

The European Society of Regional Anaesthesia and Pain Therapy and the American Society of Regional Anesthesia and Pain Medicine Joint Committee Practice Advisory on Controversial Topics in Pediatric Regional Anesthesia

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Background and Objectives: Some topics in the clinical management of regional anesthesia in children remain controversial. To evaluate and come to a consensus regarding some of these topics, The European Society of Regional Anesthesia and Pain Therapy (ESRA) and the American Society of Regional Anesthesia and Pain Medicine (ASRA) developed a joint committee practice advisory on pediatric regional anesthesia (PRA).

Methods: Representatives from both ASRA and ESRA comprised the joint committee practice advisory on PRA. Evidence-based recommendations were based on a systematic search of the literature. In cases where no literature was available, expert opinion was elicited. Experts selected controversial topics in PRA.

Results: The performance of PRA under general anesthesia or deep sedation is associated with acceptable safety and should be viewed as the standard of care (Evidence B2 and Evidence B3). Because of the difficulty interpreting a negative test dose, the use of test dosing should remain discretionary (Evidence B4). The use of either air–loss of resistance or saline–loss of resistance techniques is supported by expert opinion, but the literature supporting one technique over the other is sparse and controversial; when used appropriately, each technique may be safely used in children. There are no current evidence-based data that the use of RA increases the risk for acute compartment syndrome or delays its diagnosis in children.

Conclusions: High-level evidence is not yet available for the topics evaluated, and most recommendations are based on Evidence B studies. The ESRA/ASRA recommendations intend to provide guidance for the safe practice of regional anesthesia in children.

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The American Society of Regional Anesthesia and Pain Medicine (ASRA) and the European Society of Regional Anaesthesia and Pain Therapy (ESRA) are the primary societies for regional anesthesia in the world, and one of their goals is to create recommendations/guidelines through the collaboration of their experts.

The first result was in 2009, the publication of “The American Society of Regional Anesthesia and Pain Medicine and the European Society of Regional Anesthesia and Pain Therapy Joint Committee Recommendations for Education and Training on Ultrasound-Guided Regional Anesthesia.”¹

The 2 societies worked again together to create The European Society of Regional Anesthesia and Pain Therapy and the American Society of Regional Anesthesia and Pain Medicine Joint Committee Practice Advisory on Pediatric Regional Anesthesia (PRA). Experts from both societies discussed important and controversial topics in PRA and provide guidance, wherever possible, from an evidence-based perspective and on the basis of expert opinion when conclusive evidence is lacking in the literature. Four topics were selected by participant consensus according to the current main areas of PRA controversy: 1) the performance of regional nerve blocks under deep sedation (DS) or GA, 2) the value of a test dose, 3) the use of air versus normal saline for loss of resistance (LOR) for epidural space detection, and 4) regional anesthesia and the risk of obscuring compartment syndromes.

We are unaware of any previous practice advisories that specifically addressed controversial topics in PRA. The ASRA and the ESRA hope that this article will be useful not only to those who work every day in pediatric hospitals but also to all anesthesiologists who care for children less frequently. In addition, we intend to provide guidance and reflection on current controversial clinical issues in PRA practice.

METHODS

Representatives from both ASRA and ESRA comprised the joint committee practice advisory on PRA. Committee members met in workgroups, and decisions on topics to be addressed were made through consensus. The committee used similar methodology on the generation of practice advisories previously described by the American and European anesthesiology societies.^{2,3} In brief, an evaluation of availability and strength of the evidence was systematically performed. Scientific evidence was obtained by performing a systematic search of literature. All committee members participated in the expert opinion decisions because all involved have had extensive experience (>20 years) on the topic. No other clinician outside of the committee was consulted.

Published reports evaluating the practice of RA for pediatric patients were searched using the National Library of Medicine's

PubMed database, the Cochrane Database of Systematic Reviews, and Google Scholar inclusive to December 9, 2014. Free text and MeSH terms “block,” “regional,” “children,” “surgery,” “anesthesia,” “local,” and “pediatric” were used individually and in various combinations. No language restriction was used. No date limit was used. The search was limited to articles in subjects younger than 18 years. We reviewed the reference lists from identified studies to identify additional studies not found during our primary search. No search was performed for unpublished studies. The scientific evidence was classified according to the quality of research design as presented in Table 1, similar to what has been previously described in other practice advisories.^{2,3}

When the literature search revealed a lack of published studies or when the only evidence was generated from studies with insufficient quality because of methodological constraints, it was deemed as “insufficient literature” and expert opinion from the ESRA/ASRA joint committee was considered.

RESULTS

Performance of Regional Anesthesia Under General Anesthesia or DS

Soon after the first description by August Bier of spinal anesthesia in 1898, this regional anesthesia technique became popular for use in children on both sides of the Atlantic Ocean.^{4,5} This was later followed by the seminal publication by Campbell in 1933, which reported the use of caudal blockade for pediatric urologic procedures.⁶ However, with the many advances in the development of general anesthesia (GA) between 1940 and 1960, PRA was used only in a few specialized centers until the 1980s.

