# Complications in Pediatric Regional Anesthesia

## *An Analysis of More than 100,000 Blocks from the Pediatric Regional Anesthesia Network*

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## ABSTRACT

**Background:** Complications in pediatric regional anesthesia are rare, so a large sample size is necessary to quantify risk. The Pediatric Regional Anesthesia Network contains data on more than 100,000 blocks administered at more than 20 children's hospitals. This study analyzed the risk of major complications associated with regional anesthesia in children.

**Methods:** This is a prospective, observational study of routine clinical practice. Data were collected on every regional block placed by an anesthesiologist at participating institutions and were uploaded to a secure database. The data were audited at multiple points for accuracy.

**Results:** There were no permanent neurologic deficits reported (95% CI, 0 to 0.4:10,000). The risk of transient neurologic deficit was 2.4:10,000 (95% CI, 1.6 to 3.6:10,000) and was not different between peripheral and neuraxial blocks. The risk of severe local anesthetic systemic toxicity was 0.76:10,000 (95% CI, 0.3 to 1.6:10,000); the majority of cases occurred in infants. There was one epidural abscess reported (0.76:10,000, 95% CI, 0 to 4.8:10,000). The incidence of cutaneous infections was 0.5% (53:10,000, 95% CI, 43 to 64:10,000). There were no hematomas associated with neuraxial catheters (95% CI, 0 to 3.5:10,000), but one epidural hematoma occurred with a paravertebral catheter. No additional risk was observed with placing blocks under general anesthesia. The most common adverse events were benign catheter-related failures (4%).

**Conclusions:** The data from this study demonstrate a level of safety in pediatric regional anesthesia that is comparable to adult practice and confirms the safety of placing blocks under general anesthesia in children. **(Anesthesiology 2018; 129:721-32)**



THE use of regional anesthetics in children has grown significantly over the last decade.[1] As utilization increases, it is important to continuously reexamine safety outcomes. Severe complications of regional anesthesia are rare, so large numbers of patients are required to adequately assess the safety of this practice in children. The French-Language Society of Pediatric Anesthesia published their results of audits performed approximately 10 yr apart, both of which found a very low (less than 0.1% incidence) of long-term complications.[2,3] Another audit from the United Kingdom, consisting of more than 10,000 epidural catheters, reported similar results.[4]

The Pediatric Regional Anesthesia Network is a multicenter collaborative supporting a registry that collects data on every regional nerve block performed or supervised by an anesthesiologist at more than 20 children's hospitals. The first comprehensive analysis of the Pediatric Regional Anesthesia Network database examined almost 15,000 blocks,[5] followed by focused analyses of specific block types.[6–10]

### Editor's Perspective

#### What We Already Know about This Topic

- Regional anesthesia is associated with a low but poorly quantified incidence of complications.

#### What This Article Tells Us That Is New

- In a prospective multicenter cohort of more than 100,000 blocks in children, there were no cases of permanent neurologic deficit associated with regional anesthesia. The rate of transient neurologic deficit was low at 2.4 per 10,000, and the incidence of local anesthesia toxicity was also low at 0.76 per 10,000.

Preliminary results of this analysis were presented on October 24, 2016, at the meeting of the American Society of Anesthesiologists, Chicago, Illinois.

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There were no occurrences of severe complications. Therefore, risk assessment was limited for these important outcomes and demonstrated a need for a larger sample size. Since the publication of our 2014 study examining the safety of placing blocks under general anesthesia,[11] the number of blocks entered into the Pediatric Regional Anesthesia Network database has more than doubled.

In this article, we examine the incidence of major complications of pediatric regional anesthesia in a series of more than 100,000 blocks performed from 2007 to 2015. We chose to include the entire data set despite previous publication of some data[5–11] to increase statistical power for rare complications and perform adjusted analyses for certain risk factors, which we have not done in previous studies due to smaller sample sizes. Secondary objectives include the analysis of common patterns in clinical practice, including the technology used to perform regional anesthesia and changes in these patterns over the course of this study.

## Materials and Methods

A detailed description of the Pediatric Regional Anesthesia Network methods has been published previously.[5] The Pediatric Regional Anesthesia Network is a prospective, observational study that collects data on every regional anesthesia procedure for perioperative pain performed or supervised by an anesthesiologist in patients under 18 yr of age at each participating center. Exclusion criteria include procedures performed for the purpose of treatment or diagnosis of chronic pain and regional block procedures performed by physicians from other specialties (*e.g.*, surgery, emergency medicine). Approval for data collection was obtained from the local institutional review board of each site participating in the Pediatric Regional Anesthesia Network. All centers were granted waivers of informed consent by their review boards. The data were collected during the course of routine patient care and deidentified before entry into the database. The participating centers and local principal investigators are listed in appendix 1.

Demographic data included the patient's age, sex, weight, and American Society of Anesthesiologists (ASA) physical status classification. Technical data collected included the patient state at the time of the block (awake, sedated, or anesthetized with or without neuromuscular blockade), technology used to perform the block (none/anatomic landmarks, ultrasound, nerve stimulation, fluoroscopy/epidurogram), and whether a test dose was utilized. The type and dose of local anesthetic and any adjuvants were recorded. The time of catheter removal and reason for removal were also recorded. Complications and adverse events were defined by the presence of at least one of the following intraoperative and/or postoperative factors:

- Neurologic – paresthesia or neurologic deficit
- Local anesthetic systemic toxicity – mild (subjective symptoms, transient electrocardiogram changes) or severe (cardiac arrest or seizure)
- Infection – superficial or deep tissue/abscess
- Vascular – hematoma or puncture
- Respiratory – pneumothorax, respiratory depression
- Catheter malfunction – dislodgment, occlusion
- Dural puncture – observation of cerebrospinal fluid or postdural puncture headache
- Other

Any identified complication or adverse event was followed until the complication resolved, in most cases by clinicians on the pain service. There were rare instances when a complication or adverse event could not be definitively assigned to a specific block because multiple blocks were performed during a single operation, and it was not clear during data analysis which block was associated with the complication. To ensure the most conservative risk estimation for each single type of block, we assigned the complication to each block performed, but the complication would not be counted multiple times in the final tally of all complications in a given category (this occurred with neurologic complications). Complications were rated in severity using the following scale: resolved with no change in treatment, resolved with change in treatment, resolved with sequelae lasting less than 3 months, resolved with sequelae lasting more than 3 months, and permanent. Interventions needed (*e.g.*, imaging, consultations, antibiotic therapy) and whether the complication prolonged hospitalization were also recorded.

