 and even insulated needles111 (while others disagree).19,56,112,113 Currently, insufficient data are available to determine either the optimal techniques/equipment for these insertion modalities, as well as their associated risks and benefits.82 Case-in-point is one RCT providing contrary evidence that for popliteal-sciatic
catheters, a stimulating catheter provides improved analgesia in those successfully placed using a strict insertion protocol.\textsuperscript{63}

There are some clinical situations in which ultrasound is a superior modality—at least theoretically—such as following limb amputation,\textsuperscript{114} when solely sensory nerves are targeted,\textsuperscript{115} with concomitant anticoagulation,\textsuperscript{116} or when an electrically-induced muscle response is either undesirable\textsuperscript{117} or cannot be elicited.\textsuperscript{118} However, ultrasound nerve/plexus/needle tip visualization/identification are often difficult for relatively deep targets, in which case nerve stimulation may prove beneficial.\textsuperscript{119-121} And there are situations—such as when placing a posterior lumbar plexus catheter—that pre-puncture ultrasound visualization may aid subsequent electrical stimulation-guided catheter insertion.\textsuperscript{122} Lastly, the relative costs of each insertion modality must be accounted for, with one investigation suggesting that for single-injection peripheral nerve blocks, the use of ultrasound guidance is at least as financially competitive—and often becomes a “profit center,” depending on the clinical scenario—compared with electrical stimulation.\textsuperscript{123}
**Infusates.** Local anesthetic is the primary analgesic infused during CPNB. Although intermediate-duration agents may be used, the most commonly-reported agents are ropivacaine, bupivacaine, and levobupivacaine due to their longer duration of action and favorable sensory:motor block ratio. Since the precise equipotency ratios of local anesthetics remain unknown, comparisons are problematic. While the available data suggests bupivacaine and levobupivacaine are more potent than ropivacaine, all three provide similar analgesia, although the ropivacaine concentration is often increased up to 50% to compensate for decreased potency. One study of interscalene infusion suggested that ropivacaine 0.2% induces fewer finger paresthesias and less hand weakness than bupivacaine 0.15%. However, similar investigations using different concentrations of levobupivacaine and ropivacaine suggest that any differences in the induced motor block are minimal as long as the ropivacaine concentration is increased by approximately 50%. Conversely, there is data to suggest that when the perineural infusion is discontinued, the sensory and motor effects of bupivacaine greatly outlast those of ropivacaine. This may be relevant when titration of local anesthetic to limit undesired effects is needed (e.g., femoral perineural infusion-induced quadriceps femoris weakness limiting ambulation; or an
insensate extremity during infraclavicular or popliteal-sciatic infusion). Of note, data derived from laboratory animals suggests that both ropivacaine and bupivacaine induce tissue injury, but ropivacaine results in significantly less damage.\textsuperscript{134,135} The clinical implications of this data remain unknown.

It also remains unknown whether the primary determinant of CPNB effects is solely local anesthetic dose (mass),\textsuperscript{128,130,136,137} or if volume (rate) and/or concentration exert additional influence. For single-injection nerve blocks, volume and concentration primarily determine efficacy when dose is held constant.\textsuperscript{138,139} However, for CPNB, data from the only study that varied both the infusion rate and concentration in a static ratio so that the total dose was comparable in each treatment group suggests that—during perineural infusion—local anesthetic concentration does \textit{not} influence block effects as long as the \textit{total dose} remains constant.\textsuperscript{140} Unfortunately, the results from this study of posterior lumbar plexus ropivacaine infusion may not be applicable to other anatomic locations,\textsuperscript{137,141-143} local anesthetics,\textsuperscript{126,131-133} infusion rates,\textsuperscript{67,137,144} local anesthetic concentrations,\textsuperscript{132,137,145-147} or bolus dose/volume combinations,\textsuperscript{144} and thus further investigation is required for a definitive answer.
To complicate the issue, in the clinical setting patient-controlled bolus doses and/or an adjustable basal infusion rate are often provided, and therefore total local anesthetic dose varies depending on individual patient requirements.\textsuperscript{57,128,141-143,148,149} In these clinical cases, it appears that concentration and rate do influence infusion effects.\textsuperscript{142,143,148} Unfortunately, currently-published studies provide widely conflicting data, probably due to the multiple variables influencing infusion effects and analgesic requirements.\textsuperscript{128,141-143,148-150} For example, studies involving interscalene ropivacaine infusion report increasing local anesthetic concentration results in increased,\textsuperscript{128} decreased,\textsuperscript{141} or no\textsuperscript{149,150} difference in postoperative analgesia. Similarly, increasing local anesthetic concentration results has differing effects on the incidence of an insensate extremity depending on catheter site location: increased for infraclavicular,\textsuperscript{142} decreased for popliteal,\textsuperscript{143} no difference for axillary,\textsuperscript{150} and variable for interscalene.\textsuperscript{136,141,149} Therefore, no optimal concentration/rate combination may be recommended for all anatomic locations, and further study is warranted. For bupivacaine/levobupivacaine and ropivacaine, the most-commonly-cited concentrations are between 0.1-0.125\% and 0.1-0.2\%, respectively.
Several medications are occasionally added to local anesthetic during CPNB in an attempt to improve analgesia without increasing motor block. There are reports of the inclusion of opioid with perineural local anesthetic, but currently insufficient data exists to draw any conclusions regarding its efficacy. While clonidine was often added in the earlier years of CPNB, three subsequent RCTs failed to demonstrate any clinically-relevant benefits. An additional RCT found no benefit to adding epinephrine to perineural ropivacaine, and possible prolonged vasoconstriction places the safety of this practice into doubt. Additional possible adjuvants have been reported, but none are currently approved for perineural use in patients, and some may have unacceptable systemic effects.

**Local Anesthetic Delivery Regimens.** Infusates may be administered with three main strategies: exclusively as a basal infusion or bolus dose, as well as a combination of these two modalities. Unfortunately, similar to the data involving local anesthetic concentration, studies of delivery strategy are somewhat mixed (Table 2). In general, randomized, controlled studies involving femoral and fascia iliaca infusions have reported few differences in analgesia among the various delivery regimens (other than reduced local
anesthetic use with bolus-only dosing). Conversely, for sciatic catheters, providing a basal infusion maximizes analgesia and other benefits; although the data regarding the benefits of adding patient-controlled bolus doses is less clear.

