

# Regional anaesthesia-induced peripheral nerve injury

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## Abstract

Regional anaesthesia techniques have gained great popularity in recent years, as they provide excellent anaesthesia and analgesia for many surgical procedures. Many courses, workshops, multimedia materials and a wide access to high-end ultrasound devices have resulted in Polish anaesthesiologists eagerly performing various blockades. However, there is also a dark side to regional anaesthesia which should not be forgotten — complications. Although nerve injuries are considered to be multifactorial in nature and the vast majority of them are not due to regional anaesthesia, anaesthesiologists and anaesthetised patients must be aware of the risk involved. Due to the potentially devastating sequelae of regional blocks, updating one's knowledge of this topic is very much necessary. The aim of this review is to summarise current knowledge concerning regional anaesthesia-induced peripheral nerve injury.

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## EPIDEMIOLOGY OF PERIPHERAL NERVE BLOCK COMPLICATIONS

The data in the literature regarding the incidence of regional anaesthesia-induced neurologic complications differ markedly. These discrepancies result from the way the complications are defined, the duration of observation (different after 1 week and markedly different after 12 months), the type of surgery and block, or difficulties in determining the cause of nerve injury (anaesthetic, surgical, patient-related, etc). Early transient neurological complications are relatively common during the first days and weeks following anaesthesia. According to the meta-analysis published in 2007, the incidences of transient neurological deficits following interscalene brachial plexus block, axillary brachial plexus blocks and femoral nerve blocks are 2.84%, 1.48% and 0.34%, respectively while the incidence of permanent neurological deficits amount to only 0.04/1000 blocks [1]. More recently, Sites *et al.* [2] assessed the incidence of neurological complications following ultrasound-guided nerve blocks and noted the incidence of transient neuropathies being 1.8/1000, neuropathies persisting for at least 6 months

at 0.9/1000, and associated with interscalene blocks at 3.1/1000 blocks. Another analysis of the Italian registry of regional anaesthesia-induced complications in 2016 involving over 29,000 patients who had undergone peripheral nerve blocks revealed that transient neurological complications were observed only in 3 patients. The presented incidence of transient perioperative nerve injuries (less than 1/10,000) is probably the lowest one reported in literature. The authors, however, admit that the complications recorded in the registry regarded only the cases which were “evident during hospitalisation” while neuropathies whose symptoms may have occurred at home were not included [3].

Irrespective of inter-study differences, one element remains constant — although the initial incidence of neurological deficits is relatively high, it significantly decreases over time (to 2.2% in the first 3 months, 0.8% during the 6th month, and 0.2% after 12 months) [4]. The most commonly reported incidence of persistent (over a year) neurological injuries associated with regional anaesthesia is 2–4 per 10,000 blocks and is comparable irrespective of nerve location methods (stimulation or ultrasound) [4–10].

## PERIPHERAL NERVE ANATOMY

A peripheral nerve is comprised of axons surrounded by Schwann cells which, together with delicate connective tissue elements of the endoneurium and capillaries, are bundled into circular or oval fascicles. The individual fascicles exchange nerve fibres, morphologically resembling plexuses rather than long isolate cables. The perineurium forms the external part of fascicles — several to a dozen layers of tightly adhering fibroblasts and collagen fibres. The perineurial cells with tight junctions and non-fenestrated capillaries form the blood-nerve barrier providing a stable environment for axons. The outermost part of the nerve, rich in collagen fibres, is called the epineurium. This name pertains also to the connective tissue rich in adipose cells and a network of small blood vessels (the vasa nervorum) filling the inter-fascicle space. The nerve is surrounded by a loose connective tissue, the paraneurium, which is there to stabilise the nerve's position [11].

Some nerves, e.g. the sciatic nerve, are surrounded by a connective tissue sheath; although relatively closely attached to the nerve, the sheath is a paraneural structure independent of the epineurium [12].

