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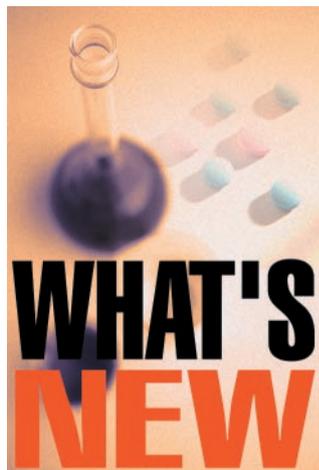
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An update of current clinical practices

# What's New in the Management of Pain in Children

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**Objectives** After completing this article, readers should be able to:

1. Describe the effects of pain and stress in neonates.
2. Delineate the general principles of pain management in children.
3. List new pharmacologic agents for treatment of pain in children.
4. Devise a program to reduce the pain associated with circumcision.
5. Describe pain assessment tools available for infants and children.

## Introduction

The past 20 years has witnessed remarkable growth in the field of pediatric pain management and the attitudes surrounding it. Controversies in the field no longer concern whether children experience pain but focus instead on how best to treat it. Pain now is perceived as a symptom worthy of independent treatment rather than merely an inevitable consequence of disease.

Why treat pain? The simple answer is that it is the humane thing to do. The relief of suffering is the moral obligation of clinicians. However, there are other reasons to treat pain. Adequate pain management reduces child and parent anxiety and increases compliance and cooperation, thereby reducing some of the burden on medical staff and resources. The long-term negative effects of pain are becoming more apparent; inadequately treated pain, particularly in the neonatal period, increases morbidity and mortality,

creates hyperalgesia, and can have a negative impact on development.

The importance of pain management has been recognized beyond the community of pediatric clinicians. The Joint Commission on Accreditation of Healthcare Organizations (JCAHO) has made pain assessment and management a focal point of their review process. The United States Food and Drug Administration has held panel discussions to define appropriate use of opioids in children. Pain is discussed frequently in the press and is a topic of numerous self-help books. Pain management in adults and children has achieved a new visibility at the professional and public level and demands attention.

In this article, we review current thinking about pain in children and its treatment. We define pain and review implications of the definition that pertain to care. We discuss emerging information on developmental neurobiology and the broad range of treatment options. Finally, we offer a selection of pharmacologic and conceptual advances.

## Definition

The International Association for the Study of Pain developed the standard

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definition of pain more than 20 years ago: Pain is “an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.” It states further that pain always is subjective and learned through experiences related to injury early in life. Alternatively, McCaffrey proposes that pain is whatever the patient says it is and that it exists whenever he or she says it does.

The standard definition incorporates the now well-accepted premise that pain is the composite of the physical stimulus and the interpretation of that stimulus through the lens of the individual's characteristics and experience. A number of factors can amplify or diminish pain, including innate characteristics such as age, gender, and temperament as well as situational and variable characteristics such as affective state, previous experience with pain, and context or meaning of the pain.

Over the past few years, several pediatric pain specialists have questioned aspects of this definition. The statement that pain is learned early in life through experience with injury is particularly irksome, implying as it does that newborns cannot experience pain because they have had no prior experience with injury. This concern, along with others in the definition, have prompted several investigators to call for a revision of the definition that states clearly that pain is an inherent quality of life that appears early in development and serves as a signal for tissue damage.

### Effects of Pain and Stress on Infants and Young Children

A review of the emerging data on newborn pain offers insight into the critical importance of pain management. Historically, newborns rarely received analgesics; in fact, until the late 1980s, they often underwent

specific surgeries without anesthesia. Recently, however, a number of studies of the developmental neurobiology of pain transmission have reframed our understanding of the preterm and term infant's response to painful stimuli.

Newborns historically were believed to experience less pain because of the immaturity of their nervous systems, but recent data support the hypothesis that the perinatal period may be a time of increased sensitivity to pain. Although the ascending pathways of the neonatal nervous system are fully developed, allowing the transmission of painful stimuli, the descending inhibitory pathways are not established. Thus, painful stimuli may reach the brain without modulation, leading to more pronounced pain sensation in neonates than in children and adults. This hypothesis is supported by clinical data that show a more pronounced physiologic response to pain and higher serum analgesic concentration requirements to produce analgesia among neonates compared with older age groups.

It also appears that hyperalgesia follows repeated painful stimuli in preterm neonates, possibly due to the phenomenon of “windup” involving increased excitability of the nociceptive neurons in the dorsal horn. This phenomenon may increase sensitivity to subsequent painful stimuli, not only from procedures, but also from routine handling of preterm neonates. As a result, sensitivity to the environment during both routine and critical care of the newborn is vital.

Recent studies also have demonstrated that infants who undergo painful procedures, a common occurrence in the newborn intensive care unit (NICU), may develop an altered response to future episodes of pain. In one study, the response to a

single heel lance was compared in two groups of infants who were each 32 weeks postconceptional age. One group was composed of 4-week-old preterm infants born at 28 weeks' gestation, and the other group was composed of babies born at 32 weeks' gestation. Response to the heel lance correlated with the total number of invasive procedures performed. In other words, babies who had had repeated heel lances responded differently from those who were receiving an initial heel lance. Similarly, Taddio and associates noted that male infants who were circumcised without analgesia responded more intensely to immunizations received 4 to 6 months later than did those who were not circumcised or those who received topical anesthesia prior to circumcision. This suggests a lasting effect of that painful procedure.

Intraventricular hemorrhage (IVH) is a cause of serious morbidity and mortality in the preterm infant, and pain may be a contributing factor. Pain in the preterm infant can lead to changes in intracranial pressure and blood volume as well as cerebral oxygen delivery. Most IVH occurs in the first few postnatal days, when infants are undergoing frequent painful procedures. Als and colleagues found that the use of a system of developmentally appropriate care in which handling and procedures were minimized was associated with a decreased incidence of IVH. Preliminary data on the use of continuous morphine in the first few days after preterm birth documented a marked decrease in the incidence of IVH (the NOPAIN trial).