Each participating center audited their data in multiple ways. First, billing records or electronic medical record reports were used to cross-match the study list and ensure that all blocks were captured in the database. Second, all centers conducted monthly audits of a random sample of 10% of all blocks (or 5 blocks if less than 50 blocks were entered) to ensure that data were entered correctly into the database. Third, all complications were audited by a principal investigator at each site to ensure that complications were entered correctly. Finally, in the process of manuscript preparation, some centers were asked to provide additional information regarding certain complications (by chart review or consultation with reporting physician), and these data were supplied in blinded manner to the authors when possible. The Pediatric Regional Anesthesia Network only analyzes data up to the most recent month for which *all* centers have audited their data so that the time epoch of all cases in the analysis is identical. The audited data in this manuscript were collected between April 1, 2007, and September 30, 2015. After data analysis and manuscript preparation were complete,

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*Members of the Pediatric Regional Anesthesia Network Investigators are listed in the appendix.

the current month for which *all* centers were audited was November 2015, with the majority of sites audited through mid-2016.

### Statistical Analysis

The data were maintained in the Pediatric Regional Anesthesia Network database by Axio Research, LLC (Seattle, Washington), and queried for analysis by Christine Wolf, M.B.S., the project manager at Axio Research. All blocks performed between April 1, 2007 (the start of data collection in this collaborative), and September 30, 2015 (all available audited data), were requested. All blocks entered during this time period were included for analysis. Each block was coded for statistical analysis using software designed by one of the authors (J.B.L.) in Perl and exported to Microsoft Excel 15.32 for Mac (Microsoft Corporation, USA). The data analysis plan, including subgroup analysis for age and other factors known or hypothesized to contribute to risk, was approved by the Pediatric Regional Anesthesia Network Steering Committee before manuscript preparation.

Estimated risk per 10,000 blocks along with 95% Agresti–Coull CI (95% CI) were reported for each complication type. Significance was assessed using a type 1 error rate of 5%. Analysis was conducted on the block level to determine the risk of complications per block. When multiple blocks were performed on a single patient, each block was considered an independent observation. For complications with blocks performed awake or under general anesthesia, a test of proportions was used to compare the risk of neurologic complications or severe local anesthetic systemic toxicity between the two groups. An age-adjusted binomial logistic regression model was constructed *post hoc* to assess a difference in risk for children 10 yr and older due to the higher incidence of neurologic complications observed in this group. To assess the influence of increased ultrasound use over time for peripheral blocks, binomial logistic regression was used to compare the risk of neurologic complications or severe local anesthetic systemic toxicity. For neurologic complications, tests of proportions were used to compare the risk for age groups, neuraxial *versus* peripheral blocks, epidural level of insertion, and ASA status. A binomial logistic regression model including single-injection *versus* catheter, local anesthetic type and concentration, and ultrasound use as dependent variables was used to explore the risk for neurologic complications. For local anesthetic systemic toxicity, analysis was conducted on the patient level to account for the scenario of multiple blocks performed on a single patient. Tests of proportions for age, test dose, and ASA status were conducted. Due to the higher incidence of local anesthetic systemic toxicity in young infants, a *post hoc* regression model adjusting for block type (caudal *vs*. other) and ultrasound use was used to determine whether the risk of severe local anesthetic systemic toxicity varies between infants under 6 months and older patients. For infection, tests of proportions were used to examine the difference in risk between neuraxial *versus* peripheral catheters and ASA status. Binomial logistic regression was used to examine the risk of complications over time. The association of risk of catheter infection and catheter duration was analyzed by a Mann–Whitney test. Adjusted risk of infection was calculated using a logistic regression model with predictors of level of insertion and catheter duration. Pairwise comparisons for infection risk between caudal and lumbar and caudal and thoracic epidural catheters were performed *post hoc*. For catheter complications, a test of proportions was performed for age groups, and a *post hoc* pairwise comparison of children younger than 3 yr old *versus* older groups was used. For dural puncture, pairwise comparisons were performed between lumbar and thoracic, as well as caudal and lumbar/thoracic. Statistical analysis was performed with R 3.4.0 using the binom package, 1.1-1 by Sundar Dorai-Raj (https://CRAN.R-project.org/package=binom; released April 21, 2017) to calculate CI.

## Results

### Demographics and Practice Patterns

There were 104,393 blocks placed in 91,701 patients during the study period (fig. 1). The number of participating centers increased over time, while five centers withdrew from the network during the study period. The relative proportion of peripheral blocks grew in comparison to neuraxial blocks until 2012, after which time the proportion was relatively stable (fig. 2). The majority (85%) of blocks were placed in ASA class 1–2 patients (fig. 3), and this distribution was consistent across all age groups.

Blocks by age group and location are described in tables 1 and 2. Overall, approximately one-third of blocks were placed in children aged 10 to 17, and one-quarter of blocks were placed in infants (1% in neonates). The most common procedure was a single-injection caudal (n = 38,116). Of the 45,324 single-injection peripheral nerve blocks, the most common were femoral (n = 8,986), sciatic (n = 3,263), popliteal (n = 2,929), and supraclavicular (n = 2,860). Over half of these were placed in children aged 10 yr and older.

There were 18,065 continuous catheters placed during the study period (table 2). Epidural and caudal catheters comprised 73% (n = 13,120) of all catheters placed, including 94% of catheters in neonates and infants. In children under 3 yr old, the use of caudal catheters threaded to more cephalad spinal positions compared to lumbar and thoracic epidural catheters decreased until 2012, after which the relative use increased slightly again (fig. 4). The majority of peripheral nerve catheters were placed in the lower extremities in children aged 10 yr and older. Neuraxial catheters outnumbered peripheral nerve catheters in all age groups.

