

Adverse Effects of Pain on the Nervous Systems of Newborns and Young Children: A Review of the Literature



Anita Mitchell, Barbara J. Boss

Abstract: There are immediate and long-lasting harmful consequences to the nervous system when infants experience severe or repetitive pain. These effects are especially significant in preterm infants, who are vulnerable to neurological damage during this critical time of neurodevelopment. Painful experiences may cause structural and physiological changes within the nervous system. Repeated painful procedures may result in decreased pain thresholds and hypersensitivity to pain. Immediate harmful effects of pain include physiologic instability and increased incidence of serious complications such as intraventricular hemorrhage. Painful stressors may lead to sleep disturbances, feeding problems, and inability to self-regulate. Long-term effects of pain may include altered pain perception, chronic pain syndromes, and somatic complaints. Repetitive pain in the preterm infant may be associated with attention deficit disorders, learning disorders, and behavioral problems in later childhood. Nursing involvement with pain management is crucial to achieve positive health outcomes for high-risk infants and older children and adults who have experienced repetitive or severe pain as infants.

The management of infant pain is important not only to provide comfort but also to prevent both immediate and long-lasting consequences that are harmful to the person's overall health. Consequences may be most severe for persons who are born prematurely and are therefore more vulnerable to nervous system damage. The third trimester of gestation is a critical time for organization of the nervous system, and this stage corresponds to the developmental stage in which preterm infants may be undergoing repetitive painful procedures in the neonatal intensive care unit (NICU). Repeated painful experiences during this period of neurological

Questions or comments about this article may be directed to: Anita Mitchell, MSN RN, University of Louisiana at Monroe, College of Nursing, 700 University Avenue, Monroe, LA 71209. She is an associate professor of nursing at the University of Louisiana at Monroe and a doctoral candidate at the University of Mississippi School of Nursing.

Barbara J. Boss, PhD RN CFNP CANP, is a professor of nursing at the University of Mississippi Medical Center, Jackson, MS.

Copyright ©2002 American Association of Neuroscience Nurses 0047-2606/02/3405/00228\$5.00

development may cause changes in pain thresholds and in the perception and tolerance of pain throughout the person's lifetime. A review of the definitions of common terms associated with pain is presented in Fig 1. This paper reviews the physiological, psychosocial, and developmental consequences of severe or repetitive pain experienced by newborns and young children.

Pain During Early Stages of Development

Preterm infants not only are neurologically capable of perceiving pain but also are more sensitive to pain than older infants or adults. There are several reasons for this increased sensitivity: (a) the number of nociceptive nerve fibers in the skin of the neonate is similar to and possibly even greater than the number found in the adult; (b) incomplete myelination of pain fibers in the preterm infant does not hinder pain transmission, and the shorter distances of the immature pain pathways offset any slowing of velocity that may be caused by lack of myelination; (c) pain neurotransmitters are found in abundance and are functional in the fetus; and (d) there are large receptive fields of neurons in the somatosensory cortex (Anand, 1998; Anand, Phil, & Carr, 1989; Perreault, et al., 1997). Fig 2 depicts the ascending pain pathway.

An important additional reason for the increased sensitivity to pain in the preterm infant is that pain transmission is well developed, but modulatory mechanisms are immature, therefore altering the infant's ability to cope with incoming pain impulses (Anand & Scalzo, 2000). There is delayed maturation of descending inhibitory pathways from supraspinal areas, delayed maturation of interneurons in the substantia gelatinosa, and a possible deficiency of inhibitory neurotransmitters. Fig 3 depicts the pain modulatory pathways. Excitatory pain neurotransmitters are plentiful by birth, but may not be balanced by an adequate supply of descending inhibitory neurotransmitters. Because of decreased pain modulation, there is increased excitability in the dorsal horn of the spinal cord and increased sensitivity to pain (Fitzgerald, 1995; Anand, 2000).

The cutaneous flexor reflex in response to painful stimuli is a sensitive method for assessing pain thresholds. To test this reflex, a noxious stimulus is applied to the sole of the foot, and the threshold for flexion

Pain threshold. The point at which the transmission of a pain stimulus begins. If the pain threshold is lowered, a weaker stimulus may be able to trigger pain transmission.

Pain perception. The point at which a person becomes aware of the pain. Awareness of pain occurs in the central nervous system (thalamus and cerebral cortex).

Pain tolerance. The degree of pain that a person can bear. Pain tolerance is influenced by psychological, social, and cultural factors.

