Best Practice & Research Clinical Anaesthesiology 33 (2019) 447–463

Contents lists available at ScienceDirect

Best Practice & Research Clinical Anaesthesiology

journal homepage: www.elsevier.com/locate/bean

7

Newer nerve blocks in pediatric surgery

Alan D. Kaye, Professor, Program Director & Chairman [a],
Jeremy B. Green, Resident [b], Kelly S. Davidson, Resident [c],
Sonja A. Gennuso, Assistant Professor [d],
Morgan L. Brown, Medical School Student [e],
Allison M. Pinner, Medical Student [f],
Jordan S. Renschler, Medical School Student [e],
Kelsey D. Cramer, Medical School Student [e],
Rachel J. Kaye, Medical School Student [g],
Elyse M. Cornett, Assistant Professor [d, *],
John A. Helmstetter, Assistant Professor [h],
Richard D. Urman, Associate Professor [i],
Charles J. Fox, Professor & Chairman [d]

[a] *Department of Anesthesiology, LSU Health Sciences Center, Room 656, 1542 Tulane Ave., New Orleans, LA 70112, United States*
[b] *Department of Anesthesiology, LSU Health Sciences Center, 1542 Tulane Ave., Suite 659, New Orleans, LA, 70112, United States*
[c] *Department of Anesthesiology, LSU Health New Orleans, 1542 Tulane Avenue, Suite 659, New Orleans, LA 70112, United States*
[d] *Department of Anesthesiology, LSU Health Shreveport, 1501 Kings Highway, Shreveport, LA 71103, United States*
[e] *LSU Health Sciences Center New Orleans, 1901 Perdido Street, New Orleans, LA 70112, United States*
[f] *Ochsner LSU Health Shreveport, 1501 Kings Highway, Shreveport, LA 71103, United States*
[g] *Medical University of South Carolina, Charleston, SC 29425, United States*
[h] *LSU Department of Anesthesiology, United States*
[i] *Department of Anesthesiology, Perioperative and Pain Medicine, Harvard Medical School, Brigham and Women's Hospital, 75 Francis St., Boston, MA 02115, United States*

* Corresponding author.
E-mail addresses: akaye@lsuhsc.edu (A.D. Kaye), jgre21@lsuhsc.edu (J.B. Green), kdav28@lsuhsc.edu (K.S. Davidson), sgennu@lsuhsc.edu (S.A. Gennuso), mbro41@lsuhsc.edu (M.L. Brown), apinn1@lsuhsc.edu (A.M. Pinner), jrensc@lsuhsc.edu (J.S. Renschler), kcrame@lsuhsc.edu (K.D. Cramer), rachelkaye17@hotmail.com (R.J. Kaye), ecorne@lsuhsc.edu, ecorne@lsuhsc.edu (E.M. Cornett), rurman@bwh.harvard.edu (R.D. Urman).

https://doi.org/10.1016/j.bpa.2019.06.006
1521-6896/Published by Elsevier Ltd.

Keywords:
pediatric
nerve blocks
regional anesthesia
pediatric regional anesthesia

Purpose of the review: The purpose of this manuscript is to provide a brief discussion of the current direction in pediatric regional anesthesia, highlighting both newer nerve blocks and techniques and traditional nerve blocks.
Recent findings: The number of nerve blocks performed in pediatric patients continues to increase. This growth is likely related in part to the recent focus on perioperative multimodal analgesia, in addition to growing data demonstrating safety and efficacy in this patient population. Multiple studies by the Pediatric Regional Anesthesia Network (PRAN) and the French-Language Society of Pediatric Anesthesiologists (ADARPEF) have demonstrated lack of major complications and general overall safety with pediatric nerve blocks. The growing prevalence of ultrasound-guided regional anesthesia has not only improved the safety profile, but also increased the efficacy of both peripheral nerve blocks and perineural catheters.
Summary: As the push for multimodal analgesia increases and the breadth of pediatric regional anesthesia continues to expand, further large prospective studies will be needed to demonstrate continued efficacy and overall safety.

Published by Elsevier Ltd.

Introduction

History of pediatric regional anesthesia

Up until the late 1980s, it was believed that a neonate's nervous system was too underdeveloped to register pain and that they required little or no analgesia. Since then, multiple studies have revealed evidence that pain in the neonatal period can have long-term neurodevelopmental consequences [1]. One study in Germany used functional magnetic resonance imaging (fMRI) to compare school-aged children who previously endured painful procedures in the neonatal intensive care unit (NICU) to school-aged children who did not require NICU care. They observed that children who had neonatal nociceptive input had developed an exaggerated response to pain based on increased activation of the primary somatosensory cortex, anterior cingulate cortex, and insula on fMRI [2]. Another study from Canada used neuroimaging to demonstrate that greater pain in the neonatal period led to a statistically significant decrease in body weight and head circumference in infants at 32 weeks' gestational age, independent of other comorbid factors [3]. These studies demonstrate the importance of adequate analgesia at all stages of development from birth and beyond, which makes regional anesthesia an attractive option as a part of a multi-modal approach to anesthesia for pediatric patients undergoing many types of procedures.

The history of regional anesthesia in the pediatric population mirrors that of the history of regional anesthesia in adults. The earliest reports of neuraxial anesthesia in children were of those performed by the surgeons Bier and Donitz in 1904 and Deetz in 1906. During this time, anesthesia was not yet a separate specialty and surgeons were responsible for the oversight and administration of anesthetics. They also performed blocks for their procedures, including neuraxial anesthesia personally. Even 100 years ago, the benefits of regional anesthesia were well recognized, such as improved operating conditions, easy access to the abdomen, earlier recovery of bowel function, decreased postoperative pain, earlier feeding, and decreased nausea and vomiting. In 1933, Meredith Campbell reported the first use of caudal anesthesia for pediatric cystoscopies [4]. Anesthesia continued to grow as a specialty through the 1950s; however, some less affluent areas still had surgeon-administered anesthesia and spinal anesthesia was preferred related to its advantages in safety, cost, and efficacy. The popularity of regional anesthesia declined during the mid-

1900s, likely related to the improvement in general anesthesia with the discovery of the muscle relaxant tubocurarine in 1941 as well as with the introduction of the inhalant volatile anesthetic halothane in 1956. In Australia, in 1968, caudal anesthesia was introduced in pediatric patients who were placed under general anesthesia before performing the block. Shortly thereafter, this technique was used commonly for urologic, lower abdominal, and lower extremity procedures [5]. In the 1970s, the first cases of nerve blocks with the use of ultrasound (US) were performed and are now used in almost all forms of regional anesthesia due to increased block success and quality [6]. While interest in pediatric regional anesthesia is prevalent, its widespread use is limited, as general anesthesia is easier and, in most cases, faster to administer. General anesthesia also tends to be more reliable than regional techniques because of the incidence, albeit small, of block failure [5].

