Fragile Infant Forums for Implementation of IFCDC Standards: Neuroprotection - Protecting the Developing Brain

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Background:

The term *neuroprotection* did not originate in the neonatal intensive care unit (NICU) or direct reference to the care of high-risk infants; yet today, many NICUs across the US are implementing strategies and policies focused on protecting the developing brain. Neuroprotection is an appropriate consideration for all hospitalized babies. This article will use the acronym "NICU" whether the baby is in a Newborn Intensive Care Unit or another Intensive Care Unit. Neuroprotection was *coined* in the laboratory to characterize substances or strategies capable of preventing cell death, such as using different substrates or pharmacologic interventions to stabilize the cell and its membranes. This is particularly important since preventing cell death in the brain appears to have both short- and long-term neurodevelopmental implications. (1) Over time, the clinical definition of neuroprotection has evolved to be more inclusive of multiple strategies or therapies that protect the neurophysiology of the brain. These interventions can be inclusive of organizational, environmental, and direct therapeutic caregiving interventions.

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The NICU environment is often overwhelming and overstimulating to parents, infants, and providers. Alarms, conversations, pumps, and equipment emit sounds and light, yet each contributes to lifesaving care. Given the nature of the NICU environment and the desire to offer the best care possible, NICU professionals have long recognized the need to mitigate these harmful effects. That is where developmental care and neuroprotection come together to support the infant experiencing life in the NICU with neuroprotective strategies and nurturing interventions. On this foundation, neuroprotective strategies have grown in prominence in the NICU. Every interaction between the infant and caregiver contributes to neurodevelopment. It requires that we, as providers and teachers of caregivers, offer developmentally appropriate care to each infant so that the cumulative effect of these interactions and interventions optimizes outcomes.

Neuroprotective strategies are being implemented in various clinical settings and continue to be studied across several disease trajectories and populations. As the findings from this research grow, so does our understanding of the importance of neuro-connectivity and how oxygen deprivation plays a role in cell death and other insults. In addition, scientists are uncovering more strategies to enhance neuro-connections and repair connections that may have been broken. (2) We know that some connections are broken more easily, and connections that are used more often become stronger over time, and those that are used less often become weaker; thus, those weaker connections can be broken more easily.

For the high-risk infant, the need for neonatal intensive care occurs during a critical window of brain development. While it is possible that neonatal intensive care itself could be characterized as

neuroprotective, it is more likely that certain caregiving activities may be neuroprotective while others may weaken brain connections or lead to brain injury. Many neonatal therapies used in the NICU save lives but often have a neurologic cost. The brain of a preterm infant is neurologically immature and not prepared for the overstimulating, bright, and stressful environment of the NICU. Evidence describing the early life stress experienced by preterm infants in the NICU is growing and is helping to shape how best we choose and implement newborn intensive care strategies and therapies. (2-4) This knowledge is also helping us to focus neonatal care with a greater emphasis on supporting neurophysiology and neuro-connections. The growing emphasis on best-supporting neuro-synaptic and neuropathway development can be seen in the inclusion of neuroprotective language in family-centered care and other developmental care models. In these frameworks, neuroprotective strategies aim to support the developing brain and have implications for promoting normal development while at the same time preventing disability. (5, 6) These interventions may begin antenatally and continue through the perinatal and postnatal period, including delivery room, NICU, and post-NICU interventions. (1)

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Supporting the evolving neurophysiology of the newborn brain is often referred to as supporting and enhancing neuroplasticity. (7) Neurons in the brain always respond to experiences internally, such as signals from other organs in the body, like those of the brain-gut connection, and externally, such as those that occur within the caregiving environment. Whether the preterm brain is developing in or outside the womb, it is a time of rapid growth for brain cells and the creation of neuropathways. Furthermore, the preterm brain is remarkably plastic (malleable) given the increasing numbers of brain cells, and environmental and human exposures are shaping the neuro-connections. Some brain cell death is normal during this time, yet how the brain is wired together is so important to later development. Proper wiring of neural circuits (neuro-connections) during development depends on internal molecular cues and activity-dependent environmental cues. These stimuli activate and adjust the strength and number of synaptic connections and, as such, shape the overall development of the brain.

Neuroprotective Strategies in the NICU:

Provision of neuroprotective care places emphasis on brain care, which may be a cultural shift for some NICU care providers. (5, 8) *how is it a shift?* Just as recent evidence conclusively demonstrated that infants feel pain (9), there is a greater emphasis on comfort and decreasing painful experiences in the NICU. Similarly, the evidence for how particular care strategies in NICU impact neuropathways are gaining traction and influencing the implementation of routine care practices.

