We conducted this retrospective study to document the efficacy and safety, and demonstrate the spectrum of indications for subcutaneously tunneled epidural catheters in the management of prolonged pain in pediatric patients. The charts of 25 patients with prolonged pain that was unresponsive to conventional opioid therapy (10: end stage malignancy, 8: extensive abdominal surgery, 7: trauma, etc.) and who received thoracic, lumbar, or caudal tunneled epidural catheters between 1995 and 1999 were reviewed for efficacy and catheter-related complications (infection or bleeding at the insertion site, toxicity related to local anesthetics, tachyphylaxis and respiratory depression). Tunneled epidural catheters were effective in providing extended analgesia in all subjects. In 14 patients with chronic pain, cumulative 48-h enteral and parenteral opioid requirements were reduced or eliminated after catheter insertion. Catheters remained in place for a median of 11 days (range, 4–240 days) until there was no further need for parenteral analgesia (n = 15), death because of the underlying disease (n = 6), accidental removal (n = 2), or possible infection (n = 2). No serious local or systemic complications (meningitis, epidural abscess, systemic infection, epidural hematoma, or spinal cord injury; seizures, local anesthetic toxicity) occurred related to this technique. Five patients were discharged from the hospital with the catheter for home analgesic therapy. The use of a percutaneously inserted, subcutaneously tunneled epidural catheter is safe, effective, and provides pain relief in situations in which conventional analgesic therapy either fails or is impractical. The technique is one that may be of great value to children suffering from pain.

(Historically, children have been under-treated for pain and for painful procedures (1). We now understand that all children, even the critically ill, respond to noxious stimuli with biochemical and physiologic stress responses that, if untreated, can lead to increased patient morbidity and mortality (2). Effective pain management produces patient benefits including reduced morbidity and mortality, early mobilization, and shortened hospital stay (3–7). Pain management has therefore become an essential component of modern pediatric, anesthetic, and surgical practice (8–11).

Analgesics with antipyretic properties (e.g., acetaminophen, ibuprofen, etc.) and opioids (e.g., codeine, morphine, etc.) are the mainstays of pediatric pain therapy. For moderate to severe pain, continuous spinal (intrathecal or epidural) analgesia, using local analgesics administered either alone or in combination with opioids, is often used. Spinal analgesia provides profound analgesia with minimal systemic side effects (e.g., sedation, respiratory depression) by blocking nociceptive impulses from entering the central nervous system (8–10,12,13). Indeed, in pediatric practice, epidural analgesia has become the most commonly performed regional anesthetic technique for the intra- and postoperative management of patients with urologic, orthopedic, and general surgical procedures below the T4 dermatomal level. It is also used in the management of pain in patients with vascular insufficiency secondary to intense vasoconstriction (e.g., purpura fulminans), sickle cell vasoocclusive crisis, and cancer that is unresponsive to parenteral and enteral opioids (14–16).

It is unknown how long an indwelling caudal or lumbar epidural catheter can be left in place without risking local or systemic infection. Serious systemic infections after short-term (3–5 days) continuous lumbar and caudal epidural analgesia have not been reported in children (17,18), although such complications have been described in adults (19–21). In clinical practice, it is common to remove epidural catheters

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within 72 h of insertion to minimize the risk of catheter colonization and systemic infection. However, there are many patients who require analgesia for longer than 72 h (17,18).

The use of percutaneously inserted epidural catheters in which a catheter segment is subcutaneously tunneled may permit the use of epidural catheterization for longer time periods. Subcutaneous tunneling of an epidural catheter may decrease the chance of accidental catheter dislodgment and, theoretically, provide additional protection against colonization much like it does for intravascular catheters. We retrospectively reviewed our experience with tunneled epidural catheters to determine the types of patients in whom this therapy offers benefit, and its efficacy, duration of use, and safety.

**Methods**

We reviewed the medical records of all 25 patients hospitalized at the Packard Children’s Hospital at Stanford (n = 10) and the Johns Hopkins Hospital (n = 15), who were managed with tunneled epidural and intrathecal catheters between January 1995 and June 1999. Catheters were inserted under general anesthesia, or under local anesthesia and sedation by an anesthesiologist using aseptic technique (8,12). In the same time period, over 2000 nontunneled catheters were inserted at both institutions together, and remained in situ for 24 to 72 h.

