Regional Anesthesia in Patients With Preexisting Neurologic Disease

Sandra L. Kopp, MD, Adam K. Jacob, MD, and James R. Hebl, MD

What's New: Since publication of initial recommendations in 2008, there is limited new information regarding the performance of regional anesthesia in patients with preexisting neurologic diseases. However, the strength of evidence has increased since 2008 regarding (1) the concern that diabetic nerves are more sensitive to local anesthetics and perhaps more susceptible to injury and (2) the concern that performing neuraxial anesthesia and analgesia in patients with preexisting spinal canal pathology may increase the risk of new or worsening neurologic symptoms. This increased evidence reinforces our initial recommendations. In addition, since the initial recommendations in 2008, the concept of postsurgical inflammatory neuropathy has been described and is potentially a contributor to postoperative neurologic dysfunction.

(*Reg Anesth Pain Med* 2015;40: 467–478)

Preexisting disorders of the peripheral nervous system (hereditary neuropathies, diabetic polyneuropathy [DPN], chemotherapy-induced neuropathies, inflammatory neuropathies), central nervous system (multiple sclerosis [MS], postpolio syndrome [PPS], amyotrophic lateral sclerosis [ALS]), and spinal canal pathology present a challenge to patients and anesthesiologists who desire to use regional anesthetic techniques. Because each of these clinical conditions involves compromise to neural structures, the concern is that further insult from surgical (eg, intraoperative stretch or compression, tourniquet ischemia, hemorrhage) or anesthetic (eg, mechanical trauma, vasoconstrictor-induced ischemia, local anesthetic toxicity) causes may result in new or worsening postoperative neurologic deficits.

Regardless of the underlying etiology, the presence of chronic neural compromise secondary to mechanical (eg, spinal stenosis or compressive radiculopathy), ischemic (eg, peripheral vascular disease), toxic (eg, vincristine or cisplatin chemotherapy), metabolic (eg, diabetes mellitus [DM]), or autoimmune (eg, MS) derangements may theoretically place patients at increased risk of further neurologic injury.[1–3] Upton and McComas[1] were the first to describe the double-crush phenomenon, which suggests that patients with preexisting neural compromise may be more susceptible to injury at another site when exposed to a secondary insult (Fig. 1). Secondary insults may include a variety of surgical or anesthetic risk factors—including regional anesthetic techniques. Osterman[2] emphasized that not only are 2 low-grade insults along a peripheral nerve trunk worse than a single site but also that the damage of the dual injury far exceeds the expected additive damage caused by each isolated insult. It may be further postulated that the second insult need not be along the peripheral nerve trunk itself but rather at any point along the neural transmission pathway. Therefore, the performance of peripheral or neuraxial regional techniques in patients with preexisting neurologic disorders may theoretically place them at increased risk of a double-crush phenomenon.

Unfortunately, the rarity of these disease processes results in a paucity of clinical data that are often conflicting in their outcomes and conclusions. As a result, definitive recommendations can rarely be made from the existing scientific literature (Table 1). However, the following commentary provides a comprehensive review of the available literature on the topic so that patients and clinicians can make an informed decision on the potential neurologic risk of performing regional anesthesia in the presence of preexisting neurologic disorders.

METHODS

Standard search engines and cross-referencing material contained therein provided the literature basis for updated material contained within this review. PubMed and Ovid were searched from 2006 onward to identify new material since our original practice advisory search. MESH terms included individual headings and their relevant combinations, including "regional anesthesia," "peripheral nerve blockade," "spinal anesthesia," "epidural anesthesia," "peripheral neuropathy," "Charcot-Marie-Tooth disease," "diabetic polyneuropathy," "chemotherapy-induced peripheral neuropathy," "Guillain-Barré syndrome (GBS)," "postsurgical inflammatory neuropathy," "post-polio syndrome," "multiple sclerosis," "amyotrophic lateral sclerosis," "traumatic spinal cord injury," "spinal stenosis," "lumbar radiculopathy," and "lumbar disk disease." All prospective randomized controlled trials, retrospective studies, case-controlled cohort studies, case series, and case reports were included for review.

PERIPHERAL NERVOUS SYSTEM DISORDERS

The peripheral nervous system is composed of numerous cell types that serve diverse sensory, motor, and autonomic functions. Signs and symptoms of impaired function depend on the distribution and severity of the injury, in addition to the specific element of the nerve that is affected. More than 100 types of peripheral neuropathy have been identified, each with its own pathophysiology, symptoms, and prognosis.[4]

Hereditary Peripheral Neuropathy

Inherited neuropathies represent a heterogeneous group of diseases that often share the features of an insidious onset and indolent course across years to decades. A wide range of genotypes may result in phenotypes ranging from mild symptoms and subclinical disease to severe debilitating conditions. The most common inherited neuropathies are a group of disorders collectively

From the Department of Anesthesiology, Mayo Clinic College of Medicine, Rochester, MN.
Accepted for publication September 5, 2014.
Address correspondence to: James R. Hebl, MD, Department of Anesthesiology, Mayo Clinic, 200 First St, SW, Rochester, MN 55905 (e-mail: hebl.james@mayo.edu).
Attribution: Department of Anesthesiology, Mayo Clinic, Rochester, Minnesota.
Financial Sources: None.
This work was presented in part at the American Society of Regional Anesthesia and Pain Medicine 37th Annual Spring Meeting, San Diego, CA (March 15–18, 2012).
The authors declare no conflict of interest.

ISSN: 1098-7339
DOI: 10.1097/AAP.0000000000000179

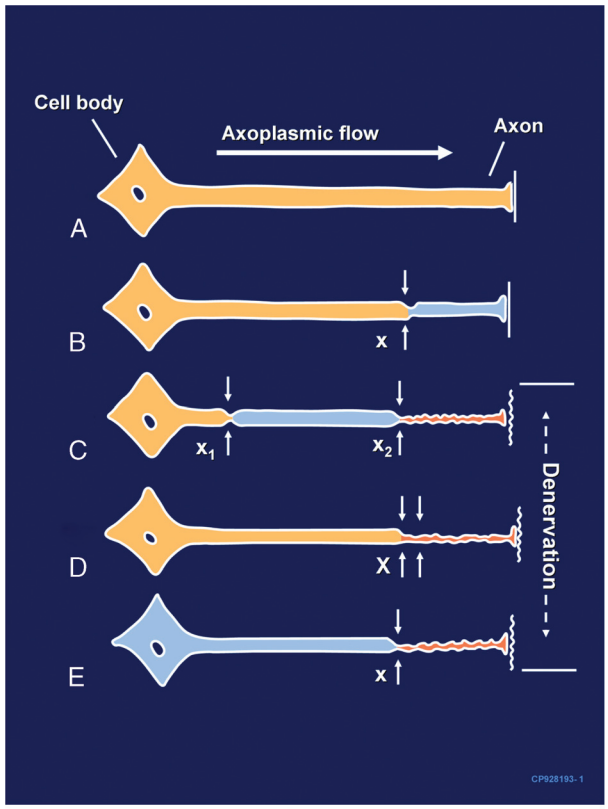

FIGURE 1. Neural lesions resulting in denervation. Axoplasmic flow is indicated by the degree of shading. Complete loss of axoplasmic flow results in denervation (C, D, E). A, Normal neuron. B, Mild neuronal injury at a single site (x) is insufficient to cause denervation distal to the insult. C, Mild neuronal injury at two separate sites (x_1 and x_2) may cause distal denervation (ie, double crush). D, Severe neuronal injury at a single site (X) may also cause distal denervation. E, Axon with a diffuse preexisting underlying disease process (toxic, metabolic, ischemic) may have impaired axonal flow throughout the neuron that may or may not be symptomatic but predisposes the axon to distal denervation after a single minor neural insult at x (ie, double crush) (by permission of Mayo Foundation for Medical Education and Research).

referred to as Charcot-Marie-Tooth (CMT) disease. Charcot-Marie-Tooth disease affects approximately 1 in 2500 people, often beginning during childhood or adolescence.[5] Charcot-Marie-Tooth neuropathies are caused from mutations in more than 30 genes responsible for manufacturing neurons or the myelin sheath.[6] Typical signs and symptoms include extreme motor weakness and muscle wasting within the distal lower extremities and feet, gait abnormalities, loss of tendon reflexes, and numbness within the lower limbs.

The reported use of peripheral[7,8] or central[9–12] regional anesthetic techniques in patients with CMT disease has been limited to small case series and anecdotal case reports. All patients made uneventful recoveries without worsening of their neurologic conditions. Of note, 2 cases involving single-injection regional techniques (epidural anesthesia using 18 mL of 0.75% ropivacaine[10] and supraclavicular analgesia using 30 mL of 0.5% bupivacaine[7]) reported a prolonged effect (12 hours and 30 hours, respectively) of the regional technique compared with the anticipated duration. In both cases, the use of higher concentrations of local anesthetic may have contributed to the delayed recovery.

Hereditary neuropathy with liability to pressure palsy (HNPP) is another rare inherited demyelinating peripheral neuropathy in which individuals have repeated motor and sensory neuropathies (pressure palsies) after a brief nerve compression or mild trauma. Discovered in the early 1990s, HNPP has been linked to a mutation on the *pmp-22* gene, resulting in reduced myelin production. Evidence discussing the use of any regional technique in the setting of HNPP has been limited to a single case report. Lepski and Alderson[13] reported the successful use of labor epidural analgesia in a 24-year-old parturient with HNPP. The patient made an uneventful recovery without worsening of her neurologic condition.