At that time, a resurgence of interest in PRA took place, perhaps best exemplified by the description of epidural anesthesia in pediatric patients by Ecoffey et al⁷ and Murat et al.⁸ Epidural anesthesia rapidly became a common modality of regional anesthesia in infants and children and was most often performed under GA. A case report of a devastating neurological complication resulting from multiple attempts at a thoracic epidural blockade performed under GA in an adult, however, provoked controversy about the safety of this practice in children.⁹ The contention was based on the supposition that improper needle placement could be detected in the awake patient by paresthesia, pain on injection, or unexpected motor responses—warning signs that would not be detectable under GA or DS (GA/DS) in children. This concern was further increased by a European publication describing serious complications after attempted epidural block placement under GA in 4 pediatric patients.¹⁰

TABLE 1. Classification of Scientific Evidence

Evidence Class	Study Design
Category A1	Sufficient number of randomized controlled trials to conduct a meta-analysis
Category A2	Several randomized controlled trial but not sufficient to conduct
Category A3	Single randomized controlled trial
Category B1	Observational comparisons between clinical interventions for a specific outcome
Category B2	Observational studies with associative statistics
Category B3	Noncomparative observational studies with descriptive statistics
Category B4	Case reports

In response to those concerns, thought leaders in pediatric anesthesiology opined that it was safe and consistently stated that it was acceptable care to perform PRA under GA/DS in children.^{11,12} Nevertheless, objective data were lacking, and the discussion about the safety of PRA during GA/DS was largely based on opinion and anecdote.¹² A 2008 ASRA practice advisory guideline acknowledged the need for performance of regional blockade under GA or DS in children.¹³

Current Evidence Base for the Safety of PRA Performed During GA/DS

Apart from reports of single-center experiences with regard to PRA,^{14,15} there are currently 4 major large-scale (>10,000 patients per study) multicenter studies available that specifically have focused on the incidence of complications after PRA.^{16–19} A summary of these seminal studies is provided below. None of the studies reported any cases of paralysis after the use of neuraxial anesthesia/analgesia, leading to an incidence (95% confidence interval [95% CI]) of 0 (0%–0.004%) for paralysis.

The first large-scale effort focused on the complications associated with the use of PRA was published by the French-Language Society of Paediatric Anaesthesiologists (ADARPEF) in 1996.¹⁶ At the 38 participating centers, all use of regional anesthesia was prospectively registered during 1 year (May 1993–April 1994), with a special focus on safety issues. There were 24,409 regional anesthetics included in the study, of which 89% were performed under GA. Neuraxial blocks were the most common; caudal blockade was by far the most common individual block performed. Peripheral blocks and local anesthesia techniques were used in only 38% of the registered cases. The overall complication rate was found to be very low (0.9 per 1000 blocks), but neuraxial blocks were found to have a higher complication rate compared with peripheral techniques (1.5 and 0 per 1000 blocks, respectively). None of the observed complications resulted in long-term disability or medicolegal action (follow-up period of 12 months) (Evidence B2).

The second large-scale effort focused on the complications associated with the use of PRA was conducted by the 2007 UK Prospective National Pediatric Epidural Audit.¹⁷ To quantify the risk associated with the use of pediatric epidural analgesia, the Association of Paediatric Anaesthetists of Great Britain & Ireland undertook a prospective audit within its membership, with the aim to include 10,000 epidural infusions. The audit was performed from 2001 to 2005. If an individual patient complication was recorded, a more detailed 12-month follow-up was undertaken. An expert panel adjudicated complications and graded the severity. A total of 10,633 epidurals in all pediatric age groups were included in the study. All but one were placed under GA. Overall, 96 incidents were reported, with the large majority being classified as minor (1:189). Only 5 incidents were recorded as serious (1 of 2000) and an additional 9 as major (1:1100). One child, who had a drug infusion error, experienced persistent paresthesia still present at the 12-month follow-up (1:10,000). Four patients developed compartment syndrome, but the expert panel judged that there was no delay in diagnosis because of the epidural infusion (Evidence B3).

The third large-scale effort focused on the complications associated with the use of PRA was the 2010 ADARPEF study.¹⁸ In this prospective 1-year study (November 2005–October 2006) including 47 different institutions, a total of 29,870 regional blocks were performed under GA and 1262 regional blocks without concomitant GA. Compared with the earlier ADARPEF study, peripheral nerve blocks were used with increasing frequency (66% peripheral vs 34% neuraxial). However, in children younger than

3 years, the use of neuraxial and peripheral blocks was similar, whereas, in older children, peripheral nerve blocks were performed 4 times more frequently than neuraxial blocks. The authors did not analyze differences in complications under GA/DS. Only 41 complications were recorded in this study (1.2:1000), and none resulted in long-term sequelae. Similar to the 1996 ADARPEF study, neuraxial blocks were associated with a 6-fold higher incidence of complications (Evidence B3).

