

Introduction

Treatment of pain following cardiac surgery is the subject of a growing number of publications and presentations given the current trend toward fast-track management of cardiac surgery patients. Tracheal extubation in the operating room or within a few hours of reaching the intensive care unit (ICU) has become common practice after the repair of simple cardiac defects.1-6 This precludes the use of large doses of systemic opioids during and after surgery due to resultant respiratory depression. An alternative approach to the treatment of postoperative pain is therefore required.

Neuraxial anesthesia involves the use of intrathecal or epidural opioids with or without local anesthetic agents. The use of neuraxial anesthesia in combination with general anesthesia for children undergoing cardiac surgery has been reported to facilitate early tracheal extubation.7,8 Reported benefits of neuraxial anesthesia in patients having cardiac surgery include attenuation of the neuroendocrine response to surgical stress, improved postoperative pulmonary function, enhanced cardiovascular stability, and improved postoperative analgesia. To the extent that neuraxial anesthesia facilitates early tracheal extubation in cardiac surgical patients, complications and costs associated with postoperative mechanical ventilation may be reduced. These benefits must, however, be weighed against the adverse effects that may accompany the use of neuraxial anesthesia. These include hypotension, postoperative respiratory depression, and epidural hematoma formation. In this chapter, the benefits and risks of neuraxial anesthesia in infants and children having open heart surgery are reviewed. In addition, specific techniques currently in use are described.

The benefits of neuraxial anesthesia in cardiac surgery

Adverse physiologic responses which occur during and after cardiac surgery include alterations in circulatory (tachycardia, hypertension, vasoconstriction), metabolic (increased catabolism), immunologic (impaired immune response), and hemostatic (platelet activation) systems.9,10 Together, these changes are referred to as the “stress response.” The stress response associated with cardiac surgery in neonates may be profound and is associated with increased morbidity and mortality. Anand et al.11 measured the stress response during and after cardiac surgery in 15 neonates anesthetized with halothane and morphine. They found elevated plasma concentrations of epinephrine, norepinephrine, cortisol, glucagon, and β-endorphin in all patients, accompanied by hyperglycemia and lactic acidemia. The four deaths in the study group occurred in neonates with the greatest stress responses.

Bromage et al.12 first demonstrated in 1971 that the stress response associated with major abdominal and thoracic surgery could be attenuated with epidural blockade. Since then, several investigators have shown that the use of neuraxial anesthesia during and after cardiac surgery (i.e. intraoperative anesthesia and postoperative analgesia) may decrease the stress response as well as morbidity and mortality.13-20 Neuraxial anesthesia (intrathecal or epidural blockade) with opioids and/or local anesthetics appears to be more effective in inhibiting the stress response associated with surgery than intravenous opioids. For example, epidural fentanyl is more effective than intravenous fentanyl in reducing the stress response after thoracotomy in adults.21 Epidural morphine administration was shown to attenuate the adverse decrease in triiodothyronine (T₃) concentration in children undergoing open heart surgery compared with general anesthesia alone.18 Epidural anesthesia with bupivacaine suppresses the increase in serum catecholamines, glucose, and adrenocorticotrophic hormone (ACTH) more effectively than intravenous fentanyl in infants.19 Epidural local anesthetics may be more efficacious than opioids in attenuating the stress response.20 In a study of fetal lambs, total spinal anesthesia completely blocked the stress response to surgical manipulation and cardiopulmonary bypass (CPB).22

Regional anesthesia and postoperative pain management

M. Gail Boltz
Gregory B. Hammer
In contrast, intravenous anesthetic techniques do not appear to mitigate the stress response. Gruber et al.\(^2\) studied the effects on the stress response of intravenous fentanyl and midazolam on 45 infants undergoing cardiac surgery. Patients were randomized to receive fentanyl 0.05–0.10 mg/kg with or without midazolam 0.10 mg/kg/hour during the surgery. Plasma epinephrine, norepinephrine, cortisol, adrenocortical hormone, glucose, and lactate were measured at five intervals during and after surgery. In all groups, plasma epinephrine, norepinephrine, cortisol, glucose, and lactate concentrations were significantly greater at the completion of surgery than prior to skin incision. The authors concluded that fentanyl dosing strategies, with or without midazolam, do not prevent a hormonal or metabolic stress response in infants undergoing cardiac surgery.

Additional benefits that may be attributed to neuraxial anesthesia include improved pulmonary function, greater circulatory stability, and reduced pain scores. Several randomized, controlled studies in adults have shown that patients receiving epidural analgesia have better pulmonary function after thoracic surgery than those treated with intravenous opioids. Thoracic epidural opioids are associated with improved pulmonary function following chest surgery compared with intravenous opioids.\(^2\) In a study comparing thoracic epidural meperidine to intravenous meperidine for postoperative analgesia, the patients receiving epidural infusions had significantly greater forced expiratory volumes in 1 second (FEV\(_1\)) and forced vital capacity (FVC), and were more cooperative with deep breathing maneuvers than those in the intravenous meperidine group.\(^2\) Thoracic epidural anesthesia may also improve respiratory performance post-operatively by effecting an improvement in diaphragmatic function.\(^2\)