Fig 1. Definitions of common terms used to describe pain

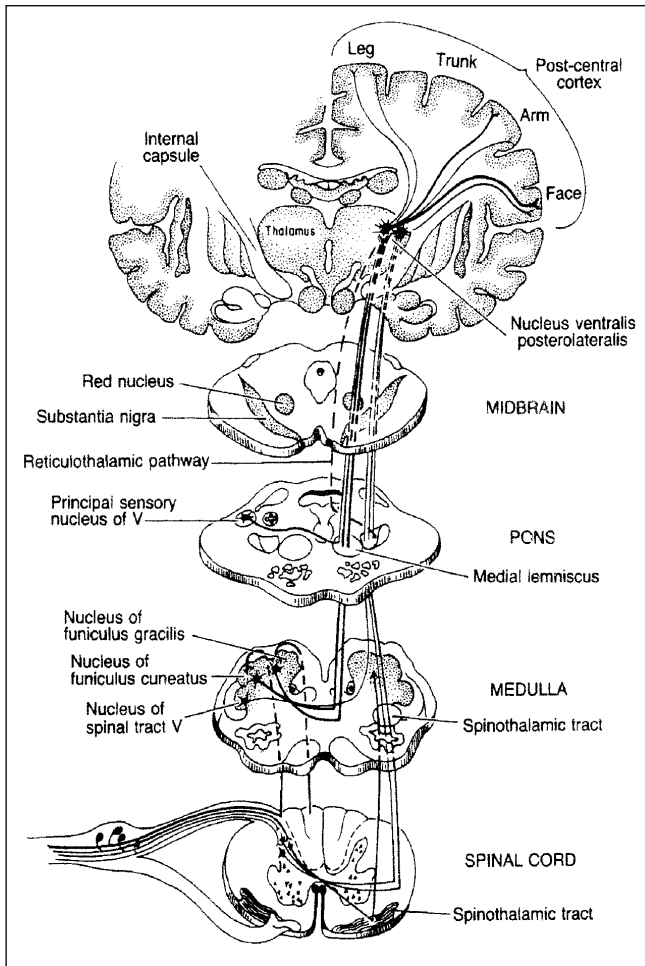


Fig 2. Ascending pain pathway. Axons of the secondary neurons that subserve pain sensation originate in laminae I, II, V, VII, and VIII of the spinal gray matter. The principal bundle decussates in the anterior spinal commissure and ascends in the anterolateral fasciculus to the brainstem and thalamic structures. [Note. From Principles of Neurology (p. 131), by R.D. Adams, M. Victor, and A.H. Ropper, 1997, New York: McGraw Hill. Copyright 1997 by McGraw Hill Companies. Reprinted with permission.]

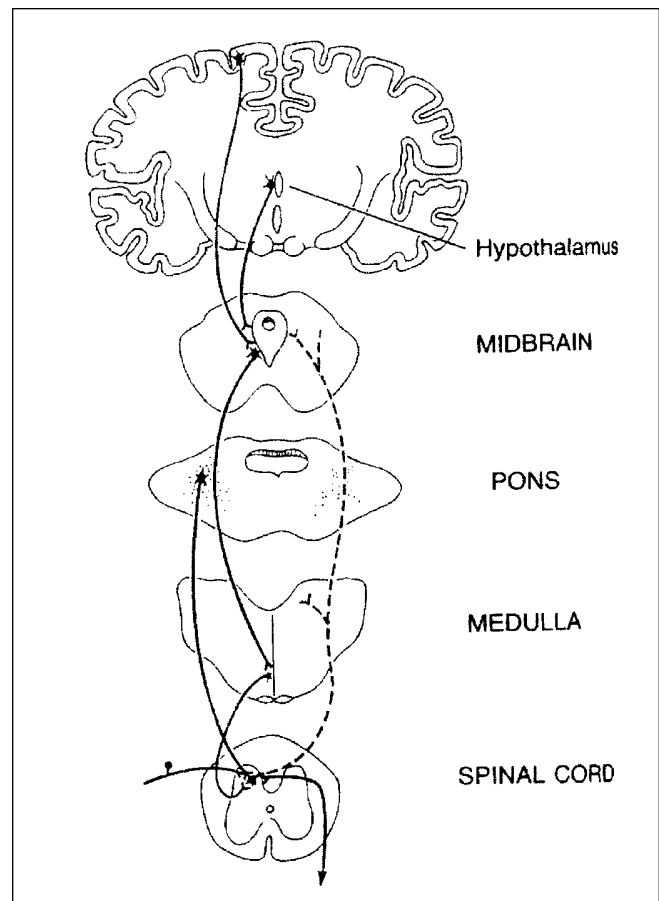


Fig 3. Pain-modulating pathways in the CNS. Impulses originating in the frontal cortex and hypothalamus project to cells in the periaqueductal gray matter of the midbrain, which control dorsal horn pain transmission cells via cells in the rostroventral medulla. [Note. From Principles of Neurology (p. 136), by R.D. Adams, M. Victor, and A.H. Ropper, 1997, New York: McGraw Hill. Copyright 1997 by McGraw Hill Companies. Reprinted with permission.]

withdrawal of the leg is measured. Preterm infants have a very low pain threshold for application of a von Frey hair to the plantar surface of the foot. A von Frey hair is a nylon monofilament that is stiff enough to apply force to the skin. The pain threshold for the withdrawal flexor reflex increases with postconceptional age (Andrews & Fitzgerald, 1994; Fitzgerald, Shaw, & MacIntosh, 1988).

Immediate Outcomes of Acute Pain in the Neonate

The need to relieve pain in the preterm infant is significant because of the harmful effects of pain on the infant's general outcome (American Academy of Pediatrics, 2000). Energy resources that the infant needs for growth and healing are used to cope with the pain. The

overall pain response results in increased heart and respiratory rates, increased blood pressure, decreased oxygen saturation, and a release of adrenal stress hormones (Anand, 1998; Anand, Phil, & Hickey, 1987, 1992; Anand, Sippell, & Aynsley-Green, 1987; Bozzette, 1993; Gonsalves & Mercer, 1993; Johnston & Stevens, 1990; Stevens & Johnston, 1994).

