Lesson 289: PeriAnesthetic Management Of the Ex-Premature Infant

Needs statement

As the management of premature infants improves, more children survive until such time that elective procedures can be undertaken. Anesthesiologists may be called on to care for these children. An understanding of the altered physiology of these patients has been identified by committee as required knowledge for anesthesia practitioners.

Learning objectives

At the end of this activity, the participant should be able to:

1. Summarize the unique pathologic conditions in the ex-premature infant.
2. Describe the impact of these conditions on the delivery of anesthesia.
3. List possible anesthetic options for the ex-premature infant.
4. Recognize the possible complications of caudal anesthesia.
5. Develop an anesthetic plan for an ex-premature infant.
6. List the pros and cons of anesthetic plans in these cases.
7. Recognize the signs and symptoms of local anesthetic toxicity.
8. Anticipate postoperative complications in the ex-premature infant.
9. Prescribe appropriate monitoring.
10. Identify steps of advanced life support in pediatric cases.
Case history

A 4-month-old boy, born prematurely at 28 weeks of gestation, was admitted for surgical repair of bilateral inguinal hernias and circumcision. The infant had been hospitalized in the neonatal intensive care unit for the first 3 months of life. His symptoms included respiratory distress syndrome, and bronchopulmonary dysplasia for which he required assisted ventilation. The infant was discharged to home, and received oxygen by nasal cannula until 2 weeks before the surgery. His medical history included additional problems related to prematurity — eg, grade 1 (mild) intraventricular hemorrhage, a patent ductus arteriosus (which was treated medically and subsequently closed), and mild retinopathy.

On examination of the infant in the preoperative holding area, he appeared to be vigorous; he weighed 5 kg, his heart rate was 137 beats per minute, oxygen saturation on room air was 96%, and respiratory rate was 40 breaths per minute. Breath sounds were clear on auscultation. No laboratory tests were ordered preoperatively. Hematocrit level was 29% at the time of discharge from the hospital 4 weeks previously. The decision was made to proceed with a spinal anesthetic, and parental consent was obtained.

Although not as stressful for the anesthesiologist as a premature infant in the neonatal intensive care unit (ICU) who requires emergency surgery, the ex-premature patient presents multiple challenges. Premature infants, because of surfactant deficiency, may develop neonatal respiratory distress syndrome or hyaline membrane disease very early in the postnatal period. Supplemental oxygen and barotrauma from mechanical ventilation can lead to bronchopulmonary dysplasia (BPD)—a destructive and chronic form of lung disease that can take months or even years to fully resolve. As a result, the ex-premature infant may require supplemental oxygen several months after discharge.

More severe BPD may result in pulmonary hypertension, fluid retention, fibrosis, and wheezing, for which diuretics and bronchodilators may be prescribed. When intubating an infant with BPD, one should anticipate the same set of problems encountered in any patient with chronic lung disease: induced bronchospasm, episodes of desaturation, and possible postoperative ventilation.

The biggest anesthetic challenge—after chronic lung disease—is the threat of postoperative apnea and bradycardia. Apnea (defined as a cessation of breathing for >20 -seconds) is due to immaturity of the respiratory regulatory centers in the brainstem or is secondary to a disease process elsewhere (sepsis, anemia, etc). Apnea generally leads to hypoxemia and then bradycardia because of the pre-dominance of parasympathetic stimulation of the neonatal heart during times of stress. Premature infants eventually outgrow episodes of apnea, but apnea may still be an active problem at the time of outpatient surgery.

Most anesthetics (inhalation agents, opioids, sedatives, induction agents) can worsen the risk for apnea; also, apnea that has resolved may reappear, or it may be induced for the first time. The infant’s risk for apnea after general anesthesia depends on postconceptual age (PCA)—the greater the PCA, the lower
the risk. Several studies have looked at the PCA at which outpatient surgery is considered safe and apnea-free. The most conservative view holds that a 60-week PCA is preferred, whereas others make the case that 45 to 50 weeks is adequate. Infants in whom PCA is below a predetermined threshold should be admitted for overnight monitoring.