Interestingly, providing *automated* hourly 5 mL bolus doses of levobupivacaine *via* a popliteal-sciatic catheter decreased pain scores compared with patients receiving a continuous 5 mL basal infusion of 0.125% levobupivacaine (although a similar investigation involving femoral ropivacaine infusion failed to detect differences in sensory or motor effects). However, by adding patient-controlled bolus doses to these two regimens, the difference in pain scores disappeared. Importantly, all investigations report a lower total consumption of local anesthetic with regimens providing patient-controlled bolus doses, suggesting the desirability of including this modality for three main reasons: (1) decreasing the required basal infusion rate and thus *theoretically* decreasing motor block [inadequately investigated to date], (2) decreasing the incidence of an insensate extremity, and (3) increasing the duration of infusion/analgesia for ambulatory patients discharged with a finite volume of local anesthetic.
In contrast to the lower extremity, investigations of interscalene\textsuperscript{144} and infraclavicular\textsuperscript{57} perineural infusion are more uniform and suggest that including a basal infusion improves baseline analgesia, decreases the incidence and severity of breakthrough pain, and decreases sleep disturbances and supplemental analgesic requirements. Furthermore, adding patient-controlled bolus doses to a basal infusion decreases total local anesthetic consumption and supplemental analgesic requirements,\textsuperscript{57,144,170} allows block reinforcement during dressing changes or physical therapy,\textsuperscript{144,175,176} and may provide increased independent activity.\textsuperscript{170}

Additional RCTs attempting to further refine interscalene dosing report provide somewhat conflicting results. One study provides evidence that a high basal rate combined with low-volume patient-controlled bolus doses reduces baseline pain scores and sleep disturbances; decrease the incidence and severity of breakthrough pain; but at a cost of increasing local anesthetic consumption.\textsuperscript{67} However, other similar investigations report few differences in varying the basal infusion rate.\textsuperscript{137,170,177}

Unfortunately, due to the heterogenicity of catheter types, insertion techniques, and a myriad of additional factors, there is little evidence for an
“optimal” infusion regimen. Until recommendations based on prospectively collected data are available, healthcare providers may wish to consider that most published investigations report a basal rate of 4-10 mL/h, a bolus volume of 2-10 mL, and a bolus lockout period of 20-60 minutes. Similarly, maximum recommended hourly total dose of local anesthetic during perineural infusion remain unknown, but a wide safety margin has been documented in numerous clinical trials, with one study reporting no toxicity signs or symptoms with perineural ropivacaine 0.2% administered at basal rates up to 14 mL/h and large repeated boluses of ropivacaine 0.5% (10-60 mL) provided for up to 27 days.

**Infusion Pumps.** While perineural local anesthetic may be provided using exclusively human-administered bolus doses, both clinical factors (e.g., basal infusion benefits) as well as logistical considerations usually dictate the use of an infusion pump. There is no single optimal device for all situations, given the multitude of clinical scenarios and practice requirements; so pump preference is usually based on the desired device characteristics. Infusion pumps may be (arbitrarily) categorized by their power source. Although spring- and vacuum-powered devices are available, neither are particularly desirable for the purpose of CPNB due to a multitude
of factors, including highly-variable basal infusion rates and relatively small local anesthetic reservoir volumes, respectively.\textsuperscript{189,190} Until recently, elastomeric infusion pumps were severely limited relative to the capabilities of electronic devices;\textsuperscript{187} however, with the advent of newer non-electronic pumps, this is no longer the case.

In general, electronic devices provide very accurate and consistent ($\pm 5\%$) basal infusion rates over the entire course of infusion.\textsuperscript{189-192} In contrast, elastomeric pumps usually over-infuse (110-130\% expected) during the initial 3-8 hours of infusion and within the final hours prior to reservoir exhaustion,\textsuperscript{189-193} resulting in a shorter infusion duration than anticipated given the initial reservoir volume and set basal infusion rate.\textsuperscript{189-192,194,195} However, whether the increased variability is clinical significant—or in which clinical situations it is relevant—remains unknown. Unlike electronic devices, the basal infusion rate of most elastomeric devices increases with increasing ambient temperature and pump height relative to the catheter insertion site,\textsuperscript{189-192,195} although these changes are probably clinically relevant only at extreme values.
An adjustable basal infusion rate allows local anesthetic administration titration in case of an insensate extremity,\textsuperscript{31} undesired side effects (e.g., muscle weakness),\textsuperscript{94,177} inadequate analgesia,\textsuperscript{167} or desire to maximize infusion duration (e.g., ambulatory patients with a set reservoir volume).\textsuperscript{57,167,174} In addition, a patient-controlled bolus function often provides multiple clinical benefits.\textsuperscript{57,144} All electronic pumps provide an adjustable basal rate, patient-controlled bolus doses, and a variable bolus lock-out period.\textsuperscript{189-192} And while most elastomeric devices provide a fixed basal infusion rate,\textsuperscript{188} a few now provide flexibility similar to their electronic counterparts. Nearly all electronic pumps use an external local anesthetic reservoir that allows for easy reservoir exchanges.\textsuperscript{115,185} In contrast, all elastomeric devices have an internal reservoir; and although refilling such devices has been investigated,\textsuperscript{196,197} this procedure is not approved by manufacturers/governments for the overwhelming majority of devices, requiring the use of an additional unit if continued infusion is desired following reservoir exhaustion.\textsuperscript{170,198-200} Regardless of reservoir type, filling the infusion pump/reservoir within the United States must now be executed within an isolation Class 5 environment, essentially requiring local anesthetic compounding within a designated pharmacy with a laminar flow workbench.\textsuperscript{201}
Non-electronic infusion pumps are often favored for their relative simplicity in both initially setting and subsequently adjusting the basal infusion rate; \textsuperscript{202} light weight and smaller size; \textsuperscript{203} lack of audible alarms \textsuperscript{203,204} (although there is no warning for a pause in the infusion); \textsuperscript{205} ease of disposability; \textsuperscript{206} and silent operation (electronic pump noise may disturb patient sleep). \textsuperscript{203} In addition, elastomeric devices with a manufacturer-fixed basal rate and no bolus dose capability are usually relatively inexpensive. \textsuperscript{188} Conversely, reusable electronic pumps use inexpensive disposable “cassettes” to provide sterile infusion for individual patients. \textsuperscript{174} A limited number of single-use electronic devices are available. \textsuperscript{141-143} Lastly, although the reliability for most infusion pumps is high—regardless of power source—certain devices are more dependable than others for both electronic \textsuperscript{204,207-210} and non-electronic pumps. \textsuperscript{193,205}