Blocks were placed under general anesthesia in 93.7% of cases (table 3). The highest rates of awake or sedated block placement were in children under 6 months or older than 10 yr. The risk of neurologic complications or severe (*i.e.*, cardiac arrest or seizure) local anesthetic systemic toxicity was

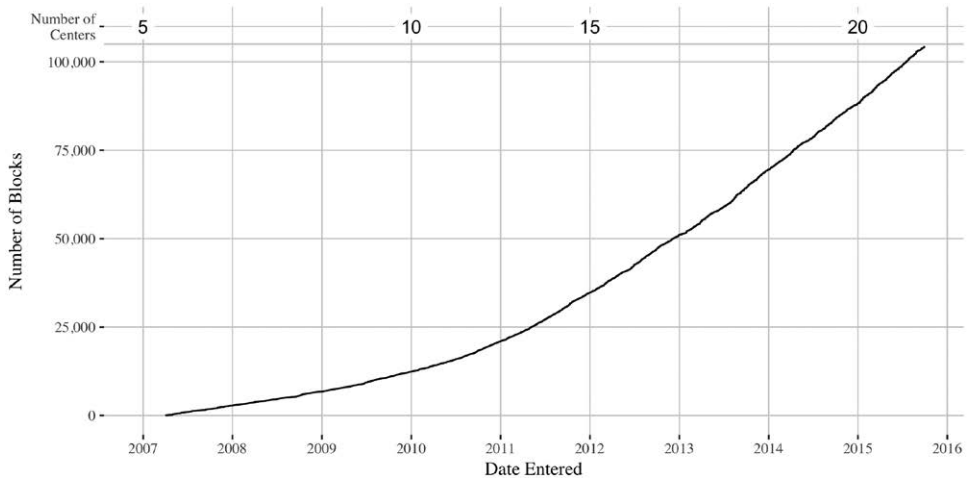


**Fig. 1.** Cumulative number of blocks entered into database.

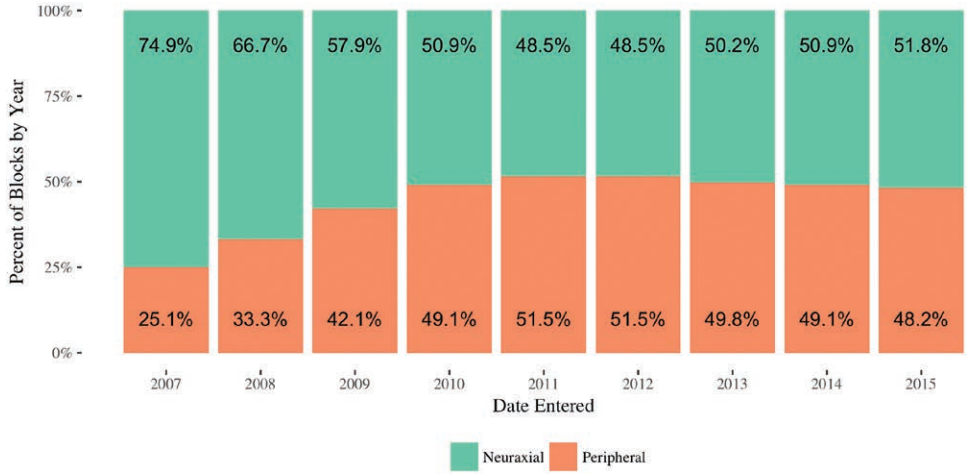


**Fig. 2.** Relative proportion of peripheral and neuraxial blocks entered by year.

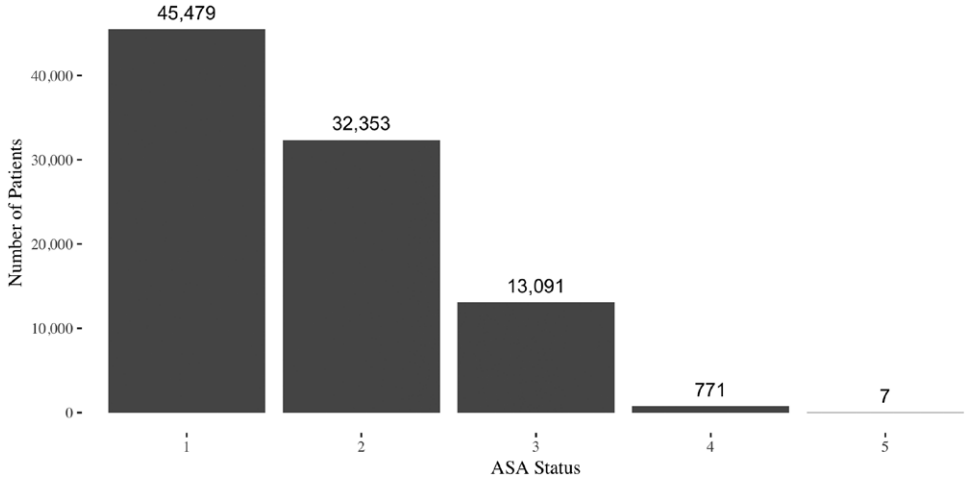


**Fig. 3.** American Society of Anesthesiologists (ASA) Physical Status Distribution.

2.2:10,000 (95% CI, 1.5 to 3.4:10,000) for blocks placed under general anesthesia and 15.2:10,000 (95% CI, 7.8 to 28.4:10,000) for blocks placed while the patient was awake or sedated. When adjusted for age, the risk of a complication remained higher for blocks placed awake or sedated (odds ratio, 2.93; 95% CI, 1.34 to 5.52; $P < 0.01$).

