Recent Litigation Regarding Necrotizing Enterocolitis

Jonathan K. Muraskas, MD, Jay P. Goldsmith, MD

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Necrotizing enterocolitis (NEC) is a disease seen primarily in preterm infants. One might consider NEC to be a single homogenous entity, but it is becoming clear that NEC is several different diseases or endotypes. NEC is the most common life-threatening gastrointestinal disease in preterm infants. Approximately 7-10% of all NICU admissions < 1500 grams are diagnosed with NEC. Mortality and poor long-term outcomes are significant, especially in surgical NEC. It is estimated that approximately one infant dies every day in the United States from NEC. The financial cost of NEC in the United States is staggering, with total annual costs approaching 1 billion dollars. Over the past three decades, the incidence of NEC has not significantly changed despite extensive research and quality improvement projects in NICUs. The specific etiologies and definitive preventative strategies have remained elusive. Epidemiologic observations strongly suggest multifactorial causes. Proposed mechanisms for NEC include ischemia (reperfusion), infection (gut colonization), mechanical injury (viscosity, embolic), iatrogenic (umbilical catheters, excessive or overaggressive enteral feedings), and immunological barrier dysfunction. Multiple risk factors have been associated with necrotizing enterocolitis:

- Formula feeding
- Asphyxia
- Intrauterine growth restriction
- Hypovolemia
- Hypothermia
- H2 blocker therapy
- Patent ductus arteriosus
- Maternal nicotine use
- Maternal cocaine use
- Packed RBC transfusions
- Maternal overuse of antibiotics
- Neonatal antibiotic use
- Preterm birth without maternal antenatal steroids
- AB blood type

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Human milk is widely considered the optimal form of infant nutrition and is endorsed by national and international health organizations. The fortification of human milk is indicated in infants with very low birth weight (VLBW) to provide sufficient protein, calories, and other elements necessary to optimize growth. Many neonatal intensive care units use bovine-based products to fortify human milk, but human milk-based fortifiers have allowed clinicians to provide infants exclusively with a human milk diet. A 2012 policy statement by the American Academy of Pediatrics titled "Breastfeeding and Use of Human Milk" referenced multiple studies that demonstrated the benefits of breast milk in reducing the incidence of NEC. (6) There has also been an evolution in the adoption of programs from this policy statement over the years, resulting in greater availability of donor milk and milk banks. Most currently available preterm formula attempts to mimic and even improve the composition of human milk concerning energy, protein, lipids, and micronutrients needed for the growth and development of preterm infants. These formulas, however, do not provide the highly bioactive components of human milk such as secretory IgA, lysozyme, lipase, alkaline phosphatase, human milk oligosaccharides, polyunsaturated fatty acids and platelet-activating factor-acetyl hydrolase. These components of human milk contribute to GI mucosal integrity and function and provide immunity against various infections. (7) Preterm infant formula is primarily used in liquid form in neonatal intensive care units and designated for use at 20, 24, and 30 kcal/oz. Cow milk-based fortifiers derived from nonhydrolyzed or extensively hydrolyzed protein are usually used to add 4 kcal/oz to human milk. A third type of cow-based formula is designated as transitional or post-discharge for home or hospital use. (8) Fortification of human milk is indicated for very low birthweight infants to provide sufficient protein, calories, and other elements necessary for optimal

growth. Many neonatal intensive care units continue to use bovine-derived human milk and bovine-derived fortifiers despite the controversy regarding its use and the incidence of NEC. Many NICUs discontinue donor milk feeds and human milk fortifiers after 34 weeks post-conceptual age. A recent study found that human milk-based fortifiers were not superior to bovine milk-based fortifiers. (9) A recent randomized controlled trial demonstrated no difference in developmental outcomes in extremely premature infants fed donor milk or preterm formula. (10)

