Neurodevelopmental care, which is any NICU intervention undertaken to improve neurodevelopmental outcome, includes NICU design, nursing routines, nursing care plans, management of pain, feeding methods and, most importantly, encouraging parental involvement with their NICU infant. Recognition that sensory stimulation can overwhelm preterm infants and increase physiologic signs of stress led to attempts to reduce sensory input. More recent approaches judiciously add back soothing sensory input (e.g., therapeutic touch, soft music). Circadian light/dark cycles and physical activity improve preterm growth. Attention to infant positioning and handling affects physiologic variables and joint mobility, if not functional motor abilities. A highly organized system of care for NICU infants is Al's NIDCAP (i.e., Neonatal Individualized Developmental Care and Assessment Program). Although NIDCAP may reduce need for respiratory support and hospital length of stay, it does not significantly influence neurodevelopmental outcome at 2–3 years. Pain management includes benign interventions (e.g., nonnutritive sucking, oral glucose), but the prolonged use of narcotics must be balanced against the consequences of sedation and dependency. The foremost challenge for NICUs remains parent disenfranchisement. Kangaroo care, which involves parent/infant skin-to-skin contact, improves preterm growth, decreases nosocomial infections and may shorten hospital length of stay. A great deal of work needs to be done to identify and demonstrate efficacy of specific interventions and changes that humanize the NICU, encourage parental involvement, support infant development and optimize preterm neurodevelopmental outcomes.

An effort to improve outcomes has shifted attention toward neuroprotective strategies and neurodevelopmental support. Neuroprotection includes giving medications (e.g., indomethacin to prevent intraventricular hemorrhage) and modifying respiratory and cardiovascular support strategies (e.g., avoiding hyperventilation and providing blood pressure support) to prevent or ameliorate central nervous system (CNS) injury [Fowlie and Davis, 2002; O’Shea, 2002]. Neurodevelopmental support includes modifying neonatal intensive care and improving neonatal intensive care unit (NICU) design to support preterm neuromaturation.

The NICU environment influences preterm neurodevelopment just as the intrauterine environment influences fetal neurological development. One example of this is that the uterus constricts fetal movement and leads to a tightly flexed fetal posture. The fullterm neonate demonstrates a high degree of flexor tone, called flexor hypertonia, which is abnormal at any other time of life. As preterm infants’ subcortical system develops, they too develop extremity flexor tone, which peaks at 38–40 weeks postmenstrual age (PMA, gestational age plus chronologic age) [Allen and Capute, 1990; Amiel-Tison, 1995]. However, preterm infants at term have less flexor hypertonia as fullterm neonates and often have more extensor tone which interferes with the development of head control, rolling over and getting into and out of sitting [Georgieff and Bernbaum, 1986]. Positioning and handling the preterm infant in a flexed posture mimics intrauterine conditions, supports the development of flexor tone prior to term and provides the infant with a sense of containment that allows better self-organization.

Understanding how the central nervous system (CNS) develops and functions is one of the most daunting challenges of science. The physiologic development of the CNS, including neuromotor, neurosensory and neurocognitive systems and later executive function are much less well understood than the fetal respiratory, cardiac or gastrointestinal systems. Neuromaturation
is the process of achieving full development and growth of the CNS. Determining how to provide NICU neurodevelopmental support requires knowledge of preterm neuromaturational, including how a fetus or preterm infant perceives surrounding auditory, visual, tactile and olfactory environmental stimuli and how the infant’s responses, posture and movement influence CNS development. It is no longer a question of genes vs environment: they continuously interact during development and determine who we are and what we become [Cotman and Berchtold, 1998; Pomeroy and Kim, 2000]. Successive turning on and then off specific genes propel CNS development forward, with genetic control of cell division, differentiation, migration and function. Surrounding cells, nutrients, temperature and many other factors influence cell division, migration, connections and function.

The intrauterine environment, including the mother’s health and adequacy of the uteroplacental supply, plays a crucial role in fetal growth and development. Likewise, fetal and preterm movement, behavioral responses and learning guide CNS shaping and remodeling [Cotman and Berchtold, 1998, Pomeroy and Kim, 2000]. The fetal heart beats and the fetus moves within weeks after the CNS begins with neural induction and neuromulation to form the brain and spinal cord. Normal limb and brain development requires fetal body movement just as normal lung development requires fetal breathing. Vast networks of neuronal interconnections are formed during synaptogenesis, and these synaptic networks are shaped by patterns of electrical activity: use fosters and drives CNS development. Later in infancy, the synaptic network is pruned and refined, according to use. CNS function is intricately related to CNS structure.

Preterm delivery dictates that interaction with the extrauterine NICU environment shapes the preterm infant’s developing CNS. Neuronal migration, differentiation, synaptogenesis, myelination and refining synaptic connections continue, even if the preterm infant has sustained CNS injury [Cotman and Berchtold, 1998]. The fragility of the developing CNS and the crudeness of a NICU’s attempts to recreate the intrauterine environment raise the question as to why all preterm infants are not disabled. In addition to medications and medical strategies to prevent or ameliorate preterm CNS injury, features of the infant’s isolette or warmer, nutrition, nursing care, medical interventions, NICU and family involve-ment can support neurodevelopment and neurorecovery. This review will begin with a historical perspective of NICU developmental intervention, then discuss a variety of interventions designed to provide neurodevelopmental support. We emphasize the importance of clinical research to evaluate efficacy (in a research environment) and effectiveness (in real NICUs) of specific interventions.