**Table 1.** Single-injection Blocks by Age Group

| | Neonate | 1–5 months | 6–11 months | 1–2 yr | 3–9 yr | ≥ 10 yr | Total |
|---|---|---|---|---|---|---|---|
| Total | 705 | 7,385 | 12,595 | 16,738 | 20,974 | 27,931 | 86,328 |
| Neuraxial | | | | | | | |
| Caudal | 520 | 5,630 | 10,918 | 12,989 | 7,515 | 544 | 38,116 |
| Lumbar epidural | 2 | 20 | 29 | 49 | 203 | 373 | 676 |
| Sacral intervertebral | 0 | 5 | 4 | 4 | 3 | 0 | 16 |
| Subarachnoid | 19 | 201 | 18 | 41 | 185 | 1,570 | 2,034 |
| Thoracic epidural | 3 | 12 | 8 | 16 | 37 | 86 | 162 |
| Upper extremity | | | | | | | |
| Axillary | 23 | 76 | 59 | 162 | 292 | 369 | 981 |
| Infraclavicular | 0 | 0 | 12 | 74 | 202 | 523 | 811 |
| Interscalene | 0 | 2 | 1 | 9 | 67 | 905 | 984 |
| Supraclavicular | 0 | 3 | 35 | 288 | 1,105 | 1,429 | 2,860 |
| Other | 0 | 0 | 3 | 10 | 9 | 39 | 61 |
| Lower extremity | | | | | | | |
| AC/saphenous | 0 | 1 | 2 | 36 | 509 | 2,196 | 2,744 |
| Femoral | 4 | 21 | 26 | 197 | 1,256 | 7,482 | 8,986 |
| Lumbar plexus | 0 | 0 | 0 | 14 | 63 | 197 | 274 |
| Popliteal | 0 | 2 | 23 | 82 | 611 | 2,211 | 2,929 |
| Sciatic | 0 | 9 | 12 | 61 | 570 | 2,611 | 3,263 |
| Other | 0 | 5 | 26 | 137 | 714 | 1,559 | 2,441 |
| Truncal | | | | | | | |
| II/IH | 5 | 100 | 154 | 468 | 2,170 | 1,133 | 4,030 |
| Intercostal | 2 | 9 | 36 | 41 | 106 | 113 | 307 |
| Paravertebral | 19 | 55 | 27 | 57 | 112 | 265 | 535 |
| Penile | 1 | 434 | 510 | 604 | 879 | 391 | 2,819 |
| Rectus sheath | 10 | 113 | 107 | 344 | 1,280 | 584 | 2,438 |
| TAP | 92 | 352 | 248 | 579 | 2,033 | 2,326 | 5,630 |
| Other | 0 | 1 | 27 | 29 | 99 | 100 | 256 |
| Head and neck | | | | | | | |
| Infraorbital | 0 | 276 | 125 | 76 | 165 | 133 | 775 |
| Maxillary/greater palatine | 0 | 4 | 35 | 26 | 31 | 3 | 99 |
| Superficial cervical plexus | 3 | 10 | 58 | 178 | 520 | 448 | 1,217 |
| Other | 2 | 41 | 83 | 147 | 191 | 241 | 705 |
| Other | 0 | 3 | 7 | 19 | 44 | 93 | 166 |

AC, adductor canal; II/IH, ilioinguinal/iliohypogastric; TAP, transversus abdominis plane.

The use of ultrasound for peripheral blocks increased over time (fig. 5). The incidence of neurologic complications with peripheral blocks decreased over time (odds ratio, 0.60; 95% CI, 0.38 to 0.90; $P = 0.02$) but not severe local anesthetic systemic toxicity (odds ratio, 1.08; CI, 0.21 to 5.43; $P = 0.9$). Utilization of nerve stimulation, alone or in conjunction with ultrasound, was relatively low by comparison and decreased over the study period. Surface landmarks were used for 95% of all neuraxial blocks (data available for 90.4% of blocks). Ultrasound (2.3%) and fluoroscopy/epidurogram (2.4%) accounted for the remainder of neuraxial blocks.

Epinephrine-containing test doses were utilized in 51.2% of neuraxial catheters and 65.4% of single-injection caudal blocks (test dose data available for 95.1% of these blocks). Positive test doses were reported in 28 (0.4%) neuraxial catheters and 49 (0.2%) single-injection caudal blocks. A test dose was utilized in 31.1% of peripheral blocks (data available for 93.6% of these blocks), and three (0.02%) positive test doses were reported. Ultrasound was associated with lower utilization of a test dose (24.6% *vs.* 49.1%).

### Complications

Neurologic complications were reported in 25 cases (2.4:10,000; 95% CI, 1.6 to 3.6:10,000). Of the 25 patients, 4 received multiple blocks. Neurologic complications were more common in children more than 10 yr of age, in whom the risk was 7.3:10,000 (95% CI, 5.0 to 10.7:10,000; $P < 0.01$) (table 4). There was no difference in the risk of neurologic complications comparing neuraxial and peripheral blocks (2:10,000, 95% CI, 1.1 to 3.7:10,000 *versus* 2.8:10,000, 95% CI, 1.6 to 4.7:10,000; $\chi^2$ on 1 df = 0.62; $P = 0.43$). Although the incidence of neurologic complications for peripheral blocks decreased over time, ultrasound use did not affect the overall risk (0:10,000, 95% CI, 0 to 4.22:10,000 *vs.* 3.6:10,000, 95% CI, 2.06 to 6.04:10,000, $\chi^2$ on 1 df = 2.74; $P = 0.98$). There was no difference in the risk of a neurologic problem comparing caudal to lumbar or thoracic

**Table 2.** Continuous Catheters by Age Group

| | Neonate | 1–5 months | 6–11 months | 1–2 yr | 3–9 yr | ≥ 10 yr | Total |
|---|---|---|---|---|---|---|---|
| Total | 353 | 1,080 | 910 | 2,013 | 4,768 | 8,941 | 18,065 |
| Neuraxial | | | | | | | |
| Caudal – lumbar | 41 | 135 | 154 | 226 | 334 | 223 | 1,113 |
| Caudal – sacral | 40 | 142 | 175 | 298 | 209 | 39 | 903 |
| Caudal – thoracic | 116 | 281 | 123 | 186 | 172 | 272 | 1,150 |
| Lumbar epidural | 43 | 150 | 172 | 527 | 2,081 | 2,740 | 5,713 |
| Sacral intervertebral | 3 | 5 | 1 | 4 | 1 | 0 | 14 |
| Thoracic epidural | 105 | 321 | 206 | 617 | 1,100 | 1,878 | 4,227 |
| Upper extremity | | | | | | | |
| Axillary | 0 | 0 | 0 | 2 | 2 | 5 | 9 |
| Infraclavicular | 0 | 0 | 2 | 9 | 31 | 91 | 133 |
| Interscalene | 0 | 1 | 0 | 0 | 8 | 94 | 103 |
| Supraclavicular | 0 | 0 | 4 | 4 | 24 | 61 | 93 |
| Lower extremity | | | | | | | |
| AC/saphenous | 0 | 0 | 0 | 0 | 32 | 213 | 245 |
| Fascia iliaca | 0 | 0 | 0 | 0 | 18 | 68 | 86 |
| Femoral | 0 | 1 | 2 | 5 | 184 | 1,365 | 1,557 |
| Lumbar plexus | 0 | 0 | 7 | 26 | 165 | 524 | 722 |
| Popliteal fossa | 0 | 0 | 2 | 11 | 88 | 454 | 546 |
| Sciatic | 0 | 2 | 6 | 11 | 161 | 502 | 682 |
| Truncal | | | | | | | |
| Paravertebral | 4 | 42 | 49 | 76 | 76 | 303 | 550 |
| TAP | 1 | 0 | 7 | 18 | 77 | 96 | 199 |
| Other | 0 | 0 | 0 | 2 | 5 | 13 | 20 |

AC, adductor canal; TAP, transversus abdominis plane.