**Ambulatory Perineural Infusion.** First described in 1997, \textsuperscript{211} CPNB may be provided to patients outside of the hospital using a portable infusion pump; and nearly every catheter type (i.e. anatomic location) has been reported in ambulatory patients. \textsuperscript{188} Perineural infusion is often provided for ambulatory surgery without an overnight hospital stay, \textsuperscript{84,86} but the technique
may be used to shorten hospitalization,\textsuperscript{175,212} or provide benefits following discharge either home or to a skilled nursing facility.\textsuperscript{33,197} Time constraints are often more restrictive in high-turnover ambulatory centers,\textsuperscript{85} making insertion techniques with documented time savings frequently desirable (e.g., ultrasound guidance).\textsuperscript{61,64,105,213} Since patients are rarely directly monitored outside of the hospital—and not all patients desire or are capable of accepting the additional responsibility of caring for the catheter and pump system—patient selection criteria are often more stringent for ambulatory CPNB. In an effort to avoid local anesthetic toxicity, patients with renal or hepatic insufficiency are often excluded from outpatient perineural infusion.\textsuperscript{179} For infusions frequently affecting the phrenic nerve and weakening the ipsilateral diaphragm (e.g., interscalene catheters),\textsuperscript{214,215} caution is warranted for individuals with heart/lung disease and in obese patients who may not be able to compensate for mild hypoxia and/or hypercarbia.\textsuperscript{216,217} Of note, age alone is not an absolute exclusion criteria, with hundreds of pediatric patients receiving at-home CPNB without complication rates or severity higher than for their adult counterparts.\textsuperscript{14,24-26}

Providing ambulatory CPNB often leads to a reduced time until discharge \textit{readiness},\textsuperscript{33,58,175,218} and in some cases, \textit{actual} discharge.\textsuperscript{175,212} Following
tricompartment knee arthroplasty, permitting early discharge with ambulatory femoral infusion results in decreased hospitalization-related costs.\textsuperscript{219} However, while ambulatory continuous femoral and posterior lumbar plexus nerve blocks decrease the time until important discharge criteria are met,\textsuperscript{33,58,218} an increased incidence of patient falls in patients receiving ropivacaine vs. saline through their catheters suggests increased caution is warranted before implementing early discharge.\textsuperscript{173} Nevertheless, relatively small published series demonstrate the feasibility of total joint arthroplasty with only a single-night hospital stay—or even on an outpatient basis—when patients are permitted to continue their hospital-based perineural infusion at home.\textsuperscript{84,199,200,220,221}

While the benefits of home CPNB are well-documented with multiple randomized, placebo-controlled studies,\textsuperscript{31,33,34,58,93,175,218,222,223} there is negligible published data regarding the optimal practice for multiple aspects of ambulatory infusion, such as the requirement of a patient caretaker;\textsuperscript{86} method/frequency of patient oversight (e.g., home nursing visits,\textsuperscript{170,224,225} telephone calls,\textsuperscript{20,202} or simply written instructions with solely patient-initiated contact); and catheter removal protocol (healthcare-provider extraction,\textsuperscript{170,225} caretaker withdrawal with instructions provided by
telephone, or simply written instructions. Of 40 patients with a hospital-based CPNB, 12.5% stated they would be unwilling to remove their catheter at home. However, of patients who previously removed a perineural catheter at home, 98% felt “comfortable” doing the procedure with instructions given by telephone, only 4% would have preferred to return to the hospital for healthcare-provider catheter removal, and 43% would have felt comfortable with exclusively written instructions. Of note, at least within the United States there are no national guidelines regarding the maximum safe CPNB duration.

**Benefits of CPNB.** While case reports and series suggest numerous possible benefits of CPNB for a wide variety of ailments, published RCTs include exclusively postoperative patients. Providing analgesia is the primary indication for postoperative CPNB, and most CPNB benefits appear to be dependent upon successfully improving pain control (Table 3). Potent analgesia is most dramatic for surgical sites that are completely innervated by nerves affected by the perineural infusion, as is often the case for shoulder and foot/ankle procedures (interscalene and sciatic nerve catheters, respectively). Unfortunately, brachial plexus infusions for procedures at or distal to the elbow appear to provide less
impressive analgesia, even though they (theoretically) cover the entire surgical site. RCT dokumented benefits of axillary, supraclavicular, paravertebral, and transversus abdominus plane infusion is severely lacking. And, while the benefits of infraclavicular infusion are validated, analgesia is often less than optimal unless a high enough dose of local anesthetic is administered which frequently renders the extremity insensate.

Similarly, femoral or posterior lumbar plexus infusion may result in unacceptable quadriceps femoris and hip adductor weakness when a high enough dose of local anesthetic is administered to optimize analgesia. In addition, a single perineural infusion for surgical sites innervated by multiple nerves—most notably the hip, knee, and ankle—may provide less-than-optimal analgesia without the concurrent use of additional analgesics. Of published reports, nearly all investigators provide a single infusion—often supplemented with a separate single-injection peripheral nerve block (e.g., sciatic block after knee surgery). Some individuals have proposed inserting a second catheter, although there is minimal—and somewhat conflicting—data to guide clinical practice. While a lumbar epidural provides roughly equivalent analgesia to femoral perineural infusion for hip
and knee arthroplasty, CPNB results in a more-favorable side-effect profile without the risk of epidural hematoma during concomitant anticoagulant administration.\textsuperscript{156,158,238,239}

Although the evidence for CPNB benefits \textit{during} local anesthetic infusion is overwhelming, there is little data demonstrating benefits \textit{following} catheter removal. Exceptions include improved analgesia after a few days\textsuperscript{2,32,240} or six months;\textsuperscript{237} more-rapid resumption of unassisted standing and lavatory use;\textsuperscript{2} and faster tolerance of passive knee flexion\textsuperscript{2} resulting in earlier discharge from hospital\textsuperscript{156} or rehabilitation\textsuperscript{158} centers. Conspicuously lacking is evidence of short- or long-term improvements in health-related quality-of-life measures.\textsuperscript{241-244}

\textbf{Complications.} As with all medical procedures, the potential CPNB benefits must be weighed against the potential risks. Fortunately, infusion-related serious and lasting injuries are uncommon, while relatively minor complications occur at a frequency similar to single-injection peripheral nerve blocks.\textsuperscript{245} Unfortunately, heterogeneous catheter insertion techniques, equipment, anatomic location, and infusions render generalizations difficult. For example, various prospective studies report an incidence of secondary
block (infusion) failure of 1%, 246 20%, 34 and 50%. 36 Thus, the specific complication rates provided in this section will not apply to all practices. CPNB-specific complications during catheter insertion include inaccurate catheter tip placement too far from the target nerve to provide postoperative analgesia, 35 and—in exceptionally rare cases—epidural, 247-249 intrathecal, 250-252 intravascular, 223, 253 intraneural, 254 and even interpleural catheter insertion. 255 Catheter migration following accurate placement has been suggested 256—but also doubted 257—and the dearth of published events suggests that it is an exceptionally rare event, if it even occurs at all.

