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Minimising complications and improving the success of peripheral regional blockade

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Abstract

Peripheral regional blockade is a type of regional anaesthesia involving depositing local anaesthetics around a specific nerve or bundle of nerves that help transmit nociceptive signals to higher centres, such as the thalamus and somatosensory cortex. It is not only a widely used technique that provides surgical anaesthesia, but also acts as an essential part of the armamentarium against postoperative pain and pain following major skeletal trauma. This article discusses the structure and function of peripheral nerves, the classification and pathophysiology of peripheral nerve injury and, finally, how practising anaesthetists are committed to maximising success and minimising harm when performing peripheral nerve blockade in the operating theatre.

Key words: Intraneuronal injection; Nerve block; Peripheral nerve injury; Regional anaesthesia

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Introduction

Safe and effective regional anaesthesia is a high-level learning outcome in the Royal College of Anaesthetists' (2021) curriculum. It is increasingly relevant to both training and practising intensivists, as the popularity of continuous peripheral nerve blocks in addressing pain in post-surgical patients and in patients following major skeletal trauma is on the rise.

This review begins by exploring the structure and function of peripheral nerves and their relevance in regional anaesthesia. Following that, the basic principles behind the knobology (the technique to manipulate ultrasound knobs and system controls to optimise the quality of the image) of ultrasound, the pathophysiology and classifications of nerve injury are discussed, along with what anaesthetists could do to maximise success and safety when performing peripheral regional blockade in the operating theatre.

Structure and function of peripheral nerves

Peripheral nerves comprise a mixture of myelinated and unmyelinated axons. Myelinated axons are encased by Schwann cells, which act as protective sheaths surrounding individual axons, decreasing the capacitance of the axonal membrane and allowing saltatory conduction to occur. The conduction velocity of peripheral nerves varies from 0.5–10 m/s in unmyelinated fibres to up to 150 m/s in myelinated fibres (Purves et al, 2001).

There are three layers of connective tissues that support the intricate structure of peripheral nerves (Reina et al, 2022):

1. Endoneurium: the innermost layer that surrounds each axon. It consists of collagen, fibroblast, capillaries, mast cells and macrophages
2. Perineurium: the dense middle layer that protects nerve fascicles (ie clusters of endoneurial tubes) from toxins and infections. Although this is made of fibroblast, the pressure exerted onto the perineurium may have an impact on the endoneurium and, thereby, the integrity of the individual axons
3. Epineurium: The outermost layer consists of dense and irregular collagenous tissue surrounding multiple nerve fascicles that comprise the peripheral nerve trunk. It has a thickness of between 1 and 100 micrometres. It is a permeable structure that consists of fibroblasts, adipocytes, mast cells, lymphatics, blood vessels and nerve fibres that innervate the vessels.

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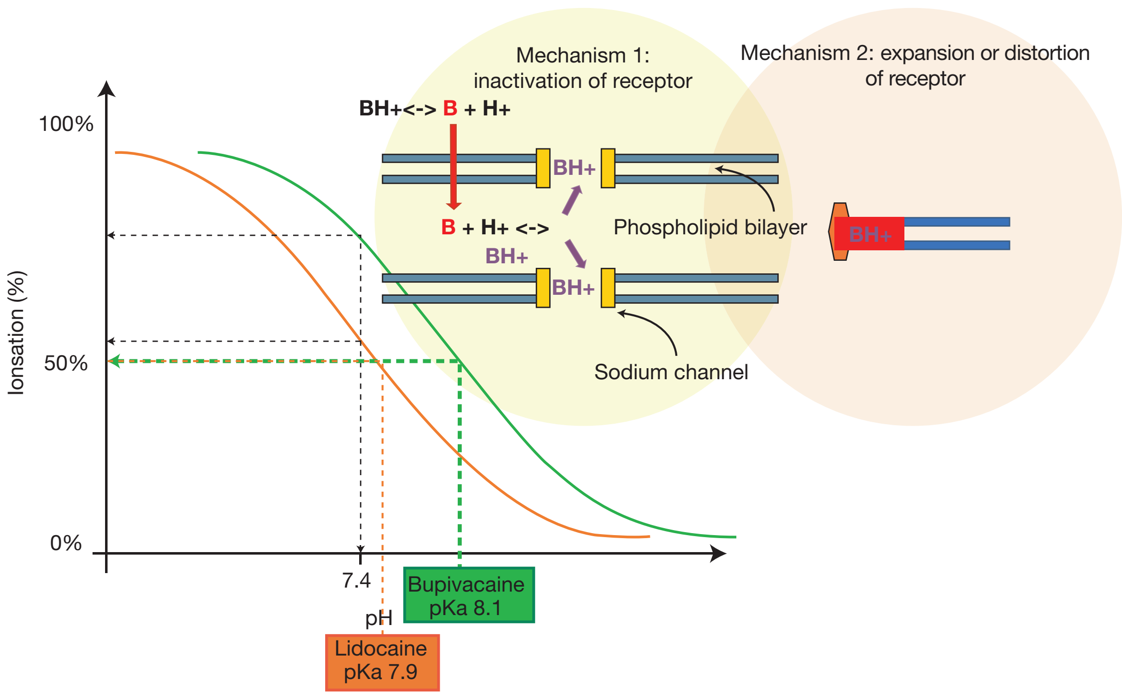

