



## Nursing Continuing Professional Development

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# Nurse-Driven Interventions for Improving ELBW Neurodevelopmental Outcomes

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### ABSTRACT

Survival rates for extremely low-birth-weight (ELBW) infants are improving as neurodevelopmental impairment (NDI) rates stay stable, thereby increasing the overall number of infants with NDI. Although there are many determinants of NDI in this population, nutritional factors are of interest because they are readily modifiable in the clinical setting. Nurses can influence nutritional factors such as improving access to human milk feeding, using growth monitoring, establishing feeding policies, implementing oral care with colostrum, facilitating kangaroo care, and providing lactation education for the mother. All of these measures assist in leading to a decrease in NDI rates among ELBW infants.

**Key Words:** extremely premature infant, growth and development, human milk, infant nutrition disorders, neonatal intensive care unit, neonatal nurses, neurodevelopmental disorders

Innovations in neonatal care have allowed for improved survival rates for extremely low-birth-weight (ELBW; <1 kg) infants, with the most significant improvement reported in infants 23 to 24 weeks of gestation from 1992 to 2012.<sup>1,2</sup> Unfortunately, because

neurodevelopmental impairment (NDI) is inversely related to gestational age, more surviving ELBW infants means that the rate of NDI increased during this period.<sup>1,3–5</sup>

Of all preterm infants, 25% develop moderate to severe NDI by age 2, and up to 50% develop mild NDI; these impairments include movement disorders such as cerebral palsy, learning disabilities, language delays, and/or behavior disorders.<sup>5,6</sup> Preterm birth accounts for more than 50% of cerebral palsy diagnoses, 15% to 20% of intellectual or developmental delays, and 10% to 15% of autism spectrum disorders.<sup>3</sup> Although there are many determinants of NDI in this population, nutritional factors are of great interest because they are more readily modifiable in a clinical setting.<sup>7</sup>

To support brain growth in the ELBW infant, adequate nutrition is paramount. Growth at both ends of the spectrum, too slow or too fast, can cause long-term sequelae for the neonate and thus must be carefully regimented and monitored.<sup>7–14</sup> To promote ideal infant nutrition, mother's own milk (MOM) is the best diet choice<sup>15–17</sup> and can improve brain growth<sup>18</sup> and neurodevelopmental outcomes<sup>19</sup> in preterm infants. In the absence of MOM, the American Academy of Pediatrics (AAP)<sup>15</sup> recommends the use of donor human milk (DHM). DHM is inferior to MOM; however, the alternative of preterm formula (PF) lacks immune support and nonnutritional components of human milk.<sup>15</sup> Additionally, the use of PF increases the risk of feeding intolerance, sepsis, and necrotizing enterocolitis (NEC) and therefore is not the first choice of diet.<sup>20–22</sup>

Nurses are of the upmost importance in promoting evidence-based care.<sup>23</sup> To promote growth of neonates in the neonatal intensive care unit (NICU), nurses can provide accurate anthropometric measurements to guide nutritional improvements,<sup>10</sup> promote evidence-based feeding policies,<sup>24</sup> and support breastfeeding NICU mothers.<sup>25</sup> Therefore, the purpose of this article is to summarize current information and provide guidance

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on many nurse-driven, low-cost methods that can guide nutrition practices and support human milk feeding, thereby working to decrease NDI rates among ELBW infants. A general search of the literature was conducted over time and completed on August 1, 2021, by the first author. The search was conducted using OVID Medline, Google Scholar, and CINAHL databases. Studies related to ELBW growth and neurodevelopmental outcomes as well as nurse-driven interventions that support ELBW growth were reviewed. See the Table 1 for the general topics identified as relevant to nursing care related to supporting growth of ELBW infants.