EARLY INTERVENTION AND SENSORY STIMULATION

Manipulations of a child’s environment to promote cognitive and neurological development have traditionally been called “early intervention.” Initial efforts were directed toward preschool children with neurodevelopmental disabilities and environmental risks factors. Extending these efforts downward to younger children culminated in the U.S. in legislation in 1986 promoting early intervention services for infants and toddlers with developmental delay or at risk for substantial delay [http://www.ed.gov/pubs/OSEP95AnlRpt/ch2a.html]. There continues to be considerable controversy as to efficacy of early intervention and/or sensory enrichment in infants with and at risk for disability [Ottenbacher and Petersen, 1984; Ottenbacher et al., 1987; Harris et al., 1988; Vargas and Camilli, 1999; Butler and Darrah, 2001].

With prematurity as a major disability risk factor, initial early intervention efforts provided sensory stimulation to preterm infants in NICUs [Masi, 1979; Field, 1980]. Stimulation included rocking, stroking, holding, moving, playing recordings of mother’s voice, providing a pacifier for nonnutritive sucking and providing visual decorations. There has been some evidence that tactile-kinesthetic, auditory or visual stimulation promoted physiologic stability, oral feeding, weight gain, responsiveness and development of preterm infants, but most studies have had serious flaws [Masi, 1979; Field, 1980; Barnard and Bee, 1983; Mueller, 1996; Vickers et al., 2002]. Flaws included unequal groups with respect to important confounders, very small sample sizes, lack of randomization, failure to measure background rate of stimulation in controls, lack of masked outcome evaluators as to treatment group and no long-term follow up. Often the subjects’ states of alertness, whether stimuli were arousing or soothing and individual differences in perceptions and responses were not considered. It is difficult to confine interventions to the study group without applying them to controls. Sick preterm infants and infants with serious medical complications were generally excluded. There has been controversy as to when supplemental stimulation should begin, what its frequency and duration should be, who should administer it and whether to continue it after discharge home. Although these intervention programs provided an opportunity to work with parents, few studies measured effects on parental behavior or parent-infant interactions.

Whether the stimulation is applied invariably or contingent on the infant’s state or behavior is an important consideration [Masi, 1979; Field, 1980; Barnard and Bee, 1983]. Learning occurs when infants can control the frequency, duration and/or intensity of stimuli. A contingency-based intervention requires infant assessment of state and response. During involuntary sensory stimulation sessions, many preterm infants closed their eyes, averted their gaze or even became physiologically unstable with color changes, apnea or bradycardia. Preterm infants in NICUs have not suffered sensory deprivation but have been bombarded by aversive stimuli, including bright fluorescent lights, noisy equipment and painful procedures [Blennow et al., 1974; Lawson et al., 1977; Gottfried et al., 1981; Newman, 1981; Robertson et al., 1998a; 1999a; b; Chang et al., 2001]. Although they habituate to repeated stimuli by 28–30 weeks postmenstrual age (PMA, chrono-
logical age plus gestational age) [Allen and Capute, 1986a], even healthy preterm infants remain vulnerable to sensory input overload.

There is no doubt that fetuses and very immature infants react to sensory stimuli [Haith, 1986]. Fetuses and preterm infants as young as 24–26 weeks gestation move in response to sound [Allen and Capute, 1986a; Johansson et al., 1992]. Movement of the mother stimulates the fetal vestibular apparatus; fetal movement provides kinesthetic stimulation; and amniotic fluid stimulates tactile receptors and conducts sound well. Visual fixation and visual pattern preference occur by 30–32 weeks gestation, as do somatosensory evoked responses to tactile stimuli [Dubowitz et al., 1980; Hack et al., 1976; 1981; Hrbek et al., 1973]. Tactile and vestibular stimuli are often used to stimulate apneic preterm infants. Sensory stimulation is part of life, and our challenge is to determine how the NICU environment can be changed to support preterm sensory, motor and cognitive neurodevelopment.

NIDCAP

Although there have been many individual contributions, many equate NICU developmental care with Heidelise Als’ highly organized system, Neonatal Individualized Developmental Care and Assessment Program (NIDCAP) [Als, 1998]. Systematic implementation requires NICU developmental care teams and training and certification of staff. Although many have voiced concerns that implementation of NIDCAP is expensive and time-consuming, NIDCAP has popularized important concepts regarding the need for infant assessment and individualizing care for infants and families.

The NIDCAP uses systematic behavioral observations of the individual at-risk newborn to provide the basis for coordinating the care of that infant. Trained observers use an instrument designed for this purpose which evaluates the infant in five systems: autonomic physiologic, motor, state organizational, attentive-interactive and self-regulatory. These include items such as respiratory status, color, visceral responses (e.g., gagging, hiccupping), tone posture, facial expressions and attention. This assessment, along with the infant’s behavioral reactions to internal and external sensory stimuli, is used to measure the infant’s ability to tolerate his or her environment and caregiving activities. An individual developmental care plan is then designed to decrease potential detrimental effects of the NICU environment.