Figure 1. pH, pKA and cellular mechanisms of local anaesthetics. B = un-ionised local anaesthetic; BH+ = ionised local anaesthetic.

Relevance in regional anaesthesia

Success in regional anaesthesia could be regarded as 'putting the right dose of the right drug in the right place' (Rajendram et al, 2011). It involves infiltrating local anaesthetics around and as close to the target nerves as possible (eg interscalene, supraclavicular, femoral or sciatic), or along fascial planes, where local anaesthetics is diffused to the nerve terminals that travel within the plane or adjacent tissues (eg spinal nerves in erector spinae plane blocks).

Right drug

Most local anaesthetics are weak bases. Their corresponding pKa will determine their readiness to dissociate and the proportion of ionised/unionised local anaesthetic present once the drug enters body tissues. The unionised drug crosses the phospholipid bilayer and penetrates the neuronal membrane. Once within the axoplasm, the local anaesthetic becomes ionised and reversibly blocks the transmission of actional potential by disturbing the voltage-gated sodium channels, rendering them inactive to prevent further depolarisation. The other mechanism involves temporary distortion of (also known as 'choking') voltage-gated sodium channels by pre-occupying local anaesthetics within the neuronal cell membrane; the theory is not often discussed and is beyond the scope of this review.

The pharmacokinetic behaviours of local anaesthetics can be categorised by the presence of ester or amide between the lipophilic aromatic and hydrophilic amine groups of the drug. Ester local anaesthetics are (often) minimally protein-bound and tend to be rapidly hydrolysed by plasma esterases. Amide local anaesthetics, in contrast, are moderately to extensively protein-bound (eg lidocaine: 60–80%, bupivacaine and ropivacaine: >90%). They are slowly broken down by liver amidases and would be more favourable to satisfy the length of anaesthesia required for most procedures. Other local anaesthetics should be used for Bier's block in preference to bupivacaine (Kraus et al, 2022), as it displays a much higher affinity to cardiac sodium channels and is cardiotoxic. Inadvertent intravascular injection of bupivacaine at a dose of over 2 mg/kg could result in cardiac arrest.

Right dose

Local anaesthetic injected outside the epineurium must travel through the epineurium, perineurium, endoneurium, myelin sheath (if present) and axoplasm to exert its effect.

Table 1. Characteristics of local anaesthetics and ways to improve success with peripheral nerve blocks

Characteristics of local anaesthetic	Determined by	Improved by
Speed of onset	pH and pKa	↑ Unionised drug to axoplasm
	Lipid solubility	↑ Lipid solubility
	Molecular weight	↓ Molecular weight, permeability α1/√molecular weight
	Concentration gradient	↑ Number of active components
		↑ Concentration (eg 4% over 1%)
	Vascularity of tissue	↓ Vascularity ↓ Systemic absorption
Potency	Lipid solubility	↑ Lipid solubility
Duration of action	Protein binding	↑ Protein binding (eg bupivacaine, lidocaine)
	Metabolism	↓ Metabolism, longer local anaesthetic availability
	Vascularity of tissue	↓ Vascularity ↓ Systemic absorption

Table 2. Potential harm relating to the use of perineural adjuncts

Agent	Potential harm
Steroid (eg, dexamethasone)	Poor postoperative blood glucose control
	Delayed wound healing
	Wound infection
	Neurotoxicity
Alpha-2 agonists (eg, clonidine and dexmedetomidine)	Bradycardia
	Hypotension
	Sedation
Adrenaline	Compromise perfusion to peripheral nerves
Buprenorphine	Pruritis
	Postoperative nausea and vomiting
Magnesium	Neurotoxicity

The onset, potency and duration of action of local anaesthetics are dependent on multiple factors, as summarised in Table 1.