Based on the lack of clinical evidence, definitive recommendations cannot be made about safety and use of regional anesthesia in patients with preexisting inherited peripheral neuropathies. However, isolated case reports would suggest that peripheral and central regional techniques *may* be used without worsening a patient's stable neurologic condition. However, caution should be used to minimize other surgical and anesthetic risk factors for perioperative nerve injury when considering the use of regional anesthesia within this patient population.

Acquired Peripheral Neuropathy

Diabetic Polyneuropathy

The increasing prevalence of DM and its associated comorbidities will likely translate into a larger number of diabetic patients presenting for surgery. However, despite the clinical benefits and widespread use of regional anesthesia (peripheral and neuraxial blockade), there remains concern regarding its use in patients with DM.[14–17] It has been suggested that patients with a history of chronic neural compromise secondary to metabolic conditions such as diabetes may be at an increased risk of worsening neurologic injury after neuraxial or peripheral nerve blockade.[14–17]

Diabetes mellitus is currently the most common cause of systemic polyneuropathy. There are several types of neuropathy associated with DM. However, distal symmetric sensorimotor polyneuropathy is the most common form and generally synonymous with the term "diabetic polyneuropathy." The frequency of DPN ranges from 4% to 8% at the time of diagnosis to more than 50% in patients with long-standing diabetes. Despite the fact that patients may be asymptomatic, nearly all will have evidence of abnormal nerve conduction.[18,19] Furthermore, it is not uncommon for patients to present for surgery with either undiagnosed DM or known diabetes with uncontrolled hyperglycemia.[20]

The pathophysiology of DPN is poorly understood and likely multifactorial. Early symptoms such as numbness, pain, and autonomic dysfunction are caused by damage to small nerve fibers, which occurs before damage to large fibers becomes apparent.[21] There is pathophysiologic evidence of abnormalities in both large and small neural blood vessels, ultimately contributing to multifocal fiber loss. Axonal degeneration is the most prominent feature of DPN and occurs secondary to the reduced delivery of essential nutrients and other components (oxygen, blood, adenosine triphosphate, glucose) to the axon. Proposed mechanisms include (1) sorbitol deposition in the nerve because of glucose accumulation, (2) local tissue ischemia in sensory and autonomic fibers secondary to endoneurial hypoxia, (3) abnormal tissue repair mechanisms caused by excess glucose, and (4) mitochondrial dysfunction within the dorsal root ganglia.[22–24]

Currently, there is an abundance of animal data that suggests diabetic nerves may have an increased risk of neurologic injury after regional anesthesia compared with nondiabetic nerves.[25–27] Kalichman and Calcutt[17] were the first to hypothesize that diabetic

nerve fibers may be more susceptible to local anesthetic neurotoxicity for 2 reasons: (1) the nerve is more susceptible to injury because of chronic ischemic hypoxia and (2) the nerves are exposed to larger concentrations of local anesthetics because of a decreased perineural blood flow. More recently, these findings were supported with both animal and clinical data. Lirk and colleagues [28] used Zucker diabetic fatty rats exposed to hyperglycemia to demonstrate that, although the overall neuronal survival difference was low, in vitro local anesthetic neurotoxicity was more pronounced in neurons from diabetic animals. The authors also reported that preexisting subclinical neuropathy led to substantial prolongation of the block duration in vivo. Kroin and colleagues[26] also reported that the duration of sciatic nerve block with lidocaine 1% or ropivacaine 0.5% was longer in streptozotocin-induced diabetic rats compared with nondiabetic rats, and that block duration actually correlated with nerve fiber degeneration. In a subsequent study, the same authors also concluded that, with continuous glycemic control, diabetic rats had a block duration that was similar to nondiabetic rats and 40 minutes shorter than rats without glycemic control.[25] Interestingly, acute glycemic control did not lessen the nerve block duration, suggesting that diabetic neuropathy is not rapidly reversed within this animal model. Currently, it is unclear whether the results from animal studies using experimentally induced hyperglycemia can be used to make recommendations about patients with long-standing DM.[29]

Although animal studies have consistently found that diabetic nerves are more sensitive to local anesthetics and potentially more susceptible to neural injury, it is unclear whether diabetic patients have a higher incidence of neurologic injury after regional anesthesia.[17,25,26,30] There is limited clinical data suggesting that the success of peripheral nerve blockade (supraclavicular brachial plexus) may be higher in diabetic patients independent of other predictors of success (eg, body mass index) compared with nondiabetic patients.[31,32] Gebhard and colleagues[30] propose several theories for this finding, including (1) a higher sensitivity of diabetic nerve fibers to local anesthetics, (2) possible unknown intraneural penetration before injection, and (3) preexisting DPN with accompanying decreased sensation. Preexisting pathology has long been reported to play a role in the development of postoperative neurologic dysfunction.[33–35] A recent case report described a persistent postoperative femoral neuropathy after discontinuing a femoral nerve catheter in a patient with a preexisting subclinical diabetic neuropathy that was undiagnosed preoperatively.[36]

In patients with DM, a decreased sensitivity to electrical stimulation combined with diminished sensory function and an increased sensitivity to local anesthetic toxicity may increase the risk of intraneural injection during peripheral nerve blockade using a peripheral nerve stimulator.[37–39] Currently, there is a lack of clinical evidence suggesting that the use of ultrasound guidance is safer than peripheral nerve stimulation within the general population.[40,41] However, this lack of clinical benefit may be less clear for diabetic patients. For example, there are a limited number of animal and clinical studies that suggest ultrasound guidance may be a more desirable method of neural localization in diabetic patients. Animal studies have shown that low-threshold electrical stimulation may not offer protection from intraneural injection in the presence of hyperglycemia. Rigaud and colleagues[42] demonstrated that all needle insertions within a hyperglycemic dog model resulted in intraneural injection (6 of 6); whereas only one (1 of 18) intraneural injection occurred among control dogs. Sites and colleagues[39] also concluded that ultrasound guidance may be a preferred method of neural localization in diabetic patients after failing to elicit a motor response or paresthesia in 2 patients undergoing sciatic nerve blockade using peripheral nerve stimulation. The authors describe a very weak motor response in both diabetic patients with a stimulating current of more than 2.4 mA despite perineural placement of the stimulating needle using ultrasound guidance. Another potential application of ultrasound technology is the ability to use the cross-sectional area of a peripheral nerve to identify a clinical or subclinical peripheral neuropathy; a diagnosis that historically would require complex nerve conduction studies.[43,44]

Findings of spinal cord involvement in diabetic patients suggest that the same or similar mechanism of injury may affect not only peripheral nerves but also neural elements within the central neuraxis as well.[45,46] Using magnetic resonance imaging, Selvarajah and colleagues[47] described early central nervous system involvement consisting of a significant reduction in spinal cord cross-sectional area in patients with both subclinical and clinically detectable diabetic peripheral neuropathy. A case report of a diabetic patient experiencing a persistent lower-extremity neuropathy after what appeared to be an uneventful epidural analgesia reinforces concerns that diabetic patients may be at an increased risk of neurologic injury after neuraxial anesthesia.[48] A retrospective review also evaluated neurologic complications in patients with preexisting peripheral sensorimotor neuropathy or DPN who subsequently underwent neuraxial anesthesia or analgesia.[22] Of the 567 patients studied, 2 (0.4%; 95% confidence interval [CI], 0.1%–1.3%) experienced new or progressive postoperative neurologic deficits when compared with preoperative findings. The authors concluded that, although the risk of severe postoperative neurologic injury among diabetic patients is rare, it appears to be higher than that reported for the general population. Although the neuraxial technique could not be definitively implicated as the primary cause of the neurologic insult, it may have been a contributing factor among patients with preexisting neural compromise. Echevarria and colleagues have also reported faster onset times, a longer duration of maximal block levels, and slower regression times of spinal anesthesia in diabetic patients compared with nondiabetic patients.[49]

In summary, patients with DPN likely have neural elements that are more sensitive to the effects of local anesthetic. As a result, diabetic peripheral nerves may be more susceptible to subsequent injury from local anesthetic toxicity or ischemic insults. Ultimately, the decision to use regional anesthesia within diabetic patients should be made on an individual basis after a thorough discussion with the patient regarding the potential risks and benefits of the technique. Consideration should be given to decreasing the concentration or total dose of local anesthetic for both peripheral and neuraxial techniques,[50] particularly in profoundly symptomatic patients. Furthermore, the use of ultrasound guidance may facilitate perineural needle placement and the use of lower local anesthetic volumes in diabetic patients; although definitive data ensuring increased safety with ultrasound guidance are currently lacking.[51] Decreasing the concentration or dose of local anesthetic or eliminating epinephrine additives should also be considered given that diabetic nerves are already at risk of neural ischemia and infarction because of changes within the endoneural microvasculature.[52]

Chemotherapy-Induced Neuropathy

Chemotherapy-induced peripheral neuropathy (CIPN) is a frequent side effect of several commonly used chemotherapeutic agents. It is a dose-limiting side effect that occurs in approximately 30% to 40% of patients.[53] The exact mechanism of injury is unclear, although damage to microtubules, interference with microtubule-based axonal transport, mitochondrial disruption, and cytotoxic effects on DNA are all possible mechanisms.[53,54]

The neurotoxicity depends on the agent used, the duration of administration, and the cumulative dose received. Cisplatin, oxaliplatin, and carboplatin characteristically induce a purely sensory painful peripheral neuropathy, whereas vincristine, paclitaxel, and suramin tend to induce a mixed sensorimotor neuropathy with or without involvement of the autonomic nervous system.[55] Symptoms are often in the "glove and stocking" distribution and consist of pain or paresthesias. Patients at risk of developing CIPN include those with preexisting neural damage secondary to DM, excessive alcohol use, or an inherited peripheral neuropathy. In general, a prolonged period of regeneration is required to restore neurologic function, with incomplete recovery being the most common outcome.[54–56] However, patients who recover from CIPN are at an increased risk of developing progressive neuropathic symptoms if exposed to additional neurotoxic agents. Local anesthetics are potentially neurotoxic, and caution should be used when deciding whether to perform regional anesthesia in patients who have received chemotherapeutic agents known to cause CIPN. It is not uncommon for patients to have a subclinical neuropathy that only presents after a second neurologic insult, such as a peripheral or neuraxial block.[16]

INFLAMMATORY NEUROPATHIES

Guillain-Barré Syndrome

Guillain-Barré syndrome is an acute, inflammatory, demyelinating polyneuropathy characterized by areflexia and diffuse ascending neuromuscular paralysis. The etiology of GBS is unclear, although infection, pregnancy, vaccinations, immunosuppression, systemic illnesses, and transfusion have all been proposed as potential triggers.[57] The degree and distribution of paralysis are variable and can include sensory nerve, cranial nerve, and autonomic nervous system involvement. Symptoms peak approximately 2 to 4 weeks after the initial onset, with most patients experiencing prolonged recovery. Unfortunately, many patients experience moderate-to-severe neurological impairment for years after the initial diagnosis.