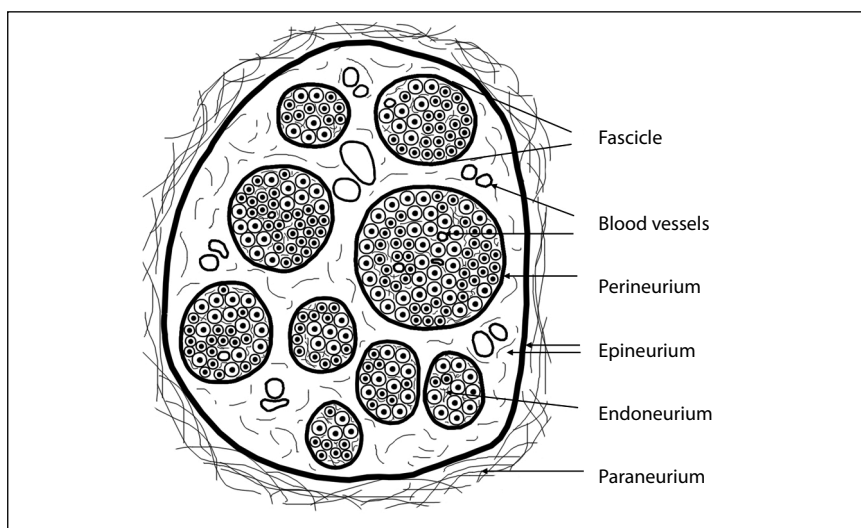
The connective tissue of nerves plays an important mechanical and protective role and its content changes along the course of individual nerves. For instance, in the brachial plexus, the ratio of nervous to non-nervous tissue within the epineurium changes from 1:1 between the scalene muscles to 1:2 in the subclavicular region. Similar relationships are found in the sciatic nerve — 2:1 in the gluteal region and 1:1 in the popliteal region. The above has relevant clinical implications as a block performed in the proximal segment theoretically creates a higher risk of neurological complications resulting from higher concentration of the nervous tissue [13, 14].

## PERIPHERAL NERVE PATHOPHYSIOLOGY

In the 1940s, Seddon and Sunderland [15] classified nerve injuries; despite certain limitations, their classifications are still valid (Table 1).

Neurapraxia is the mildest form of nerve injury in which the continuity of nerve fibres is intact and the conduction block results from axon oedema, disorganisation of neurofilaments and segmental demyelination. Remyelination and complete conduction recovery occurs within 2-12 weeks.

Axonotmesis is defined as disruption of nerve fibres with preserved epineurium continuity. Separation of the nerve cell body from its peripheral part leads to complete degeneration of the distal axon segment (and partially of the proximal segment). Following injury, biochemical and morphological changes in the peripheral axon take place within several hours. This process is called Wallerian degeneration and lasts up to 3–6 weeks. The cytoskeleton and the axon cell membrane are disintegrated and the myelin sheath is destroyed. The residual parts are eliminated by Schwann cells, as well as macrophages and granulocytes migrating into the site of injury. The severity of degenerative lesions of the nerve depends on the location and extent of injury to the nerve fibres and the surrounding connective tissue structures. Injuries close to the nerve cell body can lead to the neuron's death and lack of regeneration. The earliest symptoms of regeneration, in the form of proliferation of Schwann cells, may be observed already within the first post-injury week. The Schwann cells (the bands of Büngner) that form tubes regenerating axons. Axonotmesis is associated with poorer prognosis, as compared with neurapraxia. If the injury involves up to 20–30% of motoneurons, the function may return within 2–6 months thanks to reinnervation of the denervated



**Figure 1.** The peripheral nerve

**Table 1.** Classifications of nerve injuries according to Seddon and Sunderland

Seddon	Sunderland	Pathology	Spontaneous return of function
Neurapraxia	1	Segmental demyelination without degeneration of axons	Yes
Axonotmesis	2	Disruption of axons alone, Wallerian degeneration	Yes, slower than in neurapraxia
	3	Disruption of axons and the endoneurium; perineurium intact	Not very likely, surgical intervention may be needed
	4	Disruption of axons, the endoneurium and perineurium; epineurium intact.	Highly unlikely, surgical intervention is necessary
Neurotmesis	5	Complete disruption of the nerve (disruption of axons and all connective tissue elements).	No, surgical intervention is necessary

muscle by collaterals from adjacent intact neurocytes. If the extent of injury is larger, the main mechanism of recovery is slow regeneration of the axon stump (1–2 mm a day). In such cases, the return of nerve function is significantly longer (up to 24 months) and the target organs (muscles) remain denervated and undergo atrophy and fibrosis. The less damaged the connective tissue nerve “scaffold”, the more likely the proper regeneration is; one which is more likely after a second grade injury than after a fourth grade injury according to Sunderland.

Neurotmesis means a complete disruption of the nerve together with the external connective tissue elements (*epineurium*). In such cases, the return of nerve function is not possible without surgical intervention [15].