The fourth large-scale effort focused on the complications associated with the use of PRA was the 2014 Pediatric Regional Anesthesia Network (PRAN) report.¹⁹ To allow for prospective and continuous audit of practice trends as well as the incidence of complications, 6 academic centers in the United States pioneered an Internet-based PRAN database in 2006.²⁰ They reported on 53,564 cases of PRA prospectively collected between 2007 and 2012.¹⁹ They were able to demonstrate that performing a PRA under GA (with or without neuromuscular blockade [NB]) did not increase the risk of immediate or late complications. The incidence of neurological complications (all of which were minor with 1 exception that resolved) in patients under GA without NB was lower than that seen in any other group: 0.62 of 1000 (CI 0.4–0.92) compared with 2.4 of 1000 (CI, 1.6–3.6) in patients under GA with NB, 8.3 of 1000 (4.9–13.3) in sedated and 3.4 of 1000 (CI, 0.7–10.0) in awake patients (Evidence B2). Pediatric regional anesthesia was performed in awake patients most commonly in neonates and infants younger than 6 months ($n = 290$) and teenagers ($n = 515$); those in which sedation was used included mainly teenagers ($n = 2060$).

Cautionary Case Reports

A strong evidence base exists supporting the safety of PRA performed under GA/DS. However, this does not ensure that serious complications cannot occur under certain circumstances. Thus, if PRA is performed with the wrong type of equipment or without basic safety precautions, if the operator has insufficient training and/or skills, or if PRA is used in particularly vulnerable patient categories, serious complications may still occur, a fact that may be especially true in association with the use of epidural blockade.^{21–24} Furthermore, there is always a risk of rare complications, often of obscure or unknown etiology, that are unrelated to operator expertise and will not be an adequately identified event in large-scale studies²⁵ (Evidence B4).

Evidence-Based Conclusions and Clinical Advice

- The performance of PRA under GA/DS is associated with acceptable safety and should be viewed as the standard of care (Evidence B2 and Evidence B3).
- The overall risk for complications is 0.66% (95% CI, 0.6%–0.7%), whereas the risk of paralysis is estimated at 0 (95% CI, 0%–0.004%) (Evidence B2 and Evidence B3).
- Despite the reassuring safety of PRA performed under GA/DS, serious complications may still occur. In the event of an unexpected clinical outcome, especially unanticipated motor blockade during continuous postoperative regional block after the use of PRA, a high index of suspicion for neurological injury is warranted and appropriate diagnostic and therapeutic measures must be performed without delay (Evidence B4).

Test Dose and Intravascular Injection

Because differences exist in both the physiological and clinical conditions under which regional anesthetics are administered in children compared with adults, there is considerable controversy and disparity of practice regarding the use of local anesthetic

(LA) test doses in children. The epinephrine-containing test dose initially was designed to be used in awake adults who were not receiving β -blocking agents to detect accidental intravascular injection during epidural anesthesia.²⁶ In an awake adult, the injection of 3 mL of an LA solution containing 15 μ g epinephrine produces hemodynamic effects (mainly tachycardia) if injected intravascularly. Most children, however, have their regional blocks placed while under GA/DS, making the recognition of accidental intravascular injection of LA with epinephrine more difficult.

To detect accidental intravascular injection of an LA solution in children, some practitioners add epinephrine to the LA solution at a concentration of 2.5 or 5 μ g/mL, a concentration of 1/400,000 or 1/200,000, respectively. However, a small child's increased resting heart rate, combined with the fact that most regional blocks are performed under GA/DS, means that the utility and accuracy of test dosing remain a matter of controversy among pediatric anesthesiologists.

The volume of a pediatric test dose was empirically defined as a volume of 0.1 mL/kg of an LA solution containing 5 μ g/mL of epinephrine, that is, a dose of 0.5 μ g/kg epinephrine.²⁷ This was thought to be sufficient to induce an easily detectable hemodynamic change but also small enough to avoid complications and is supported by a dose-response study.²⁸

Incidence of Accidental Intravenous Injection of LA During Regional Anesthesia in Children

In the first prospective study of ADARPEF, 6 of the 25 complications observed were caused by the accidental intravascular injection of the LA¹⁶ (Evidence B3). The second ADARPEF study reported 15 cases of LA toxicity, of which 6 had a negative test dose¹⁸ (Evidence B3). In a prospective study of 1100 caudal blocks, the incidence of unintentional vascular puncture was 6.9% and 8 (0.7%) accidental intravascular (IV) injections, all occurring in infants weighing less than 10 kg, were observed²⁹ (Evidence B4).

In another prospective study including 742 epidural caudal or lumbar blocks, a 5.6% incidence of unintentional vascular injections was observed. In addition, in 12 cases out of 36, aspiration for blood had been negative before the injection of the epinephrine-containing LA³⁰ (Evidence B3). In an audited cohort from the PRAN database composed of a total of 26,949 blocks using a test dose, there was a 0.21% incidence of positive test doses, almost all of which occurred during caudal or epidural placement²⁰ (Evidence B3). There were no positive test doses in other blocks, with the exception of 1 single-injection truncal block, although test doses were less frequently used in non-neuraxial blocks when ultrasound guidance was used.

All the aforementioned studies attested to the importance of dose calculation and staying below the maximum recommended LA dose to avoid complications related to LA toxicity.