The synactive theory of development (Als, 1982) described subsystems within the infant that become unbalanced and unstable when the infant is exposed to stressors such as pain. Instability within the autonomic subsystem is reflected in vital sign and oxygen saturation changes. The motor subsystem becomes unstable when the infant moves limbs in a disorganized way in response to the pain. Disturbances within the sleep/wake state subsystem lead to disturbed sleep cycles. There are also feeding problems and even altered maternal/infant interaction patterns. Pain relief helps the infant regulate the subsystems and return to a balanced state.

The experiences of the newborn infant control the development of synapses.

The disturbed sleep cycle resulting from pain can have both immediate and long-term consequences. The neurological systems that control attention, emotion, and sleep/wake states in the brain interact. Therefore, early pain and stress resulting in repeated disruption of the sleep cycle can affect the child's neurodevelopment and may put the child at risk for attention deficits and emotional disturbances (Grunau, 2000).

Responses to pain cause increased intracranial pressure and diaphragmatic splinting with secondary increases in intracranial blood volume. These changes lead to an increased incidence of intraventricular hemorrhage (IVH) and periventricular leukomalacia (PVL) in the preterm infant and subsequent neurological injury (Anand, 1998).

In a study involving 124 preterm infants with gestational ages 32–34 weeks, researchers analyzed heart rate, oxygen saturation, and intracranial pressure during heel stick and heel squeeze (Stevens & Johnston, 1994). Significant increases in heart rate and intracranial pressure and significant decreases in oxygen saturation were found between baseline and heel-stick phases and between baseline and heel-squeeze phases. The group of physiological variables examined together showed a significant multivariate main effect of phase ($F = 16.19, p < .0001$).

Significant harmful responses to pain were demonstrated in a randomized trial with neonates during cardiac surgery. Fifteen neonates received lighter anesthesia with halothane, ketamine, and repeated doses of morphine during surgery. These 15 infants then received intermittent doses of morphine and diazepam for

analgesia and sedation following surgery. Thirty neonates received deeper anesthesia with sufentanil during surgery and continuous infusions of fentanyl for 24 hours following surgery. Infants who received the deeper anesthesia and continuous postoperative fentanyl demonstrated a significantly decreased stress response as measured by decreased epinephrine, norepinephrine, glucagon, beta-endorphin, aldosterone, and cortisol levels. Those infants who received more pain medication also had a lower incidence of sepsis ($p = .03$), metabolic acidosis ($p < .01$), disseminated intravascular coagulation ($p = .03$), and death ($p < .01$). Infants receiving a lighter anesthesia demonstrated more severe hyperglycemia and lactic acidemia during surgery, indicating more intense physiologic stress responses ($p < .025$, Anand et al., 1992).

Painful Experiences Cause Structural and Physiological Changes

All neurologic structures and neurotransmitters required for the transmission and interpretation of pain impulses are present at birth. However, pain pathways continue to develop during infancy and childhood. Thus, painful experiences shape the development of the overall pain system and may "determine the final architecture of the adult brain" (Anand, Phil, & Carr, 1989, p. 800).

Around the time of birth, there is a "critical window of neonatal brain development" (Anand & Scalzo, 2000, p. 75) and a period of rapid brain growth. Plasticity of the brain, meaning that the development of pain and other pathways is ongoing, makes the brain of the newborn infant more vulnerable to harmful effects of pain.

The experiences of the newborn infant control the development of synapses. Normally, the number of synapses in the brain of the neonate is "pruned back" because there is an overproduction of synapses at the time of birth. Daily experiences of the infant determine which synapses are retained and which are pruned. Repetitive painful experiences may result in the retention of a high number of synapses that would otherwise be deleted or in the formation of abnormal connections. The result of these abnormal connections and higher numbers of synapses may be increased sensitivity to pain (Anand, Grunau, & Oberlander, 1997; Grunau, 2000).

There is a peak density of N-methyl-d-aspartate (NMDA) receptors around the dorsal horn of the spinal cord and in supraspinal areas in the newborn infant, and an increased magnitude of calcium currents resulting from NMDA receptor activity. Prolonged firing of C-fiber nociceptors releases the neurotransmitter glutamate, which acts on NMDA receptors in the spinal cord. The young brain is susceptible to NMDA-induced excitotoxicity. Anand and Scalzo (2000) hypothesized that repeated painful procedures in the premature infant may cause excessive activation of excitatory amino acids and

NMDA receptors, leading to damage to the developing neurons. Effects of damage to developing neurons may include a decreased pain threshold, or "windup" phenomenon, and central sensitization. Central sensitization means that the spinal cord neurons become more responsive to all input. Recent studies suggest that NMDA-mediated mechanisms may lead to a susceptibility to chronic pain states in persons who have experienced repeated painful experiences (Chiang, Hu, & Sessle, 1997; McCormack, Prather, & Chapleo, 1998).

Fitzgerald (1995) stated that repeated painful stimuli in the neonate results in hyperinnervation, with sprouting of both A and C pain fibers. This sprouting is partially due to an increased supply of nerve growth factor, which is more available in newborns than in older infants or adults. A study with neonatal rats involving skin wounds in the foot demonstrated long-lasting sprouting of sensory nerve terminals with resulting hyperinnervation and decreased pain thresholds even after the wounds healed (Reynolds & Fitzgerald, 1995). The authors attributed this phenomenon of hypersensitivity to the plasticity of the nervous system in the very young infant and to the effects of pain on sensory fibers during a critical phase of neurological development. Prolonged hypersensitivity even decreases the pain threshold to the point that the preterm infant may perceive normally non-noxious stimuli such as routine handling as painful (Evans, Vogelpohl, Bourguignon, & Morcott, 1997).