Informed parental consent and, when appropriate, the child’s assent were obtained before catheter insertion. A commercially available epidural anesthesia kit with a FlexTip Plus® catheter, AK 05520-P (Arrow International, Inc., Reading, PA) was used in all patients. Before inserting the epidural needle, the overlying skin was cleaned and prepared with povidone solution and then draped with sterile towels. By using either a lumbar or caudal approach, epidural catheters were percutaneously inserted and advanced cephalad until the catheter tip was presumptively situated at a level appropriate to the dermatomal level of pain. Then the catheters were tunneled subcutaneously, 3–6 cm into the epidural space; a 2-mm horizontal incision is made ultimately underwent placement of a tunneled intrathecal catheter using a Dacron-cuffed silicon catheter that was attached to a subcutaneous port.

Local anesthetic infusions were prepared in a sterile manner in the hospital pharmacies. In one patient at the Packard Children’s Hospital at Stanford, the epidual solution contained 0.1% (1 mg/mL) bupivacaine and fentanyl 2 μg/mL diluted in 0.9% sodium chloride without preservative. In the other Packard Children’s Hospital patients, hydromorphone 3 μg/mL was administered in the epidural solution with bupivacaine as follows. For pain below the umbilicus, bupivacaine was initially infused at a rate of 0.2 mg · kg<sup>−1</sup> · h<sup>−1</sup> (0.6 μg · kg<sup>−1</sup> · h<sup>−1</sup> hydromorphone or 0.4 μg · kg<sup>−1</sup> · h<sup>−1</sup> fentanyl). For pain above the umbilicus, bupivacaine was initially infused at a rate of 0.3 mg · kg<sup>−1</sup> · h<sup>−1</sup> (0.9 μg · kg<sup>−1</sup> · h<sup>−1</sup> hydromorphone). The maximum bupivacaine dose was limited to 0.4–0.5 mg · kg<sup>−1</sup> · h<sup>−1</sup> (or 14–16 mL/h) (22–24). At the Johns Hopkins Hospital, the epidural solution contained 0.1%–0.5% (1–5 mg/mL) lidocaine with or without fentanyl 1–2 μg/mL diluted in 0.9% sodium chloride without preservative. The initial lidocaine infusion provided 1.5 mg · kg<sup>−1</sup> · h<sup>−1</sup> lidocaine and 0.5 μg · kg<sup>−1</sup> · h<sup>−1</sup> fentanyl. The maximum infusion rate was 20 mL/h. In both institutions, the epidural solutions and the infusion sets were changed at least every 72 h in hospitalized patients, and once weekly in outpatients (25).

All patients who were opioid naïve were monitored with continuous electrocardiogram and chest wall impedance plethysmography as well as continuous pulse oximetry. Opioid-tolerant patients, such as those with chronic cancer pain, were so monitored for the first...
24–48 h of neuraxial opioid administration, until a stable effective dose was obtained.

Demographic data and patient characteristics such as age, weight, primary diagnosis, and any relevant surgical data, were recorded (Table 1). Detailed information concerning the tunneled epidural catheters included level of placement, duration of use, clinical analgesic effect, reason for removal, and medication

