Neurologic Complications of Peripheral Nerve Blocks

Terese T. Horlocker, MD

Perioperative nerve injuries have long been recognized as a complication of regional anesthesia. Fortunately, severe or disabling neurologic complications rarely occur. Risk factors contributing to neurologic deficit after regional anesthesia include neural ischemia (hypothesized to be related to the use of vasoconstrictors or prolonged hypotension), traumatic injury to the nerves during needle or catheter placement, infection, and choice of local anesthetic solution.[1–3] In addition, postoperative neurologic injury due to pressure from improper patient positioning or from tightly applied casts or surgical dressings, as well as surgical trauma are often attributed to the regional anesthetic.[4] Lynch et al.[5] reported a 4.3% incidence of neurologic complications following total shoulder arthroplasty. The neurologic deficit localized to the brachial plexus in 75% of affected patients. Importantly, the level of injury occurred most commonly at the upper and middle nerve trunks- the level at which an interscalene block is performed, making it impossible to determine the etiology of the nerve injury (surgical versus anesthetic). Patient factors such as body habitus and preexisting neurologic dysfunction may also contribute. For example, the incidence of peroneal nerve palsy following total knee replacement is increased in patients with significant valgus or a preoperative neuropathy (Table 1).[6,7]

The safe conduct of regional anesthesia involves knowledge of the large patient surveys as well as individual case reports of neurologic deficits following regional anesthetic techniques. Prevention of complications, along with early diagnosis and treatment are important in the management of regional anesthetic risks.

INCIDENCE AND ETIOLOGY OF NEUROLOGIC COMPLICATIONS

A prospective survey in France recently evaluated the incidence and characteristics of serious complications related to regional anesthesia.[1] A total of 103,730 regional anesthetics, including 21,278 peripheral nerve blocks, were performed over a five-month period. The incidence of cardiac arrest and neurologic complications was significantly higher after spinal anesthesia than other types of regional procedures (Table 2). Neurologic complications related to the regional anesthetic technique occurred in 34 patients; recovery was complete within three months in 19 of 34 patients. In all cases of nerve injury peripheral block, needle placement was associated with either paresthesia during needle insertion, or pain with injection. In all cases, the postoperative deficit had the same topography as the associated paresthesia. The authors concluded that needle trauma and local anesthetic neurotoxicity were the etiologies of most neurologic complications. This study demonstrated that the incidence of severe anesthesia-related complications is very low. However, since serious complications were noted to occur even in the presence of experienced anesthesiologists, continued vigilance in patients undergoing regional anesthesia is warranted. In a follow-up study involving over 150,000 regional anesthetics, Auroy et al.[8] reported a decrease in the frequency of serious complications related to the anesthetic technique.

Cheney et al.[9] examined the American Society of Anesthesiologists Closed Claims database to determine the role of nerve damage in malpractice claims filed against anesthesia care providers. Of the 4,183 claims reviewed, 670 (16%) were for anesthesia-related nerve injury. The most frequent sites of injury were the ulnar nerve (190 claims), brachial plexus (137 claims), lumbosacral roots (105 claims), or spinal cord (84 claims). Regional anesthesia was more frequently associated with nerve damage claims. Ulnar nerve injuries were more often associated with general anesthesia. However, spinal cord and lumbosacral nerve root injuries having identifiable etiology were associated predominantly with a regional anesthetic technique, and were related to paresthesias during needle or catheter placement or pain during injection of local anesthetic. It is also notable that despite intensive medicolegal investigation, a definite mechanism of injury is rarely determined. The lack of apparent mechanism often led the patient (and consulting specialists) to assume that something most have been done incorrectly during the perioperative period to cause the nerve injury.