During the perineural infusion, more-common (and benign) complications include catheter dislodgement or obstruction, 115, 170, 246 fluid leakage at the catheter site; 170, 223 infusion pump malfunction, 204, 258 undesired pause, 205 or disconnection; 33 skin irritation or allergic reactions to the catheter dressing and/or liquid adhesive; 259 and catheter-induced brachial plexus irritation. 260 In addition, a CPNB-induced insensate extremity may prove disconcerting to patients, 261 impedes physical therapy and/or ambulation, 132, 218 and considered a risk factor for injury by some investigators. 142, 143 In these cases, the infusion pump is usually paused until sensory perception begins to return, after which the infusion is restarted at a lower basal rate. 31, 58
Conversely, inadequate analgesia or breakthrough pain may occur, and is often treated by increasing the basal infusion and providing patient-controlled bolus doses, respectively.\textsuperscript{31,223}

More serious (but rare) complications include myonecrosis with repeated large boluses of bupivacaine;\textsuperscript{262} local anesthetic toxicity,\textsuperscript{125,179,263,264} prolonged Horner’s syndrome;\textsuperscript{265} and catheter knotting,\textsuperscript{75,76,266} retention,\textsuperscript{57,267} shearing,\textsuperscript{125,268,269} or breakage.\textsuperscript{270} Although infusions potentially effecting the phrenic nerve may have minimal pulmonary effects for relatively healthy patients,\textsuperscript{152,214,271} dyspnea in often-heavy patients is somewhat common,\textsuperscript{67} and lower lobe collapse has occurred.\textsuperscript{217} There is limited evidence that the risk of nerve injury from prolonged local anesthetic exposure may be increased in patients with diabetes\textsuperscript{272,273} and/or preexisting neuropathy.\textsuperscript{274}

There are case reports of peri-catheter hematoma formation,\textsuperscript{268,275} often with concurrently-administered low molecular weight heparin for thromboprophylaxis.\textsuperscript{276-278} Most are self-limiting,\textsuperscript{277} but more dramatic cases require surgical evacuation.\textsuperscript{275} The most-recent (Third) American Society of Regional Anesthesia consensus statement on neuraxial anesthesia and anticoagulation explicitly recommends precautions for neuraxial
techniques and anticoagulation be exercised for “deep” perineural catheters (undefined): specifically, that any catheter be removed prior to administration of various anticoagulants;\textsuperscript{279} although this practice has been questioned by various investigators.\textsuperscript{280-285} Also concerning is the association between perineural infusions affecting the femoral nerve and patient falls following hip and knee arthroplasty,\textsuperscript{173} possibly due to CPNB-induced sensory, proprioception, and/or quadriceps weakness.\textsuperscript{94} Correlation does not prove causation; however, until further evidence is published, practitioners should consider interventions that may decrease the risk of falls, such as limiting the local anesthetic dose/mass,\textsuperscript{140} providing crutches/walker and a knee immobilizer during ambulation,\textsuperscript{286} and educating surgeons, nurses, and physical therapists of possible CPNB-induced weakness and fall precautions.

While the reported rate of inflammation (3-4\%)\textsuperscript{246,258,287} and catheter bacterial colonization (6\%-57\%) are seemingly high,\textsuperscript{288,289} clinically-relevant infection is relatively rare (incidence 0-3\%;\textsuperscript{290,291} but most reports <1\%).\textsuperscript{38,125,245,288,292} Risk factors include admission to an intensive care unit, absence of perioperative antibiotic prophylaxis, and male sex.\textsuperscript{258} Although one multicenter study found a higher risk with axillary and femoral catheters,\textsuperscript{258} others have report the interscalene location as the most
Risk of infection is also correlated with infusion duration. Nonetheless, infusions provided during extended medical transport for up to 34 days and provided at home for up to 83 days have been reported with a minimal incidence of infection. There is limited evidence that subcutaneous catheter tunneling may decrease the risk of bacterial colonization and infection. Abscesses have occurred—although the incidence remains unknown—and occasionally require surgical treatment, but often do not if timely antibiotic coverage is provided. And, while life-threatening catheter-related infections/sepsis have been reported, there is currently no case of permanent injury due to CPNB-related infection within the English-language literature.

Perhaps the most feared post-infusion complication is neurologic injury. It is often difficult to determine how much of a neurologic deficit—if any—is attributable to CPNB since all surgical procedures are associated with a variable incidence of nerve injury, regardless of the application of a regional anesthetic/analgesic. With this critical limitation in mind, the incidence of transient adverse neurologic symptoms associated with CPNB is 0-1.4% for interscalene, 0.4-0.5% for femoral, and 0-1.0% for sciatic catheters. An additional investigation found a 0.2%

...
incidence of neurologic deficits lasting longer than 6 weeks in nearly 3,500 catheters from multiple anatomic locations.\textsuperscript{246} In this latter study, it remains unknown if the deficits resolved after the 6-week study period; but multiple prospective investigations report that the overwhelming majority of neurologic symptoms present at 4-6 weeks resolve spontaneously within three months of surgery.\textsuperscript{38,245,258}

There are reported cases of \textit{long-term} and/or \textit{permanent} nerve injury \textit{associated} with perineural infusion.\textsuperscript{304} Five large,\textsuperscript{38,245,258,264,268} prospective series that followed patients for at least three months found 3 cases of unresolved adverse neurologic events: a brachial plexus lesion following interscalene infusion (followed 9 months);\textsuperscript{245} a femoral neuropathy presumably the result of a retroperitoneal hematoma (cause undetermined; months followed not reported);\textsuperscript{268} and a persistent paraesthesia following a popliteal-sciatic catheter (followed through 18 months).\textsuperscript{264} Combining the results of these studies (4,148 total subjects) suggests the risk of neurologic injury lasting longer than nine months \textit{associated} with CPNB is 0.07\%.\textsuperscript{38,245,258,264,268} While ultrasound-guidance may decrease the incidence of many/most of these reported complications,\textsuperscript{305} to date there are few data
supporting this proposition,\textsuperscript{306,307} and case reports suggest that completely abolishing such events is unlikely.\textsuperscript{308-310}

