

Inadequate Pain Management During Routine Childhood Immunizations: The Nerve of It

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ABSTRACT

Background: Immunization is regarded as one of the most significant medical achievements of all time. Recently, increasing attention has been paid to the pain resulting from routine childhood immunizations.

Objective: This narrative review summarizes existing knowledge about: (1) the epidemiology of childhood immunization pain; (2) the pain experience of children undergoing immunization; (3) current analgesic practices; (4) barriers to practicing pain management in children; and (5) recommendations for improvements in pain management during immunization.

Methods: We conducted a search of MEDLINE, PsycINFO, EMBASE, CINAHL, and the Cochrane Central Register of Controlled Trials for primary research and review articles published from inception of the databases through October 2008. Key search terms included *immunization, pain, child/infant, vaccine, and intervention*. Additional studies were identified through searches of the reference lists in the retrieved articles. No language restrictions were imposed regarding the type of article (eg, full article, abstract) or language.

Results: Vaccine injections are the most common iatrogenic procedure performed in childhood and a major source of distress for children (of all ages), their parents, and the participating health care professionals,

as well as a direct cause of vaccine nonadherence. In addition, lack of adequate pain management during immunization exposes children to unnecessary suffering and the potential for long-term consequences, such as fear of needles. Numerous pain management strategies are available to reduce vaccine injection pain, including: (1) physical interventions and injection techniques; (2) psychological interventions; and (3) pharmacologic and combined interventions. However, adoption of pain-relieving techniques into clinical practice has been suboptimal. The underutilization of pain management strategies can be attributed to a lack of knowledge about pain and effective pain prevention strategies, and the persistence of attitudes about pain that interfere with optimal clinical practices. Current analgesic practices could be improved substantially if all stakeholders involved in immunization (eg, policy makers, practitioners, consumers) participate in efforts to reduce pain. Treating pain during childhood immunization has the potential to reduce distress during the procedure and greatly improve satisfaction with the immunization experience through more positive experience.

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riences for children and their families. Other potential benefits include improved adherence to immunization schedules and reduced sequelae of untreated pain.

Conclusion: Immunization is a global health priority. Medical care can be improved if pain management becomes a routine aspect of the delivery of vaccine injections. (*Clin Ther.* 2009;31[Suppl B]:S152–S167) © 2009 Excerpta Medica Inc.

Key words: immunization, pain, infant/child, pain management.

INTRODUCTION

Vaccines are regarded as one of medicine's greatest achievements. Since the implementation of immunization programs worldwide, there has been a substantial reduction in both morbidity and mortality caused by infectious diseases.¹ Most vaccines, however, require a needle puncture, or "shot." Although it is widely recognized that vaccine injections are distressing for children, their families, and the participating health care professionals, little attention has been given to minimizing the pain associated with these procedures.^{2,3}

Medical societies are taking initiative to address pain in childhood.^{4–6} Relief of pain and suffering has been identified as an important quality of pediatric medical care.⁷ Recently, the Brighton Collaboration (<http://brightoncollaboration.org>), a global vaccine safety effort founded in 1999, acknowledged pain as an adverse event of immunization, and is developing a standardized definition of vaccine injection pain intended for safety monitoring of immunizations worldwide. Efforts aimed at disseminating and implementing effective pain management strategies are therefore both timely and highly relevant. This article is a narrative review of the existing knowledge about, and the rationale for, pain reduction during immunization, including: (1) the epidemiology of childhood immunization pain; (2) the pain experience of children undergoing immunization; (3) current analgesic practices; (4) barriers to practicing pain management in children; and (5) recommendations for improvements in pain management during immunization.

We conducted a search of MEDLINE, PsycINFO, EMBASE, CINAHL, and the Cochrane Central Register of Controlled Trials for primary research and review articles published from inception of the databases through October 2008. Key search terms included *immunization, pain, child/infant, vaccine, and interven-*

tion. Additional studies were identified through searches of the reference lists in the retrieved articles. No restrictions were imposed regarding the type of article (eg, full article, abstract) or language.

EPIDEMIOLOGY OF CHILDHOOD IMMUNIZATION PAIN

Routine immunizations are the most frequent painful medical procedures during childhood.⁸ The World Health Organization estimates that 12 billion injections are given annually, and that ~5% are childhood vaccinations.^{9,10} The number and types of vaccines administered depend on the geographic region, with each area developing its own vaccination schedule according to the regional disease epidemiology, the economic impact on the region, and health policy priorities.

Within Canada, the national vaccine schedule currently recommends immunization against 17 specific infectious diseases. According to the schedule, children will receive up to 20 separate vaccine injections by the time they reach school age (4–6 years). If they have underlying medical conditions, they will receive considerably more injections.¹¹ In the United States, the immunization schedule recommends that children receive up to 5 shots during a single office visit.¹² An even greater number of injections can be anticipated with the development of new vaccines to counter other emerging or reemerging infectious diseases.^{13,14}

The continuing addition of new vaccines to national immunization programs has led to satirical descriptions of children as "targets for pain" or "pin cushions."¹⁵ The availability of combination vaccines has reduced the number of needle punctures by two thirds.¹⁶ In addition, innovative noninvasive technology is being investigated to avoid injection pain by using mucosal and topical routes of vaccine administration. However, such noninvasive technology is not expected to replace needles anytime soon,¹⁵ and needles will continue to be the primary method of vaccine delivery and the "negative symbol" of routine childhood immunization for many years to come.

Guiding Principles for Pain Relief During Immunization

The importance of pain avoidance in the delivery of health care is recognized in the medical principle to "first do no harm." Pain relief is considered a basic human right,¹⁷ and reducing iatrogenic pain in children is a priority identified by health care agencies,

researchers, and parents.^{4–6,18,19} The concept of *atraumatic care*, defined as the provision of therapeutic care in a way that minimizes physical and emotional distress to children and families,²⁰ has been promoted as a framework for performing needle punctures in children.

Children are typically not involved in decision making about prophylactic interventions such as immunizations.²¹ Prerequisite conditions that ensure protection of the child's rights have been proposed by bioethicists and include: (1) use of the least invasive treatment option; (2) minimal negative impact on health; and (3) the ability to provide informed consent (as appropriate).²¹

The cumulative effect of pain that is inflicted by vaccinations needs to be addressed. Teenagers are increasingly being selected for additional immunizations to prevent sexually transmitted diseases (eg, human papilloma virus) or to boost waning immunity.¹³ Pain is a prominent feature of the vaccination experience of teenagers,²² and public health providers need to devote attention to it. Any aversion to needle sticks is likely to compound doubts about the value of new vaccines and willingness to submit to them.

THE PAIN EXPERIENCE OF CHILDREN UNDERGOING IMMUNIZATION

The International Association for the Study of Pain defines *pain* as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. Furthermore, pain is always subjective. Each individual learns the application of the word through experiences related to injury in early life.”²³ This definition of pain highlights the individuality of pain and importance of life experiences, especially those in early life, in shaping the pain response.²⁴ The inability to verbally communicate pain, as occurs in young infants, does not negate its presence. At the time of birth, the basic nociceptive connections are already formed. However, immaturity of the pain system, which includes the presence of larger receptive fields and lack of inhibitory controls of pain, may lead infants to have greater responses from the same sensory input compared with adults.²⁵

Immunizations make up the majority of a healthy child's early life experiences with iatrogenic (medical) pain, and therefore have the potential to play a significant role in shaping the child's pain during similar events in the future. It has been reported that chil-

dren's perceptions of immunization pain differ from those of adults; they perceive immunizations as more painful.^{26,27} For children, any procedure involving a needle puncture is viewed as one of the most frightening and painful health-related events.^{20,28–30} In an article titled “The needle is like an animal: How children view injections,”³¹ Lewis presented a child's account of injections:

“When the doctors give the shots

They don't know how it feels.