The NIDCAP program recommends salaried positions for a developmental specialist and a developmental care nurse educator, a 6–7 member multidisciplinary leadership support team and a trained core group of nursing staff. The training involves 2 levels: NIDCAP level I consists of training in the infant behavioral observation, developmental care planning, and implementation of the care plan based on the behavior observation. Level II training includes consultation to the NICU regarding its environment, the building of a developmental team, and implementation of developmental care, with specific training for the developmental specialist, the developmental care nurse educator and consultation to the multidisciplinary support team. The full development of the program is expected to be a five-year process.

Several studies have attempted to evaluate the effect of the NIDCAP interventions by looking at various short and long-term outcomes. In two trials by Als [Als et al., 1986; 1994], infants receiving routine care were compared to infants cared for by those specially trained in NIDCAP. The NIDCAP intervention group had a decrease in the total number of ventilator days, in addition to fewer tube feeding days, shorter hospital stays and discharge at an earlier gestational age. There was no difference in the incidences of intraventricular hemorrhage, retinopathy of prematurity, or weight gain between the groups. In the later study [Als et al., 1994], the NIDCAP intervention group had higher scores on their Bayley developmental assessment at 9 months of age.

A randomized trial of routine care compared to NIDCAP found no group differences in death, retinopathy of prematurity, weight gain or days on a ventilator [Westrup et al., 2000]. However, the NIDCAP group had fewer days on CPAP and supplemental oxygen and lower postmenstrual age (PMA, gestational age plus chronologic age) at discharge than the routine care group. Others have reported that very low birthweight infants who received developmental care had lower hospital costs due to an earlier move to a transitional unit with lower nursing costs, and an earlier discharge [Petryshen et al., 1997]. However, this study did not take into account the cost of the program and the need for specially trained personnel. Studies assessing developmental outcome at two and three years of age [Ariagno et al., 1997; Kleberg et al., 2000] have not found differences in the developmental quotient in those infants who received NIDCAP care as a newborn compared with those who did not.

Most of the trials of NIDCAP suffer from small sample size, lack of masking for those assessing outcomes and use of historical controls. Meta-analysis of the three trials [Als et al., 1986; 1994; Westrup et al., 2000] that meet at least some of the criteria for inclusion in a Cochrane Review (i.e., masked randomization, masked intervention, complete follow-up and masked outcome assessors) provides evidence that NIDCAP decreases duration of oxygen support (weighted mean difference, –39.4 days, 95% CI — 64.6, –14.1), number of tube feeding days (weighted mean difference, –32.0 days, 95% CI — 48.4, –15.6), and length of hospital stay, as measured by lower PMA at discharge (weighted mean difference, –2.19 weeks, 95% CI — 4.33, –0.05) [Symington and Pinelli, 2002]. The evidence for improved neurodevelopmental outcome is conflicting, with most of the improved development being demonstrated at earlier ages but no significant differences at two to three years.

Despite the potential benefits, the NIDCAP has not been universally adopted. In a survey of developmental care in NICUs, half of the respondents had NIDCAP certified staff at their institution, but most initiated consults only “when the need arises” rather than as a protocol [Ashbaugh et al., 1999]. Only 30% of NICUs with a developmental care team had a dedicated budget. Implementation as outlined by NIDCAP was unusual. Because NIDCAP incorporates stimuli reduction, nursing interventions and modification of the NICU environment for each infant, it is not clear which aspects are more beneficial, and assumes

Sensory stimulation is part of life, and our challenge is to determine how the NICU environment can be changed to support preterm sensory, motor and cognitive neurodevelopment.
that all excess stimuli are detrimental. Many NICUs incorporated aspects of the NIDCAP that are widely acknowledged to be sensible (e.g., coordinating an infant’s cares with feedings to prolong sleep time) and promote family interactions with their infant.

Studies evaluating other individualized developmental care programs not based on NIDCAP have found no differences in weight gain, hospital charges or length of stay [Brown et al., 1980; Fleisher et al., 1995]. One study did find a decrease in ventilator days in infants receiving developmental care [Fleisher et al., 1995]. There were no differences in 12 month developmental outcome [Brown et al., 1980].

THE NICU ENVIRONMENT

Many studies have attempted to intervene in specific areas of the NICU environment in order to assess its individual contribution to outcome. It is well known that excessive exposure to loud sound can be damaging to hearing. It is not as clear what level and duration of sound exposure is harmful to the developing auditory system of a preterm infant. As a result, the focus in NICUs has been to minimize excess noise exposure [Saunders, 1995; Robertson et al., 1998b; 1999a; b: Philbin et al., 1999; Walsh-Sukys et al., 2001]. Less clear are the potential positive effects of either quiet or soothing stimuli such as lullabies or maternal voice. Minimizing auditory input by placing ear muffs on preterm infants for 2 days found no acute changes in physiologic parameters [Zahr and de Traversay, 1995]. Decreasing sound and light for 12 hours at night resulted in improved weight gain and increased time sleeping [Mann et al., 1986]. The use of lullaby or parent voice during feeding has not been shown to improve growth or duration of tube feeding [Chapman, 1984; Gatts et al., 1994], but when combined with rocking, it decreased hospital length of stay [Gatts et al., 1994].