Former preterm infants exhibit differences in pain response that may extend well beyond infancy. In one investigation, 18-month-old former preterm infants, especially those whose birthweights were less than

1,000 g, were less reactive to daily bumps and scrapes than larger preterm or term infants. In contrast, somatization (the occurrence of multiple complaints that remained unexplained medically, such as stomachaches, headaches, and leg pains) were much more common in 4- to 5-year-old former preterm infants than in age-matched controls. At ages 8 to 10 years, former preterm infants gave higher ratings to illustrations of painful events than their age-matched controls. Interestingly, the duration of NICU stay was correlated with higher pain ratings, even 8 to 10 years later.

Inadequate analgesia can have negative effects on children. A placebo-controlled study evaluating administration of transmucosal oral fentanyl prior to painful procedures was performed in the mid-1990s. Both groups (initial placebo and initial active drug) were given fentanyl for subsequent procedures. Children younger than age 8 years who had received placebo initially consistently rated the pain of subsequent procedures as higher, despite receiving adequate analgesia for the current procedure. The authors suggested that this emphasized the importance of adequate analgesia for painful procedures, especially when multiple procedures can be anticipated in the future.

## Treatment

### General Principles

A number of general principles can be applied to the management of acute or chronic pain in children:

*1. Prevention of pain.* If it can be anticipated, pain should be treated prophylactically. More medication must be administered to ameliorate pain that has occurred than to prevent its occurrence. Because all infants, children, and adults have pain following surgery, it makes little

sense and is inhumane to wait until the individual reports discomfort.

*2. Adequate assessment.* Assessment is the cornerstone of adequate treatment. Developmentally appropriate assessment of pain and of the results of intervention is critical.

*3. Multimodal approach.* Pain is the composite of the nociceptive stimulus and the individual's interpretation of it. As such, it can and should be approached at multiple levels through numerous strategies. Modalities that should be considered include analgesics (both systemic and topical); physical strategies such as massage, transcutaneous electrical nerve stimulation (TENS), heat, cold, and acupuncture; and behavioral/cognitive/psychological ap-

proaches, including hypnosis, distraction, preparation, and rehearsal.

diagnostic and treatment procedures can create an atmosphere of anxiety and increased pain during subsequent procedures that can color the child's relationship with the physician and hospital. Pain associated with initial diagnostic procedures should be treated aggressively to avoid a disturbing outcome.

### Pain Assessment

Pain assessment is the key to good pain management. Pain often is underestimated in children because of the inability of caretakers to assess their pain. Although physiologic parameters and parental observations can be helpful in assessing pain in children, self-report is the gold standard. Children older than 8 years of

**Newborns** experience pain at least as much as older children and have increased sensitivity with subsequent painful stimuli.

proaches, including hypnosis, distraction, preparation, and rehearsal.

*4. Parental involvement.* Parents are the best source of information about their child and should be involved in all decisions about treatment. They can be taught techniques to help their child with pain, particularly during procedures. Such an approach can reduce both parent and child anxiety and helplessness, which reduces pain.

*5. Nonnoxious routes.* The route through which analgesia is administered should be as painless as possible. Painful injections to reduce pain often produce reluctance to report pain in the future.

*6. Pain control during procedures.* Inadequate treatment of pain during

age generally can use the standard visual analog scale that commonly is used in adults and involves a 10-cm line anchored at either end ("no pain" and "worst pain imaginable"). Between the ages of 3 and 8 years, children can assess their pain if given developmentally appropriate tools. Numerous modified self-report instruments have been developed that employ various modalities, including cartoon faces and photographs of people in pain, "pieces of pain," and colors to allow children to quantify the degree of pain they are experiencing.

There has been a great deal of interest and effort in developing validated scales for the assessment of neonatal pain. Because verbal self-

**Table 1. Clinical Assessment of Pain**

Physiologic	Behavioral	Self Report	Composite
<ul style="list-style-type: none"> <li>• Respiratory rate</li> <li>• Heart rate</li> <li>• Blood pressure</li> <li>• Cortisol levels</li> <li>• Palmar sweating</li> </ul>	<ul style="list-style-type: none"> <li>• Body movement</li> <li>• Facial action</li> <li>• Crying</li> <li>• Posturing</li> <li>• State of arousal</li> <li>• Breathing pattern</li> </ul>	<p>Age 3 to 8 Years</p> <ul style="list-style-type: none"> <li>• Oucher Scale</li> <li>• Faces Scale</li> <li>• Poker Chip Tool</li> <li>• Colored Analogue Scale</li> <li>• Pain Thermometer</li> </ul> <p>Age 9+ Years</p> <ul style="list-style-type: none"> <li>• Visual Analogue Scale</li> <li>• McGill Pain Questionnaire</li> </ul>	<p>Infancy</p> <ul style="list-style-type: none"> <li>• CRIES</li> <li>• Neonatal Facial Action Coding System</li> <li>• NAPI</li> <li>• NIPS</li> <li>• PIPP</li> <li>• SUN</li> <li>• OPS</li> </ul> <p>Age 2+ Years</p> <ul style="list-style-type: none"> <li>• CHEOPS</li> <li>• COMFORT</li> <li>• OSBD</li> <li>• Toddler Preschooler Postoperative Pain Scale</li> </ul> <p>Age 8+ Years</p> <ul style="list-style-type: none"> <li>• Adolescent Pediatric Pain Tool</li> <li>• Varni-Thompson Pediatric Pain Questionnaire</li> </ul>

report is not possible in this population, scales use a combination of physiologic, behavioral, and observational parameters as well physiologic state and gestational age to document pain. Physiologic indicators include increased heart rate, respiratory rate, and stress hormone release. Behavioral indicators of pain encompass facial expression, cry, gross motor movements, changes in behavioral state, and changes in behavior patterns such as sleep. Several composite scales use both of these elements to yield a score that theoretically represents the degree of pain the baby is experiencing. Many different scales are available and are known by their acronyms. Details of these instruments are available from other sources, but at this time there is no uniformly accepted newborn pain scale. The ideal scale is the one that works best in an individual neonatal unit. Table 1 lists some of the available instruments to assess pain in infants and children.