They say it's not gonna hurt

Only because it doesn't hurt them.”

Furthermore, the question most frequently asked by children when entering the doctor's office is: “Am I going to get a shot?”^{8,32} Children are clearly concerned about needle pain.

Vaccine injections cause acute pain through activation of peripheral nociceptors during 2 separate events: (1) when the needle punctures the skin and tissues; and (2) when the vaccine constituents are deposited into the tissue. In children, vaccine injections elicit more distress than would be expected from the extent of physical injury that is sustained from the procedure. The planned nature of the vaccination event tends to induce anticipatory fear responses (distress before pain is inflicted due to anticipation of pain). It is normal for children to fear potentially threatening situations and situations that have caused previous harm, such as vaccine injections.³³ Anticipatory fear, however, can increase the pain and distress experienced during the actual procedure. Contrary to popular belief, children do not habituate to painful procedures over time. Instead, they rapidly develop conditioned anxiety responses to them,³⁴ which manifest as anticipatory fear. Factors that influence the degree of anticipatory fear include a child's age (cognitive development, ability to understand the value of the procedure), procedural factors (chaotic environment, inadequate treatment of pain and distress, lack of control), the presence or absence of supportive adults (they rely on adults to help them when they are in pain), and memory factors (the child may have fragmented traumatic memories of previous procedures and/or distorted or exaggerated memories).^{24,30}

Individual child factors such as developmental level, temperament, and sex may have a considerable effect on a child's response to immunization. On average, younger children exhibit more distress and pain than do older children. More than 90% of toddlers

and 50% of primary school-aged children exhibit severe distress during immunization.³⁵ Children classified as being more difficult (temperamental) may have enhanced reactions to pain.^{36,37} Studies have not implicated sex as a significant determinant of pain response for infants and young children undergoing immunization.^{38–43} In general, however, females tend to report more pain than do males as adults.^{24,44} It has been suggested that these sex differences develop during adolescence.²⁴

In addition, procedural factors, including analgesia and environmental setting, can have a considerable impact on a child's response during immunization. Effective pain management strategies are recommended, including: (1) physical interventions and injection techniques (eg, rapid injection without aspiration); (2) psychological interventions (eg, cognitive-behavioral strategies such as distraction); and (3) pharmacologic and combined interventions (eg, topical local anesthetics, sweetening agents such as sucrose solutions, breastfeeding) (see the articles by Taddio et al,⁴⁵ Chambers et al,⁴⁶ and Shah et al⁴⁷ in this supplement) (Table I). In terms of setting, a comfortable room free of visual or acoustic distress-provoking stimuli should be used.⁴ In doctors' offices, this can be accomplished using private patient examination

rooms. In school-based immunization clinics, a room separated from peers may be needed to minimize environmentally induced distress.

A substantial body of research has reported that parental (and other adult) behaviors during painful procedures are associated with children's pain and distress.^{36,48–53} A child's pain and distress during such procedures are reduced when adults are calm and use coping-promoting strategies such as engaging in non-procedural talk, coaching, or distraction (diverting a child's attention from the procedure). Conversely, children's pain and distress are increased when adults are anxious or use distress-promoting strategies such as making apologies, criticizing, providing reassurance, or showing empathy (focusing a child's attention on the procedure).

It is important to note that children want their parents to be with them when they have pain, and parents want to be with their children when they are experiencing pain.^{54–56} Generally, parents are present at vaccine injections performed in doctors' offices. However, parents cannot be present in all instances when their children receive vaccine injections (eg, clinics offered in schools). Both parents and health care staff can be easily instructed to use coping-promoting strategies to minimize pain and distress in children.⁵²

Table I. Evidence-based interventions for reducing childhood vaccine injection pain.*

Intervention	Strategy
Physical interventions and injection techniques ⁴⁵	Use the least painful formulation of a vaccine that is commercially available Position children sitting up (or hold infants) Stroke the skin close to the injection site Inject the most painful vaccine last when ≥ 2 vaccines are being injected sequentially during a single office visit Use rapid intramuscular injection without aspiration
Psychological interventions ⁴⁶	Breathing exercises Child-directed distraction Nurse-led distraction Combined cognitive-behavioral interventions
Pharmacologic interventions ⁴⁷	Topical local anesthetics (eg, lidocaine–prilocaine) Sweetening agents (eg, sucrose [for infants])
Combined interventions ⁴⁷	Breastfeeding (for infants) Combinations of physical, psychological, and pharmacologic interventions

*See the 3 separate systematic reviews in this supplement for more details.

Parents, nurses, and physicians become distressed when they witness a child in pain, and they are often uncomfortable with injection of multiple vaccines during a single office visit.^{15,57} Parental concern for their child suffering during medical procedures is not limited to vaccine injections; in 1 study,²⁰ parents rated needle punctures as the second most distressing event during their child's hospitalization, second only to waiting for their child during surgery.²⁰ Parents report a willingness to pay (\$25–\$50) to reduce the number of injections their children receive.⁵⁸

Long-Term Effects of Pain in Children

There are many documented adverse sequelae of untreated procedural pain in childhood. These include: anticipatory fear at future procedures due to negative memories of past procedures,⁵⁹ sensitization to future pain due to changes in how the nervous system processes pain,⁶⁰ reduced effectiveness of analgesics,⁶¹ difficulty carrying out procedures,⁶² and needle phobia⁶³ (an unusual fear of needles, diagnosable by criteria in the *Diagnostic and Statistical Manual of Mental Disorders*⁶⁴).

The amount of distress a child experiences during a procedure is particularly important for how the child remembers the event. Greater distress is associated with more negative memories, which lead to more reports and displays of pain and distress at future encounters of the same stressful events.^{35,36,65} A lack of verbal report of pain or overt distress during immunization does not imply a lack of physiologic consequences or distorted negative recall of the pain experienced.^{30,66}

Studies have reported that painful events in the newborn period can lead to changes in future pain responses.^{60,67–69} In 2 separate studies,^{67,68} circumcised newborn male infants had more pain at routine 4- and 6-month immunizations than did their uncircumcised peers. Pretreatment of circumcision pain with topical local anesthesia prevented the heightened pain response at immunization.⁶⁸ Infants of diabetic mothers, who undergo repeated heel lances in the first 2 days of life, had greater pain responses to subsequent venipunctures than did matched control infants.⁶⁹ Changes in future pain responses also occurred in hospitalized preterm and full-term infants.⁶⁰

Children may have increased analgesic requirements at future procedures if pain is inadequately managed early in life. In a study of children with newly diag-

nosed cancer, those given a placebo instead of an oral analgesic during the first lumbar puncture reported more pain during subsequent procedures than did those given an oral analgesic at the first lumbar puncture, even though both groups of children received the oral analgesic at subsequent procedures.⁶¹

Distress and pain experienced by children during medical procedures can affect a child's level of cooperative behavior and need for physical restraint to allow completion of the procedure. There is a risk of failing to carry out required medical procedures if children are highly distressed.⁶² The provision of analgesia can facilitate procedure completion. In 2 separate studies,^{70,71} venous cannulation success rate on the first attempt was significantly higher for children who received topical local anesthetics compared with those who received no anesthetic ($P = 0.03$). Moreover, the improved success rate was associated with a significant reduction in overall procedure time ($P = 0.04$).⁷⁰

Needle phobia is a widely publicized adverse consequence of untreated needle pain and develops in ~10% of the population.⁶³ Needle phobia usually develops in childhood, after a negative experience at the doctor's office.⁶³ Children with needle phobia struggle to avoid procedures and may sustain trauma during procedures due to falling (as a result of fainting or resistance to being restrained).⁶³ The fear may also become generalized to individuals, objects, and situations related to needles, such as doctors, nurses, syringes, white laboratory coats, and examination rooms.⁶³ It is important to note that even children who do not meet the criteria for a diagnosable needle phobia can still experience substantial anticipatory anxiety and fear regarding immunizations.