Early tracheal extubation is an important factor in reducing ICU length of stay and the duration of hospitalization.\(^4\) Especially in children with single ventricle physiology (e.g. following bilateral cavopulmonary anastomosis or modified Fontan operations), spontaneous ventilation may result in improved hemodynamics by decreasing intrathoracic pressure and thereby increasing pulmonary blood flow.\(^2\) Early tracheal extubation may also obviate or reduce complications associated with mechanical ventilation, including trauma to the lungs and airways, inadvertent dislodgement or malpositioning of the tracheal tube, and adverse hemodynamic changes associated with tracheal suctioning. The cost of mechanical ventilation can be avoided in patients who are extubated in the operating room.\(^4\) A number of studies have shown that infants and children can be safely extubated within several hours following the completion of surgery.\(^1,2,6,25\) The majority of reports of early extubation following open heart surgery in infants and children include a period of 6–8 hours of mechanical ventilation in the ICU after surgery. A limited number of reports describe tracheal extubation in the operating room at the completion of surgery.

### Early extubation without neuraxial anesthesia

In an early report of tracheal extubation in the operating room following congenital heart surgery, Schuller et al.\(^3\) reviewed the records of 209 children who had undergone repair of congenital heart defects. Fifty-two percent of infants between the ages of 3 and 12 months and 88% of patients over the age of 12 months were extubated in the operating room. Four patients were reintubated in the operating room or ICU. Inhaled agents were supplemented with low doses of fentanyl to provide anesthesia. Similarly, Burrows et al.\(^3\) reviewed the management of 36 children undergoing repair of secundum atrial septal defects under isoflurane and fentanyl anesthesia. The tracheas of 19 children (53%) were extubated in the operating room. Compared to those children receiving postoperative mechanical ventilation, these patients had shorter CPB times (24 vs. 32 minutes) and received lower doses of fentanyl (5.9 vs. 35.1 µg/kg).

Laussen et al.\(^5\) reported tracheal extubation in the operating room after atrial septal defect repair as part of a clinical practice guideline in children. Of 66 children reviewed subsequent to the implementation of the practice guideline, 25 patients (38%) were extubated in the operating room while the remainder received postoperative mechanical ventilation. The children in the early extubation group received less fentanyl (6.0 vs. 27.5 µg/kg), were more likely to have a respiratory acidosis on admission to the ICU, and had an increased frequency of vomiting in the ICU. Eight children in the early extubation group received caudal morphine 50–75 µg/kg vs. two children in the postoperative mechanical ventilation group. There was no difference in ICU stay or in clinical outcomes. The patients extubated in the operating room had significantly lower hospital charges due to the absence of postoperative mechanical ventilation.

Cray et al.\(^6\) reported the use of propofol with “low dose” opioid anesthesia to facilitate early tracheal extubation following cardiac surgery in children between the ages of 6 months and 18 years. Isoflurane and fentanyl (up to a maximum dose of 20 µg/kg) were given prior to and during CPB. In patients for whom early tracheal extubation was considered, a propofol infusion was started at 50 µg/kg/minute as well as a morphine infusion at a dose of 10–40 µg/kg/minute. The median time to tracheal extubation was 5 hours. The goal of extubation within 6 hours was achieved in 56 children (62%). Causes for prolonged intubation included bleeding and phrenic nerve palsy. One child was reintubated shortly following extubation due to excessive respiratory depression.

### Neuraxial anesthesia and early extubation

Neuraxial anesthesia techniques have been used to facilitate
early tracheal extubation following cardiac surgery, improve postoperative analgesia, and reduce the incidence of side effects caused by intravenous opioids. Jones et al. reported the use of intrathecal morphine for postoperative analgesia in 56 children undergoing cardiac surgery. Following induction of anesthesia, patients received intrathecal morphine 0.02 or 0.03 mg/kg. Tracheal extubation was performed in all patients after admission to the ICU shortly following the completion of surgery. The duration of analgesia in both groups was similar, with two-thirds of patients requiring no supplemental analgesia for more than 18 hours.

In a retrospective review of pain control in 91 children undergoing cardiac surgery, Shayevitz et al. compared lumbar epidural morphine infusions to intravenous opioid analgesia. In the epidural analgesia group, lumbar epidural catheters were placed following induction of anesthesia. Preservative-free morphine sulfate was administered in an initial dose of 0.05 mg/kg followed by a continuous infusion of 0.003–0.004 mg/kg/hour during and after surgery. Children in the intrathecal morphine group received an initial dose of fentanyl 0.05 mg/kg i.v. followed by a continuous infusion of 0.018 mg/kg/hour i.v. during surgery. The fentanyl infusion was reduced to 0.006 mg/kg/hour i.v. postoperatively. Patients in the epidural analgesia group had significantly lower pain scores and received significantly less supplemental analgesia postoperatively than patients in the intrathecal morphine group.

In a prospective, randomized, controlled study, Rosen and Rosen evaluated the efficacy of caudal epidural morphine compared with intravenous morphine in 32 children following open cardiac surgery. Patients in the study group received a caudal injection of preservative-free morphine sulfate 0.075 mg/kg in the operating room following surgery prior to awakening and tracheal extubation. Children in the control group received intravenous morphine alone for postoperative analgesia. Supplemental doses of intravenous morphine were given to children in both groups as needed, prior to which pain scores were recorded. Children having received caudal morphine required significantly less intravenous morphine and had significantly lower pain scores postoperatively than patients in the control group. The mean duration of complete analgesia in children receiving caudal morphine was 6 hours (range 2–12 hours), but decreased analgesic requirements were noted for the entire 24-hour study period.