### Drug Selection

A simple, effective ladder for escalation of analgesic drug therapy was devised for cancer pain by the World Health Organization in 1990. This ladder is effective in relieving the pain of approximately 90% of patients. It provides a stepped approach to drug selection that is effective for most children who complain of pain. It progresses as follows:

- Acetaminophen or a nonsteroidal anti-inflammatory drug (NSAID) for mild-to-moderate pain. Adjuvant drugs (antidepressants, anti-convulsants, topical anesthetics, stimulants) may be used at any step to enhance analgesic efficacy, treat concurrent symptoms that exacerbate pain, and provide independent analgesic activity for specific types of pain.
- When pain persists or increases, an opioid such as codeine or hydrocodone is added (not substituted) to the NSAID. Opioids at this step often are administered in fixed

dose combinations with acetaminophen because this combination provides additive analgesia. Fixed-combination products may be limited by the content of acetaminophen or NSAID, which may produce dose-related toxicity.

- When higher doses of opioid are necessary, separate dosage forms of the opioid and nonopioid analgesic are used to avoid exceeding maximally recommended doses of acetaminophen or NSAID.
- Pain that is persistent or moderate-to-severe at the outset is treated by increasing opioid potency or by using higher dosages. Drugs such as codeine or hydrocodone are replaced with more potent opioids (usually morphine, hydromorphone, methadone, or fentanyl).
- Medications for persistent pain are administered around the clock, with additional pro re nata (prn) doses, because regularly scheduled dosing maintains a constant level of drug in the body and helps to prevent pain recurrence.

## Widely Used Drugs NSAIDS

It is important to understand the benefits and limitations of the common pain medications when selecting the appropriate drug for pain therapy. NSAIDs are very effective for the management of mild-to-moderate pain or in combination with opioids for more severe pain. Among the drawbacks to these anti-inflammatory medications are effects on the gastric mucosa and platelet aggregation. A class of NSAIDs that somewhat overcomes these drawbacks, the cyclooxygenase (COX) 2 inhibitors, is discussed later in this article. NSAIDs also are subject to a ceiling effect, in which a maximum dose of an NSAID is achieved, after which no additional analgesic benefit is derived. In contrast, opioids have no ceiling effect; increasing the dose generates more analgesic effect.

## OPIOIDS

The choice of an opioid is dictated by the clinical situation. Parenteral opioids that have a moderate duration of action, such as morphine or hydromorphone, are used for the patient who is suffering from acute pain. For procedural pain control, a short-acting opioid such as fentanyl may be more appropriate. Oral opioids, in some cases in combination with an NSAID, are more appropriate for mild-to-moderate pain. Long-acting, controlled-release forms of opioids such as oxycodone or morphine are ideal for chronic pain associated with cancer or other illness. They are used in conjunction with a shorter-acting opioid for breakthrough pain. Meperidine is problematic because its metabolite normeperidine can cause hallucinations, agitation, and seizures. Meperidine also can cause catastrophic interactions when used in conjunction with monoamine oxidase inhibitors.

Contrary to popular belief, meperidine does not offer advantages over morphine in terms of sphincter of Oddi pressure or bowel motility. For these reasons, meperidine is used only rarely for pain control. Opioids can be administered via the oral, intramuscular, intravenous, intranasal, subcutaneous, intraspinal, transdermal, transmucosal, or nebulized route.

The predictable adverse effects of opioids include pruritus, constipation, sedation, dysphoria, and respiratory depression and should be anticipated whenever these drugs are used. Pruritus can be treated by using antihistamines, by employing an alternate opioid, or by placing the hospitalized patient on a low-dose naloxone infusion or intermittent nalmeferene (a long-acting opioid antagonist). Constipation should be expected for all patients receiving chronic opioid therapy and treated aggressively with laxatives. Careful monitoring and judicious use of opioid antagonists can reduce the risk of respiratory depression. Patients who are receiving chronic opioid therapy and experience sedation can be treated with a stimulant such as methylphenidate or an alternative opioid.

## Behavioral/Cognitive/ Psychological Approaches

A number of techniques generally categorized as “cognitive/behavioral/psychological” can improve pain control when used alone or in combination with pharmacologic strategies. Generally, these techniques are effective during painful procedures, but they may be beneficial at other times as well.

Developmentally appropriate discussion about the procedure and the sensations associated with it has been shown to decrease both the anxiety and pain associated with painful procedures.



**Figure.** Distraction unit that includes a bubble column, light wands, and imagery projector.

Parents, once actively banned from treatment rooms, now not only are allowed but are encouraged to be active participants. Parents are critical sources of information about how children handle pain and procedures, but they may act as coaches by using behavioral/cognitive techniques to comfort the child. Parental presence decreases both parent and child anxiety and offers a sense of control during times of helplessness.

Breathing, distraction, and hypnosis help to relax the child and reduce anxiety. They may involve merely deep breathing or counting or the use of pinwheels or a party blower. More complex approaches include guided imagery or active use of fantasy and suggestion. Some hospitals have incorporated these principles into care by equipping treatment rooms with distraction units (Figure)

Table 2. Topical Anesthetics

Drug	Application Time	Comments
EMLA <sup>®</sup> (lidocaine–prilocaine) (AstraZaneca)	60 min minimum	Most well studied; safe in neonates
Amethocaine	30 to 40 min	Not available in United States
Ela-Max <sup>®</sup> (liposomal lidocaine) (Ferndale Laboratories)	30 min	Data limited
Numby Stuff <sup>®</sup> (lidocaine iontophoresis) (Iomed)	10 min	Requires electric current
Vapocoolant sprays	Seconds	No efficacy in neonates

that are inviting to children and parents and reduce anxiety and improve coping. Although many clinicians and parents use these strategies intuitively, more formal training can be obtained through multiple venues, including the annual hypnosis course of the Society for Developmental and Behavioral Pediatrics ([www.sdbp.org](http://www.sdbp.org)).