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Catheter insertion site</th>
<th>Age (yr)</th>
<th>Weight (kg)</th>
<th>Diagnosis</th>
<th>Indication</th>
<th>Duration (days)</th>
<th>Reason for removal</th>
<th>Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Thoracic</td>
<td>5</td>
<td>21</td>
<td>Abdominal trauma</td>
<td>Abdominal pain</td>
<td>7</td>
<td>Resolution (s.a. Case Report 1)</td>
<td>Bupivacaine + hydromorphone</td>
</tr>
<tr>
<td>2</td>
<td>Thoracic</td>
<td>36</td>
<td>37</td>
<td>Cystic fibrosis</td>
<td>Chronic chest pain</td>
<td>16</td>
<td>Transition to transdermal fentanyl</td>
<td>Bupivacaine + hydromorphone</td>
</tr>
<tr>
<td>3</td>
<td>Thoracic</td>
<td>7</td>
<td>26</td>
<td>Recurrent metastatic Stage 3 anaplastic Wilms tumor</td>
<td>Left anterior chest wall and flank pain unresponsive to IV PCA</td>
<td>22</td>
<td>Death</td>
<td>Bupivacaine + hydromorphone</td>
</tr>
<tr>
<td>4</td>
<td>Lumbar</td>
<td>8</td>
<td>53</td>
<td>Leukemia</td>
<td>Wound care and dressing changes</td>
<td>5</td>
<td>Resolution</td>
<td>Bupivacaine + hydromorphone</td>
</tr>
<tr>
<td>5</td>
<td>Lumbar</td>
<td>17</td>
<td>52</td>
<td>Recurrent metastatic synovial cell sarcoma</td>
<td>Intractable pain unresponsive to IV PCA</td>
<td>54</td>
<td>Death (s.a. Case Report 2)</td>
<td>Bupivacaine + fentanyl</td>
</tr>
<tr>
<td>6</td>
<td>Lumbar</td>
<td>21</td>
<td>68</td>
<td>Osteosarcoma high grade of the left femur with pulmonary mets</td>
<td>Left hip and back pain</td>
<td>11</td>
<td>Accidental dislodgement at home</td>
<td>Bupivacaine + hydromorphone</td>
</tr>
<tr>
<td>7</td>
<td>Lumbar</td>
<td>15</td>
<td>45</td>
<td>Chronic regional pain syndrome Type I</td>
<td>Intensive physical therapy</td>
<td>7</td>
<td>Resolution</td>
<td>Bupivacaine + hydromorphone</td>
</tr>
<tr>
<td>8</td>
<td>Lumbar</td>
<td>15</td>
<td>36</td>
<td>Sickle cell disease</td>
<td>Painful crisis</td>
<td>9</td>
<td>Resolution</td>
<td>Bupivacaine + hydromorphone</td>
</tr>
<tr>
<td>9</td>
<td>Lumbar</td>
<td>13</td>
<td>42</td>
<td>Disseminated blue cell tumor</td>
<td>Chronic abdominal pain with obstruction</td>
<td>10</td>
<td>Death (s.a. Case Report 3)</td>
<td>Bupivacaine + hydromorphone</td>
</tr>
<tr>
<td>10</td>
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<td>7</td>
<td>25</td>
<td>Motor vehicle accident</td>
<td>Degloving leg injury</td>
<td>27</td>
<td>Resolution (s.a. Case Report 4)</td>
<td>Chloroprocaine</td>
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<tr>
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<td>Lumbar</td>
<td>17</td>
<td>71</td>
<td>Ovarian cancer with ileus</td>
<td>Nausea, severe pain</td>
<td>240</td>
<td>Death</td>
<td>Epidural; morphine, intrathecal: morphine + bupivacaine</td>
</tr>
<tr>
<td>12</td>
<td>Lumbar</td>
<td>6</td>
<td>22</td>
<td>Bladder extrophy</td>
<td>Postoperative pain</td>
<td>9</td>
<td>Resolution</td>
<td>Lidocaine + fentanyl</td>
</tr>
<tr>
<td>13</td>
<td>Lumbar</td>
<td>12</td>
<td>30</td>
<td>HgbS beta thalassemia</td>
<td>Pain crisis of lower back and sternum</td>
<td>4</td>
<td>Tenderness and induration at catheter site</td>
<td>Bupivacaine + hydromorphone</td>
</tr>
<tr>
<td>14</td>
<td>Lumbar</td>
<td>10</td>
<td>36</td>
<td>Bilateral hip pain, s/p Grice procedure</td>
<td>Severe pain and spasticity</td>
<td>9</td>
<td>Resolution</td>
<td>Bupivacaine + hydromorphone</td>
</tr>
<tr>
<td>15</td>
<td>Lumbar</td>
<td>6</td>
<td>25</td>
<td>Traumatic amputation right calf, crush laceration left leg</td>
<td>Severe bilateral leg pain</td>
<td>16</td>
<td>Resolution</td>
<td>Bupivacaine + hydromorphone</td>
</tr>
<tr>
<td>16</td>
<td>Caudal</td>
<td>0.5</td>
<td>9</td>
<td>Bladder extrophy</td>
<td>Postoperative pain</td>
<td>14</td>
<td>Resolution</td>
<td>Lidocaine + fentanyl</td>
</tr>
<tr>
<td>17</td>
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<td>1 day</td>
<td>3.5</td>
<td>Omphalocele</td>
<td>Postoperative pain</td>
<td>5</td>
<td>Resolution</td>
<td>Lidocaine</td>
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<tr>
<td>18</td>
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<td>3</td>
<td>14</td>
<td>Recurrent metastatic Stage D neuroblastoma</td>
<td>Intractable pain unresponsive to IV PCA</td>
<td>7</td>
<td>Death</td>
<td>Lidocaine + fentanyl, Day 3 with bupivacaine</td>
</tr>
<tr>
<td>19</td>
<td>Caudal</td>
<td>7</td>
<td>23</td>
<td>Recurrent metastatic Grade III neuroblastoma</td>
<td>Abdominal and right flank pain unresponsive to IV PCA</td>
<td>17</td>
<td>Death</td>
<td>Bupivacaine + hydromorphone</td>
</tr>
<tr>
<td>20</td>
<td>Caudal</td>
<td>5</td>
<td>17</td>
<td>Bladder extrophy</td>
<td>Postoperative pain</td>
<td>42</td>
<td>Resolution</td>
<td>Lidocaine + fentanyl</td>
</tr>
<tr>
<td>21</td>
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<td>0.9</td>
<td>10</td>
<td>Bladder extrophy</td>
<td>Postoperative pain</td>
<td>8</td>
<td>Fever</td>
<td>Lidocaine + fentanyl</td>
</tr>
<tr>
<td>22</td>
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<td>11</td>
<td>Bladder extrophy and epispidias</td>
<td>Postoperative pain</td>
<td>14</td>
<td>Resolution</td>
<td>Lidocaine + fentanyl</td>
</tr>
<tr>
<td>23</td>
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<td>5</td>
<td>18</td>
<td>Bladder extrophy</td>
<td>Postoperative pain</td>
<td>26</td>
<td>Resolution</td>
<td>Lidocaine + fentanyl</td>
</tr>
<tr>
<td>24</td>
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<td>7.2</td>
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<td>11</td>
<td>Accidental dislodgement</td>
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</tr>
<tr>
<td>25</td>
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<td>11</td>
<td>Bladder extrophy</td>
<td>Postoperative pain</td>
<td>24</td>
<td>Resolution</td>
<td>Bupivacaine + hydromorphone</td>
</tr>
</tbody>
</table>