Safety of regional anesthesia in children

Regional anesthesia comes with a set of challenges unique to the pediatric population. Most regional anesthesia techniques are performed on adults while they are awake and responsive, which was thought to increase safety and decrease complications. Pediatric patients lack the cooperation of adults; thus, blocks are performed while the patient is at various levels of consciousness, ranging from mild sedation to general anesthesia. Contrary to this theory, safety appears to be improved in pediatric patients when general anesthesia is employed, as patients are less likely to move and cause injury. In addition, it removes the stress and anxiety associated with awake nerve blocks. Analysis of the Pediatric Regional Anesthesia Network (PRAN) database, which includes information on nearly 15,000 blocks performed on 13,725 patients over a 3-year period, found zero reports of death secondary to regional anesthesia, with a few reported complications lasting less than 3 months. Greater than 95% of these patients were anesthetized at the time of block placement [6]. In 1996, the French-Language Society of Pediatric Anesthesiologists (ADARPEF) performed large, successive prospective trials, which have also failed to demonstrate an increased incidence of complications when regional anesthesia techniques were performed under general anesthesia. In this analysis, they found that in children less than 6 months of age, the complication rate was four times higher and recommended that regional anesthesia in these patients be performed only by specialized pediatric anesthesiologists. In addition, it was observed that greater complication rates were associated with central nerve blocks with a sixfold increase in complications when compared with that of peripheral techniques. The most common adverse events in this trial were unintentional dural puncture and unintentional intravascular injection [7]. Twelve years later, a follow-up prospective study of greater than 30,000 blocks yielded similar results. The overall rate of adverse events was 0.12%. It was again reported that infants younger than 6 months of age were having complication rates four times that of infants greater than 6 months; 0.4% compared with 0.1%, respectively. They also observed a sixfold risk increase in risk for complications when neuraxial anesthesia techniques were used as opposed to peripheral nerve blocks. Other potential complications associated with regional anesthesia are listed in Table 1 and include, but are not limited to, infection, hematoma, meningitis, and local anesthetic toxicity [6].

Pharmacology and toxicology of local anesthetics in infants and children

Local anesthetics are small molecules that contain an aromatic ring, an amide group, and a hydrophilic residue with a tertiary amine. They are lipid-soluble weak bases that easily traverse cell membranes. These properties are utilized to block the impulses of nerve fibers by inactivating voltage-gated sodium channels. Local anesthetics cross cell membranes in a unionized form and become ionized once inside the cell to bind and mechanically block pores in the membrane. At higher concentrations, local anesthetics are also able to block potassium and calcium channels. Amide local anesthetics distribute themselves into red blood cells and bind to serum proteins in the blood. As weak bases, local anesthetics are able to bind to α1-acid glycoprotein (AGP) and human serum albumin. α1-Acid glycoprotein is the primary protein that binds local anesthetics despite its low concentration in serum [8]. AGP concentration is low at birth and increases throughout the first year of life. For this reason, neonates and infants have a higher free fraction of local anesthetics than adults, potentially increasing the risk of systemic local anesthetic toxicity in this demographic [9]. In addition, AGP is an

Table 1
Complications associated with regional anesthesia.

Neurologic
• Paresthesias
• Neurologic Deficit
• Postdural puncture headache
• Neuropathy
• Compressive Hematoma
Systemic (intravascular injection)
• Local anesthetic systemic toxicity (LAST)
o Transient ECG changes
o Seizures
o Arrhythmias
o Cardiac arrest
Respiratory
• Pneumothorax
• Respiratory Depression
• Phrenic Nerve Blockade
Infection
• Epidural Abscess
• Meningitis
• Skin and soft tissue infection or deep abscess formation
Catheter Related
• Retained epidural catheter
• Kinking, dislodgement, and occlusion

acute phase protein, and its concentrations increase in the inflammatory state associated with the postoperative period. This leads to an overall increase in protein binding and a concomitant decrease in total clearance. All amide local anesthetics are metabolized by cytochrome P450 enzymes in the liver. These enzymes are immature at birth and undergo changes in their activity levels throughout development. A specific factor influencing the metabolism of local anesthetics is the CYP1A2 enzyme, which metabolizes lidocaine and ropivacaine. This enzyme is immature before 4–7 years of age. Levobupivacaine is primarily metabolized by the CYP3A4/7 enzyme, which does not have full enzymatic capacity until the age of 1 year. Concentrations that cause toxicity in neonates and infants are widely unknown. Neonates and infants have a higher predisposition for developing systemic toxicity when treated with local anesthetics as a result of enzymatic immaturity, leading to lower clearance and a higher serum-free fraction from variable levels of AGP.

Local anesthetic systemic toxicity (LAST) is a rare but life-threatening complication of local anesthetics. Local anesthetics used for regional anesthesia are most often utilized in children under general anesthesia [10]. As a result, the neurological signs of LAST are absent, and hemodynamic compromise may be the only indicator that LAST has occurred. The mechanism of this toxicity is the inhibition of ionotropic and metabotropic cell signaling, as well as mitochondrial dysfunction [11]. These alterations in cellular function lead to central nervous system excitation, cardiac dysfunction, and circulatory collapse. Airway management, oxygenation, ventilation, and life support are the first steps in the management of a patient with LAST [12]. Lipid resuscitation is a well-supported method to reverse systemic toxicity associated with local anesthetics and is the next step in the management of these patients. The mechanism of lipid resuscitation is most likely the establishment of a new equilibrium between the local anesthetic residing in the blood and body tissues and the anesthetic in the lipid component of the plasma [9]. Lipid resuscitation also likely affects tissue binding and has other metabolic effects. The cardiac manifestations of LAST primarily include arrhythmias. The majority of the electrical conduction in the heart, the exception being nodal conduction, relies on sodium channels like those targeted by local anesthetics. Local anesthetics with longer half-lives decrease conduction velocity in the ventricles; this effect is intensified by tachycardia. As a result, neonates and infants with more rapid heart rates than adults are more likely to be affected by local anesthetic-induced blocks. In addition, the low protein binding and decreased clearance of local anesthetics in infants causes them to be more prone to LAST than adults. Decreased ventricular conduction can result in bradycardia, QRSwidening, and Torsades de pointes that can progress to ventricular fibrillation or asystole [1].

Neurotoxicity in LAST manifests in the form of seizures [13]. These complications can culminate in death caused by apnea and cardiovascular collapse [9].

Intralipid is the lipid emulsion utilized in the reversal of LAST. The dosing guidelines for the treatment of LAST with Intralipid in pediatrics include administration of 1.5 ml/kg of 20% lipid emulsion IV for more than 1 min, followed by a repeat dose every 3–5 min to a maximum of 3 ml/kg (up to a total dose of 10 ml/kg). Maintenance infusion of 0.25 ml/kg/min is then given until circulation is restored. The establishment of safe dosing limits for lipid resuscitation in neonates and children must be determined to prevent complications resulting from lipid overload [6]. Neonates who receive IV nutritional support can be subject to lipid overload after treatment with Intralipid. There have been several cases of fat embolism in infants who have received lengthy courses of intravenous infusion of fat (Intralipid 20%). These cases have culminated in the complication known as "fat overloading syndrome," which resembles a post-traumatic fat embolism clinically. Transiently high rates of infusion of Intralipid seem to have been part of the etiology of the fat embolism [14]. These complications exemplify the importance of establishing appropriate dosing guidelines in this vulnerable population. The efficacy of lipid rescue depends on the time of administration in the course of LAST. A study has shown that lipid resuscitation should be administered as soon as it becomes available and not as a last resort [9]. Intralipid is utilized for its stabilizing effects on hemodynamics for patients with LAST.

Maximum recommended dose of local anesthetic in children

Local	Maximum Dose (mg/kg)	Infusion Dose (mg/kg/hr)	Approximate Duration of Action (min)
Lidocaine	5	–	90–200
Bupivacaine	2.5	0.2–0.4	180–600
Ropivacaine	2.5	0.2–0.5	180–600
Levobupivacaine	2.5	0.2–0.5	180–600
Procaine	10	–	60–90
2-Chloroprocaine	20	–	30–60
Tetracaine	1.5	–	180–600

Note: Adapted from NYSORA: regional anesthesia in pediatric patients: general considerations.

Cellular and metabolic differences between neonates/infants and adults must be taken into consideration when determining the dose and efficacy of local anesthetics. This population has a greater predilection for the development of systemic toxicity (LAST) following the use of local anesthetics. LAST can cause acute neurological and cardiovascular manifestations that can lead to circulatory collapse and death. The use of Intralipid rescue in patients experiencing LAST can help to hemodynamically stabilize and restore the patient to a stable physiological state.