Watching a procedure on a videotape, speaking to someone who has experienced it, or practicing the procedure on a stuffed animal can increase a child's familiarity and sense of mastery, which can reduce pain during the procedure itself.

### Physical Approaches

Several physical strategies have demonstrated efficacy in pain management for children. These include the use of heat, cold, and massage. TENS often is very effective in situations in which the pain is well localized. Graded physical exercise, often under the auspices of a physical therapist, is extremely valuable in chronic pain situations such as fibromyalgia to prevent deconditioning and promote function. Acupuncture may have value for selected pain problems in children. Recent studies have shown acupuncture to be both acceptable and helpful for pediatric patients who have chronic pain.

## What's New

### Drugs

#### TOPICAL ANESTHETICS

Immunizations, intravenous lines, and venipuncture produce pain and

are often the most anxiety-producing medical procedures for children. EMLA<sup>®</sup> Cream (AstraZaneca), a combination of lidocaine and prilocaine, was introduced in the early 1990s and has been successful in providing topical anesthesia for a myriad of painful procedures in children (Table 2). However, at least 1 hour is required to provide acceptable anesthesia, it must be used with an occlusive dressing, it provides a depth of anesthesia of only 3 to 4 mm, and its vasoconstricting effects may affect venous access negatively. The cream formulation may leak out from the occlusive dressing and prevent anesthesia of the desired area. Recently, EMLA<sup>®</sup> has been formulated into a disc that is easier to apply, obviates the need for an occlusive dressing, and provides more reliable anesthesia.

Amethocaine is 4% tetracaine cream that provides equivalent anesthesia to EMLA<sup>®</sup> for procedures such as venipuncture, venous cannulation, and subcutaneous port access. Amethocaine requires only 30 to 40 minutes to be effective and, unlike EMLA<sup>®</sup>, is a vasodilator. It is available in Europe and Canada but currently not approved for use in the United States.

ElaMax<sup>®</sup> (Ferndale Laboratories) is a topical formulation of 4% lidocaine. The lidocaine is encapsulated by liposomes, which create lipid solubility and allow transdermal drug delivery and anesthesia. ElaMax<sup>®</sup> provides anesthesia in about 30 min-

utes if placed under an occlusive dressing. It is available without a prescription. However, it is too early to recommend this formulation due to the limited published data regarding its use.

Lidocaine iontophoresis allows for the active transdermal delivery of lidocaine under the influence of a low-level electric current. This technique, currently available under the name Numby Stuff<sup>®</sup> (Iomed Inc), provides topical anesthesia in as few as 10 minutes. Lidocaine iontophoresis is superior to EMLA<sup>®</sup> for venous cannulation because it provides considerably deeper anesthesia (8 to 9 mm versus 3 to 4 mm). Iontophoresis requires a system that includes an electric current delivery device connected via wires to two patches. Some patients report tingling or itching associated with iontophoretic drug delivery and find it aversive, but most children accept the system easily. Smaller and easier-to-use iontophoretic systems are in development.

Vapocoolant sprays such as ethyl chloride or fluoromethane have been shown to be effective in reducing the pain of immunizations in 4- to 6-year-old children. They have not been proven effective for this procedure in infants or for placement of intravenous needles in children of any age. They can be sprayed directly onto the skin or onto a cotton ball, provide anesthesia in 15 to 30 seconds, and are considerably less ex-

Table 3. New Drugs for Pain Management

Drug	Brand Name	Dose	Comments
Celecoxib	Celebrex® (Pfizer/Pharmacia & Upjohn)	100 to 200 mg BID	Contains sulfa
Rofecoxib	Vioxx® (Merck)	12.5 to 25 mg QD	Liquid available
Tramadol	Ultram® (Ortho-McNeil)	50 to 100 mg q 6 h	No selective serotonin reuptake inhibitors or tricyclic antidepressants
Gabapentin	Neurontin® (Parke-Davis)	30 mg TID	Increase gradually
Clonidine		2 to 4 mcg/kg (to treat withdrawal)	Also available in transdermal patch

Dosages based on published pediatric experience. No formal United States Food and Drug Administration indications for use in children.

pensive than other available topical anesthetics.

#### COX-2 INHIBITORS

NSAIDs are potent inhibitors of the COX pathway that prevent the formation of mediators of pain, inflammation, and fever such as prostaglandins. Unfortunately, drugs such as ibuprofen, naproxen, and indomethacin also inhibit the cytoprotective effects of prostaglandins and prostanoids on the gastric mucosa and, therefore, can cause gastritis, gastric or duodenal ulceration, and painless bleeding. NSAIDs also inhibit platelet aggregation, which can result in bleeding.

A new group of NSAIDs, the COX-2 inhibitors (Table 3), have been developed to address these specific issues. COX-2 inhibitors selectively target only COX-2, the type of cyclooxygenase present in response to inflammation and other physiologic and hormonal stresses. They do not affect COX-1, which synthesizes the prostaglandins that protect the gastric mucosa and regulate platelet aggregation. There are currently two COX-2 inhibitors on the market, although they are not approved for use in children: celecoxib (Celebrex® [Pfizer/Pharmacia & Upjohn]) and rofecoxib (Vioxx® [Merck]). Rofecoxib is administered once daily and is available in liquid

form. Celecoxib is administered twice daily and is not available as a liquid. Celecoxib is contraindicated in patients who are sensitive to sulfa. These drugs should be reserved for patients who require long-term NSAID administration, such as those who have chronic pain syndromes or rheumatologic disease, and for those who do not tolerate regular NSAIDs.