The consequences of needle fears are considerable. For example, children with needle fears and their parents avoid seeking medical care.^{63,72} As adults, these children decline dental treatments, avoid regular health care visits, and are nonadherent to preventive health care measures (eg, vaccination, blood donation) and medical treatment regimens (eg, insulin injections for diabetes).^{63,73–80} Thus, individuals with needle fears are assuming higher risks than the general public for morbidity and mortality.⁶³

Concerns about vaccination pain are present during immunizations performed in adulthood as well.^{79,81} Up to 25% of adults are estimated to have considerable fear of needles.⁴ One study⁸¹ suggests that the majority of the adult working population does not

want to be vaccinated. In that study, only 12.7% of 12,582 individuals who were offered a free influenza vaccine elected to receive it. In the group that elected vaccination, 97% chose to receive the intranasal formulation rather than the injectable one. Fear of injections was the primary reason given for choosing the intranasal formulation in 14% of the vaccinated individuals. Influenza vaccination rates also have been reported to be consistently low for health care workers, a group of individuals specifically targeted for vaccination. Each year, it is estimated that only 30% to 40% of health care workers are vaccinated.⁸² This rate increases to only 50% to 60% with implementation of intensive voluntary campaigns. One of the factors leading to poor compliance may be lingering memories of negative pain experiences in childhood contributing to negative attitudes about immunization in adulthood.

Effects of Immunization Pain on Adherence to Vaccination Schedules

Vaccinations are not administered according to recommended schedules in up to 25% of children.^{83,84} Concerns about the pain and discomfort associated with injections have been identified as an important factor for immunization adherence.^{85–87} In particular, parents report delaying immunization because they do not want to see their children cry or do not want all shots to be given at once.^{88,89} Furthermore, both parents and physicians report nonadherence to vaccine schedules and may avoid elective immunizations in an attempt to reduce the pain in children.^{57,88,90–93} This results in inadequate protection against infectious diseases at a time when protection is needed. In addition, nonadherence leads to an increased risk of not completing the vaccination course.⁸⁷ This places societal childhood immunization programs at risk of failure and results in resurgence of infectious diseases.⁹⁴ As long as vaccination programs rely on voluntary adherence, they must start and continue to address the issue of vaccine injection pain.

CURRENT ANALGESIC PRACTICES

As concluded in the 3 separate systematic reviews in this supplement,^{45–47} numerous evidence-based interventions are available for reducing vaccine injection pain (Table I). Moreover, practice guidelines have already been developed.^{4,8} However, adoption of the available research knowledge into clinical practice has

been suboptimal. In a recent audit of analgesic practices during routine immunization,² we found that effective analgesic strategies were rarely used in clinical practice. Of 274 children included in the audit, only 4 (1%) were treated with topical local anesthetics to reduce vaccine injection pain, a proven pain-relieving intervention for immunization pain.⁴⁷ Sixteen percent of mothers reported feeding infants, and none reported administering sweetening agents (eg, sucrose solutions).³

In addition, although recent evidence supports rapid intramuscular injection without aspiration as a technique to reduce vaccine injection pain,⁹⁵ only one third of 140 participating physicians reported that they injected the vaccine without aspiration.³ Interestingly, both rapid and slow vaccine injection speeds were cited by respondents as a method of reducing pain: 50% of physicians reported injecting the vaccine quickly to try to mitigate pain, whereas 20% injected the vaccine slowly.³ The technique of rapid injection without aspiration⁹⁵ is an evidence-based pain management approach that is cost free and could easily be adopted in practice.

In contrast, 80% of mothers reported holding their children and 70% reported distracting them as a comforting strategy during immunization.³ Although holding and distraction can be effective strategies for reducing pain,^{45,46} it was not clear from the responses whether mothers were restraining rather than supporting or comforting their children, which could have a paradoxical effect,⁹⁶ or whether attempts at distraction were effective. Parent-led distraction has not been shown to be a reliable method of pain management for children undergoing immunization, contrary to child-directed or nurse-led distraction (see the systematic review by Chambers et al⁴⁶ in this supplement).

Does elimination of pain during immunization prevent future fear of needles?⁹⁷ In 1 study,⁶⁶ the use of psychological and pharmacologic pain-relieving strategies reduced recall of pain and distress in 8- to 11-year-old children 6 months after immunization compared with those who received no intervention ($P = 0.017$). Consistent pain management is the only recommended approach for children undergoing repeated medical procedures.⁴

The use of analgesics alone may not be sufficient to prevent the development of fear because fear depends on multiple factors, not just physical pain. These fac-

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tors include previous experience, social learning, and situational circumstances.^{98,99} A comprehensive approach that addresses all potential sources of distress is required to minimize the development of needle fears. At a minimum, the basic principles of pain management include: (1) preparation of children before the procedure; (2) use of effective pain management interventions (eg, topical local anesthetics, distraction techniques, optimal vaccine injection techniques); (3) the presence of calm adults who can coach children during the procedure; and (4) a comfortable environment.

BARRIERS TO PRACTICING PAIN MANAGEMENT IN CHILDREN

The underutilization of pain management strategies during childhood immunization can be attributed to a lack of knowledge about pain, a lack of knowledge about effective pain prevention, and the persistence of attitudes about pain from medical procedures that interfere with optimal clinical practices.^{100,101} **Some of the commonly held myths about procedural pain in children and the respective truths are presented in Table II.**

Parental Lack of Knowledge About Pain

Parents report insufficient information as the primary reason for not managing immunization pain in their children.² In general, they report being unfamiliar with the classes of drugs that are used to manage vaccine injection pain (eg, topical local anesthetics), and they express skepticism about their effectiveness and concerns about additive adverse effects of the vaccines.² Parents rely on their physicians to teach them about how to help their children during immunization,^{2,30} and physicians' advice is predictive of analgesic utilization by parents.² However, parents report that their physicians do not routinely advise them about pain management.² Physicians acknowledge that they do not offer instruction to parents about pain if parents do not explicitly request it and do not routinely use analgesics in their practices.² Instead, they focus on educating parents about the adverse effects of the vaccine that develop later, when at home (eg, fever).³⁰

Another problem is that parents may not recognize that their children are experiencing pain.¹⁰² Many behavioral cues signal the presence of pain. In preverbal children, these include responses such as crying, facial grimacing, and writhing body movements. Be-

cause some of these markers (eg, crying) are nonspecific (ie, they occur in both the presence and absence of pain), the potential exists for adults (both parents and health care providers) to discount or ignore them. Health care providers may also perceive crying as a normal response of children in health care settings.¹⁰³ The presence of nonspecific indicators of pain suggests the need to perform additional actions to eliminate all potential sources of distress. In older, verbal children (>3 years of age), pain may be exhibited with similar behaviors; however, children can supplement behaviors with a self-report, which is considered the primary source for pain assessment. In all age groups, pain may be accompanied by physiologic changes (eg, increases in heart rate, blood pressure, and respiratory rate) as well as biochemical changes (eg, increased levels of cortisol and adrenaline); monitoring of these responses, however, is limited to hospital or research settings.

