5 Mechanisms of Neurologic Complications with Peripheral Nerve Blocks

Alain Borgeat, Stephan Blumenthal, and Admir Hadžić

Although there are relatively few published reports of anesthesia-related nerve injury associated with the use of peripheral nerve blocks (PNBs), it is likely that the commonly cited incidence (0.4%) of severe injury is underestimated because of underreporting.[1–3] 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. Although neurologic complications after PNBs can be related to a variety of factors related to the block (e.g., needle trauma, intraneuronal injection, neuronal ischemia, and toxicity of local anesthetics), a search for other common causes should also include surgical factors (e.g., positioning, stretching, retractor injury, ischemia, and hematoma formation). In some instances, the neurologic injury may be a result of a combination of these factors.

In this chapter, we will discuss mechanisms and consequences of acute neurologic injury related to the nerve block procedures. Specific nerve injuries associated with upper and lower nerve block techniques, neuraxial anesthesia, and local anesthetic toxicity will be discussed elsewhere in the text.

Functional Histology of the Peripheral Nerves

To understand the mechanisms of peripheral nerve injury, one must be familiar with the functional histology of the peripheral nerve. Peripheral nerves are complex structures consisting of fascicles held together by the *epineurium* – an enveloping, external connective sheath (Figure 5-1). Each fascicle contains many nerve fibers and capillary blood vessels embedded in a loose connective tissue, *the endoneurium*.[4] The *perineurium* is a multilayered epithelial sheath that surrounds individual fascicles and consists of several layers of perineural cells. Therefore, in essence, a fascicle is a group of nerve fibers surrounded by *perineurium*. Of note, fascicles can be organized in one of three common arrangements: *monofascicular* (single, large fascicle); *oligofascicular* (few fascicles of various sizes); and *polyfascicular* (many fascicles of various sizes).[5]

Nerve fibers can be myelinated or unmyelinated; sensory and motor nerves contain both in a ratio of 4:1, respectively. Unmyelinated fibers are composed of several

B. T. Finucane (ed.), *Complications of Regional Anesthesia*

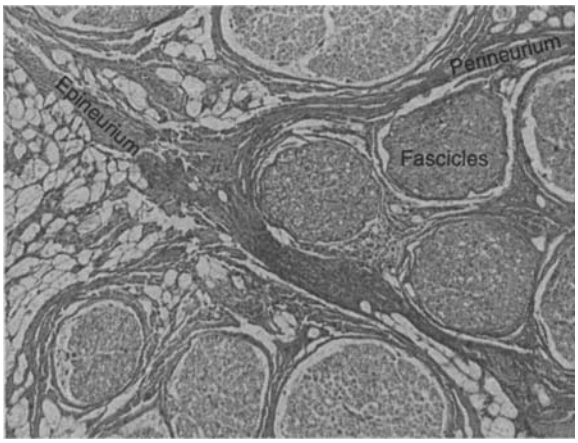

FIGURE 5-1. Histology of the peripheral nerve. A peripheral nerve is a complex structure consisting of fascicles held together by the epineurium. Fascicles contain many nerve fibers and capillary blood vessels embedded in a loose connective tissue, the endoneurium. The perineurium is a multilayered epithelial sheath that surrounds individual fascicles.

axons, wrapped by a single Schwann cell. The axons of myelinated nerve fibers are enveloped individually by a single Schwann cell. A thin layer of collagen fibers, the *endoneurium*, surrounds the individually myelinated or groups of unmyelinated fibers.

Nerve fibers depend on a specific endoneurial environment for their function. 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 neurovascular bed is regulated by the sympathetic nervous system, and its blood flow can be as high as 30–40 mL/100 g/minute. 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.

Mechanisms of Peripheral Nerve Injury

The etiology of peripheral nerve injury related to the use of PNBs falls into one of four categories (Table 5-1). *Laceration* results when the nerve is cut partially or completely, such as by a scalpel or a large-gauge cutting needle. *Stretch injuries* to the nerves may result when nerves or plexuses are stretched in a nonphysiologic or exaggerated physiologic position, such as during shoulder manipulation under an interscalene block. *Pressure*, as a mechanism of nerve injury, is relatively common. A typical example of this mechanism is chronic compression of the nerves by neighboring structures, such as fibrous bands, scar tissue, or abnormal muscles, where they pass through fibro-osseous spaces if the space is too small, such as the carpal tunnel. Such chronic compression syndromes are called *entrapment neuropathies*. Examples of pressure injuries applicable to PNBs include external pressure over a period of hours (e.g., a "Saturday night palsy" resulting from pressure of a chair back on the radial nerve of an intoxicated person). The pressure may be repeated and have a cumulative effect (e.g., an ulnar neuropathy resulting from habitually leaning on the elbow). Such a scenario is conceivable, for instance, with a patient who positions the anesthetized arm (e.g., long-acting or continuous brachial plexus block) in a nonphysiologic position for a few hours. Another example of pressure-related nerve injury is prolonged use