Aside from the above considerations of drug and dose, the quality (defined here as prolonging analgesia without lengthening motor block) of regional anaesthesia can be improved by using steroids, alpha-2 agonists (clonidine or dexmedetomidine), adrenaline, buprenorphine and magnesium as adjuncts to supplement the effect of local anaesthetics.

Despite encouraging results from clinical trials, using these agents as perineural adjuncts is not without risk (Table 2); neither has received approval from medicine regulation agencies, such as the Food and Drug Administration and the Medicine and Healthcare product Regulatory Agency.

Right place

To limit wastage and ensure effective transfer of local anaesthetics through the nerve sheaths, connective tissues and the axonal sodium channels, local anaesthetics must be deposited as

Table 3. Benefits of using ultrasound for nerve localisation and peripheral nerve blocks
Allows visualisation of needle path and tip
Allows refinement and precise placement of block needle in between fascia planes
Allows placement of block needle as close and as safely to the target nerves as possible
Allows visualisation of target nerves and surrounding structures (eg, blood vessels and pleura)
Allows real-time and continuous visualization of the spread of local anaesthetics around the structure of interest
Allows differentiation of intravascular and extravascular injections and, if resolution allows, of intraneural and extraneural injection
Allows lean regional anaesthesia (ie to achieve the same effect with less local anaesthetic, to enhance patient safety)

close and safely as possible to the nerves that supply nociception to the area that requires surgery. The injection of local anaesthetics, either sub-epineural or sub-perineurally, which is also known as an intraneural injection, is detrimental.

Evolution of nerve localisation techniques

Traditionally, regional anaesthesia was heavily reliant on surface anatomy-based techniques. These techniques (eg palpation of landmarks, feeling for fascia clicks, eliciting paraesthesia and transarterial injections) are not necessarily the safest in non-expert hands, so are being gradually replaced by ultrasound-guided techniques in modern medical training. The benefits of using ultrasound in peripheral nerve block are listed in Table 3.

Fundamentals in image optimisation using ultrasound

Spatial resolution refers to the ability of an imaging system to distinguish between two structures that are close to each other. In two-dimensional ultrasound, spatial resolution is dependent on axial and lateral resolutions (Ng and Justiaan, 2011).

Axial resolution

Axial resolution refers to the minimum distance required for the ultrasound to differentiate two reflecting objects positioned parallel to the beam. Mathematically, this is represented by half of the spatial pulse length, which is the product of the wavelength and the number of cycles within an ultrasound pulse. Axial resolution is high when the spatial pulse length is short.

Lateral resolution

Lateral resolution refers to the minimum distance required to distinguish two side-by-side reflectors positioned perpendicularly to the direction of the ultrasound beam. Lateral resolution correlates well with the frequency of ultrasound beams, but is poor when neighbouring structures are located within the same beam width. This could be optimised by placing the structures of interest at a point where the width of ultrasound beams is the narrowest, and ideally no more than two focal zones away (Figure 2), as this may compromise the ability of ultrasound to capture instantaneous events of evolving structures, such as the displacement of nerves and vasculatures following the injection of local anaesthetics.

A high-frequency probe (eg 10–13 MHz) will give the operator the best axial resolution and lateral resolution to perform superficial blocks (eg brachial plexus). Where deeper nerves are to be anaesthetised (eg gluteal sciatic or popliteal), the frequency of the probe would have to be sacrificed in exchange for better penetration of structures below the skin. When a lower frequency probe (eg 2–10 MHz) is needed, operators must recall the PART mnemonic (pressure, alignment, rotation and tilting) when trying to achieve image optimisation (Orebaugh and Kirkham, 2022):

- Pressure: compressing the subcutaneous tissue may bring the target nerves closer to the skin, thereby reducing the penetration and depth required for image acquisition

