Complications of regional anesthesia
J. Eric Greensmith and W. Bosseau Murray

Purpose of review
The use of regional anesthesia, either alone or as an adjunct to general anesthesia, is at an all-time high. Demonstrated benefits include reduced side effects, more efficient use of facilities and enhanced patient satisfaction with the improved postoperative pain relief. New advances in equipment, techniques and medications have been incorporated over the past 10 years, and especially over the last 2 years. As the number of practitioners and procedures increase, the number of complications may rise as well.

Recent findings
The specific issues of nerve damage, treatment of local anesthetic toxicity with lipid solutions and prevention of wrong-sided procedures are examined with special reference to recent publications.

Summary
Specific needle shapes, appropriate pharmacologic resuscitation from intravascular injection of local anesthetics and institutional procedures to positively identify patients and the correct block location are all part of a strategy to minimize the occurrence of adverse outcomes and to mitigate the consequences of those adverse events when they do occur. More importantly, these are changes that can be instituted immediately with minimal expense to the institution and great benefit to the patient.

Keywords
complications, local anesthetic toxicity, nerve injury, regional anesthesia, wrong-sided procedure

Introduction
Recent national publications document the fact that perioperative pain is poorly managed. Regional anesthesia has been proposed as a key component of a comprehensive multimodal approach to the prevention of postoperative pain.

The last decade, and particularly the last 5 years, have witnessed a significant increase in the use of regional anesthesia. Purported benefits of regional anesthetic techniques range from reduced mortality and reduced major morbidity [1], reduction in minor (albeit annoying) morbidities [2], to enhanced tissue oxygenation, and improved outpatient pain management [3**4].

Sales of regional anesthesia textbooks, videos, interactive DVDs, regional anesthesia equipment and journals, as well as visits to regional websites, are at an all-time high. New developments have been reported in nerve stimulators [5], as well as novel drug delivery technologies (pumps, deposition release medications [6*], and transcutaneous drug-delivery systems).

The enhanced numbers of practitioners of regional anesthesia, and a logarithmic growth in procedures performed, similarly increase the potential for complications and adverse outcomes. This review will examine three areas of challenge and progress with regards to complications in the practice of regional anesthesia: direct and pressure-induced nerve injury, local anesthetic toxicity and wrong-site regional procedures.

New information regarding direct nerve injury
The public perception of the danger in peripheral neural blockade largely centers around concerns of direct nerve injury by the use of a needle, for instance paralysis after a ‘needle in the back/spine’.

Studies by Dag Selander and colleagues in the 1970s [7] demonstrated that blunt or ‘B bevel’ needles (see Fig. 1) are less likely to penetrate a nerve, and thus, less likely to cause nerve damage, than a long, sharp cutting edge needle [7]. There was a brief flurry of controversy over this after Rice and McMahon’s report in 1992 [8] that long bevel (i.e. sharp) needles were less likely to cause nerve damage than B-bevel needles – an apparent refutation of Selander’s work. This apparent discrepancy is explained by the methodologic differences wherein Rice and McMahon’s in-situ model guaranteed that the nerve was impaled by the needle whereas Selander’s work...
(and most biologic scenerios) allow the nerve to move freely and thus passively slide away from all but the most resolute needle approaches. Recent application of high-resolution ultrasound technology confirms, in real time, Selander’s premise [7] that major nerves approached by a blunt bevel block needle in unconfined spaces are rarely penetrated by the needle and generally slide away from the needle after any contact. Nerves being blocked in confined spaces (e.g. the ulnar nerve at the olecranon fossa, the fibular nerve at the head of the fibula) may not enjoy this relative protection due to their lack of mobility in their anatomic confinement. In a recent review, Marhofer et al. [9] suggested that not only can ultrasound guidance ensure a high block success rate, but also can nearly eliminate needle complications.