In another prospective, randomized, controlled study, Hammer et al. compared postoperative analgesia in children receiving a remifentanil-based anesthetic with or without spinal anesthesia for open heart surgery. Patients in both groups were extubated in the operating room immediately following the completion of surgery. Intravenous fentanyl was administered according to age-appropriate pain scores postoperatively. Patients in the spinal anesthesia group received significantly less fentanyl during the initial 8- and 24-hour periods following surgery than those in the control group ($P < 0.01$, $P = 0.02$, respectively). There was a trend toward lower pain scores in patients receiving spinal anesthesia compared with those in the control group.

In addition to the benefits of improved lung function and pain control, patients receiving neuraxial anesthesia have fewer opioid-related side effects than patients treated with intravenous opioids. Patients receiving epidural anesthesia have more rapid return of bowel function following surgery compared with those receiving intravenous analgesics. In a recent review of 16 studies comparing epidural and systemic analgesia with regard to postoperative recovery of gastrointestinal function, all eight studies with epidural catheter placement above T12 showed more rapid recovery of bowel function when epidural analgesia was used. The use of postoperative thoracic epidural analgesia with bupivacaine and morphine was associated with earlier return of gastrointestinal function and decreased hospital costs due to shortened hospital stay compared with intravenous morphine patient-controlled analgesia (PCA). A study comparing epidural vs. intravenous fentanyl analgesia following thoracotomy also reported a lower incidence of nausea, shorter duration of ileus, and earlier hospital discharge in the epidural analgesia group.

**Adverse effects of neuraxial anesthesia for cardiac surgery**

Although neuraxial anesthesia offers many benefits, adverse effects may occur. The most serious complications that may be associated with neuraxial anesthesia for cardiac surgery are hypotension, respiratory depression, and epidural hematoma formation.

Systemic arterial hypotension is an undesired effect of intrathecal and epidural local anesthetic blockade. In adults with coronary artery stenosis and myocardial ischemia, local anesthetic-induced blockade of cardiac sympathetic nerve activation alleviates angina and improves coronary blood flow and ventricular function. However, local anesthetic blockade to upper thoracic dermatomes produces hypotension accompanied by a decrease in coronary artery perfusion. In infants and young children, local anesthetic blockade to T3–T5 does not produce significant changes in blood pressure nor heart rate. This may be attributable to increased sympathetic innervation of the lower extremities and/or immaturity of the sympathetic nervous system in young children. In two recent studies of high spinal blockade in children undergoing open heart surgery, hemodynamic stability was demonstrated in all patients.

Respiratory depression may be seen in children following the administration of epidural opioids in doses exceeding 0.05 mg/kg. However, in a study of children undergoing cardiac surgery and receiving epidural morphine in an initial
dose of 0.05 mg/kg followed by a continuous infusion, respiratory depression did not occur.32 Several other studies in children have shown excellent analgesia and no evidence of respiratory depression when the dose of epidural morphine does not exceed 0.05 mg/kg.44–46

Similarly, doses of intrathecal morphine exceeding 0.02 or 0.03 mg/kg may result in significant respiratory depression following cardiac surgery in children.31 Intrathecal morphine 0.01 mg/kg has also been associated with respiratory depression postoperatively when combined with midazolam and intravenous fentanyl 0.02 mg/kg in adult patients undergoing cardiac surgery.47 However, in a review of children given intrathecal morphine in a dose of 0.02 mg/kg in whom no intravenous opioids were administered during surgery, no patient had postoperative respiratory depression.48 In addition, no child required supplemental opioid analgesia for at least 15 hours following surgery. In a recent study comparing intrathecal morphine in doses of 0.005, 0.007, and 0.010 mg/kg in children having open heart surgery, the trachea of each patient was extubated at the conclusion of surgery and no patient had signs of respiratory depression.49 Hammer et al.50 reported results of a study of postoperative respiratory depression in children anesthetized with remifentanil with or without spinal anesthesia for open heart surgery. The authors found only mild elevation in arterial carbon dioxide tension in children in both groups following surgery. No patient required intervention for respiratory depression.

Epidural hematoma formation following epidural or spinal anesthesia is a rare but potentially catastrophic complication of neuraxial blockade. In an analysis of 20 series, including more than 850,000 cases of epidural blockade and 650,000 cases of spinal anesthesia in adult patients, only three case reports of epidural hematoma were documented.51 Based on these data, the author estimated the risk of epidural hematoma to be 1:150,000 following epidural anesthesia and 1:220,000 following spinal anesthesia. Unfortunately, it is unknown what the incidence of clotting disorders, use of anticoagulants, or traumatic procedures was in these reports.