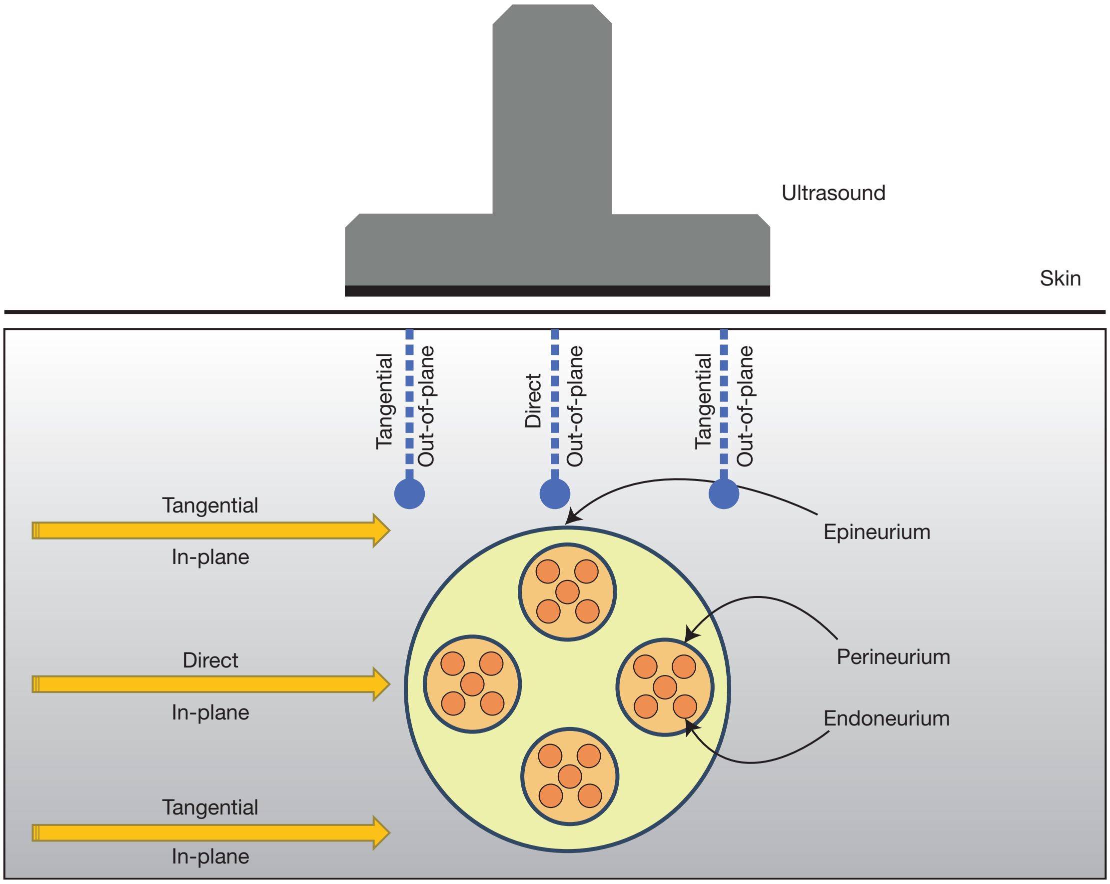

Figure 2. Needling approach to reduce the harm of intraneural injection.

- Alignment: focusing the target nerves in the centre of the screen may improve axial and/or lateral resolution and allow vital structures (eg the subclavian artery in supraclavicular blocks) to be visualised
- Rotation and tilting: fine-tuning manoeuvres to maximise the number of returning echoes by bringing the face of the ultrasound probe into a better perpendicular arrangement with the target structures and block needle.

Classification of peripheral nerve injury

The definition of nerve injuries varies with different classifications, but, as a general rule, they should be suspected when the following complaint(s) arise:

- New onset of pain, weakness (see Table 4 for the nerve roots and function of myotomes), paraesthesia or any other abnormal sensation
- Effects of block lasting beyond the usual duration of the specific block (for example exceeding 48 hours).