In the past, a hematocrit level maintained near 30%, and transfusions and the administration of a central stimulant such as caffeine, were strategies believed to prevent postoperative apnea. It is hard to justify transfusion therapy with its attendant risks, particularly when intraoperative blood loss is not anticipated to be high. If an infant is receiving a methylxanthine, it makes sense to continue it throughout the perioperative period. However, prophylactic caffeine or theophylline in an infant who is not already receiving it should be administered with caution.

**Choice of Anesthetic Technique**

Because of possible preexisting lung disease and the risk for postoperative apnea in the ex-premature infant, regional anesthesia (spinal, caudal) is an attractive alternative to general anesthesia. Studies have shown that regional anesthesia leads to less apnea and fewer other postoperative complications. However, an infant may develop postoperative apnea if sedatives are administered during regional procedures. Also, spinal anesthesia itself may cause apnea due to loss of accessory muscle action, but this generally occurs immediately after placement.

Recent reports of neurotoxicity in neonatal animals exposed to general anesthetics may prompt some to avoid these agents in favor of regional techniques in human infants. Although there are published reports that caution about anesthetic exposure and learning disabilities in children, there is as yet no definitive evidence that regional anesthesia results in less neuropathology.

**Neuraxial Techniques in the Ex-Premature Infant**

Spinal anesthesia has a long record of safety and effectiveness in infants, including premature and ex-premature infants. Spinal techniques typically are used to provide anesthesia in subumbilical surgery, but its use for procedures above the umbilicus also has been described. A single-shot spinal with either 1% tetracaine or 0.5% bupivacaine with epinephrine 1:200,000 (0.5-1.0 mg/kg) reliably yields a mid-thoracic sensory level with little or no hemodynamic compromise for up to 2 hours. The spinal cord descends to L1-2 in the neonate; thus, attempts to administer spinal anesthesia should be below this level. The periosteum of the neonatal vertebra bleeds very easily and “bloody taps” therefore are not uncommon. The failure rate for single-shot spinals in infants is between 10% and 20%.

Caudal anesthesia as the sole anesthetic technique in the ex-premature infant is a reasonable alternative in the event of a failed spinal, or as a first-line technique. A single-shot caudal requires the injection of a larger volume of local anesthetic (0.7-1 mL/kg) for inguinal anesthesia. Caudal anesthesia as the sole anesthetic for supra-umbilical surgery in critically ill premature infants has been described. One advantage of caudal anesthesia over spinal anesthesia is the ability to redose by keeping an angiocatheter in place through the sacral hiatus, or by threading an epidural catheter into the sacral canal or higher into the lumbar or thoracic spine. A recent retrospective comparison of spinal and caudal blocks in awake ex-premature infants found that caudals were technically easier to perform, and required fewer attempts than the subarachnoid approach.
A combined spinal–epidural technique is an option that entails the placement of a spinal block initially, followed by a caudally threaded epidural catheter for long procedures above and below the umbilicus.\(^\text{19}\) A combined -caudal–epidural technique also has been described, in which a caudally threaded epidural catheter is preceded by a single-shot caudal block.\(^\text{20}\) Another option is the sacral interspinous approach to the caudal space, although the risk for dural puncture increases.\(^\text{21}\)

General anesthesia is reserved as a backup whenever regional anesthesia is planned in an infant. Technical difficulties in administering a spinal or caudal anesthetic in an awake infant are real, and mandate discussion with parents prior to surgery. A caudal block is an adjunct to general anesthesia in all pediatric patients which can reduce perioperative requirements for opioids—useful in the ex-premature infant given that perioperative opioids can lead to postoperative apnea.