NERVE INJURY FROM NEEDLE AND CATHETER PLACEMENT

Many anesthesiologists intentionally elicit a paresthesia during the performance of peripheral regional techniques. Although the elicitation of a paresthesia may represent direct needle trauma and increase the risk of persistent paresthesia associated with regional anesthesia, there are no clinical studies that definitively either prove or refute the theory.[10–13] Selander

Table 1. Risk Profile for Peroneal Nerve Palsy After Total Knee Arthroplasty

Risk factor	Peroneal palsy (n = 8)	No peroneal nerve palsy (n = 353)
Age (yr)	64 ± 10	69 ± 10
Valgus (degrees)	13 ± 5*	9 ± 7
Tourniquet time (min)	141 ± 52*	103 ± 28
Neurologic condition	4*	30
Anesthetic technique	3	112
General		
Spinal	1	67
Epidural	4	174
Epidural analgesia	4**	104
Postoperative bleeding	3*	4

* $P < 0.05$.

** Although postoperative epidural analgesia was not a risk factor for peroneal nerve palsy, all cases of peroneal nerve palsy with motor deficits occurred in patients with postoperative epidural analgesia. Adapted from Horlocker et al. (6). Used with permission.

et al.[10] reported a higher incidence of postoperative nerve injury in patients where a paresthesia was sought during axillary block (2.8%) compared to those undergoing a perivascular technique (0.8%). However, the difference was not significant. Importantly, 40% of patients in the perivascular group reported unintentional paresthesias during the procedure, demonstrating the difficulty with standardization of technique and analysis of neural injury. Postoperative neurologic deficits ranged from slight hypersensitivity to severe paresis, and persisted from two weeks to greater than one year. In a prospective study utilizing a variety of regional anesthetic approaches including paresthesia, transarterial and nerve stimulator techniques, Urban and Urquhart[12] noted that mild paresthesias were common the day after surgery, occurring after 9% of interscalene blocks and after 19% of axillary blocks. At two weeks the incidence had decreased significantly, with near complete resolution noted at four weeks. Stan et al.[11] reported a 0.2% incidence of neurologic complications after axillary blocks performed with the transarterial approach. However, vascular complications such as transient arterial spasm, unintentional vascular injection and hematoma formation occurred in 1.4% of patients. Theoretically, localization of neural structures with a nerve stimulator would allow a high success rate without increasing the risk of neurologic complications, but this has not been formally evaluated. Fanelli et al.[13] prospectively evaluated 3996 patients undergoing sciatic-femoral, axillary, and interscalene blocks using a multiple injection/nerve stimulator technique. During the first month after surgery, 69 patients (1.7%) developed neurologic dysfunction; recovery was complete in all but one in 4–12 weeks. (This frequency is similar to that reported using a paresthesia technique). The only variable associated with neurologic injury was tourniquet inflation pressure >400 mm | Hg. Use of a nerve stimulator does not prevent intraneural injection. Indeed, serious neurologic injury has been reported following uneventful brachial plexus block using a nerve stimulator technique.[14,15] Equally interesting are the cases in which apparent intraneural injection did not result in neurologic injury.[16,17] Currently, no compelling evidence exists to endorse a single technique as superior with respect to success rate or incidence of complications. Needle gauge, type (short vs long bevel), and bevel configuration may also influence the degree of nerve injury, although the findings are conflicting and there are no confirmatory human studies.[18,19]

The passage and presence of an indwelling catheter into a peripheral nerve sheath presents an additional source of direct trauma. The risk of neurologic complications resulting from plexus or peripheral nerve catheters remains undefined.[20,21] While difficulty during catheter insertion may lead to vessel puncture, tissue trauma and bleeding, significant complications are uncommon and permanent sequelae are rare. In a series of 405 continuous brachial plexus blocks, Bergman et al.[22] reported 9 complications in 8 patients for an overall frequency of 2.2%. Complications included one each of the following: localized infection (treated with catheter removal and antibiotics), axillary hematoma, and retained catheter fragment requiring surgical excision. In addition, two patients reported signs and symptoms of systemic (pre-seizure) local anesthetic toxicity. Four (1.0%) patients reported new neurologic deficits postoperatively. In two patients, the neural dysfunction was non-anesthesia related. In a more recent prospective study involving 1,416 patients with continuous catheters, there were 12 patients (0.84%) experiencing serious adverse events and three (0.21%) patients had neurologic lesions attributed to the continuous peripheral nerve catheter.[23]