TABLE 5-1. Mechanism of Peripheral Nerve Injury Related to PNBs

Mechanical-acute
Laceration
Stretch
Intraneural injection
Vascular
Acute ischemia
Hemorrhage
Pressure
Extraneural
Intraneural
Compartment syndrome
Chemical
Injection of neurotoxic solutions

of a high-pressure tourniquet. Finally, an intraneural injection may lead to sustained high intraneural pressure, which exceeds capillary occlusion pressure, leading to nerve ischemia.[6] *Vascular nerve damage* after nerve blocks can occur when there is acute occlusion of the arteries from which the vasa nervora are derived or from a hemorrhage within a nerve sheath. With *injection injuries*, the nerve may be directly impaled and the drug injected directly into the nerve, or the drug may be injected into adjacent tissues, causing an acute inflammatory reaction or chronic fibrosis, both indirectly involving the nerve. *Chemical nerve injury* is the result of tissue toxicity of injected solutions (e.g., local anesthetic toxicity or neurolysis after alcohol or phenol injections).

Clinical Classification of Acute Nerve Injuries

Classification of acute nerve injuries is useful in considering the physical and functional state of damaged nerves. In his classification, Seddon[7] introduced the terms *neurapraxia*, *axonotmesis*, and *neurotmesis*; Sunderland[8] subsequently proposed a five-grade classification system.

Neurapraxia refers to nerve dysfunction lasting several hours to 6 months after a blunt injury to the nerve. In neuropraxia, the nerve axons and connective tissue structures remain intact. The nerve dysfunction probably results from several factors, of which *focal demyelination* is the most important abnormality. Intraneural hemorrhage, changes in the vasa nervora, disruption of the blood-nerve barrier and axon membranes, and electrolyte disturbances all may add to the impairment of nerve function. Because the nerve dysfunction is rarely complete, clinical deficits are partial and recovery usually occurs within a few weeks, although some neurapraxic lesions (with minimal or no axonal degeneration) may take several months to recover.

Axonotmesis consists of *physical interruption of the axons* but within intact Schwann cell tubes and intact connective tissue structures of the nerve (i.e., the endoneurium, perineurium, and epineurium). Sunderland subdivided this group, depending on which of the three structures were involved (Table 5-2). With axonotmesis, the nerve sheath remains intact, enabling regenerating nerve fibers to find their way into the distal segment. Consequently, efficient axonal regeneration can eventually take place.

Neurotmesis refers to a *complete interruption of the entire nerve* including the axons and all connective tissue structures (epineurium included). Clinically, there is total nerve dysfunction. With both axonotmesis and neurotmesis, axonal disruption leads to Wallerian degeneration, from which recovery occurs through the slow process of axonal regeneration. However, with neurotmesis, the two nerve ends may be

TABLE 5-2. Classification of Nerve Injuries

Seddon	Sunderland	Structural and functional processes
Neurapraxia	1	Myelin damage, conduction slowing, and blocking
Axonotmesis	2	Loss of axonal continuity, endoneurium intact, no conduction
	3	Loss of axonal and endoneurial continuity, perineurium intact, no conduction
	4	Loss of axonal, endoneurial, and perineurial continuity; epineurium intact; no conduction
Neurotmesis	5	Entire nerve trunk separated; no conduction

Source: Based on data from Seddon,[7] Sunderland,[8] and Lundborg.[9]

completely separated, and the regenerating axons may not be able to find the distal stump. For these reasons, effective recovery does not occur unless the severed ends are sutured or joined by a nerve graft. With closed injuries, the only way to distinguish clearly between axonotmesis and neurotmesis is surgical exploration and intraoperative inspection of the nerve.

It should be noted that most acute nerve injuries are mixed lesions.[7] Different fascicles and nerve fibers typically sustain different degrees of injury, which may make it difficult to assess the type of injury and predict outcome even by electrophysiologic means. Recovery from a mixed lesion is characteristically biphasic; it is relatively rapid for fibers with neurapraxic damage, but much slower for axons that have been totally interrupted and have undergone Wallerian degeneration.

Mechanical Nerve Injury

Intraneural Injection

As opposed to a relatively clean injury caused by a needle, intraneural injection has the potential to create structural damage to the fascicle(s) that is more extensive and less likely to heal (Figure 5-2). Indeed, the devastating sequelae of sensory and motor loss after injection of various agents into peripheral nerves has been well documented.[10]

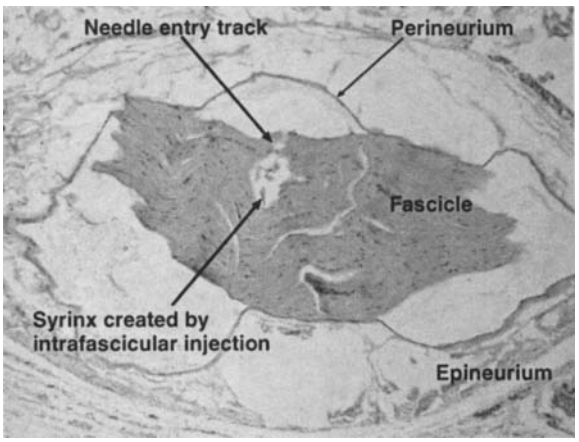

FIGURE 5-2. Mechanical nerve injury after an intraneural injection in a sciatic nerve of a rat. Shown are bulging of the perineurium, needle insertion track, and a syrinx created by intrafascicular injection. (Reproduced with permission from Deschner S, Borgeat A, Hadzic A. Neurologic complications of peripheral nerve blocks. In Hadzic A, ed. Regional Anesthesia and Acute Pain Management, 2007;967–997. McGraw-Hill, New York).