### MECHANISMS OF PERIOPERATIVE NERVE INJURY

The mechanisms of perioperative nerve injury can be divided into 4 major groups: chemical, mechanical, vascular and inflammatory. These may be associated with anaesthetic and surgical factors, as well as the patient’s predisposition (neuropathy). To illustrate the complexity of the issue, the following situation may be considered: during anaesthesia, the anaesthesiologist introduces the tip of the needle into the bundle, injuring the epi- and endoneurial blood vessels. If undiagnosed and the local anaesthetic is administered under high pressure, three kinds of injuries can be observed, namely: mechanical (direct injury to the nerve and pressure insult caused by the administration of the solution and formation of an intra-nerve haematoma); chemical (exposure to high concentrations of local anaesthetics (LAs), direct contact with blood); and vascular (a haematoma can locally limit the blood supply). If all this happens to a patient with a pre-existing nerve injury, e.g. in diabetic patient (the patient-dependent factor) and the procedure is associated with an increased risk of nerve injury (the surgical factor), the probability of severe nerve injury is extremely high. Although the causes of nerve injuries will be further discussed separately, they cannot be practically separated as the nerve injury is often the result of many of them (Table 2).

**Table 2.** Mechanisms of perioperative nerve injury

Chemical	Toxicity of LAs, adjuvants, blood
Mechanical	Needle (cut, tear) Compression from the outside (tourniquets, high volume of an anaesthetic, oedema or haematoma of the adjacent tissues) High pressure in the nerve (intraneural injection) Stretching (patient’s positioning, surgical method)
Vascular	Vasoconstriction (LAs, adjuvants) Ischaemia caused by constriction of nerve vessels (compression from the inside or outside, oedema, haematoma, tourniquets)
Inflammatory	Local anaesthetics Disinfectants Ultrasound gel Perinervous haematoma Surgical insult (postsurgical inflammatory neuropathy [PSIN])

### CHEMICAL INJURY — TOXICITY OF THE AGENT ADMINISTERED

Almost 40 years ago it was found that the basic tools of regional anaesthesia, i.e. local anaesthetics, exert cytotoxic effects on cell cultures, inhibiting cell growth and survival and that such effects intensify with prolonged exposure time and increasingly high LA concentrations [16, 17]. In clinical practice, the place of deposition of LAs is essential for increased toxic effects. As mentioned earlier, the perineurium with the endothelium of subperineural capillaries functions as a blood-nerve barrier limiting the entry of various substances into the nerve bundle. The administration of LAs outside the perineurium only slightly affects the efficiency of the blood-nerve barrier, although increases its permeability. In such cases, the fluid within the endoneurium changes from hypertonic to hypotonic due to the difference in osmolarity, which causes oedema and leads to an increase in intra-fascicular pressure [18]. Irrespective of oedema, high extrafascicular concentrations of LAs can damage axons [19]. Local administration of bupivacaine or lidocaine to the nerve reduces the blood flow in the nerve, which can contribute to its ischaemic injury (concentration-dependent) [20, 21].

Although the vasoconstrictive effect is unequivocal, it does not seem to play a relevant clinical role in the majority of patients [22]. An exception may be patients with baseline disorders of blood supply to the nerves, e.g. smokers and diabetic patients. Even a small amount of LA injected into the bundle causes significantly more serious sequels, such as demyelination and Wallerian degeneration of axons and this effect is concentration-dependent [23, 24]. LAs injure not only axons but also the Schwann cells and this effect is also exposure time- and concentration-dependent [25].

To date, the cause of LA neurotoxicity at the cellular level has not been explicitly determined. According to in vivo studies, LAs uncouple oxidative phosphorylation in the mitochondria and activate neurone apoptosis via the activation of p38 mitogen-activated protein kinase and caspases. Moreover, neurotoxicity is modulated by the phosphoinositide 3-kinase (P13k)/Akt pathway [26].

In order to improve the quality of blocks and lengthen them, various adjuvants are added to LAs, e.g. adrenaline, clonidine, buprenorphine, dexamethasone or dexmedetomidine. Adrenaline added to LAs as an agent lengthening the duration of a block and a marker of intravascular administration, enhances the vasoconstrictive effect and prolongs the contact of nervous structures with LAs [21, 27]. Moreover, adrenaline increases axon degeneration after the administration of bupivacaine into the bundle [28]. In in vitro studies, cytotoxicity of buprenorphine was observed during the 24-hour exposure of neurones to adjuvants (although lesser than that of ropivacaine alone). Clonidine was found less toxic while dexamethasone was the least toxic agent. After the 2-hour exposure of neurones to the mixture of adjuvants with ropivacaine, clonidine increased the toxicity of ropivacaine while dexamethasone and buprenorphine did not [29]. Dexmedetomidine can attenuate the bupivacaine-induced inflammatory reaction around the nerve [30]. Likewise, dexamethasone, added as an adjuvant to an LA, can reduce the toxicity of bupivacaine by increasing the activity of the Akt pathway [31].