Table 2. Complications Related to Regional Anesthesia

Technique	Cardiac arrest	Death	Seizure	Neurologic injury
Spinal (N = 40,640)	26 (3.9–8.9)	6 (0.3–2.7)	0 (0–0.9)	24 (3.5–8.3)
Epidural (N = 30,413)	3* (0.2–2.9)	0 (0–1.2)	4 (0.4–3.4)	6* (0.4–3.6)
Peripheral blocks (N = 21,278)	3+ (0.3–4.1)	1 (0–2.6)	16# (3.9–11.2)	4# (0.5–4.8)
IV regional (N = 11,229)	0 (0–3.3)	0 (0–3.3)	3 (0.5–7.8)	0 (0–3.3)

Data presented are number and (95% confidence interval). * Epidural versus spinal ($P < 0.05$).

+ Peripheral nerve blocks versus spinal ($P < 0.05$). # Peripheral nerve blocks versus epidural ($P < 0.05$).

Adapted from Auroy et al. (1). Used with permission.

LOCAL ANESTHETIC TOXICITY

Neurologic complications following regional anesthesia may be a direct result of local anesthetic toxicity. Although most local anesthetics administered in clinical concentrations and doses do not cause nerve damage, prolonged exposure, high dose and/or high concentrations of local anesthetic solutions may result in permanent neurologic deficits. There is both laboratory and clinical evidence that local anesthetic solutions are potentially neurotoxic and that the neurotoxicity varies among local anesthetic solutions.[2,24–27] Differences in neurotoxicity are dependent on pKa, lipid solubility, protein binding and potency. In histopathologic, electrophysiologic, and neuronal cell models, lidocaine and tetracaine appear to have a greater potential for neurotoxicity than bupivacaine at clinically relevant concentrations.[25,28] Additives such as epinephrine and bicarbonate may also affect neurotoxicity. Addition of 5 μg/mL of epinephrine increases the toxicity of both lidocaine and bupivacaine. The presence of a preexisting neurologic condition may predispose the nerve to the neurotoxic effects of local anesthetics.[6,12] The presumed mechanism is a "double crush" of the nerve at two locations resulting in a nerve injury of clinical significance.[29] The double crush concept suggests that nerve damage caused by traumatic needle placement/local anesthetic toxicity during the performance of a regional anesthetic may worsen neurologic outcome in the presence of an additional patient factor or surgical injury. Finally, intraneuronal injection may potentiate the neurotoxic effects of higher concentrations of local anesthetic as well as the addition of vasoconstrictors.

NEURAL ISCHEMIA

Peripheral nerves have a dual blood supply consisting of intrinsic endoneural vessels and extrinsic epineural vessels. A reduction or disruption of nerve blood flow may result in neural ischemia. Intraneural injection of volumes as small as 50-l00 μL may generate intraneural pressures which exceed capillary perfusion pressure for as long as 10 minutes and thus cause neural ischemia.[30] Endoneural hematomas have also been reported after intraneural injection.[19] Epineural blood flow is also responsive to adrenergic stimuli.[31,32] The use of local anesthetic solutions containing epinephrine theoretically may produce peripheral nerve ischemia, especially in patients with microvascular disease.[2,26]

Neural ischemia may also result from expanding hematoma. In the series of 1000 transarterial axillary blocks, Stan et al.[11] reported vascular complications such as transient arterial spasm, unintentional vascular injection and hematoma formation occurred in 1.4% of patients. A case report of axillary block complicated by hematoma and radial nerve injury has been described.[33]