In light of these data, parents require education about how to recognize pain in their children. Parents should also be given written information (including pictures illustrating appropriate application methods) and practice/demonstration opportunities for ways to minimize pain in their children. Finally, parents should be educated about adult behaviors during the procedure that promote coping and, conversely, distress in their children, so they can effectively manage their child's distress during procedures.

Children, too, should be prepared for upcoming vaccine injections.³⁵ Preparation of the child promotes trust and allows the child time to think about how they might respond and plan coping mechanisms. In addition, the time invested to prepare children may be offset by the time saved during the procedure because of enhanced cooperation.⁵⁶ The optimal timing and content of the preparation relative to the procedure are unclear.¹⁰⁴ As little as 1 day of advance preparation may be sufficient for school-aged children.¹⁰⁵ For toddlers and infants, preparation is recommended immediately before the procedure.^{104,105} Children should, at a minimum, be told: (1) what will be done (ie, steps involved in the procedure); (2) how it will feel, being careful to use words that are explanatory without evoking anxiety (eg, *pressure*, *squeezing*, and *poking* instead of *pain*, *hurt*, and *shot*)^{24,104}; and (3) how to minimize discomfort.²⁹ Age-appropriate language and demonstration with dolls, books, or pamphlets can be used.²⁴

Table II. Myths and truths about immunization pain management in children.

Myth	Truth
It only hurts for a minute; there are no long-term effects.	The effects of pain can last a lifetime. Untreated pain can leave a permanent scar, or imprint, on the nervous system that changes how children respond to pain in the future. It also leads to fears of needles, doctors, and nurses.
Most immunizations happen when kids are infants, and they don't remember the pain.	The nervous system forms permanent memories of pain in infancy. Children also learn to associate the doctor or nurse with painful events and develop a fear of doctors and nurses at a young age. Parents are present at immunizations performed in early infancy and recall the pain their children experienced. They are less likely to adhere to immunization schedules because of it.
This is not an issue for most kids.	More than 90% of toddlers and 50% of primary school-aged children exhibit severe distress during immunization. Even children who do not appear to be distressed may have considerable distress.
It's only a needle.	For children, procedures involving a needle puncture are viewed as one of the most frightening and painful health-related events. The most common question a child asks when entering a doctor's office is "Am I getting a shot today?" Children are preoccupied by needle pain.
I give a lot of injections; I just want to get it over with quickly.	Adopting a child-focused approach to immunization will allow vaccinators to open their minds to an alternative method of immunization that does not involve distress for children, parents, or themselves. If pain management is practiced with every injection, children will learn to manage pain, remain calm during procedures, and develop trusting relationships with health care professionals. It also saves time because children will be more cooperative.
The problem is that hysterical parents are causing their child to have fears about getting shots. It is all psychological.	Getting shots is stressful for everyone—the child, the parent, and the health care worker performing the injection. At least 5% to 10% of parents delay immunization or don't have their children immunized because of pain. Fears develop because of a negative past experience with receiving injections, but can be avoided if proper pain management strategies are used every time. Parents can be trained to use pain-relieving techniques that will minimize their child's fear about getting shots.
Pain management is the parent's problem.	Parents have little information about how to manage pain during immunization. Health care providers have the opportunity to fill this knowledge gap.
Fear of shots is the only long-term effect of immunizations, and it is rare.	Up to 25% of adults are estimated to have a considerable fear of needles. Approximately 1 of every 10 people develops a needle phobia, usually in childhood, as a consequence of a negative experience with needles. This is common enough that everyone knows someone with a needle phobia. Fear of needles leads to avoidance of preventive and therapeutic health care measures in childhood and adulthood, which negatively impacts health.
We need to immunize quickly; we don't have time for all this pain management stuff.	When pain management is practiced routinely, it does not have to add extra time to the procedure. Parents and children can read about pain management beforehand, and measures can be put in place to mitigate pain during immunization.

(continued)

Table II (continued).

Myth	Truth
My doctor (nurse) knows best and tells me not to worry about the pain.	In the past, pain during medical procedures (eg, immunization) was viewed as a benign adverse effect. New scientific evidence has changed that view. Pain is now regarded as a harmful effect that should be prevented. Not everyone is familiar with the current scientific evidence. By delivering the message that pain management is important, and by using pain management strategies for their own children, parents can help change dismissive attitudes about pain.
We've never managed pain before, and everything has been just fine. Everyone gets through it.	Although immunization pain has not been managed routinely, it is not true that everything has been fine. There are many negative consequences of untreated pain in childhood, including increased pain at future procedures due to changes in how the nervous system processes pain, anxiety at future procedures, and needle fears. We have always accepted pain as a part of immunization, but that can change. With modern technology, we have the ability to treat immunization pain effectively. We can have the benefits of immunization AND no pain.
Children need to learn to cope with pain. Pain is a part of life.	Dismissive views about children's pain are counterproductive and lead children to mistrust health care workers. Children learn to cope with pain by practicing effective pain management, not by being forced to endure the pain. Children are cognitively immature. They feel more pain than adults do during immunizations, do not have coping strategies, and can suffer psychological trauma.
They cry anyway, so what's the difference?	Crying is a nonspecific measure of distress and does not confirm or negate the presence of pain. However, crying is not an excuse to deny pain relief to the child. Rather, it suggests that additional efforts are required to eliminate all potential sources of distress.
Children get used to getting shots.	On the contrary, children may display increased distress with repeated procedures. The best way to ensure that a child "gets used to" procedures is to provide adequate pain management in every instance.
We are already giving a vaccine. We shouldn't give children any pain medications if we don't have to. It is unsafe.	Vaccine injections are given to children to prevent them from developing infectious diseases that can make them sick. However, these injections can have adverse effects. The most common side effect is pain during injection. We use pain medications to prevent injection pain. Pain medications have been found to be effective and tolerable for children of all ages, even the youngest preterm infants, and do not interfere with the effects of vaccines.
The analgesic cream doesn't work.	Numerous well-designed studies have found that topical local anesthetics (ie, analgesic creams that numb the skin) reduce vaccine injection pain. On their own, they might not block all sensation, and a number of children still report some pain. The pain-relieving effects can be augmented if used in combination with other analgesic strategies such as distraction.
The analgesic cream costs too much, and parents wouldn't pay for it.	Parents are willing to pay for pain medication for their children, just as they are willing to pay for fever medication. They will follow their health care professional's advice on how to manage immunization pain.

(continued)

Table II (continued).