In a thorough review of the literature from 1906 through 1994, Vandermeulen et al.52 found 61 published cases of epidural or subdural hematoma following epidural or spinal anesthesia in adult patients. Of these 61 cases, 42 occurred in patients with impaired coagulation function prior to epidural or spinal needle placement, including 25 patients receiving heparin. In 15 patients, the procedure was reported to be difficult and/or traumatic. A clotting disorder or difficult/traumatic needle placement was present in 53 of the 61 cases (87%).

In a series of over 4000 epidural or spinal anesthetics performed prior to anticoagulation with heparin for vascular surgery, no cases of epidural hematoma were reported.53 The authors highlighted important precautions that were undertaken in these patients, including delaying surgery for at least 1 hour between needle placement and heparin administration. Other recommended precautions include use of the smallest dose of heparin necessary to achieve therapeutic objectives and removal of epidural catheters only when normal coagulation function has been restored.54 Although traumatic needle placement may increase the risk of hemorrhage, there are no data to guide the practitioner as to whether or not surgery should be cancelled. Patients must be monitored postoperatively for signs of unexpected motor blockade suggestive of epidural hematoma formation. When epidural analgesia is used following surgery, the minimum effective concentration of local anesthetic should be administered to allow early detection of an epidural hematoma.55 Epidural hematoma formation has not been reported in a patient following spinal anesthesia performed prior to CPB.

Pediatric data regarding neuraxial hematoma are sparse, but a symptomatic intraspinal hematoma has been reported in a neonate undergoing non-cardiac surgery from a caudal epidural catheter threaded to the lumbar level.56 In the largest series reported to date, 961 pediatric patients undergoing cardiothoracic surgery who received catheter epidural techniques were studied.57 Caudal, lumbar, and thoracic sites were studied, and heparinized and non-heparinized cases, as well as coarctation of aorta repairs were included. There was a 7.9% incidence of observing blood through the needle or catheter during placement, and 88% of these incidents were with caudal catheters. Surgery apparently was not delayed in these cases, but a median of 90 minutes elapsed between catheter placement and heparinization for caudal catheters, and 183 minutes for thoracic epidurals. No neurologic deficits attributable to the epidurals were noted in any patient, including 60 patients undergoing coarctation repair, three of whom bled during catheter placement. Despite the lack of reports of neurologic injury with neuraxial techniques and their benefits to facilitate early extubation and pain control, neuraxial anesthesia for cardiac surgery in children remains a very controversial topic, and awaits large-scale controlled studies.58

**Neuraxial anesthesia techniques**

A variety of neuraxial blockade techniques have been reported in children undergoing cardiac surgery. These include intrathecal (spinal) and epidural techniques utilizing opioids and/or local anesthetics. Epidural approaches include single dose (“single shot”) caudals as well as thoracic, lumbar, and caudal catheter techniques.

**Intrathecal (spinal) techniques**

The use of spinal opioid analgesia as an adjunct to general anesthesia was first described by Mathews and Abrams in 1980. In this report, 40 adults received intrathecal morphine...
in a dose of 1.5–4.0 mg prior to surgery. All patients remained comfortable for more than 24 hours. Subsequently, many studies have demonstrated the efficacy of spinal opioids, primarily morphine, in producing analgesia following cardiac surgery in adult patients. These reports have been summarized elsewhere. Although intrathecal morphine alone has not been shown to attenuate the stress response associated with cardiac surgery per se, it may attenuate the stress response in the immediate postoperative period.

In order to augment the effects of intrathecal opioids in reducing the stress response and circulatory instability in patients undergoing cardiac surgery, local anesthetics have been used in combination with intrathecal opioids. In adults, however, intrathecal injection of local anesthetics in doses needed to attain high spinal blockade results in hypotension. Young children, on the other hand, do not develop hypotension following high spinal blockade. Finkel et al. studied the hemodynamic effects of spinal anesthesia in children undergoing cardiac surgery. In this study, 30 children between the ages of 7 months and 13 years received intrathecal morphine mixed with tetracaine following induction of general anesthesia and tracheal intubation. The dose of tetracaine was adjusted for age, according to the estimated volume of cerebrospinal fluid. Patients aged 6–12 months received intrathecal tetracaine 2.0 mg/kg, those between the ages of 1 and 3 years received 1.0 mg/kg, and those over the age of 4 years received 0.5 mg/kg. Tetracaine was mixed with 10% dextrose to yield a 0.5% hyperbaric solution, and all patients received preservative-free morphine in a dose of 0.005–0.010 mg/kg. Patients were placed in a 30° head-down (Trendelenberg) position for a minimum of 10 minutes following administration of the intrathecal solution. Although there was mild slowing of the heart rate in children over age 4 years, there was no clinically significant bradycardia nor hypotension observed. Hammer et al. have also reported hemodynamic stability following intrathecal tetracaine/morphine in children undergoing cardiac surgery.

The use of spinal anesthesia in combination with general anesthesia has been reported in children for whom tracheal extubation is planned prior to leaving the operating room following open heart surgery. Surgical procedures included repair of atrial and/or ventricular septal defects, anomalous pulmonary venous return, aortic or pulmonary valvuloplasty, right ventricular-to-pulmonary artery conduit placement or exchange, bidirectional cavopulmonary shunt, and the modified Fontan procedure. Spinal anesthetic blocks were performed immediately after tracheal intubation (i.e. prior to placement of arterial and central venous catheters) in order to maximize the time interval between spinal anesthetic block and heparinization for CPB. Patients were placed with the head of the table 30° down for a minimum of 15 minutes following spinal anesthetic block. No intravenous opioids were administered intraoperatively. The authors’ dosing regimen for spinal anesthetic blocks is shown in Table 17.1.