Conclusions. Although the published literature presented in this review article provides a plethora of information involving CPNB, many aspects of perineural infusion have yet to be fully elucidated, including the optimal catheter insertion modality and technique; infusate(s) and adjuvants; local anesthetic delivery regimen; details of optimizing ambulatory infusion; possible infusion benefits; and the incidence of all possible risks. Furthermore, while CPNB appears to provide far-more-potent analgesia than wound catheters\textsuperscript{311-313}—and often fewer undesirable side effects than epidural infusion\textsuperscript{23,156,158,239,311}—many questions remain regarding the optimal analgesic technique for multiple surgical procedures.\textsuperscript{314,315} Lastly, perineural infusion must be adequately compared with possible new analgesic techniques.\textsuperscript{316} Only through prospective research will we fully reveal and maximize the potential benefits—while minimizing the potential risks—of CPNB for our patients.
Table 1. Catheter locations (selected references only due to publication limitations; similarly, only randomized, controlled trials included when at least one study with this design is available)

<table>
<thead>
<tr>
<th>Surgical Site</th>
<th>Major Approaches</th>
<th>Evaluated with RCT?</th>
<th>Comments</th>
<th>Comparative CPNB Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Head</strong></td>
<td>Mandibular and maxillary nerves</td>
<td>No&lt;sup&gt;17,317,318&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Shoulder and proximal humerus</strong></td>
<td>Interscalene</td>
<td>Yes&lt;sup&gt;34,93,170,175,214, 226,319-324&lt;/sup&gt;</td>
<td>Validated with nerve stimulation&lt;sup&gt;34,38,170,175,214,226,319-321&lt;/sup&gt; and ultrasound guidance&lt;sup&gt;93,322&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Cervical paravertebral</td>
<td>No&lt;sup&gt;325&lt;/sup&gt;</td>
<td></td>
<td>Nearly all publications from a single group</td>
<td></td>
</tr>
<tr>
<td>Intersterno-cleidomastoid</td>
<td>No&lt;sup&gt;326&lt;/sup&gt;</td>
<td></td>
<td>Nearly all publications from a single group</td>
<td></td>
</tr>
<tr>
<td>Supraclavicular</td>
<td>No&lt;sup&gt;228,229&lt;/sup&gt;</td>
<td></td>
<td>Effectiveness of technique for postoperative analgesia unclear without RCT</td>
<td></td>
</tr>
</tbody>
</table>

There are no studies comparing these CPNB techniques.
<table>
<thead>
<tr>
<th>Technique</th>
<th>Effectiveness</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Elbow, forearm, and hand</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suprascapular</td>
<td>No(^{327})</td>
<td>Effectiveness of technique unclear without RCT</td>
</tr>
<tr>
<td>Supraclavicular</td>
<td>Yes(^{227})</td>
<td>Caution regarding pneumothorax risk(^{328}) (including with ultrasound guidance)(^{329})</td>
</tr>
<tr>
<td>Infraclavicular</td>
<td>Yes(^{223})</td>
<td>Provides superior analgesia to both supraclavicular(^{227}) and axillary* catheters</td>
</tr>
<tr>
<td>Axillary</td>
<td>Yes(^{150,*})</td>
<td>No benefit of ropivacaine 0.1% or 0.2% over placebo infusion</td>
</tr>
<tr>
<td>Median nerve</td>
<td>No(^{330})</td>
<td></td>
</tr>
<tr>
<td><strong>Thorax and breast</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paravertebral</td>
<td>Yes(^{230})</td>
<td>RCT for mastectomy only: no infusion benefits over single-injection(^{230})</td>
</tr>
<tr>
<td>Intercostal</td>
<td>No(^{331,332})</td>
<td>Approach aims to place catheter tip in paravertebral space. Effectiveness of this technique unclear without RCT.</td>
</tr>
<tr>
<td><strong>Abdomen, iliac crest, and inguinal</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transversus abdominus plane</td>
<td>No(^{231,333-336})</td>
<td>Relatively new technique with risks and benefits yet to be thoroughly investigated. Retrospective study suggests decreased opioid</td>
</tr>
<tr>
<td>Region</td>
<td>Yes/No</td>
<td>Studies Ref</td>
</tr>
<tr>
<td>------------------------</td>
<td>--------</td>
<td>-------------</td>
</tr>
<tr>
<td>Posterior lumbar plexus</td>
<td>Yes</td>
<td>13,33,210,235,337-339</td>
</tr>
<tr>
<td>Femoral</td>
<td>Yes</td>
<td>210,234,239,337,340,341</td>
</tr>
<tr>
<td>Parasacral</td>
<td>No</td>
<td>342</td>
</tr>
<tr>
<td>Location</td>
<td>Used</td>
<td>Reference(s)</td>
</tr>
<tr>
<td>------------------------</td>
<td>------</td>
<td>--------------</td>
</tr>
<tr>
<td>Posterior lumbar plexus</td>
<td>Yes</td>
<td>163,236,343</td>
</tr>
<tr>
<td>Femoral</td>
<td>Yes</td>
<td>32,36,49,58,147,156,158,163,164,218,236,240,311,315,344-348</td>
</tr>
<tr>
<td>Fascia iliaca</td>
<td>Yes</td>
<td>344,345,349,350</td>
</tr>
<tr>
<td>Parasacral</td>
<td>No</td>
<td>342,351</td>
</tr>
<tr>
<td>Labat and Raj</td>
<td>No</td>
<td>30,354</td>
</tr>
<tr>
<td>Subgluteal</td>
<td>Yes</td>
<td>352,353</td>
</tr>
<tr>
<td>Popliteal</td>
<td>Yes</td>
<td>23,31,170,212,222</td>
</tr>
<tr>
<td>Tibial nerve</td>
<td>No</td>
<td>224,355</td>
</tr>
<tr>
<td>Femoral</td>
<td>Yes</td>
<td>237</td>
</tr>
</tbody>
</table>
place of—popliteal infusion for major ankle surgery