## MECHANICAL INJURY

As the amount of connective tissue inside the nerve is large, its perforation with the needle usually does not disrupt the continuity of nerve fibres as the needle tip may be inside the nerve, namely under the epineurium, outside the fascicle or between the fascicles. If the needle tip is inserted into the fascicle, the continuity of perineurium and nerve fibres is directly disrupted. Both the thickness and type of the needle are of importance. The penetration of the nerve/fascicle with short-bevelled needles is much more difficult, as compared with pencil-pointed needles; whenever this happens, the injury is more extensive [32]. In animal models, the intraneural placement of the needle, even without

damaging the fascicles or vessels, induced an inflammatory reaction with resultant demyelination and transient impairment of the nerve function [33]. It seems, however, that an isolated needle injury does not lead to serious sequels unless accompanied by intrafascicular deposition of an LA when a high neurotoxic concentration is achieved. High intrafascicular pressure leads to mechanical disruption of nervous structures and the occlusion of blood vessels [34].

From the anaesthesiologist's point of view, it is essential that some surgical procedures *per se* are associated with a significant percentage of neurological complications which can be attributed to regional anaesthesia. A representative example is brachial surgery in which the majority of complications is caused by physical injury, e.g. by instruments or excessive traction-pulling of the limb when the head and neck being bent to the side opposite to that being operated on, stretches the brachial plexus. In such cases, the percentage of neurological complications, mainly short-lasting, is very high and in arthroscopic procedures reaches even 10% [35]. The incidence of neurological complications following total hip arthroplasty is about 1%. These complications most commonly affect the common peroneal nerve, less commonly femoral and sciatic nerves [35]. Transient injuries to the lateral femoral cutaneous nerve are extremely common (up to 88%) while performing the procedure from the anterior access [36]. The percentage of neurological complications following total knee arthroplasty ranges from 0.3% to 9.5% [35]. The more severe the preoperative knee deformity (e.g. valgity), the higher the risk of common peroneal nerve injury. Commonly performed knee arthroscopies are associated with a high percentage (up to 25%) of transient dysaesthesia within the anterior knee. In cases of anterior cruciate ligament reconstruction, this percentage can reach even 75% [37, 38].

## VASCULAR INJURY — ISCHAEMIA

As mentioned earlier, LAs and adjuvants can directly constrict blood vessels. However, it seems that impaired blood supply to the nerve, caused by the injury to the vasa nervorum or nerve compression (e.g. by a haematoma caused by anaesthetic or surgical intervention) and leading to vasoconstriction, is more important clinically. The nerve structures within the fascial compartments of low resilience are at the highest risk. For instance, under unfavourable conditions, the vessel injection during brachial plexus block from the axillary access can lead to the development of medial brachial fascial compartment syndrome, which can cause severe neurological complications [39]. Another common cause of ischaemia of nervous structures is the use of tourniquets. Acute ischaemia causes depolarisation and generates spontaneous nerve discharges, which are felt by patients as paresthesias. Prolonged ischaemia blocks

slow-conducting fibres, or even all fibres [40]. If ischaemia lasts less than 2 hours, the nerve functions are restored within 6 hours. Reperfusion causes oedema and degenerative changes in axons followed by a phase of regeneration which lasts several weeks. Ischaemia up to 6 hours does not cause permanent structural lesions [41].

### INFLAMMATORY INJURIES

Kaufman *et al.* [42] described a series of 14 cases of persistent diaphragmatic paralysis following interscalene brachial plexus blockade. The cause of phrenic nerve neuropathy detected during surgical revision was nerve entrapment in the scar tissue resulting from chronic inflammatory lesions. Inflammatory lesions can also be caused by haematomas around the nerve or the ultrasound gel applied close to it [44, 45]. The stress factor, i.e. surgical intervention, can trigger an inflammatory response involving the peripheral nerves (PSIN), as well as other structures. The symptoms of this inflammatory neuropathy can be uni- or multifocal and are accompanied by muscle weakness and muscle pain [46].

### RISK FACTORS OF PERIOPERATIVE NERVE INJURY

Although perioperative peripheral nerve injuries can result from regional anaesthesia, recent studies have paradoxically failed to demonstrate that peripheral nerve blocks are an independent risk factor of such injuries [4]. In the cohort retrospective studies conducted at the Mayo Clinic, the incidence of neurological complications following orthopaedic procedures was assessed. The incidence of peripheral nerve injuries associated with hip, knee and shoulder arthroplasty was found to be 0.72%, 0.79% and 2.2%, respectively. The risk factors of nerve injuries in hip arthroplasty included younger age and the duration of tourniquet use. Peripheral nerve anaesthetics did not increase the total incidence of postoperative neuropathies [46, 47]. Nevertheless, one should be aware that the orthopaedic literature tends to attribute a higher percentage of complications to nerve blocks than the anaesthesiological literature [48, 49].