Still, it is apparent that nerves can be penetrated by needle placement with variable sequelae – ranging from no demonstrable change in function to permanent sensory and motor dysfunction. What accounts for this range of outcomes for direct nerve injury? Clinical experience (but not examined in any prospective experimental fashion) with ultrasound guided blocks suggests that early recognition of intraneural injection is readily apparent as the nerve is seen to swell with the first few milliliters of local anesthetic injected. Immediate cessation of injection and repositioning of the needle to an extraneural location have been associated with the absence of demonstrable neural deficit in the postoperative period (V. Chan, 2006, personal communication). While this ‘absence of proof, is not proof of absence’, it suggests a fruitful line of investigation for avoidance of nerve damage.

Unfortunately, there are several case reports with what appear to be direct intraneural injections and resultant permanent dyesthesias in patients who were lightly sedated – or not sedated at all – and the patients did not report any pain in the course of the local anesthetic injection [10]. Since intraneural injection of local anesthetic may give a very brief paresthesia that is rapidly extinguished by the presence of the local anesthetic within the nerve [11], it has been suggested that use of 1 ml of saline should be administered for the initial Raj test so that any painful intraneural injections would not be masked by the presence of local anesthetic within the nerve fiber. Since cessation of muscular contraction with the nerve stimulator occurs rapidly, the small injection of the Raj test is thought to be due to charge dissipation; the use of saline in lieu of local anesthetic should still be predictive of a successful block [12].

Another line of investigation suggests that postregional/postoperative nerve injury may be a function of peripheral nerve ischemia. Among possible contributors to peripheral nerve ischemia is the addition of low-dose (5 µg/ml) epinephrine to the local anesthetic mixture. Selander performed topical endoneural and intrafascicular injections of saline with various concentrations of bupivacaine in the presence or absence of epinephrine in rabbit sciatic nerves in vivo. While intrafascicular injections inevitably were associated with neuronal degeneration, endoneurial injections seemed to be associated with degeneration based on the presence of epinephrine at 5 µg/ml. Perhaps nerves with a generous collateral blood supply may be less vulnerable than those in a watershed area between two tenuous vascular arcades, such as the sciatic nerve. So at least for the sciatic nerve, the recommendation has been to forgo the addition of epinephrine, especially for the use of long-acting agents such as bupivacaine.

Neural ischemia may also arise from a variety of other impediments to blood flow, such as a tourniquet occluding the blood supply to a nerve, hypotension and/or increases in intraneural pressure that cause temporary cessation of nutrient blood flow. Hadzic and colleagues [13] demonstrated in an anesthetized dog model that low pressure nerve injections – both perineurally (into the epineurium) and intraneurally (within the perineurium) – were not permanently injurious to the nerves in the dogs, whereas higher pressure injections (>11 psi) were associated with severe fascicular injury and persistent neurologic injury.

In a simulation study designed to examine pressures that anesthesiologists achieved during regional anesthetic
injections, Claudio et al. [14] demonstrated that the vast majority of anesthesiologists generated pressures greater than 20 psi and 10% exerted greater than two atmospheres (30 psi) – all well beyond the 11 psi ‘breakpoint’ for permanent nerve injury in cases of intraneural injection. This study went on to illustrate how unreliable the nebulous parameter of ‘syringe feel’ is for predicting true injection pressures.

In truth, all of these factors (and others to be discovered) may well coexist in cases of nerve injury. Nerves already compromised by poor vascular supply may be damaged by needle contact, particularly if entrapped and incapable of sliding away from a needle with a cutting taper. Any ensuing injection, especially an intraneural position and/or injected at high pressure, may bring nutrient blood flow to a halt. Neural ischemia would be even more severe if vasoconstrictors were added to the local anesthetic. Strategies to minimize complications will work best when brought to bear on all the risk factors that potentiate nerve injury risk.

New developments in the treatment of systemic local anesthetic toxicity

Systemic local anesthetic toxicity and its consequences are major sources of complications in regional anesthesia. The two most problematic consequences of toxicity are seizures and cardiac toxicity. While absolute limits and weight-scaled limits have been proposed, debated and refuted in the literature, it is clear that location of [15] local anesthetic injection is at least as important as the absolute mass of drug administered.