Few data exist on the risk of hemorrhagic complications in patients undergoing peripheral block while receiving hemostasis-altering medications. Although the Consensus Statements on Neuraxial Anesthesia and Anticoagulation published by the American Society of Regional Anesthesia[34] could be applied to any regional anesthetic technique, a more liberal application, taking into account the compressibility of the needle insertion site and the vascular structure at risk.[35–37] Bleeding into a nerve sheath does not represent the same catastrophe as bleeding into the spinal canal, both in severity and significance of neural compromise. Certainly, cardiac catheterization involves the placement of a large cannula in a femoral or brachial vessel with subsequent anticoagulation, yet the frequency of neurologic dysfunction is rare. Indeed, single dose and continuous peripheral blocks may represent a suitable alternative to neuraxial techniques in the anticoagulated patient. Communication between clinicians involved in the perioperative management of patients receiving anticoagulants for thromboprophylaxis is essential in order to decrease the risk of serious hemorrhagic complications. Patients should be closely monitored in the perioperative period for early signs of neural compression such as pain, numbness, or weakness. A delay in diagnosis and intervention may lead to irreversible neural ischemia.

INFECTIOUS COMPLICATIONS

Infection can complicate any regional technique, but neurologic sequelae are rare. The infectious source can be exogenous due to contaminated equipment or medication, or endogenous secondary to a bacterial source in the patient seeding to the remote site of needle or catheter insertion. Although infection at the site of needle insertion is an absolute contraindication to regional anesthesia, common sense dictates that encroaching cellulitis, lymphangitis, or erythema would also preclude a regional technique. Indwelling catheters theoretically increase the risk of infectious complications. However, while colonization may occur, infection is rare.[22,23,38–40] Local infections are treated with catheter removal and antibiotics. Retained catheter fragments may be a source of infection.[22] Strict attention to aseptic technique is crucial to reducing regional anesthesia related infections, particularly in the presence of indwelling catheters.[41]

PATIENTS WITH PREEXISTING NEUROLOGIC DISORDERS

Patients with preexisting neurologic disease present a unique challenge to the anesthesiologist. The cause of postoperative deficits is difficult to evaluate, because neural injury may occur as a result of surgical trauma, tourniquet pressure, prolonged labor, improper patient positioning, and/or anesthetic technique. Progressive neurologic diseases may coincidentally worsen perioperatively, independent of the anesthetic method.[42,43] The decision to proceed with a regional anesthesia in these

patients should be made on a case-by-case basis and involves understanding the pathophysiology of neurologic disorders, the mechanisms of neural injury associated with regional anesthesia, and the overall incidence of neurologic complications after regional techniques. If a regional anesthetic is indicated or requested, the patient's preoperative neurologic examination should be formally documented and the patient must be made aware of the possible progression of the underlying disease process.

The presence of preexisting deficits, signifying chronic neural compromise, theoretically places these patients at increased risk for further neurologic injury.[29] It is difficult to define the actual risk of neurologic complications in patients with preexisting neurologic disorders who receive regional anesthesia; no controlled studies have been performed, and accounts of complications have appeared in the literature as individual case reports. In a study examining the effect of local anesthetics on nerve conduction block and injury in diabetic rats, Kalichman and Calcutt[26] reported that the local anesthetic requirement is decreased and the risk of local anesthetic-induced nerve injury is increased in diabetes. Clinically, the success rate of regional techniques is increased in diabetic patients.[44] These findings suggest that diabetic patients may require less local anesthetic to produce anesthesia and that a reduction in dose may be necessary to reduce the risk of neural injury by doses considered safe in nondiabetic patients. However, confirmatory human studies are lacking. Conversely, Hebl et al.[45] noted no difference in neurologic function in patients undergoing ulnar nerve transposition under axillary block versus general anesthesia. However, all patients in the axillary block group with postoperative worsening of neurologic function had an ulnar paresthesia or nerve stimulator response reported during their regional technique.