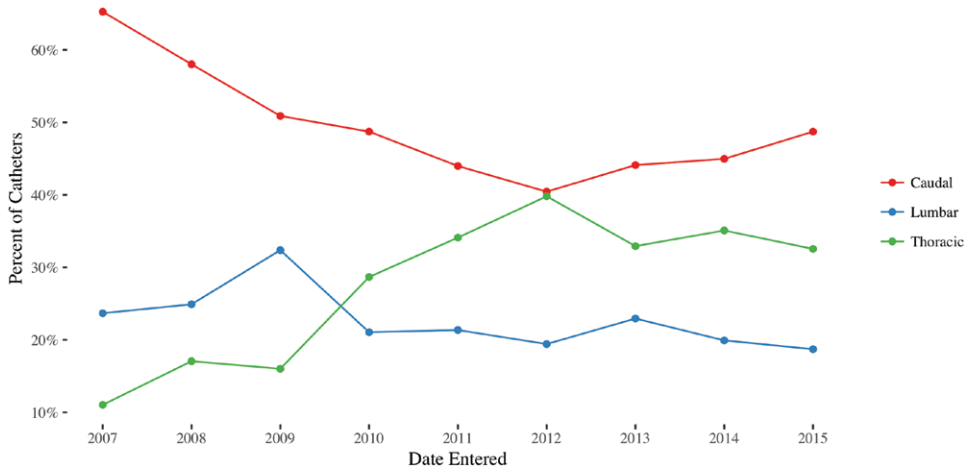


**Fig. 4.** Proportion of caudal, lumbar, and thoracic epidural catheters over time in children under 3 yr of age.

approaches (CI of difference, −17.8 to 3.96:10,000, $\chi^2$ on 1 df = 0.67; $P$ = 0.41) or when directly comparing lumbar and thoracic approaches (CI of difference −11.4 to 11.9:10,000, $\chi^2$ on 1 df = 0.002; $P$ = 0.96). Using logistic regression, there was no difference in neurologic problems when comparing catheter to single-injection blocks (odds ratio, 0.63; 95% CI, 0.21 to 2.74; $P$ = 0.47), local anesthetic type (bupivacaine *vs.* ropivacaine, odds ratio, 3.57; 95% CI, 0.99 to 22.8; $P$ = 0.09), or local anesthetic concentration more than 0.25% (odds ratio, 2.63; 95% CI, 0.98 to 8.3; $P$ = 0.06). Neurologic complications were primarily sensory in nature and resolved over a period of weeks to months, with only two cases demonstrating a sensory deficit beyond 3 months. There were no cases of permanent motor deficit recorded (95% CI, 0–0.4:10,000). ASA status of 3 or greater was not associated with an increased risk of neurologic complications (CI of difference, −2.9 to 2.7:10,000; $\chi^2$ on 1 df < 0.01, $P$ = 1).

Severe local anesthetic systemic toxicity was reported in 7 cases (0.76:10,000, 95% CI, 0.3 to 1.6:10,000). Details of these cases are provided in table 5. Five cases were in infants, three of which were less than 6 months old (table 6). Local anesthetic systemic toxicity presented as cardiac arrest in

**Table 3.** Sedation Status for Block Placement

| Age Group | Blocks | General Anesthesia, % | Awake/Sedated, % |
|---|---|---|---|
| Neonate | 1,058 | 983 (92.9) | 75 (7.1) |
| 1–5 months | 8,465 | 8,051 (95.1) | 414 (4.9) |
| 6–11 months | 13,505 | 13,413 (99.3) | 92 (0.7) |
| 1–2 yr | 18,751 | 18,602 (99.2) | 149 (0.8) |
| 3–9 yr | 25,742 | 25,285 (98.2) | 457 (1.7) |
| ≥ 10 yr | 36,872 | 31,491 (85.4) | 5,381 (14.6) |
| Total | 104,393 | 97,825 (93.7) | 6,568 (6.3) |

four cases and seizure in three cases. Three cases involved single-injection caudal blocks. An epinephrine-containing test dose was used in all cases involving caudals or epidurals. All cases of severe local anesthetic systemic toxicity involved bolus dosing of local anesthetic and were not seen with continuous infusion techniques. Using a logistic regression model adjusting for age, block type (caudal *vs.* other blocks), and use of ultrasound, infants under 6 months old were at significantly greater risk of severe local anesthetic systemic toxicity than other children (odds ratio, 7.42; 95% CI, 1.31 to 39.25; $P = 0.02$). ASA class (CI of difference, −2.9 to 1.5:10,000; $\chi^2$ on 1 df = 0.201; $P = 0.65$) and block type (CI of difference, −1.2 to 1.1:10,000; $\chi^2$ on 1 df; $P = 0.95$) were not independent predictors for the risk of local anesthetic systemic toxicity. Use of ultrasound (CI of difference, −1.6 to 1.0:10,000; $\chi^2$ on 1 df; $P = 0.59$) or a test dose (CI of difference, −1.5 to 0.8:10,000; $\chi^2$ on 1 df; $P = 0.51$) did not affect the risk of local anesthetic systemic toxicity. There were also 11 additional cases of mild local anesthetic systemic toxicity reported, which were characterized by patient report of subjective symptoms (*e.g.*, metallic taste in mouth, tinnitus) or the clinician noting small electrocardiographic changes. All of these additional cases were reported in the postoperative period, and all symptoms resolved with decreasing the rate of or discontinuing the local anesthetic infusion.