RCT: randomized, controlled trial

CPNB: continuous peripheral nerve block

* Unpublished data, Mariano and Ilfeld (2011)
**Table 2.** Local anesthetic delivery regimens for continuous peripheral nerve blocks (exclusively selected randomized, controlled trials specifically investigating varying delivery method due to publication limitations)

<table>
<thead>
<tr>
<th>Catheter Location</th>
<th>Infusate(s)</th>
<th>Treatment Groups</th>
<th>Primary Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>n</td>
<td>Basal (mL/h)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20</td>
<td>10</td>
</tr>
<tr>
<td><strong>Interscalene</strong></td>
<td>bupivacaine</td>
<td>20</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>[0.125%]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>clonidine</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>[1 µg/mL]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>sufentanil</td>
<td>20</td>
<td>--</td>
</tr>
<tr>
<td></td>
<td>[0.1 µg/mL]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interscalene</td>
<td>Type</td>
<td>Dose</td>
<td>Pain</td>
</tr>
<tr>
<td>-------------</td>
<td>------</td>
<td>------</td>
<td>------</td>
</tr>
<tr>
<td>177</td>
<td>nonstimulating catheter, ultrasound-guided posterior approach</td>
<td>ropivacaine [0.2%]</td>
<td>38 2 5 60</td>
</tr>
<tr>
<td>67</td>
<td>stimulating catheter, anterolateral approach</td>
<td>ropivacaine [0.2%]</td>
<td>12 8 2 60</td>
</tr>
<tr>
<td>170</td>
<td>nonstimulating catheter, anterolateral approach</td>
<td>ropivacaine [0.2%]</td>
<td>15 7 -- --</td>
</tr>
</tbody>
</table>

Note that this group self-administered 6 mandatory bolus doses daily in addition to as-needed bolus doses.
<table>
<thead>
<tr>
<th>Location</th>
<th>Local Anesthetic</th>
<th>Concentration</th>
<th>Supplemental Analgesics</th>
<th>Breakthrough Pain</th>
<th>Local Anesthetic Consumption</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infraclavicular</strong>&lt;sup&gt;57&lt;/sup&gt;</td>
<td>ropivacaine</td>
<td>[0.2%]</td>
<td>Increased supplemental analgesics vs. basal-bolus</td>
<td>Increased breakthrough pain incidence and intensity as well as sleep disturbances vs. basal-bolus</td>
<td>No clinical differences between groups; but, study most-likely underpowered to detect any difference</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Note that this group received automated hourly bolus doses of 10 mL without additional optional bolus doses</td>
</tr>
<tr>
<td><strong>Axillary</strong>&lt;sup&gt;8&lt;/sup&gt;</td>
<td>bupivacaine</td>
<td>[0.25%]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Femoral</strong>&lt;sup&gt;151&lt;/sup&gt;</td>
<td>bupivacaine</td>
<td>[0.125%]</td>
<td>Increased dynamic pain vs. 5 mL bolus group and increased local anesthetic consumption vs. others</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>clonidine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Possibly lower incidence of “slight paresthesia” (data combined with popliteal infusion)
<table>
<thead>
<tr>
<th>Approach</th>
<th>Local Anesthetic</th>
<th>Concentration</th>
<th>Time (min)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femoral</td>
<td>Bupivacaine</td>
<td>[0.125%]</td>
<td>15-10-30</td>
<td>Increased local anesthetic consumption vs. other two groups</td>
</tr>
<tr>
<td></td>
<td>Clonidine</td>
<td>[0.1 µg/mL]</td>
<td>15-5-30</td>
<td>Trend towards less supplemental analgesic requirements ($p=0.10$) than other two groups</td>
</tr>
<tr>
<td>Fascia Iliaca</td>
<td>Ropivacaine</td>
<td>[0.2%]</td>
<td>46-10-60</td>
<td>Least local anesthetic consumption vs. other two groups</td>
</tr>
</tbody>
</table>

- **Femoral**
  - for knee arthroplasty
  - inguinal perivascular approach
  - nonstimulating catheter

- **Fascia Iliaca**
  - for knee surgery
  - nonstimulating catheter
| Seldinger technique | Subgluteal-Sciatic\(^{168}\) | Ropivacaine [0.2%] | 25 | 10 | -- | -- | Increased consumption of local anesthetic
| | Subgluteal-Sciatic | Nonstimulating catheter | Inserted 3-4 cm | 25 | 5 | 5 | 60 |
| | Popliteal-Sciatic\(^{167}\) | Ropivacaine [0.2%] | 10 | 12 | -- * | -- | Increased consumption of local anesthetic with a shorter duration of infusion and analgesia
| | | Stimulating catheter | Posterior approach | 10 | 8 | 4 | 60 |
| | | Posterior approach | 10 | -- * | 9.9 | 60 |
| | Popliteal-Sciatic\(^{171}\) | Levo-bupivacaine [0.125%] | 22 | 5 | -- | -- | Increased baseline and breakthrough pain intensity; a trend towards increased rescue analgesic requirement \((p=0.055)\)
| | | Nonstimulating catheter | 22 | -- | 5 | 60 |

Note that this group received automated hourly
| **Popliteal-Sciatic**<sup>172</sup> | levo-bupivacaine [0.125%] | 25  | 5   | 3   | 15   | Increased local anesthetic consumption
|                            |                            |     |     |     |      | *Note that this group received automated hourly bolus doses of 5 mL; and optional 3 mL bolus doses
| **Popliteal-Sciatic**<sup>170</sup> | ropivacaine [0.2%] | 15  | 7   | --  | --   | Possibly increased assistance with daily activity and time until 10 minutes of ambulation (data combined with interscalene infusion; no p-value provided for ambulation)
|                            |                            |     |     |     |      | Possibly lower incidence of “slight paresthesia” (data combined with interscalene infusion)

--: not included for this treatment group

*: nominal basal infusion rate or bolus volume provided to retain treatment group masking
Table 3. Benefits of continuous peripheral nerve blocks documented in randomized, controlled trials including at least one treatment group without a regional analgesic (selected references included due to publication limitations)