A pain threshold study with preterm infants who ranged from 27 to 32 weeks at birth demonstrated that flexion reflex thresholds on the side of the heel undergoing heel lances were half that of the thresholds on the side of the heel not used for heel lances. Subsequent treatment of the lanced heel with EMLA cream (lidocaine 2.5% and prilocaine 2.5%) every 4 hours for 2 weeks reversed the hypersensitivity. Significant differences ($p < .01$) were found between flexion reflex thresholds in infants whose heels were treated with EMLA and those treated with a placebo cream (Fitzgerald, Millard, & McIntosh, 1989).

Recent research indicates that excitotoxic chemicals released during repetitive painful events experienced by neonatal rats may result in damage to the developing central nervous system that affects not only pain thresholds but also long-term behaviors. Anand, Coskun, Thrivikraman, Nemeroff, and Plotsky (1999) carried out research on neonatal rat pups, attempting to simulate conditions in the NICU, where preterm infants may be receiving repetitive heel sticks. The researchers estimated that the neurological maturity of a neonatal rat approximates that of a 24-week preterm infant. They administered repetitive paw manipulations to rat pups for 7 days. Three experimental groups of rat pups experienced insertion of a 25-gauge needle into the paw once hourly,

twice hourly, or four times hourly. Three control groups experienced touching of the paw with a cotton swab at the same times and frequency as the experimental groups. After the NICU simulation, pain thresholds were measured by noting time to withdrawal following exposure to a hot plate. Rats that had received the four noxious paw sticks every hour had significantly decreased pain thresholds ($p < .05$ at age 16 days, $p < .005$ at age 22 days). Excitotoxic damage may stimulate inappropriate innervation in the dorsal horn with a corresponding decrease in pain threshold. Rats who received four noxious paw sticks every hour also demonstrated an increased preference for alcohol as adults ($p = .004$) and increased behavioral disorders such as anxiety and defensive withdrawal behavior. The reason for increased alcohol preference is unknown, but may involve alterations in dopaminergic and serotonergic pathways, nor-epinephrine release, and function of opioid receptors (Anand et al., 1999).

There is evidence that painful procedures such as circumcisions during the neonatal period may alter pain thresholds later in infancy.

The combination of pain and maternal separation in neonatal rats activates the hypothalamic-pituitary-adrenal (HPA) axis in neonatal rats. Anand et al., (1999) stated that more attention needs to be given to supraspinal mechanisms that influence long-term effects of pain. Increased activation of the HPA axis may lead to long-term or permanent changes in behavioral and endocrine responses to stress. For example, HPA activation may result in increased glucocorticoid response and impaired feedback control mechanisms in the hypothalamus (Anand, Grunau, & Oberlander, 1997).

Altered Pain Thresholds in Later Infancy

There is evidence that painful procedures such as circumcisions during the neonatal period may alter pain thresholds later in infancy. In a retrospective study, the pain responses of 4- to 6-month-old male infants receiving immunizations were examined on the basis of whether the infant had been circumcised as a neonate. Pain responses during DPT immunizations were scored by a pediatrician and an observer by using a visual analogue scale (VAS). Median VAS scores in infants who had been circumcised were significantly higher (40 mm) than those in infants who had not been circumcised (26 mm, $p = .03$). In addition to the VAS scores, a coder who was blind to the infants' history and to the treatment taking place reviewed videotapes of the immunizations and scored behavioral pain responses based on facial activity, cry, and body movements. There was a trend toward less crying in infants who had not been circumcised, but no

significant difference in the behavioral pain score ($p = 0.2$, Taddio, Goldbach, Ipp, Stevens, & Koren, 1995).

A second part of this study focused on 18 infants who were receiving the HIB immunization in addition to the DPT. Net pain scores in the infants who received the HIB vaccine were positively correlated with a history of circumcision ($r = 0.67$, $p = .002$). Behavioral pain scores ($r = 0.61$, $p = .007$) and duration of crying ($r = 0.57$, $p = .02$) also were correlated positively with history of circumcision. Researchers suggested that more research is needed to explore the role of excitatory amino acids, C-fiber neuropeptides, and NMDA receptors that are stimulated during painful situations and may cause a central sensitization or hypersensitivity to pain for a period following the initial sensitization. Limitations to this study include the retrospective design and the small sample size.

However, based on the findings of this study, Taddio, Katz, Ilersich, and Koren (1997) carried out a prospective cohort study with a larger sample to examine possible long-term effects of neonatal pain.

There may be long-term consequences of pain without conscious recall.

The pain responses of 87 healthy male infants were again measured during routine immunizations at 4–6 months of age. The control group comprised 32 infants who were not circumcised at birth based on parents' choice. The remaining infants had been randomly assigned either to a group that was circumcised using EMLA cream as an analgesic or to a group that had been circumcised following application of a placebo cream. Pain responses during immunizations 4–6 months later were videotaped, and pain scores were calculated based on facial expression, cry duration, and VAS score. The research assistant who scored the videotapes was blind to the procedure and to the infants' history. Infants who had been circumcised with use of a placebo cream had significantly higher difference scores than infants who were uncircumcised for VAS score (5.1 versus 3.1 cm, respectively; $p < .05$), percentage cry duration (53.8% versus 24.7%, respectively), and percentage facial action (136.9% versus 77.5%, respectively; Taddio et al., 1997).