#### TRAMADOL

Tramadol (Ultram® [Ortho-McNeil]) is an analgesic medication that can be used to treat mild-to-moderate pain. Its dual mechanism of action includes agonistic effects at the mu receptor and inhibition of serotonin and norepinephrine reuptake. Tramadol is available in 50-mg tablets and can be given in doses up to 100 mg every 6 hours. It does not have a pediatric indication at present, but numerous pediatric studies support its safety and efficacy. Tramadol may be useful for the management of acute pain, such as in traumatic injuries. It also is used for patients who have chronic pain, but it cannot be used in conjunction with selective serotonin reuptake inhibitors or tricyclic antidepressants because of the possible development of "serotonin syndrome," which may result in jitteriness, irritability, and seizures. Because tramadol is metab-

olized by the P450 system, interactions with other medications may alter its therapeutic response. Although tramadol had been believed to have low addiction potential, as a mu agonist, it can result in physical dependence and addiction. It must be tapered, as must all opioids, after chronic use to avoid symptoms of withdrawal.

#### NITROUS OXIDE

Although not new, nitrous oxide has enjoyed a resurgence of interest for procedural pain management and sedation in children. The ideal medication for sedation and analgesia for a child undergoing a procedure would have a noninvasive delivery mechanism, rapid onset, and short duration of activity and be safe and well tolerated. Nitrous oxide meets these standards. Systems that allow for continuous flow of nitrous oxide at concentrations of 50% or less provide rapid sedation, analgesia, and amnesia without cardiorespiratory adverse effects. These systems can be used to sedate children as young as age 2 years prior to brief painful procedures.

The ideal setting for nitrous oxide use is the pediatric emergency department. With the use of nitrous oxide, procedures such as suturing, intravenous cannulation, lumbar puncture, fracture reduction, and

sexual abuse evaluation can take place without the use of an intravenous set and often without physical restraint. In an ideal world, every treatment room would have nitrous oxide available to minimize the anxiety and pain that many children experience in the hospital.

Nitrous oxide must be used carefully, however. Delivery systems should have a safety valve to prevent the administration of more than 70% nitrous oxide and an automatic shut-off if oxygen becomes unavailable. Toxicity such as bone marrow suppression and central nervous system, liver, and testicular dysfunction occur rarely with repeated chronic exposure. The teratogenic effects of nitrous oxide are controversial.

States. When it is crushed and inhaled intranasally, high doses of opioid can be absorbed rapidly. Such use has resulted in several deaths. Articles highlighting the abuse of this drug, but not its effectiveness in the treatment of chronic pain, have been cover stories in major magazines and newspapers. Some of the progress made in the treatment of severe pain with opioids has been undone by these events. Prescriptions for all opioid medications over the past year have decreased; the fears of both physicians and the public about opioid addiction have increased.

#### GABAPENTIN

Gabapentin is a structural analog of gamma-aminobutyric acid (GABA)

dromes I and II (formerly known as reflex sympathetic dystrophy), abdominal pain, headache, fibromyalgia, and chronic fatigue. The usual starting dose for adolescents is 200 to 300 mg at bedtime, which can be increased by 100 mg every few days. The usual therapeutic dose is 300 mg TID, but occasional patients may not achieve pain relief until the total dose is 2 to 3 g/d. The primary adverse effects seen with gabapentin are somnolence, dizziness, confusion, and weight gain. The sedation often associated with gabapentin dissipates over time and can be diminished further by reducing the rate of dose escalation.

#### ALPHA-2 AGONISTS

Alpha-2 agonists have been used successfully to treat hypertension since the early 1970s. Their use in the field of pain management has blossomed over the past several years because of diverse responses produced by these medications, including analgesia, anxiolysis, and sedation. Alpha-2 agonists have been used successfully in the treatment of intraoperative and postoperative pain and chronic pain as well as in the control of symptoms of withdrawal in opioid-dependent individuals. Clonidine and, more recently, dexmetomidine have been shown to be useful in both the operative and intensive care unit settings.

Clonidine can be administered via an epidural catheter either intra- or postoperatively, prolonging and intensifying surgical anesthesia and postoperative pain management. In combination with opioids, clonidine offers the additional advantage of a reduced dose for each component with correspondingly fewer adverse effects. Epidural clonidine has been used successfully to treat cancer and neuropathic pains. Clonidine also has been used intravenously to decrease

## For neonates, non-nutritive sucking and maintaining skin-to-skin contact during breastfeeding decrease pain associated with procedures.

A scavenging device is essential to minimize ambient levels of gas and exposure to health care workers.

#### LONG-ACTING OPIOIDS

The development of long-acting opioids has been a blessing for patients who have chronic pain. These medications, which include long-acting preparations of oxycodone and morphine, must be swallowed whole to provide continuous pain relief. Long-acting opioids are appropriate for patients who suffer severe pain from malignancy, arthritis, and chronic pain syndromes. They should not be used for acute pain.

Unfortunately, long-acting oxycodone has become a popular drug of abuse in some areas of the United

States that was introduced in 1994 as an antiepileptic medication especially for partial seizures. Other antiepileptics such as carbamazepine have been useful as adjuncts for the treatment of chronic pain, as has gabapentin. It seems to be most successful when used to treat neuropathic pain states. Although the mechanism of action remains unclear, clinical data suggest that gabapentin is most helpful in reducing paroxysmal pain that has lancinating or burning qualities. Randomized, controlled data comparing the efficacy of gabapentin with other adjunctive medications are limited.

Gabapentin may be used for a variety of chronic pain problems, including complex regional pain syn-

the opioid requirement of patients suffering from extensive burns. When administered orally or transdermally, clonidine can ameliorate symptoms of opioid or benzodiazepine withdrawal for patients who are being weaned after long stays in the intensive care unit. In this setting, clonidine usually is administered at a dose of 2 to 4 mcg/kg every 4 to 6 hours. Further study is required to define the potential for alpha-2 agonist use in pediatric pain management.

### Specific Populations Neonatal Pain

Interest in the area of neonatal pain has exploded lately. It has become obvious that neonates not only feel pain, but remember it and even may experience pain more intensely than older children and adults. Some basic strategies can decrease the pain associated with common neonatal procedures. Encouraging nonnutritive sucking by simply allowing the infant to suck on a pacifier has been shown to decrease the pain of a heel lance. Maintaining skin-to-skin contact or breastfeeding during the procedure also has been shown to decrease pain.