Relative toxicities of the various ester and amide local anesthetics have been calculated and expressed as a ratio to the nerve blocking potency and as a ratio of the cardiac to central nervous system (CNS) toxicity [16]. Bupivicaine, a favored amide local anesthetic, has a narrow CNS to cardiac toxicity ratio [17]. High doses or rapid increases in plasma bupivicaine levels can predispose the heart to a variety of brady-dysrhythmias as well as ventricular tachycardia and ventricular fibrillation. Due to the high affinity of bupivicaine for cardiac sodium channels (as well as other myocardial sites) [18], bupivicaine cardiac toxicity can be extremely refractory to all conventional treatment strategies. Paradoxically, the bupivicaine binding to sodium channels greatly retards myocardial cellular metabolism, affording a measure of cellular protection in the face of ischemia [19]. Thus, bupivicaine is, ironically, a myocardial preservative. Strategies that rapidly reduce bupivicaine levels (the functional equivalent of a chelator or binding agent) or support circulation (cardiopulmonary bypass) until bupivicaine levels drop by redistribution, metabolism and clearance may result in an amazingly well preserved myocardial function despite an asystolic myocardial arrest.

Bupivicaine is very lipid soluble, suggesting that infusion of a lipid may serve to chelate (bind) the local anesthetic and lower free plasma levels of the drug. Isolated heart experiments show that radiolabeled bupivicaine had a much faster washout rate from the myocardium when a lipid emulsion was infused through the coronary circulation. Time to recovery of intrinsic rhythm, time to recovery of baseline pressure and rate pressure product were all significantly reduced by intravascular lipid emulsion therapy [20].

In-vivo rat experiments by Weinberg et al. in the late 1990s [21] demonstrated a protective shift in the cardiac toxic dose of bupivicaine when administered after lipid infusion. Intravenous lipids remained merely as a theoretic antidote to the specter of bupivicaine toxicity until this year, when the first case report of a successful human resuscitation from bupivicaine toxicity using lipids was published.

In a recent extraordinary case report [22], a 58-year-old, 82 kg male, with a history of coronary bypass surgery was administered a supraclavicular block for arm surgery. Ninety seconds after receiving a mixture of 20 ml each of mepivicaine 1.5% and bupivicaine 0.5%, the patient began to seizure and demonstrated premature ventricular contractions, followed by ventricular tachycardia that progressed on to a complete asystolic cardiac arrest. The seizure was rapidly recognized as due to local anesthetic toxicity and rapidly truncated with 100 mg of intravenous propofol. Cardiopulmonary resuscitation (CPR) was initiated and epinephrine, 1 mg, was administered three times, plus a loading dose of amiodarone as well as vasopressin along with a total of four direct current countershocks without success. At this point 100 ml of 20% lipid emulsion was given as an intravenous bolus. The patient received a fifth attempt at direct current defibrillation; the patient had one sinus beat followed by resumption of a normal sinus rhythm at 90 beats per minute. The patient was eventually discharged home, neurologically intact. This case is very impressive in that bupivicaine toxicity – if it progressed to the point of cardiac standstill – has been almost uniformly lethal. A lipid emulsion – cheap and readily available – may be our first effective antidote to this most dreaded of all regional anesthesia complications.

This case report [22] is accompanied by a leading editorial [23] emphasizing the clinical importance of the use of lipids, especially as the basic science and animal work has such a solid basis.

Wrong-sided and wrong-site procedures

In a field proudly featuring exceptional achievements of nerve localization, imaging, nerve stimulation and reductions in mortality and morbidity, it may seem trivial
and incongruous to discuss the (seemingly) simple concept of wrong-sided procedures [24]. It is not trivial. Figure 2 shows the number of wrong-site surgeries by year over the past decade. While there is no comparable registry for wrong-sided regional anesthetics (yet), it is probable that the trend would be similar.

In May 2003, the Joint Commission on HealthCare Organizations (JCAHO) and its corporate members sponsored a Wrong-Site Summit. More than 50 participants discussed a root cause analysis of wrong-site procedures and identified potential barriers to elimination of those root causes. At this summit, five key areas were identified:

1. Preoperative verification;
2. A defined ‘timeout’ prior to the procedure;
3. Unambiguous surgical site marking;
4. Special situations and settings outside of the operating room;
5. Physician buy-in.