<table>
<thead>
<tr>
<th>Benefit</th>
<th>Brachial Plexus</th>
<th>Femoral Nerve</th>
<th>Sciatic Nerve</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Inter-scalene</td>
<td>Infraclavicular</td>
<td>Posterior Lum.Plexus</td>
</tr>
<tr>
<td>Resting Analgesia</td>
<td>RCT 170,214,319-322,324* MPC 34,93,175</td>
<td>MPC 223 RCT 13,235,337 §</td>
<td>RCT 2,156,158,234</td>
</tr>
<tr>
<td>Break-through</td>
<td>RCT 322 MPC 34,93,175</td>
<td>MPC 223</td>
<td>RCT 2,137 §</td>
</tr>
<tr>
<td>Dynamic</td>
<td>RCT 170,214,324* MPC 175</td>
<td>RCT 235,337 §</td>
<td></td>
</tr>
<tr>
<td>&gt; 1 day after catheter</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>removal</td>
<td>Oral opioids</td>
<td>Intravenous opioids</td>
<td>NSAID</td>
</tr>
<tr>
<td>---------</td>
<td>--------------</td>
<td>---------------------</td>
<td>-------</td>
</tr>
<tr>
<td></td>
<td>MPC\textsuperscript{34,93,175} MPC\textsuperscript{223}</td>
<td>RCT\textsuperscript{321,324} MPC\textsuperscript{175,226}</td>
<td>RCT\textsuperscript{170\textcopyright}</td>
</tr>
<tr>
<td></td>
<td>RCT\textsuperscript{240} MPC\textsuperscript{32}</td>
<td>RCT\textsuperscript{337,339}</td>
<td>RCT\textsuperscript{158,239,337,347}</td>
</tr>
<tr>
<td></td>
<td>Sedation, fatigue, dizziness, or bowel function</td>
<td>Sleep disturbance</td>
<td>Awakenings</td>
</tr>
<tr>
<td>------------------------</td>
<td>------------------------------------------------</td>
<td>------------------</td>
<td>------------</td>
</tr>
<tr>
<td>RCT</td>
<td>RCT(^{170,*}) MPC(^{34}) MPC(^{223})</td>
<td>RCT(^{234})§</td>
<td>MPC(^{349})</td>
</tr>
<tr>
<td>MPC</td>
<td>MPC(^{175}) MPC(^{33}) MPC(^{58,218})</td>
<td>MPC(^{33})</td>
<td>MPC(^{58,218})</td>
</tr>
<tr>
<td>Resumption of passive joint range-of-motion (accelerated)</td>
<td>Shoulder</td>
<td>MPC$^{175}$</td>
<td>RCT$^{2,36,156,158}$, $^{234}$</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Knee</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hip</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Resumption of ambulation or other functioning (accelerated)</th>
<th></th>
<th>RCT$^{170}$$^*$</th>
<th>RCT$^{337}$</th>
<th>RCT$^2$</th>
<th>RCT$^{170}$$^*$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>MPC$^{343}$</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Inflammation or pro-inflammatory markers (decrease)</th>
<th></th>
<th></th>
<th>RCT$^{235}$$^\S$</th>
<th>RCT$^2$</th>
<th>RCT$^{235}$$^\S$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Lum.Plexus: lumbar plexus
RCT: randomized, controlled trial (either no placebo control or at least one clinical group unmasked to treatment allocation)

MPC: RCT with all clinical groups masked to treatment allocation and including a placebo control

NSAID: non-steroidal anti-inflammatory drug

*: Study by Capdevila, et al.,170 did not separate results for interscalene and popliteal-sciatic catheters, and therefore one or both of these anatomic locations may account for all of the difference between treatment groups

$: Studies by Bagry, et al.,235 Mistraletti, et al.,234 and Blumenthal, et al.,237 compared two concurrent continuous peripheral nerve blocks vs. no regional intervention, and therefore one or both of these anatomic catheter locations may account for all of the difference between treatment groups
Acknowledgements: The author would like to thank Eliza Ferguson, BS, research coordinator extraordinaire (University of California San Diego, San Diego, California), for her assistance with the myriad of articles used in this review.
References


40. Torkki PM, Marjamaa RA, Torkki MI, Kallio PE, Kirvela OA: Use of anesthesia induction rooms can increase the number of urgent orthopedic cases completed within 7 hours. Anesthesiology 2005; 103: 401-405


55. Ilfeld BM, Wright TW, Sessler DI, Chmielewski TL: Valid and relevant outcome measures are critical for objective hypothesis-testing. Anesth Analg 2008; 107: 722-723

57. Ilfeld BM, Morey TE, Enneking FK: Infraclavicular perineural local anesthetic infusion: a comparison of three dosing regimens for postoperative analgesia. Anesthesiology 2004; 100: 395-402


60. Hubler M, Stehr SN: Not all reasons for difficult peripheral nerve blocks are at the proximal end of the needle. Anesth Analg 2006; 102: 649


65. Ilfeld BM, Morey TE, Thannikary LJ, Wright TW, Enneking FK: Clonidine added to a continuous interscalene ropivacaine perineural infusion to improve postoperative analgesia: a randomized, double-blind, controlled study. Anesth Analg 2005; 100: 1172-1178


70. Tsui BC, Kropelin B: The electrophysiological effect of dextrose 5% in water on single-shot peripheral nerve stimulation. Anesth Analg 2005; 100: 1837-1839
designed, self-coiling catheters for regional anesthesia-an imaging study. Regional
anesthesia and pain medicine 2011; 36: 171-6

80. Borgeat A, Ekatodramis G, Dumont C: An evaluation of the infraclavicular
block via a modified approach of the Raj technique. Anesth Analg 2001; 93: 436-441

81. Ilfeld BM SN, Loland VJ, Suresh PJ, Mariano ER, Madison SJ, Bishop ML,
Schwartz AK, Lee DK: Ultrasound-guided (needle in-plane) perineural catheter
insertion: the effect of catheter insertion distance on postoperative analgesia. Reg
Anesth Pain Med: In Press

82. Ilfeld BM, Fredrickson MJ, Mariano ER: Ultrasound-guided perineural
catheter insertion: three approaches but few illuminating data. Reg Anesth Pain Med
2010; 35: 123-126

83. Davis JJ, Swenson JD, Greis PE, Burks RT, Tashjian RZ: Interscalene block for
postoperative analgesia using only ultrasound guidance: the outcome in 200

84. Swenson JD, Bay N, Loose E, Bankhead B, Davis J, Beals TC, Bryan NA, Burks
RT, Greis PE: Outpatient management of continuous peripheral nerve catheters
2006; 103: 1436-1443

85. Fredrickson MJ, Ball CM, Dalgleish AJ: Successful continuous interscalene
analgesia for ambulatory shoulder surgery in a private practice setting. Reg Anesth
Pain Med 2008; 33: 122-128