Noxious stimuli are unfortunately common in the NICU due to the need for frequent monitoring and procedures related to caring for a critically ill infant. Providing soothing measures such as nonnutritive sucking during minor procedures may be of benefit [Field and Gokslon, 1984; Stevens et al., 1999]. In addition to minimizing tactile stimulation through clustering of cares and treating or supporting infants during noxious stimuli, there has been interest in providing positive tactile stimulation, such as stroking or massage. Positive stimulation around the time of feeding has been shown to improve weight gain that persists through 12 months PMA, but has not changed the time needed to become fully nipple fed [Helders et al., 1989; Gaebler and Hanzlik, 1996].

In an attempt to simulate the rhythmic motions found in the in utero environment, a number of investigators have looked at providing vestibular stimulation to preterm infants. Rhythmic stimulation has been provided by use of devises such as oscillating or rocking mattresses, waterbeds, and a breathing teddy bear that is placed in isolettes. Vestibular stimulation facilitates quiet sleep [Thoman et al., 1991] but has no impact on weight gain, feeding outcomes or apnea [Saigal et al., 1986; Henderson-Smart and Osborn, 2002]. Developmental assessment at 12 months [Saigal et al., 1986] and 18 months [Darrab et al., 1994] was not different between groups.

The sudden exposure to bright light after the darkened in utero environment has brought concerns of the effect of light on the immature retina. Most NICUs have significantly decreased ambient lighting [Walsh-Sukys et al., 2001], and the addition of isoflurane covers reduces light to the infant even further. Although avoiding bright light exposure makes sense, reduction of light exposure has not been shown to reduce the incidence of retinopathy of Prematurity [Reynolds et al., 1998; Phelps and Watts, 2002]. Although it is the practice in many NICUs to wear isoflurane and minimize light exposure, isoflurane covers should not totally block a preterm infant from view, because of the need in intensive care to view the patient as well as respond to alarms.

Infants demonstrate variations in their vital signs in accordance with a circadian cycle, and may respond to interventions differently based on that cycle [Glotzbach et al., 1995]. The in utero environment establishes rhythmic patterns from the influences of maternal sleep, temperature, heart rate and hormonal cycles. The continuous reduction of light and other sensory input may make it more difficult for the preterm infant to establish circadian rhythms. Cycling light exposure may provide a beneficial rhythmicity for the infants. Brandon et al. [2002] assigned preterm infants to one of three groups: cycled light from birth, cycled light beginning at 32 weeks PMA, or cycled light beginning at 36 weeks PMA in preparation for discharge. Those infants receiving cycled light from birth and 32 weeks PMA gained weight faster than those who did not receive cycled light until 36 weeks PMA. There were no differences in length of stay or number of ventilator days. Interestingly, those infants in near darkness until 36 weeks appeared to have more severe retinopathy of prematurity earlier than those in cycled light do.

POSITIONING AND HANDLING

Because of the fragility of preterm infants, most NICUs have adopted a minimal handling and stimulation approach for very immature and/or sick infants [Ashbaugh et al., 1999]. Nurses have primary responsibility for positioning NICU infants for monitoring and accessibility (e.g., to allow stabilization of the infant’s airway and intravascular or arterial catheters) and for rotating their position on a regular basis. Attention should always be paid to the infant’s physiologic parameters: heart and respiratory rate, oxygen saturations, blood pressure, ease of breathing and perfusion. When supine, 21 intubated NICU infants on ventilators had evidence of obstructed cerebral venous drainage when their heads were turned to the side, which suggests that acutely ill infants in supine should be positioned with their heads midline [Pellicer et al., 2002]. Several studies have found more effective breathing and oxygenation in preterm infants with lung disease in the prone position (compared to supine and side-lying) [Martin et al., 1979; Liory and Manginello, 1988; Baird et al., 1991; Mizuno and Aizawa, 1999; Maynard et al., 2000; Chang et al., 2002], but not in healthy preterm infants [Fox et al., 1993]. Repositioning the infant is an effective method for treating apnea of prematurity. Preterm infants symptomatic with apnea of prematurity had no significant differences between prone and supine positions in frequency of apnea, bradycardia or desaturations [Keene et al., 2000]. Neonates with narcotic abstinence syndrome had fewer signs of withdrawal and lower caloric intake in the prone vs the supine position [Matchuk et al., 1999].

Promoting neuromaturation is the goal of positioning and handling convalescent infants, but is also a consideration for more acutely ill infants. Although several small randomized controlled trials did not find that a positioning and handling program conducted by physical therapists altered incidence of disability in preterm infants [Goodman et al., 1985; Piper et al., 1986], failure to attend to how preterm infants are positioned in the NICU influences infant posture and motor function. Many of the common neuromotor abnormalities (e.g., asymme-
tries, extensor hypertonia) seen in preterm infants during their first year that do not signal disability may be the result of positioning while in the NICU [Georgieff and Bernbaum, 1986; Downs et al., 1991; de Groot et al., 1995, Konishi et al., 1986; 1987; 1997; Bracewell and Marlow, 2002].