There was one epidural abscess reported (0.76:10,000, 95% CI 0 to 4.8:10,000) in a 2-month-old who had a lumbar epidural. The catheter was removed on postoperative day 4, and purulent drainage from the insertion site was noted on the day following removal. A lumbar laminectomy was performed to evacuate the abscess on postoperative day 6, and the child made a full recovery. There were 92 local cutaneous infections reported in 18,065 continuous catheters (53:10,000, 95% CI, 43 to 64:10,000) (table 7). There was a higher rate of infection reported with neuraxial catheters (60:10,000, 95% CI, 48 to 75:10,000) when compared to peripheral catheters (26:10,000, 95% CI, 15 to 45:10,000; $P < 0.01$). Using logistic regression adjusted for catheter duration and level of insertion, no difference was found in risk of infection between caudal and lumbar (odds ratio, 0.58; 95% CI, 0.31 to 1.10; $P = 0.093$) or between caudal and thoracic catheters (odds ratio, 1.51; 95% CI, 0.88 to 2.66; $P = 0.14$). Cases of infection had a significantly longer median catheter duration of 4 days (interquartile range, 2 to 5 days) compared to cases without infection, which had a median duration of 2 days (interquartile range, 1 to 3 days; $P < 0.01$). The risk of infection increased by 6.7% for each additional catheter day (odds ratio, 1.067; 95% CI, 1.02 to 1.12; $P < 0.01$). ASA class 3 or greater was independently associated with the risk of infection (CI of difference, −36.1 to −18.4:10,000; $\chi^2$ on 1 df; $P < 0.01$). Patients received antibiotic therapy in 29 of 92 cases. The remaining cases were treated with removal of the catheter only. There were no infections associated with single-injection blocks (95% CI, 0 to 1.02:10,000).

There were no hematomas reported with neuraxial catheters (95% CI, 0 to 3.5:10,000). There was one hematoma associated with bilateral paravertebral catheters (18.2:10,000, 95% CI, 0 to 113:10,000). Pain and swelling were noted on one side, which prompted magnetic resonance imaging showing a hematoma that tracked into the epidural space from T1 to T10. There were no associated

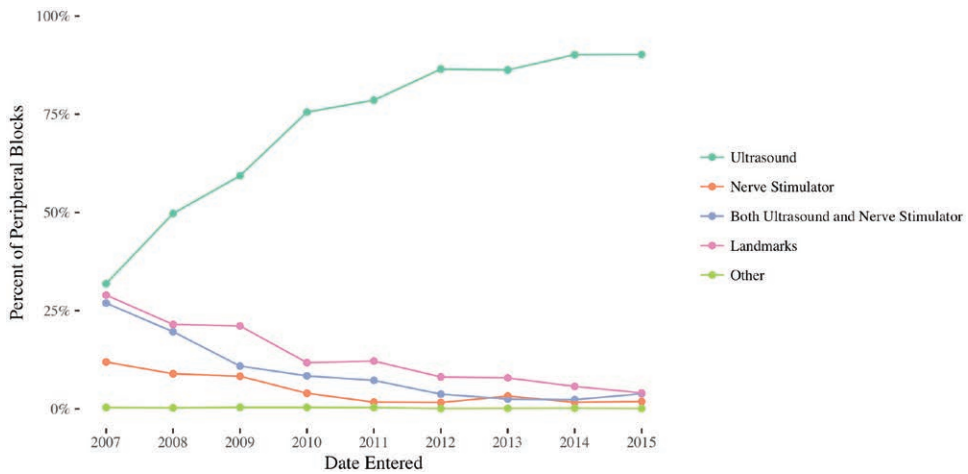


**Fig. 5.** Technology used for peripheral blocks. Data were available for 92.3% of blocks.

**Table 4.** Neurologic Complications by Age Group (N = 104,393 Blocks)

| Age Group | Cases | Blocks | Incidence | 95% CI |
|---|---|---|---|---|
| Neonate | 0 | 1,058 | 0:10,000 | 0–43.7 |
| 1–5 months | 0 | 8,465 | 0:10,000 | 0–5.5 |
| 6–11 months | 0 | 13,505 | 0:10,000 | 0–3.4 |
| 1–2 yr | 0 | 18,751 | 0:10,000 | 0.02–4 |
| 3–9 yr | 3 | 25,742 | 1.2:10,000 | 0.2–3.6 |
| ≥10 yr | 27 | 36,872 | 7.3:10,000* | 5–10.7 |

*$P < 0.01$. Cases total more than 25 because 4 patients received multiple blocks (3 patients received 2 blocks, and 1 patient received 3 blocks).

neurologic deficits. This was treated conservatively without surgical intervention, and the patient made a full recovery.

One pneumothorax was reported in a 2-yr-old child who received a single-injection supraclavicular block under ultrasound guidance. This was managed conservatively and did not require a thoracostomy tube. There was also one case of a caudal catheter that was unintentionally placed into the abdominal cavity in a neonate. The catheter was placed using nerve stimulation and recognized with a radiographic catheter injection for confirmation of placement. This did not result in further sequelae. Two cases of needle breakage during block placement (penile and superficial cervical plexus) were reported. In both cases, the needle was removed by a surgeon without further sequelae. Finally, there was one report of a wrong-sided femoral block in a 9-yr-old child.

### *Adverse Events*

The most common adverse events were catheter complications (*e.g.*, dislodgement, occlusion, disconnection, *etc.*), occurring in 4% of cases. Adverse catheter events were more common in children under 3 yr of age (CI of difference, 234 to 395:10,000; $\chi^2$ on 1 df = 83.2; $P < 0.01$). Overall, catheters were removed in 7.5% of cases due to the occurrence of a complication (either a catheter-related complication as described or another category of complication).

Respiratory depression occurred in 18 cases, all associated with neuraxial catheters (14:10,000, 95% CI, 9 to 22:10,000). The epidural infusion contained opioid in 15 of these cases, and all resolved by changing or pausing the infusion. Additionally, a case of intraoperative apnea occurred after a subarachnoid block in a 2-month-old child.