The symptomatic or subclinical nerve dysfunctions (neuropathies) present prior to anaesthesia are likely to increase the risk of perioperative deterioration of nerve function (the hypothesis of "double crush injury"). The other risk factors include peripheral nerve diseases, vasculitis, tobacco smoking, and arterial hypertension [4].

Diabetic peripheral polyneuropathy is a common complication of diabetes mellitus and the most commonly diagnosed peripheral neuropathy. Neuraxial anaesthesia in diabetic patients is associated with a significantly higher risk of neurological deficits, as compared with the general population (0.4%). In this group of patients, the motor stimulation threshold can be markedly higher than in healthy

patients, which can increase the risk of intraneural insertion of the needle [50]. Moreover, diabetic patients have been demonstrated to have higher success rates of blocks, as well as longer and metabolic compensation-dependent duration of blocks [52–54].

Among the other causes of neuropathy that should be considered are alcoholism (which can be associated with vitamin deficiencies), chemotherapy and congenital factors (Charcot-Marie-Tooth neuropathies, and hereditary neuropathy with pressure palsies [HNPP], in particular) [55].

### SAFETY OF NERVE LOCATION METHODS

#### NERVE STIMULATION

Relatively recently, needle-nerve contact causing parasthesias was considered indispensable to provide the block. However, it appears that the lack of parasthesias does not exclude intraneural location of the needle tip [56–58]. Nerve injuries can occur even when the injection is immediately discontinued once parasthesias and pain have been reported by the patient [5]. On the other hand, some discomfort can be a natural and harmless symptom while performing the block and there are no explicit data confirming that the induction of parasthesias is an independent factor of postoperative neurological disorders. The symptoms reported by patients are insufficient to prevent nerve injuries.

A huge step forward in the techniques of nerve location was the introduction of nerve stimulators to everyday practice. A current intensity of 0.2 mA, causing a motor response, is most likely associated with intraneural location of the needle. Finding the minimal current intensity, which locates the nerve with high sensitivity and specificity without its puncture, is a much more important issue. In cases of supraclavicular blocks, the use of typical stimulation thresholds of 0.2–0.5 mA may be connected with a high percentage (54%) of intraneural needle tip location; in popliteal blocks — even 94% of cases. The disappearance of motor responses at > 0.5 mA is also associated with intraneural location of the needle tip; in supraclavicular blocks in 10% of cases and even in 90% (!) of cases in popliteal sciatic blocks [59–63]. The lack of motor response to markedly higher current intensities (1.5 mA) does not exclude intraneural location of the needle tip [61]. The lack of motor response to an intensity of 2.4 mA was observed in many diabetic patients, despite explicit, ultrasound-confirmed needle-nerve contact [50]. There is a high individual variability in the threshold current intensity required to induce a motor response, while such extremely high intensities of the stimulation current, although more commonly observed in diabetic patients, with diabetic neuropathy, in particular, have also been found in healthy individuals [64].

Important data determining the dependence of stimulation current intensity on needle-nerve contact may be found in the study carried out by Vassiliou *et al.* [65]. In the swine model, the risk of needle-nerve contact at 0.5 mA was found to be 0.5, while at 0.9 and 1.1 mA — 0.13 and 0.1, respectively.

Newer nerve stimulators have an additional option, namely enabling bioimpedance measurements for the flowing current. The nerve is composed of a higher number of lipid elements and lower amounts of water compared to the surrounding tissue; therefore, if the needle tip has penetrated the nerve, the stimulator shows a significant increase in resistance [66].

### ULTRASONOGRAPHY

As the epineurium is composed of relatively compact connective tissue, after contact with the needle, the nerve is initially moved away. Prior to the nerve puncture by a needle, an “indentation” can be observed on the nerve surface [67]. After forcing the superficial epineurium, the needle tip will be more likely to penetrate looser connective tissue between the fascicles than in the fascicles themselves.

Sonographic signs of intraneural administration are an increased transverse cross-sectional area with decreased echogenicity of the nerve. Another later finding is the “halo” sign, namely a concentric, hypoechogenic area around the nerve visible proximally and distally in relation to the site of injection visualising subepineural spread of anaesthetics [68, 70]. In some cases, the “halo” sign evidences the LA spread in the paraneural sheath. In a study regarding the sciatic nerve sheath, Andersen *et al.* [12] performed intraneural injections and observed an increase in the cross-sectional area of the nerve followed by gradual “permeation” of the injected fluid, which caused the separation of the sheath from the epineurium. An increase of 9% in the cross-sectional area together with decreased echogenicity after the administration of 0.5 mL of volume enables highly sensitive detection of intraneural administration. Unfortunately, in practice even experts are not able to detect 1/6 of intraneural administrations, and less experienced individuals not even 1/3 of such cases [68, 70]. The difficulties in early detection of intraneural administration using ultrasound result both from equipment-associated limitations and insufficient experience. The incidence of unintended intraneural administrations during ultrasound-guided brachial plexus blocks (interscalene and supraclavicular) performed by experienced physicians is up to 17% [71]. Similar incidences (16.3%) were found for sciatic nerve blocks from the subgluteal approach [72].