PCA = patient-controlled analgesia.
administered via the catheter. The charts were also reviewed for evidence of any complications related to the tunneled epidural catheters, notably infection, bleeding, toxicity related to local anesthetic or opioids, tachyphylaxis, pruritus, urinary retention, or respiratory depression. In addition to the descriptive information on the clinical effect of tunneled epidural catheters provided in the chart records, the cumulative dosages of parenteral and enteral opioid therapy (adjusted to morphine equivalents and body weight) (26–28) administered during the 48 h before catheter insertion were calculated and compared with the cumulative opioid dose administered in the first 48 h after catheter insertion. In those individuals who had not received enteral or parenteral opioids before the catheter insertion (e.g., trauma patients and patients in whom the catheter was inserted intraoperatively), the need for supplemental opioids for pain control after the catheter insertion was assessed. Therapy was considered successful if systemic opioid therapy was reduced or eliminated in the former patients, and if no supplemental opioids were administered in the latter patients. Data were presented as the median and range.

Results
Between January 1995 and June 1999, 25 patients (median age 7 yr, range 1 day to 36 yr; median body weight 25 kg, range 3.5 to 71 kg) had tunneled epidural catheters placed for long-term analgesia (Table 1). The indications for catheter insertion were acute pain caused by trauma, extensive abdominal surgery (omphalocele, bladder extrophy repair), acute pain because of chronic disease (β-thalassemia), and chronic pain (end-stage malignancy, cystic fibrosis). Subjects 3, 5, 6, 11, and 19 were discharged from the hospital and managed with their catheters in their homes.

Tunneled epidural catheters were effective in providing extended analgesia in all patients: In none of the subjects with acute indications for catheter placement (e.g., trauma, postoperatively) were supplemental enteral or parenteral opioids administered. In 14 patients with “chronic” indications for catheter insertion, systemic cumulative opioid dosage (administered parenterally or entally) decreased dramatically or was eliminated completely (Fig. 2). Catheters functioned for a median of 11 days (range 4 to 240 days). They remained in place until there was no further need for parenteral analgesia (n = 15), death because of the underlying disease (n = 6), accidental removal (n = 2), or possible infection (n = 2).