Nearly, all experimental studies on this subject have demonstrated that the site of injection is critical in determining the degree and nature of injury. More specifically, to induce neurologic injury, the injectate must be injected intrafascicularly; extrafascicular injections of the same substance typically do not cause nerve injury.[11] Thus, the main factor leading to a severe peripheral nerve damage associated with injection techniques is injection of local anesthetic into a fascicle or group of faciles bound together. This causes mechanical destruction of the fascicular architecture and sets into motion a cascade of pathophysiologic changes including inflammation, cellular infiltration, axonal degeneration, and others, all possibly leading to nerve scarring.

Histologic features after intraneural injection are rather nonspecific and range from simple mechanical disruption and delamination to fragmentation of the myelin sheath and marked cellular infiltration. A vast array of cellular changes occur after peripheral nerve trauma, and these have been documented using a variety of animal models.[11] The extent of actual neurologic damage occurring after an intrafascicular injection can range from neuropraxia with minimal structural damage to neurotmesis with severe axonal and myelin degeneration, depending on the needle–nerve relationship, agent injected, and dose of the drug used.[12–15] In general, subperineural changes tend to be more prominent, compared with the central area of the fascicle.[16] Additionally, injury to primary sensory neurons, which is not detectable histologically, causes a shift in membrane channel expression, sensitivity to algogenic substances, neuropeptide production, and intracellular signal transduction, both at the injury site and in the cell body in the dorsal root ganglion. All of this leads to increased excitability and the occurrence of acute or chronic pain, often experienced by patients with neurologic injury. It should be noted that intraneural injection and its resultant mechanical injury are merely the inciting mechanisms; a host of additional changes occur involving inflammatory reactions such as chemical neuritis and intraneural hemorrhage, all of which eventually may lead to nerve scarring and chronic neuropathic pain (Figure 5-3).

Prevention of Intraneural Injection

Pain on Injection

Little is known about how to avoid an intraneuronal injection. Pain with injection has long been thought of as the cardinal sign of intraneuronal injection; consequently, it is frequently suggested that blocks be avoided in heavily premedicated or anesthetized patients. However, case reports suggest that pain may not be reliable as a sole warning sign of impending nerve injury, and it may be present in only a minority of cases.[17–20] For instance, Fanelli and colleagues[3] have reported unintended paresthesia in 14% of patients in their study; however, univariate analysis of potential risk factors for

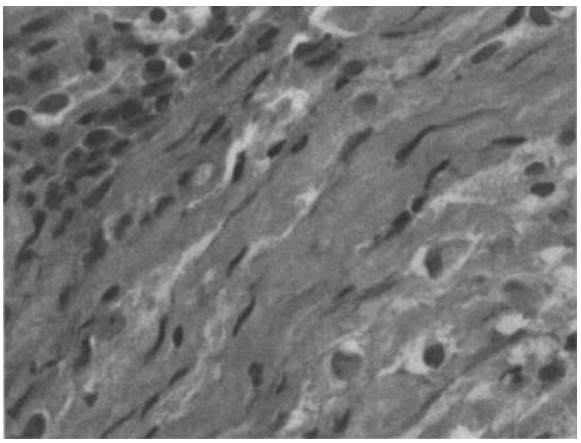

FIGURE 5-3. Inflammatory changes in a nerve fascicle after an intraneural injection.

postoperative neurologic dysfunction failed to demonstrate paresthesia as a risk factor. In addition, the sensory nature of the pain-paresthesia can be difficult to interpret in clinical practice.[21] A certain degree of discomfort on injection ("pressure paresthesia") is considered normal and affirmative of impending successful blockade because it indicates that injection of local anesthetic has been made in the vicinity of the targeted nerve.[21] In clinical practice, however, it can be difficult to discern when pain-paresthesia on injection is "normal" and when it is the ominous sign of an intraneural injection.[22] Moreover, it is unclear how pain or paresthesia on injection, even when present, can be used clinically to prevent development of neurologic injury. For instance, in a prospective study on neurologic complications of regional anesthesia by Auroy and colleagues,[2] neurologic injuries occured even when the participating anesthesiologists did not continue to inject local anesthetic when pain on injection was reported by the patients.