Unique metabolic characteristics in Pediatrics affecting local anesthetic metabolism

α1-Acid glycoprotein concentration	α1-Acid glycoprotein concentration is low at birth and increases throughout the first year of life – as a result neonates/infants have a higher free fraction of local anesthetics than adults.
Cytochrome P450 Enzyme immaturity	CYP1A2 that metabolizes lidocaine and ropivacaine is immature before the age of 4–7 years CYP3A4/7 lacks full capacity to metabolize levobupivacaine until the age of 1 year.
Rapid heart rate	In local anesthetics with longer half-lives, tachycardia decreases the ventricular conduction velocity and can cause bradycardia, QRS widening, and Torsades de pointes that can lead to ventricular fibrillation or asystole. Pediatric populations have more rapid heart rates than adults and are predisposed to these adverse effects.
Net effect of low protein binding/decreased clearance of local anesthetics=	Predisposition to local anesthetic systemic toxicity

Head and neck blocks

Blocks of the head and neck, while not common place, are increasing in popularity, primarily because of their relative ease, safety profile, and postoperative analgesic effects.

Supraorbital and supratrochlear nerves (V1 division of the trigeminal nerve)

The supraorbital, supratrochlear, and ophthalmic nerves arise from V1 of the 5th cranial nerve, the Trigeminal nerve. V1 passes through the cranium at the superior orbital fissure before dividing into the lacrimal, frontal, and nasociliary nerves. The supraorbital and supratrochlear nerves are both frontal nerve branches that pass through the supraorbital and supratrochlear notches and are responsible for the innervation of the frontal scalp, forehead, medial upper eyelid, and nasal bridge [15]. Supraorbital and supratrochlear nerve blocks are indicated for procedures at or immediately cephalad to the eyebrow and the upper eyelid region. These procedures include ventriculoperitoneal shunt placement, skin lesions of the scalp, Ommaya reservoir placements in neonates [16], and midline skin procedures.

Following induction, the supraorbital foramen is easily located by palpating the midline of the orbital rim, which typically correlates to the midpoint of the pupil. When palpation is challenging, the distance of the infraorbital foramen from the midline is nearly 21 mm plus 0.5 multiplied by the age in years [17]. After cleansing the area, the needle is advanced through the skin until contact is made with the bone. Following withdrawal of approximately 1 mm and negative aspiration, an injection of 0.5–1 ml of local anesthetic is deposited subcutaneously. Pressure is then applied to the area to ensure spread of the local anesthetic and to prevent hematoma formation. Complications for this particular block are rare but include intravascular injection, hematoma, and eye globe damage.

Infraorbital nerve (V2 division trigeminal nerve)

The infraorbital nerve is a branch of the maxillary nerve (V2). It passes through the infraorbital foramen, which is located below the inferior orbital rim, before dividing into the inferior palpebral, external nasal, and superior labial nerves. It supplies sensation to the orbital floor and lower eyelid, as well as the upper lip, tip of the nose, and a portion of the nasal septum. Patients undergoing surgeries such as cleft lip repair, nasal septum repair, and endoscopic sinus surgery can benefit from the infraorbital block [18].

Two techniques have been described in the literature to block the infraorbital nerve: the extraoral approach and the intraoral approach. For the extraoral approach, the infraorbital foramen is palpated on the floor of the orbital rim. A 27-gauge needle may then be advanced through the foramen, and following negative aspiration, 0.5–1 ml of local anesthetic may be injected into the area [16]. Once the needle is withdrawn, apply pressure for 1 min to the area.

When attempting the intraoral approach, the infraorbital foramen is again identified as a landmark. At the canine or first premolar tooth, a needle is advanced through buccal mucosa at the sub-sulcal groove in the direction of the infraorbital foramen. Bending the needle to approximately 70° may aid in passing the needle on the maxillary process. Following negative aspiration, 0.5–1 ml of local anesthetic may be injected into the area. A finger should be placed externally at the infraorbital foramen to prevent the penetration of the globe of the eye [16]. Following the procedure, care should be taken to prevent the biting of the upper lip, as sensation to this area may remain numb for several hours.

Greater auricular nerve (superficial cervical plexus)

The superficial cervical plexus innervates the lateral scalp, posterior auricular area, anterior-lateral skin of the neck, and parotid gland, making it a good target for procedures involving the ear, such as tympanomastoid surgery, as well as procedures of the neck, like thyroid and anterior cervical surgery.

The greater auricular nerve is a branch of the superficial cervical plexus, which is formed by the ventral rami of the C2–C4 nerve roots. Near the midpoint of the posterior border of the sternocleidomastoid, the superior cervical plexus divides, giving rise to the great auricular, lesser occipital,

supraclavicular, and transverse cervical nerves. Following induction, a line can be drawn from the level of Chassaignac's tubercle at C6 to the posterior border of the clavicular head of the sternocleidomastoid muscle. A 27-gauge needle with a 60-degree bend cephalad is then advanced along the posterior border of the sternocleidomastoid. Following negative aspiration, a subcutaneous injection of 1–2 ml of local anesthetic may be performed. Complications following this block are related to intravascular injection or deep cervical plexus blockade and can include Horner's syndrome (unequal size of pupil, eyelid drooping, raising of the lower eyelid, and light-colored iris), unilateral phrenic nerve paralysis, and hematoma.

Occipital nerve

The posterior rami of nerve roots C2 and C3 give rise to the greater occipital nerve, which is responsible for the innervation of the skin of the posterior scalp. The greater occipital nerve initially travels cephalad and medial to the occipital artery. However, it is noted that the nerve will eventually become lateral to the artery. Ultimately, it becomes superficial at the level of the superior nuchal line at the occipital protuberance. Greater occipital nerve blocks may be used as adjuncts for posterior fossa surgery, or as treatment migraine and cervicogenic headaches [19], as well as occipital neuralgia [20]. Using the landmark technique, the occipital protuberance is located. The occipital artery runs inferior and lateral to the occipital protuberance. Once the artery is identified via palpation, a 27-gauge needle is used to aspirate and inject 2–3 ml of local anesthetic lateral to the artery. Gentle pressure may be applied following injection to ensure spread of the local anesthetic.

Recently, the US technique has been described for occipital nerve blocks [21]. The spinous process of the C1 vertebra is identified using a linear probe before moving caudad to identify the bifid C2 vertebra. After rotating the probe by 90°, it is then moved laterally to identify the greater occipital nerve, which runs along the obliquus capitis muscle [15]. Using a 27-gauge needle, aspiration and injection of 2 ml of local anesthetic solution are performed using the in-plane approach. Complications are rare with both approaches, but include intravascular injection.

Greater palatine nerve (V2)

The greater palatine nerve innervates the mucous membrane of the hard palate and gums, making it a common block used in cleft palate repair. Arising from the pterygopalatine ganglion, the greater palatine nerve passes through the greater palatine foramen and lies in the groove of the hard palate [15]. Following the induction of general endotracheal anesthesia, the patient is positioned in the supine position with the head in a neutral midline position. A bite block is used to maintain the mouth in an open position. The palatine foramen is located medial and anterior to the first molar. Aspiration and injection of 1 ml of local anesthetic in the mucosa are performed using a 27-gauge needle. Potential complications include intraneural and intravascular injection.

Pediatric upper, mid, and lower abdomen blocks

Truncal blocks such as the transversus abdominis plane, ilioinguinal/iliohypogastric, and rectus sheath blocks are becoming more commonplace as an adjunct for postoperative pain control following abdominal and inguinal surgeries.

Transversus abdominis plane (TAP) block

The transversus abdominis plane (TAP) is located between the internal oblique and transversus abdominis muscle layers. Within this plane lie the thoracolumbar nerve roots supplying sensory innervation to the anterior abdominal wall. The TAP block is indicated in pediatric patients for post-operative pain control at the anterior abdominal wall, particularly for laparoscopic surgeries and other abdominal incisions.