### Table 17.1

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Tetracaine (mg/kg)</th>
<th>Morphine (mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1</td>
<td>2.0</td>
<td>0.007</td>
</tr>
<tr>
<td>1–3</td>
<td>1.0</td>
<td>0.007</td>
</tr>
<tr>
<td>4–8</td>
<td>0.5</td>
<td>0.007</td>
</tr>
<tr>
<td>&gt; 8</td>
<td>0.0</td>
<td>0.010</td>
</tr>
</tbody>
</table>

### Epidural techniques

The use of postoperative epidural analgesia in patients undergoing open heart surgery was first described by Hoar et al. in 1976. Subsequently, El-Baz and Goldin reported the use of epidural blockade initiated prior to surgical incision. In 1989, Rosen and Rosen first reported the efficacy of epidural morphine analgesia in children undergoing cardiac surgery. Since then, many studies have reported favorable results with epidural anesthesia and analgesia for cardiac surgery.

In general, epidural anesthesia is used in patients undergoing open heart surgery for whom tracheal extubation is planned in the operating room following the completion of surgery or shortly thereafter. The epidural technique most commonly used in children is the administration of a single dose of morphine injected into the caudal epidural space. Morphine is favored for caudal epidural administration due to its low lipid solubility and tendency to spread cephalad to thoracic dermatomes. Following induction of general anesthesia and tracheal intubation, preservative-free morphine sulfate is injected in a dose of 0.05–0.10 mg/kg into the caudal epidural space via an epidural needle or intravenous catheter. Intravenous opioids, if administered intraoperatively, are given in restricted doses (e.g. fentanyl 0.01–0.02 mg/kg).

Alternatively, a caudal epidural catheter may be inserted to facilitate continuous administration of morphine during and after surgery. Following an initial dose of epidural morphine 0.04 mg/kg, a continuous infusion is begun in a dose of 0.0075 mg/kg/hour. The infusion is continued throughout the intraoperative period and maintained postoperatively for 48–72 hours. If the patient appears overly somnolent the infusion is decreased in increments of 0.0025 mg/kg/hour (pers. comm., D. Rosen to G.B. Hammer, January 2000).

In order to attenuate the stress response associated with cardiac surgery and CPB as well as optimize postoperative analgesia, a combination of epidural opioids and local anesthetic agents may be used. Although local anesthetic agents may spread to thoracic dermatomes when administered via the caudal epidural space, potentially toxic doses of local anesthetics may be required to achieve thoracic analgesia. Thoracic epidural blockade may be achieved with greater safety and efficacy by placing the epidural catheter tip in proximity to the spinal segment associated with surgical

---

**CHAPTER 17** Regional anesthesia and postoperative pain management

---
Pared with “single shot” techniques is that adjustments can be made in dosing postoperatively according to the patient’s level of comfort. For example, a “bolus” of epidural anesthetic agents may be given and the infusion rate increased if the patient is experiencing pain. Alternatively, the infusion may be decreased if the patient becomes somnolent. Table 17.3 lists suggested regimens for thoracic epidural opioids.

Ropivacaine is a newer long-acting local anesthetic agent that has the advantage of reduced cardiotoxicity and neurotoxicity compared to bupivacaine.69,70 It also has less propensity to cause motor blockade in children.71 Its pharmacokinetics for long-term (2–4 days) infusion via lumbar or low thoracic epidural catheter has been studied, and plasma levels are well within the safe range in children 4 months to 7 years in age undergoing major abdominal surgery.72 Analgesia was excellent and side effects few with 0.2% ropivacaine infused at 0.4 mg/kg/hour. Of note is that starting doses for neonates and young infants under 3 months of age should be reduced by 50% because of reduced clearance of all agents due to renal and hepatic immaturity in this age group.

Side effects related to neuraxial opioids include nausea and vomiting, pruritus, somnolence, respiratory depression, and urinary retention. Nausea and vomiting as well as pruritus appear to be relatively uncommon in infants and are primarily seen in children over the age of 3 years. These side effects are more common with morphine compared with hydromorphone and fentanyl.73 Due to greater rostral spread, respiratory depression is also more common when morphine is used compared with hydromorphone.63,73 Urinary retention is seen most commonly during the initial 24 hours of therapy, during which time the majority of patients have urinary