Konishi et al. [1986; 1987; 1997] found that a preterm infant’s predominant position in the NICU influenced infant motor development. One study assigned low risk preterm infants by date of birth to predominantly prone or supine positions in the NICU. [Konishi et al., 1987] The groups were comparable with respect to birthweight, gestational age, sex, respiratory distress, apnea and length of hospital stay. Infants positioned predominantly in supine were more likely to demonstrate 1) a marked preference for turning to the right and keeping their head on the right, 2) an asymmetric posture, 3) asymmetrical occipital skull flattening, 4) an asymmetrical trunk at 6 months, 5) an early (before 6 months) right hand preference, and 6) an asymmetrical gait with a mild gait disturbance. A marked lateral head preference can therefore promote asymmetric movements in early infancy. This may be related to the asymmetric tonic neck reflex (when the infant’s head is turned to the side, limbs on the occiput side flex and on the face side extend) in preterm infants from 30 weeks PMA until it is suppressed by higher cortical function at 4–6 months from term [Allen and Capute, 1986b; 1990].

A developmental study of 213 preterm infants with birthweights below 1750 grams found that prone positioning improved head control but not performance on the Bayley Mental or Psychomotor Scales at 56 and 92 weeks [Ratliff-Schaub et al., 2001]. Prone position gives infants opportunities to strengthen muscles and utilize balance skills when lifting their heads. Parents should be encouraged to play with their awake preterm infant in prone on a firm surface (not a soft mattress) [Mildred et al., 1995, Ratliff-Schaub et al., 2001] because play in prone facilitates upper body antigravity control, trunk and shoulder stability, fine motor function and bringing their hands to the midline.

In a similar manner, positioning preterm NICU infants in flexion mimics intrauterine posture and supports the development of flexor tone, which normally peaks at term [Allen and Capute, 1990]. Placing rolled towels or blankets to position the infant with flexed limbs and shoulders slightly forward also helps to contain the infant, providing firm boundaries. The infant’s head should be neither flexed nor extended, but in line with the body. It is not necessary to position infants with respiratory distress with neck extension; in fact too much neck extension collapses the airway just as too much neck flexion does. Lack of attention to flexed posture and neutral head position leads to the higher neck, trunk and extremity extensor tone seen in preterm infants in NICUs and follow-up clinics [de Groot et al., 1995; Georgieff and Bernbaum, 1986].

The neck extensor muscles are stronger than flexors at approximately 32-34 weeks gestation [Amiel-Tison, 1995], giving preterm infants a slight tendency to position themselves with their neck extended. By 30 weeks gestation, most of the primitive reflexes seen in full term infants are evident in preterm infants [Allen and Capute, 1986b]. This includes the tonic labyrinthine, in which the trunk and legs extend and shoulders retract with neck extension and neck flexion leads to lower extremity flexion and shoulder protraction. Positioning a preterm infant in supine with neck extension stimulates the tonic labyrinthine reflex, thereby promoting shoulder retraction and the extensors of the neck, trunk and legs. This posture can persist during infancy [Georgieff and Bernbaum, 1986; de Groot et al., 1995] and interfere with midline hand play (a 3 month skill), rolling over (4-5 months), sitting well (6-8 months) and getting into and out of sitting (7-8 months). When staff recognize signs of neck extensor hypertonia in a NICU infant, careful positioning and handling of that infant is indicated to keep the infant contained or snug with firm boundaries, neck neutral, shoulders protracted, and body symmetric.

Pediatric physical and occupational therapists can be an important resource for NICUs because of their experience with neuromotor abnormalities in infants with cerebral palsy. They may function as part of a NICU developmental team, or may be consulted about specific patients. The NICU infant with neck extensor hypertonia who is difficult to position warrants consultation with a therapist, who may demonstrate how to swaddle the infant or use sandbags to position the infant in a lateral decubitus position with head neutral. Therapists can also help develop intervention strategies for infants with asymmetries, infants with hand abnormalities (e.g., cortical thumbs) and infants with joint contractures. Most importantly, therapists can play a major role in working with parents on developmental handling and positioning techniques.

One type of joint contracture that can be avoided by careful positioning is hip abduction and external rotation contracture (also known as tensor fascia latae contracture or shortened tibial band) [Amiel-Tison and Grenier, 1986]. Sick, sedated or very immature infants tend to lie frog-legged in either prone or supine. Frog-legged posture for days to weeks (especially if paralyzed) fixes the hips in abduction and results in contractures that interfere with subsequent neuromotor development (e.g., rolling over, getting into and out of sitting). Positioning an infant’s legs with hips neutral (with some abduction) can prevent this unnecessary complication of hypotonia [Downs et al., 1991].

Neonates have traditionally been swaddled. Wrapping them tightly in a blanket with limbs flexed, hips neutral without rotation, shoulders forward, head neutral and hands accessible for exploration provides containment and predictable support, mimicking the security of the womb. They should be moved slowly, with attention to how they are positioned. This is especially true for irritable infants with narcotic withdrawal symptoms, chronic lung disease or the hyperexcitability of hypoxic-ischemic encephalopathy. Even very preterm infants when placed in an isolette tend to migrate towards a side or corner. Strategies that use positioning aids (e.g. blanket rolls, support wedges) to contain the infant in flexion and with hips neutral are often rewarded by reduced signs of stress. Vulnerable preterm infants should be moved carefully as a whole, keeping body and head aligned and limbs tucked in.