Possible Interfering Factors Specific to Efficacy of the Test Dose in Children

One of the main problems is interpreting the hemodynamic response induced by an IV injection of LA mixed with a small dose of epinephrine.^{31,32} The following factors have been demonstrated or theorized to alter the reliability of a test dose: 1) the general anesthetic agent used and its dose at the time of injection of the test dose; 2) a higher basal heart rate in infants and small children; 3) a possible age-dependent variation of the reactivity of the cardiovascular system to epinephrine; 4) the premedication received; 5) the LA used; and 6) the GA technique used.^{32–36}

In children under sevoflurane anesthesia, the IV injection of 0.1 mL/kg of an LA solution containing 5 or 2.5 μ g/mL epinephrine produces (Evidence B3):

1) An early modification (within 20–40 seconds) of the T wave morphology on the electrocardiogram (ECG): the increase in T wave amplitude is more pronounced in younger children.²⁸ In older children, adolescents, and adults, inversion of the T wave is observed.³⁵ These modifications are best observed in leads I, II, III, or V5 on the ECG.³⁷ The pathophysiology of this modification of the T wave is unknown: it can be observed after the accidental IV injection of a large dose of a mixture of lidocaine and bupivacaine without epinephrine but also when a small dose of epinephrine is injected IV without any LA.³⁸

2) A change in heart rate: this is most often manifested as a heart rate increase of more than 10 beats/min observed somewhat later than the T wave changes. However, bradycardia or other dysrhythmias may be observed, too, and about 25% of patients may not demonstrate any change in rate.

3) A transient increase in systolic blood pressure: this can be missed during intermittent noninvasive measurement of blood pressure, as is usually the case in routine pediatric anesthesia cases.

4) In children receiving GA with propofol and remifentanyl-based total intravenous anesthesia, the T wave amplitude changes are highly inconsistent—elevation is seen in only 25% of cases, whereas no change or depression is seen equally in the remainder.³⁹ Other hemodynamic criteria need thus to be defined in this context. Diastolic blood pressure elevation, measured between 1 and 2 minutes after injection, was reported to be a highly sensitive indicator and was observed in all cases studied.

Evidence-Based Conclusions and Clinical Advice

- Because of the difficulty interpreting a negative test dose, the use of test dosing should remain discretionary. In clinical practice, if a test dose is used, there may be false-negative results, especially when the test dose is only partially administered intravenously or when the general anesthetic agents can blunt the hemodynamic effects of epinephrine. A negative result after the injection of a test dose therefore is reassuring but does not rule out vascular placement of needle or catheter. Any injection of an LA solution should be performed slowly, in small aliquots (0.1–0.2 mL/kg) and with intermittent aspiration and observation of the ECG tracing (Evidence B4).
- In all experimental studies using the deliberate IV injection of an LA solution containing epinephrine to model accidental IV injection, no false-positive results were observed: any modification of the T wave or of the heart rate within 30 to 90 seconds after the injection of a test dose should thus be interpreted as an accidental IV injection until disproven (Evidence B3).
- Imaging modalities (ultrasound, fluoroscopy) may help to avoid or visualize accidental intravascular needle placement in peripheral blocks, but data are lacking in PRA to determine the value of these techniques (expert opinion).^{40,41}

Loss of Resistance

Despite the introduction of ultrasound guidance as a complement to regular LOR, the traditional LOR techniques using air or saline still remain the most widely used techniques for detecting needle placement in the epidural space.^{42,43}

In 1995, a case series was published reporting a serious complication after the use of air-LOR in children, which immediately triggered an intense discussion regarding whether saline-LOR is a safer option and therefore should be the only recommended technique¹⁰ (Evidence B4). This discussion has since been ongoing and has divided the pediatric anesthesia community into 2 camps,

those in favor of saline-LOR and those who prefer to use air-LOR. Recently, a third option has been advocated as a “compromise”—use of a combination of air and saline.⁴⁴

Air-LOR

Several complications related to the air-LOR technique have been published (nerve root compression, pneumocephalus, incomplete analgesia, and venous air embolism)^{8,10,45–48} (Evidence B4). However, all these complications were associated with the total amount of air injected (eg, multiple attempts, large injection volume). Thus, expert consensus is that the amount of air in the syringe should be limited to a maximum of 0.5 to 1 mL and used only to detect the change of resistance, releasing the pressure on the plunger immediately on entry into the epidural space. Restricting the volume of air that is/can be injected will on theoretical grounds substantially limit the risk for any air-related complications. The use of air-LOR is currently the preferred choice in some countries.⁴⁹

Other gases have been tried as alternatives to air for LOR. From a theoretical point of view, CO₂ may offer some theoretical advantages.⁵⁰ Carbon dioxide is extremely soluble in blood and therefore will mitigate the risk of air embolism; in addition, CO₂ may possess bactericidal properties. However, the availability of CO₂ is limited in most operating rooms and may therefore be an impractical alternative as compared with either air or saline.