### Table 17.2 Local anesthetic dosing regimens for thoracic epidural anesthesia.

<table>
<thead>
<tr>
<th>Epidural local anesthetics</th>
<th>Intraoperative dosing</th>
<th>Postoperative infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bupivacaine</td>
<td>0.25%: 0.5 mL/kg initial, then 0.3 mL/kg every 90 seconds</td>
<td>0.1%: 0.15–0.30 mL/kg/h, max. dose 0.4 mg/kg/h</td>
</tr>
<tr>
<td>Ropivacaine</td>
<td>0.2%: 0.5 mL/kg initial, then 0.3 mL/kg every 90 seconds</td>
<td>0.1%: 0.15–0.30 mL/kg/h, max. dose 0.4 mg/kg/h</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Agent</th>
<th>Intraoperative bolus</th>
<th>Postoperative infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fentanyl (thoracic)</td>
<td>1–2 µg/kg</td>
<td>1–5 µg/mL: 0.25–1.00 µg/kg/h</td>
</tr>
<tr>
<td>Hydromorphone (caudal/lumbar)</td>
<td>7–8 µg/kg</td>
<td>10–30 µg/mL: 2–3 µg/kg/h</td>
</tr>
<tr>
<td>Morphine (caudal/lumbar)</td>
<td>50–75 µg/kg</td>
<td>50 µg/mL: 4–6 µg/kg/h</td>
</tr>
</tbody>
</table>

Reduce doses of all agents 50% for infants under 3 months of age; use local anesthetic doses at lower end of range for thoracic epidural catheters.

Incision. Segmental anesthesia may then be achieved with lower doses of local anesthetic than those needed when the catheter tip is distant from the surgical site. In infants, a catheter can be advanced from the caudal to the thoracic epidural space.65 For example, with the infant in the lateral decubitus position, a 20-gauge epidural catheter may be inserted via an epidural needle or an 18-gauge intravenous catheter placed through the sacrococcygeal membrane. The epidural catheter is then advanced 16–18 cm to the mid-thoracic epidural space. Minor resistance to passage of the catheter may be overcome by simple flexion or extension of the spine. If continued resistance is encountered, no attempt should be made to advance the catheter further, as the catheter may become coiled within or exit the epidural space. A newly described method to guide placement of caudal epidural catheters at thoracic dermatomes is to use the electrocardiogram (ECG).68 All catheters in this report were within two vertebrae of the target. Radiographic confirmation of tip location may be undertaken following placement or postoperatively. In older children, a thoracic epidural catheter may be inserted directly between T4 and T8 to provide intraoperative anesthesia and postoperative analgesia. As with spinal anesthetic block, epidural catheter placement should be performed immediately following tracheal intubation in order to maximize the time elapsed prior to heparin administration for CPB. Hammer et al.7 reported the use of an initial dose of hydromorphone 0.007–0.008 mg/kg and 0.25% bupivacaine 0.5 mL/kg. Subsequent doses of 0.25% bupivacaine 0.3 mL/kg are administered intraoperatively at approximately 90 minute intervals. No intravenous opioids are given during surgery. Postoperatively, a continuous infusion of 0.10% bupivacaine and hydromorphone 0.003 mg/mL is administered at a rate of 0.3 mL/kg/hour. Intraoperative and post-operative thoracic epidural local anesthetic regimens are listed in Table 17.2. An advantage of epidural catheter compared with “single shot” techniques is that adjustments can be made in dosing postoperatively according to the patient’s level of comfort. For example, a “bolus” of epidural anesthetic agents may be given and the infusion rate increased if the patient is experiencing pain. Alternatively, the infusion may be decreased if the patient becomes somnolent. Table 17.3 lists suggested regimens for thoracic epidural opioids.

Ropivacaine is a newer long-acting local anesthetic agent that has the advantage of reduced cardiotoxicity and neurotoxicity compared to bupivacaine.69,70 It also has less propensity to cause motor blockade in children.71 Its pharmacokinetics for long-term (2–4 days) infusion via lumbar or low thoracic epidural catheter has been studied, and plasma levels are well within the safe range in children 4 months to 7 years in age undergoing major abdominal surgery.72 Analgesia was excellent and side effects few with 0.2% ropivacaine infused at 0.4 mg/kg/hour. Of note is that starting doses for neonates and young infants under 3 months of age should be reduced by 50% because of reduced clearance of all agents due to renal and hepatic immaturity in this age group.

### Treatment of side effects

Side effects related to neuraxial opioids include nausea and vomiting, pruritus, somnolence, respiratory depression, and urinary retention. Nausea and vomiting as well as pruritus appear to be relatively uncommon in infants and are primarily seen in children over the age of 3 years. These side effects are more common with morphine compared with hydromorphone and fentanyl.73 Due to greater rostral spread, respiratory depression is also more common when morphine is used compared with hydromorphone.63,73 Urinary retention is seen most commonly during the initial 24 hours of therapy, during which time the majority of patients have urinary
To provide supplemental analgesia, a variety of drugs may be used. Recently, the use of epidural and intrathecal clonidine to provide postoperative analgesia has been described. Clonidine has been shown to prolong and potentiate the effects of local anesthetics by as much as 50–114%. The administration of clonidine in an initial dose of 1–2 µg/kg followed by a continuous infusion of 0.08–0.12 µg/kg/hour with bupivacaine or ropivacaine appears safe and effective for use in children. Motsch et al. compared caudal clonidine 5 µg/kg with 0.175% bupivacaine to 0.175% bupivacaine alone. The authors reported a prolongation of caudal blockade with the use of clonidine.

### Adjuncts and alternatives to neuraxial analgesia

In order to decrease the incidence and magnitude of side effects associated with spinal and epidural opioids, a variety of drugs may be used to provide supplemental analgesia.