Myth	Truth
Analgasic creams take too long to work, and we don't have time in our clinic.	Parents can apply topical local anesthetic creams at home, before coming to the clinic appointment, so that no extra time is needed in the clinic. Educating parents up front about pain management can help offset longer procedure times because of improved child cooperation and reduced recovery time.
Kids come in with the analgesic cream in the wrong place.	Well-designed studies have proven that parents can apply topical local anesthetics correctly when given instructional pamphlets or prior demonstration.
Pain management can't work in large, school-based programs. We can't possibly be expected to do it in schools, where we vaccinate dozens of children, or more, at a time.	Pain management can be practiced in any setting, including schools. Information about pain management can be included with vaccine information that is sent home before the day of vaccination. Topical local anesthetics can be applied at school. Children can pick a distraction item from a toolkit during an injection (the toolkit contains many options), or they may want to use their own personal possession. In addition, performing injections in a private and comfortable room, separated from peers and free of visual or acoustic cues, can help minimize distress.
We can't give sugar water to infants. It interferes with breastfeeding.	Sugar water is being used as a pain treatment, not as a food. Infants are given a small volume that is similar to the volume of other drugs they get when treating other conditions, such as fever or infections.
Giving sugar water will damage infants' teeth.	The risk of tooth decay from the therapeutic use of sugar water to manage immunization pain is negligible due to its intermittent use. It is an inexpensive, easy, and effective way of managing pain during immunization.
Infants cannot breastfeed during immunization. They will choke.	Breastfeeding is a cost-free and effective pain management strategy. Choking has not been reported in infants that breastfed during immunization, and breastfeeding during immunization is considered safe.
If I breastfeed my baby during immunization, won't my baby associate me with pain?	The risk of a baby associating his/her mother with painful procedures is negligible due to the intermittent occurrence of immunization injections. Cuddling and hugging infants comforts them during procedures and should be done even if infants are not breastfed.

Health Care Professional Misperceptions About Pain Management

Considering that immunizations are primarily planned procedures, there is ample time and opportunity to plan for pain management. Vaccinators, however, currently hold a procedure-focused "get it over with" approach¹ to immunization that does not include planning for pain management. This approach does not address the child's main concern about pain.

Health care professionals harbor beliefs about the feasibility of analgesics that are consistent with a procedure-focused approach and contribute to sub-

optimal analgesic utilization.^{2,3} For instance, physicians report that topical anesthetics are not easily accommodated in practice because of the extra cost and time needed.² In addition, they express concerns about parental competence regarding correct application methods. These beliefs, however, contradict the results of well-designed studies that reported a willingness of parents to pay for analgesics (\$10–\$25) to reduce immunization pain,^{2,106} and parental competence regarding administration of topical local anesthetics.^{107,108} Application of topical local anesthetics by parents avoids delays at the doctor's office.

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Moreover, parents report that they would accommodate topical local anesthetics in their schedules.^{107,109}

Health care professionals also question the effectiveness of analgesics for managing pain during immunization in childhood (data on file). The benefits of topical local anesthetics are dismissed for a variety of reasons, including: (1) failure to acknowledge pain as an adverse effect of immunization that warrants therapy; (2) failure to discriminate responses of children who receive them versus those who do not because other situational factors that affect response are not accounted for; (3) misperceptions that they interfere with the effectiveness of vaccines⁴⁷; and (4) failure to value topical local anesthetics because they do not eliminate all pain.

The efficacy of topical local anesthetics has been discounted because they do not completely eliminate pain. In reality, analgesics do not have “all-or-none” effects. Effectiveness is increased by either increasing the dose of the analgesic or adding another analgesic. Within the context of immunization, strong evidence supports a clinically significant reduction in pain from topical local anesthetics, but not for elimination of pain (see the systematic review by Shah et al⁴⁷ in this supplement). Adjuvant strategies are required to reliably eliminate pain. Understandably, there may be reluctance on the part of health care professionals to tackle the issue of immunization pain management because it involves more than just applying topical local anesthetics.

Adopting a child-focused approach that recognizes and treats pain allows vaccinators to realize an alternative model of immunization that does not involve distressed children, parents, or health care professionals. If pain management is practiced with every injection, children will learn to manage pain, remain calm during procedures, and develop trusting relationships with health care professionals.⁴

Societal Attitudes About Pain

Parents may not ask for pain relief for their children, and physicians may not offer it, in part because of cultural attitudes toward pain.^{110,111} These include dismissiveness of children’s pain, relative diminutive importance given to pain and suffering (or quality of life) relative to overall health (or saving life), and the notion that pain is part of normal life and thus makes children better and stronger adults.¹¹² Past experiences, historical and religious expectations, and the

notion that there needs to be a trade-off between good health outcomes and quality of life also contribute to apparent apathy about management of pain in children. Parents may, in fact, worry about pain in their children but underrate that concern¹¹³ because of these attitudes and fears of negative repercussion for their children if they complain about pain, and then feel enormous guilt or betrayal for allowing their children to suffer.

Advocates of immunization, in particular, accept that rare and serious adverse effects are an unavoidable consequence for the few to the benefit of the many. They also accept implicitly that the pain of immunization, albeit unpleasant, is a cost of achieving widespread immunity and disease eradication.¹¹⁴ Fundamental changes are needed to alter the behavior of immunization providers and society’s views of iatrogenic pain in childhood. We need to acknowledge that iatrogenic pain in children may not simply be a short-lived experience that must be endured as part of medical care, but rather, a potential traumatic experience associated with long-term adverse sequelae that can be prevented as part of good medical care. The accumulating scientific evidence of harm from untreated pain in childhood, coupled with the availability of numerous effective analgesic strategies in modern society, permits us the opportunity to achieve both good health outcomes (ie, long-term protection against disease) and quality of life (ie, no pain) simultaneously for children undergoing immunization.

RECOMMENDATIONS FOR IMPROVEMENTS IN PAIN MANAGEMENT DURING IMMUNIZATION

Childhood immunization is a public health priority. Injection pain is the most frequent adverse effect of immunization, and undertreatment of that pain contributes to the development of alterations in future pain responses, anticipatory fear, and needle phobias.^{59–63} Furthermore, untreated pain leads to dissatisfaction with the immunization experience and contributes to low vaccine uptake.^{90–92,115,116}

Evidence-based analgesic strategies are available for managing pain, including: (1) physical interventions and injection techniques⁴⁵; (2) psychological interventions⁴⁶; and (3) pharmacologic and combined interventions.⁴⁷ Despite compelling evidence regarding the efficacy of these pain-relieving strategies, pain continues to be scarcely addressed within the context of immunization health policy. The fact that evidence-

based pain management strategies for childhood immunization exist and that they have not been widely adopted in clinical practice implies a failure of knowledge transfer (incorporating research evidence into clinical practice).^{104,117} We need buy-in¹¹⁸ for implementation of analgesic strategies among all the relevant stakeholders involved in immunization (eg, policy makers, practitioners, consumers) to optimally facilitate effective uptake of research knowledge into practice.

If all the stakeholders become invested partners in reducing pain, they can promote pain management for all aspects of the immunization enterprise, from vaccine development to vaccine delivery to public education. This could have a dramatic effect on current practices. For instance, pharmaceutical manufacturers and governmental agencies could begin to systematically investigate and promote vaccines and administration techniques that reduce pain in children. This includes concomitant administration of analgesics in vaccine trials. Health care professionals performing immunizations could be trained in the use of effective pain management strategies. Information pamphlets could be distributed to parents and children that describe preparation of children for procedures, adult behaviors that minimize distress, and analgesic strategies. In addition, a variety of age-appropriate cognitive-behavioral techniques (eg, bubbles, toys, books, games, music as distraction aids) and rewards (eg, stickers) could be made available for use during vaccine injections in settings where vaccine injections are performed.

If such initiatives were undertaken, parents, children, and health care professionals likely would report improved satisfaction with the immunization experience and a greater willingness to adhere to immunization schedules. Beyond immunization, these initiatives would promote satisfaction and trust in the health care system in general because of more positive experiences for children and their families.

Lack of adequate analgesia during needle-puncture procedures exposes children to needless suffering, poor immunization compliance, and long-term negative effects. Pain relief is a basic human right, and it is unethical to impose pain in children without making efforts to minimize it when effective and available treatments exist. Together we can make a difference.