The incidence of unintentional dural puncture in lumbar (86:10,000, 95% CI, 66 to 112:10,000) and thoracic (66:10,000, 95% CI, 46 to 95:10,000) epidural needle insertions was not significantly different (CI of difference, −1.5 to 5.5:10,000; $\chi^2$ on 1 df = 1.1; $P = 0.29$). The dural puncture rate associated with caudal needle insertion was 10:10,000 (95% CI, 7 to 14:10,000), significantly lower than lumbar or thoracic approaches (CI of difference, −85.2 to −50.3:10,000; $\chi^2$ on 1 df = 159.8; $P < 0.01$). Postdural puncture headache occurred in 11 (7%) of the dural puncture cases, and 7 of these 11 patients received an epidural blood patch. The overall block failure rate was 1.05%.

## Discussion

The larger sample size for this analysis of the entire Pediatric Regional Anesthesia Network data set has allowed us to better define the upper limits of conservative risk assessment for pediatric regional anesthesia. Previous analyses that included peripheral blocks have consisted primarily of head and neck and truncal blocks,[3] which are known to be lower risk.[10] The peripheral blocks in our cohort were primarily femoral, sciatic, popliteal, and supraclavicular, which have a higher risk of complications.

Despite this large sample size, we did not identify any permanent motor neurologic deficits. In adults, the risk of permanent neurologic deficit is estimated to be 2 to 4:10,000 for peripheral blocks and 1 to 2:10,000 for neuraxial blocks.[12] In major pediatric audits, only one permanent neurologic deficit has been reported (resulting from a pump programming error).[3,4] Our large data set allows for lower conservative risk estimates (*i.e.*, the upper limit of the 95% CI) for transient sensory (3.6:10,000) and permanent motor (0.4:10,000) deficits that are 30 to 40% lower than the previous analysis of the Pediatric Regional Anesthesia Network data.[11] However, case reports confirm the risk of permanent neurologic injury in children, primarily with epidural analgesia.[13–15] The French-Language Society of Pediatric Anesthesia audit found a lower risk of overall complications with peripheral compared to neuraxial blocks,[3] but our data do not show a difference. Although there was an association with older children for the incidence of neurologic complications, this is likely due to challenges in diagnosing subtle neurologic complications in preverbal/nonverbal children.

**Table 5.** Characteristics of Severe Local Anesthetic Systemic Toxicity Cases

| Age | Block | Sedation | Technology | Local Anesthetic | Test Dose | Symptoms | Lipid Emulsion |
|---|---|---|---|---|---|---|---|
| 1 month | Caudal | GA | Landmarks | 1.5 mg/kg R | Yes | Seizure | No |
| 2 months | Thor epid catheter | GA | Ultrasound | 1.3 mg/kg B | Yes | Cardiac arrest | Yes |
| 2 months | Subarachnoid | Awake | Landmarks | 0.75 mg/kg B | Unknown | Cardiac arrest | Yes |
| 3 months | Caudal | GA | Landmarks | 2.5 mg/kg B | Yes | Cardiac arrest | Unknown |
| 9 months | Paravertebral catheter | GA | Ultrasound | 30 mg/kg CP | No | Seizure | No |
| 3 yr | Caudal | GA | Landmarks | 1.1 mg/kg B | Yes | Cardiac arrest | No |
| 13 yr | Infraclavicular | Sedated | Ultrasound | 1.28 mg/kg B | No | Seizure | Yes |

B, bupivacaine, CP, chloroprocaine; GA, general anesthesia; R, ropivacaine; Thor epid, thoracic epidural.

**Table 6.** Local Anesthetic Systemic Toxicity by Age Group

| Age Group | Cases | Total Patients | Incidence | 95% CI |
|---|---|---|---|---|
| Neonate | 0 | 998 | 0:10,000 | 0–46.3 |
| 1–5 months | 4 | 7,935 | 5.0:10,000 | 1.5–13.5 |
| 6–11 months | 1 | 12,943 | 0.8:10,000 | 0–4.8 |
| 1–2 yr | 0 | 17,829 | 0:10,000 | 0–2.6 |
| 3–9 yr | 1 | 22,702 | 0.4:10,000 | 0–2.8 |
| ≥ 10 yr | 1 | 29,294 | 0.3:10,000 | 0–2.1 |
| Total | 7 | 91,701 | 0.76:10,000 | 0.3–1.6 |

In addition, younger children have an enhanced capacity to recover from peripheral nerve insults relative to older children and adults, so a neurologic insult may not be as likely to result in a long-term deficit.[16,17]

Our study also confirmed the safety of placing blocks in children under general anesthesia, consistent with expert guidelines.[12,18] In fact, we actually observed a higher risk for local anesthetic systemic toxicity or neurologic complications when blocks were placed in sedated or awake patients, even when adjusted for age. The majority (80%) of awake or sedated blocks were placed in children 10 yr of age and older, who should be able to convey subjective symptoms of local anesthetic systemic toxicity or potential neurologic injury. However, the sample size for awake/sedated block placement was relatively small (n = 6,568), limiting the statistical validity of a comparison between the two groups. An appropriately conservative interpretation of the data indicates that the risk of placing nerve blocks under general anesthesia in children is comparable to the risk in awake adults.

Since our last major analysis,[11] only two additional cases of severe local anesthetic systemic toxicity have been reported to the database, reducing the conservative risk estimate by approximately 25%. Large pediatric audits have demonstrated a rate of 0.4 to 1:10,000,[4,15] which is similar to our results and lower than reports from adult studies.[19] It is not surprising that the use of a test dose did not reduce the risk of local anesthetic systemic toxicity, because it has been shown to have a limited negative predictive value under general anesthesia. Therefore, it cannot be recommended universally for all neuraxial procedures or those performed without ultrasound.[18] However, it should be noted that there were 80 positive test doses reported to the database, and given the high positive predictive value of the test dose, it is possible that many more cases of local anesthetic systemic toxicity were avoided.

All of the severe cases of local anesthetic systemic toxicity were associated with bolus dosing, whereas the majority of mild cases were noted in the postoperative period with continuous infusions. Doses in cases of severe local anesthetic systemic toxicity were within published guidelines in all cases.[20] However, we should emphasize that developmental pharmacokinetics in neonates and infants under 6 months require consideration of a dose reduction in some cases.[21] Overall, our data demonstrate that infants under 6 months are at higher risk for local anesthetic systemic toxicity, but it is often not a consequence of excessive local anesthetic dosing. Rather, it is likely due to other factors such as unrecognized intravascular injection, rapid absorption and distribution, or decreased hepatic $\alpha_1$-acid glycoprotein synthesis in young infants.