## MEASURING GROWTH IN NEONATES

In utero fetal growth rates are the historical standard for ELBW infants' ideal growth trajectories since 1977 but may not be appropriate indicators of successful growth in ELBW infants and are challenging to attain.<sup>26–28</sup> Although postnatal growth failure rates are improving, half of ELBW infants at discharge still exhibit postnatal growth failure and do not meet the standards of the 1977 AAP guidelines demonstrating the urgent need for improved nutrition.<sup>29</sup>

Instead, acknowledging that growth is not constant throughout gestation and using an evidence-based growth chart, such as the Fenton,<sup>30</sup> may more accurately guide expectations for growth velocity, or growth measurements over time.<sup>31</sup> Once underlying growth expectations and patterns are understood, nutrition can be meaningfully improved using international guidelines for infant growth, weight, length, and occipital frontal circumference (OFC). These measurements should be obtained at least weekly to follow growth velocities and alter diets as needed to improve outcomes.<sup>11,32</sup> Growth velocities are a better indicator of each neonate's nutritional accretion than a single measurement in time.<sup>11,32</sup>

Weight, length, and OFC are all pieces of the nutritional puzzle. Using only a single measure, such as weight, which correlates with brain growth but does not distinguish lean mass from adipose tissue, can lead to a short-stature, heavy infant.<sup>7</sup> Importantly, weight gain, in the absence of linear growth, does not improve neurodevelopmental outcomes.<sup>14</sup> Length is also an important measurement as it indexes with skeletal growth, lean body mass, and organ growth.<sup>9</sup> OFC is a rudimentary approximation for brain growth.<sup>9</sup> For the

**Table 1. Nursing interventions to support ELBW growth and nutrition and decrease NDI**

Nursing intervention	Rationale
Use a length board for precise measurements vs a tape measure	Length board provides more accurate measures, which allow for tracking of neonatal growth <sup>10</sup>
Support and follow a uniform feeding policy for ELBW infants	Use of feeding policies has shown to improve growth and decrease NEC <sup>24</sup>
Support early initiation of enteral feeds	Early enteral nutrition has been shown to improve neurodevelopmental outcomes <sup>41</sup>
Support human milk fortification	Fortification improves nutrient delivery, especially protein to ELBW infants <sup>42</sup>
Offer DHM as a bridge to MOM	DHM diet increases feeding tolerance, decreases the risk of NEC, and decreases NDI when compared with formula <sup>69</sup>
Promote MOM even during maternal COVID-19 infection or after COVID-19 vaccination	Mothers can safely provide pumped human milk during COVID-19 infection by using universal precautions, <sup>79</sup> and maternal COVID-19 infection and COVID-19 vaccination provide antibodies to COVID-19 in MOM <sup>81,82</sup>
Teach mothers how to pump as soon as possible after delivery and continue to provide lactation support during NICU admission	Mothers should be taught to express milk using a hospital-grade, double electric pump every 2-3 h day and night for about 20-min each session to promote an adequate supply of 720-1050 mL per day by 2 wk postpartum. <sup>94–96</sup> These practices improve the rate of breastfeeding at discharge, which is associated with decreased NDI. <sup>97,98</sup>
Encourage colostrum for oral care	This practice is safe, and it improves infant outcomes, increases MOM supply, and increases breastfeeding rates at discharge and through 6 wk of life <sup>99–101</sup>
Support skin-to-skin holding for caregivers	Skin-to-skin holding has been shown to increase milk supply, improve bonding, reduce maternal stress, improve neonatal growth, and decrease neonatal infections <sup>102, 103</sup>

Abbreviations: DHM, donor human milk; ELBW, extremely low-birth-weight; MOM, mother's own milk; NDI, neurodevelopmental impairments; NEC, necrotizing enterocolitis; NICU, neonatal intensive care unit.