Initially, it was suggested that EMLA<sup>®</sup> use in neonates might be inappropriate because of the potential for an increased risk of methemoglobinemia. Data from studies involving EMLA<sup>®</sup> use for procedures ranging from circumcision to venipuncture have demonstrated that it can be used safely in newborns and even in preterm infants. Other methods of topical anesthesia have been less well studied in neonates.

It appears that a spoon full of sugar does help the medicine go down; more accurately, a spoonful of sugar is the medicine! Sucrose water (12% to 50%; typically, 1 packet of sugar in 10 mL of water) administered just prior to a procedure has

been shown to decrease the pain associated with heel lance, venipuncture, and immunization. Remarkably, sucrose seems to use opioid pathways. In fact, in a rat model, the effect of sucrose can be blocked by the use of an opioid antagonist such as naloxone. Sucrose can be administered via a pacifier or directly instilled into the mouth with a small syringe. It works best in the neonatal period and loses its efficacy by 4 to 6 months of age. Interestingly, this effect recently was shown to occur with an artificial sweetener (saccharin) as well. The combination of direct parental contact and sucrose seems to have an additive effect on pain reduction.

Because of the recent recognition of the potential for long-term consequences from the inadequate treatment of pain in even common neonatal procedures, significant attention has focused on pain relief during circumcisions and heel lance. Pain control in circumcision, the most commonly performed surgical procedure in the United States, now is considered an essential aspect of the surgery. Despite a revised consensus statement from the American Academy of Pediatrics urging the use of anesthesia/analgesia for circumcision, many procedures are performed without pain relief because of time constraints and lack of knowledge. Multiple studies have shown that a nerve block, either the dorsal penile nerve block or a ring block, is safe and dramatically decreases the pain associated with circumcision. A nerve block can be used in conjunction with EMLA<sup>®</sup> cream to minimize pain further. In addition to the use of a nerve block, the choice of clamp can influence the pain of circumcision. Research comparing the Mogen clamp, which is used routinely by ritual circumcisers, and the more commonly used Gomco clamp found

the Mogen clamp to be faster and considerably less painful. A padded restraint board and the use of sucrose prior to the procedure further decreases the distress associated with the procedure.

Although sucrose may be helpful, topical anesthetics do not appear to be effective in alleviating the pain of a heel lance. Some evidence supports the use of autoinjectors to lance the heel instead of a manually directed lancet. A number of studies have suggested that venipuncture be considered for routine blood draws in the newborn period because it appears to be less painful than heel lance, and pain can be reduced further through the use of a topical anesthetic. Venipuncture may become the preferred method of obtaining blood specimens from the neonate in the future.

### Children Who Have Neurologic Impairment

Another conceptual advance in the field of pediatric pain is the increased recognition of pain in children who have neurologic impairments and developmental disabilities. Historically, this population was as disenfranchised as the neonatal population. Children who are cognitively impaired or technologically dependent often are unable to describe their pain with any subtlety or request relief. In addition, because they frequently have damaged or altered nervous systems, the myth that pain transmission in this population is altered and most likely diminished has persisted. In addition to discrimination due to inadequate assessment and attitude, many children who have neurologic handicaps have unique pain problems such as spasticity that require medications that are not familiar to most physicians.

In the past 5 years, a number of articles have been published that review this vexing problem. New as-

assessment techniques for cognitively and motorically impaired individuals have been developed and standardized. Understanding of the neurologic basis of pain transmission has grown, and the addition of new animal models has provided further insight into the pain suffered by individuals who have sustained neurologic insults. New drugs for spasticity as well as new delivery systems such as implantable pumps are available for the unique subset of problems that these children may encounter.

tective function has shifted. Instead of focusing solely on pain, the emphasis is now on rehabilitation. Success should be gauged by return of function (school attendance and performance, social engagement) and not merely by reduction of discomfort. For these problems, exercise, physical and occupation therapy, cognitive and behavioral approaches to pain, and physical strategies such as massage, TENS, and acupuncture should be the mainstays of treatment. A coordinated team effort is critical.

tics, the following principles generally are followed:

- Parents and children are informed that pain control is a “right” through signs in the institution and discussion on arrival. Their active participation is encouraged.
- Protocols for pain control are developed and displayed prominently to minimize variability of knowledge among staff.
- Aggressive use of local anesthetics is advocated, and impediments to their use are identified.
- Use of the treatment room and play therapists in the child life program is encouraged for procedures.
- Assessment techniques are standardized throughout the institution, and compliance with them is monitored by quality assurance programs.

A systematic approach to pain management assures that all children receive sophisticated pain care, not only those for whom consultation with the pain service is obtained.

### JCAHO

JCAHO, the accrediting body for hospitals, recently acknowledged the importance of pain assessment and management in the overall safety and well-being of hospitalized patients. In 2000, JCAHO finalized standards on pain assessment and management that now are incorporated into the survey process.

These standards have at their core the philosophy that “all patients have a right to pain relief,” a statement that must be included in the patient’s bill of rights and displayed prominently around the hospital. Key components required by JCAHO are documentation of initial assessment and regular reassessment of pain in all patients, education of relevant clinicians in pain assessment and management, and education of patients and

**Improvement** in pain control requires medical institutions to have a clear plan for pain management. “All patients have a right to pain relief.”