The TAP block is performed with US guidance. The probe is placed adjacent to the umbilicus and moved laterally until the three abdominal muscle layers (external oblique, internal oblique, and

transversus abdominis) are identified. The needle is then advanced through the external oblique, into the plane between the internal oblique and transversus abdominis [13]. Proper placement of the needle will demonstrate hydrodissection between the two planes as the local anesthetic is injected. Alternatively, US guidance may be used to perform the TAP from a posterior approach. Using this method, the local anesthetic is injected under the anterior border of the quadratus lumborum muscle [22]. In pediatric patients, the anterior approach is more commonly used because it provides greater spread of the local anesthetic and therefore more adequate analgesia [23]. Low concentrations (0.2–0.3 ml/kg) of ropivacaine and bupivacaine are most commonly used.

TAP blocks in the pediatric population have been shown to reduce early and late postoperative pain, as well as opioid consumption 24 h after surgery [22], and in some cases, the blocks have completely eliminated the need for opioids. The TAP block has been shown to be more effective when performed preoperatively, with an association between higher anesthetic doses and length of analgesia.

Overall, the TAP block is considered a safe nerve block. Complications of the TAP block include infection, local anesthetic toxicity, peritoneal puncture, bowel puncture, and intravascular injection [13]. The PRAN has collected data on the safety of TAP blocks, with a study by Polaner and colleagues, showing a complication rate of 0.7% [13]. Additional studies by Long et al. showed a 0.3% complication rate and included the vascular aspiration of blood and peritoneal rupture [22].

Ilioinguinal/Iliohypogastric (IL/IH) nerve block

The ilioinguinal and iliohypogastric (IL/IH) nerves, which supply sensation to the posterolateral gluteal region, inguinal region, and anterior scrotum, run just medial to the anterior superior iliac spine and between the internal oblique and transversus abdominis muscles. However, the location of the IL and IH nerves has been shown to vary significantly by age group in pediatric patients. In a study performed by Hong et al., the IH nerve was not identified on the line between the anterior portion of the superior iliac spine and umbilicus in 12.5% of patients (25 out of 200) [24]. Therefore, age must be considered when locating these nerves based on anatomical landmarks rather than US guidance.

The IL/IH nerve block is indicated for postoperative analgesia following inguinal surgery such as inguinal hernia repair, orchiopexy, and hydrocelectomy, while it may also be used for the diagnosis and treatment of ilioinguinal/iliohypogastric neuralgia, groin pain, inguinal pain, pelvic plain, and post-herpetic neuralgia [25].

The IL/IH nerve block is performed with US guidance with the probe positioned medial to the anterior superior iliac spine at the level of the umbilicus. Once the three abdominal muscle layers are identified, the IL and IH nerves should be located between the transversus abdominis and internal oblique muscles. The needle is then advanced to the nerves and the anesthetic is injected [13].

The IL/IH nerve block is increasing in popularity as it has proven to be superior to both intravenous opioids and TAP blocks. In a study performed by Karan et al., pediatric patients who received the IL/IH nerve block had greater post-op analgesia and less rescue medications required in the first 24 h. In patients who received ropivacaine with adjunct dexmedetomidine, the mean duration of analgesia was 970.23 ± 47.61 min [26].

Similar to the TAP, IL/IH nerve blocks are relatively safe. Complications include infection, local anesthetic toxicity, bowel puncture, pelvic hematoma, femoral nerve palsy, and intravascular injection. Femoral nerve blockade may result in the temporary paresis of the quadriceps muscles and numbness of the femoral nerve distribution. A study by Polaner and colleagues showed the rate of such complications at 0.4% [13], while a study by Karan et al. showed no complications in the 60 pediatric patient participants who received the IL/IH nerve block [26].

Rectus sheath block

Another block for postoperative analgesia of the anterior wall is the rectus sheath block. Sensation to the umbilicus is supplied bilaterally by thoracoabdominal intercostal nerves, which travel between the sheath and posterior wall of the rectus abdominis muscle. The rectus sheath is formed by the aponeuroses of the internal oblique, external oblique, and transversus abdominis muscles and consists of anterior and posterior sheaths, which encase the rectus abdominis muscle. This block is particularly

useful for midline abdominal incisions and is commonly used postoperatively after an umbilical hernia repair or laparoscopic procedures.

The rectus sheath block is performed under US guidance, with the probe is placed just lateral to the umbilicus to identify the rectus abdominis muscle. The needle is then advanced medially between the rectus abdominis and posterior rectus sheath and the anesthetic, most commonly bupivacaine, is injected [13].

A study performed by Relland et al. comparing rectus sheath blocks, caudal analgesia, and surgical site infiltration for postoperative analgesia after pediatric umbilical herniorrhaphy showed that all three approaches were effective in providing postoperative analgesia and decreasing the need for opioids. Although there was no significant difference in postoperative analgesia between these three methods, the rectus sheath block is considered superior because of its greater accuracy, safety, and lower volume of anesthetic injectate required [27].

Complications of the rectus sheath block include infection, local anesthetic toxicity, bowel puncture, and intravascular injection. Because the rectus sheath block requires less anesthetic to be injected, it decreases the risk of anesthetic systemic toxicity. According to the PRAN, the rate of such complications is 0 out of 294 procedures [13]. Therefore, this has proven to be a relatively safe form of analgesia.

TAP Block	IL/IH Block	Rectus Sheath Block
Post-op analgesia of the anterior abdominal wall abdominal wall incisions, and laproscopic procedures	Post-op analgesia of the inguinal region and scrotum Inguinal hernia repair, Orchiopexy, and Hydrocelectomy	Post-op analgesia of the anterior abdominal wall midline abdominal incisions, Umbilical hernia repair, and laparoscopic procedures

Pediatric upper extremity blocks

The advent of US-guided regional anesthesia, has allowed for non-invasive real time visualization of nerves and their surrounding structures, allowing for both a higher rate of successful blocks, as well as a decrease in the risk of regional anesthesia, such as neuronal damage, intravascular injection, and pneumothorax [28]. US guidance increases the efficacy of blocks by allowing closer proximity of injections to nerves, while decreasing the risk of hitting structures [29]. Implementation of US guidance is of particular use in the pediatric population as anatomy is more variable, rendering the use of bony landmarks to isolate nerves that are less reliable. Additionally, vessels and nerves are smaller and more closely associated in children, increasing the risk of puncturing vessels on needle insertion. Children also have higher body water content than adults, allowing for a more distinct image of the structures deep to the probe [30]. Less subcutaneous fat and more superficially located nerves also contribute to the ability to more clearly visualize structures using US in the pediatric population.

The upper limb is supplied by nerves from the brachial plexus, which is composed of the ventral rami of nerves C5–C8 and a part of the T1 ventral ramus. Brachial plexus nerve blocks are indicated for surgeries of the upper extremity and impair sensation and motor ability. Employing the appropriate approach to blocking at different locations of the brachial plexus allows for selective peripheral nerve block. The European Society of Regional Anesthesia (ESRA) and the American Society of Regional Anesthesia and Pain Medicine (ASRA) formed a joint committee in 2018 to determine and recommend safe dosages for local anesthetics in regional anesthesia for children. They advised that US-guided upper extremity peripheral nerve blocks are safe and effective with a local anesthetic dose of bupivacaine or ropivacaine of 0.5–1.5 mg/kg, and dexmedetomidine is a safe adjunct to injections to prolong the nerve blocks [31]. A major concern for blocking at the brachial plexus for the upper

extremity is the superior extent of the lung in the pediatric population, which extends above the superior thoracic aperture. US guidance allows for the visualization and reduction of risks associated with upper extremity nerve blocks [32].