ELBW infant, slow growth in any of these 3 areas of measurement is associated with an increase in NDI.<sup>7,9,14</sup>

### Anthropometric practice

Anthropometric measurement practices in the NICU vary widely and lead to inaccuracies.<sup>10</sup> To improve reliability, INTERGROWTH-21st guidelines recommend each measure be done by 2 trained professionals and compared.<sup>11</sup> Length measurement guidelines dating back to 1931<sup>33</sup> support the use of a length board for precise measurements, but a recent study of measurement practices in the NICU found that only 19.4% of nurses used a length board versus a tape measure.<sup>10</sup>

### NUTRITIONAL CONCERNS

Providing sufficient nutrition during the first year of life has profound implications for brain growth and neurodevelopment. However, too much growth too fast can also cause long-term harm, as first reported by Barker and associates in 1989.<sup>8</sup> The “Barker hypothesis” describes the association between low-birth-weight (LBW) and a higher risk of coronary heart disease, hypertension, and arteriosclerosis in adulthood. LBW infants often have a period of rapid growth (catch-up growth) that may create a potential for insulin resistance, obesity, and cardiovascular diseases.<sup>8,12,13,34</sup> This phenomenon has also been described for ELBW infants.<sup>35–37</sup> Therefore, close monitoring of excessive growth is essential.

### Feeding policy

One way to support appropriate anthropometric progression is to standardize nutrition delivery via a feeding policy. A recent systematic review by Jasani and Patoli<sup>24</sup> found a significant decrease in NEC, a severe intestinal disease that affects about 10% of ELBW infants, with the use of a standardized feeding policy. The review did not give specific details of the feeding policies but explained that by simply standardizing the progression and fortification of feedings in the NICU, the incidence of NEC decreased, and growth improved. It is important to note that NEC significantly increases the risk of NDI for preterm infants.<sup>38</sup> The best practice is to use MOM as much as available, start early, and increase prescriptively as tolerated using bolus feeds, as delays in full oral feeds increase the infant’s length of stay.<sup>24,39,40</sup> Early enteral feeds have been shown to improve neurodevelopmental outcomes in ELBW infants.<sup>41</sup>

### Fortification

For preterm infants born at less than 1800 g, feedings should be fortified as the standard of practice to support

their growth.<sup>42–44</sup> Adding a human milk fortifier (HMF) to MOM or DHM increases macronutrients, especially protein, to improve nutrition delivery to the ELBW infant.<sup>42</sup> Recent literature shows enteral feeds can safely be fortified as early as 60 mL/kg/day.<sup>45</sup>

One option for human milk fortification is a bovine-based HMF. In a systematic review, human milk fortified with bovine-based HMF versus unfortified human milk increased in-hospital growth slightly, but did not improve cognitive outcomes.<sup>46</sup> Another option is a human milk-based HMF that is made from pasteurized DHM.<sup>47</sup> Since human milk is better tolerated and the chosen diet for ELBW infants,<sup>15</sup> human milk-based HMF appears ideal. However, currently, evidence of the superiority of human milk-based HMF over bovine-based HMF is insufficient.<sup>48</sup> Overall, human milk-based HMF is considered a safe and promising alternative to bovine-based HMF.<sup>48</sup> Due to the higher cost of human milk-based HMF, more evidence is needed before it becomes recommended for use. An additional factor to consider is that the volume of human milk-based HMF is greater than that of bovine-based HMF and can displace more MOM than bovine-based HMF, resulting in a decreased amount of MOM fed to the infant.<sup>49</sup>

### CHOICE OF DIET

The choice of diet also alters the growth trajectory and tolerance of feedings. The choices for enteral feeding in ELBW neonates are MOM, DHM, or PF. Of note, the macronutrients and micronutrients in both MOM and DHM vary, whereas PF is standardized (see the Figure 1).

MOM	DHM	PF (Similac Special Care 20)
<ul style="list-style-type: none"> <li>Day 1-3               <ul style="list-style-type: none"> <li>2.7 grams protein</li> </ul> </li> <li>Day 4-7               <ul style="list-style-type: none"> <li>1.6 grams protein</li> <li>3.5 grams of fat</li> <li>68 kcal Total calories</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>0.9-1.3 grams protein</li> <li>2.2-3.5 grams of Fat</li> <li>62-67 kcal Total calories</li> </ul>	<ul style="list-style-type: none"> <li>2 grams protein</li> <li>3.6 Fat</li> <li>67 kcal Total calories</li> </ul>
Abbreviations: MOM, mother's own milk; DHM, donor human milk; PF, preterm infant formula. *All measurements are per 100 milliliters.		