There are several reports of GBS occurring in the postoperative period after a variety of surgical procedures and types of anesthetics.[58–60] However, case reports of regional anesthesia use in patients with GBS are generally limited to the obstetric population.[61–64] Some patients with GBS may have autonomic instability and subsequently experience an exaggerated response to neuraxial blockade,[63] whereas other patients exhibit a normal response to neuraxial anesthesia.[61,64] Although there have been reports of successful neuraxial anesthesia in parturients with GBS, the theoretical concern of local anesthetics interacting with peripheral myelin or direct nerve trauma cannot be ignored.[21] There is some evidence to suggest that epidural anesthesia may precipitate or reactivate GBS hours to weeks after surgery.[58,65,66] However, it is difficult to determine if this is caused by the effects of the epidural, the natural progression of the disease, the surgical procedure, or the stress response related to surgery.

Although it has been suggested that acute neuronal inflammation may be a relative contraindication to regional anesthesia, existing data provide little information regarding the safety of neuraxial anesthesia or peripheral nerve blockade in patients with GBS.[21] Ultimately, the decision to perform regional anesthesia should be made on an individual basis after a thorough discussion with the patient regarding the potential risks and benefits.

Postsurgical Inflammatory Neuropathy

Recently, neurologists have become aware that an autoimmune or inflammatory process may be the cause of severe postoperative neurologic deficits. Staff and colleagues[67] recently described a series of 33 patients who developed postsurgical inflammatory neuropathy (PSIN) within 30 days of surgery. The diagnosis was confirmed in most patients after a peripheral nerve biopsy. Postsurgical inflammatory neuropathy is believed to be an idiopathic immune-mediated response to a physiologic stress such as an infectious process, a vaccination, or a surgical procedure.[67] The condition may present as focal, multifocal, or diffuse neurologic deficits in the setting of a negative radiographic imaging. Complicating the diagnosis, the onset of neurologic deficits may not be apparent during the immediate postoperative period; and the deficits may be in an anatomic distribution remote from the surgical site or regional anesthetic technique. Risk factors or potential triggers for PSIN include malignancy, DM, tobacco use, systemic infection, volatile anesthetic use, and recent blood transfusion.[67] Suppression of the immune response with prolonged high-dose corticosteroids or intravenous immunoglobulin is the current treatment of choice. The goal of treatment is to sufficiently blunt the inflammatory response to allow for axonal regeneration. Fortunately, most patients improve with current treatment recommendations, with pain and sensory deficits improving before the motor deficits.[67]

The degree to which inflammatory mechanisms play a role in postoperative neurologic dysfunction is unknown and poorly characterized particularly within the anesthesia literature.[68] As a result, anesthesia providers and surgeons rarely consider this potential etiology of nerve injury when evaluating patients with postoperative deficits. This is problematic because the common approach of watchful waiting and conservative management will not be effective in patients with PSIN. Rather, PSIN is a clinical condition that must be suspected early in the disease process so that a definitive diagnosis can be obtained (nerve biopsy) and aggressive immunotherapy can be initiated to potentially improve neurologic outcome.[67]

CENTRAL NERVOUS SYSTEM DISORDERS

Historically, neuraxial anesthesia techniques have not been offered to patients with preexisting neurologic disorders of the central nervous system (MS, PPS, ALS) for fear of worsening neurologic outcome.[69–72] In fact, many historians believe that the recommendation by Dripps and Vandam[70] in 1956 to avoid regional anesthesia in patients with preexisting neurologic disorders has impacted clinical management for nearly half a century. Several theoretical mechanisms have been proposed based on the double-crush phenomenon, including neurologic injury from needle- or catheter-induced trauma, local anesthetic neurotoxicity, and neural ischemia caused by local anesthetic additives. However, the avoidance of regional anesthesia within this patient population may also be caused by physician and patient biases or potential medicolegal concerns. There are several confounding factors (age, body habitus, surgical trauma, tourniquet times and pressures, positioning, anesthetic technique) that make it difficult to determine the etiology of worsening postoperative neurologic deficits.

A recent review evaluated 139 patients with a history of one or more central nervous system disorders that subsequently underwent a neuraxial anesthetic technique.[71] Preoperative neurologic disorders included primarily PPS, MS, ALS, and traumatic spinal cord injury. In contrast to the findings of Dripps and Vandam several decades ago, the authors identified no new or worsening postoperative neurologic deficits (0.0%; 95% CI, 0.0%–0.3%) within their patient cohort. This was despite the fact that 74% of the patients reported active neurologic symptoms (paresthesias, dysesthesias, hyperreflexia) or sensorimotor deficits during the immediate preoperative period and subsequently

received standard doses of local anesthetics. Two smaller reviews in parturients receiving smaller doses of local anesthetic for labor analgesia have reported similar results.[73,74]

Clearly, further investigations with more patients are needed to make definitive recommendations. However, the current data suggest that the decision to perform neuraxial anesthesia in patients with preexisting central nervous system disorders be based on the risks and benefits for each individual patient. Some authors have postulated that the neurologic risk may be higher in patients who have progressive neurologic deficits when compared with those patients with chronic stable sensorimotor symptoms that have not changed during the course of several months or years.

Multiple Sclerosis

Multiple sclerosis is an inflammatory autoimmune disorder of the central nervous system with a lifetime risk of 1 in 400, making it the most common debilitating neurologic disease in young adults.[75] It is a chronic degenerative disease characterized by focal demyelination within the spinal cord and brain. The demyelination results in a fluctuating conduction block that causes a classic "waxing and waning" of symptoms that is characteristic of the disease. Signs and symptoms include sensory or motor deficits, diplopia or vision loss, bowel or bladder dysfunction, and ataxia. The precise etiology is unclear; however, a combination of genetic risk factors and environmental factors likely plays a role. Twenty-five percent of MS patients are essentially asymptomatic, and their activities of daily living are unaffected. However, up to 15% of patients may become severely disabled, with significant sensorimotor deficits within a short period.[76]

Several factors common to surgery can negatively impact the disease process, including hyperpyrexia, emotional stress, and infection.[77] The mechanism of worsening neurologic function in patients with MS is unclear and may occur coincidentally within the postoperative period independent of the anesthetic technique. Evidence regarding the risk of regional anesthesia in patients with MS is limited. Despite some evidence for demyelination of the peripheral nerves in MS, peripheral nerve blockade has traditionally been considered safe.[78] However, a recent report of severe brachial plexopathy after an ultrasound-guided interscalene block has raised the concern that a segment of MS patients may have subclinical peripheral neuropathy.[79] Several investigators have demonstrated evidence of axonal demyelinating peripheral lesions (sensory > motor) in patients with MS.[80–82] Misawa and colleagues[81] demonstrated that peripheral demyelination may occur in 5% of MS patients, whereas Pogorzelski and colleagues[80] report peripheral demyelination may occur in up to 47% of patients. Similarly, Sarova-Pinhas and colleagues[82] describe nerve conduction abnormalities in up to 14.7% of peripheral nerves within MS patients compared with only 2.4% of nerves within the general population. Despite this evidence, the overall incidence and clinical relevance of this underlying peripheral neuropathy remain undefined in the setting of performing peripheral nerve blockade in patients with MS.

In contrast to peripheral nerve blockade, the potential risk of new or progressive neurologic deficits in MS patients after spinal anesthesia was first described in 1937. Critchley[83] described 3 patients with "disseminated (multiple) sclerosis" that experienced worsening of symptoms after spinal anesthesia. The author concluded that "spinal anesthesia may be a precipitating agent in the evolution of disseminated (multiple) sclerosis." Several subsequent studies demonstrated similar outcomes with the development of new or worsening neurologic deficits or a higher likelihood of symptom exacerbation after spinal anesthesia.[69,72,84,85] In contrast, a more recent study demonstrated no new or worsening neurologic symptoms after spinal anesthesia in 35 MS patients undergoing a variety of surgical procedures.[22]

The safety of epidural anesthesia and analgesia in MS patients has been focused almost exclusively within the obstetric population, which may not accurately represent the nonpregnant MS patient. Pregnancy is frequently associated with a decrease in disease relapses, whereas the postpartum period is often associated with an increased risk of relapse. The transition from cellular immunity to humoral immunity required for the mother's immune system to tolerate the fetus is thought to be protective during pregnancy.[73] However, as cell-mediated immunity rebounds during the postpartum period, patients will often experience transient worsening of neurologic symptoms that could be falsely attributed to recent regional anesthetic techniques.