The Effects of Early Pain Experiences on Children

An area of concern for healthcare providers and parents is the extent to which an infant will remember painful experiences and how these experiences will affect the child and adult later in life. Grunau (2000) stated that when a pain message is sent, there are molecular changes in the nervous system and a biologic marker is placed. This is implicit memory, meaning that the child will not have conscious recall, but that there is memory

at the subconscious level. Implicit memory may involve the brainstem, the basal ganglia, and the cerebellum. There may be long-term consequences of pain without conscious recall.

Preterm infants who undergo frequent painful procedures may experience altered responses to pain later in life. One study compared temperament and pain sensitivity (reactivity) among extremely low-birth-weight (ELBW) infants, heavier preterm infants, and full-term infants at 18 months of age. Note that in this study researchers did not measure the pain thresholds of children participating in the study, but examined their behavioral responses to pain. Parents of ELBW infants rated their infants as less sensitive (reactive) to pain as compared to ratings by parents of heavier preterm infants and full-term infants ($F = 4.43$, $p = .005$). Temperament of the toddlers was related to pain sensitivity in all groups except for the lowest-birth-weight group weighing less than 800 g. The authors suggested that the lack of association between temperament and pain sensitivity (or pain reactivity) for this ELBW group could be due to painful experiences in the NICU, neurological immaturity, or unknown factors. There were no significant relationships between pain sensitivity ratings and parenting styles (Grunau, Whitfield, & Petrie, 1994).

In a study that examined 8- to 10-year-old children's judgments about pain, two groups of children were used: 47 children who had weighed less than 1,000 g at birth and 37 children who were full term and weighed more than 2,500 g at birth. Children viewed pictures from the Pediatric Pain Inventory that illustrated painful events from medical, recreational, daily living, and psychosocial experiences. They were then asked to rate (a) pain intensity using a Color Analog Scale and (b) pain affect using the Facial Affective Scale. The low-birth-weight group rated medical pain significantly higher than psychosocial pain ($p < .004$), but there were no significant differences between medical and psychosocial pain ratings for the full-term group. For low-birth-weight infants, there was a significant correlation between number of days spent in the NICU and affect associated with pain in daily living ($r = 0.37$, $p < .01$) and recreation ($r = 0.30$, $p < .04$). The authors recommended continued research in the area of neonatal experiences and pain judgment in children (Grunau, Whitfield, & Petrie, 1998).

Preterm infants who were extremely low birth weight (<1,000 g) may have a tendency to have more somatic or physical complaints later in childhood than children who were born full term. In one study, 36 children born full term were compared with 36 ELBW children at 3 years of age and again at 4 years of age. Mother-child interaction was observed, and psychological assessment including administration of the Personality Inventory for Children was carried out. Children who had been

Table 1. Neurological Consequences of Pain in Infants

Problem Associated with Pain	Immediate Consequences	Long-Term Consequences
Disruption of sleep cycle	Lack of sleep, wasted energy	
Disruption of normal interaction between brain systems that control sleep/wake states, attention, and emotion (secondary to disruption of sleep cycle)		Risk for attention deficits, emotional disturbances, and behavioral problems
Disruption of self-regulation	Inability to calm self and organize behavior	Risk for attention deficits
Feeding problems	Wasted energy and risk for nutritional problems	Risk for consequences of nutritional deficits
Fluctuating intracranial blood volume and increased intracranial pressure	Intraventricular hemorrhage, periventricular leukomalacia	Neurological deficits, cognitive deficits, cerebral palsy
Modification of pain pathways and synapses		
(a) Retention of higher numbers of synapses and formation of abnormal connections*	Increased sensitivity to pain/decreased pain threshold	
(b) NMDA-induced excitability, excessive activity of excitatory amino acids and NMDA receptors (fiber firing yields glutamate), NMDA receptors in dorsal horn and supraspinal areas increase in density*	Decreased pain threshold, "wind-up" phenomenon, central sensitization	Possible susceptibility to chronic pain syndrome states, altered pain experiences, somatization (physical complaints)
(c) Sprouting of both A and C pain fibers (hyperinnervation)	Decreased pain threshold	
Increased activation of the HPA axis (hypothalamic-pituitary-autonomic nervous system)*		Changes in behavioral and hormonal responses to stress
Memory of pain at the subconscious level		Possible altered response to pain and altered judgment concerning painful events
Altered relationships between pain, emotion, and attention centers in the area of the brain associated with the anterior cingulate cortex		Possible attention deficits and emotional problems
Generalized, cumulative effects of repeated pain in low-birth-weight infants as a result of multiple factors: modified pain pathways, disruption of self-regulation and sleep cycles, brain damage from blood volume disturbances, association of pain with attention and emotion		May contribute to multidimensional problems such as <ul style="list-style-type: none"> • chronic pain syndrome states • somatic complaints • cognitive defects • learning disorders • attention deficits • poor motor performance • psychosocial problems • inability to cope or to adapt to new situations (Pain may contribute to neurodevelopmental problems such as these, but other factors also play a part.)

*Hypothesized changes in the nervous system associated with pain; research is ongoing.

preterm had significantly higher somatization scores than full-term infants ($\chi^2 = 10.29, p = .001$). Somatization refers to numerous pains that cannot be accounted for medically. There were no significant differences in medical problems between low-birth-weight children with high somatization scores and low-birth-weight children with lower somatization scores. The researchers suggested that the frequent painful procedures experienced by low-birth-weight infants may contribute to pain syndromes and increased somatic complaints, but state the need for additional research in this area (Grunau, Whitfield, Petrie, & Fryer, 1994).