These injuries could be transient or permanent. Following an extensive review of the literature, the Royal College of Anaesthetists estimated that transient nerve injury from peripheral nerve block could happen in fewer than 1 in 10 nerve blocks, with full recovery expected between 4–6 weeks in 92–97% of the affected individuals. It was stated that permanent nerve injury is believed to be rare, but may occur between 1 in 2000 and 1 in 5000 cases (Royal College of Anaesthetists, 2017). The British Orthopaedic Association and RA-UK have jointly published a protocol for the initial management of unexpected or persistent neurological dysfunction following peripheral nerve block (Sebastian et al, 2022). The protocol is accessible via the RA-UK and the British Orthopaedic Association's websites.

The two commonly used classifications of peripheral nerve injuries are the Seddon (neuropraxia, axonotmesis, neurotmesis) and Sunderland (grade 1–5) classifications. The ascending order of severity is based on pathophysiological mechanisms, ranging from local myelin sheath injury to incomplete axonal injury (interruption of axoplasmic flow

Table 4. Myotomes: their nerve roots and function		
	Myotome	**Responsible nerves**
Shoulder abduction	C5	Complex movement, innervated by a mixture of nerves that part originated from C5, including supraspinous, axillary and long thoracic nerves; also innervated by the accessory nerve which is originated from cranial nerve XI
Elbow flexion	C5–7	Musculocutaneous nerve
Elbow extension	C7–8	Radial nerve
Wrist extension	C7	Radial nerve
Grip (finger flexion)	C8–T1	Median and ulnar nerves
Finger extension	C7	Radial nerve
Finger abduction	T1	Ulnar nerve
Thumb abduction	T1	Median nerve
Hip flexion	L1–3	Femoral nerve
Hip extension	L5–S2	Inferior gluteal nerve
Knee extension	L3–4	Femoral nerve
Knee flexion	L5–S1	Sciatic nerve
Ankle dorsiflexion	L4–5	Common peroneal nerve
Ankle plantarflexion	S1–2	Tibial nerve
Ankle eversion	L5–S1	Common peroneal nerve
Ankle inversion	L4–5	Tibial nerve
Big toe extension	L4–5	Common peroneal nerve

> endoneurial injury > perineural injury), the complete loss of continuity of axon and axoplasmic disruption of the entire nerve trunk.

Pathophysiology of nerve injury and ways to improve safety when performing peripheral nerve blocks

Numerous factors could predispose peripheral nerve injuries. The following safety considerations are important when performing peripheral nerve block.

Mechanical injury

Forceful needle-to-nerve contact and intraneural injection may cause partial to complete lacerations to the peripheral nerves. Using smaller echogenic needles will likely reduce the risk of mechanical injury. The safety margin will only improve if a tangential (Figure 3), rather than direct, approach is used to anaesthetise the peripheral nerve (Sermeus et al, 2017). The selection of needle-tip is also essential. Short-bevelled and blunt or non-cutting needles may have the advantages of providing better tactile feedback, as they are 'popping' through the fascia and reducing mechanical injury by accidental penetration of the nerve, as opposed to than long-bevelled needles. However, it is imperative to recall that the damage caused by short-bevelled needles is more significant than by long-bevelled needles. The increased force needed to penetrate the fascia using blunt needles may cause overshooting and inadvertent damage to the peripheral nerve.

Pressure injury

Sustained or continuous high intraneural pressure could lead to peripheral nerve ischaemia. The risk is even higher in the context of pre-existing hypoperfusion, hypoxia and acidosis.