### Technical Aspects of Caudal Anesthesia in Infants: Ultrasound and Needle Selection

A successful caudal block depends on accurate identification of the sacral hiatus, the distal opening in the sacrum that is covered by skin and the sacrococcygeal ligament. Palpation of the area usually suffices, but can be inaccurate and difficult in some infants because of anatomic variation. Portable ultrasonography is a valuable tool for correctly identifying sacral anatomy and “visualizing” local anesthetic as it is injected into the sacral canal.\(^\text{22}\) First described by Roberts et al for use in the longitudinal plane,\(^\text{23}\) ultrasound also can be used for this purpose in the transverse plane. One looks for turbulence and dilation within the sacrum or changes in a Doppler signal (Figures 1-3). Holding the ultrasound probe over the sacral hiatus can help identify the correct caudal needle placement.
Figure 3. Infiltrate within the canal using the Doppler mode. An injection not in the caudal canal would be seen as dilation to the right or left of the sacral apex (white arrow). Detection using ultrasound is quicker than using palpation.

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Ultrasound is more reliable than other methods for confirming correct needle placement within the caudal canal\(^{24}\) and can be used to locate the tip of an epidural catheter if one is threaded up from the caudal space (Figures 4 and 5).

![Figure 4. The tip of a caudally threaded thoracic epidural catheter is shown in the longitudinal plane.](image)

![Figure 5. The tip of the catheter is shown in cross-section.](image)

Opinions vary as to which needle is optimal for caudal placement. Styletted spinal needles reduce the theoretical migration of mitotic epidermal cells into the sacral canal. Blunt-tipped regional needles increase tactile “feel” and theoretical safety against intravascular injection. Other anesthesiologists (the author included) use angiocatheters because it is difficult to smoothly advance the catheter over the needle unless it is placed correctly in the caudal canal. Long beveled hypodermic needles should be used with extreme caution, as accidental placement into the soft back wall of the sacrum may result in negative aspiration of blood, little resistance to injection, and intravascular toxicity.

Regardless of the needle used, injection of local anesthetic should only follow a negative aspiration for blood and cerebrospinal fluid (CSF), and be slow and incremental with electrocardiographic (EKG) monitoring.\(^{25}\) Epinephrine included in the injectate provides additional safety by inducing early tachycardia if the injection is intravascular.

### Cardiac Toxicity of Local Anesthetics In Infants

Local anesthetics are more toxic in infants than in older children and adults due primarily to decreased protein binding in infants, thus generating a greater fraction of free (unbound) drug. The prolonged elimination of local-anesthetic amide compounds because of immature hepatic enzyme systems also contributes to increased toxicity in infants.

Of the available local anesthetics, bupivacaine, a long-acting amide, has the longest track record, clinically. Bupivacaine produces a reliable block when given caudally, but its major drawback is cardiac toxicity when given inadvertently as an intravascular bolus. The slow reversibility of its binding to sodium channels in the heart causes conduction delay and arrhythmias from escape pathways. Bupivacaine also is a direct myocardial depressant. It may produce severe arrhythmias and ventricular
fibrillation after rapid IV administration; cardiac resuscitation may be very difficult.
The maximum dose of bupivacaine that should be administered in a pediatric caudal block is 2.5 mg/mL (1 mL/kg of 0.25% solution). By comparison, ropivacaine—another long-acting amide that consists of an L-enantiomer—has a shorter plasma half-life and less lipid solubility than bupivacaine. Ropivacaine is an effective agent for pediatric caudal anesthesia with equivalent sensory block—but less motor block—than bupivacaine. The decreased cardiac toxicity associated with ropivacaine is balanced against its slightly decreased anesthetic potency. Cardiac toxicity in an infant following a caudal block with ropivacaine has recently been described.26

L--bupivacaine (ie, containing only the L--enantiomer) has the best safety profile for cardiac toxicity of the long-acting, local-anesthetic amides. When used for caudal blocks in children, it has been shown to be as effective as bupivacaine.27 Unfortunately, it is not yet available in the United States.