Patients with preoperative neurologic deficits may undergo further nerve damage more readily from needle or catheter placement, local anesthetic systemic toxicity, and vasopressor-induced neural ischemia. Dilute or less potent local anesthetic solutions should be used when feasible to decrease the risk of local anesthetic toxicity. The use of epinephrine-containing solutions in patients with preexisting neurologic deficits is controversial. The potential risk of vasoconstrictor-induced nerve ischemia must be weighed against the advantages of improved quality and duration of block. Because epinephrine and phenylephrine also prolong the block and therefore neural exposure to local anesthetics, the appropriate concentration and dose of local anesthetic solutions must be thoughtfully considered.[2]

PERFORMANCE OF REGIONAL TECHNIQUES IN ANESTHETIZED PATIENTS

The performance of regional blockade on anesthetized patients theoretically increases the risk of perioperative neurologic complications, since these patients are unable to respond to the pain associated with needle- or catheter-induced paresthesias or intraneural injections. However, there are few data to support these concerns. Cases are typically reported individually; no randomized study or large review has been performed to date.[14,15] There are also medicolegal issues. The actual risk of neurologic complications in patients undergoing regional techniques while anesthetized or heavily sedated has not been formally evaluated. The apparent safety of performing regional techniques under general anesthesia that is demonstrated in the pediatric literature must be carefully interpreted. As previously mentioned, epidemiologic series report direct trauma and toxicity as the etiologies of most neurologic complications, and have identified pain during needle placement or injection of local anesthetic as risk major factors.[1,8,9]

Peripheral and plexus blocks (compared to neuraxial techniques) represent additional risk when performed on an anesthetized patient. The larger dose of local anesthetic given as a single bolus over a relatively short interval increases the risk of systemic toxicity while heavy sedation or general anesthesia diminishes the patient's ability to report early signs of rising local anesthetic blood levels. In addition, although some peripheral techniques are performed as a field block, most require that the nerve or sheath be directly identified by eliciting a paresthesia or nerve stimulator response or by locating an adjacent vascular structure. However, the use of a nerve stimulator does not replace the patient's ability to respond to the pain of needle trauma or intraneural injection. Urmey et al.[46] performed interscalene blocks on unpremedicated patients using the paresthesia technique with insulated (10 patients) and noninsulated (20 patients) needles. Paresthesias were elicited with the nerve stimulator power off. Upon elicitation of the paresthesia, the nerve stimulator was turned on and the amperage slowly increased to a maximum of 1.0 milliamperes. Only 30% of patients exhibited any motor response. There was no correlation between site of paresthesia and associated motor response. These results suggest that since it is possible to have sensory nerve contact and not elicit a motor response, use of a nerve stimulator does not protect the anesthetized patient from nerve injury. Passannante[15] described a case report of spinal anesthesia and permanent brachial plexopathy in a patient who underwent an interscalene block using a nerve stimulator while anesthetized. Motor response in the hand was obtained at 0.2 milliamperes; no blood or CSF was aspirated. It was postulated the needle tip was in a dural sleeve or the subarachnoid space, with a portion of the local anesthetic injected intraneurally. The patient's inability to respond to pain allowed a larger intraneural injection and increased the severity of nerve injury. Benumof[14] reported four cases of permanent cervical spinal cord injury following interscalene

Table 3. EMG Abnormalities After Axonal Injury

Time after injury	Insertional activity	Fibrillation	Recruitment	Amplitude
Acute (<14 d)	Normal	Absent	Reduced	Normal
Subacute (14–21 d)	Increased	Present	Reduced	Normal
1–3 month	Increased	Present	Reduced	May be increased
>6 month	May be increased	Present, but decreased	Reduced	Increased

From Hogan et al. (50). Used with permission.

block performed with the patient under general anesthesia or heavy sedation. In three cases, a nerve stimulator was used to localize the brachial plexus.

DIAGNOSIS AND EVALUATION OF NEUROLOGIC COMPLICATIONS

Neurologic deficits that arise within the first 24 hours most likely represent extra- or intraneural hematoma, intraneural edema, or a lesion involving a sufficient number of nerve fibers to allow immediate diagnosis. However, in many cases of persistent paresthesias after regional anesthesia, the symptoms of nerve injury do not develop immediately after the injury, but have their onset days or weeks later.[10] In a study evaluating nerve conduction after nerve block at the elbow, Löfström et al.[47] observed that while ulnar nerve action potential had returned to normal 24 hours after injection, subsequent examinations at weekly intervals detected abnormally low amplitudes in 3 of 28 subjects, although only 1 complained of neurologic dysfunction. Late disturbances in nerve function have also been reported after human microneurography, a technique involving percutaneous electrical stimulation of a nerve.[48] The presentation of late disturbances in nerve function suggests an alternative etiology such as tissue reaction or scar formation, although it is not possible with the existing data to determine whether this reaction is due to mechanical trauma, chemical trauma, or both.