JCAHO maintains an extensive website (http://www.jointcommission.org) with explicit guidelines on the ‘universal protocol’ for avoiding ‘wrong side’ surgery. The pre-regional anesthetic ‘timeout’ should be implemented prior to the surgical timeout and is analogous in many ways.

Preoperative block placements often occur outside of the operating room setting and, therefore, are somewhat removed from the remainder of the preoperative safety checks. Furthermore, patients are not infrequently blocked at anatomical locations remote from their surgical site. A patient having ankle surgery may have a femoral/sciatic block combination to block both operative and tourniquet pain. Finally, for some midline or unilateral structures – such as partial or total thyroidectomy – it may be appropriate to block the superficial cervical plexus bilaterally – even though the surgery may be one sided.

Although there are no formal statistical data available on this point, front/back block combinations seem to be particularly vulnerable to wrong-sided blocks. The patient may be positioned prone for a sciatic block of any approach with the operator standing ipsilateral to the side to be blocked. When the patient is subsequently turned supine for a femoral or saphenous nerve block, operators must switch sides or they are now standing on the side of the extremity not to be blocked and thus at risk for a wrong-sided block.

Deschner and colleagues [25], in an abstract at the 2006 American Society of Regional Anesthesia (ASRA) meeting, describe a systematic ‘timeout’ approach before sedation of a block procedure is initiated (see Fig. 3). The mnemonic ‘ECT’ is used to denote equipment check, consent check and timeout check for correct, and labeled block site. Analogous to the pilot preflight checklist, a formal, systematic preprocedural review such as this is the best systems defense against a wrong-sided procedure.

At our institution, we have recently instituted the following process: the initial event in a patient encounter in the block room is a ‘timeout/check in’. The patient’s name band is checked and confirmed with the patient and the chart. The allergy, anticoagulant and fasting (NPO) histories are checked, along with the patient’s understanding of what surgery is to be performed. The anesthesiologists put their initials on the front and back of the extremity to be blocked. A circumferential band of 10 cm (4 inch) wide blue masking tape is placed loosely around the extremity to be blocked. The patient is positioned and draped such that the blue band of marking tape is

---

**Figure 2** The increase in the number of reported wrong-site surgeries over the last decade

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of events reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>1995</td>
<td>0</td>
</tr>
<tr>
<td>1996</td>
<td>10</td>
</tr>
<tr>
<td>1997</td>
<td>20</td>
</tr>
<tr>
<td>1998</td>
<td>30</td>
</tr>
<tr>
<td>1999</td>
<td>40</td>
</tr>
<tr>
<td>2000</td>
<td>50</td>
</tr>
<tr>
<td>2001</td>
<td>60</td>
</tr>
<tr>
<td>2002</td>
<td>70</td>
</tr>
<tr>
<td>2003</td>
<td>80</td>
</tr>
<tr>
<td>2004</td>
<td>90</td>
</tr>
<tr>
<td>2005</td>
<td>100</td>
</tr>
</tbody>
</table>

Adapted from the Joint Commission on HealthCare Organizations (JCAHO) website at http://www.jointcommission.org.
Future trends

New improvements in medications, training, procedural techniques, neural localization, and safety procedures are frequently reported. Future trends are always difficult to predict, and many a prognostication has appeared foolish in retrospect, but two unrelated areas of basic science research bear scrutiny.

The first is use of the high conductance properties of major nerve tracts to map these nerves transcutaneously (http://www.nervonix.com). Since nerves have a low impedance to current flow – lower than surrounding muscle, bone and connective tissue – it may be possible to apply small currents in higher frequency ranges that take advantage of the conductive properties of individual nerves and search for an increased current flow ‘down-stream’ as the nerve is approached by the stimulating current.

Secondly, a new facet may be entering the regional anesthesia/general anesthesia debate in the dual nature of opiate analgesics – specifically the ability to ameliorate acute pain contrasted with the long-term sequelae of pain sensitization [26]. While it is clear that opiates are unsurpassed among intravenous and oral medications in the treatment of pain, there is a growing body of literature to suggest that these same medications may set up a postoperative hypersensitivity. It is possible that the concept of ‘preemptive analgesia’ may, in fact, be a manifestation of ‘opiate sparing’ and a lack of the postoperative sensitization by perioperative narcotic administration [27]. If, in fact, opiates exacerbate the postoperative pain experience, this will lend a new impetus to the search for ever more effective means of multimodal analgesia that are opiate sparing and thus, ultimately, pain sparing.