Confavreux and colleagues[73] have performed one of the few prospective studies evaluating risk factors associated with disease relapse during the postpartum period. They concluded that epidural analgesia during labor and delivery did not contribute to a higher risk of relapse compared with patients not receiving neuraxial techniques. Similarly, Kuczkowski[86] found no association between any form of obstetric regional analgesia and the worsening of MS symptoms among obstetric patients. Epidural anesthesia and analgesia have traditionally been recommended over spinal anesthesia in MS patients because the concentration of local anesthetic in the white matter of the spinal cord is one fourth the level after epidural injection compared with intrathecal injection.[87] It is believed that the lack of myelin may leave the spinal cord susceptible to the neurotoxic effects of local anesthetics.[87] Although definitive studies on the pharmacological effects of local anesthetic concentrations and doses are lacking, many recommend limiting neuraxial local anesthetic doses and concentrations to the lowest level possible. There is some evidence that lidocaine can reversibly worsen symptoms of MS.[88] This is thought to occur when sodium channels in demyelinated areas are blocked enough to unmask lesions that would otherwise be below the level of clinical detection. With regard to the obstetric patient, the risk of neuraxial anesthesia or analgesia needs to be weighed against the increased risk of general anesthesia. A recent survey demonstrated that 99% of obstetric anesthesiologists would perform neuraxial anesthesia for an emergency cesarean delivery in an MS patient after carefully weighing the potential risks and benefits.[89]

In summary, there remains little conclusive evidence to support or refute the use of regional anesthesia in patients with MS. Peripheral nerve blockade has not been definitively shown to be harmful in the setting of MS and, therefore, should not be considered an absolute contraindication. In contrast, given that demyelinated fibers may be more prone to the toxic effects of local anesthetics, epidural anesthesia and analgesia may be considered safer than spinal anesthesia techniques. However, reducing the local anesthetic concentration and total dose to the lowest effective level(s) may be prudent for both peripheral and neuraxial blockade. All decisions regarding the use of regional anesthesia and analgesia in patients with MS need to be made after careful consideration of the potential risks and benefits. Regardless of the anesthetic technique chosen, patients should be informed about the risk of new or worsening neurologic symptoms during the postoperative period because of exposure to multiple exacerbating factors.

Postpolio Syndrome

Postpolio syndrome refers to new-onset neurologic symptoms that develop several years after an acute poliomyelitis infection. The onset of new or progressive symptoms may occur up to

30 years after the initial episode of poliomyelitis. PPS affects anterior horn cells within the anterior portion of the spinal cord and is, therefore, considered a lower motor neuron disorder.[90] Initial symptoms include muscle weakness, fatigue, gait instability, joint pain, and muscle atrophy within muscle groups that were previously affected by the disease. Sensory deficits are generally not characteristic of the syndrome and are only observed if a secondary disorder is present (ie, compression radiculopathy or disk herniation). The muscle effects of PPS are thought to be related to an ongoing process of denervation and reinnervation that ultimately ends when denervation is no longer compensated for by reinnervation.[90]

Postpolio syndrome is the most prevalent motor neuron disease in North America. Furthermore, because acute poliomyelitis continues to occur in developing countries, PPS will likely remain an anesthetic concern for years to come.[21] It is not uncommon for patients with PPS to require orthopedic procedures; therefore, it is important to determine the safety of regional anesthetic techniques under these clinical circumstances. Although patients with PPS have fewer motor neurons than normal, it is difficult to know whether remaining motor neurons are more susceptible to the toxic effects of local anesthetics. There have been no reports of worsening neurologic status after neuraxial anesthesia with normal doses of tetracaine and bupivacaine in patients with PPS.[91,92] However, this does not imply that regional anesthetic techniques are without risk.[93] As with all patients, the potential risk of regional anesthesia must be balanced against the disadvantages of general anesthesia, including a hypersensitivity to sedative or opioid medications, risk of muscle relaxant use, and the risk of hypoventilation and aspiration. The largest series of patients with PPS (n = 79) undergoing neuraxial anesthesia or analgesia demonstrated no worsening of neurologic symptoms during the postoperative period.[71] However, the paucity of clinical data on this topic prevents clear recommendations from being made regarding the safety of neuraxial anesthesia or peripheral nerve blockade in patients with PPS. Ultimately, the decision to use regional anesthesia should be made on an individual basis after a thorough discussion of the potential risks and benefits with each patient. Given the increased sensitivity to opioid and sedative medications within this patient subgroup, these medications should always be used with caution.

Amyotrophic Lateral Sclerosis

Amyotrophic lateral sclerosis is a common form of motor neuron disease characterized by adult-onset degeneration of both the upper and lower motor neurons. Unfortunately, in the majority of patients, death from respiratory failure occurs within a few years of disease onset.[94]

The existing evidence, albeit limited, has not supported the fear that neuraxial or peripheral blockade will exacerbate preexisting symptoms in ALS patients.[65,95–99] However, given the potential for worsening respiratory failure after general anesthesia because of the use of muscle relaxants and opioid medications, the ability to avoid airway manipulation may be considered a benefit within this high-risk patient population. Regardless of the anesthetic technique, the possibility of postoperative respiratory or neurologic deterioration is quite high in patients with ALS. Ultimately, the decision to use regional anesthesia should be made on an individual basis after a thorough discussion of the potential risks and benefits with each patient.

SPINAL CANAL PATHOLOGY

Spine and spinal canal pathology has been proposed as a potential risk factor for neurologic complications after neuraxial blockade. Several mechanisms of injury have been proposed, including an ischemic or compressive effect after the injection of large volumes of local anesthetic into a relatively confined space (ie, epidural anesthesia) as well as local anesthetic neurotoxicity (ie, spinal anesthesia). Although the precise mechanism(s) of injury remain unclear, there are several isolated case reports and large case series that are believed to support these hypotheses.

Spinal Stenosis and Lumbar Disk Disease

Spinal stenosis occurs as age-related changes within the intervertebral disks and facet joints result in narrowing of the spinal canal or neural foramina. Changes include disk degeneration, facet joint hypertrophy, osteophyte formation, and infolding of the ligamentum flavum. The precise mechanism by which spinal nerve root compression results in signs or symptoms of spinal stenosis is not completely understood.[100] Classic symptoms include back and leg radicular pain that significantly worsens with extension and is alleviated with flexion. Preexisting spinal stenosis or compressive lumbar disk disease has been proposed as a potential risk factor for neurologic complications after a neuraxial (spinal or epidural) technique. Proposed mechanisms of injury include mechanical trauma,[101,102] local anesthetic neurotoxicity,[103,104] ischemia,[105–107] or a multifactorial etiology.[108,109] Pathophysiologically, patients with spinal stenosis have a reduction in the diameter of the spinal canal, resulting in less anatomic space for fluid collections such as blood or local anesthetic. As a result, small quantities of fluid may result in significant increases in pressure around the neuraxis that would otherwise have no clinical effect in a widely patent spinal canal.

Two relatively large case series and several case reports have been published that suggest undiagnosed spinal stenosis may be a risk factor for neurologic complications after neuraxial blockade.[101,103,105,108,110] The majority of cauda equina cases involved epidural analgesia, which may suggest an ischemic component (mechanical compression of the cord by the infusing local anesthetic) to the injury.[106] Hebl and colleagues[108] performed a retrospective review of patients with preexisting spinal stenosis or lumber disk disease with and without a history of prior spinal surgery and concluded that this cohort of patients was at an increased risk for the development or worsening of neurologic deficits when compared with the general population undergoing a neuraxial technique. In addition, patients with more than one neurologic diagnosis (eg, spinal stenosis, compressive radiculopathy, preexisting peripheral neuropathy) appeared to have an even higher risk of injury. Moen and colleagues[103] also performed a large epidemiologic survey in Sweden that revealed similar trends. During a 10-year study period, 1,260,000 spinal anesthetics and 450,000 epidural blocks were evaluated. Overall, the authors identified 127 serious complications, including 85 (67%) patients with permanent injuries. Although 14 patients had preexisting spinal stenosis, 13 (93%) of these were diagnosed in the postoperative period during the evaluation of the neurologic deficit. The authors concluded that the incidence of severe anesthesia-related complications may not be as low as previously reported, and preexisting spinal canal pathology may be a "neglected risk factor." Finally, although patients with prior spine surgery may have an increased risk of paraplegia after transforaminal epidural steroid injections,[111,112] no similar risk has been found in patients after neuraxial anesthesia or analgesia.

In summary, although it appears that patients with spinal stenosis or compressive lumbar disk disease may be at increased risk of neurologic complications after neuraxial blockade, the existing literature fails to provide a direct comparison of surgical patients with similar spinal pathology undergoing general anesthesia.

Therefore, it is unclear whether the higher incidence of neurologic complications is caused by surgical factors, the anesthetic technique, the natural progression of the disease process, or a combination of these factors.