Although most neurologic complications resolve completely within several days or weeks, significant neural injuries necessitate neurologic consultation to document the degree of involvement and coordinate further work-up. Neurophysiologic testing, such as nerve conduction studies, evoked potentials, and electromyography are often useful in establishing a diagnosis and prognosis.[49,50] A reduced amplitude in evoked responses indicates axonal loss, while increased latency occurs in the presence of demyelination. Fibrillation potentials are present during active axonal degeneration. They appear 2–3 weeks after injury and are maximal at 1–3 months (Table 3). Because of the decreased number of axons present in patients with neurologic conditions, there is a reduction in neuron recruitment during voluntary effort. The degree of reduction parallels the severity of the disorder. Despite many applications, nerve conduction studies have several limitations. Typically only the large sensory and motor nerve fibers are evaluated; dysfunction of small unmyelinated fibers would not be detected. In addition, abnormalities will not be noted on EMG immediately after injury, but rather require several weeks to evolve. Although it is often recommended to wait until evidence of denervation has appeared before performing neurophysiologic testing, a baseline study (including evaluation of the contralateral extremity) would be helpful in ruling out underlying pathology or a preexisting condition.

In conclusion, major complications after regional anesthetic techniques are rare, but can be devastating to the patient and the anesthesiologist. Prevention and management begin during the preoperative visit with a careful evaluation of the patient's medical history and appropriate preoperative discussion of the risks and benefits of the available anesthetic techniques. Alternative anesthetic techniques such as peripheral blocks or general anesthesia should be considered for patients at increased risk for neurologic complications following neuraxial block. The decision to perform a regional anesthetic technique on an anesthetized patient must be made with care since these patients are unable to report pain on needle placement or injection of local anesthetic. Efforts should also be made to decrease neural injury in the operating room through careful patient positioning. Postoperatively, patients must be followed closely to detect potentially treatable sources of neurologic injury, including hematoma or abscess, constrictive dressings, improperly applied casts, and increased pressure on neurologically vulnerable sites. New neurologic deficits should be evaluated promptly by a neurologist, or neurosurgeon, to document formally the patient's evolving neurologic status, arrange further testing or intervention, and provide long-term follow-up.

REFERENCES

1. Auroy Y, Narchi P, Messiah A. Serious complications related to regional anesthesia. Anesthesiology 1997;87:479–86
2. Myers RR, Heckman HM. Effects of local anesthesia on nerve blood flow: studies using lidocaine with and without epinephrine. Anesthesiology 1989;71:757–62
3. Rigler ML, Drasner K, Krejcie TC. Cauda equina syndrome after continuous spinal anesthesia. Anesth Analg 1991;72:275–81
4. Brull R, McCartney CJ, Chan VW. Effect of transarterial axillary block versus general anesthesia on paresthesiae 1 year after hand surgery. Anesthesiology 2005;103:1104–5
5. Lynch NM, Cofield RH, Silbert PL, Hermann RC. Neurologic complications after total shoulder arthroplasty. J of Shoulder and Elbow Surgery 1996;5:53–61
6. Horlocker TT, Cabanela ME, Wedel DJ. Does postoperative epidural analgesia increase the risk of peroneal nerve palsy after total knee arthroplasty? Anesth Analg 1994;79:495–500
7. Horlocker TT, Hebl JR, Gali B. Anesthetic, patient, and surgical risk factors for neurologic complications after prolonged total tourniquet time during total knee arthroplasty. Anesth Analg 2006;102:950–5