Although no definitive data have been published regarding a reasonable period of time to redose after a single caudal block, in the author’s practice the wait is at least 3 hours, based on the half-life of bupivacaine; a dose half as concentrated as the first (eg, 0.125% bupivacaine) is then administered.

### Treatment of Cardiac Toxicity From Local Anesthetics

In the event of an intravascular bolus of local anesthetic with cardiac decompensation, treatment must be prompt and organized. Help should be summoned. Initiation of cardiovascular and ventilatory support with cardiopulmonary resuscitation (CPR) is the first step, as outlined in the pediatric advanced life support (PALS) manual of the American Academy of Pediatrics and American Heart Association.28,29 In general, 2-rescuer CPR with a compression-to-ventilation ratio of 15:2 should begin (heart rate of 100 bpm). The infant’s trachea is already intubated, so 8 to 10 breaths per minute should be provided without pause for chest compressions. This ratio emphasizes chest compressions with blood flow to the coronary and cerebral vasculature over ventilation. Excessive ventilation during resuscitation can impede venous return and cardiac output. All inhalation anesthetics should be discontinued because they cause myocardial depression and vasodilatation.

The PALS algorithm for pediatric pulseless arrest (Table) should be followed—in this case, the arm for shockable rhythms, ventricular tachycardia/ventricular fibrillation (VT/VF). The algorithm is designed to provide periods of effective, uninterrupted CPR with efficient delivery of electrical therapy. An initial asynchronous shock of 2 J/kg is followed by immediate resumption of CPR if a stable rhythm is not observed. The shorter the interval between the last compression and the shock delivery, the greater the probability of shock success.

### Table. PALS Algorithm for Pulseless VT/VF

<table>
<thead>
<tr>
<th>Action</th>
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<tbody>
<tr>
<td>Initiate CPR</td>
</tr>
<tr>
<td>Defibrillation, 2 J/kg</td>
</tr>
<tr>
<td>Reinitiate CPR</td>
</tr>
<tr>
<td>Repeat defibrillation if rhythm is still unstable; increase J setting to 4 J/kg</td>
</tr>
<tr>
<td>Reinitiate CPR</td>
</tr>
<tr>
<td>Check rhythm; if still in VT/VF, administer medication</td>
</tr>
<tr>
<td>Epinephrine (1:10,000), 0.01 mg/kg IV; may be repeated every 3-5 minutes</td>
</tr>
<tr>
<td>Repeat defibrillation if still unsuccessful (4 J/kg)</td>
</tr>
<tr>
<td>Reinitiate CPR</td>
</tr>
<tr>
<td>Check rhythm; if still in VT/VF, administer medication</td>
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<tr>
<td>Amiodarone, 5 mg/kg IV bolus,</td>
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<tr>
<td>or Lidoxxcaine, 1 mg/kg IV,</td>
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<tr>
<td>or Magnesium, 25-50 mg/kg IV (for torsades de pointes)</td>
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<tr>
<td>Repeat defibrillation/CPR/epinephrine, if still unsuccessful</td>
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</tbody>
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Based on reference 26.

CPR, cardiopulmonary resuscitation; IV, intravenous; J, joule; PALS, Pediatric Advanced Life Support; VF, ventricular fibrillation; VT, ventricular tachycardia
mg/kg (0.1 mL/kg=1:10,000). Rhythm should be
assessed—these interruptions should last no longer than 10 seconds—and chest compressions should be resumed. A third shock should be administered (4 J/kg), followed by continuous CPR.

If VT/VF persists, an antiarrhythmic drug such as amiodarone (Vaughan-Williams class III; 5 mg/kg) should be considered. Alternatives include lidocaine (1 mg/kg) and magnesium sulfate (25-50 mg/kg), with the latter indicated for VF with torsades de pointes.