**Figure 1.** Macronutrient comparison of diets.<sup>51,64,66,105–107</sup> All measurements are per 100 mL. DHM indicates donor human milk; MOM, mother's own milk; PF, preterm infant formula. This figure is available in color online ([www.jpnnjournal.com](http://www.jpnnjournal.com)).

## Mother's own milk

As the ELBW infant grows and develops, macronutrients of human milk change over the duration of each mother's lactation. For example, MOM for ELBW infants is higher in fat, protein, and carbohydrates compared to MOM for late preterm and term infants.<sup>43,50</sup> MOM also changes in response to stress, maternal diet, and the time of day, among other factors.<sup>43,51</sup> The fat content of human milk also varies significantly from the beginning to the end of each milk extraction as well as over the weeks and months of lactation.<sup>51</sup> Despite all the variation, MOM is still superior in improving long-term neurodevelopmental outcomes.<sup>18,52–56</sup>

Human milk has an optimal bioavailability of components, rendering it easier to tolerate and digest.<sup>22</sup> Feeding intolerance is a significant iatrogenic contributor to postnatal growth failure for ELBW infants, as it often results in frequent starts and stops to enteral feeds<sup>57</sup> and postnatal growth failure increases the risk of NDI.<sup>40</sup> MOM, in contrast to PF, also contains nonnutritional components that help with the immune system and tolerance of feedings, including anti-infective factors, immunoglobulins, stem cells, enzymes, electrolytes, hormones, pre- and probiotic properties, and antioxidants that can decrease inflammation and its associated conditions.<sup>22</sup>

## Donor human milk

Many benefits of a human milk diet are conferred by DHM. These include being easy to tolerate and digest as well as immunologically protective.<sup>58</sup> However, DHM may be lower in calories than MOM or PF, as DHM is often donated near the end of a mother's lactation journey and, therefore, lower in macronutrients, which can lead to poor growth.<sup>51,59</sup> For this reason, 2 to 5 DHM samples are pooled before pasteurization to help with the variability of nutrients.<sup>51</sup> Because DHM is lower in macronutrients, namely protein, some suggest DHM may need fortification beyond that required for MOM.<sup>60,61</sup> Nonetheless, having DHM available in NICUs has been shown to improve breastfeeding rates at discharge by 10% to 13% compared with units where DHM is not available.<sup>61,62</sup> The reason for this association is unclear but may be due to NICU staff's acknowledgment of the importance of human milk for ELBW infants and subsequent support of the mother to provide MOM. A systematic review and meta-analysis by Williams et al<sup>63</sup> found an overall increase in MOM administration rates at measured time points when DHM was used for supplementation; however, 1 of 10 included studies showed a decrease in the use of MOM when DHM was available. The motive for initiation of DHM availability varied in studies and may explain why one

study found a decrease in MOM use at measured time points.

Before arriving at the ELBW infant's bedside, DHM undergoes many processes that render it less nutritive than MOM. Fat is often lost in DHM, as it is not homogenized, and it undergoes multiple container changes, leaving small amounts of adhered fat in each container.<sup>58</sup> During pasteurization, DHM also loses many bioactive components.<sup>51,64</sup> To retain the highest fat and biofunctionality of DHM, such as antimicrobial and growth-promoting activity, it should be used within 3 months of expression.<sup>65,66</sup> Newer methods of pasteurization show promising results in maintaining more bioactive components of DHM, but further research is needed to evaluate their effectiveness and feasibility on a larger scale.<sup>67</sup>