Axillary block

The axillary approach to upper extremity block is one of the most common and safest blocks in children. The approach delivers local anesthesia to the radial, median, and ulnar nerves, resulting in analgesia to the hand, forearm, and elbow. It is of use in orthopedic and plastic surgical repairs in a child with a full stomach, when the risk of aspirating gastric contents is higher under deeper sedation. At this level, the ulnar nerve lies anterior and inferior to the axillary artery, while the radial nerve lies posterior to the artery. The median nerve is located anterior and superior to the axillary artery. The musculocutaneous nerve is located between the biceps brachii and coracobrachialis outside of the neurovascular sheath and must be blocked separately. With the US probe oriented transverse to the humerus, an in-plane technique is used to deliver multiple injections of the local anesthetic around the nerve [13]. Repositioning of the needle between injections facilitates complete block of the nerve. Potential complications of the axillary block include neural injury, intravascular injection, and puncture site infection; however, the risk of adverse events is minimized with US guidance.

Interscalene block

The interscalene block is often reserved for older children and teenagers undergoing shoulder surgery and is rarely performed in younger children. Blocking the brachial plexus at the interscalene groove provides best access to the C5, C6, and C7 nerve roots. The block is performed at the level of the sixth cervical vertebra, where the trunks and roots of the brachial plexus are situated in between the anterior and middle scalene muscles and posterior to the sternocleidomastoid muscle. For best access to the plexus, the child should be positioned supine with their arms extended inferiorly and their head turned toward the contralateral side [30]. The US probe is oriented in the transverse plane at the level of cricoid cartilage on the lateral border of the sternocleidomastoid muscle. Complications of this approach make it less common in pediatrics, with adverse sequelae being potentially fatal [30]. Interscalene block risks include pneumothorax, vertebral artery injection, and intrathecal injection. Successfully completed interscalene blocks are often associated with hemidiaphragmatic paralysis, recurrent laryngeal nerve block, and Horner's syndrome, although these outcomes are reduced with the use of US guidance [33].

Supraclavicular block

The supraclavicular block covers the trunks and divisions of the brachial plexus, which are located lateral and superficial to the subclavian artery in the supraclavicular fossa. The first rib is inferior and medial to brachial plexus; and the pleura is found within 1–2 cm of the plexus. The supraclavicular block is indicated for upper arm surgical procedures. The US probe is oriented in the coronal–oblique plane superior to the upper border of mid-clavicle for this approach. The needle is then inserted superior and lateral to the artery and advanced medially in the direction of the plexus to minimize the risk of vascular puncture and intraneural injection. Because of the proximity of the pleura to the brachial plexus, pneumothorax is again a potential complication. Intravascular injection into the vertebral artery is also a risk of this approach.

Infraclavicular block

The infraclavicular block provides arm and elbow analgesia by blocking at the level of the cords of the brachial plexus. This block is of particular use when injury, such as fracture, makes abduction of the arm painful [34]. The cords of the plexus are medial and inferior to the coracoid process of the scapula. The pectoralis major and pectoralis minor muscles are superficial to the cords, and the axillary artery and vein lie deep to the cords. The medial cord is situated between the axillary artery and vein, and the

posterior cord is located deep to the artery. The infraclavicular block employs a lateral approach to the brachial plexus with the US probe oriented in the transverse plane. The needle is inserted inferior to the probe, and an out-of-plane technique is used to advance the needle to the lateral aspect of the plexus. Complications of this approach include the pneumothorax and puncture of the axillary artery or vein.

Approach	Portion of Brachial Plexus Blocked
Axillary	Branches
Interscalene	Trunks and Roots
Supraclavicular	Trunks and Divisions
Infraclavicular	Cords

Pediatric lower extremity blocks

Femoral nerve block

The femoral nerve is the largest branch of the lumbar plexus and is formed from the dorsal rami of L2-L4 spinal nerves. It provides sensory innervation to the anterior and medial thigh, as well as most of the femur, hip joint, and knee joint. After exiting the lumbar plexus, the femoral nerve courses inferiorly under the inguinal ligament, superficial to the iliopsoas muscle. The nerve bundle lies just laterally to the femoral sheath, which contains the femoral artery and the femoral vein most medially. The femoral nerve and femoral sheath are contained underneath the fascia iliaca in the femoral triangle. After a course of a few centimeters in the thigh, the femoral nerve divides into anterior and posterior divisions. The anterior branch provides sensory innervation for anterior, medial, and lateral thigh, and the hip joint. The posterior branch provides sensory info for the knee joint and the saphenous nerve region [35,36].

There are several indications for a femoral nerve block in the pediatric patient population. Acutely, femoral nerve blocks can be used in emergency departments to provide analgesia in cases of hip fractures, femur fractures, patellar injuries, and anterior thigh wounds [35]. When femoral nerve blocks are appropriately performed in the emergency department, pediatric patients report 2–3 times longer lasting analgesic effect compared to a dose of a systemic analgesic medication such as morphine. Decreasing the amount of opioid medications given to pediatric patients reduces the risk of adverse events such as apnea or nausea. Additionally, decreased opioid use leads to less nursing interventions and clinical time spent titrating pain medication dosing [37]. Femoral nerve blocks can also be used in surgical cases, such as the repair of a quadriceps tendon, or to supplement other lower extremity blocks including sciatic and popliteal blocks [36].

Point of care US guidance allows for easy location of the femoral nerve when it is just distal to the inguinal ligament. On US, the femoral nerve is hyperechoic and triangular in appearance. A useful landmark is the pulsatile femoral artery just medial to the femoral nerve [35]. If no point of care US is available, the location of the femoral nerve can be triangulated using the femoral artery pulse and the inguinal ligament. In this method, the femoral nerve is approximately 1 cm lateral of the artery just distal to the inguinal ligament [36].

After the patient is draped and the injection location is determined, a small amount of lidocaine should be injected into the superficial tissue to minimize procedure discomfort [35]. Then, the nerve block needle is advanced, ideally a needle with the ability to be connected to a nerve stimulator. The injector may feel a “pop” sensation with the puncture of the fascia iliaca. It is imperative to get under this thick fascia for an effective nerve block. Once under the fascia iliaca, stimulation of the femoral nerve should yield quadriceps contractions. At this point, the needle should be pulled back just until the nerve and needle are not in contact. Pulling back off a quadriceps contraction combined with a negative aspiration should indicate the correct needle placement for the local anesthetic injection – under the fascia but not directly into the nerve or vasculature. This placement technique is the same for a one-time injection or for catheter placement for an infusion or repeated boluses [36]. The first amount of local anesthetic should be injected underneath the nerve, to “float” the nerve fibers making

the subsequent injections around the nerve easier. The US should show the anesthetic medication dissecting through the fascial layers around the nerve fibers, if the injection is in the correct place [35].

Complications of lower extremity peripheral nerve blocks are reduced with the point of care US guidance but there remain inherent procedural risks for nerve blocks [35]. These risks include injection infiltration into vasculature, hematoma formation, direct nerve injury, and injection site infection. Local anesthetic toxicity is dose dependent, which makes accurate weight-based dose calculations and proper time recording particularly important in the pediatric population. In addition to these standard peripheral nerve block risks, there is a patient fall risk associated with femoral blocks from sensory and motor blockade to lower extremity muscles [35,36]. These complications and safety concerns are always in addition to the underlying primary diagnosis that indicated a nerve block such as compartment syndrome or hematoma formation after a femur fracture. Femoral nerve blocks are contraindicated with local anesthetic allergy, uncooperative patients, and patients at risk for immediate complications such as evolving compartment syndrome [35].

Saphenous nerve block

The saphenous nerve is a cutaneous branch of the femoral nerve. It provides sensory innervation to the knee and the medial lower leg, running alongside the sartorius muscle in its path down the leg. The saphenous nerve can be blocked distally to provide analgesia to the medial lower leg or it can be blocked proximally to additionally provide analgesia to the knee joint [13].