Neural Tube Defects

Neural tube defects are congenital anomalies of neural development that primarily affect the cranium or spine. Clinical manifestations vary widely and include cranial defects (eg, anencephaly, exencephaly, encephalocele), open spinal dysraphisms, and closed spinal dysraphisms. Open spinal dysraphisms, often referred to as *spina bifida cystica*, occur at a frequency of 0.5 to 8 cases per 1000 live births and include conditions in which neural tissue is exposed to the external environment.[113] The most common open spinal dysraphisms are meningocele (exposed meninges) and meningomyelocele (exposed meninges and spinal cord tissue). In contrast, closed spinal dysraphisms are characterized by unexposed neural tissue with abnormalities ranging from isolated defects in the fusion of the posterior vertebral column (ie, spina bifida occulta) to more serious spinal cord malformations such as diastematomyelia (split cord malformations), tethered spinal cord syndrome, and dural ectasia (lumbosacral widening or caudal displacement of the dural sac).[114] The etiology of neural tube defects are believed to be multifactorial, with both genetic and environmental factors equally implicated.[115]

Open spinal dysraphisms are commonly treated with surgical intervention during the early neonatal period. Clinical outcomes may vary from no neurologic sequelae to sensorimotor deficits, lower extremity paraplegia, and bowel and bladder dysfunction. Four anecdotal case reports have been described in the literature in which epidural analgesia[116,117] or spinal anesthesia[118,119] has been used in parturients during labor and delivery with a history of spina bifida cystica and subsequent surgical correction. In all but 1 case, the authors describe extensive cranial spread of local anesthetic and dense neural blockade with normal or reduced doses of local anesthetic. Limited spread of local anesthetic caudad to the site of surgical intervention was also noted. None of the patients experienced an inadvertent dural puncture, postdural puncture headache, or new or progressive neurologic dysfunction after the regional technique. Tidmarsh and May[120] have also described the use of epidural analgesia in four parturients who previously underwent meningomyelocele repair during infancy. Clinical outcomes included extensive cranial spread of local anesthetic (n = 1), poor sacral analgesia (n = 1), and successful epidural analgesia (n = 2). The authors cautioned that performing neuraxial techniques within this patient population can be technically challenging, with an increased risk of inadvertent dural puncture and unpredictable local anesthetic spread.[120] If neuraxial anesthesia or analgesia is performed under these clinical circumstances, it is recommended that the site of needle insertion occurs at a level above the original lesion because of limitations in local anesthetic spread.[116]

Spina bifida occulta is a common closed spinal dysraphism that is thought to be a normal variant of vertebral column development. Studies report an incidence of 10% to 24% within the general population.[114] *Isolated* spina bifida occulta involves the failure of a single-level vertebral arch (usually the lamina) from fusing, with no clinical signs or symptoms. There is no external lesion, and the spinal cord and meninges are not involved. The use of regional anesthesia in parturients with isolated spina bifida occulta has been reported but is limited to anecdotal case reports[121] and small case series.[120,122] Within this collection of 11 reported cases, successful epidural analgesia was achieved with normal doses of local anesthetic without extensive cranial spread of local anesthetic, sacral sparing, or adverse neurologic sequelae. One patient experienced technical difficulties during block placement, including the elicitation of a transient paresthesia and inadvertent dural puncture.[121] If neuraxial anesthesia or analgesia is performed in patients with isolated spina bifida occulta, it is generally recommended that the site of needle insertion occur at a level above the vertebral abnormality.[116]

In contrast to patients with isolated spina bifida, *complex* spina bifida may occur in conjunction with more severe closed spinal dysraphisms. Patients with spina bifida and (*a*) associated cutaneous manifestations (eg, hairy patch, subcutaneous lipoma, skin sinus), (*b*) involvement of more than one lamina, (*c*) neurologic symptoms, or (*d*) associated bowel or bladder dysfunction commonly have more severe coexisting conditions such as tethered spinal cord syndrome or diastematomyelia.[123] Under these clinical circumstances, neuraxial techniques should be considered contraindicated because neurologic complications have been reported after spinal,[124] epidural,[125] and combined spinal-epidural[126] techniques in patients with previously unrecognized tethered spinal cord syndrome and/or diastematomyelia.

Dural ectasia is the abnormal widening or ballooning of the dural sac, most commonly within the lumbosacral region of the spinal cord. It is common among patients with Marfan syndrome, occurring in 63% to 92% of cases.[127,128] Dural ectasia is also known to occur in patients with Patau syndrome (trisomy 13),[129] Ehlers-Danlos syndrome, neurofibromatosis type I, and ankylosing spondylitis.[130] Several case reports have described inadvertent dural puncture during caudal anesthesia[129,131,132] and incomplete spinal anesthesia[133] in patients with dural ectasia.

In summary, neural tube defects encompass a wide range of spinal cord malformations, ranging from asymptomatic single-level vertebral canal abnormalities (ie, spina bifida occulta) to meningomyelocele with paraplegia after surgical repair. Given the wide spectrum of clinical abnormalities, the varied risk, and the paucity of clinical data for any one diagnosis, definitive recommendations cannot be made regarding the safety of neuraxial anesthesia or analgesia in patients with neural tube defects. However, it is clear that regional anesthesia should be avoided in patients with documented tethered spinal cord syndrome, diastematomyelia, or spina bifida with associated cutaneous lesions, multilevel vertebral body involvement, neurologic deficits, or bowel or bladder dysfunction.

The neuroanatomy of all other neural tube defects (eg, isolated spina bifida occulta, prior meningo-myelocele repair) should be clearly documented with radiographic imaging before neuraxial anesthesia or analgesia is considered. If radiographic imaging can exclude the coexistence of complex closed spinal dysraphisms (eg, tethered spinal cord, diastematomyelia) within these patients, then regional anesthesia may be considered after a comprehensive risk/benefit discussion with the patient, highlighting the risk of technical difficulties, extensive cephalad spread of local anesthetic, sacral sparing, inadvertent dural puncture, and neurologic injury. If neuraxial anesthesia or analgesia is performed under these clinical circumstances, it is recommended that the site of needle insertion occurs at a level above the vertebral abnormality or site of prior surgical repair.[116]

RECOMMENDATIONS

The following recommendations (Table 1) are intended to encourage quality patient care, although observing them cannot guarantee any specific patient outcome. Their value should ultimately be determined by those who use them. The recommendations are subject to revision from time to time, as warranted by the evolution of technology, scientific evidence, and clinical practice. Importantly, the recommendations address only the issue of

TABLE 1. Recommendations: Regional Anesthesia in Patients With Preexisting Neurologic Disease

Peripheral Nervous System Disorders

Hereditary Peripheral Neuropathies

- Patients with Charcot-Marie-Tooth (CMT) disease and hereditary neuropathy with liability to pressure palsy (HNPP) may have a clinical or subclinical evidence of a preexisting peripheral neuropathy caused by neural compromise from the disease state (Class I).
- Anecdotal case reports and small case series suggest that both peripheral and neuraxial regional techniques may be used in patients with stable CMT or HNPP disease states without worsening their neurologic symptoms. However, a careful discussion regarding the potential risks and benefits of performing regional anesthesia in patients with preexisting neural compromise is strongly recommended (Class III).

Acquired Peripheral Neuropathies

- Patients with diabetic peripheral neuropathy or previous exposure to chemotherapy (eg, cisplatin or vincristine) may have a clinical or subclinical evidence of a preexisting peripheral neuropathy caused by neural compromise from the disease state (Class I).
- An abundance of animal data and limited clinical data support the concern that diabetic nerves are more sensitive to local anesthetics and perhaps more susceptible to injury. Therefore, peripheral and neuraxial blockade may theoretically increase the risk of new or progressive neurologic deficits in patients with diabetic peripheral neuropathy (Class II).
- When regional anesthesia is thought to be appropriate in patients with acquired peripheral neuropathy (eg, diabetic peripheral neuropathy or chemotherapy-induced neuropathy), consideration should be given to modify the anesthetic technique (ie, decreasing the concentration of local anesthetic, reducing the total dose of local anesthetic, eliminating or reducing the concentration of vasoconstrictors such as epinephrine) to minimize the potential additive risk (Class II).
- The use of ultrasound guidance may facilitate (a) perineural needle placement and (b) a reduction in the total dose (volume) of local anesthetic administered. However, clinical data demonstrating a reduction in neurologic injury with ultrasound guidance are currently lacking (Class II).

Inflammatory Neuropathies

- Patients with inflammatory neuropathies such as Guillain-Barré syndrome and postsurgical inflammatory neuropathy are at risk of new or worsening neurologic deficits during the postoperative period regardless of anesthetic technique (Class II).
- Neural compromise secondary to acute neuronal inflammation may be a relative contraindication to regional anesthesia. However, the existing literature can neither support nor refute this claim. Therefore, the decision to perform neuraxial or peripheral nerve blockade in patients with inflammatory neuropathies should be made on an individual basis after a thorough discussion of the potential risks and benefits with the patient (Class III).

Central Nervous System Disorders

- Patients with central nervous system disorders (eg, multiple sclerosis, postpolio syndrome, amyotrophic lateral sclerosis) may have clinical or subclinical evidence of a preexisting neurologic deficit caused by neural compromise from the disease state. Furthermore, it is not uncommon for patients with central nerve system disorders to experience worsening of their neurologic symptoms during the postoperative period regardless of the anesthetic technique (Class I).
- Anecdotal case reports and small case series suggest that neuraxial anesthesia and analgesia may be used in patients with stable neurologic symptoms without worsening their neurologic deficits. However, *definitive* evidence supporting this practice is lacking. Therefore, a careful discussion regarding the potential risks and benefits of performing regional anesthesia in patients with preexisting neural compromise is strongly recommended (Class II).

Spinal Canal Pathology

Spinal Stenosis or Lumbar Disk Disease

- Patients with spinal canal pathology (eg, spinal stenosis, lumbar disk disease) may have clinical or subclinical evidence of a preexisting neurologic deficit caused by neural compromise from the disease state (Class I).
- Large case series suggest that the performance of neuraxial anesthesia and analgesia in patients with preexisting spinal canal pathology may result in new or worsening neurologic symptoms. However, *definitive* evidence suggesting an increased risk of neurologic complications is lacking (Class II).
- Currently, it is unclear whether the development of new or worsening neurologic symptoms after neuraxial anesthesia or analgesia is caused by surgical factors, the anesthetic technique, the natural progression of the spinal pathology, or a combination of these factors (Class II).