CONCLUSIONS

Vaccine injections are the most common source of iatrogenic pain in childhood and a significant source

of distress for children undergoing the procedure, their parents, and the clinicians performing the procedure. Pain from vaccine injections has been identified as a direct cause of vaccine nonadherence. Untreated pain in childhood may lead to changes in future pain responsivity, including fear of needles. Although various pain-relieving interventions exist, they are not routinely used in clinical practice. Barriers to pain management include lack of knowledge about effective pain management techniques and attitudes, and misbeliefs about pain and its effects. Efforts to reduce the gap between research knowledge and clinical practice are needed to improve current practices.

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REFERENCES

1. Ulmer JB, Valley U, Rappuoli R. Vaccine manufacturing: Challenges and solutions. *Nature Biotechnol.* 2006;24:1377–1383.
2. Taddio A, Manley J, Potash L, et al. Routine immunization practices: Use of topical anesthetics and oral analgesics. *Pediatrics.* 2007;120:e637–e643.
3. Taddio A. Proceedings of the Workshop Conquering Pain: The Hidden Cost of Immunization. University of Toronto, Toronto, Ontario, Canada. March 20, 2008.
4. Guideline statement: Management of procedure-related pain in children and adolescents. *J Paediatr Child Health.* 2006;42(Suppl 1):S1–S29.
5. Batton DG, Barrington KJ, Wallman C, for the American Academy of Pediatrics Committee on Fetus and Newborn; American Academy of Pediatrics Section on Surgery; Canadian Paediatric Society Fetus and Newborn Committee. Prevention and management of pain in the neonate: An update [published correction appears in *Pediatrics.* 2007; 119:425]. *Pediatrics.* 2006;118:2231–2241.
6. Taylor EM, Boyer K, Campbell FA. Pain in hospitalized children: A prospective cross-sectional survey of pain prevalence, intensity, assessment and management in a Canadian pediatric teaching hospital. *Pain Res Manag.* 2008;13:25–32.
7. American Academy of Pediatrics. Committee on Psychosocial Aspects of Child and Family Health; Task Force on Pain in Infants, Children, and Adolescents. The assessment and management of acute pain in infants, children, and adolescents. *Pediatrics.* 2001;108:793–797.

Clinical Therapeutics

8. Schechter NL, Zempsky WT, Cohen LL, et al. Pain reduction during pediatric immunizations: Evidence-based review and recommendations. *Pediatrics*. 2007;119:e1184–e1198.
9. World Health Organization. Vaccines and Biologicals. <http://www.who.int/vaccines-documents/docs/PDF00/www505.pdf>. Accessed January 9, 2009.
10. Giudice EL, Campbell JD. Needle-free vaccine delivery. *Adv Drug Deliv Rev*. 2006;58:68–89.
11. Public Health Agency of Canada. Immunization schedules: Recommendations from the National Advisory Committee on Immunization (NACI). <http://www.phac-aspc.gc.ca/im/is-cv/index-eng.php#a>. Accessed January 9, 2009.
12. Middleton DB, Zimmerman RK, Mitchell KB. Vaccine schedules and procedures, 2007. *J Fam Pract*. 2007;56(Suppl Vaccines):S47–S60, C4–C8.
13. Rappuoli R. Current developments in new vaccines for adolescents. *Biologicals*. 1997;25:159–163.
14. Wilson K. Protecting vaccine programs and the public. *CMAJ*. 2007;176:1681, 1683.
15. Woodin KA, Rodewald LE, Humiston SG, et al. Physician and parent opinions. Are children becoming pincushions from immunizations? *Arch Pediatr Adolesc Med*. 1995;149:845–849.
16. Zareba G. A new combination vaccine for measles, mumps, rubella and varicella. *Drugs Today (Barc)*. 2006;42:321–329.
17. Brennan F, Carr DB, Cousins M. Pain management: A fundamental human right. *Anesth Analg*. 2007;105:205–221.
18. Anand KJ, Aranda JV, Berde CB, et al. Summary proceedings from the neonatal pain-control group. *Pediatrics*. 2006;117:S9–S22.
19. Southall DP, Burr S, Smith RD, et al. The Child-Friendly Healthcare Initiative (CFHI): Healthcare provision in accordance with the UN Convention on the Rights of the Child. Child Advocacy International. Department of Child and Adolescent Health and Development of the World Health Organization (WHO). Royal College of Nursing (UK). Royal College of Paediatrics and Child Health (UK). United Nations Children's Fund (UNICEF). *Pediatrics*. 2000;106:1054–1064.
20. Ellis JA, Sharp D, Newhook K, Cohen J. Selling comfort: A survey of interventions for needle procedures in a pediatric hospital. *Pain Manag Nurs*. 2004;5:144–152.
21. Hodges FM, Svoboda JS, Van Howe RS. Prophylactic interventions on children: Balancing human rights with public health. *J Med Ethics*. 2002;28:10–16.
22. Benin AL, Wu AC, Holmboe E, Shapiro ED. Communication about vaccines for teenagers: A qualitative study with teens and their parents. *PAS*. 2005;57:1803. Abstract.
23. Pain terms: A list with definitions and notes on usage. Recommended by the IASP Subcommittee on Taxonomy. *Pain*. 1979;6:249.
24. Young KD. Pediatric procedural pain. *Ann Emerg Med*. 2005;45:160–171.
25. Fitzgerald M, Walker SM. Infant pain management: A developmental neurobiological approach. *Nat Clin Pract Neurol*. 2009;5:35–50.
26. Schneider EM, LoBiondo-Wood G. Perceptions of procedural pain: Parents, nurses, and children. *Child Health Care*. 1992;21:157–162.
27. Goodenough B, Perrott DA, van Dongen K, et al. Children's response to vaccine fluid injection versus needle puncture pain during routine immunization. *Amb Child Health*. 2008;6:91–100.
28. Hart D, Bossert E. Self-reported fears of hospitalized school-age children. *J Pediatr Nurs*. 1994;9:83–90.
29. Broome ME, Hellier AP. School-age children's fears of medical experiences. *Issues Compr Pediatr Nurs*. 1987;10:77–86.
30. Megel ME, Hesser R, Matthews K. Parents' assistance to children having immunizations. *Issues Compr Pediatr Nurs*. 2002;25:151–165.
31. Lewis N. The needle is like an animal: How children view injections. *Child Today*. 1978;7:18–21.
32. Reis EC, Jacobson RM, Tarbell S, Weniger BG. Taking the sting out of shots: Control of vaccination-associated pain and adverse reactions. *Pediatr Ann*. 1998;27:375–386.
33. Chapman HR, Kirby-Turner NC. Dental fear in children—a proposed model. *Br Dent J*. 1999;187:408–412.
34. Kuttner L. Management of young children's acute pain and anxiety during invasive medical procedures. *Pediatrician*. 1989;16:39–44.
35. Jacobson RM, Swan A, Adegbenro A, et al, for the Vaccine Research Group. Making vaccines more acceptable—methods to prevent and minimize pain and other common adverse events associated with vaccines. *Vaccine*. 2001;19:2418–2427.
36. Rocha EM, Prkachin KM, Beaumont SL, et al. Pain reactivity and somatization in kindergarten-age children. *J Pediatr Psychol*. 2003;28:47–57.
37. Bustos T, Jaaniste T, Salmon K, Champion GD. Evaluation of a brief parent intervention teaching coping-promoting behavior for the infant immunization context: A randomized controlled trial. *Behav Modif*. 2008;32:450–467.
38. Eland JM. Minimizing pain associated with prekindergarten intramuscular injections. *Issues Compr Pediatr Nurs*. 1981;5:361–372.
39. Ipp M, Taddio A, Goldbach M, et al. Effects of age, gender and holding on pain response during infant immunization. *Can J Clin Pharmacol*. 2004;11:e2–e7.
40. Sparks L. Taking the “ouch” out of injections for children. Using distraction to decrease pain. *MCN Am J Matern Child Nurs*. 2001;26:72–78.
41. Megel ME, Houser CW, Gleaves LS. Children's responses to immunizations: Lullabies as a distraction. *Issues Compr Pediatr Nurs*. 1998;21:129–145.