Many studies have revealed that intraneural injection of LAs during brachial plexus or sciatic nerve blocks does not lead to remote neurological sequels, although it produces explicit ultrasound signs [59–61, 68–70]. Based on the above

studies, it may be concluded that intraneural injections to the external part of the epineurium but extrafascicularly, both intended and unintended, are relatively safe. Unfortunately, the studies mentioned were performed in small groups of patients (up to several dozen), which is undeniably insufficient to conclude that this management strategy is harmless. Additionally, although modern ultrasound devices generate images of increasingly high quality, in practice, it is still impossible to differentiate extra- and intrafascicular locations of the needle tip. The linear resolution of the 10 MHz transducer is about 1 mm, while in the case of deeper blocks it is necessary to use lower frequencies, which translates into even lower resolution. Only in cases of superficially running nerves (e.g. in forearm blocks) and the use of transducers of high resolution (e.g. 18 MHz), is the quality of nerve structure images good.

Given the current state of knowledge, it seems that it is better to move the needle tip slightly further away from the nervous structures, even at the expense of worse quality and shortened duration of blocks. Such a management option is suggested in those studies comparing the efficacy of interscalene brachial plexus blocks depending on the site of LA deposition, namely intraplexus or periplexus. In one of the above studies, no differences in block onset time and block quality were demonstrated; however, a significant prolongation of the blockade was observed after intraplexus administration. Another study disclosed quicker blocks albeit also higher incidences of transient parasthesias after intraplexus LA administration [73, 74].

Although the use of ultrasound accelerates and facilitates the provision of blocks, reduces the risk of vessel puncture and enables the administration of lower amounts of LAs, it does not reduce the risk of neurological complications [2, 68, 75].

### MONITORING OF INJECTION PRESSURE

To differentiate intra- and extrafascicular administration, the assessment of pressure with which LA is applied may be useful. Animal studies carried out several years ago suggested that the high pressure of an injection (> 25psi) was likely to indicate intrafascicular administration due to low compliance of the fascicle [78]. What then should be the injection pressure? Autopsy studies have demonstrated various patterns of increases in pressure and peak pressures depending on the injection site, namely: to the nerve root; to the peripheral nerve; and perineuronally. Administration to the nerve root was associated with a peak pressure of 60.2 psi, intrafascicular administration to the peripheral nerve with 52.9 psi, and extrafascicular administration with 22.4 psi. Moreover, the authors pointed out that the peak pressure was achieved after more than several seconds, i.e. once a certain volume of the anaesthetic had been deposited [77].

From the clinical point of view, it is more useful to determine the pressure in the syringe-catheter-needle system, at which the injection can be started, called “the opening pressure”. In cases of interscalene brachial plexus anaesthetics, direct needle-nerve contact is connected with an opening pressure exceeding 15 psi. The withdrawal of the needle tip by 1 mm significantly reduces the opening pressure [56]. Likewise, in femoral nerve blocks whenever the needle tip touches the nerve or iliac fascia, it is not possible to start the injection with an opening pressure lower than 15 psi in the majority of cases [78]. Recent autopsy studies confirm that the opening pressure in femoral, femoro-crural, sciatic, common peroneal and tibial nerve blocks is several times higher when the needle tip is placed inside the fascicle, as compared with perineurial insertion and always exceeds 15 psi; at the rate of administration of  $10 \text{ ml min}^{-1}$ , this pressure is achieved after 10–12 seconds [79].

It is extremely difficult to “feel” the opening pressure. In one study, the pressure with which anaesthesiologists injected LAs was measured: 70% of them started the injection at a pressure of > 20 psi; 50% at > 25 psi; and 10% at > 30 psi [80].

Two devices that help to reduce the risk of LA injection at too high a pressure are available on the market. One of these is a sensor which warns one against excessive pressure using colours while the other is a pressure limiter, which prevents LA administration at a pressure higher than 15 psi.

According to the above-mentioned studies, if the motor response subsides at a current intensity higher than 1 mA, the needle tip on the US image, as assessed by the observer, is outside the nerve and the pressure during LA administration does not exceed 15 psi, then it is highly likely that the needle tip is not actually in contact with the nerve (triple guidance). In this “trinity”, stimulation is probably of least importance while pressure monitoring is crucial.