94. Charous MT MS, Suresh PJ, Sandhu NS, Loland JV, Mariano ER, Donohue MC, Dutton PH, Ferguson EJ, Ilfeld BM: Continuous femoral nerve blocks: varying local anesthetic delivery method (bolus vs. basal) to minimize quadriceps motor block while maintaining sensory block. Anesthesiology: In Press


112. Chelly JE, Casati A: Perineural infusion of local anesthetics: "more to the review". Anesthesiology 2007; 106: 191-192

113. Boezaart AP: That which we call a rose by any other name would smell as sweet and its thorns would hurt as much. Reg Anesth Pain Med 2009; 34: 3-7


123. Liu SS, John RS: Modeling cost of ultrasound versus nerve stimulator
guidance for nerve blocks with sensitivity analysis. Reg Anest Pain Med 2010; 35:
57-63


125. Bergman BD, Hebl JR, Kent J, Horlocker TT: Neurologic complications of 405

Fraschini G, Chelly JE: Lidocaine versus ropivacaine for continuous interscalene
47: 355-360

127. Butterworth JFt: Potency ratios for local anesthetics in regional blocks: how
long must we wait? Regional anesthesia and pain medicine 2008; 33: 1-3

P, Sassoli V, Luppi M, Casati A: Pain relief and motor function during continuous
interscalene analgesia after open shoulder surgery: a prospective, randomized,
double-blind comparison between levobupivacaine 0.25%, and ropivacaine 0.25%
or 0.4%. Eur.J Anaesthesiol. 2006; 23: 1005-1009

129. Heid F, Muller N, Piepho T, Bares M, Giesa M, Drees P, Rumelin A, Werner C:
Postoperative analgesic efficacy of peripheral levobupivacaine and ropivacaine: a
prospective, randomized double-blind trial in patients after total knee arthroplasty.
Anest Analg 2008; 106: 1559-61, table
130. Casati A, Vinciguerra F, Cappelleri G, Aldegheri G, Grispigni C, Putzu M, Rivoltini P: Levobupivacaine 0.2% or 0.125% for continuous sciatic nerve block: a prospective, randomized, double-blind comparison with 0.2% ropivacaine. Anesth Analg 2004; 99: 919-23, table


136. Borgeat A, Aguirre J, Marquardt M, Mrdjen J, Blumenthal S: Continuous interscalene analgesia with ropivacaine 0.2% versus ropivacaine 0.3% after open rotator cuff repair: the effects on postoperative analgesia and motor function. Anesth Analg 2010; 111: 1543-7


141. Le LT, Loland VJ, Mariano ER, Gerancher JC, Wadhwa AN, Renehan EM, Sessler DI, Shuster JJ, Theriaque DW, Maldonado RC, Ilfeld BM: Effects of local anesthetic concentration and dose on continuous interscalene nerve blocks: a dual-


147. Seet E, Leong WL, Yeo AS, Fook-Chong S: Effectiveness of 3-in-1 continuous femoral block of differing concentrations compared to patient controlled


149. Fredrickson MJ, Price DJ: Analgesic effectiveness of ropivacaine 0.2% vs 0.4% via an ultrasound-guided C5-6 root/superior trunk perineural ambulatory catheter. Br.J Anaesth. 2009; 103: 434-439


152. Pere P: The effect of continuous interscalene brachial plexus block with 0.125% bupivacaine plus fentanyl on diaphragmatic motility and ventilatory function. Reg Anesth 1993; 18: 93-97


159. Ilfeld BM, Morey TE, Enneking FK: Continuous infraclavicular perineural infusion with clonidine and ropivacaine compared with ropivacaine alone: a randomized, double-blinded, controlled study. Anesth Analg 2003; 97: 706-712

161. Weber A, Fournier R, Van Gessel E, Riand N, Gamulin Z: Epinephrine Does Not Prolong the Analgesia of 20 mL Ropivacaine 0.5% or 0.2% in a Femoral Three-In-One Block. Anesth Analg 2001; 93: 1327-1331


173. Ilfeld BM, Duke KB, Donohue MC: The association between lower extremity continuous peripheral nerve blocks and patient falls after knee and hip arthroplasty. Anesth Analg 2010; 111: 1552-4


175. Ilfeld BM, Vandenborne K, Duncan PW, Sessler DI, Enneking FK, Shuster JJ, Theriaque DW, Chmielewski TL, Spadoni EH, Wright TW: Ambulatory continuous interscalene nerve blocks decrease the time to discharge readiness after total shoulder arthroplasty: A randomized, triple-masked, placebo-controlled study. Anesthesiology 2006; 105: 999-1007


185. Bleckner LL, Bina S, Kwon KH, McKnight G, Dragovich A, Buckenmaier CC, III: Serum ropivacaine concentrations and systemic local anesthetic toxicity in trauma
patients receiving long-term continuous peripheral nerve block catheters. Anesth Analg 2010; 110: 630-634

186. Paauwe JJ, Thomassen BJ, Weterings J, van Rossum E, Ausems ME: Femoral nerve block using ropivacaine 0.025%, 0.05% and 0.1%: effects on the rehabilitation programme following total knee arthroplasty: a pilot study. Anaesthesia 2008; 63: 948-953


188. Ilfeld BM, Enneking FK: Continuous peripheral nerve blocks at home: A review. Anesth Analg 2005; 100: 1822-1833


223. Ilfeld BM, Morey TE, Enneking FK: Continuous infraclavicular brachial plexus block for postoperative pain control at home: a randomized, double-blinded, placebo-controlled study. Anesthesiology 2002; 96: 1297-1304


228. Cornish PB: Supraclavicular regional anaesthesia revisited--the bent needle technique. Anaesthesia and intensive care 2000; 28: 676-9


304. Dullenkopf A, Zingg P, Curt A, Borgeat A: [Persistent neurological deficit of the upper extremity after a shoulder operation under general anesthesia combined with a preoperatively placed interscalene catheter]. Anaesthesist 2002; 51: 547-551

305. Swenson JD, Davis JJ: Ultrasound-guided regional anesthesia: why can't we all just stay away from the nerve? Anesthesiology 2008; 109: 748-749


308. Neal JM, Wedel DJ: Ultrasound guidance and peripheral nerve injury: is our vision as sharp as we think it is? Reg Anesth Pain Med 2010; 35: 335-337


355. Larrabure P, Pandin P, Vancutsem N, Vandesteene A: Tibial nerve block:
280