Previous Spine Surgery

- Prior spine surgery is not a contraindication to the performance of neuraxial anesthesia or analgesia. However, before performing a regional technique, a review of the patient's radiologic imaging or the use of fluoroscopy is recommended to identify the optimal approach to the neuraxis (Class I).
- Under most clinical circumstances, spinal anesthesia may be (a) technically easier to perform and (b) more reliable (ie, higher success rates) than epidural techniques in patients who have previously undergone spine surgery. Patients undergoing neuraxial anesthesia or analgesia after a previous spine surgery do not appear to be at higher risk of new or progressive neurologic deficits (Class II).

Neural Tube Defects

- Neural tube defects encompass a wide range of spinal cord malformations, including both open (eg, meningocele, meningomyelocele) and closed (eg, spina bifida occulta, tethered spinal cord syndrome, diastematomyelia, dural ectasia) spinal dysraphisms. Patients with neural tube defects may have clinical or subclinical evidence of a preexisting neurologic deficit caused by neural compromise from the disease state (Class I).
- Because of the wide range and severity of possible spinal cord and vertebral column malformations, patients with neural tube defects should undergo radiographic imaging to fully evaluate and define the extent of their disease state before considering neuraxial anesthesia or analgesia (Class II).

Continued next page

TABLE 1. *(Continued)*

- Anecdotal case reports and small case series suggest that the performance of neuraxial anesthesia and analgesia in patients with complex closed spinal dysraphisms (ie, tethered spinal cord syndrome or diastematomyelia) may result in new or progressive neurologic symptoms. However, *definitive* evidence suggesting an increased risk of neurologic complications is lacking (Class II).
- Anecdotal case reports and small case series suggest that neuraxial anesthesia and analgesia may be used in patients with *isolated* spina bifida occulta (without associated tethered spinal cord syndrome or diastematomyelia) without an increased risk of neurologic injury. However, *definitive* evidence supporting this practice is lacking. Therefore, a careful discussion regarding the potential risks (technical difficulties, unpredictable local anesthetic spread, inadvertent dural puncture, neural injury) and benefits of performing regional anesthesia in patients with isolated spina bifida occulta is strongly recommended (Class II).

TABLE 2. Strength of Recommendations

Classification	
I	Animal and/or human evidence and/or general agreement of expert opinion supports the effectiveness and usefulness of the recommendation.
II	The weight of conflicting evidence and/or the weight of expert opinion supports the usefulness of the recommendation.
III	The usefulness of the recommendation is limited by absent or conflicting evidence and/or divergent expert opinion.

This classification system is significantly modified from the American College of Cardiology/American Heart Association construct for classifying strength of evidence.[134]

regional anesthesia in patients with preexisting peripheral and neurologic disorders.

The recommendation classification scheme (Table 2) is a modification from the American College of Cardiology/American Heart Association construct for classifying strength of evidence.[134]

REFERENCES

1. Upton AR, McComas AJ. The double crush in nerve entrapment syndromes. *Lancet*. 1973;2:359–362.
2. Osterman AL. The double crush syndrome. *Orthop Clin North Am*. 1988; 19:147–155.
3. Neal JM, Bernards CM, Hadzic A, et al. ASRA Practice Advisory on Neurologic Complications in Regional Anesthesia and Pain Medicine. *Reg Anesth Pain Med*. 2008;33:404–415.
4. Jacob AK, Kopp SL. Regional anesthesia in the patient with preexisting neurologic disorders. *Adv Anesth*. 2011;29:1–18.
5. Skre H. Genetic and clinical aspects of Charcot-Marie-Tooth's disease. *Clin Genet*. 1974;6:98–118.
6. Saporta AS, Sottile SL, Miller LJ, Feely SM, Siskind CE, Shy ME. Charcot-Marie-Tooth disease subtypes and genetic testing strategies. *Ann Neurol*. 2011;69:22–33.
7. Bui AH, Marco AP. Peripheral nerve blockade in a patient with Charcot-Marie-Tooth disease. *Can J Anaesth*. 2008;55:718–719.
8. Dhir S, Balasubramanian S, Ross D. Ultrasound-guided peripheral regional blockade in patients with Charcot-Marie-Tooth disease: a review of three cases. *Can J Anaesth*. 2008;55:515–520.
9. Fernandez Perez AB, Quesada Garcia C, Rodriguez Gonzalez O, Besada Estevez JC. Obstetric epidural analgesia, a safe choice in a patient with Charcot-Marie-Tooth disease [in Spanish]. *Rev Esp Anestesiol Reanim*. 2011;58:255–256.
10. Schmitt HJ, Muenster T, Schmidt J. Central neural blockade in Charcot-Marie-Tooth disease. *Can J Anaesth*. 2004;51:1049–1050.
11. Sugai K, Sugai Y. Epidural anesthesia for a patient with Charcot-Marie-Tooth disease, bronchial asthma and hypothyroidism [in Japanese]. *Masui*. 1989;38:688–691.
12. Tanaka S, Tsuchida H, Namiki A. Epidural anesthesia for a patient with Charcot-Marie-Tooth disease, mitral valve prolapse syndrome and 2nd degree AV block [in Japanese]. *Masui*. 1994;43:931–933.
13. Lepski GR, Alderson JD. Epidural analgesia in labour for a patient with hereditary neuropathy with liability to pressure palsy. *Int J Obstet Anesth*. 2001;10:198–201.
14. Horlocker TT, O'Driscoll SW, Dinapoli RP. Recurring brachial plexus neuropathy in a diabetic patient after shoulder surgery and continuous interscalene block. *Anesth Analg*. 2000;91:688–690.
15. Waters JH, Watson TB, Ward MG. Conus medullaris injury following both tetracaine and lidocaine spinal anesthesia. *J Clin Anesth*. 1996;8: 656–658.
16. Hebl JR, Horlocker TT, Pritchard DJ. Diffuse brachial plexopathy after interscalene blockade in a patient receiving cisplatin chemotherapy: the pharmacologic double crush syndrome. *Anesth Analg*. 2001;92:249–251.
17. Kalichman MW, Calcutt NA. Local anesthetic–induced conduction block and nerve fiber injury in streptozotocin-diabetic rats. *Anesthesiology*. 1992;77:941–947.
18. Dyck PJ, Kratz KM, Karnes JL, et al. The prevalence by staged severity of various types of diabetic neuropathy, retinopathy, and nephropathy in a population-based cohort: the Rochester Diabetic Neuropathy Study. *Neurology*. 1993;43:817–824.
19. Ross MA. Neuropathies associated with diabetes. *Med Clin North Am*. 1993;77:111–124.
20. Centers for Disease Control and Prevention. *2011 National Diabetes Fact Sheet*. Atlanta, GA: Centers for Disease Control and Prevention, US Department of Health and Human Services; 2011.
21. Lirk P, Birmingham B, Hogan Q. Regional anesthesia in patients with preexisting neuropathy. *Int Anesthesiol Clin*. 2011;49:144–165.
22. Hebl JR, Kopp SL, Schroeder DR, Horlocker TT. Neurologic complications after neuraxial anesthesia or analgesia in patients with preexisting peripheral sensorimotor neuropathy or diabetic polyneuropathy. *Anesth Analg*. 2006;103:1294–1299.
23. Krishnan AV, Kiernan MC. Altered nerve excitability properties in established diabetic neuropathy. *Brain*. 2005;128(pt 5):1178–1187.
24. Sinnreich M, Taylor BV, Dyck PJ. Diabetic neuropathies. Classification, clinical features, and pathophysiological basis. *Neurologist*. 2005;11:63–79.
25. Kroin JS, Buvanendran A, Tuman KJ, Kerns JM. Safety of local anesthetics administered intrathecally in diabetic rats. *Pain Med*. 2012;13:802–807.
26. Kroin JS, Buvanendran A, Williams DK, et al. Local anesthetic sciatic nerve block and nerve fiber damage in diabetic rats. *Reg Anesth Pain Med*. 2010;35:343–350.
27. Williams BA. Toward a potential paradigm shift for the clinical care of diabetic patients requiring perineural analgesia: strategies for using the diabetic rodent model. *Reg Anesth Pain Med*. 2010;35:329–332.