For the proximal block, the injection location is lateral to the femoral artery at the upper border of the sartorius muscle, at the branch point of the saphenous nerve from the femoral nerve. Point of care US can be used to identify the correct depth and angle of injection. At this location, the saphenous nerve is coursing next to the motor innervation to the vastus medialis muscle. Using the nerve stimulation technique, vastus medialis contraction indicates that the needle is in the right location. A saphenous nerve block here will also block motor innervation to vastus medialis [38]. To block the saphenous nerve distally, the child's leg should be abducted and laterally rotated while lying supine. With the US probe just above the medial aspect of the knee joint, the saphenous nerve can be visualized near the insertion of the sartorius muscle and blocked from that location [13]. Complications, contraindications, and safety concerns are the same as that of a femoral block. It is worth noting that saphenous blocks have historically had a higher failure rate, calculated to about 20%, because the saphenous nerve is purely sensory and harder to locate with the nerve stimulation technique. With the increasing use of the point of care US, this failure rate is expected to decrease [38].

Sciatic nerve block

The sciatic nerve is composed of fibers from L4-S3 and arises in the sacral plexus. After leaving the pelvis through the greater sciatic foramen, the sciatic nerve courses between the ischial tuberosity and greater trochanter of the femur. At emergence from the subgluteal space, the sciatic nerve runs down the femur alongside the adductor magnus muscle to the popliteal fossa. At the knee, it divides into two nerves, the common fibular nerve and the tibial nerve. A sciatic nerve block provides analgesia to the posterior thigh, the lower leg, and the foot [38,39].

The technique for a sciatic block differs from previously discussed lower extremity blocks in that a longer needle and lower frequency US probe is needed to reach the deep nerve fibers [39]. There are several different approaches to blocking the sciatic nerve: most typically used in pediatrics are the subgluteal and popliteal approaches. For the subgluteal approach, US is used to locate the sciatic nerve at one of the more superficial locations, between the ischial tuberosity and the greater trochanter. The nerve will appear hyperechoic and flat on US between the gluteus maximus and the quadriceps femoris muscles [39]. It is important to chart the course of the nerve down the leg because it can easily be confused for the biceps femoris tendon, which will transition into muscle fibers as the nerve continues. For the popliteal approach, the injection can either be between the lateral border of the biceps femoris and the medial border of semimembranosus/semitendinosus tendons or can be between the groove of the biceps femoris and the vastus lateralis on the lateral aspect if the thigh is at the distal 1/3 mark from

the hip to the knee [39]. The popliteal approach is an ideal location to leave a catheter to continue the peripheral block postoperatively in painful conditions such as clubfoot surgery [38].

The complications of the sciatic block include the complications discussed above that pertain to all peripheral nerve blocks as well as increased risk of falling. Additionally, the proximal sciatic blocks, including the subgluteal approach, require higher doses of local anesthetic than other locations. The use of US in pediatric sciatic blocks decreases the amount of needle passes, increases the duration of analgesia, and decreases the total amount of anesthetic needed [39].

Lumbar plexus block

The lumbar plexus includes the nerve roots of T12-L5 and is located deep to the paravertebral muscles, within the psoas muscle. The plexus branches innervate the lower abdomen and upper leg. Specifically, it innervates the anterior thigh and the anteromedial lower leg up to the medial foot [39]. Blocking the lumbar plexus along with the sciatic nerve of the same leg will provide complete anesthesia to the limb [13].

The technique of a lumbar plexus block is difficult, even with US, because of the intramuscular location of the plexus. To reach the lumbar plexus, the injection will first have to pass through the erector spinae and quadratus lumborum muscles. The patient should be placed in the lateral decubitus position with the US probe placed lateral to the midline between the iliac crest and the spinous processes, at the level of the L4 or L5 transverse processes. Nerve stimulation is needed to confirm that the needle is in the right location within the psoas muscle [13]. Then, the injection technique is the same as other peripheral blocks, including intermittent negative aspirations. Lumbar plexus blocks have the same complications as other standard peripheral nerve blocks and additionally pose a fall risk due to lower extremity muscle innervation by branches of the plexus.

Pediatric central neuraxial techniques

Caudal analgesia

Caudal anesthesia is the most commonly used approach to regional anesthesia in pediatric patients [40]. Caudal analgesia is indicated to reduce anticipated pain in surgical procedures of the midthoracic to lumbosacral dermatomes, including the sex organs, bladder, pelvis, and perineum. Utilization of caudal blocks promotes early ambulation, hemodynamic stability in the operative period, and spontaneous breathing in patients whose airways may be difficult to secure [41].

For this approach, the child is situated in a prone or lateral decubitus position. A short-bevel styletted needle is typically introduced through the sacral hiatus, which is located approximately 5 cm cephalad from the coccyx. The needle is inserted through the sacrococcygeal ligament into the caudal space, and resistance should be felt as the needle traverses the ligament. Once into the caudal space, the needle should be directed cephalad, parallel to the plane of the back. The needle is then aspirated to check for the presence of cerebrospinal fluid (CSF) or blood. A test injection of 2–4 mL should be performed while examining for systemic effects, such as arrhythmias or hypotension, a feeling of resistance to the injection, or a bump in the surrounding tissue. If the test injection is performed without adverse events, the local anesthetic is then injected in increments. US guidance or nerve stimulation may be used to assist with the placement of the needle.

Caudal analgesia can be given independently, or in combination with general anesthesia. ASRA guidelines state that the benefit of guaranteed cooperation of children under generalized anesthesia may outweigh the risk of performing the neuraxial blockade with heavy sedation or general anesthesia. The ESRA and ASRA guidelines state that a bupivacaine dose of 1 mg/kg for newborns and infants and 0.5 mg/kg in children greater than 1 year of age can be performed. Tetracaine 0.5% is recommended for spinal anesthesia at a dosage of 0.07–0.13 mL/kg [4]. If the surgery is greater than 3 h, a second injection, at half-dose, can be given at the conclusion of the surgery to prolong analgesia.

Clonidine or dexmedetomidine can be used as adjuvants to caudal analgesia blocks with local anesthetics. These α-2 adrenergic agonists have been demonstrated to extend regional analgesia to up to 3 times longer than the administration of local anesthetic alone. They also reduce rescue analgesia without any significant added side effects [42,43]. Studies examining the effects of alternative adjuvants to local anesthetics demonstrated that arousable sedation time was prolonged with adjuvant clonidine and fentanyl; however, fentanyl was associated with pruritus and urinary retention [44]. A 2018 review of literature evaluating the use of dexmedetomidine as an adjuvant for caudal blockade determined that dexmedetomidine extended postoperative analgesia longer than fentanyl and morphine. The review also reported better postoperative behavior scores and higher sedation scores associated with adjuvant dexmedetomidine, in the absence of respiratory depression. The review concluded that the addition of dexmedetomidine to local anesthetic is supported in pediatric patients undergoing infraumbilical and lower extremity surgeries [45].

Continuous neuraxial catheters

In comparison to single-dose caudal anesthesia as described above, a continuous catheter delivering spinal anesthesia allows for smaller doses of local anesthetics and adjuvants over an indefinite amount of time [46]. Lower, more frequent doses allow for more control over duration and location of the anesthetic, decreasing adverse hemodynamic effects and anesthesia to undesired locations, such as sacral roots controlling bowel and bladder function in some cases [46]. Catheters can be placed in thoracic, lumbar, or caudal regions and even threaded up cephalad from a caudal insertion to find the desired nerve roots for blockade [13]. Continuous spinal anesthesia should be considered as an option instead of or in combination with general anesthesia for children with certain conditions such as difficult airways, neonatal respiratory distress, or children/preterm infants who have a history of respiratory depression episodes [41]. In addition to operative anesthetic effects, epidural catheters are often used to control postoperative pain in infants and children [13].