Offering DHM as a bridge, an inferior yet safe short-term alternative while the mother establishes her milk supply, can motivate mothers to pump.<sup>62,64</sup> Using DHM as a bridge for MOM has been shown to increase the rate of MOM use by 10% and decrease the rate of NEC by 2.6%.<sup>62</sup> While using DHM, healthcare providers must account for variations in macronutrients that may require higher amounts of fortification to meet each infant's caloric needs.<sup>68</sup> Overall, a DHM diet increases feeding tolerance, decreases the risk of NEC and, therefore, decreases NDI when compared with formula.<sup>69</sup>

## Preterm formula

PF differs from full-term infant formula, as it is higher in protein, minerals, and calories, which are helpful for the ELBW infant's growth.<sup>4</sup> PF supports faster growth but does not improve cognitive outcomes.<sup>69</sup> PF also increases the risk of NEC, which increases the risk for NDI.<sup>1,70</sup> The only confirmed measure for decreasing the risk of NEC is an exclusively human milk diet.<sup>15,20,58,65,71</sup> Infants fed formula are at almost twice the risk of developing NEC than those fed human milk.<sup>69</sup> For this reason, PF is used with caution in ELBW infants.

## COVID-19 influence

The demand for DHM is increasing, but a current concern is that DHM donations may decline owing to the coronavirus disease-2019 (COVID-19) pandemic. Physical distancing restrictions and fewer donations pose unique challenges for collection sites, prompting concern that DHM may not be shipped to banks for timely processing.<sup>72</sup> Creative measures, such as home visits to draw donating mothers' blood for testing and pickup options for donated milk, can be taken to ensure mothers may continue to donate human milk safely and in a timely manner. Knowing that DHM remains the best alternative to MOM, many units are revising their

feeding policies to only use DHM for infants under 1500 g in anticipation of a potential shortage.<sup>72</sup> Furthermore, DHM should still be regarded as safe, as COVID-19 is inactivated with the current pasteurization process.<sup>73</sup>

Clinical guidelines for mothers during the COVID-19 pandemic have varied.<sup>74</sup> However, human milk remains the best choice of diets for all infants<sup>75–77</sup> and risk of COVID-19 neonatal infections is low.<sup>78</sup> If pumping mothers become infected, they should continue to pump while taking extra precautions to wash their hands before expressing milk, wear a face covering while expressing milk, and clean all pump parts after each use.<sup>79</sup> If the mother chooses to receive the COVID-19 vaccine, it is safe to continue breastfeeding.<sup>80</sup> Additionally, providing human milk during COVID-19 infection or after vaccination may protect the infant, as anti-SARS-CoV-2 immunoglobulin A had been detected in MOM.<sup>81,82</sup>

## DIET AND NEURODEVELOPMENTAL IMPAIRMENT

Nutrition during the NICU stay has lasting implications for the ELBW infant, especially during the first 2 weeks of life. Studies have found that higher protein and calorie intake in the first 1 to 2 weeks of life positively correlated with improved neurodevelopmental outcome scores by 2 years of age.<sup>83</sup>

ELBW infants have many complications, aside from nutrition, that increase NDI. Intraventricular hemorrhage, periventricular leukomalacia, infections, sepsis, meningitis, and posthemorrhagic hydrocephalus are commonly reported conditions in ELBW infants with poor long-term neurodevelopmental outcomes.<sup>84–86</sup> The incidence of these disorders increases as gestational age decreases. Even in the absence of a significant brain injury, ELBW infants are at higher risk for NDI.<sup>87</sup>

Prevention of NEC is of great importance, as it can be deadly to the ELBW infant<sup>69</sup> and increases the risk of NDI.<sup>70</sup> Feeding with MOM for greater than 50% of total feeds in the first 2 weeks of life significantly decreases the ELBW infant's risk of NEC.<sup>58,88</sup> The decrease occurs as the bioactive components in MOM protect the immature ELBW infant's gut by lowering gastric pH,<sup>89</sup> decreasing epithelial permeability,<sup>90</sup> improving intestinal motility,<sup>91</sup> and optimizing the microbiota.<sup>92</sup>