Although there is no evidence that range of motion exercises or other forms of physical activity influence later neuromotor development, 2 small randomized controlled studies in preterm NICU infants found greater weight gain and bone mass (bone length, area and mineral content) with physical activity [Moyer-Mileur et al., 1995; 2000]. These studies reassure us that once infants have achieved physiologic stability, NICU staff and families should not be afraid to hold and handle them. A sensible approach is to incorporate movement and gentle tactile, vestibular and kinesthetic stimulation into therapeutic holding, positioning and handling preterm infants in a NICU.

NON-NUTRITIVE SUCKING

Non-nutritive sucking behavior is present in the preterm infant as early as 27 weeks gestation [Håfström and Kjellner, 2000].
and Kennel [1982] recognized the importance of the time immediately following delivery, when the infant is generally in a quiet alert state and both mother and infant are most receptive to bonding. When given the opportunity to hold their baby for the first time, mothers look into the baby’s eyes, talk to them and examine them, from head to toe. Failure to form an attachment during the first few weeks and months, or disruption of the attachment process, leads to a higher risk of abuse and neglect of the dependent infant. Because this process is disrupted when the infant is sick or premature, NICU staff realized that they had to promote family involvement in the care of their preterm infant. Because this process is disrupted when the infant is sick or premature, NICU staff realized that they had to promote family involvement in the care of their preterm infant.

**Family-centered NICU care, the ideal for which most NICUs strive, promotes family involvement in child care activities and empowers parents to nurture their child even in the highly technical NICU environment.**

FAMILY INVOLVEMENT

An essential component of any neurodevelopmental intervention program is family involvement. Parent involvement in the care of preterm infants has varied markedly during the last century. Pierre Budin promoted maternal involvement in the care of their preterm infants in his book Les Nourrissons published in 1900 (in English in 1907). Subsequent endeavors focused on technological details of preterm care, including feeding and temperature control in isolettes. Most early preterm nurseries tended to isolate preterm infants from their families who were often unable to visit their infants because of distance and other factors. Typically, preterm infants who survived delivery at home would be transported to the nursery (by the family, or in some cases by specialized transport vehicles staffed and maintained by the nursery). When the infant had grown and developed sufficiently to be discharged from the nursery, the parents would be notified to come pick up their infant.

The importance of parent involvement in the care of their preterm infant became clear when tertiary care centers noted a high incidence of child abuse and neglect in these preterm children. Klaus and Kennel [1982] recognized the importance of the time immediately following delivery, when the infant is generally in a quiet alert state and both mother and infant are most receptive to bonding. When given the opportunity to hold their baby for the first time, mothers look into the baby’s eyes, talk to them and examine them, from head to toe. Failure to form an attachment during the first few weeks and months, or disruption of the attachment process, leads to a higher risk of abuse and neglect of the dependent infant. Because this process is disrupted when the infant is sick or premature, NICU staff realized that they had to promote family-infant attachment by providing opportunities for parents to visit, hold and talk to their infant. Recognition came much later that the NICU is often an ideal place to work with young and inexperienced mothers on parenting skills and developmental support of their infant.

Family-centered NICU care, the ideal for which most NICUs strive, promotes family involvement in child care activities and empowers parents to nurture their child even in the highly technical NICU environment [McGrath, 2000]. In an effort to provide family-centered care, most NICUs have twenty-four hour a day visiting policies for parents, encourage sibling visitation, have parental support groups and attempt to arrange specific child care activities, like nipple feeding, bathing and time for kangaroo care, around parents schedules. Decoration of their infant’s isolette with family pictures individualizes the infant by enabling staff to picture the infant as part of a family.

Although most would agree that parental participation in child care during the NICU hospitalization is essential for parental coping and promotes a long-term healthy parent-child relationship, how this participation occurs remains one of the biggest challenges to NICU care. Family-centered care assumes that parents want to be actively involved in the day-to-day care and decision-making regarding their child. The literature suggests however, that many parents do not wish to assume this level of responsibility [Coyne, 1995]. Some parents are comfortable providing nurturing care such as holding, comforting and feeding but do not want to perform tasks that NICU nurses perceive as part of the child’s daily care, such as changing dressings, giving medication and trouble shooting equipment alarms. These differences in perceptions make providing family-centered care particularly challenging for NICU nurses. Family-centered care requires a partnership between parents and the NICU staff with both parties realizing that every child and family is different and what works for one may not work for another.