### Models of Care and Regulatory Efforts

#### Multidisciplinary Pain Teams and Clinics

Current understanding of the multifactorial nature of pain suggests that pain cannot be managed adequately by pharmacotherapy alone. All pain problems, whether acute or chronic, benefit from multidisciplinary evaluation and treatment. General and subspecialty pediatricians, nurses, psychologists, psychiatrists, anesthesiologists, rehabilitation specialists, occupational therapists, physical therapists, and parents and siblings have important roles to play in alleviating a child’s pain. For children who have chronic pain, involvement of the child’s school also is essential. In addition, the approach to treatment of chronic pain problems (eg, fibromyalgia, complex regional pain syndrome, chronic fatigue, headache) in which pain no longer has a neuropro-

### Institutional Strategies

Significant improvement in pain control for all children can be accomplished only by changing the culture of medical institutions rather than focusing on the unique pain problems of selected individuals. Strategies are required to overcome many of the impediments to pain management, such as attitudes that promote undertreatment, inadequate assessment, lack of staff knowledge and sophistication, continuously changing personnel who do not share the same knowledge base or beliefs, and a lack of financial incentive. A number of institutions around the United States, ranging from community hospitals to large academic medical centers, have implemented a series of reforms that attempt to guarantee that each child who enters the institution receives state-of-the-art pain control. Although the specific strategies vary, depending on local legis-

families, when appropriate, regarding their roles in managing pain as well as the potential limitations and adverse effects of pain treatments.

Although JCAHO does not mandate the manner by which these standards are implemented, their directives have caused hospitals nationwide to re-evaluate their approach to pain and vigorously address deficiencies in assessment, management, documentation, and discharge planning. The development of a systematic approach to pain management in hospitals predated the JCAHO pain initiative, but such programs clearly have been validated and encouraged by the JCAHO mandate.

## Conclusion

Dramatic changes have occurred in the past 20 years in conceptualizing and treating pain. Untreated pain may have significant consequences for the individual. New assessment techniques allow better identification of pain in children, and new pharmacologic and behavioral approaches allow more successful treatment. Populations in whom pain treatment was not a strong consideration in the past have been shown to require and benefit from appropriate pain control. It is imperative that these advances be available to all children and that systems be implemented to assure children and families that their suffering will be addressed compassionately.

## Suggested Reading

Als H, Lawhon G, Doffy F, et al. Individualized developmental care for the very

- low birth weight pre-term infant: medical and neurofunctional effects. *JAMA*. 1994;272:853–858
- American Academy of Pediatrics. Task Force on Circumcision. Circumcision policy statement. *Pediatrics*. 1999;103:686–693
- Anand KJS. Consensus statement for the prevention and management of pain in the newborn. *Arch Pediatr Adolesc Med*. 2001;155:173–180
- Finley GA, Mocrath PJ. *Measurement of Pain in Infants and Children: Progress in Pain Research and Management*. Vol 10. Seattle, Wash: IASP Press; 1998
- French GM, Painter EC, Coury DL. Blowing away shot pain: a technique for pain management during immunization. *Pediatrics*. 1994;93:384–388
- Gray L, Watt L, Blass EM. Skin-to-skin contact is analgesic in healthy newborns. *Pediatrics*. 2000;105:e14. Available at [pediatrics.aappublications.org/cgi/content/full/105/1/e14](http://pediatrics.aappublications.org/cgi/content/full/105/1/e14)
- Kemper KJ, Sarah R, Silver-Highfield E, et al. On pins and needles? Pediatric pain patients' experience with acupuncture. *Pediatrics*. 200;105:941–947
- Larsson BA, Tannfeldt G, Lagercrantz H, et al. Venipuncture is more effective and less painful than heel lancing for blood tests in neonates. *Pediatrics*. 1998;101:882–886
- Lawson RA, Smart NG, Gudgeon C, et al. Evaluation of an amethocaine gel preparation for percutaneous analgesia before venous cannulation in children: *Br J Anaesth*. 1995;75:282–285
- Luhmann JD, Kennedy RM, Porter FL, Miller JP, Jaffe DM. A randomized clinical trial of continuous-flow nitrous oxide and midazolam for sedation of young children during laceration repair. *Ann Emerg Med*. 2001;37:20–27
- McCaffery M, Beebe A. *Pain: Clinical Manual for Nursing Practice*. St. Louis, MO: CV Mosby; 1989
- McGrath PJ, Finley GA. *Chronic and Recurrent Pain in Children and Adolescents: Progress in Pain Research and Management*. Vol 13. Seattle, Wash: IASP Press; 1999
- Reis EC, Holubkov R. Vapocoolant spray is equally effective as EMLA cream in reducing immunization pain in school-aged children. *Pediatrics*. 1997;100:e5. Available at [pediatrics/aappublications.org/cgi/content/full/100/6/e5](http://pediatrics/aappublications.org/cgi/content/full/100/6/e5)
- Schechter NL, Berde CB, Yaster M. *Pain in Infants, Children, and Adolescents*. Philadelphia, Pa: Lippincott Williams and Wilkins; 2003
- Schechter NL, Blankson V, Pachter LM, et al. The ouchless place: no pain, children's gain. *Pediatrics*. 1997;99:890–894
- Stang HJ, Snellman LW, Condon L, et al. Beyond dorsal penile nerve block: a more humane circumcision. *Pediatrics*. 1997;100:e3. Available at [pediatrics/aappublications.org/cgi/content/full/100/2/e3](http://pediatrics/aappublications.org/cgi/content/full/100/2/e3)
- Stevens B, Taddio A, Ohlsson A, et al. The efficacy of sucrose for relieving procedural pain in neonates—a systematic review and meta-analysis. *Acta Paediatr*. 1997;86:837–842
- Sugarman LI. Hypnosis: teaching children self-regulation. *Pediatr Rev*. 1996;17:5–11
- Taddio A, Katz J, Ilersich AL, et al. Effect of neonatal circumcision on pain response during subsequent routine vaccination. *Lancet*. 1997;349:599–603
- Taddio A, Ohlsson A, Einarson TR, Stevens B, Koren G. A systematic review of lidocaine-prilocaine cream (EMLA) in the treatment of acute pain in neonates. *Pediatrics*. 1998;101:e1. Available at [pediatrics/aappublications.org/cgi/content/full/101/2/e1](http://pediatrics/aappublications.org/cgi/content/full/101/2/e1)
- Weisman SJ, Bernstein B, Schechter NL. Consequences of inadequate analgesia during painful procedures in children. *Arch Pediatr Adolesc Med*. 1998;152:147–149
- Yaster M. Acute pain in children. *Pediatr Clin North Am*. 2000;47:3
- Zempsky WT, Anand KS, Sullivan KM, et al. Lidocaine iontophoresis for topical anesthesia before intravenous line placement in children. *J Pediatr*. 1998;132:1061–1063

## PIR Quiz

Quiz also available online at [www.pedsinreview.org](http://www.pedsinreview.org).