## Supporting mothers

Human milk is vital to decreasing NDI in premature infants. However, many mothers who deliver prematurely have problems achieving an adequate milk supply.<sup>93</sup> Some barriers to providing MOM are low milk production, difficulty expressing milk, and separation from the

infant.<sup>93</sup> Those who care for ELBW infants need to advocate and teach the benefits of breastfeeding, be aware of the risks associated with formula, and develop skills for supporting the breastfeeding dyad.<sup>15</sup>

The first step in supporting mothers of ELBW infants through their lactation journey is to educate them on the benefits of human milk for their infant shortly after birth and continue, as they navigate the establishment and maintenance of their milk supply. Mothers should be taught to express milk using a hospital-grade, double electric pump every 2 to 3 hours day and night for about 20 minutes each session to promote an adequate supply of 720 to 1050 mL per day by 2 weeks postpartum.<sup>94–96</sup> These practices improve the rate of breastfeeding at discharge, which is associated with decreased NDI.<sup>97,98</sup>

The second step to supporting mothers of ELBW infants is by using their colostrum for their infant's oral care. Expressing human milk for an ELBW infant can be overwhelming, but focusing on such a small volume needed for oral care is more feasible and can empower mothers to, hopefully, set the stage for a positive lactation experience. This practice is safe, and it improves infant outcomes, increases MOM supply, and increases breastfeeding rates at discharge and through 6 weeks of life.<sup>99–101</sup> For best absorption of colostrum immune components, 0.1 mL delivered by a needleless, tuberculin syringe in bilateral buccal cavities is recommended.<sup>100</sup>

The final step that encourages lactation in the NICU is kangaroo care, or skin-to-skin holding. Kangaroo care has been shown to increase milk supply, improve bonding, reduce maternal stress, improve neonatal growth, and decrease neonatal infections.<sup>102,103</sup> Once the infant is deemed stable by the medical team, the infant, dressed only in a diaper, should be held directly against the mother's bare skin for continuous, extended periods.<sup>103</sup> Contact between a mother and an infant, as achieved with kangaroo care and breastfeeding, allows for MOM leukocytes to change in response to neonatal infection, thereby providing immunity to the infant and perhaps explaining the decreased neonatal infections associated with this practice.<sup>104</sup> Kangaroo care is a low-cost, high-impact intervention that can change how parents interact with their ELBW infants.

## DISCUSSION

Many variables that effect neurodevelopmental outcomes in the NICU are not modifiable. However, supporting early nutrition with human milk, prioritizing MOM, to promote growth for ELBW infants *is* modifiable. As NICU care providers seek to improve nutrition and neurodevelopmental outcomes for ELBW infants, the amount of published literature is overwhelming. The information presented helps to provide guidance on

nursing practices that may improve ELBW infant neurodevelopmental outcomes.

### Implications for future study

Understanding the extremely complex nature of MOM and its benefits to the ELBW infant in their care may help NICU providers to support lactating mothers further. Also, studies that evaluate storage and administration on the components of MOM will be helpful to improve the process. Does offering fresh MOM confer more immunological benefits over frozen milk? Finally, studies evaluating the changing policies related to human milk use and breastfeeding, as well as shortages in DHM supply during the COVID-19 pandemic, will help the medical community prepare for future crises.

### CONCLUSION

As neonates grow and progress in the NICU, they are subjected to many experiences that can negatively affect the brain's maturation at a critical time, even when a direct insult has not occurred.<sup>6</sup> To mitigate the risk for NDI in ELBW infants, ensuring proper growth and nutrition is paramount. Keeping in mind that growth alone may not be enough to ameliorate NDI, the key to improving outcomes may lie in the multiple non-nutritional components of human milk. Following the evidenced-based recommendations provided here can help improve daily practices in a way that ameliorates the neurodevelopmental outcomes of the ELBW infants in our care.

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