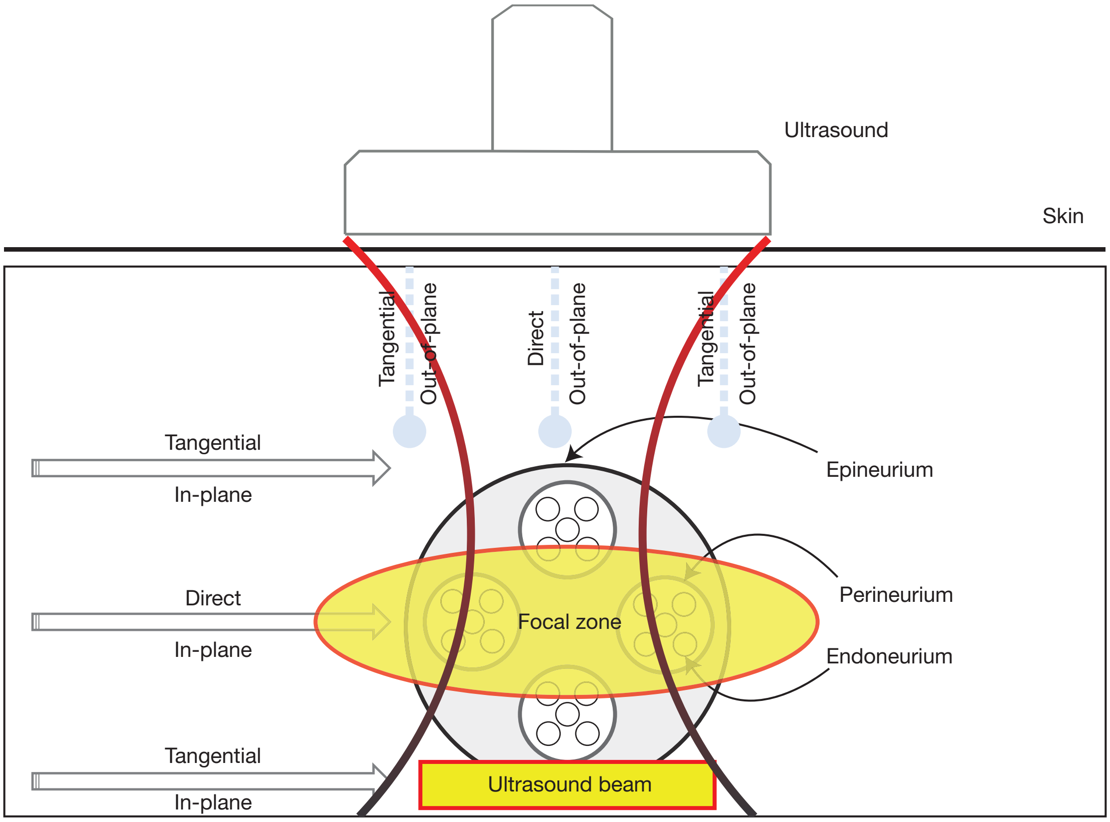

Figure 3. Ultrasound optimisation to ensure the best spatial resolution.

Comments of feeling ‘hard to inject’ by the assistant are subjective. However, an immediate re-evaluation of the needle-tip position should be undertaken, as this may suggest needle-to-bone, -tendon or -nerve contact or intraneural or intra-fascicular injection. Using an inline injection manometer gives an objective, easy-to-use visual aid to reduce pressure-related injuries during peripheral nerve block. An (opening) injection pressure of over 15 psi (pounds per square inch) may indicate the undesirable spread of local anaesthetics into poorly compliant tissues, for the reasons stated above, or around the neuraxis.

Chemical injury

Direct injection of toxic chemicals into a peripheral nerve is inevitably harmful. An in vitro study has demonstrated that local anaesthetics, in their clinically relevant concentrations, is neurotoxic. The degree of toxicity has been demonstrated to be concentration-dependent but class (ester/amide) independent (Werdehausen et al, 2009). Besides local anaesthetics, operators should also be mindful of the apoptotic effect of chlorhexidine and never attempt needle-to-skin contact before the chlorhexidine has air-dried. The joint guideline published by four UK anaesthetic associations concerning skin antisepsis for central neuraxial blockade suggested that chlorhexidine, at a concentration of 2%, did not offer any statistically improved antibacterial effect than its 0.5% counterpart (Campbell et al, 2014). The authors believe that this finding should be translated to the practice of peripheral nerve block.

Vascular injury

Whether intraneural or extraneural, the haematoma will likely compromise peripheral nerve blood flow. When performing peripheral nerve block on a patient who uses anticoagulants or experiences coagulation disorders, it is important to refer to the relevant professional guidance – for instance, the regional anaesthesia and patients with abnormalities of coagulation guidelines (Working Party et al, 2013).

Safe use of adrenaline is also vital. The use of adrenaline at concentration >5 ug/ml (ie <1:200 000) may potentiate greater alpha than beta activity and negatively impact neuronal blood flow, particularly in poorly vascularised peripheral nerves.

Minimising complications and improving success when performing peripheral nerve blocks

Preparation is key to minimise harm and promote success when performing peripheral nerve blocks. The determining factors are summarised below.