Two catheters were removed because of concern of infection: one child had a postoperative fever without evidence of a catheter-related infection, and the other developed cellulitis at the catheter exit site. In the former patient, the epidural catheter was removed after it had been in place for 8 days along with all other indwelling IV and urinary catheters, because there was no known source of the fever. The fevers subsequently subsided, but the source of fever was not clinically identified. This child was not treated with antibiotics. In the latter patient, the skin overlying the exit site was erythematous and tender 4 days after catheter insertion. Both the catheter and the wound site were sterile on bacterial culture. This child was empirically treated with cephalexin until the cultures were reported as negative, then antibiotics were discontinued. One patient who had been discharged home with an epidural catheter had an accidental dislodgment, and another had accidental dislodgment while in the hospital. No cardiorespiratory complications related to the epidural analgesia were identified in any of the patients. In each case, there was a significant reduction in, or total elimination of, the requirement for IV analgesics and sedatives, as illustrated in the following case descriptions.

Case Reports
Case 1
A 5-yr-old girl suffered severe abdominal wall trauma after a motor vehicle accident. After several days in intensive care, she required continuous administration of fentanyl at a dose of 5 μg·kg⁻¹·h⁻¹ to maintain adequate comfort, and additionally needed general anesthesia with IV propofol for daily dressing changes. We elected to convert her therapy from IV analgesics and anesthetics to epidural analgesia to eliminate the occurrence of physiologic drug dependence to
opioids, and obviate the need and concomitant expense and risk of daily administration of general anesthesia. After placement of a tunneled epidural catheter, the need for IV opioids for continuous analgesia and general anesthetics for daily dressing changes was eliminated. Analgesia was maintained with an epidural infusion of bupivacaine and hydromorphone, and she was able to undergo daily dressing changes while awake without supplemental medication. After placement and dosing of the epidural catheter, IV fentanyl was weaned over a 5-day period during which the patient was carefully monitored for signs of opioid abstinence syndrome. These did not occur.

The catheter remained in place for 7 days until dressing changes were no longer required and pain resolved.

**Case 2**

A 17-yr-old girl with end-stage metastatic synovial cell carcinoma was administered IV morphine sulfate at 100 mg/h (2.5 mg · kg⁻¹ · h⁻¹) to control severe abdominal pain caused by malignant ascites. Despite this, analgesia remained inadequate, and she had severe opioid-induced side effects (nausea, over-sedation) and secondary loss of quality of life. Because epidural analgesia could effectively provide abdominal analgesia without the untoward side effects of parenteral large-dose opioids, a tunneled epidural catheter was placed under ketamine anesthesia to establish prolonged epidural analgesia. After epidural administration of local anesthetic, the patient became apneic and required small-dose naloxone (1.0 µg/kg, followed by a continuous infusion of 0.5 µg · kg⁻¹ · h⁻¹) for 24 h. Apnea was not attributed to high spinal anesthesia, but rather to residual parenteral opioid effects after complete resolution of pain. Pain relief was complete, and opioids were weaned slowly over 5 days to avoid withdrawal symptoms. She did not need supplemental opioid analgesics until death occurred because of metastatic disease 2 mo later.

**Case 3**

A 13-yr-old girl with an end-stage metastatic abdominal blue cell tumor required methadone 60 mg/day to relieve pain secondary to disseminated intraabdominal metastatic disease and organomegaly. Methadone therapy did not adequately control her pain and produced unacceptable opioid-induced side effects (somnolence, nausea). An attempt to change the opioid to IV fentanyl neither improved analgesia nor eliminated the undesired opioid side effects. Therefore, a tunneled epidural catheter was inserted; IV analgesia was weaned over a 48-h period to prevent opioid abstinence syndrome after epidural analgesia was instituted. She remained pain free for the next 10 days until she died from her metastatic disease.