**BREASTFEEDING**

Breastfeeding is one of the primary ways mothers can be involved in their child’s care from the time of birth throughout the NICU hospitalization. Breastfeeding or providing pumped breastmilk allows mothers to nurture their child when there is little else they can do [Meier, 2001]. Mothers who have been encouraged to breastfeed report that providing breastmilk helped them cope with the NICU and kept them connected to their infant during the long hospitalization [Kavanaugh et al., 1997].
Breastfeeding is beneficial for both mother and child. Infants who are breastmilk fed have a reduced risk of infection and necrotizing enterocolitis [AAP, 1997]. Breastmilk may also provide a protective effect against the development of chronic diseases of the gastrointestinal tract and allergies [AAP, 1997]. When an infant cannot be put to the breast, bottle feeding breastmilk may decrease the risk of aspiration. Mizuno et al. [2002] has shown that newborns demonstrate a more coordinated suck/swallow/breathing pattern when bottle feeding breastmilk compared with bottle feeding formula or sterile water. Infants feeding breastmilk are much less likely to inspire after swallowing, a pattern which places the child at increased risk for aspiration, than when bottle feeding other liquids. Recent evidence suggests that duration of breastfeeding also exerts a positive effect on intelligence in young adults with mean adjusted scores on the Wechsler Adult Intelligence Scale of 99.4, 101.7, 102.3, 106.0 and 104.0 for those who were breastfed for less than 1 month, 2 to 3 months, 4 to 6 months, 7 to 9 months and more than 9 months, respectively [Mortensen et al., 2002].

Women who breastfeed have less postpartum blood loss, enhanced bone mineralization and a reduced risk of ovarian and breast cancer [AAP, 1997].

Mothers of NICU infants also report that breastfeeding allowed them to feel like they had some control over their child’s care and were directly contributing to their child’s well-being. Physicians and nurses are instrumental in a NICU mother’s decision to breastfeed. As many as 40% of mothers who are undecided about how they want to feed their child chose to breastfeed after talking with NICU staff about the benefits of breastmilk [Meier, 2001]. Speaking with other NICU mothers who have breastfed also plays an influential role in the decision to continue breastfeeding or providing pumped breastmilk throughout the NICU hospitalization [Meier, 2001]. Furman et al. [2002] reported that mothers of very low birthweight infants were more likely to continue to breastfeed beyond 40 weeks PMA if they began expressing breastmilk before 6 hours after delivery, pumped at least 5 times each day, and practiced kangaroo care.

KANGAROO CARE

Kangaroo care or skin-to-skin contact between mother and infant was developed in Bogotá, Columbia as a low cost way to assist low birthweight infants with thermal regulation and provide nutrition and stimulation [Charpak et al., 1996]. Patterned after marsupial caregiving behaviors, kangaroo care involves placing the naked infant against the mother’s bare chest, between her breasts, in an upright position for several hours a day and providing breastmilk only.

A Cochrane Review of kangaroo care [Conde-Agudelo et al., 2002] cited nine trials comparing kangaroo care with conventional care, only three of which were randomized [Sloan et al., 1994; Charpak et al., 1997; Cattaneo et al., 1998]. Each of the randomized trials was conducted in a developing country using a similar intervention protocol. In each study, infants were eligible for kangaroo care only after a period of routine care stabilization. On average, infants were randomized to conventional or kangaroo care at 3 to 13 days of age and weighed 1574 to 1715 grams. Kangaroo care was associated with a reduction in nosocomial infections (relative risk 0.49, 95% CI 0.25, 0.93), severe illness (relative risk 0.30, 95% CI 0.14, 0.67) and respiratory disease (relative risk 0.37, 95% CI 0.15, 0.89) at 6 months follow-up. Although encouraging, these data were provided by only one trial. There was no association with rehospitalization. Infants who received kangaroo care gained, on average, 3.6 grams more weight each day than those who did not received kangaroo care (weighted mean difference, 95% CI 0.8, 6.4), a small and probably clinically significant difference. Similarly, women who provided kangaroo care were less likely to discontinue breastfeeding prior to hospital discharge than those who did not (likelihood of not exclusive breastfeeding at discharge, relative risk 0.41, 95% CI 0.25, 0.68), but there was no difference between the groups at one and six month follow-up. Again, this endpoint was reported in only one trial. Mothers providing kangaroo care were less likely to be dissatisfied with NICU care (relative risk 0.41, 95% CI 0.22, 0.75) than those who did not in the single trial that studied this endpoint. Data concerning length of hospitalization is conflicting between the three randomized trials, providing no clear evidence that kangaroo care decreases duration of hospitalization.

Kangaroo care may provide protection from infection in the NICU environment, increase daily weight gain and improve maternal satisfaction with hospital care. Future research is needed to define how kangaroo care can benefit children and parents in developed countries.
because of these early experiences, preterm infants may have both structural and functional reorganization of their nervous system, similar to the effects seen in animal studies of prolonged pain exposure. This reorganization could result in long-term alterations in pain response [Anand, 1998; Grunau et al., 1998]. Clinical studies seem to support this hypothesis.

Lower gestational age and increased number of previous painful procedures were independently related to diminished behavioral and autonomic pain reactivity to an invasive procedure performed at 32 weeks PMA in two separate studies of preterm infants [Johnston and Stevens, 1996; Grunau et al., 2001]. Grunau et al. [1998] reported that at eight to ten years of age, extremely low birthweight children rated the perceived intensity of pain related to pictures of medical procedures (stitches in the arm) as higher than the perceived pain related to pictures of psychosocial embarrassing situations (reprimanded by teacher). This is in direct contrast to how their full-term peers rated the pain intensity in the two situations.