Saline-LOR

The use of saline avoids most of the issues related to the use of air. However, as with air, it is essential to limit the volume of the injectate because excessive amounts of saline may dilute subsequently injected LA, may make the identification of unintentional dural puncture more difficult, and can together with the volume of LAs cause transient reduction in cerebral blood flow in small infants.⁵¹ Despite these issues associated with the use of saline-LOR, the exclusive use of saline has been recommended by some experts and has become the general practice in some countries.^{52,53}

Air/Saline-LOR

One publication involving 500 pediatric epidural blocks described the use of saline with a bubble of air in the syringe⁴⁴ (Evidence B3). This was reported to permit easy detection of the epidural space with a lower incidence of dural puncture (0.5%) than what has been reported for exclusive use of air or saline.⁵⁰

Evidence-Based Conclusions and Clinical Advice

- The use of either air-LOR and saline-LOR techniques are supported by different international experts, and the literature supporting 1 technique over the other is sparse; as long as either technique is used appropriately, each may be safely used in infants and children. The combination of air and saline may represent a better alternative that will minimize the risk of injecting air and reduce the volume of saline injected. This method is also associated with a low risk for unintentional dural puncture (expert opinion).
- There are insufficient data in children to determine if using LOR to air or saline to detect needle entry into the epidural space will result in clinically significant differences regarding safety, accuracy, and subsequent efficacy of the injected LA (Evidence B3 and Evidence B4). Thus, both the aforementioned alternatives are acceptable if care is taken to keep the injected volume at a minimum.

- In neonates and infants, the volume of air contained in the syringe should be limited to less than 1 mL and air injections should not be repeated if multiple attempts are made to enter the epidural space (expert opinion).
- Although the committee recognizes that an air embolism with hemodynamic consequences is rare when LOR-air is used, enough evidence is lacking regarding the brain safety even for small amounts of air in the presence of a right-to-left cardiac shunt.

Compartment Syndrome

Acute compartment syndrome (ACS) of a limb is caused by high pressure in the closed noncompliant muscle compartment, which leads to compromised circulation, ischemia, and, if unrecognized, to motor and sensory impairment, neuronal death, and myonecrosis.⁵³ Therefore, the time to diagnosis of ACS is essential because a delay in treatment of more than 4 hours can lead to irreversible limb damage and possible limb loss.

Both adults and children develop this syndrome, which is generally associated with trauma, fracture with subsequent casting, prolonged malpositioning during surgery, or ischemia-reperfusion injury.⁵⁴⁻⁶¹ External or internal compression creates excessive pressure in a closed fascial compartment and leads to excruciating pain that cannot be ascribed to the trauma or surgery. A compartment pressure greater than 30 mmHg is the commonly accepted trigger for emergency intervention.⁶²

The hypothesis that RA delays diagnosis and treatment of ACS is one that continues to generate debate. Only isolated case reports describe this event, and any evidence-based conclusion is difficult. Moreover, in children, especially in preverbal or nonverbal children, the recognition of ACS is more difficult because of its unreliable warning signs (Evidence B4). Furthermore, several case reports suggest that breakthrough pain in a patient with a previously well-functioning continuous block may be an early warning sign of ACS and enhance its detection if caregivers are vigilant (Evidence B4).

Epidural infusions and peripheral single-dose and continuous LA infusions have been stated to be responsible for delayed diagnosis in children, but without convincing evidence of causation⁶³⁻⁶⁵ (Evidence B4). In many cases, the main root cause was not caused by the regional anesthetic technique but because of inadequate observation or to surgical malposition of the patient. Kanj and colleagues,⁶⁶ evaluating 23 children undergoing fasciotomy for ACS of the upper limb, showed that pain and swelling were the main symptoms of excessively high compartment pressure (>30 mmHg) in all but 2 patients, and that diagnosis in children is difficult and “associated with a prolonged clinical time course” (Evidence B4).

Johnson et al⁶⁷ reviewed 12 pediatric cases of ACS associated with epidural analgesia reported in the literature. They identified the following clinical signs for impending compartment syndrome in the lower limbs (Evidence B4): 1) increasing pain with increasing need for analgesics, 2) pain remote to the site of surgery, 3) paresthesia that is not attributable to analgesia technique, 4) signs of reduced perfusion of the painful site, 5) local swelling, and 6) pain on passive movement of the limb. Mar et al,⁶⁸ correlating ACS and type of analgesia (opioids or regional anesthetics), concluded that “There is no convincing evidence that patient-controlled analgesia, opioids, or regional analgesia delays the diagnosis of compartment syndrome provided that patients are adequately monitored. Regardless of the type of analgesia used, a high index of clinical suspicion, ongoing assessment of patients, and compartment pressure measurement are essential for early diagnosis.”