6. A 2-day-old boy is scheduled to undergo circumcision. He was born after an uncomplicated pregnancy and delivery. His mother is concerned about pain associated with circumcision. Of the following, a *true* statement regarding pain in the newborn is that:
  - A. Ascending neural pathways transmitting pain are well developed at birth, but descending inhibitory pathways are not.
  - B. Experiencing pain early in life helps children deal with adversity more effectively later in life.
  - C. Feeling of pain is a learned phenomenon through postnatal experience with injury.
  - D. Neonatal pain response is transient and not as pronounced as in older children and adults.
  - E. Repeated procedures such as heel sticks result in habituation, with decreasing response to painful stimuli.
  
7. A 12-year-old girl is admitted after repair of idiopathic scoliosis. She has no other significant medical history. Of the following, the *best* means of assessing her pain is via:
  - A. Behavioral indicators.
  - B. Nursing staff assessment.
  - C. Parental assessment.
  - D. Patient self-assessment.
  - E. Physiologic indicators.
  
8. An 8-year-old boy underwent thoracotomy to remove a chronically infected bronchiectatic left lower lobe. Of the following, a *correct* statement regarding postoperative pain management in this boy is that:
  - A. Both nonsteroidal anti-inflammatory drugs (NSAIDs) and opioids have a maximum dose after which a higher dose does not provide additional analgesic benefit (ceiling effect).
  - B. Different classes of pain medications, such as an NSAID and an opioid, should not be combined.
  - C. Objective means of assessing pain, such as a validated pain scale, are more accurate than patient self-assessment.
  - D. Opioids should not be used as the first-line drugs in management of postoperative pain because of their adverse effects.
  - E. Pain medication should be administered around the clock, with additional doses in between as required.
  
9. A 2-day-old girl is admitted for management of suspected sepsis and dehydration. The management plan includes obtaining blood samples and initiating intravenous antibiotics and fluid therapy. Which of the following statements regarding painful procedures in this patient is *true*?
  - A. Development of neural pathways involving pain is not appreciable before 1 week of age.
  - B. Experiencing pain in the neonatal period has been shown to be of little or no consequence later in life.
  - C. Heel lancing is less painful than venipuncture for obtaining blood samples.
  - D. Oral administration of sucrose water is effective in reducing pain associated with venipuncture.
  - E. Topical anesthetic cream made of lidocaine and prilocaine should not be used in newborns because of the risk of methemoglobinemia.

## What's New in the Management of Pain in Children

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Pain Management in Children An Integrative Approach Susie Gerik, MD Children's Center for Restorative Care UTMB  
Children's Hospital Definition of Pain As defined by the International Association for the Study of Pain (IASP), pain is "an unpleasant sensory and emotional experience associated with actual or potential damage, or described in terms of such damage." Physiology of Pain Nocioception is a physiologic mechanism of noxious stimulus transduction Requires a nociceptor Not necessarily the same as "pain" Biologic role is protective Nociceptors Nociceptors are free nerve endings Ubiquitous distribution An introduction to controlling pain in children. What is pain? How pain is expressed? How pain is assessed? Pain in children has several unique features which make appropriate management challenging. In the past, pain has been poorly managed in paediatric patients due to the false belief that neonates and children do not experience pain or require pain relief, as commonly as adults. It was thought that neonates did not experience or remember pain due to their immature nervous systems. Perhaps the greatest challenge of pain management in children, is gaining an objective assessment of the level of pain. Infants and young children cannot verbalise their pain levels so rely on adults' and health professional's interpretations of external manifestations of the pain. Procedural sedation in children outside of the operating room. Scrotal trauma in children and adolescents. Urinary tract infections in infants older than one month and young children: Acute management, imaging, and prognosis. Causes of scrotal pain in children and adolescents. View in Chinese. The most common causes of acute scrotal pain in children and adolescents include testicular torsion, torsion of the appendix testis, and epididymitis. In one review of 238 consecutive boys, ages 0 to 19 years, who presented with acute scrotal pain to a children's hospital over a two-year period, 16 percent had testicular torsion, 46 percent had torsion of the appendix testis, and 35 percent had epididymitis [1]. TESTICULAR TORSION.

What are the causes and effects of pain? Pain management is an important concern for a child with cancer or other pain-causing disease. When a child has cancer, one of their greatest fears, and the fear of parents, is pain. Every effort should be made to ease the pain during the treatment process. Pain is a sensation of discomfort, distress, or agony. Because pain is unique to each person, a child's pain can't be measured with a lab test or imaging study. Healthcare providers can evaluate pain by observing a child and asking about it. Nonpharmacological pain management is the management of pain without medicines. This method utilizes ways to alter thinking and focus to decrease pain. Methods include The science of pain assessment for infants and children has grown substantially in the past several decades to the point that valid and reliable methods for pain assessment are available for use in clinical settings. Accurate pain assessment requires consideration of children's developmental level, type of pain experienced, history and context of pain, family influences, and interaction with the health care team. 2. Delineate the general principles of pain management in children. 3. List new pharmacologic agents for treatment of pain in children. 4. Devise a program to reduce the pain associated with circumcision. 5. Describe pain assessment tools available for infants and children. All children with burns will experience pain, regardless of the cause, size, or burn depth. Undertreated pain can result in noncompliance with treatment and, consequently, prolonged healing. It is acknowledged that the monitoring and reporting of pain in children with burns has generally been poor. Management of pain is important during all stages of treatment including in the emergency department, during procedures such as dressing changes and after discharge when complex neuropathic pain syndromes may develop [18]. 6. Measurement Tools. A major contributing factor to poor pain management is the difficulty children have in expressing their pain and problems that the health professionals may have in interpreting and assessing this information correctly.