Morphine and fentanyl are the most commonly used pharmacological agents in the NICU for pain management [Stevens et al., 2000]. Both drugs provide analgesic effects for mild to severe pain in neonates as agonists for endogenous opioid receptors. Although concern about respiratory depression has historically limited use of these analgesics, recent evidence suggests that morphine may be beneficial to the neurological outcome of preterm infants. Anand et al. [1999] reported a decreased incidence of death, severe IVH or PVL among preterm infants that received continuous, low-dose morphine (4%) when compared to infants that received either midazolam (32%) or 10% dextrose (24%). In contrast, animal studies of mice and one study of preterm infants has suggested that fentanyl may increase the risk of PVL [Gressens et al., 2002]. Other pharmacologic agents are available to reduce pain in the NICU setting, including non-opioid analgesics such as acetaminophen and topical anesthetics such as EMLA.

Oral sucrose is the most widely studied non-pharmacological intervention for pain relief in neonates. There have been 17 randomized controlled trials that meet Cochrane Review criteria that compared physiologic and behavioral responses, and scores on pain scales between infants given oral sucrose and those given placebo (generally water) after a heelstick or venapuncture [Stevens et al., 2002]. Eleven out of twelve studies that assessed crying as an endpoint reported decreased crying behavior for infants that received sucrose administration compared to controls. Seven of the eleven studies that assessed heart rate also reported decreased heart rate among infants receiving sucrose. The majority of studies (5/6) that used a behavior pain scale reported decreased scores among infants receiving sucrose. For the three studies that utilized the Premature Infant Pain Profile, a behavioral, physiologic and contextual measure of pain, scores were reduced for those infants receiving sucrose compared with controls at 30 seconds [weighted mean difference, −1.64 (95% CI−2.47, −0.81)] and 60 seconds after a heelstick [weighted mean difference, −2.05 (95% CI−3.08, −1.02)]. Only one of the four studies that evaluated adverse effects reported problems with sucrose administration; three infants had desaturations when receiving sucrose by syringe (this did not occur when given in conjunction with a pacifier) and 3 infants in the control group desaturated or choked when receiving water, with or without a pacifier. None of the infants required intervention. Sucrose administration appears to be a safe and effective strategy for reducing pain associated with blood drawing.

Additional research is critical to the development of a comprehensive approach to pain management in the NICU. Strategies must weigh the potential risks and benefits of both pharmacological and behavioral interventions without losing sight of the human factors of pain and suffering.

CONCLUSIONS

Providing neurodevelopmental support in a NICU is more than a protocol or an order list. It is an attitude that should be shared by every staff member and every discipline providing care to infants and families in the NICU. It should be shared by everyone who enters the NICU: visitors, technicians, maintenance workers and administrators should be cautioned to keep their voices low, avoid shining bright lights in an infant’s face, respect a family’s privacy and be supportive in any way they can. Some of the proposed interventions discussed in this review require a great deal of training, preparation, organization, time and money and their influence on neurodevelopmental outcome is uncertain. However, many others are inexpensive, non-time-consuming, family-centered interventions that can easily be implemented. Many can be incorporated into an infant’s care without taking extra time. Many merely involve changing how we do things or changing our attitude towards what we are doing.

Assessing each infant and individualizing care has been a central feature of many proposed intervention strategies, but NIDCAP has made a major contribution to the field by popularizing this concept. Preterm infants are individuals who differ a great deal with respect to size, maturity, medical status, nutritional status and neuromotor and neurobehavioral abilities. Their families also differ as to their needs, strengths, capabilities, degree of understanding of medical and neonatal intensive care, community supports and socioeconomic status. All supportive intervention, for the child and family, needs to be individualized for it to be most effective. The major challenge is to determine who benefits from which intervention, applied in what way for how long.

There is no doubt that one of the most effective neurodevelopmental interventions that a NICU can provide is to promote family involvement and guidance regarding neurodevelopmental support. Even the busiest NICUs with the sickest infants should not lose sight of their overall goals, and how important families are to these goals. Nurturing and enrichment experiences support a child’s development and have effects that continue throughout that child’s lifetime. Every NICU should be easily accessible to families, value effective parent communication, have a sibling visitation program and provide guidance to parents in how they can support their infant’s neuromaturation.

Efforts to determine efficacy and effectiveness of specific NICU neurodevelopmental interventions have continued over the last two decades, utilizing a variety of outcomes. What are we trying to change when we introduce interventions? Primary outcome variables are measures of cognitive, neuromotor and neurosensory abilities generally obtained at 1-2 years or later. A less expensive and time-consuming approach has been to utilize variables related to earlier discharge to a more nurturing environment (i.e., home or a convalescent care unit). Many studies therefore utilize length of hospital stay, weight gain and duration of mechanical ventilation or supplemental oxygen. A few studies have directly measured the preterm infant’s neurobehavioral status at term or NICU discharge, but how these measures relate to later neurodevelopmental outcome remains a question. Rate of neuromaturation has not been specifically measured or used as
outcome measures. The work that has been done raises many questions that require further research.

The fragility and health of the preterm infant and family must be taken into account when formulating a plan for neurodevelopmental support. Any interventions that pose a degree of risk to the fragile preterm infant must be postponed or abandoned. A central feature of neurodevelopmental support is that it must be individualized. There is no doubt that there is an exciting potential to design the NICU and neonatal intensive care of infants and their families in a way that enhances normal CNS development, supports recovery from CNS injury and protects the developing CNS from further injury.

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