Intensity of the Stimulating Current

In current clinical practice, development of nerve localization and injection monitoring techniques to reliably prevent intraneural injection remain inconclusive.[18] Nerve stimulators are very useful for nerve localization; however, the needle–nerve relationship cannot be adequately, precisely, and reliably ascertained as early literature suggested.[23] Response to nerve stimulation with a frequently used current intensity (1 mA) may be absent even when the needle makes physical contact with or is inserted into a nerve.[24,25] Occurrence of nerve injuries despite using nerve stimulation to localize the nerve further suggests that nerve stimulators can, at best, provide only a rough approximation of the needle–nerve relationship.[1] The current interest in ultrasound-assisted nerve localization holds promise for facilitating nerve localization and administration of nerve blocks; however, the image resolution of this technology is insufficient to visualize nerve fascicles and prevent intrafascicular injection.

The optimal current intensity resulting in accurate localization of a nerve has been a topic of controversy for many years.[23,26–29] For instance, stimulation at currents higher than 0.5 mA may result in block failure because the needle tip is distant from the nerve, whereas stimulation at currents lower than 0.2 mA theoretically may pose a risk of intraneuronal injection (http://www.nysora.com, January 1, 2003). Some authors suggest that a motor response with a current intensity between 1.0 and 0.5 mA is sufficient for accurate placement of the block needle,[23] whereas others advise using a current of much lower intensity (0.5–0.1 mA).[26,28] Others simply suggest stimulating with currents less than 0.75 mA,[29,30] or progressively reducing the current to as low a level as possible while still maintaining a motor response.[27] Methods in most recently published reports have suggested obtaining nerve stimulation with currents of 0.2–0.5 mA (100 ms) before injecting local anesthetics, believing that motor response with current intensities lower than 0.2 mA may be associated with intraneural needle placement. However logical these beliefs might sound, there are no published reports substantiating these concerns.

Resistance to Injection

Assessing resistance to injection is a common practice, similar to loss of resistance to injection of air or saline using a "syringe feel" during administration of epidural, paravertebral, or lumbar plexus blocks. Similarly, assessing tissue resistance and injection compliance is another means of estimating the anatomic location of the needle tip during the practice of PNBs. For this, many clinicians use a syringe feel to estimate what may be an abnormal resistance to nerve block injection and thus reduce the risk of intraneural injection.[6,28,31] However, this practice has significant inherent limitations.[32] For instance, the resistance to injection is greater with smaller needles that are used for nerve blocks, introducing a confusion factor as to what is "normal" or "abnormal" resistance. Second, as opposed to "loss of resistance" in an epidural

injection, there is no baseline pressure information or a change in tissue compliance during nerve block injection. In a study by Claudio and colleagues,[32] all anesthesiologists detected a change in pressure of as little as 0.5 psi during a simulated nerve block injection. However, when gauging the absolute pressure, they substantially varied (by as much as 40 psi) in their perception of what constituted an appropriate resistance to injection. Finally, until recently, no information has been available on what constitutes "normal" and "abnormal" injection pressure during nerve block performance. For these reasons, subjective estimation of resistance to injection is at least as inaccurate as perhaps estimating blood pressure by palpating the radial artery pulse. Objective means of assessing resistance to injection should be far superior in standardizing injection force and pressure.

To explain the mechanisms responsible for development of neuraxial anesthesia after an interscalene block,[33,34] Selander and Sjostrand[35] injected solutions of local anesthetic into rabbit sciatic nerves and traced the spread of the anesthetic along the nerve sheath. They postulated that an intraneural injection results in significant spread of local anesthetic *within the nerve sheath*. In their model, these investigators incidentally noticed that intraneural injections often resulted in higher pressures (up to 9 psi) than those required for perineural injections (<4 psi). Injection into a nerve fascicle resulted in rupture of the *perineurium* and histologic evidence of disruption of the fascicular anatomy. This study, however, used a small-animal model, microinjections (10–200 μL), miniature needles, clinically irrelevant injection rates (100–300 μL/min), and did not include neurologic evaluation after intraneural injections. It is perhaps for these reasons that their foretelling results on the association of injection pressure with intrafascicular injection did not gain the deserved acceptance in clinical practice.

More recent studies, however, have used clinically more-applicable injection speeds and volumes of local anesthetic in a canine model of nerve injury.[36] The results of these studies unequivocally suggested that high-injection pressures (>20 psi) may indicate intrafascicular injection and carry a risk of neurologic injury (Figure 5-4).[37] Specifically, intraneural injections resulting in pressures >20 psi have been associated with clinically detectable neurologic deficits as well as histologic evidence of injury to nerve fascicles (Figure 5-5).

Current evidence suggests that neurologic injury does not always develop after an intraneural injection.[38] In fact, injection after an intraneural needle placement is more likely to result in deposition of the local anesthetic between and not into the fascicles.[36] Intraneural, but *extrafascicular* (interfascicular) injection probably occurs more fre-

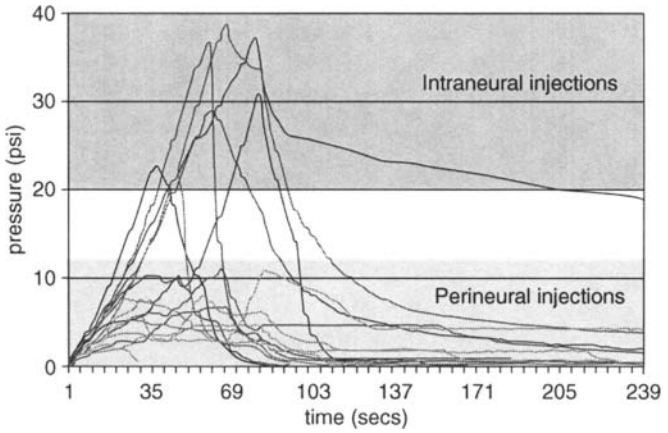

FIGURE 5-4. Injection pressure tracings during sciatic nerve blockade in a canine model. Perineural injections result in low pressures, whereas intraneural, intrafascicular injections are associated with significantly higher injection pressures.