<table>
<thead>
<tr>
<th>Side effect</th>
<th>Treatment</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea/vomiting</td>
<td>Metoclopramide 0.1–0.2 mg/kg/dose i.v. Q 6 h</td>
<td>Extrapyramidal reactions may occur but are uncommon</td>
</tr>
<tr>
<td></td>
<td>Maximum dose: 10 mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Droperidol 0.025–0.05 mg/kg i.v. Q 6 h p.r.n.</td>
<td>Very sedating—avoid if somnolent</td>
</tr>
<tr>
<td></td>
<td>Maximum dose: 1.25 mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diphenhydramine 0.5–1.0 mg/kg i.v. Q 6 h p.r.n.</td>
<td>Very sedating—avoid if somnolent</td>
</tr>
<tr>
<td></td>
<td>Maximum dose: 50 mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ondansetron 0.1–0.2 mg/kg i.v. Q 6 h p.r.n.</td>
<td>May substitute other S-HT3 antagonist, e.g. granisetron or dolasetron</td>
</tr>
<tr>
<td></td>
<td>Maximum dose: 4 mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nalbuphine 0.1 mg/kg i.v. Q 6 h p.r.n.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Naloxone 0.001–0.005 mg/kg/h infusion</td>
<td>Excessive doses may compromise analgesia</td>
</tr>
<tr>
<td></td>
<td>Propofol 0.001–0.010 mg/kg/h infusion</td>
<td></td>
</tr>
<tr>
<td>Pruritus</td>
<td>Diphenhydramine 0.5–1.0 mg/kg i.v. Q 6 h p.r.n.</td>
<td>Very sedating—avoid if somnolent</td>
</tr>
<tr>
<td></td>
<td>Maximum dose: 50 mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nalbuphine 0.1 mg/kg i.v. Q 6 h p.r.n.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Naloxone 0.001–0.005 mg/kg/h infusion</td>
<td>Excessive doses may compromise analgesia</td>
</tr>
<tr>
<td>Somnolence</td>
<td>Decrease epidural opioid infusion</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Consider low dose naloxone infusion (above)</td>
<td></td>
</tr>
<tr>
<td>Respiratory depression</td>
<td>Severe: Administer 100% oxygen via facemask</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Initiate positive pressure ventilation p.r.n.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Naloxone 0.001–0.010 mg/kg i.v.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Stop epidural infusion</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Subsequently/Mild–moderate depression:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Increase FIO$_2$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Reduce epidural opioid infusion</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Naloxone 0.001–0.005 mg/kg/h infusion</td>
<td></td>
</tr>
<tr>
<td>Urinary retention</td>
<td>Replace urinary catheter p.r.n.</td>
<td></td>
</tr>
</tbody>
</table>
addition of clonidine, but some sedation, hypotension and bradycardia were seen at this dose.

For patients who are not receiving a regional anesthetic technique to provide postoperative analgesia, systemic opioids are used to treat postoperative pain. Although intermittent intramuscular and subcutaneous injections have been used widely in the past, these routes of administration are painful and are associated with unpredictable and erratic uptake and distribution. Intermittent intravenous injections with opioids of short or moderate duration are also associated with periods of excessive sedation and inadequate analgesia. Continuous analgesia may be achieved when opioids are administered by continuous intravenous infusion with or without PCA dosing.

Morphine is commonly used for postoperative analgesia. In neonates less than 1 month of age, clearance is reduced and elimination half-life is prolonged and is about three times that in adults. For continuous infusions of morphine, a loading dose of 0.025–0.075 mg/kg followed by infusion rates of 0.005–0.015 mg/kg/hour result in therapeutic plasma concentrations in neonates. Older infants and children require a loading dose of 0.05–0.10 mg/kg/hour followed by an initial infusion rate of 0.01–0.03 mg/kg/hour. In children receiving PCA, dosing in the range of 0.01–0.03 mg/kg with a lock-out interval of 6–10 minutes with or without a continuous infusion has been recommended. In children at risk for morphine-induced histamine release, fentanyl (0.0005–0.001 mg/kg/hour ± 0.0005–0.001 mg/kg PCA dose) or hydromorphone (0.003–0.005 mg/kg/hour ± 0.003–0.005 mg/kg PCA dose) may be used. Patient-controlled analgesia dosing regimens are listed in Table 17.5.

The use of methadone, which has a half-life of approximately 17 hours in children over the age of 1 year, may provide more continuous analgesia than shorter-acting agents. For moderate-to-severe pain, intermittent intravenous doses of methadone between 0.05 and 0.08 mg/kg as needed may be given. The side effects that may occur with intravenous opioid administration are similar to those described with epidural opioids, and may be treated similarly (see Table 17.4). With epidural or intravenous techniques, improved analgesia and a decrease in opioid dosing (and side effects) may be achieved with concomitant administration of non-opioid analgesic agents. Ketamine has been administered in a sub-analgesic dose by continuous infusion to achieve sedation and analgesia in adults during mechanical ventilation after major surgery. In a study by Hartvig et al., 10 children were given continuous infusions of ketamine supplemented with intermittent doses of midazolam to provide analgesia and sedation after cardiac surgery. Ketamine infusions were administered in doses of 1 and 2 mg/kg/hour. Both ketamine infusion regimens provided acceptable analgesia and sedation during and after weaning from mechanical ventilation. Psychomimetic effects were not seen and may have been suppressed by the supplemental use of midazolam. Ketamine infusions can also be used to decrease morphine requirements and may be useful in patients developing signs of spinal cord sensitization.