Patient factors

- Managing expectations and improving compliance are essential. To enhance patients' preparedness for a peripheral nerve block, it is possible that they could be shown informational videos produced by organisations such as RA-UK (2016)
- Although the absence of sensation does not preclude intraneural injection, a peripheral nerve block should be performed in an awake patient whenever possible, to allow real-time reporting of paraesthesia and any symptoms and signs of local anaesthetic systemic toxicity. Those who require a peripheral nerve block, but who are likely to be non-compliant or uncooperative, should be consented to having the block performed under sedation or general anaesthesia, after consideration of the benefits and risks.

Equipment factors

- The combination of ultrasound-guided nerve block, nerve stimulation technique and injection pressure monitoring may improve safety when performing aperipheral nerve block. This technique is infrequently practised, and no data support the suggestion that this practice is any better than either of these techniques alone.
- Comparison of image acquisition techniques:
  - In-plane: moving the needle perpendicularly to the transducer is generally more tolerable. The in-plane approach reduces the distance required for the needle to travel within the skin to reach the target nerve, but may have a higher chance of intraneural injection or needle misplacement
  - Out-of-plane: moving the needle parallel or diagonally to the ultrasound beam allows visualisation of the needle shaft throughout the procedure. This technique increases the potential for block success and minimises complications. It is preferable for superficial blocks. However, when inserting block needles at steeper angles to reach for deeper structures, refraction will increase, and the quality of ultrasound may be compromised.
- Peripheral nerve stimulator: a nerve stimulator is traditionally used as a nerve-seeking device. The device is highly sensitive. Motor response elicited at ≤0.2 mA indicates intraneural contact or breach. It is also noteworthy that a sudden change in electrical impedance may imply needle-tip migration from the extra- to intraneural compartments.

Organisational factors

The Medical Defence Union (2022) suggested that needle misplacement, including during central and peripheral nerve block, was the third most common negligence claim in anaesthetics. The wrong-sided block is a 'never event', according to NHS England (Pandit et al, 2017). The campaign 'Stop Before You Block' was introduced to address human factors that have been associated with performing the wrong-sided block (RA-UK, 2022). Despite this, incident reports suggested that this continues to occur in roughly 1 in 6520 regional anaesthesia (Pandit et al, 2017). The 'Mock Before You Block' approach is a newer methodology that incorporates both a verbal trigger, similarly to Stop Before You Block, and an action trigger before the performance of the block. Authors of this new action-check model hypothesised that Mock Before You Block would be a much safer technique, as two successive errors would have to be made before triggering this severe incident; the probability for that would be $1/6520^2$ (NHS Improvement, 2021).

Conclusions

The use of peripheral regional blockade extends far beyond providing anaesthesia and analgesia for patients to undergo surgical procedures. When used appropriately, peripheral nerve blocks may also help improve function and reduce opioid-related side effects in patients who experience major skeletal trauma. As hospital clinicians, it is essential to recall

Key points

- Safe and effective regional anaesthesia is a high-level learning outcome in the 2021 Royal College of Anaesthetists curriculum. Putting the correct dose of the right drug in the right place is likely to improve success and minimise harm when performing regional nerve blocks.
- Perineural adjuncts may extend the analgesic effect, but without prolonging the motor block of peripheral nerve blocks; these agents are currently unlicensed in the UK.
- A good understanding of the dermatome and myotome anatomy and classifications of nerve injuries is likely to facilitate the initial management of unexpected or persistent neurological dysfunction following peripheral nerve block.
- Intraneural injection could cause mechanical, pressure, chemical or vascular injury. Ultrasound, nerve stimulator, and injection pressure monitoring may reduce harm when performing peripheral nerve blocks.
- The wrong-sided block is a never event. Anaesthetists must practice ‘Stop before you block’ or ‘Mock before you block’ before attempting any regional blocks.

the applied anatomy, myotomes, the classification and pathophysiology of nerve injury relating to peripheral nerve blockade. Any patients with suspected injury should prompt immediate investigation, as per the local trust policy or the joint guidance published by the British Orthopaedic Association and RA-UK. Anaesthetists-in-training should endeavour to ensure that all precautions are taken before the performance of the block, not only to maximise the chance of success but also to minimise harm. A block safety culture should be cultivated by ensuring that the stop or mock before you block techniques are performed appropriately. The use of a combination of ultrasound, nerve stimulation and injection pressure monitoring to perform peripheral regional blockades should also be considered.

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Conflicts of interest
The authors declare that there are no conflicts of interest.

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