The neurodevelopmental outcomes of preterm infants are partly mediated by neonatal illness. However, pain experiences also may determine cognitive and psychosocial outcomes of low-birth-weight infants. Repetitive pain and environmental stress in ELBW infants (<1,000 g) is associated with cognitive defects, learning disorders, poor motor performance, attention deficits, psychosocial problems, and inability to adapt and cope in new situations and social situations (Anand, Grunau, & Oberlander, 1997; Grunau, 2000). Grunau (2000) cited the following mechanisms as possible connections between early pain experiences and cognitive and emotional developmental outcomes: (a) modification of pain pathways and synapses, (b) changes in cerebral blood volume with resultant brain damage, (c) disruption of sleep cycles, (d) disruption of self-regulation, (e) association of pain with attention and subsequent cognitive development, and (f) association of pain with emotion and subsequent social and emotional development.

There is a relationship among pain, attention, and emotion. According to blood flow patterns visualized with positron emission tomography (PET) scans, the anterior cingulate cortex is the part of the brain most affected by pain. This area of the brain has a close connection with areas of the brain associated with emotion and attention. Therefore, repetitive pain in the developing brain may affect the capacity for sustained attention and alter the emotional makeup of the brain (Grunau, 2000).

Nursing Implications

It is important for nurses who care for infants to

prevent or eliminate pain as much as possible to promote positive neurodevelopmental outcomes during infancy and also in later childhood and adulthood. Table 1 presents a summary of neurological consequences of pain in infants. The American Association of Pediatrics (AAP, 2000) statement outlines concepts that must form the basis for pain management for the term and preterm neonate. In this statement, the AAP stresses the importance of pain management for infants, emphasizing that the neonate is capable of perceiving pain and may suffer consequences of pain both during the neonatal period and later in life. Concepts from the AAP statement are outlined in Fig 4.

Pain must be prevented as much as possible; unnecessary painful procedures must be avoided; and nurses must explore additional ways to assess and relieve infant pain. Assessing pain in infants and young children is challenging, but valid instruments that are feasible for use in clinical practice have been developed. A list of instruments for assessing pain in infants is presented in Table 2.

Nurses must provide follow-up care for infants who have experienced excessive or repetitive pain and offer intervention as needed for long-term consequences of pain in children and adults. Fig 5 offers suggestions for assessment components for children and adults with chronic pain syndromes or somatic complaints. Nurses can also develop policy within individual institutions to manage infant pain, educate healthcare professionals on the importance of pain management for infants, and continue to carry out research to examine adverse effects of pain or to design more effective pain management strategies.

Table 2. Infant Pain Assessment Tools

Name of Tool	Age Group	Author, Date
Premature Infant Pain Profile (PIPP)	Preterm infants	Stevens, Johnston, Petryshen, and Taddio, 1996
CRIES (Postoperative scale)	Infants	Krechel & Bilder, 1995
Scale for Use in Newborns (SUN)	Neonates	Blauer & Gertsman, 1998
Neonatal Facial Coding (NFCS)	Neonates	Grunau & Craig, 1990; Grunau, Oberlander, Holsti, & Whitfield, 1998
Neonatal Infant Pain Scale (NIPS)	Neonates	Lawrence, Alcock, McGrath, Kay, MacMurray, & Dulberg, 1993
Children & Infants Post-op Pain Scale (CHIPPS)	Infants, children	Buttner & Finke, 2000
Distress Scale for Ventilated Newborns (DSVNI)	Neonates	Sparshott, 1996
Echelle Douleur Inconfort Nouveau-Né (EDIN) Scale for Prolonged Pain	Preterm infants	Debillon, Zupan, Ravault, Magny, & Dehan, 2001

- The neonate is neurologically capable of pain perception (Anand, Phil, & Carr, 1989; Fitzgerald, Millard, & McIntosh, 1989; Fitzgerald, Shaw, & McIntosh, 1988; Perreault et al., 1997).
- Pain that is severe or prolonged increases morbidity in the neonate (Anand, 1998; Anand, Phil, & Hickey, 1987; Anand, Sippell, & Aynsley-Green, 1987).
- Pain during the neonatal period alters the infant's pain responses later in life (Grunau, 2000; Johnston & Stevens, 1996; Taddio, Goldbach, Ipp, Stevens, & Koren, 1995; Taddio, Katz, Ilersich, & Koren, 1997).
- It is possible to assess pain and evaluate effects of pain-relieving interventions in the neonate (Grunau & Craig, 1987; Grunau & Craig, 1990; Stevens, Johnston, Petryshen, & Taddio, 1996).
- When an analgesic is required, the neonate may not be comforted by other means (McIntosh, 1997).
- Lack of crying does not mean that the neonate is not experiencing pain (Stevens et al., 1996).