Non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used as an adjunct to other forms of analgesia after thoracic surgery, but their use after cardiac surgery is controversial. Non-steroidal anti-inflammatory drug use in cardiac surgical patients has been limited by the risks of gastritis, renal impairment, and inhibiton of platelet aggregation. Non-steroidal anti-inflammatory drugs exert their antinociceptive action by blocking the peripheral synthesis of prostaglandins through inhibition of the cyclo-oxygenase enzymes (COX-1 and COX-2). A central mechanism has also been proposed. Inhibition of COX-2 causes gastritis, platelet dysfunction, and renal impairment. Studies evaluating the use of NSAIDs after cardiac surgery have concluded that a morphine-sparing effect is present. In 120 patients scheduled for elective CAGB surgery, diclofenac, ketoprofen, and indomethacin were compared to placebo. Diclofenac appeared to have the best analgesic effect as evidenced by reducing the need for morphine and other analgesic agents postoperatively. The short-term use of NSAIDs in the postoperative period does not appear to be associated with increased bleeding from the surgical site nor with an increased incidence of gastrointestinal bleeding. New COX-2 inhibitors, including celecoxib and rofecoxib, specifically inhibit synthesis of prostaglandins that produce pain, inflammation, and fever.

Acetaminophen suppositories are a frequently overlooked but effective adjunct to other analgesic methods in infants and children following major surgery. An initial dose of 30–45 mg/kg (maximum dose 1000 mg), followed by 20 mg/kg every 6 hours, for 48–72 hours, has a narcotic sparing effect, with negligible danger of toxicity.

Table 17.5 Intravenous patient-controlled analgesia regimens.

<table>
<thead>
<tr>
<th>Agent</th>
<th>Bolus dose (µg/kg)</th>
<th>Continuous rate (µg/kg/h)</th>
<th>4-h limit (µg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>15–25</td>
<td>4–15</td>
<td>300</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>3–5</td>
<td>1–3</td>
<td>60</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>0.25</td>
<td>0.15</td>
<td>4</td>
</tr>
</tbody>
</table>

Patient should be developmentally normal 6–7 years of age or older; meperidine is contraindicated for patient-controlled analgesia.

Conclusion

The use of epidural and spinal anesthesia in infants and children may attenuate the stress response and thereby decrease morbidity and mortality associated with cardiac surgery. In
addition, the use of these neuraxial anesthesia techniques during and after cardiac surgery may result in improved pulmonary function, greater circulatory stability, and better postoperative pain control compared with general anesthesia and postoperative intravenous opioid analgesia. To the extent that neuraxial anesthesia may facilitate tracheal extubation in the operating room immediately following surgery, complications and the expense associated with mechanical ventilation in the postoperative period may be avoided. In those patients who undergo tracheal extubation in the ICU, cost savings may be achieved due to reductions in time of mechanical ventilation and ICU length of stay, as well as earlier resumption of a regular diet.

The risks of epidural and spinal anesthesia in these patients include undesired side effects (nausea and vomiting, pruritus), hypotension, respiratory depression, and epidural hematoma formation. The incidence of side effects does not appear to exceed that associated with intravenous opioid analgesia. Hypotension, associated with local anesthetic spinal and epidural blockade in adult patients, is uncommon in infants and young children. Postoperative respiratory depression is greatly reduced by avoiding intraoperative opioids and using prudent doses of spinal and epidural opioids.

The risk of epidural hematoma formation is small but finite. This risk can be minimized by employing reasonable safeguards. Appropriate precautions include selecting patients with normal coagulation function prior to needle placement, abandoning the neuraxial anesthesia technique if needle placement is difficult, and delaying surgery in the event of return of blood via the needle or epidural catheter. The time interval between needle placement and heparin administration should be maximized, allowing for an interval of at least 60 minutes. Epidural catheters should be removed only after normal coagulation function has been restored following surgery.

Future studies may provide additional information regarding the dose–response relationships of neuraxial anesthetic agents in patients undergoing cardiac surgery. Modulation of the stress response in neonates, e.g. utilizing spinal anesthesia, warrants investigation. In addition, strategies to decrease the incidence of opioid-related side effects (e.g. prophylactic antiemetic therapy) may be developed.

References

23 Gruber EM, Laussen PC, Casta A. Stress response in infants undergoing cardiac surgery: A randomized study of fentanyl bolus,
PART 4 Management

54 Chaney MA. Intrathecal and epidural anesthesia and analgesia for cardiac surgery. Anesthesiology 1997; 84: 1211–21.


64 Dahlstrom B. Pharmacokinetics and pharmacodynamics of epidural and intrathecal morphine. Int Anesthesiol Clin 1986; 24: 29–42.


69 Graf BM, Abraham I, Eberbach N et al. Differences in cardio-toxicity of bupivacaine and ropivacaine are the result of physico-chemical and stereoselective properties. Anesthesiology 2002; 96: 1427–34.