Since 2006, reports have been published of lipid emulsion therapy for local anesthetic toxicity. To date, there are numerous case reports of successful resuscitation following intralipid administration, including one in an infant who received a caudal block. These reports follow many years of animal research that showed the beneficial resuscitative effects of intralipids after infusion of local anesthetics. Currently, the recommendation for local anesthetic–induced cardiac arrest is conventional resuscitative therapy; if that proves unsuccessful, intralipid 20% (1-2 mL/kg for 1 minute) is administered, followed by an infusion at a rate of 0.25 mL/kg per minute. The bolus can be repeated every 3 to 5 minutes, up to a dose of 3 mL/kg, and the infusion increased to 0.5 mL/kg per minute. Further studies will no doubt clarify the role of intralipids in toxin-induced resuscitations; meanwhile, a supply of intralipid should be readily available anytime regional blocks, including caudals, are performed.

Safety of Caudal Blocks in Infants

Caudal blocks in children are generally very safe, with a very low incidence of serious complications. Most serious complications develop in infants less than 6 months old. The keys to safe caudal administration in infants include correct anatomic localization, avoidance of sharp beveled needles, safe dosages of local anesthetic, and slow incremental injection while monitoring the EKG. The use of ultrasound to define anatomy and verify placement also can increase the overall safety of the procedure.

Management of the Case Presented

A peripheral IV cannula was placed. The patient’s back was cleansed, and lidocaine 1% was injected in the skin above the L4-5 interspace. Because of the infant’s movement and difficulty with his positioning, 0.1 mg of midazolam was administered twice. The infant became calmer, but after multiple passes with a short 22-gauge spinal needle, blood was obtained each time. The infant was positioned upright, but the result was the same and the technique was abandoned.

General anesthesia with a caudal block was planned. Endotracheal intubation with a 3.5-mm endotracheal tube was achieved after administration of 10 mg of propofol and 5 mg of rocuronium. The infant was placed in the left lateral position, and the sacral hiatus located by palpation. Several passes were made with a 21-gauge long beveled needle. After a negative aspiration for blood and CSF, 5 mL of bupivacaine 0.25% was injected.

After completion of the caudal block, the infant was repositioned and surgery commenced. No changes in vital signs were noted at the time of incision. The surgery proceeded uneventfully. Throughout the procedure, a 2-L flow of sevoflurane 1% in an oxygen-nitrous oxide mixture of 50% was maintained. No opioids were administered. Surgical repair was slow and difficult. After 2.5 hours the patient’s heart rate increased slightly from 130 to 145 bpm, which was treated by increasing the sevoflurane concentration to 2%. Surgery lasted 3 hours. Plans were made for the infant to stay overnight in a monitored pediatric
ICU/step-down unit.
After surgery, preparations were made for a second caudal block. The infant was again placed in the left lateral position, still intubated and mechanically ventilated. Injection of another 5 mL of bupivacaine 0.25% was begun. The infant was placed supine, but perfusion appeared to be poor with mottling in all extremities. EKG showed a wide, complex sinusoidal rhythm at 220 bpm (Figure 6). Capnometry revealed an end-tidal CO2 concentration of 15 torr. Pulse oximetry and noninvasive blood pressure measurements were not registering.

CPR was initiated. Sevoflurane and nitrous oxide were discontinued. Asynchronous defibrillation was attempted 3 times in rapid succession in doses of 2 J/kg (10 J), 4 J/kg (20 J), and 4 J/kg. The rhythm remained unchanged. Epinephrine 0.5 mL (1:10,000) was administered. Another attempt at defibrillation was unsuccessful. Subsequently, a 5-mg/kg dose of amiodarone was administered. Defibrillation with 20 J resulted in a sinus rhythm at a rate of 110 with return of pulses and improved perfusion. Because local anesthetic toxicity was highly suspected, 5 cc of 20% intralipid was infused for 1 minute, followed by an infusion at 0.25 mL/kg per minute. The infant’s vital signs were stable, and he was taken to the pediatric ICU. Later that day, he was extubated, and he was discharged home the following day. A follow-up examination revealed no sequela.