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There have been at least 750 lawsuits filed to date, as well as some legal judgments because preterm infants who were fed cow-based formula or fortifier developed NEC. In a July 2024 court decision in St. Louis, Missouri, Abbott Laboratories was found liable for both punitive damages and economic damages totaling $495 million for the use of their bovine-derived formula in premature neonates who developed NEC. Also, in 2024, an Illinois jury awarded $60 million to a mother whose infant died from NEC after using Enfamil formula. Both court decisions have been appealed. (11,12) Many of these lawsuits are not only directed at the companies that make bovine-derived formula (Abbott Nutrition, Mead Johnson Nutrition), but hospitals, physicians, and healthcare systems are also named as defendants for using these products and not warning parents of the increased incidence of NEC in patients fed formula rather than breast milk. These litigations have raised significant concerns among doctors regarding formula availability and have affected medical decision-making. Abbott CEO Robert Ford told investors in October 2024 that it would be exceedingly difficult for any company to remain on the market with these products in the face of indefinite liability. Abbott and Mead Johnson agree that a mother's breastmilk and donated human milk protect against NEC, but they believe that formula does not cause NEC. Unlike pharmaceuticals, nutritional products are not FDA-approved; however, there is regulatory oversight of their manufacturing and labeling. Allegations of plaintiffs are that hospital purchasers and administrators should have known that cow's milk formula increases the risk of necrotizing enterocolitis at least 3-fold. Other studies have shown that using donor breastmilk when the mother's milk was low or unavailable was associated with an earlier initiation of enteral feedings, faster return to birthweight, and a reduced incidence of necrotizing enterocolitis.

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Recent articles by Goldstein and Hageman addressed this controversy. (13,14) They stressed the need for informed consent before initiating a cow-based formula or fortifier for preterm infants. The plaintiff's legal strategy has focused on the hospital's negligence in failing to notify parents of the potential risk associated with cow's milk formula and not seeking alternate nutritional options. They target companies that manufacture specialized formulas for preterm infants and continue to market them as "safe and effective." Arguments from the defense state that formula remains part of the standard of care in feeding premature infants, and there is no evidence that cow milk-based products are the principal cause of NEC. However, they acknowledge the validity of studies showing breast milk reduces the risk of NEC based on the baseline risk of prematurity/low birthweight. On 10/3/2024, the FDA/CDC/NIH released a consensus statement for premature infants in situations where the supply of human milk is insufficient that standard available bovine-derived premature formulas are part of the standard of care. (15) No conclusive evidence exists that preterm infant formulas cause NEC. Despite significant improvements in policy to support breastfeeding and human milk donations, it is unlikely that an all-human milk-based diet could be available for many years, if ever, for most of the approximately 55,000 very low birthweight (<1500 grams) preterm infants born in the United States every year. Advocates of formula point out the acute shortage of infant formula in 2022 demonstrated the critical role of formula in the public marketplace in the care of premature infants.

These multiple lawsuits have implications for all of us who care for critically ill newborns. From a medical and legal perspective, can a Daubert challenge be initiated for a defense expert who opines

that formula does not cause NEC? What is the difference between association and causation? We would argue that NEC has multifactorial etiologies associated with multiple risk factors. Can one state with a reasonable degree of medical probability (>50%) that using cow-derived formulas and/or fortifiers causes NEC when clinicians and scientists do not know the specific etiology? The evidence strongly suggests that using breast milk significantly reduces the incidence of NEC. Does the use of cow-based products for preterm infants cause NEC? A court should not determine biological causality. Objective scrutiny of evidence to date neither answers whether formula causes NEC nor whether pasteurized human donor milk is a better or a safe alternative. (16) These lawsuits drive physicians to practice defensive medicine that is not rooted in evidence. We must uphold ethical standards and let evidence-based medicine guide us in this national controversy.

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Recommendations:

1. Document the conversation with the mother in the medical record on the role of breast milk in reducing the risk of infection and NEC. Note if the mother refuses to attempt to provide breast milk.
2. Note in the medical record if donor breast milk is available in your hospital and is permitted by the mother. Some cultures are strongly opposed to donor breast milk.
3. Limit the overuse of antibiotics in your premature patients.
4. Do not use H2 blockers for reflux or other gastrointestinal conditions.
5. Have a standardized approach to feeding a VLBW infant.

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Disclosure: *In reviewing this case, the authors adhered to HIPAA guidelines regarding the confidentiality of private patient information. Only those facts reported in the press and the public court records were reviewed here. One of the authors (JPG) was an expert witness at the trial.*

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Jonathan K. Muraskas, M.D.
Professor of Pediatrics
Co-director, Neonatal ICU
Director, Neonatal-Perinatal Research
Loyola University Medical Center
2160 S First Ave
Maywood, Illinois 60153
email: JMURASK@lumc.edu

Corresponding Author

Jay P. Goldsmith, M.D.
Clinical Professor of Pediatrics
Tulane University School of Medicine
4740 S I-10 Service Rd, West, Suite 120
Metairie, LA 70001
Email: jgoldsmi@tulane.edu