Evidence-Based Conclusions and Clinical Advice

- There is no current evidence that the use of regional anesthetics increases the risk for ACS or delays its diagnosis in children.
- A comprehensive preoperative discussion with the patient’s family and the surgical team should be performed to inform them of this rare but serious complication.
- As with many controversies linked to PRA, it is almost impossible to give unequivocal statements or recommendations. We suggest the following “best practice rules” to reduce or avoid the risk of compartment syndrome in children undergoing surgery with perioperative PRA: 1) single shot for both peripheral and neuraxial blocks: use 0.1% to 0.25% bupivacaine, levobupivacaine, or ropivacaine concentrations because they are less likely to mask ischemic pain and/or produce muscle weakness than more concentrated solutions (Evidence B4); 2) for continuous infusions, bupivacaine, levobupivacaine, or ropivacaine concentrations should be limited up to 0.1%; 3) in cases of patients having tibial compartment surgery or other high-risk surgeries for compartment syndrome, restricting both volume and concentration in sciatic catheters is advisable; 4) the use of LA additives should be with caution because they can increase the duration and/or density of the block; 5) high-risk patients should have appropriate follow-up by acute pain services to allow early detection of potential signs and symptoms; and 6) if ACS is suspected, compartment pressure measurements should be urgently assessed.

CONCLUSIONS

Notwithstanding the evidence of the value, safety, and efficacy of PRA, some aspects of it remain controversial. The ASRA and the ESRA have worked together on the main controversies and present their conclusions. High-level evidence is not yet available for these controversies, and most recommendations are based on Evidence B-level studies.

A practice advisory based on consensus should only be considered within its inherent limitations. First, it may become obsolete as new information becomes available from future studies. It is, therefore, likely that this practice advisory will need to be reviewed and updated periodically. It is possible that anesthesiologists practicing PRA may encounter system and individual barriers to implement the proposed recommendations. Nevertheless, the ESRA/ASRA joint commission hopes that barriers to implementation will be overcome with the publication of this international practice advisory.

REFERENCES

1. Sites B, Chan V, Neal J, Grau T, Koscielnak-Nielsen Z, Ivani G. The American Society of Regional Anesthesia (ASRA) and the European Society of Regional Anesthesia (ESRA) Joint Committee: recommendations for Education and Training in Ultrasound Guided Regional Anesthesia. *Reg Anesth Pain Med.* 2009;1:40-46.
2. Apfelbaum JL, Caplan RA, Barker SJ, et al. American Society of Anesthesiologists Task Force on Operating Room Fires. Practice advisory for the prevention and management of operating room fires: an updated report by the American Society of Anesthesiologists Task Force on Operating Room Fires. *Anesthesiology.* 2013;118:271-290.
3. Kozek-Langenecker SA, Afshari A, Albaladejo P, et al. Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology. *Eur J Anaesthesiol.* 2013;30:270-382.
4. Gray HT. A study of spinal anaesthesia in children and infants. *Lancet.* 1909;174:913-917.
5. Farr R. Local anaesthesia in infancy and childhood. *Arch Pediatr.* 1920;37:381-383.