**Conclusion**

As a patient, the ex-premature infant presents numerous challenges. Persistent risks for apnea and residual lung disease are major concerns. Regional anesthesia is a good choice for outpatient infrarumbilical surgery because it avoids many of the potential risks associated with general anesthesia. Regional anesthesia options are many; spinal and caudal techniques are preferred, but caudal block in combination with a general anesthetic can reduce the need for opioids and muscle relaxants. Factors that can increase the safety of caudal blocks in infants include the use of ultrasound, avoidance of beveled needles, safe dosing of local anesthetics, and slow, incremental injections. All pediatric anesthesiologists should follow the PALS algorithm in the event that an inadvertent intravascular injection of local anesthetic leads to cardiac toxicity. The use of intralipid 20% as an antidote has shown promise.

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References


Post-test

1. All of the following needles are acceptable for caudal blocks in infants, except:
   a. 20-gauge angiocatheter
   b. styletted spinal
   c. 21-gauge beveled hypodermic
   d. 22-gauge angiocatheter

2. The most likely reason that an ex-premature infant would require supplemental oxygen is:
   a. bronchopulmonary dysplasia
   b. apnea of prematurity
   c. hyaline membrane disease
   d. surfactant deficiency

3. Which statement is false regarding post-operative apnea in the ex-premature infant?
   a. Apnea will not develop in a patient who did not have it prior to surgery.
   b. Transfusing to a hematocrit level of 30% may prevent apnea.
   c. Postoperative apnea is less likely to develop in an infant of 58 weeks postconceptual age than in one of 40 weeks postconceptual age.
   d. Methylxanthines have been shown to help prevent apnea.

4. Which statement is true regarding the use of ultrasonography when performing a caudal block in infants?
   a. Ultrasound can only be used in the transverse plane.
   b. Injectate can be seen in the sacral canal when using the Doppler mode.
   c. Needle identification is key when using ultrasound during caudals.
   d. It is difficult to identify the sacral hiatus by an ultrasound examination.

5. When administering a caudal block with 0.25% bupivacaine in an infant:
   a. 2 mL/kg is a safe dose
   b. the solution contains only an L-enantiomer
   c. 1 mL/kg should not be exceeded
   d. the total volume can be administered quickly
6. **In the event of pulseless ventricular tachycardia following the administration of local anesthetic:**
   a. a bolus of intralipid should be the first intervention
   b. cardiopulmonary resuscitation should be administered, followed by asynchronous shocks of 1 J/kg
   c. amiodarone should be administered before epinephrine
   d. a bolus of 1 to 2 mL/kg of 20% intralipid should be given if conventional resuscitation is not successful

7. **Which of the following is a true statement about regional anesthesia in ex-premature infants?**
   a. A spinal approach is easier to perform than a caudal approach.
   b. An advantage of spinal over caudal anesthesia is that an indwelling catheter can be placed to redose the spinal block.
   c. A spinal is better than a caudal for a mid-thoracic block.
   d. Spinals generally require a higher volume of drug.

8. **Which anesthesia option is not recommended for an ex-premature infant undergoing unilateral hernia repair?**
   a. Local anesthetic infiltration supplemented with IV midazolam and fentanyl
   b. Spinal anesthesia, if IV sedatives are administered
   c. Caudal anesthesia, if IV sedatives are administered
   d. General anesthesia, if opioids are administered

9. **Regional anesthesia is preferred over general anesthesia in ex-premature infants because:**
   a. general anesthesia has been proven to cause neurotoxicity in infants
   b. apnea is less likely following regional anesthesia, if the patient undergoes little or no sedation
   c. monitoring of infants is not required when regional anesthesia is used
   d. infants can be sent home the same day when regional anesthesia is used

10. **Which of the following describes a way to make caudal blocks safer in the ex-premature infant?**
    a. Avoid using beveled hypodermic needles.
    b. Inject local anesthetics slowly and incrementally.
    c. Use epinephrine containing local anesthetic, and carefully monitor the electrocardiogram.
    d. All of the above are correct.