8. Auroy Y, Benhamou D, Bargues L. Major complications of regional anesthesia in France: the SOS Regional Anesthesia Hotline Service. Anesthesiology 2002;97:1274–80
9. Cheney FW, Domino KB, Caplan RA, Posner K. Nerve injury associated with anesthesia: a closed claims analysis. Anesthesiology 1999;90:1062–9
10. Selander D, Edshage S, Wolff T. Paresthesiae or no paresthesiae? Acta Anaesthesiol Scand 1979;23:27–33
11. Stan TC, Krantz MA, Solomon DL, Poulos JG, Chaouki K. The incidence of neurovascular complications following axillary brachial plexus block using a transarterial approach: a prospective study of 1000 consecutive patients. Reg Anesth 1995; 20:486–92
12. Urban MK, Urquhart B. Evaluation of brachial plexus anesthesia for upper extremity surgery. Reg Anesth 1994;19:175–82
13. Fanelli G, Casati A, Garancini P. Nerve stimulator and multiple injection technique for upper and lower limb blockade: failure rate, patient acceptance, and neurologic complications. Anesth Analg 1999;88:847–52
14. Benumof JL. Permanent loss of cervical spinal cord function associated with interscalene block performed under general anesthesia. Anesthesiology 2000;93:1541–4
15. Passannante AN. Spinal anesthesia and permanent neurologic deficit after interscalene block. Anesth Analg 1996;82:873–4
16. Bigeleisen PE. Nerve puncture and apparent intraneural injection during ultrasound-guided axillary block does not invariably result in neurologic injury. Anesthesiology 2006;105:779–83
17. Borgeat A. Regional anesthesia, intraneural injection, and nerve injury: beyond the epineurium. Anesthesiology 2006;105:647–8
18. Rice ASC, McMahon SB. Peripheral nerve injury caused by injection needles used in regional anaesthesia: influence of bevel configuration, studied in a rat model. Br J Anaesth 1992;69:433–8
19. Selander D, Dhuner KG, Lundborg G. Peripheral nerve injury due to injection needles used for regional anesthesia. Acta Anaesthesiol Scand 1977;21:182–8
20. Motamed C, Bouaziz H, Mercier FJ, Benhamou D. Knotting of a femoral catheter. Reg Anesth Pain Med 1997;22:486–7
21. Sada T, Kobayashi T, Murakami S. Continuous axillary brachial plexus block. Can Anaesth Soc J 1983;30:201–5
22. Bergman BD, Hebl JR, Kent J, Horlocker TT. Neurologic complications of 405 consecutive continuous axillary catheters. Anesth Analg 2003;96:247–52
23. Capdevila X, Pirat P, Bringuier S. Continuous peripheral nerve blocks in hospital wards after orthopedic surgery: a multicenter prospective analysis of the quality of postoperative analgesia and complications in 1,416 patients. Anesthesiology 2005;103:1035–45
24. Drasner K, Sakura S, Chan VW. Persistent sacral sensory deficit induced by intrathecal local anesthetic infusion in the rat. Anesthesiology 1994;80:847–52
25. Hodgson PS, Neal JM, Pollock JE, Liu SS. The neurotoxicity of drugs given intrathecally (spinal). Anesth Analg 1999;88:797–809
26. Kalichman MW, Calcutt NA. Local anesthetic-induced conduction block and nerve fiber injury in streptozotocin-diabetic rats. Anesthesiology 1992;77:941–7
27. Ready LB, Plumer MH, Haschke RH. Neurotoxicity of intrathecal local anesthetics in rabbits. Anesthesiology 1985;63:364–70
28. Neal JM, Hebl JR, Gerancher JC, Hogan QH. Brachial plexus anesthesia: essentials of our current understanding. Reg Anesth Pain Med 2002;27:402–28
29. Upton AR, McComas AJ. The double crush in nerve entrapment syndromes. The Lancet 1973;2:359–62
30. Selander D, Sjostrang J. Longitudinal spread of intraneurally injected local anesthetics. Acta Anaesthesiol Scand 1978;22:622–34