6. Campbell M. Caudal anesthesia in children. *Am J Urol.* 1933;30:245–249.
7. Ecoffey C, Dubousset AM, Samii K. Lumbar and thoracic epidural anesthesia for urologic and upper abdominal surgery in infants and children. *Anesthesiology.* 1986;65:87–90.
8. Murat I, Delleur MM, Esteve C, Egu JF, Raynaud P, Saint-Maurice C. Continuous extradural anaesthesia in children. Clinical and haemodynamic implications. *Br J Anaesth.* 1987;59:1441–1450.
9. Bromage PR, Benumof JL. Paraplegia following intracord injection during attempted epidural anesthesia under general anesthesia. *Reg Anesth.* 1998;23:104–107.
10. Flandin-Bléty C, Barrier G. Accidents following extradural analgesia in children. The results of a retrospective study. *Paediatr Anaesth.* 1995;5: 41–46.
11. Krane EJ, Dalens BJ, Murat I, Murrell D. The safety of epidurals placed during general anesthesia. *Reg Anesth Pain Med.* 1998;23:433–438.
12. Bosenberg AT, Ivani G. Regional anaesthesia—children are different. Editorial. *Paediatr Anaesth.* 1998;8:447–450.
13. Bernards CM, Hadzic A, Suresh S, Neal JM. Regional anesthesia in anesthetized or heavily sedated patients. *Reg Anesth Pain Med.* 2008;5: 449–460.
14. Ivani G, Conio A, Papurel G, Ciliberto F, Vitale P. 1,000 consecutive blocks in a children's hospital: How to manage them safely. *Reg Anesth Pain Med.* 2001;26:93–94.
15. Rochette A, Dadure C, Raux O, Troncin R, Mailhé P, Capdevila X. A review of pediatric regional anesthesia practice during a 17-year period in a single institution. *Paediatr Anaesth.* 2007;17:874–880.
16. 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;83:904–912.
17. Llewellyn N, Moriarty A. The national pediatric epidural audit. *Paediatr Anaesth.* 2007;17:520–533.
18. Ecoffey C, Lacroix F, Giaufré E, Orliaguet G, Courrèges P. Association des Anesthésistes Réanimateurs Pédiatriques d'Expression Française (ADARPEF). Epidemiology and morbidity of regional anesthesia in children: a follow-up one-year prospective survey of the French-Language Society of Paediatric Anaesthesiologists (ADARPEF). *Paediatr Anaesth.* 2010;20:1061–1069.
19. Taenzer AH, Walker BJ, Bosenberg AT, et al. Asleep versus awake: does it matter? Pediatric regional block complications by patient state: a report from the Pediatric Regional Anesthesia Network. *Reg Anesth Pain Med.* 2014;39:279–283.
20. 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: 1353–1364.
21. Kasai T, Yaegashi K, Hirose M, Tanaka Y. Spinal cord injury in a child caused by an accidental dural puncture with a single-shot thoracic epidural needle. *Anesth Analg.* 2003;96:65–67.
22. Rose JB. Spinal cord injury in a child after single-shot epidural anesthesia. *Anesth Analg.* 2003;96:3–6.
23. Aldrete JA, Ferrari H. Myelopathy with syringomyelia following thoracic epidural anaesthesia. *Anaesth Intensive Care.* 2004;32:100–103.
24. Meyer MJ, Krane EJ, Goldschneider KR, Klein NJ. Case report: neurological complications associated with epidural analgesia in children: a report of 4 cases of ambiguous etiologies. *Anesth Analg.* 2012;115: 1365–1370.
25. Alnaami I, Lam FC, Steel G, et al. Arteriovenous fistula and pseudoaneurysm of the anterior spinal artery caused by an epidural needle in a 5-year-old patient. *J Neurosurg Pediatr.* 2013;11:340–345.
26. Moore DC, Batra MS. The components of an effective test dose prior to epidural block. *Anesthesiology.* 1981;55:693–696.
27. Desparmet J, Mateo L, Ecoffey C, Mazoit X. Efficacy of an epidural test dose in children anaesthetized with halothane. *Anesthesiology.* 1990;72: 249–251.
28. Tanaka M, Nishikawa T. Evaluating T-wave amplitude as a guide for detecting intravascular injection of a test dose in anesthetized children. *Anesth Analg.* 1999;88:754–758.
29. Veyckemans F, Van Obbergh L, Gouverneur JM. Lessons from 1,100 caudal blocks in a teaching hospital. *Reg Anesth.* 1992;17:119–125.
30. Fisher QA, Shaffner DH, Yaster M. Detection of intravascular injection of regional anaesthetics in children. *Can J Anaesth.* 1997;44:592–598.
31. Tobias JD. Caudal epidural block: a review of test dosing and recognition of systemic injection in children. *Anesth Analg.* 2001;93:1156–1161.
32. Sethna NF, McGowan FX. Do results from studies of a simulated epidural test dose improve our ability to detect unintentional epidural vascular puncture in children? *Paediatr Anaesth.* 2005;15: 711–715.
33. Varghese E, Deepak KM, Chowdary KVR. Epinephrine test dose in children : is it interpretable on ECG monitor? *Paediatr Anaesth.* 2009;19: 1090–1095.
34. Shiga M, Nishina K, Mikawa K, Uesugi T, Maekawa N, Obara H. Oral clonidine premedication does not change efficacy of simulated epidural test dose in sevoflurane-anesthetized children. *Anesthesiology.* 2000;93: 954–958.
35. Kozek-Langenecker SA, Marhofer P, Jonas K, Macik T, Urak G, Semsroth M. Cardiovascular criteria for epidural test dosing in sevoflurane- and halothane- anesthetized children. *Anesth Analg.* 2000;90:579–583.
36. Sethna NF, Sullivan L, Retik A, McGowan FX, Di Canzio J, Zurakowski D. Efficacy of simulated epinephrine-containing epidural test-dose after intravenous atropine during isoflurane anesthesia in children. *Reg Anesth Pain Med.* 2000;25:566–572.
37. Osagawara K, Tanaka M, Nishikawa T. Choice of electrocardiography lead does not affect the usefulness of the T-wave criterion for detecting intravascular injection of an epinephrine test dose in anesthetized children. *Anesth Analg.* 2003;97:372–376.
38. Tanaka M, Nitta R, Nishikawa T. Increased T-wave amplitude after accidental intravascular injection of lidocaine plus bupivacaine without epinephrine in a sevoflurane-anesthetized child. *Anesth Analg.* 2001;92: 915–917.
39. Polaner DM, Zuk J, Luong K, Pan Z. Positive intravascular test dose criteria in children during total intravenous anesthesia and remifentanyl are different than during inhaled anesthesia. *Anesth Analg.* 2010;110:41–45.
40. Roberts SA, Guruswamy V, Galvez I. Caudal injectate can be reliably imaged using portable ultrasound—a preliminary study. *Paediatr Anaesth.* 2005;15:948–952.
41. Wang L-Z, Hu X-X, Zhang Y-F, Chang X-Y. A randomized comparison of caudal block by sacral hiatus injection under ultrasound guidance with traditional sacral canal injection in children. *Paediatr Anaesth.* 2013;23: 395–400.
42. Shenouda PE, Cunningham BJ. Assessing the superiority of saline versus air for use in the epidural loss of resistance technique: a literature review. *Reg Anesth Pain Med.* 2003;28:48–53.
43. Willschke H, Marhofer P, Bosenberg A, et al. Epidural catheter placement in children: comparing a novel approach using ultrasound guidance and a standard loss-of-resistance technique. *Br J Anaesth.* 2006;97:200–207.
44. Roelants F, Veyckemans F, Van Obbergh L, et al. Loss of resistance to saline with a bubble of air to identify the epidural space in infants and children: a prospective study. *Anesth Analg.* 2000;90:59–61.
45. Dalens B, Bazin JE, Haberer JP. Epidural bubbles as a cause of incomplete analgesia during epidural anesthesia. *Anesth Analg.* 1987;66:679–683.
46. Beilin Y, Arnold I, Telfeyan C, Bernstein HH, Hossain S. Quality of analgesia when air versus saline is used for identification of the epidural space in the parturient. *Reg Anesth Pain Med.* 2000;25:596–599.