28. Lirk P, Flatz M, Haller I, et al. In Zucker diabetic fatty rats, subclinical diabetic neuropathy increases in vivo lidocaine block duration but not in vitro neurotoxicity. *Reg Anesth Pain Med*. 2012;37:601–606.
29. Williams BA, Murinson BB. Diabetes mellitus and subclinical neuropathy: a call for new paths in peripheral nerve block research. *Anesthesiology*. 2008;109:361–362.
30. Gebhard RE, Nielsen KC, Pietrobon R, Missair A, Williams BA. Diabetes mellitus, independent of body mass index, is associated with a "higher success" rate for supraclavicular brachial plexus blocks. *Reg Anesth Pain Med*. 2009;34:404–407.
31. Cuvillon P, Reubrecht V, Zoric L, et al. Comparison of subgluteal sciatic nerve block duration in type 2 diabetic and non-diabetic patients. *Br J Anaesth*. 2013;110:823–830.
32. Sertoz N, Deniz M, Ayanoglu H. Relationship between glycosylated hemoglobin level and sciatic nerve block performance in diabetic patients. *Foot & Ankle Intl*. 2013;34:85–90.
33. Alvine FG, Schurrer ME. Postoperative ulnar-nerve palsy. Are there predisposing factors? *J Bone Joint Surg Am*. 1987;69:255–259.
34. Chaudhry V, Glass JD, Griffin JW. Wallerian degeneration in peripheral nerve disease. *Neurol Clin*. 1992;10:613–627.
35. Selander D, Edshage S, Wolff T. Paresthesiae or no paresthesiae? Nerve lesions after axillary blocks. *Acta Anaesthesiol Scand*. 1979;23:27–33.
36. Blumenthal S, Borgeat A, Maurer K, et al. Preexisting subclinical neuropathy as a risk factor for nerve injury after continuous ropivacaine administration through a femoral nerve catheter. *Anesthesiology*. 2006; 105:1053–1056.
37. Bigeleisen PE. Nerve puncture and apparent intraneural injection during ultrasound-guided axillary block does not invariably result in neurologic injury. *Anesthesiology*. 2006;105:779–783.
38. Lok C, Kirk P. Problems performing a sciatic nerve block in an amputee. *Anaesthesia*. 2003;58:289–290.
39. Sites BD, Gallagher J, Sparks M. Ultrasound-guided popliteal block demonstrates an atypical motor response to nerve stimulation in 2 patients with diabetes mellitus. *Reg Anesth Pain Med*. 2003;28:479–482.
40. Liu SS, Ngeow JE, Yadeau JT. Ultrasound-guided regional anesthesia and analgesia: a qualitative systematic review. *Reg Anesth Pain Med*. 2009;34:47–59.
41. Sites BD, Taenzer AH, Herrick MD, et al. Incidence of local anesthetic systemic toxicity and postoperative neurologic symptoms associated with 12,668 ultrasound-guided nerve blocks: an analysis from a prospective clinical registry. *Reg Anesth Pain Med*. 2012;37:478–482.
42. Rigaud M, Filip P, Lirk P, Fuchs A, Gemes G, Hogan Q. Guidance of block needle insertion by electrical nerve stimulation: a pilot study of the resulting distribution of injected solution in dogs. *Anesthesiology*. 2008;19:473–478.
43. Lucchetta M, Pazzaglia C, Granata G, Briani C, Padua L. Ultrasound evaluation of peripheral neuropathy in POEMS syndrome. *Muscle Nerve*. 2011;44:868–872.
44. Riazi S, Bril V, Perkins BA, et al. Can ultrasound of the tibial nerve detect diabetic peripheral neuropathy? A cross-sectional study. *Diabetes Care*. 2012;35:2575–2579.
45. Eaton SE, Harris ND, Rajbhandari SM, et al. Spinal-cord involvement in diabetic peripheral neuropathy. *Lancet*. 2001;358:3536.
46. Varsik P, Kucera P, Buranova D, Balaz M. Is the spinal cord lesion rare in diabetes mellitus? Somatosensory evoked potentials and central conduction time in diabetes mellitus. *Med Sci Monit*. 2001;7:712–715.
47. Selvarajah D, Wilkinson ID, Emery CJ, et al. Early involvement of the spinal cord in diabetic peripheral neuropathy. *Diabetes Care*. 2006;29: 2664–2669.
48. Al-Nasser B. Toxic effects of epidural analgesia with ropivacaine 0.2% in a diabetic patient. *J Clin Anesth*. 2004;16:220–223.
49. Echevarria M, Hachero A, Martinez A, Ramallo E, Garcia-Bernal D, Ramos M, Fernandez A. Spinal anesthesia with 0.5% isobaric bupivacaine in patients with diabetes mellitus: the influence of CSF composition on sensory and motor block. *Eur J Anaesthesiol*. 2008;25:1014–1019.
50. Drasner K. Local anesthetic neurotoxicity: clinical injury and strategies that may minimize risk. *Reg Anesth Pain Med*. 2002;27:576–580.
51. Koscielniak–Nielsen ZJ. Ultrasound-guided peripheral nerve blocks: what are the benefits? *Acta Anaesthesiol Scand*. 2008;52:727–737.
52. Williams BA, Murinson BB, Grable BR, Orebaugh SL. Future considerations for pharmacologic adjuvants in single-injection peripheral nerve blocks for patients with diabetes mellitus. *Reg Anesth Pain Med*. 2009;34:445–457.
53. Pachman DR, Barton DL, Watson JC, Loprinzi CL. Chemotherapy-induced peripheral neuropathy: prevention and treatment. *Clin Pharmacol Ther*. 2011;90:377–387.
54. Peters CM, Jimenez-Andrade JM, Kuskowski MA, Ghilardi JR, Mantyh PW. An evolving cellular pathology occurs in dorsal root ganglia, peripheral nerve and spinal cord following intravenous administration of paclitaxel in the rat. *Brain Res*. 2007;1168:46–59.
55. Quasthoff S, Hartung HP. Chemotherapy-induced peripheral neuropathy. *J Neurol*. 2002;249:9–17.
56. Pignata S, De Placido S, Biamonte R, et al. Residual neurotoxicity in ovarian cancer patients in clinical remission after first-line chemotherapy with carboplatin and paclitaxel: the Multicenter Italian Trial in Ovarian cancer (MITO-4) retrospective study. *BMC Cancer*. 2006;6:5.
57. Pithadia AB, Kakadia N. Guillain-Barré syndrome (GBS). *Pharmacol Rep*. 2010;62:220–232.
58. Bamberger PD, Thys DM. Guillain-Barré syndrome in a patient with pancreatic cancer after an epidural-general anesthetic. *Anesth Analg*. 2005;100:1197–1199.
59. Gautier PE, Pierre PA, Van Obbergh LJ, Van Steenberge A. Guillain-Barré syndrome after obstetrical epidural analgesia. *Reg Anesth*. 1989;14: 251–252.
60. Heyworth BE, Fabricant PD, Pizzurro MM, Beksac B, Salvati EA. Guillain-Barré syndrome mimicking nerve injury after total hip arthroplasty. *HSS J*. 2011;7:286–289.
61. Alici HA, Cesur M, Erdem AF, Gursac M. Repeated use of epidural anaesthesia for caesarean delivery in a patient with Guillain-Barré syndrome. *Int J Obstet Anesth*. 2005;14:269–270.
62. McGrady EM. Management of labour and delivery in a patient with Guillain-Barré syndrome. *Anaesthesia*. 1987;42:899.
63. Perel A, Reches A, Davidson JT. Anaesthesia in the Guillian-Barré syndrome. A case report and recommendations. *Anaesthesia*. 1977;32: 257–260.
64. Vassiliev DV, Nystrom EU, Leicht CH. Combined spinal and epidural anesthesia for labor and cesarean delivery in a patient with Guillain-Barré syndrome. *Reg Anesth Pain Med*. 2001;26:174–176.
65. Otsuka N, Igarashi M, Shimodate Y, Nakabayashi K, Asano M, Namiki A. Anesthetic management of two patients with amyotrophic lateral sclerosis (ALS) [in Japanese]. *Masui*. 2004;53:1279–1281.
66. Steiner I, Argov Z, Cahan C, Abramsky O. Guillain-Barré syndrome after epidural anesthesia: direct nerve root damage may trigger disease. *Neurology*. 1985;35:1473–1475.
67. Staff NP, Engelstad J, Klein CJ, et al. Post-surgical inflammatory neuropathy. *Brain*. 2010;133:2866–2880.
68. Ahn KS, Watson JC, Scott KP, Trousdale RT, Hebl JR. Postsurgical inflammatory neuropathy. *Reg Anesth Pain Med*. 2011;36:403–405.
69. Bamford C, Sibley W, Laguna J. Anesthesia in multiple sclerosis. *Can J Neurol Sci*. 1978;5:41–44.