31. Neal JM. Effects of epinephrine in local anesthetics on the central and peripheral nervous systems: Neurotoxicity and neural blood flow. Reg Anesth Pain Med 2003;28:124–34
32. Bouaziz H, Iohom G, Estebe JP. Effects of levobupivacaine and ropivacaine on rat sciatic nerve blood flow. Br J Anaesth 2005;95:696–700
33. Ben-David B, Stahl S. Axillary block complicated by hematoma and radial nerve injury. Reg Anesth Pain Med 1999;24:264–6
34. Horlocker TT, Wedel DJ, Benzon H. Regional anesthesia in the anticoagulated patient: defining the risks. The Second ASRA consensus conference on neuraxial anesthesia and anticoagulation. Reg Anesth Pain Med 2003;28:172–97
35. Klein SM, D'Ercole F, Greengrass RA, Warner DS. Enoxaparin associated with psoas hematoma and lumbar plexopathy after lumbar plexus block. Anesthesiology 1997;87:1576–9
36. Maier C, Gleim M, Weiss T. Severe bleeding following lumbar sympathetic blockade in two patients under medication with irreversible platelet aggregation inhibitors. Anesthesiology 2002;97:740–3
37. Weller RS, Gerancher JC, Crews JC, Wade KL. Extensive retroperitoneal hematoma without neurologic deficit in two patients who underwent lumbar plexus block and were later anticoagulated. Anesthesiology 2003;98:581–3
38. Gaumann DM, Lennon RL, Wedel DJ. Continuous axillary block for postoperative pain management. Reg Anesth 1988;13:77–82
39. Nseir S, Pronnier P, Soubrier S. Fatal streptococcal necrotizing fasciitis as a complication of axillary brachial plexus block. Br J Anaesth 2003;92:427–9
40. Adam F, Jaziri S, Chauvin M. Psoas abscess complicating femoral nerve block catheter. Anesthesiology 2003;99:230–1
41. Hebl JR. The importance and implications of aseptic techniques during regional anesthesia. Reg Anesth Pain Med 2006;31:311–23
42. Blumenthal S, Borgeat A, Maurer K. Preexisting subclinical neuropathy as a risk Factor for nerve injury after continuous ropivacaine administration through a femoral nerve catheter. Anesthesiology 2006;105:1053–6
43. Candido KD, Sukhani R, Doty R Jr. Neurologic sequelae after interscalene brachial plexus block for shoulder/upper arm surgery: the association of patient, anesthetic, and surgical factors to the incidence and clinical course. Anesth Analg 2005;100:1489–95
44. Singelyn F. The influence of diabetes mellitus on the success rate of posterior popliteal sciatic nerve blockade. Anesthesiology 2004 (abstract)
45. Hebl JR, Horlocker TT, Sorenson EJ, Schroeder DR. Regional anesthesia does not increase the risk of postoperative neuropathy in patients undergoing ulnar nerve transposition. Anesth Analg 2001;93:1606–11
46. Urmey WF, Stanton J. Inability to consistently elicit a motor response following sensory paresthesia during interscalene block administration. Anesthesiology 2002;96:552–4
47. Löfström B, Wennberg A, Widen L. Late disturbances in nerve function after block with local anaesthetic agents. Acta Anaesthesiol Scand 1966;10:111–22
48. Eckberg DL, Wallin BG, Fagius J, Lundberg L, Torebjork HE. Prospective study of symptoms after human microneurography. Acta Physiol Scand 1989;137:567–9
49. Aminoff MJ. Electrophysiologic testing for the diagnosis of peripheral nerve injuries. Anesthesiology 2004;100:1298–1303
50. Hogan QH, Hendrix L, Jaradej S. Neurologic injury following regional anesthesia. In: Finucane BT (ed). Complications of Regional Anesthesia, Second edition. New York, Springer 2007:386–409

AUTHOR QUERIES

AUTHOR PLEASE ANSWER ALL QUERIES **1**