47. Schwartz N, Eisenkraft JB. Probable venous air embolism during epidural placement in an infant. *Anesth Analg*. 1993;76:1136–1138.
48. Sethna NF, Berde CB. Venous air embolism during identification of the epidural space in children. *Anesth Analg*. 1993;76:925–927.
49. Busoni P, Messeri A. Loss of resistance technique to air for identifying the epidural space in infants and children. Use an appropriate technique! (Letter). *Paediatr Anaesth*. 1995;5:397.
50. Dalens B, Chrysostome Y. Intervertebral epidural anaesthesia in paediatric surgery: success rate and adverse effects in 650 consecutive procedures. *Paediatr Anaesth*. 1991;1:107–117.
51. Lundblad M, Forestier J, Marhofer D, Eksborg S, Winberg P, Lönqvist PA. Reduction of cerebral mean blood flow velocity and oxygenation after high-volume (1.5 mL kg⁻¹) caudal block in infants. *Br J Anaesth*. 2014; 113:688–694.
52. Russell R, Douglas J. Loss of resistance to saline is better than air for obstetric epidurals. *Int J Obstet Anesth*. 2001;10:302–306.
53. Ames WA, Hayes JA, Pétriz GC, Roy WL. Loss of resistance to normal saline is preferred to identify the epidural space: a survey of Canadian pediatric anesthesiologists. *Can J Anaesth*. 2005;52:607–612.
54. Walker BJ, Noonan KJ, Bosenberg AT. Evolving compartment syndrome not masked by a continuous peripheral nerve block. *Reg Anesth Pain Med*. 2012;3:393–397.
55. Erdos J, Dlaska C, Szatmary P. Acute compartment syndrome in children: a case series in 24 patients and review of the literature. *Int Orthop*. 2011; 35:569–575.
56. Paletta CE, Dehghan K. Compartment syndrome in children. *Ann Plast Surg*. 1994;2:141–144.
57. Ramos C, Whyte CM, Harris BH. Nontraumatic compartment syndrome of the extremities in children. *J Pediatr Surg*. 2006;41:5–7.
58. Moen TC, Sarwark JF. Compartment syndrome following intraosseous infusion. *Orthopedics*. 2008;31:815.
59. Prasarn ML, Ouellette EA, Livingstone A. Acute pediatric upper extremity compartment syndrome in the absence of fracture. *J Pediatr Orthop*. 2009;29:263–268.
60. Ebbesen RL, De Kock MJ, Penny N. Rhabdomyolysis, acute renal failure, and compartment syndrome in a child with parainfluenza type 1 infection. *Pediatr Infect Dis J*. 2009;28: 850–852.
61. Mulcahey M, Thakur N, Tocci S. Compartment syndrome in a child secondary to acute osteomyelitis of the ulna. *Pediatr Infect Dis J*. 2009;28: 258–259.
62. Staudt JM, Smeulders MJ, van der Horst CM. Normal compartment pressures of the lower leg in children. *J Bone Joint Surg Br*. 2008; 90:215–219.
63. Dunwoody J, Reichert CC, Brown KL. Compartment syndrome associated with bupivacaine and fentanyl epidural analgesia in pediatric orthopaedics. *J Pediatr Orthop*. 1997;17:285–328.
64. Hyder N, Kessler S, Jennings A, et al. Compartment syndrome in tibial shaft fracture missed because of a local nerve block. *J Bone Joint Surg*. 1996;78-B:499–500.
65. Tang W, Chiu K. Silent compartment syndrome complicating total knee arthroplasty. *J Arthroplasty*. 2000;15:241–243.
66. Kanj WW, Gunderson MA, Carrigan RB, Sankar WN. Acute compartment syndrome of the upper extremity in children: diagnosis, management, and outcomes. *J Child Orthop*. 2013;7: 225–233.
67. Johnson DJG, Chalkiadis GA. Does epidural analgesia delay the diagnosis of lower limb compartment syndrome in children? *Paediatr Anaesth*. 2009;19:83–91.
68. Mar GJ, Barrington MJ, McGuirk BR. Acute compartment syndrome of the lower limb and the effect of postoperative analgesia on diagnosis. *Br J Anaesth*. 2009;102:3–11.