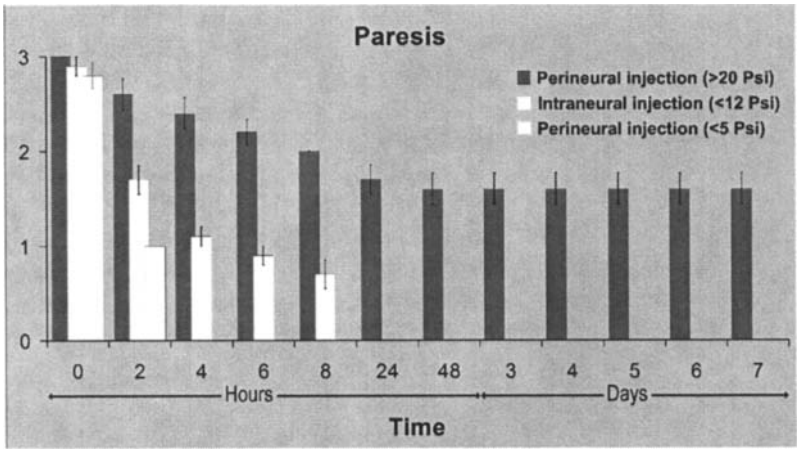

FIGURE 5-5. Duration of sciatic nerve blockade in the canine model of sciatic block. Perineural injections with 2% lidocaine result in motor block lasting up to 3 hours; intraneural but extrafascicular injections result in denser and longer blockade (up to 8 hours) but no permanent injury; intraneural intrafascicular injections (pressures >20 psi) result in blockade lasting >7 days and neurologic injury. (Reprinted with permission from Acta Anaesthesiol Scand. November 1, 2006 [Epub ahead of print]).

quently than thought in clinical practice.[38] Such an injection results in a block of unusually fast onset and long duration rather than in a neurologic injury. This is because an intraneural but extrafascicular injection leads to intimate exposure of nerve fascicles to high concentrations and doses of local anesthetics. However, permanent neurologic injury does not develop because the local anesthetic is deposited *outside* the fascicles and the blocks slowly resolve after the injection, without evidence of histologic derangement.

Needle Design and Direct Needle Trauma

Needle tip design and risk of neurologic injury have been matters of considerable debate for more than 3 decades. Nearly 30 years ago, Selander and colleagues[39] suggested that the risk of perforating a nerve fascicle was significantly lower when a short-bevel (e.g., 45°) needle was used as opposed to a long-bevel (12°–15°) needle. The results of their work are largely responsible for the prevalent trend of using short-bevel needles (i.e., angles 30°–45°) for the majority of major peripheral nerve conduction blocks. However, the work by Rice and McMahon[40] suggests that short-beveled needles, when placed intraneurally, tend to cause more mechanical damage than the long-beveled needles. In their experiment in a rat model, after deliberately penetrating the largest fascicle of the sciatic nerve with 12°- to 27°-beveled needles, the degree of neural trauma on histologic examination was greater with short-beveled needles. Their work suggests that sharp needles produce cleaner, more-likely-to-heal cuts, whereas blunt needles produced noncongruent cuts and more extensive damage. In addition, the cuts produced by the sharper needles were more likely to recover faster and more completely than were the irregular, more traumatic injuries caused by the blunter, short-beveled needles. Although the data on needle design and nerve injury have not been clinically substantiated, the theoretical advantage of short-beveled needles in reducing the risk of nerve penetration has influenced both practitioners and needle manufacturers. Consequently, whenever practical, most clinicians today prefer to use short-beveled needles for major conduction blocks of the peripheral nerves and plexuses. Sharp beveled, small-gauge needles, however, continue to be used routinely for many nerve block procedures, such as axillary transarterial brachial plexus block, wrist and ankle blocks, cutaneous nerve block, and others.