Using a catheter to deliver local anesthetics mixed with the adjuvants discussed in the previous section decreases the reliance on postoperative opioid use, sparing children from many adverse events, including respiratory depression. Risks of continuous catheter use are the same as the single injection risks of local anesthetics plus additional risks associated with catheter placement, leading to a slightly higher complication rate in catheter use, often outweighed by the benefits of continuous anesthesia [47].

Paravertebral block

A paravertebral block refers to blocking somatic and sympathetic fibers, where the spinal nerves are leaving the intervertebral foramina. The paravertebral space is a potential space deep to intercostal/paraspinal muscles. This space is bounded posteriorly by the superior costotransverse ligament, anteriorly by the parietal pleura, medially by the intervertebral discs, and superiorly by the head/neck of the ribs [13]. The paravertebral space communicates with the epidural space medially and the intercostal space laterally [48].

Paravertebral blocks provide anesthesia or analgesia to abdominal and thoracic dermatomes [48]. These blocks are typically unilateral as bilateral sympathetic denervation leads to increased risks of hypotension and hemodynamic compromise; however, bilateral blocks have been reported [48]. Unilateral paravertebral blocks have fewer reported contraindications and adverse events than caudal neuraxial blocks in situations where they will provide sufficient anesthesia for breast surgeries, cholecystectomies, and thoracotomies [13]. Common uses for analgesic paravertebral blocks in the pediatric population are sustained postoperative analgesia and after rib fractures in patients with painful breathing [48].

The injection technique is similar to that of a peripheral nerve block. The US probe is placed at the transverse processes of the desired vertebrae at a 90° angle to the skin. The needle is introduced in plane with the probe into the paravertebral space. Depth blockers or measured needles are encouraged, as the injection needs to be through the intercostal/paravertebral muscles but not through the parietal pleura [48]. To confirm that the needle has not punctured any vessels, a negative aspiration should occur before injection. Then, a small bolus of saline into the paravertebral space will help visualize the

potential space on US. The block can be a single injection or a catheter for continued analgesia can be placed [13].

In addition to the complications from injections and the use of local anesthetics and adjuvants discussed earlier in the section, paravertebral block complications also include pleural puncture, pneumothorax, and hemodynamic compromise from sympathetic blockade [13]. A benefit of the paravertebral block is that the child has no fall risk from the block, the lower limb sensation and musculature will remain intact [48].

Conclusion

As the emphasis on perioperative multimodal analgesia, improved patient outcomes, and improved patient satisfactions continues to increase, so too will the use of regional anesthesia, particularly in the pediatric population. Regional anesthesia has been shown to be both safe and efficacious in children and, as just discussed, offers an adjunct solution for postoperative pain control across a number of different surgeries. As the use of US and complexity in nerve blocks continue to increase in children, further prospective studies will be needed to ensure continued safety and efficacy in the pediatric patient population.

Summary

This manuscript highlights some of the newer blocks available and emphasizes newer techniques of regional anesthesia in pediatric surgery. The blocks presented include the head/neck region; upper, mid, and lower abdomen; and lower extremity. It will also address neuraxial anesthesia. The manuscript concludes with the discussion of outcomes and safety concerns.

Practice points

- There is a demonstrated general overall safety and a lack of major complications associated with pediatric nerve blocks.
- The growing prevalence of ultrasound (US)-guided regional anesthesia has improved the safety profile and increased the efficacy of both peripheral nerve blocks and perineural catheters.
- Local anesthetic toxicity is dose dependent, which makes accurate weight-based dose calculations and proper time recording particularly important in the pediatric population.
- The establishment of safe dosing limits for lipid resuscitation in neonates and children must be determined to prevent complications resulting from lipid overload.
- The use of US in pediatric sciatic blocks decreases the amount of needle passes, increases the duration of analgesia, and decreases the total amount of anesthetic needed.

Research agenda

- As the use of US and complexity in nerve blocks continue to increase in children, further prospective studies will be needed to ensure continued safety and efficacy in the pediatric patient population.
- Studies evaluating the safety and efficacy of US-guided nerve blocks in all ages of children are especially important. Other important future research factors in this population include gender, race, and comorbidities.