**Case 4**

A 7-yr-old girl suffered a severe degloving injury of the leg with secondary soft tissue infections after a motor vehicle accident. Similarly to Case 1, she underwent painful debridement and dressing changes three times a day under general anesthesia until a decision was made to place a tunneled epidural catheter to obviate this need with its attendant risk and expense. After the placement of the tunneled epidural catheter, she was able to undergo debridement and dressing changes on the nursing unit under epidural analgesia that consisted of epidural infusion of 10 mL of 2% chloroprocaine. Chloroprocaine administration was initially performed by a physician member of the pain management service, and after several doses was subsequently administered using the “loading dose” function of an epidural infusion pump by the unit nurses. Between dressing changes, the epidural catheter was infused with a mixture of 0.1% bupivacaine and hydromorphone 3 µg/mL at a rate of 0.2 mL · kg⁻¹ · h⁻¹. After several days, the continuous infusion of local anesthetic and opioid was discontinued because continuing wound pain became less severe, but the catheter continued to be used for dressing changes. The catheter remained in place for 27 days until the wound was grafted and dressing changes were no longer necessary.

**Discussion**

In this retrospective review, we describe the overall effectiveness of percutaneously inserted, subcutaneously tunneled epidural and intrathecal catheters for prolonged pain relief in pediatric patients. Each patient had significant benefit from the tunneled catheter technique as determined by a substantial reduction in pain and by the elimination or reduction in the need for supplemental opioids (Fig. 2).

This method was used in two types of patients: patients with chronic pain, in whom conventional anaglgesic therapy failed (e.g., a cancer patient with pathological fractures, nerve entrapment, etc.), and patients with a prolonged need for acute analgesia in whom opioid-induced side effects significantly affected the quality of life. Although the patient groups were different, the analgesic technique was appropriate for both.

Epidural catheters can be inserted at the caudal, lumbar, or thoracic level. Because local anesthetic toxicity is directly related to the total amount of drug infused, catheter placement plays a very important role in the overall safety of this technique (29,30). Epidural placement via the caudal and lumbar approaches is most common, although thoracic placement is equally feasible when indicated.

Short-term studies demonstrate that epidural catheters can remain safely in place for 72 hours. Strafford et al. (17) suggested that, for patients in the final stages of a terminal disease, the risk of infection with long-term epidural catheters appears acceptable. In this review, conditions associated with epidural abscess were immunocompromised state, concomitant steroid use, trauma, diabetes, sepsis, or a distal site of infection.

One of the most comprehensive reports of infections of chronically implanted epidural catheters was by Du Pen et al. (31) in a study that included 350 adult patients with pain from either cancer or acquired immunodeficiency syndrome treated for up to 457 days. He described 30 superficial epidural catheter track infections (cellulitis), 8 deep tissue infections (fasciitis), and 15 epidural space infections, representing a
total frequency of infection of 23.7%. Patients were treated with antibiotics, and no infection required surgical management or led to morbidity. Two-thirds of the infections occurred in the first 190 days of therapy. Finally, in one group of patients with reflex sympathetic dystrophy, Rauck et al. (32) reported an infection frequency of 19%.

With intravascular catheters, infection begins by invasion of microorganisms along the transcutaneous portion of the catheter (33). The larger the number of organisms at the insertion site, the larger the rate of colonization and bacteremia (2,3,34). Epidural catheters, such as intravascular catheters, traverse the integument and thereby interfere with the natural host defenses of the skin. Studies with intravascular catheters have found that aseptic technique during placement of the catheter, minimal handling of the catheter hub and the infusion tubing, tunneling the catheter, and central preparation of the infusate reduce, but do not eliminate, the risk of contamination (2,25).

The number of subjects in this report is too small to define reliably the risk of infection associated with long-term tunneled catheter placement in the pediatric population. In addition, we must emphasize that retrospective reviews may not define the precise magnitude of the risk of infection, respiratory depression, bleeding, and other complications of epidural and intrathecal catheterization. These questions, and the definition of which local anesthetic and opioids are superior, can best be answered by large prospective studies.

The placement of epidural or intrathecal catheters requires an anesthesiologist trained in regional anesthesia in children, repeated examination of the child and catheter site, and strict attention to prevention of infection. With careful nursing care and supervision by a pediatric pain specialist, prolonged spinal analgesia is both feasible and safe, and with proper teaching and home nursing care, patients may be sent home with the tunneled catheter. This therapy offers pain relief in situations in which conventional analgesic therapy either fails or is impractical, and is one that may be of great value to children suffering from pain.

References