Regardless of the considerations related to the needle design and risk of nerve injury, the actual clinical significance of isolated, direct needle trauma remains unclear. For instance, it is possible that both paresthesia and nerve stimulation techniques of nerve localization may often lead to unrecognized intraneural needle placement, yet the risk of neurologic injury remains relatively low. Similarly, during femoral arterial cannulation, it is likely that the needle is often inserted into the femoral nerve, yet reported injuries to the nerve are rare, and when they occur, they are usually attributed to hematoma formation rather than needle injury. It is possible that needle-related trauma without accompanying intraneural injection results in injury of a relatively minor nature, which readily heals and may go clinically undetected. In contrast, needle trauma coupled with injections of local anesthetics into the nerve fascicle carry a risk of much more severe injury.[37]

Toxicity of Injected Solution

Nerves can be injured by direct contact with a needle, injection of a drug into or around the nerve, pressure from a hematoma, or scarring around the nerve.[41-44] Experimental studies have shown that the degree of nerve damage after an injection depends on the exact site of the injection and the type and quantity of the drug used.[45] The most severe damage is produced by intrafascicular injections, although extrafascicular (subepineurial) injections of some particularly noxious drugs can also produce nerve damage.[14,46] Benzylpenicillin, diazepam, and paraldehyde are the most damaging, but certain other antibiotics, analgesics, sedatives, and antiemetic medications are also capable of damaging peripheral nerves when injected experimentally or accidentally.[45]

Local anesthetics produce a variety of cytotoxic effects in cell cultures, including inhibition of cell growth, motility, and survival, as well as morphologic changes. The extent of these effects is proportionate to the length of time the cells are exposed to the local anesthetic solutions and occur in concentrations normally used in clinical practice. Within normal ranges, the cytotoxic changes are greater as concentrations increase. In the clinical setting, the exact site of local anesthetic deposition has a critical role in determining the pathogenic potential.[47] After applying local anesthetics outside a fascicle, the regulatory function of the perineural and endothelial blood-nerve barrier is only minimally compromised. High concentrations of extrafascicular anesthetics may produce axonal injury independent of edema formation and increased endoneural fluid pressure.[48] As with the effects of local anesthetics in cell cultures, the duration of exposure and concentration of local anesthetic determine the degree and incidence of local-anesthetic–induced residual paralysis. Neurotoxicity of local anesthetics will be discussed in greater detail elsewhere in this textbook.

Neuronal Ischemia

Lack of blood flow to the primary afferent neuron results in metabolic stress. The earliest response of the peripheral sensory neuron to ischemia is depolarization and generation of spontaneous activity, symptomatically perceived as paresthesias. This is followed by blockade of slow-conducting myelinated fibers and eventually all neurons, possibly through accumulation of excess intracellular calcium, which accounts for the loss of sensation with initiation of limb ischemia. Nerve function returns within 6 hours if ischemic times are less than 2 hours. Ischemic periods of up to 6 hours may not produce permanent structural changes in nerves. However, detailed pathologic examination after ischemia initially shows minimal changes, but with 3 hours or more of reperfusion, edema and fiber degeneration develops that lasts for 1–2 weeks, followed by a phase of regeneration lasting 6 weeks. In addition to neuronal damage, oxidative injury associated with ischemia and reperfusion also affects the Schwann cells, initiating apoptosis.

The perineurium is a tough and resistant tissue layer. An injection into this compartment or a fascicle can also result in a prolonged increase in endoneurial pressure, exceeding the capillary perfusion pressure. This pressure, in turn, can lead to endoneural ischemia.[35] The addition of vasoconstricting agents theoretically can enhance ischemia because of the resultant vasoconstriction and reduction in blood flow. The addition of epinephrine has been shown, in vitro, to decrease the blood supply to intact nerves in the rabbit. However, in patients undergoing lower-extremity surgery, addition of epinephrine to the local anesthetic solution used in combined femoral and sciatic nerve blocks has not been shown to be a risk factor for developing postblock nerve dysfunction.[3]

Tourniquet Neuropathy

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 to be 1 in 8000 operations. A prospective study of lower-extremity nerve blockade suggests that higher tourniquet inflation pressures (>400 mm Hg) were associated with an increased risk of transient nerve injury.[3] 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 90–120 minutes.[49] Even with these recommendations, post-tourniquet-application neuropraxia may occur, particularly in the setting of preexisting neuropathy.

Compressive Hematoma

Few data exist regarding the safety of PNB in patients treated with anticoagulants. Compressive hematoma formation leading to neuropathy has been associated with needle misadventures when performing lower extremity PNB, particularly with concomitant treatment with anticoagulants. However, as opposed to spinal or epidural hematoma, peripheral neuropathy from this etiology typically resolves completely.[50,51] Regardless, these reports emphasize the important differences in the risk–benefit ratio of PNBs compared with neuraxial blocks in patients receiving anticoagulant therapy.

Conclusion

The published data suggest that neurologic complications of PNBs are relatively rare. However, the severity of consequences and lack of prevention strategies continue to present a source of concern for both clinicians and patients. The main inciting mechanism of neurologic injury with PNBs seems to be an intrafascicular or intraneural injection. However, it is fortunate that peripheral nerves possess an inherent natural protection. Intraneural injections do not always result in intrafascicular needle placement and, therefore, do not necessarily lead to nerve injury. It is often suggested that the use of short-beveled needles and avoidance of excessive sedation and general anesthesia to decrease the risk of nerve injury. However, these frequently voiced recommendations have recently been challenged. In addition, avoidance of adequate premedication may have a significant negative impact by decreasing the patient's acceptance and satisfaction with PNBs. The relatively low incidence rate of complications with PNBs, coupled with the lack of objective documentation and means to more precisely monitor administration of nerve blocks, make retrospective analyses of cases of nerve injury largely speculative with regard to the actual mechanism of nerve injury in clinical practice.