References

[1] Marchant A. “Neonates do not feel pain”: a critical review of the evidence. Biosci Horizons 2014;7:hzu006. https://doi.org/10.1093/biohorizons/hzu006.
[2] Hohmeister J, Kroll A, Wollgarten-Hadamek I, et al. Cerebral processing of pain in school-aged children with neonatal nociceptive input: an exploratory fMRI study. Pain 2010;150:257–67. https://doi.org/10.1016/j.pain.2010.04.004.
[3] Vinall J, Miller SP, Chau V, et al. Neonatal pain in relation to postnatal growth in infants born very preterm. Pain 2012;153:1374–81. https://doi.org/10.1016/j.pain.2012.02.007.
[4] Campbell MF. Caudal anesthesia in Children1Read before the American society of regional anesthesia, New York academy of medicine, February 14, 1933. J Urol 1933;30:245–50. https://doi.org/10.1016/S0022-5347(17)72472-X.
[5] Brown TCK. History of pediatric regional anesthesia. Pediatr Anesth 2012;22:3–9. https://doi.org/10.1111/j.1460-9592.2011.03636.x.
*[6] Davis PJ, Cladis FP. Smith's anesthesia for infants and children. 7th ed. 2017. Philadelphia.
[7] Giaufré E, Dalens B, Gombert A. Epidemiology and morbidity of regional anesthesia in children: a one-year prospective survey of the French-Language Society of Pediatric Anesthesiologists. Anesth Analg 1996;83:904–12.
[8] Mazoit J-X. Local anesthetics and their adjuncts. Paediatr Anaesth 2012;22:31–8. https://doi.org/10.1111/j.1460-9592.2011.03692.x.
[9] Lo P. Toxicity of local anesthetic drugs : a pediatric perspective 2012;22:39–43. https://doi.org/10.1111/j.1460-9592.2011.03631.x.
[10] Mauch J, Jurado OM, Spielmann N, et al. Resuscitation strategies from bupivacaine-induced cardiac arrest 2012;22:124–9. https://doi.org/10.1111/j.1460-9592.2011.03688.x.
[11] Weinberg G. Lipid rescue resuscitation from local anaesthetic cardiac toxicity. Toxicol Rev 2006;25:139–45.
[12] Weinberg GL. Treatment of local anesthetic systemic toxicity (LAST). Reg Anesth Pain Med 2010;35:188–93. https://doi.org/10.1097/AAP.0b013e3181d246c3.
[13] Shah RDD, Suresh S. Applications of regional anaesthesia in paediatrics. Br J Anaesth 2013;111:114–24. https://doi.org/10.1093/bja/aet379.
[14] Barson AJ, Chiswick ML, Doig CM. Fat embolism in infancy after intravenous fat infusions, 53; 1978.
[15] Suresh S, Voronov P. Head and neck blocks in infants, children, and adolescents. Pediatr Anesth 2012;22:81–7. https://doi.org/10.1111/j.1460-9592.2011.03701.x.
[16] Belvis D, Voronov P, Suresh S. Head and neck blocks in children. Tech Reg Anesth Pain Manag 2007;11:208–14. https://doi.org/10.1053/j.trap.2007.09.009.
[17] Suresh S, Voronov P, Curran J. Infraorbital nerve block in children: a computerized tomographic measurement of the location of the infraorbital foramen. Reg Anesth Pain Med 2006;31:211–4. https://doi.org/10.1016/j.rapm.2005.11.017.
*[18] Local and regional anesthesia for ophthalmic surgery - NYSORA. https://www.nysora.com/regional-anesthesia-for-specific-surgical-procedures/head-and-neck/ophthalmic/local-regional-anesthesia-ophthalmic-surgery/. [Accessed 7 April 2019].
[19] Bovim G, Sand T. Cervicogenic headache, migraine without aura and tension-type headache. Diagnostic blockade of greater occipital and supra-orbital nerves. Pain 1992;51:43–8. https://doi.org/10.1016/0304-3959(92)90007-X.
[20] Naja ZM, El-Rajab M, Al-Tannir MA, et al. Repetitive occipital nerve blockade for cervicogenic headache: expanded case report of 47 adults. Pain Pract 2006;6:278–84. https://doi.org/10.1111/j.1533-2500.2006.00096.x.
[21] Greher M, Moriggl B, Curatolo M, et al. Sonographic visualization and ultrasound-guided blockade of the greater occipital nerve: a comparison of two selective techniques confirmed by anatomical dissection. Br J Anaesth 2010;104:637–42. https://doi.org/10.1093/bja/aeq052.
*[22] Visoiu M. Paediatric regional anaesthesia: a current perspective. Curr Opin Anaesthesiol 2015;28:577–82. https://doi.org/10.1097/ACO.0000000000000238.
[23] Bhalla T, Sawardekar A, Dewhirst E, et al. Ultrasound-guided trunk and core blocks in infants and children. J Anesth 2013;27:109–23. https://doi.org/10.1007/s00540-012-1476-5.
[24] Hong J-Y, Kim WO, Koo BN, et al. The relative position of ilioinguinal and iliohypogastric nerves in different age groups of pediatric patients. Acta Anaesthesiol Scand 2010;54:566–70. https://doi.org/10.1111/j.1399-6576.2010.02226.x.
[25] Hubbell III PJ. Chapter 59: Ilioinguinal and Iliohypogastric Nerve Blocks. In: Diwan Sudhir, Staats Peter S, editors. Atlas of Pain Medicine Procedures Copyright © 2015 by McGraw-Hill Education.
*[26] Karan D, Swaro S, Mahapatra PR, et al. Effect of dexmedetomidine as an adjuvant to ropivacaine in ilioinguinal-iliohypogastric nerve blocks for inguinal hernia repair in pediatric patients: a randomized, double-blind, control trial. Anesth Essays Res 2018;12:924–9. https://doi.org/10.4103/aer.AER_169_18.
*[27] Relland LM, Tobias JD, Martin D, et al. Ultrasound-guided rectus sheath block, caudal analgesia, or surgical site infiltration for pediatric umbilical herniorrhaphy: a prospective, double-blinded, randomized comparison of three regional anesthetic techniques. J Pain Res 2017;10:2629–34. https://doi.org/10.2147/JPR.S144259.
[28] Guay J, Suresh S, Kopp S. The use of ultrasound guidance for perioperative neuraxial and peripheral nerve blocks in children. Anesth Analg 2017;124:948–58. https://doi.org/10.1213/ANE.0000000000001363.
[29] Marhofer P, Sitzwohl C, Greher M, et al. Ultrasound guidance for infraclavicular brachial plexus anaesthesia in children. Anaesthesia 2004;59:642–6. https://doi.org/10.1111/j.1365-2044.2004.03669.x.
[30] Khan ZH, Karvandian K, Zanjani AP, et al. Archives of anesthesiology and critical care, 3. Tehran University of Medical Sciences, Department of Anesthesiology and Critical Care; 2017.
*[31] Suresh S, Ecoffey C, Bosenberg A, et al. The European society of regional anaesthesia and pain therapy/American society of regional anesthesia and pain medicine recommendations on local anesthetics and adjuvants dosage in pediatric regional anesthesia. Reg Anesth Pain Med 2018;1. https://doi.org/10.1097/AAP.0000000000000702.
[32] Lam DKM, Corry GN, Tsui BCH. Evidence for the use of ultrasound imaging in pediatric regional anesthesia: a systematic review. Reg Anesth Pain Med 2016;41:229–41. https://doi.org/10.1097/AAP.0000000000000208.
[33] Fredrickson M. Ultrasound-assisted interscalene catheter placement in a child: EBSCOhost. Anaesth Intensive Care 2007;807–8.

*[34] Cote CJ, Lerman J, Anderson B. A Practice of anesthesia for infants and children. 2019. p. 988–1022.
[35] Baker MD, Gullett JP. Ultrasound-guided femoral nerve blocks. Pediatr Emerg Care 2015;31:864–8. https://doi.org/10.1097/PEC.0000000000000634.
[36] New York School of Regional Anesthesia. Femoral nerve block - landmarks and nerve stimulator technique - NYSORA. https://www.nysora.com/techniques/lower-extremity/femoral/femoral-nerve-block/.
[37] Turner AL, Stevenson MD, Cross KP. Impact of ultrasound-guided femoral nerve blocks in the pediatric emergency department. Pediatr Emerg Care 2014;30:227–9. https://doi.org/10.1097/PEC.0000000000000101.
[38] Dalens B. Lower extremity nerve blocks in pediatric patients. 2003. https://doi.org/10.1053/trap.2003.123520.
[39] Ganesh A, Gurnaney HG. Ultrasound guidance for pediatric peripheral nerve blockade peripheral nerve block pediatric ultrasound guidance regional anesthesia post operative analgesia. Anesthesiol Clin 2009;27:197–212. https://doi.org/10.1016/j.anclin.2009.06.001.
*[40] Tsui BCH. Epidural and caudal anesthesia. Pediatr. Atlas ultrasound- nerve stimul. Reg. Anesth.. New York, NY: Springer New York; 2016. p. 495–525. https://doi.org/10.1007/978-0-387-79964-3_33.
[41] Wiegele M, Marhofer P, Lönnqvist P-A. Caudal epidural blocks in paediatric patients: a review and practical considerations. Br J Anaesth 2019. https://doi.org/10.1016/J.BJA.2018.11.030.
[42] Priolkar S. Efficacy and safety of clonidine as an adjuvant to bupivacaine for caudal analgesia in paediatric infra-umbilical surgeries. J Clin DIAGNOSTIC Res 2016. https://doi.org/10.7860/JCDR/2016/19404.8491.
[43] Kamal M, Mohammed S, Meena S, et al. Efficacy of dexmedetomidine as an adjuvant to ropivacaine in pediatric caudal epidural block. Saudi J Anaesth 2016;10:384. https://doi.org/10.4103/1658-354X.177325.
*[44] Abdel Aziz M, Abdelfatah A, Abdel Hamid H. Ultrasound-guided caudal analgesia using fentanyl versus dexmedetomidine as an adjuvant for levobupivacaine in infraumbilical pediatric surgeries. Ain-shams J Anaesthesiol 2016;9:542. https://doi.org/10.4103/1687-7934.198267.
*[45] Trifa M, Tumin D, Tobias JD. Dexmedetomidine as an adjunct for caudal anesthesia and analgesia in children. Minerva Anestesiol 2018;84:836–47. https://doi.org/10.23736/S0375-9393.18.12523-5.
[46] Moore JM. Continuous spinal anesthesia. Am J Ther 2009;16:289–94. https://doi.org/10.1097/MJT.0b013e3181729d2a.
[47] Polaner DM, Taenzer AH, Walker BJ, et al. Pediatric Regional Anesthesia Network (PRAN): a multi-institutional study of the use and incidence of complications of pediatric regional anesthesia. Anesth Analg 2012;115:1353–64. https://doi.org/10.1213/ANE.0b013e31825d9f4b.
[48] NYSORA. Thoracic and lumbar paravertebral block - landmarks and nerve stimulator technique. https://www.nysora.com/regional-anesthesia-for-specific-surgical-procedures/abdomen/thoracic-lumbar-paravertebral-block/.