We observed a low rate of cutaneous infection and only one epidural abscess. Other large pediatric audits have reported an incidence of 1 to 3:10,000 for serious infection, which is similar to our results.[4,22] Cutaneous infections were generally mild in this series, and antibiotics were infrequently needed. The incidence of superficial infection for neuraxial catheters in our database (60:10,000) was slightly higher than that observed in the audit from the United Kingdom (24:10,000),[4] but clinician judgment may vary regarding the diagnosis of superficial infection, and the difference is not clinically significant. In our adjusted analysis, it is notable that we did not observe an increased incidence of infection with caudal catheters, which are considered higher risk for infection. We did observe a higher incidence of infection with neuraxial *versus* peripheral catheters. This may be due to the site being exposed to more moisture from leakage or perspiration when the patient is supine or simply more irritation at the site causing local erythema. Overall, our data suggest that the risk of infection is not related to the level of insertion but more likely associated with a longer duration of catheter use, as well as patient-related factors given the association with higher ASA class.

The only epidural hematoma reported to our database did not require surgical intervention, and the patient made a full recovery. Epidural hematoma associated with a regional

**Table 7.** Cutaneous Catheter Infections by Site

| Catheter Location | Infections | Catheters | Duration | Incidence | 95% CI |
|---|---|---|---|---|---|
| Caudal | 18 | 3,166 | 2 (0–3) | 57:10,000 | 34–90 |
| Lumbar epidural | 21 | 5,713 | 2 (1–3) | 38:10,000 | 24–58 |
| Thoracic epidural | 40 | 4,227 | 3 (2–4) | 99:10,000 | 72–134 |
| Upper extremity | 1 | 338 | 2 (1–3) | 30:10,000 | 1–164 |
| Lower extremity | 11 | 3,838 | 3 (2–3) | 29:10,000 | 14–51 |
| Paravertebral | 1 | 550 | 3 (2–5) | 18:10,000 | 0–101 |
| Other | 0 | 233 | 3 (2–4) | 0:10,000 | 0–195 |
| Total | 92 | 18,065 | 2 (1–3) | 53:10,000 | 43–64 |

Catheter duration is reported in days as median (interquartile range) for all catheters in each category.

anesthetic has not been reported in any of the large pediatric audits.[2–4] In our review of the literature, we found only a single case report of subarachnoid hematoma, resulting from a direct puncture of the spinal cord with an epidural needle in a child with an undiagnosed arteriovenous fistula.[23] There has been one additional case of a thoracic epidural hematoma entered in the Pediatric Regional Anesthesia Network database after the current data collection period.[24] A recent investigation from the Multicenter Perioperative Outcomes Group reported an incidence of epidural hematoma in adults of 1.1:10,000 for nonobstetric neuraxial procedures,[25] which is within the upper limit of our CI (3.5:10,000).

### Limitations

These data should be interpreted cautiously. Although our database contains a larger sample size than previous pediatric audits, the event rate was still low. This limits the statistical power for some of our adjusted analyses. In addition, other unknown confounders may affect our adjusted analyses, and the Pediatric Regional Anesthesia Network does not collect any information on patient comorbidities beyond ASA status. Finally, some analyses were performed *post hoc* after significance was found across multiple groups. Given the large sample size with many subgroups, performing a considerable number of statistical tests increases the risk of type 1 error.

Despite a robust auditing process, the Pediatric Regional Anesthesia Network relies on self-reporting for all events. Given the sensitive nature of some complications, there is a risk of reporting bias on the part of physicians.[26] The details of follow-up processes differ at each institution, but most have a dedicated acute pain service for inpatients and telephone follow-up for single-injection blocks and ambulatory continuous catheters. Detection of delayed complications occurring after discharge from follow-up relies on voluntary reporting from patients, families, or surgeons. As we noted regarding neurologic complications, it is difficult to detect subtle complications in preverbal and nonverbal children. Despite these limitations, we strongly believe that serious complications, such as permanent neurologic deficits or cases of severe local anesthetic systemic toxicity, would be identified and reported in all patients. Furthermore, Pediatric Regional Anesthesia Network centers are deidentified for data analysis, so we are not able to account for heterogeneity in reporting. With sites both entering and leaving the network over the study period, we cannot easily discern whether trends in complication rates or practice patterns are due to changes in institutions participating in the database. This analysis includes data only through September 2015, the most current month for which *all* centers were audited. Including further audited data (currently only through November 2015 for all centers) would not add many blocks to this already large sample size, and we believe would not change the conclusions of the study.

The Pediatric Regional Anesthesia Network database does not include surgical procedure data; therefore, it cannot assess relative risk or recommend a particular approach for different surgical procedures. Neither does the database include data about the efficacy or quality of analgesia. At the initiation of the database, attempts were made to collect pain scores as a marker of efficacy, but we were unable to ensure uniformity and reliability of scoring among different institutions and patients. This parameter was later omitted from the database because the data quality was judged to be poor. Efficacy data require standardized postoperative treatment protocols, comparison to a control group receiving a different form of analgesia, and data on rescue analgesic administration,[27] which are more suitable for prospective, randomized clinical trials.

### Conclusions

Our data from a diverse group of children's hospitals demonstrate that regional anesthesia in children is a safe practice, including performing neuraxial and peripheral nerve blocks under general anesthesia. Although there were no serious neurologic complications reported in this study, case reports do exist describing permanent injury. Our data also confirm the safety of caudal catheters, with a similar infection rate and lower dural puncture rate compared to thoracic and lumbar approaches. They are a suitable alternative to direct lumbar or thoracic approaches, as long as the appropriate catheter tip location is confirmed. There was also a relatively large catheter-adverse event rate, suggesting the need for improvement in both catheter and fixation technology.

Physicians should continue to exercise caution when applying these techniques, especially in infants. Future research should focus on prospective, randomized trials to examine efficacy and outcome benefits for regional anesthesia in children. Safety concerns should not represent a barrier to further study of regional techniques in the pediatric population.

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## Competing Interests

The authors declare no competing interests.

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