Few publications have had a greater impact on the clinical practice of anesthesiology than the American Society of Anesthesiologists (ASA) practice guidelines.[52]

These practice guidelines have been designed to enhance and promote the safety of anesthetic practice and have made the practice of general anesthesia much safer. Such guidelines are much needed but currently do not exist with regard to the practice of PNBs. This is likely because administration of PNBs has been traditionally based on individual preferences, clinical impressions, and other subjective methods. Future efforts should be directed toward developing more objective and exacting nerve localization and injection monitoring techniques to more reliably detect and prevent intraneural intrafascicular injection. The results of these efforts will inevitably be of crucial importance to the future of PNBs and their role in practice of modern anesthesiology.

References

1. Auroy Y, Benhamou D, Bargues L. Major complications of regional anesthesia in France: the SOS regional anesthesia hotline service. Anesthesiology 2002;97:1274–1280.
2. Auroy Y, Narchi P, Messiah A, et al. Serious complications related to regional anesthesia: results of a prospective study in France. Anesthesiology 1997;87:479–486.
3. Fanelli G, Casati A, Garancini P, et al. Nerve stimulator and multiple injection technique for upper and lower limb blockade: failure rate, patient acceptance, and neurologic complications. Study Group on Regional Atesthesia. Anesth Analg 1999;88:847–852.
4. Sunderland S. Nerve and Nerve Injury. Edinburgh: Churchill Livingstone; 1978:31–32.
5. Millesi H, Terzis JK. Nomenclature in peripheral nerve surgery. Clin Plast Surg 1984;11:3–8.
6. Selander D. Peripheral nerve injury after regional anesthesia. In: Finucane B, ed. Complications of Regional Anesthesia. New York: Churchill Livingstone; 1999:105–115.
7. Seddon HJ. Three types of nerve injury. Brain 1943;66:236–288.
8. Sunderland S. A classification of peripheral nerve injuries producing loss of function. Brain 1951;74:491–516.
9. Lundborg G. Nerve Injury and Repair. New York: Churchill Livingstone; 1988.
10. Hudson AR, Kline D, Gentili F. Management of peripheral nerve problems. In: Omer G, Spinner M, eds. Peripheral Nerve Injection Injury. Philadelphia: WB Saunders; 1980: 639–653.
11. Mackinnon SE, Dellon AL. Classification of nerve injuries as the basis of treatment. In: Mackinnon SE, Dellon AL, eds. Surgery of the Peripheral Nerve. New York: Thieme Medical Publishers; 1988:35–63.
12. Gentili F, Hudson A, Kline D, et al. Early changes following injection injury of peripheral nerves. Can J Surg 1980;23:177–182.
13. Mackinnon SE, Hudson AR, Gentili F, et al. Peripheral nerve injury with steroid agents. Plast Reconstr Surg 1982;69:482–489.
14. Mackinnon SE, Hudson AR, Llamas F, et al. Peripheral nerve injury by chymopapain injection. J Neurosurg 1984;61:1–8.
15. Strasberg JE, Atchabahian A, Strasberg SR, et al. Peripheral nerve injection injury with antiemetic agents. J Neurotrauma 1999;16:99–107.
16. Hadzic A, Dilberovic F, Shah S, et al. Combination of intraneural injection and high injection pressure leads to fascicular injury and neurologic deficits in dogs. Reg Anesth Pain Med 2004;29:417–423.
17. Bhananker SM, Domino KB. What actions can be used to prevent peripheral nerve injury. In: Fleisher LA, ed. Evidence-based Practice of Anesthesiology. New York: Elsevier; 2004: 228–235.
18. Fremling MA, Mackinnon SE. Injection injury to the median nerve. Ann Plast Surg 1996;37:561–567.
19. Lim E, Pereira R. Brachial plexus injury following brachial plexus block. Anesthesia 1984; 39:691–694.
20. Gillespie JH, Menk EJ, Middaugh RE. Reflex sympathetic dystrophy. A complication of interscalene block. Anesth Analg 1987;66:1316–1317.
21. Winnie AP. Interscalene brachial plexus block. Anesth Analg 1970;49:455–466.
22. Barutell C, Vidal F, Raich M, et al. A neurological complication following interscalene brachial plexus block. Anaesthesia 1980;35:365–367.