70. Dripps RD, Vandam LD. Exacerbation of pre-existing neurologic disease after spinal anesthesia. *N Engl J Med*. 1956;255:843–849.
71. Hebl JR, Horlocker TT, Schroeder DR. Neuraxial anesthesia and analgesia in patients with preexisting central nervous system disorders. *Anesth Analg*. 2006;103:223–228, table of contents.
72. Keschner M. The effect of injuries and illness on the course of multiple sclerosis. *Res Publ Assoc Res Nerv Ment Dis*. 1950;28:533–547.
73. Confavreux C, Hutchinson M, Hours MM, Cortinovis-Tourniaire P, Moreau T. Rate of pregnancy-related relapse in multiple sclerosis. Pregnancy in Multiple Sclerosis Group. *N Engl J Med*. 1998;339:285–291.
74. Crawford JS. Epidural analgesia for patients with chronic neurological disease. *Anesth Analg*. 1983;62:621–622.
75. Noseworthy JH, Lucchinetti C, Rodriguez M, Weinshenker BG. Multiple sclerosis. *N Engl J Med*. 2000;343:938–952.
76. Compston A, Coles A. Multiple sclerosis. *Lancet*. 2002;359:1221–1231.
77. Korn-Lubetzki I, Kahana E, Cooper G, Abramsky O. Activity of multiple sclerosis during pregnancy and puerperium. *Ann Neurol*. 1984;16:229–231.
78. Pollock M, Calder C, Allpress S. Peripheral nerve abnormality in multiple sclerosis. *Ann Neurol*. 1977;2:41–48.
79. Koff MD, Cohen JA, McIntyre JJ, Carr CF, Sites BD. Severe brachial plexopathy after an ultrasound-guided single-injection nerve block for total shoulder arthroplasty in a patient with multiple sclerosis. *Anesthesiology*. 2008;108:325–328.
80. Pogorzelski R, Baniukiewicz E, Drozdowski W. Subclinical lesions of peripheral nervous system in multiple sclerosis patients [in Polish]. *Neurol Neurochir Pol*. 2004;38:257–264.
81. Misawa S, Kuwabara S, Mori M, Hayakawa S, Sawai S, Hattori T. Peripheral nerve demyelination in multiple sclerosis. *Clin Neurophysiol*. 2008;119:1829–1833.
82. Sarova-Pinhas I, Achiron A, Gilad R, Lampl Y. Peripheral neuropathy in multiple sclerosis: a clinical and electrophysiologic study. *Acta Neurol Scand*. 1995;91:234–238.
83. Critchley EP. Multiple sclerosis initially presenting as facial palsy. *Aviat Space Environ Med*. 2004;75:1001–1004.
84. Hammes E. Neurological complications associated with spinal anesthesia (Eight cases). *Minn Med*. 1943;36:339–345.
85. Stenuit J, Marchand P. Sequelae of spinal anesthesia [in French]. *Acta Neurol Psychiatr Belg*. 1968;68:626–635.
86. Kuczkowski KM. Labor analgesia for the parturient with neurological disease: what does an obstetrician need to know? *Arch Gynecol Obstet*. 2006;274:41–46.
87. Warren TM, Datta S, Ostheimer GW. Lumbar epidural anesthesia in a patient with multiple sclerosis. *Anesth Analg*. 1982;61:1022–1023.
88. Sakurai M, Mannen T, Kanazawa I, Tanabe H. Lidocaine unmasks silent demyelinative lesions in multiple sclerosis. *Neurology*. 1992;42:2088–2093.
89. Drake E, Drake M, Bird J, Russell R. Obstetric regional blocks for women with multiple sclerosis: a survey of UK experience. *Int J Obstet Anesth*. 2006;15:115–123.
90. Gonzalez H, Olsson T, Borg K. Management of postpolio syndrome. *Lancet Neurol*. 2010;9:634–642.
91. Bordes J, Gaillard PE, Lacroix G, Palmier B. Spinal anaesthesia guided by computed tomography scan in a patient with severe post-polio sequelae. *Br J Anaesth*. 2010;105:702–703.
92. Higashizawa T, Sugiura J, Takasugi Y. [Spinal anesthesia in a patient with hemiparesis after poliomyelitis]. *Masui*. 2003;52:1335–1337.
93. Lambert DA, Giannouli E, Schmidt BJ. Postpolio syndrome and anesthesia. *Anesthesiology*. 2005;103:638–644.
94. Pratt AJ, Getzoff ED, Perry JJ. Amyotrophic lateral sclerosis: update and new developments. *Degener Neurol Neuromuscul Dis*. 2012;2012:1–14.
95. Chen LK, Chang Y, Liu CC, Hou WY. Epidural anesthesia combined with propofol sedation for abdominal hysterectomy in a patient with amyotrophic lateral sclerosis–a case report. *Acta Anaesthesiol Sin*. 1998;36:103–106.
96. Hara K, Sakura S, Saito Y, Maeda M, Kosaka Y. Epidural anesthesia and pulmonary function in a patient with amyotrophic lateral sclerosis. *Anesth Analg*. 1996;83:878–879.
97. Hobaika AB, Neves BS. Combined spinal-epidural block in a patient with amyotrophic lateral sclerosis: case report. *Rev Bras Anestesiol*. 2009;59:206–209.
98. Kitoh T, Kobayashi K, Ina H, et al. Effects of lumbar sympathetic ganglion block for a patient with amyotrophic lateral sclerosis (ALS). *J Anesth*. 2006;20:109–112.
99. Kochi T, Oka T, Mizuguchi T. Epidural anesthesia for patients with amyotrophic lateral sclerosis. *Anesth Analg*. 1989;68:410–412.
100. Katz JN, Harris MB. Clinical practice. Lumbar spinal stenosis. *N Engl J Med*. 2008;358:818–825.
101. Stambough JL, Stambough JB, Evans S. Acute cauda equina syndrome after total knee arthroplasty as a result of epidural anesthesia and spinal stenosis. *J Arthroplasty*. 2000;15:375–379.
102. Tetzlaff JE, Dilger JA, Wu C, Smith MP, Bell G. Influence of lumbar spine pathology on the incidence of paresthesia during spinal anesthesia. *Reg Anesth Pain Med*. 1998;23:560–563.
103. Moen V, Dahlgren N, Irestedt L. Severe neurological complications after central neuraxial blockades in Sweden 1990–1999. *Anesthesiology*. 2004;101:950–959.
104. Yuen EC, Layzer RB, Weitz SR, Olney RK. Neurologic complications of lumbar epidural anesthesia and analgesia. *Neurology*. 1995;45:1795–1801.
105. de Seze MP, Sztark F, Janvier G, Joseph PA. Severe and long-lasting complications of the nerve root and spinal cord after central neuraxial blockade. *Anesth Analg*. 2007;104:975–979.
106. Hooten WM, Hogan MS, Sanemann TC, Maus TJ. Acute spinal pain during an attempted lumbar epidural blood patch in congenital lumbar spinal stenosis and epidural lipomatosis. *Pain Physician*. 2008;11:87–90.
107. Usubiaga JE, Wikinski JA, Usubiaga LE. Epidural pressure and its relation to spread of anesthetic solutions in epidural space. *Anesth Analg*. 1967;46:440–446.
108. Hebl JR, Horlocker TT, Kopp SL, Schroeder DR. Neuraxial blockade in patients with preexisting spinal stenosis, lumbar disk disease, or prior spine surgery: efficacy and neurologic complications. *Anesth Analg*. 2010;111:1511–1519.
109. Horlocker TT. Neuraxial blockade in patients with spinal stenosis: between a rock and a hard place. *Anesth Analg*. 2010;110:13–15.
110. Kubina P, Gupta A, Oscarsson A, Axelsson K, Bengtsson M. Two cases of cauda equina syndrome following spinal-epidural anesthesia. *Reg Anesth*. 1997;22:447–450.
111. Houten JK, Errico TJ. Paraplegia after lumbosacral nerve root block: report of three cases. *Spine J*. 2002;2:70–75.
112. Huntoon MA, Martin DP. Paralysis after transforaminal epidural injection and previous spinal surgery. *Reg Anesth Pain Med*. 2004;29:494–495.
113. Saitsu H, Yamada S, Uwabe C, Ishibashi M, Shiota K. Development of the posterior neural tube in human embryos. *Anat Embryol (Berl)*. 2004;209:107–117.
114. Kaplan KM, Spivak JM, Bendo JA. Embryology of the spine and associated congenital abnormalities. *Spine J*. 2005;5:564–576.

115. Detrait ER, George TM, Etchevers HC, Gilbert JR, Vekemans M, Speer MC. Human neural tube defects: developmental biology, epidemiology, and genetics. *Neurotoxicol Teratol*. 2005;27:515–524.

116. Vaagenes P, Fjacrestad I. Epidural block during labour in a patient with spina bifida cystica. *Anaesthesia*. 1981;36:299–301.

117. Altamimi Y, Pavy TJG. Epidural analgesia for labour in a patient with a neural tube defect. *Anaesth Intensive Care*. 2006;34:816–819.

118. Nuyten F, Gielen M. Spinal catheter anaesthesia for cesarean section in a patient with spina bifida. *Anaesthesia*. 1990;45:846–847.

119. Broome IJ. Spinal anaesthesia for caesarean section in a patient with spina bifida cystica. *Anaesth Intensive Care*. 1989;17:377–379.

120. Tidmarsh MD, May AE. Epidural anaesthesia and neural tube defects. *Intl J Obstet Anesth*. 1998;7:111–114.

121. McGrady EM, Davis AG. Spina bifida occulta and epidural anaesthesia. *Anaesthesia*. 1988;43:867–869.

122. Rosaeg OP, Yarnell RW, Lindsay MP. The obstetrical anaesthesia assessment clinic: a review of six years experience. *Can J Anaesth*. 1993;40:346–356.

123. Ali L, Stocks GM. Spina bifida, tethered cord and regional anaesthesia. *Anaesthesia*. 2005;60:1149–1150.

124. Wenger M, Hauswirth CB, Brodhage RP. Undiagnosed adult diastematomyelia associated with neurological symptoms following spinal anaesthesia. *Anaesthesia*. 2001;56:764–767.

125. Morgenlander JC, Redick LF. Spinal dysraphism and epidural anesthesia. *Anesthesiology*. 1994;81:783–785.

126. Xue JX, Li B, Lan F. Accidental conus medullaris injury following combined epidural and spinal anesthesia in a pregnant woman with unknown tethered cord syndrome. *Chin Med J (Engl)*. 2013;126:1188–1189.

127. Pyeritz RE, Fishman EK, Bernhardt BA, Siegelman SS. Dural ectasia is a common feature of the Marfan syndrome. *Am J Hum Genet*. 1988;43:726–732.

128. Fattori R, Nienaber CA, Descovich B, et al. Importance of dural ectasia in phenotypic assessment of Marfan's syndrome. *Lancet*. 1999;354:910–913.

129. Cohen IT. Caudal block complication in a patient with trisomy 13. *Paediatr Anaesth*. 2006;16:213–215.

130. Liu CC, Lin YC, Lo CP, Chang TP. Cauda equina syndrome and dural ectasia: rare manifestations in chronic ankylosing spondylitis. *Br J Radiol*. 2011;84:123–125.

131. Rishimugesh Kanna P, Sekar C, Prasad Shetty A, Rajasekaran S. Transient paraplegia due to accidental intrathecal bupivacaine infiltration following pre-emptive analgesia in a patient with missed sacral dural ectasia. *Spine (Phila Pa 1976)*. 2010;35:1444–1446.

132. Visoiu M, Lichtenstein S. 25 Years of experience, thousands of caudal blocks, and no dural puncture. What happened today? *Paediatr Anaesth*. 2012;22:304–305.

133. Lacassie HJ, Millar S, Leithe LG, et al. Dural ectasia: a likely cause of inadvertent spinal anaesthesia in two parturients with Marfan's syndrome. *Br J Anaesth*. 2005;94:500–504.

134. Eagle KA, Berger PB, Calkins H, et al. ACC/AHA guideline update for perioperative cardiovascular evaluation for noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1996 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery). *J Am Coll Cardiol*. 2002;39:542–553.