42. Broome ME, Endsley RC. Group preparation of young children for painful stimulus. *West J Nurs Res.* 1987;9:484-502.
43. Cassidy KL, Reid GJ, McGrath PJ, et al. Watch needle, watch TV: Audio-visual distraction in preschool immunization. *Pain Med.* 2002;3:108-118.
44. Unruh AM. Gender variations in clinical pain experience. *Pain.* 1996; 65:123-167.
45. Taddio A, Ilersich AL, Ipp M, et al. Physical interventions and injection techniques for reducing injection pain during routine childhood immunizations: Systematic review of randomized controlled trials and quasi-randomized controlled trials. *Clin Ther.* 2009;31(Suppl B):XX-XX.
46. Chambers CT, Taddio A, Uman LS, McMurty CM, for the HELPinKIDS Team. Psychological interventions for reducing pain and distress during routine childhood immunizations: A systematic review. *Clin Ther.* 2009;31(Suppl B):S77-S103.
47. Shah V, Taddio A, Rieder MJ, for the HELPinKIDS Team. Effectiveness and tolerability of pharmacologic and combined interventions for reducing injection pain during routine childhood immunizations: Systematic review and meta-analysis. *Clin Ther.* 2009;31(Suppl B): S104-S151.
48. Blount RL, Bunke V, Cohen LL, Forbes CJ. The Child-Adult Medical Procedure Interaction Scale-Short Form (CAMPIS-SF): Validation of a rating scale for children's and adults' behaviors during painful medical procedures. *J Pain Symptom Manage.* 2001;22:591-599.
49. Sweet SD, McGrath PJ. Relative importance of mothers' versus medical staffs' behavior in the prediction of infant immunization pain behavior. *J Pediatr Psychol.* 1998;23:249-256.
50. Cohen LL, Bernard RS, Greco LA, McClellan CB. A child-focused intervention for coping with procedural pain: Are parent and nurse coaches necessary? *J Pediatr Psychol.* 2002;27:749-757.
51. Gonzalez JC, Routh DK, Armstrong FD. Effects of maternal distraction versus reassurance on children's reactions to injections. *J Pediatr Psychol.* 1993;18:593-604.
52. Cohen LL. Behavioral approaches to anxiety and pain management for pediatric venous access. *Pediatrics.* 2008;122(Suppl 3):S134-S139.
53. Frank NC, Blount RL, Smith AJ, et al. Parent and staff behavior, previous child medical experience, and maternal anxiety as they relate to child procedural distress and coping. *J Pediatr Psychol.* 1995;20:277-289.
54. Ross DM, Ross SA. Childhood pain: The school-aged child's viewpoint. *Pain.* 1984;20:179-191.
55. Gonzalez JC, Routh DK, Saab P, et al. Effects of parent presence on children's reactions to injections: Behavioral, physiological, and subjective aspects. *J Pediatr Psychol.* 1989;14:449-462.
56. Stephens BK, Barkey ME, Hall HR. Techniques to comfort children during stressful procedures. *Adv Mind Body Med.* 1999;15:49-60.
57. Madlon-Kay DJ, Harper PG. Too many shots? Parent, nurse, and physician attitudes toward multiple simultaneous childhood vaccinations. *Arch Fam Med.* 1994;3:610-613.
58. Lieu TA, Black SB, Ray GT, et al. The hidden costs of infant vaccination. *Vaccine.* 2000;19:33-41.
59. Taddio A. Effects of early pain experience (the human literature). In: McGrath PJ, Finley GA, eds. *Chronic and Recurrent Pain in Children and Adolescents.* Seattle, Wash: IASP Press; 1999:57-74.
60. Taddio A, Katz J. The effects of early pain experience in neonates on pain responses in infancy and childhood. *Pediatr Drugs.* 2005;7:245-257.
61. Weisman SJ, Bernstein B, Schechter NL. Consequences of inadequate analgesia during painful procedures in children. *Arch Pediatr Adolesc Med.* 1998;152:147-149.
62. O'Brien L, Kemp S, Dupuis L, Taddio A. Pharmacologic management of painful oncology procedures in pediatric patients. *Am J Cancer.* 2003;2:403-426.
63. Hamilton JG. Needle phobia: A neglected diagnosis. *J Fam Pract.* 1995; 41:169-175.
64. *Diagnostic and Statistical Manual of Mental Disorders.* 4th ed. Arlington, Va: American Psychiatric Association; 1994.
65. Chen E, Zeltzer LK, Craske MG, Katz ER. Children's memories for painful cancer treatment procedures: Implications for distress. *Child Dev.* 2000;71:933-947.
66. Cohen LL, Blount RL, Cohen RJ, et al. Children's expectations and memories of acute distress: Short- and long-term efficacy of pain management interventions. *J Pediatr Psychol.* 2001;26:367-374.
67. Taddio A, Goldbach M, Ipp M, et al. Effect of neonatal circumcision on pain responses during vaccination in boys. *Lancet.* 1995;345:291-292.
68. Taddio A, Katz J, Ilersich AL, Koren G. Neonatal circumcision on pain response during subsequent routine vaccination. *Lancet.* 1997;349:599-603.
69. Taddio A, Shah V, Gilbert-MacLeod C, Katz J. Conditioning and hyperalgesia in newborns exposed to repeated heel lances. *JAMA.* 2002; 288:857-861.
70. Taddio A, Soin H, Schuh S, et al. Liposomal lidocaine to improve procedural success rates and reduce procedural pain among children: A randomized controlled trial. *CMAJ.* 2005;172:1691-1695.
71. Baxter A, Ewing PH, Manworren RCB, et al. EMLA application in triage improves venipuncture success. *PAS.* 2005;57:2902. Abstract.
72. Pate JT, Blount RL, Cohen LL, Smith AJ. Childhood medical experiences