Fig 4. American Association of Pediatrics (AAP) Statement on Infant Pain (2000)

Birth and Neonatal History

- Weeks of gestation (greater prematurity, greater risk)
- Birth weight
- Presence of any congenital defects
- History of admission to neonatal intensive care unit (NICU)
 - Medical diagnosis/es
 - Nature of diagnostic tests conducted: blood tests, lumbar punctures, eye examinations, etc.
 - Nature of treatments carried out: mechanical ventilation, intravenous therapy, placement of any tubes, etc.
 - Nature of any surgery or surgical procedures
 - Length of NICU stay
 - Discharge diagnosis/es

History of Infancy

- History of admissions to hospital during first year of life
 - Admitting diagnosis/es
 - Nature of diagnostic tests conducted
 - Nature of treatments carried out
 - Nature of surgery or surgical procedures
 - Length of hospital stay
 - Discharge diagnosis/es
- History of outpatient medical/surgical care during first year of life
 - Medical diagnosis/es
 - Nature of diagnostic tests conducted
 - Nature of treatments carried out
 - Nature of surgery or surgical procedures

Fig 5. Assessment components for children and adults with chronic pain syndromes or somatic complaints

Summary

Nurses must meet the challenge of preventing and relieving pain in infants. Preterm infants especially are very sensitive to pain, and their immature nervous systems make them more vulnerable to adverse effects of pain. Painful experiences during the neonatal period may have immediate harmful consequences and may even lower the pain threshold through various physiological and structural mechanisms.

Early painful experiences may alter responses to pain later in life and contribute to chronic pain syndromes and increased physical complaints. Repetitive painful experiences early in life may alter cognitive and emotional development. Current knowledge of the immediate and long-term effects of severe or repetitive pain in the infant population places a mandate on nurses to assess the problem and to intervene in order to promote positive health outcomes for infants, children, and adults.

References

- Als, H. (1982). Toward a synactive theory of development: Promise for the assessment and support of infant individuality. *Infant Mental Health Journal*, 3(4), 229–243.
- American Academy of Pediatrics. (2000). Prevention and management of pain and stress in the neonate. *Pediatrics*, 105(2), 454–461.
- Anand, K.J.S. (1998). Clinical importance of pain and stress in preterm neonates. *Biology of the Neonate*, 73, 1–9.
- Anand, K.J.S. (2000). Effects of perinatal pain and stress. *Progress in Brain Research*, 122, 117–129.
- Anand, K.J.S., Coskun, V., Thirivikraman, K.V., Nemeroff, C.B., & Plotzky, P.M. (1999). Long-term behavioral effects of repetitive pain in neonatal rat pups. *Physiology and Behavior*, 66(4), 627–637.
- Anand, K.J.S., Grunau, R.V.E., & Oberlander, T.F. (1997). Developmental character and long-term consequences of pain in infants and children. In S.J. Weisman (Ed.), *Pain Management in Children, Child and Adolescent Psychiatric Clinics of North America*, 6(4), 703–724.
- Anand, K.J.S., Phil, D., & Carr, D.B. (1989). The neuroanatomy, neurophysiology and neurochemistry of pain, stress, and analgesia in newborns and children. *Pediatric Clinics of North America*, 36(4), 795–822.
- Anand, K.J.S., Phil, D., & Hickey, P.R. (1987). Pain and its effects in the human neonate and fetus. *New England Journal of Medicine*, 317(21), 1321–1329.
- Anand, K.J.S., Phil, D., & Hickey, P.R. (1992). Halothane-morphine compared with high-dose sufentanil for anesthesia and postoperative analgesia in neonatal cardiac surgery. *New England Journal of Medicine*, 326(1), 1–9.
- Anand, K.J.S., & Scalzo, F.M. (2000). Can adverse neonatal experiences alter brain development and subsequent behavior? *Biology of the Neonate*, 77, 69–82.
- Anand, K.J.S., Sippell, W.G., & Aynsley-Green, A. (1987). A randomized trial of fentanyl anesthesia in preterm neonates undergoing surgery: Effects of the stress response. *Lancet*, 1, 243–248.
- Andrews, K., & Fitzgerald, M. (1994). The cutaneous withdrawal reflex in human neonates: Sensitization, receptive fields, and the effects of contralateral stimulation. *Pain*, 56, 95–101.
- Blauer, T., & Gertsman, D. (1998). A simultaneous comparison of three neonatal pain scales during common NICU procedures. *Clinical Journal of Pain*, 14(1), 39–47.