Thirdly, a call has been made for more radiological studies after suspected subdural placement of an epidural catheter, in an attempt to better understand the physiology. A novel case of rapid onset (6 min) massive subdural anesthesia with cardiovascular collapse was reported by Wills [28]. The position of the epidural catheter was radiologically confirmed after successful resuscitation. We highlight this case because of the rarity of subdural blocks, and the consequent tendency for practitioners not to test the height of the block after the test dose.

Fourthly, although infectious complications of regional anesthesia have not been a focus of this article, they remain a dreaded, albeit rare, threat, and readers are directed to a recent review of this topic [29].

Finally, two recent reviews are commended to the reader.

The first is a brief review of perioperative nerve dysfunction by Ridgeway and Herrick [30]. This describes three key points.

1. Temporary postoperative paraesthesia is not uncommon, even with no known errors occurring.
2. The incidence of permanent nerve damage is approximately one in 5000.
3. A nerve stimulator will not necessarily prevent nerve damage.

Patient positioning and surgery are often implicated in perioperative nerve damage.

The second is a comprehensive review of peripheral nerve block catheters by Andre’ Boezaart [31]. This review includes an extensive review of complications of perineural blocks under the headings nerve injury, infection, associated unwanted nerve blockade, complications due to drug effects, and pain during catheter placement. The conclusion is that in spite of these rare complications, it is still valuable to place such nerve catheters, as this technique is the only one enabling pain relief not only during periods of immobility, but also during mobilization and movement of the extremities, for instance, during physical therapy.
Conclusion

Complications in regional anaesthesia range from trivial to life threatening. Incidence and prevalence figures for morbidity and mortality vary with the procedure and health status of the patient. Although there are data from closed claims analyses [32], small randomized trials, as well as from large individual case series compared with historic controls [33], it is difficult to get accurate incidence figures with a reliable denominator of procedures performed.

Using the methodology of surveillance studies that has proven helpful in infection control research, Schulz-Stüber and colleagues at the University of Iowa have recently organized the Regional Anesthesia Surveillance System (http://www.uirass.com) in an effort to assemble large numbers of patient experiences with regional anaesthesia, such that accurate statements can be made about incidence, type and prevalence of complications. Tim Cook from the Royal College of Anaesthetists of Great Britain is organizing a comparable audit of major complications of neuraxial anaesthesia (tcok@rcoc.ac.uk). Out of these large aggregate experiences, it is hoped that meaningful trends will become apparent and benchmark statistics can be derived against which individual practitioners and institutions can compare their performance.

This brief survey has looked at technical, pharmacologic and administrative advances to minimize complications and enhance safety in the practice of regional anaesthesia. As the advantages of regional anaesthesia become apparent and the numbers of procedures performed multiply, it is imperative that we enhance the safety and quality of the practice in parallel as a duty to our patients.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 583–584).


4 Hadzic A, Karaca PE, Hobpeka P, et al. Peripheral nerve blocks result in superior recovery profile compared with general anaesthesia in outpatient knee arthroscopy. Anesth Analg 2005; 100:976–981. Head on head trial of general anaesthesia compared with combined lumbar plexus and sciatric blocks for efficiency, side effects, and pain during outpatient knee surgery. This study shows a clearly superior outcome with regional anaesthesia.


20 Weinberg GL, Ripper R, Murphy P, et al. Lipid infusion accelerates removal of bupivacaine and recovery from bupivacaine toxicity in the isolated rat heart. Reg Anesth Pain Med 2006; 31:296–303. Good entry point into the basic (animal) science literature for local anesthetic metabolism (‘binding’) using lipids. This will change clinical practice by encouraging the use of lipids early in the resuscitation of bupivacaine toxicity. The ‘lipid’ used for this purpose is the standard lipid used for total parenteral nutrition (‘hyperalimentation’).


31 Boezaart AP. Perineural infusion of local anesthetics. Anesthesiology 2006; 104:872–880.