Producers of ultrasound devices and needles for regional blocks are constantly developing new technologies which can improve safety. The visualisation of the needle along its entire course, especially when advanced under a high angle towards the front of the transducer can be extremely problematic. Therefore, the majority of producers of regional anaesthesia sets offer needles with technology improving their visibility in the ultrasound beam. The use of highly efficient piezoelectric monocrystals in some ultrasound transducers provides higher resolution and deeper penetration, hence better images of nervous structures. Some ultrasonographs are equipped with software automatically improving needle visibility. Some other devices use the needle-induced electromagnetic field changes for virtual 3D tracking, even if the needle is outside the ultrasound beam. The above solution can be extremely useful in deep blocks, especially in an out-of-plane approach.

## SYMPTOMS OF NERVE INJURY

The onset of neuropathic symptoms following the injuring stimulus may be acute (hours, days) or delayed (weeks). Acute onset is associated with direct nerve injury, and delayed onset with oedema and inflammation. Nerve injury symptoms are likely to include abnormal sensations (hypoesthesia, parasthesias, pain, allodynia, hyperesthesia), muscle weakness, disorders of the autonomic system. These may occur in various configurations and affect one's quality of life depending on their severity, location or the patient's age. It is difficult to determine the cause of injury based only on symptoms. Small nervous fibres are more susceptible to chemical injuries; therefore, the most common symptoms of their injury are parasthesias and abnormal pain and temperature sensations rather than disorders of deep sensations and of movement. As neuropathy caused by surgical tourniquets concerns mainly thick myelinated fibres, its symptoms include motor, touch, vibration and position disorders with heat, cold and pain sensations preserved and without parasthesias. When the tourniquet is placed on the arm, the symptoms of neuropathy mainly concern the radial nerve and not the medial/ulnar nerve, as opposed to neuropathies following the axillary block where the symptoms mainly concern the medial nerve (exclusively or together with the ulnar nerve [28, 38].

## DIAGNOSTIC MANAGEMENT

In order to effectively implement diagnostic-therapeutic management, it is essential that a nerve injury is suspected as early as possible. This is extremely difficult if anaesthesiologist-patient contact ends in the recovery room. In many cases, the anaesthesiologist is informed about the most severe complications detected in surgical wards with delay; less severe complications (parasthesias subsiding within several days or weeks) may not be even reported to the surgeon, not to mention the anaesthesiologist. The simplest screening method for nerve injuries (used in our centre) is the anaesthetic visit during which the basic examination, including the neurological evaluation, is carried out after the anticipated duration of anaesthesia. In the early post-operative period, such an assessment may be hindered due to residual sedation, limb immobilisation or the presence of a catheter; however, this approach can accelerate the decision to eliminate any potentially reversible causes of disorders (e.g. removal of a haematoma compressing the nerve) and facilitates further contact with patients with suspected injuries. Moreover, the post-anaesthesia visit is the right time to discuss possible causes of injuries, diagnostic procedures, prognosis, and referral to appropriate outpatient clinics. Moreover, conducting an assessment after anaesthesia is important as a high proportion of patients cannot precisely determine the onset of symptoms; even when they develop

symptoms with a week's delay, after some time they can interpret them as lasting from the procedure. If a haematoma compressing the nerve is suspected or there is a risk that the cause of nerve injury is surgical, it is worth talking to the surgeon to determine whether the nerve could have been injured (cuts, stretching, suture entrapment) or whether fascial compartment syndrome should be considered and find out if revision is possible. In each case in which the motor component of the block persists, the block intensifies or returns after earlier subsidence, neurological consultation is required. Early diagnostic imaging procedures involve basic ultrasound examinations, e.g. to exclude the haematoma. Theoretically, more advanced examinations can also be performed, e.g. MRI, enabling the assessment of morphological changes of the nerve — prolonged T2 relaxation and enhanced signals in the STIR sequence may be observed earlier than the changes typical of denervation. Moreover, for instance, a haematoma compressing the nerve can be visualised [81].

However, neurophysiological examinations are far more important for the diagnosis of nerve injuries. The electrophysiological tests applied most commonly are a nerve conduction study (NCS) and electromyography (EMG). Nerve conduction tests are performed by stimulating the nerve in two separate locations along its course with the receiving electrode placed over the muscle supplied by this nerve, or along the course of the sensory nerve. They measure the following: amplitude reflecting the number of depolarised fibres; latency, i.e. the time between a stimulus and the appearance of a response — compound motor action potential (CMAP) or sensory nerve action potential (SNAP); and conduction velocity — the speed with which the stimulus spreads along the thickest myelinated axons. Based on the analysis of such tests, one can assess whether the nerve has been injured, and if so, determine the level of injury. Moreover, the test results should demonstrate whether this is a case of demyelination (neurapraxia) or the loss of axons (axonotmesis). Then, based on baseline values, the regeneration can be monitored.