23. Raj PP, De Andrés J, Grossi P, et al. Aids to localization of peripheral nerves. In: Raj P, ed. Textbook of Regional Anesthesia. New York: Churchill Livingstone; 2002:251–284.
24. Urmey WF, Stanton J. Inability to consistently elicit a motor response following sensory paresthesia during interscalene block administration. Anesthesiology 2002;96:552–554.
25. Choyce A, Chan VW, Middleton WJ, et al. What is the relationship between paresthesia and nerve stimulation for axillary brachial plexus block? Reg Anesth Pain Med 2001; 26:100–104.
26. Brown DL. Local anesthetics and regional anesthesia equipment. In: Brown DL, ed. Atlas of Regional Anesthesia. Philadelphia: WB Saunders; 1992:3–11.
27. Chelly J. Nerve stimulator. In: Chelly J, ed. Peripheral Nerve Blocks. A Color Atlas. Philadelphia: Lippincott Williams & Wilkins; 1999:7–10.
28. Jankovic D, Wells C. Brachial plexus. In: Jankovic D, Wells C, eds. Regional Nerve Blocks. Berlin: Blackwell Publishers; 2001:58–86.
29. Jankowski CJ, Hebl JR, Stuart MJ, et al. A comparison of psoas compartment block and spinal and general anesthesia for outpatient knee arthroscopy. Anesth Analg 2003; 97:1003–1009.
30. Tonidandel WT, Mayfield JB. Successful interscalene block with a nerve stimulator may also result after a pectoralis major motor response. Reg Anesth Pain Med 2002;27:491–493.
31. Weaver MA, Tandatnick CA, Hahn MB. Peripheral nerve blockade. In: Raj P, ed. Regional Anesthesia. New York: Churchill Livingstone; 2002:857–870.
32. Claudio RE, Hadzic A, Shih H, et al. Injection pressures by anesthesiologists during simulated peripheral nerve block. Reg Anesth Pain Med 2004;29:201–205.
33. Passannante AN. Spinal anesthesia and permanent neurologic deficit after interscalene block. Anesth Analg 1996;82:873–874.
34. Dutton RP, Eckhardt WF 3rd, Sunder N. Total spinal anesthesia after interscalene blockade of the brachial plexus. Anesthesiology 1994;80:939–941.
35. Selander D, Sjostrand J. Longitudinal spread of intraneurally injected local anesthetics. An experimental study of the initial neural distribution following intraneural injections. Acta Anaesthesiol Scand 1978;22:622–634.
36. Hadzic A. Combination of intraneural injection and high-injection pressure leads to fascicular injury and neurologic deficit in dogs. Reg Anesth Pain Med 2005;30:309–310.
37. Hadzic A, Dilberovic F, Shah S, et al. Combination of intraneural injection and high injection pressure leads to severe fascicular injury and neurologic deficits in dogs. Reg Anesth Pain Med 2004;29:417–423.
38. Sala-Blanch X, Pomes J, Matute P, et al. Intraneural injection during anterior approach for sciatic nerve block. Anesthesiology 2004;101:1027–1030.
39. Selander D, Dhuner K, Lundborg G. Peripheral nerve injury due to injection needles used for regional anesthesia. Acta Anaesthesiol Scand 1977;21:182–189.
40. 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;9:433–438.
41. Sunderland S. The sciatic nerve and its tibial and common peroneal divisions: anatomical and physiological features. In: Sunderland S, ed. Nerves and Nerve Injuries. Edinburgh: Churchill Livingstone; 1978:925–991.
42. Rousseau JJ, Reznik M, LeJeune GN, et al. Sciatic nerve entrapment by pentazocine-induced muscle fibrosis: a case report. Arch Neurol Psychiatry 1979;36:723–724.
43. Obach J, Aragones JM, Ruano D. The infrapiriformis foramen syndrome resulting from intragluteal injection. J Neurol Sci 1983;58:135–142.
44. Napiontek M, Ruszkowski K. Paralytic drop foot and gluteal fibrosis after intramuscular injections. J Bone Joint Surg Br 1993;75:83–85.
45. Gentili F, Hudson AR, Hunter D. Clinical and experimental aspects of injection injuries of peripheral nerves. Can J Neurol Sci 1980;7:143–151.
46. Mackinnon SE, Hudson AR, Gentili F, et al. Peripheral nerve injury with steroid agents. Plast Reconstr Surg 1982;69:482–489.
47. Selander D. Neurotoxicity of local anesthetics: animal data. Reg Anesth 1993;18:461–468.
48. Kaneko S, Matsumoto M, Tsuruta S, et al. The nerve root entry zone is highly vulnerable to intrathecal tetracaine in rabbits. Anesth Analg 2005;101:107–114.
49. Sharrock NE, Savarese JJ. Anesthesia for orthopedic surgery. In: Miller R, ed. Anesthesia. New York: Churchill Livingstone; 2000:2118–2139.

50. Klein SM, D'Ercole F, Greengrass RA, et al. Enoxaparin associated with psoas hematoma and lumbar plexopathy after lumbar plexus block. Anesthesiology 1997;87:1576–1579.
51. Weller RS, Gerancher JC, Crews JC, et al. Extensive retroperitoneal hematoma without neurologic deficit in two patients who underwent lumbar plexus block and were later anticoagulated. Anesthesiology 2003;98:581–585.
52. American Society of Anesthesiologists. Policy statement on practice parameters. In: ASA Standards, Guidelines and Statements. American Society of Anesthesiologists Publication; October 3, 1999.