- Bozette, M. (1993). Observation of pain behavior in the NICU: An exploratory study. *Journal of Perinatal and Neonatal Nursing*, 7(1), 76–87.
- Buttner, W., & Finke, W. (2000). Analysis of behavioural and physiological parameters for the assessment of postoperative analgesia demand in newborns, infants and young children: A comprehensive report on seven consecutive studies. *Paediatric Anaesthesiology*, 10(3), 303–318.
- Chiang, C.Y., Hu, J.W., & Sessle, B.J. (1997). NMDA receptor involvement in neuroplastic changes induced by neonatal capsaicin treatment in trigeminal nociceptive neurons. *Journal of Neurophysiology*, 78, 2799–2803.
- Debillon, T., Zupan, V., Ravault, N., Magny, J.F., & Dehan, M. (2001). Development and initial validation of the EDIN scale, a new tool for assessing prolonged pain in preterm infants. *Archives of Diseases in Childhood Fetal & Neonatal Edition*, 85, F36–F41.
- Evans, J.C., Vogelpohl, D.G., Bourguignon, C.M., & Morcott, C.S. (1997). Pain behaviors in LBW infants accompany some nonpainful caregiving procedures. *Neonatal Network*, 16(3), 33–40.
- Fitzgerald, M. (1995). Developmental biology of inflammatory pain. *British Journal of Anaesthesia*, 75, 177–185.
- Fitzgerald, M., Millard, C., & MacIntosh, N. (1989). Cutaneous hypersensitivity following peripheral tissue damage in newborn infants and its reversal with topical anesthesia. *Pain*, 39, 31–36.
- Fitzgerald, M., Millard, C., & MacIntosh, N. (1988). Hyperalgesia in premature infants. *Lancet*, 1, 292.
- Fitzgerald, M., Shaw, A., & McIntosh, N. (1988). Postnatal development of the cutaneous flexor reflex: Comparative study of preterm infants and newborn rat pups. *Developmental Medicine and Child Neurology*, 30, 520–526.
- Gonsalves, S., & Mercer, J. (1993). Physiological correlates of painful stimulation in preterm infants. *Clinical Journal of Pain*, 9(2), 88–93.
- Grunau, R.V.E. (2000). Long-term consequences of pain in human neonates. In K.J.S. Anand, B.J. Stevens, & B.J. McGrath (Eds.), *Pain in neonates: Vol 10. Pain and research clinical management* (2nd. Rev. enl. ed., pp. 55–76). Amsterdam: Elsevier.
- Grunau, R.V.E., & Craig, K.D. (1987). Pain expression in neonates: Facial action and cry. *Pain*, 28, 395–410.
- Grunau, R.V.E., & Craig, K.D. (1990). Facial activity as a measure of neonatal pain expression. In D.C. Tyler & E.J. Krane (Eds.), *Advances in pain research and therapy: Vol. 15. Pediatric pain*. New York: Raven Press.
- Grunau, R.V.E., Oberlander, T., Holsti, L., & Whitfield, M.F. (1998). Bedside application of the Neonatal Facial Coding System in pain assessment of premature neonates. *Pain*, 76, 277–286.
- Grunau, R.V.E., Whitfield, M.F., & Petrie, J. (1994). Pain sensitivity and temperament in extremely low-birth-weight premature toddlers and preterm and full-term controls. *Pain*, 58, 341–346.
- Grunau, R.V.E., Whitfield, M.F., & Petrie, J. (1998). Children's judgments about pain at age 8–10 years: Do extremely low-birthweight (<1000 g) children differ from full birthweight peers? *Journal of Child Psychology and Psychiatry*, 39(4), 587–594.
- Grunau, R.V.E., Whitfield, M.F., Petrie, J.H., & Fryer, E.L. (1994). Early pain experience, child and family factors, as precursors of somatization: A prospective study of extremely premature and full term children. *Pain*, 56, 353–359.
- Johnston, C.C., & Stevens, B. (1990). Pain assessment in newborns. *Perinatal Neonatal Nursing*, 4(1), 41–52.
- Johnston, C.C., & Stevens, B. (1996). Experience in a neonatal intensive care unit affects pain response. *Pediatrics*, 98(5), 925–930.
- Krechel, S.W., & Bildner, J. (1995). CRIES: a new neonatal postoperative pain measurement score: Initial testing of validity and reliability. *Paediatric Anaesthesiology*, 5(1), 53–61.
- Lawrence, J., Alcock, D., McGrath, P., Kay, J., MacMurray, S.B., & Dulberg, C. (1993). The development of a tool to assess neonatal pain. *Neonatal Network*, 12(6), 59–66.
- McCormack, K., Prather, P., & Chapleo, C. (1998). Some new insights into the effects of opioids in phasic and tonic nociceptive tests. *Pain*, 78, 79–98.
- McIntosh, N. (1997). Pain in the newborn: A possible new starting point. *European Journal of Pediatrics*, 156(3), 173–177.
- Perreault, T., Fraser-Askin, D., Liston, R., McCourt, C., Oh, W., Ohlsson, A., et al. (1997). Pain in the neonate. *Paediatric Child Health*, 2(3), 201–209.
- Reynolds, J.L., & Fitzgerald, M. (1995). Long-term sensory hyperinnervation following neonatal skin wounds. *Journal of Comparative Neurology*, 358, 487–498.
- Sparshott, M. (1996). The development of a clinical distress scale for ventilated newborn infants: Identification of pain and distress based on validated behavioral scores. *Journal of Neonatal Nursing*, 2(2), 5–11.
- Stevens, B., & Johnston, C.C. (1994). Physiological responses of premature infants to a painful stimulus. *Nursing Research*, 43(4), 226–231.
- Stevens, B., Johnston, C.C., Petryshen, P., & Taddio, A. (1996). Premature infant pain profile: Development and initial validation. *Clinical Journal of Pain*, 12(1), 13–22.
- Taddio, A., Goldbach, M., Ipp, M., Stevens, B., & Koren, G. (1995). Effect of neonatal circumcision on pain responses during vaccination in boys. *Lancet*, 345, 291–292.
- Taddio, A., Katz, J., Ilersich, A.L., & Koren, G. (1997). Effect of neonatal circumcision on pain response during subsequent routine vaccination. *Lancet*, 349, 599–603.

Continuing Education Credit

The *Journal for Neuroscience Nursing* is pleased to offer the opportunity to earn neuroscience nursing CE for this article online. Go to www.aann.org, and select "Continuing Education." There you can read the article again or go directly to the posttest assessment. The cost is \$15 for each article. You will be asked for a credit card or online payment service number.

The posttest consists of 10 questions based on the article, plus several assessment questions (e.g., How long did it take you to read the article and complete the posttest?). A passing score of 80% (8 of 10 questions correct) on the posttest and completion of the assessment questions yields 1 hour of continuing education credit in neuroscience nursing for each article.