The loss of myelin (demyelinating neuropathies) decreases the conduction velocity and lengthens the latency while the CMAP amplitudes remain normal, or are only slightly reduced. In neuropathies with a reduced number of axons (axonal), CMAP and SNAP amplitudes are decreased at normal latency and conduction velocity. In cases of nerves with impaired conduction caused by segmental demyelination, the amplitude of CMAP evoked above the focus is markedly reduced, as compared with stimulation below the focus. The response to normal stimulation induces the orthodromic response. Supraliminal stimulation additionally induces antidromic impulse conduction, which depolarises the cells of the anterior horns of the spinal cord and delays

the response in muscle cells (F wave). Prolonged F waves are typical of demyelinating injuries while their absence evidences an axonal or severe demyelinating injury. The examinations of sensory nerve conduction, particularly of fine cutaneous branches in patients with abundant subcutaneous tissue, are much more difficult to perform due to lower amplitudes of evoked potentials.

The axonal parts distal to the injury site remain excitable for many days after injury. CMAP and SNAP amplitudes do not decrease for 2-3 days. Moreover, CMAP amplitudes do not achieve their lowest point until 9 days after the insult, and SNAP amplitudes — until 10-11 days post-injury [82].

During this time, stimulation distal to the site of injury may not disclose the evident pathology while stimulation proximal to the site of injury will not allow differentiating demyelination and the loss of axons. Therefore, it is more reasonable to perform nerve conduction examinations after 10-14 days following the occurrence of damage and not earlier.

EMG assesses only the motor functions of nerves. A needle electrode inserted directly in the muscle can record spontaneous potentials in the denervated muscle, namely fasciculations and sharp waves. Moreover, motor unit potentials (MUPs) are assessed, i.e. the sum of potentials of all muscle fibres innervated by one stimulated nerve. In cases of neurapraxia, EMG does not show significant changes, except for reduced MUP recruitment. Up to 21 days after major nerve injuries, electromyographic changes resemble those mentioned above, although between days 14 and 21, the spontaneous muscle activity begins in the form of fasciculations and sharp waves mentioned earlier. In cases of completely cut nerves, MUPs are not recorded.

Although in cooperation with the neurologist, electrophysiological tests may be performed immediately after the insult, such tests are rather to determine the pre-existing pathology. In most cases, the first tests are performed 3 weeks after injury, follow-ups after 3-6 months and 12 months, if required. [83].

## STRATEGIES REDUCING THE RISK OF NERVE INJURY

Prior to surgery:

1. Practicing and continuously improving one's skills.
2. Screening for patients with neuropathies. If a regional block has been decided upon, adrenaline (as an adjuvant) should be avoided and a reduction in LA concentration should be considered.
3. Providing the patient with detailed information about possible complications of the suggested procedure, as well as alternative techniques, and obtaining patient's informed consent. Unfortunately, even in the United States, anaesthesiologists eagerly inform patients about the advantages of regional anaesthesia



and usually mention only mild complications (transient parasthesias, haematomas) while the potentially life-threatening complications, such as toxicity of local anaesthetics or neuropathies leading to disability, are often passed over [84].

In the operating suite:

1. Combine the location methods (ultrasound, injection pressure monitoring, and stimulation — triple guidance).
2. Do not use a current intensity of < 0.5 mA for nerve stimulation.
3. Use needles clearly visible in the ultrasound beam
4. In each case in which the patient reports severe pain radiating along the limb during needle manipulations or the administration of LA, the administration of LA should be immediately discontinued and the needle withdrawn.
5. Choose co-anaesthetics individually, bearing in mind that perineural administration of dexamethasone is off-label and adrenaline is contraindicated in diabetic patients.
6. Careful positioning of the patient on the operating table, namely the arm abducted to 90 degrees in the reverse position, the places of compression protected; the elbow bent to < 90 degrees; lateral decubitus with the hip flexed to < 120 degrees.
7. Attentive monitoring and recording of the time of tourniquet use and the pressure within it.

## SUMMARY

Huge advances in regional anaesthesia have been observed in recent years. “Old” techniques are being improved and new ones designed; better ultrasound devices and anaesthesia sets are available. Nevertheless, the incidence of complications has not changed. It can even be cautiously assumed that the number of patients with complications is likely to increase as regional anaesthesia methods are becoming increasingly popular. The paper summarises the present state of knowledge about nerve injuries and the strategies concerning their prevention and management.

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