Clinical Therapeutics

- and temperament as predictors of adult functioning in medical situations. *Children's Health Care*. 1996; 25:281-298.
73. Page AC. Blood-injury-injection fears in medical practice. *Med J Aust*. 1996;164:189.
 74. Searing K, Baukus M, Stark MA, et al. Needle phobia during pregnancy. *J Obstet Gynecol Neonatal Nurs*. 2006;35:592-598.
 75. Harrington M, Sweeney MR, Baile K, et al. What would encourage blood donation in Ireland? *Vox Sang*. 2007;92:361-367.
 76. Oswalt RM, Napoliello M. Motivations of blood donors and nondonors. *J Appl Psychol*. 1974;59:122-124.
 77. McConnell EM, Harper R, Campbell M, Nelson JK. Achieving optimal diabetic control in adolescence: The continuing enigma. *Diabetes Metab Res Rev*. 2001;17:67-74.
 78. Enkling N, Marwinski G, Johren P. Dental anxiety in a representative sample of residents of a large German city. *Clin Oral Investig*. 2006;10: 84-91.
 79. Heimberger T, Chang HG, Shaikh M, et al. Knowledge and attitudes of healthcare workers about influenza: Why are they not getting vaccinated? *Infect Control Hosp Epidemiol*. 1995;16:412-415.
 80. Nir Y, Paz A, Sabo E, Potasman I. Fear of injections in young adults: Prevalence and associations. *Am J Trop Med Hyg*. 2003;68:341-344.
 81. Sendi P, Locher R, Bucheli B, Battegay M. Intranasal influenza vaccine in a working population. *Clin Infect Dis*. 2004;38:974-980.
 82. Tilburt JC, Mueller PS, Ottenberg AL, et al. Facing the challenges of influenza in healthcare settings: The ethical rationale for mandatory seasonal influenza vaccination and its implications for future pandemics. *Vaccine*. 2008;26(Suppl 4):D27-D30.
 83. Barker L, Luman E, Zhao Z, et al, for the Centers for Disease Control and Prevention (CDC). National, state, and urban area vaccination coverage levels among children aged 19-35 months—United States, 2001. *MMWR Morb Mortal Wkly Rep*. 2002;51:664-666.
 84. Meyerhoff AS, Jacobs RJ. Do “too many shots due” lead to missed vaccination opportunities? Does it matter? *PAS*. 2004;1188. Abstract.
 85. Mills EJ, Montori VM, Ross CP, et al. Systematically reviewing qualitative studies complements survey design: An exploratory study of barriers to paediatric immunisations. *J Clin Epidemiol*. 2005;58:1101-1108.
 86. Yawn BP, Xia Z, Edmonson L, et al. Barriers to immunization in a relatively affluent community. *J Am Board Fam Pract*. 2000;13:325-332.
 87. Guerra FA. Delays in immunization have potentially serious health consequences. *Paediatr Drugs*. 2007;9: 143-148.
 88. Abbotts B, Osborn LM. Immunization status and reasons for immunization delay among children using public health immunization clinics. *Am J Dis Child*. 1993;147:965-968.
 89. Samad L, Butler N, Peckham C, Bedford H, for the Millennium Cohort Study Child Health Group. Incomplete immunisation uptake in infancy: Maternal reasons. *Vaccine*. 2006;24:6823-6829.
 90. Harrington PM, Woodman C, Shannon WF. Vaccine, yes; injection, no: Maternal responses to the introduction of Haemophilus influenzae type b (Hib) vaccine. *Br J Gen Pract*. 1999;49:901-902.
 91. Harrington PM, Woodman C, Shannon WF. Low immunisation uptake: Is the process the problem? *J Epidemiol Community Health*. 2000; 54:394-400.
 92. Askew GL, Finelli L, Lutz J, et al. Beliefs and practices regarding childhood vaccination among urban pediatric providers in New Jersey. *Pediatrics*. 1995;96:889-892.
 93. Roberts RJ, Sandifer QD, Evans MR, et al. Reasons for non-uptake of measles, mumps, and rubella catch up immunisation in a measles epidemic and side effects of the vaccine. *BMJ*. 1995;310:1629-1632.
 94. The measles epidemic. The problems, barriers, and recommendations. The National Vaccine Advisory Committee. *JAMA*. 1991;266: 1547-1552.
 95. Ipp M, Taddio A, Sam J, et al. Vaccine-related pain: Randomised controlled trial of two injection techniques. *Arch Dis Child*. 2007; 92:1105-1108.
 96. Broome ME, Endsley RC. Maternal presence, childrearing practices, and children's response to an injection. *Res Nurs Health*. 1989;12: 229-235.
 97. McGrath PJ, McAlpine L. Psychologic perspectives on pediatric pain. *J Pediatr*. 1993;122:S2-S8.
 98. Kleinknecht RA. Acquisition of blood, injury, and needle fears and phobias. *Behav Res Ther*. 1994;32: 817-823.
 99. Ost LG. Age of onset in different phobias. *J Abnorm Psychol*. 1987;96: 223-229.
 100. Melhuish S, Payne H. Nurses' attitudes to pain management during routine venepuncture in young children. *Paediatr Nurs*. 2006;18: 20-23.
 101. Lebovits AH, Florence I, Bathina R, et al. Pain knowledge and attitudes of healthcare providers: Practice characteristic differences. *Clin J Pain*. 1997;13:237-243.
 102. Parvez E. Mothers' beliefs about analgesia during childhood immunization: A qualitative study. MSc Thesis, University of Toronto, 2008.
 103. Hatfield L, Messner ER, Lingg K. Evidence-based strategies for the pharmacological management of pediatric pain during minor procedures in the emergency department. *Top Emerg Med*. 2006;28: 129-137.
 104. Schechter NL. Treatment of acute and chronic pain in the outpatient

- setting. In: Finley GA, McGrath PJ, Chambers CT, eds. *Bringing Pain Relief to Children: Treatment Approaches*. Totowa, NJ: Humana Press; 2006:31–58.
105. Broome ME. The child in pain: A model for assessment and intervention. *Crit Care Quarter*. 1985;8:47–55.
 106. Meyerhoff AS, Weniger BG, Jacobs RJ. Economic value to parents of reducing the pain and emotional distress of childhood vaccine injections. *Pediatr Infect Dis J*. 2001;20 (Suppl):S57–S62.
 107. Taddio A, Nulman I, Goldbach M, et al. Use of lidocaine-prilocaine cream for vaccination pain in infants. *J Pediatr*. 1994;124:643–648.
 108. Koh JL, Fanurik D, Stoner PD, et al. Efficacy of parental application of eutectic mixture of local anesthetics for intravenous insertion. *Pediatrics*. 1999;103:e79.
 109. Hansen BW, Sørensen PV. The EMLA cream versus placebo in MMR vaccination of older children in general practice [in Danish]. *Ugeskr Laeger*. 1993;155:2263–2265.
 110. Lovering S. Cultural attitudes and beliefs about pain. *J Transcult Nurs*. 2006;17:389–395.
 111. Lewis T, DiLillo D, Peterson L. Parental beliefs regarding developmental benefits of childhood injuries. *Am J Health Behav*. 2004;28 (Suppl 1):S61–S68.
 112. Craig KD, Lilley CM, Gilbert CA. Social barriers to optimal pain management in infants and children. *Clin J Pain*. 1996;12:232–242.
 113. Arvidsson SB, Ekroth RH, Hansby AM, et al. Painless venipuncture. A clinical trial of iontophoresis of lidocaine for venipuncture in blood donors. *Acta Anaesthesiol Scand*. 1984;28:209–210.
 114. Petousis-Harris H. Vaccine injection technique and reactogenicity—evidence for practice. *Vaccine*. 2008; 26:6299–6304.
 115. Niederhauser VP, Markowitz M. Barriers to immunizations: Multi-ethnic parents of under- and immunized children speak. *J Am Acad Nurse Pract*. 2007;19:15–23.
 116. Thomas M, Kohli V, King D. Barriers to childhood immunization: Findings from a needs assessment study. *Home Health Care Serv Q*. 2004;23:19–39.
 117. Azocar F, Cuffel B, Goldman W, McCarter L. The impact of evidence-based guideline dissemination for the assessment and treatment of major depression in a managed behavioral health care organization. *J Behav Health Serv Res*. 2003; 30:109–118.
 118. Barwick MA, Boydell KM, Stasiulis E, et al. Knowledge transfer and implementation of evidence-based practices in children's mental health. Ontario, Canada: Children's Mental Health Ontario; 2005. <http://resources.cpha.ca/CCIAP/data/700e.pdf>. Accessed January 25, 2009.

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