NICU professionals need to consider how their NICU environment currently supports neuroprotective strategies. There are likely current strategies, therapies, and even standards of care that are neuroprotective and developmentally supportive. Using the term neuroprotective to describe these interventions helps us to reflect and consider the impact of our care on the developing brain. We must recognize that for many years, NICU professionals have strived to implement developmentally supportive care based on the seminal work of Dr. Als and her Synactive Theory of Development. From this work, more attention was placed on reading infant cues, positioning, bundling of care activities, attention to sound, stimulation, and treatments provided to NICU infants.

Nevertheless, developmentally supportive care has often been viewed as those 'nice to have' and not 'must-have' activities. With the growing attention to neuroprotection, many NICU professionals are calling for a reconceptualization of developmentally supportive care – which is, in fact, neuroprotective. It is not possible to have one without the other. This reconceptualization calls for *all* neonatal care to be viewed as developmentally appropriate and neuroprotective. This means providing caregiving activities so that the potential effect on the developing brain is foundational to decision-making, such as choosing when to add or delete an intervention.

For example, implementing Golden Hour activities following a high-risk delivery decreases risks for neurologic disability by decreasing the occurrence of intraventricular hemorrhage in the short term and enhancing overall developmental outcomes in the long term. (10) These activities might include the judicious implementation of admission activities, such as keeping noise and activity to a minimum, using humidity to support skin development, and early skin-to-skin activities for newborns and their parents. (11)

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The importance of the family, parents or other social connections on neuropathways cannot be emphasized enough. (12-14) Unlimited parental presence in the NICU is a neuroprotective strategy, regardless of family needs, social status, or ability. Strategies such as skin-to-skin and the Eat, Sleep, Console protocol for substance-exposed infants are care bundles focused on neuroprotective care. It has been well demonstrated that infants with the opportunity to engage in skin-to-skin, or "kangaroo care," demonstrate greater physiologic stability and better developmental outcomes. (14, 15) Just as neuropathways create connections between a vast network of cells, similarly, neurodevelopment relates to many other health and developmental outcomes such as

stress resilience, sleep integrity, parental bonding (15), and autonomic stability. Thus, supporting neuroprotection through developmentally sensitive and appropriate care supports all aspects of an infant's health and development.

Efforts to implement neuroprotective strategies and unlimited parental presence also present the opportunity to improve health equity in the NICU. If every baby routinely receives individually tailored, developmentally appropriate, and neuroprotective care, we may be able to close the gap in racial and ethnic disparities in infant outcomes. This will likely require NICU professionals to take an uncomfortable view of how systemic racist practices may be present in the current NICU climate. For instance, are there differences in rates of chestfeeding in your NICU? Do certain groups of parents engage more with infant care? Are certain procedures recommended more or less to certain infants? Is pain relief adequately administered across all infants based on their medical conditions? Answering these questions, where known disparities persist, is the first step in addressing systemic racism in healthcare and our neonatal community. There are a few NICUs in the US where nurses have instituted health equity initiatives, such as monthly seminars and workshops that provide opportunities for discussion, growth, and elimination of bias in healthcare. These initiatives are a great starting place to bring awareness to cultural issues and begin the work of dismantling racist practices and advancing health equity.

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Conclusions:

Embracing new technology or equipment can sometimes be easier to integrate into neonatal care than examining the *how* and *why* of neonatal practices and therapies. The Vermont Oxford Organization, a national NICU quality collaborative, has coined the phrase *"all care is brain care"* to help caregiving professionals consider best practices in delivering NICU strategies. We want to extend this phrase by saying that *all care is developmental care and developmental care is neuroprotective*. This includes administering medications, infant positioning, feeding behaviors, responding to an infant's cues, and encouraging parent-infant interaction. It also may be as simple as implementing protocols for better blood draws from a heal stick, how and when antibiotic treatment is provided, or how a nasal gastric tube is placed. Additionally, the strategies can be more complex such as examining how a high-risk infant is admitted to the NICU (i.e., golden hour protocols), integrating interventions based on their level of intrusiveness, or complimenting neonatal care with positive touch times for infants via, touch and massage strategies.

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Our goal as NICU professionals is to empower infants to engage, mature, and thrive in their world rather than tolerate or defend themselves. No matter what name or label is given to the type of care you provide, every interaction with a NICU infant influences their growth and development, and with our actions, we have the opportunity to provide developmentally supportive care or not. Integration of neuroprotective strategies during the newborn period means taking advantage of what is known about neural plasticity and aligning neuroprotective strategies during this critical period in development when the brain is malleable. The growing attention on neuroprotection in the NICU provides the space for caregivers to influence neural connectivity and enhance long-term developmental outcomes positively. We conclude by encouraging neonatal caregivers and scientists to explore more opportunities to make the most of the *potential* of the developing brain during intensive caregiving. We cannot emphasize enough how everything we do -- does matter!

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