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## EDITORIAL Surgical necrotizing enterocolitis defined

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Ever since Bell *et al.*<sup>1</sup> first attempted to define necrotizing enterocolitis (NEC) through clinical staging criteria, there have been concerns with our ability to distinguish NEC from other disease entities. The field of neonatology has modified those criteria on multiple occasions as our understanding of the pathogenesis of NEC has evolved.<sup>2–4</sup> One of the most important factors in this continual evolution was the identification of spontaneous intestinal perforation (SIP) as a separate disease entity from NEC.<sup>5</sup> We have since learned that NEC and SIP have different short and long term outcomes; information that is indispensable when providing pre-surgical counseling to families.<sup>6</sup>

Even though our knowledge of acquired neonatal gut diseases has grown, many studies have continued to lump all variants of disease into a single category. The largest surgical trial evaluating laparotomy versus peritoneal drainage suffered greatly by combining these varied disease entities.<sup>7,8</sup> Other multicenter studies continued to use this umbrella definition of NEC, typically focusing on two elements (perforation and pneumoperitoneum) to the exclusion of other factors.<sup>9–12</sup> The Vermont Oxford Network, neonatology's largest clinical database, continues to define focal intestinal perforation (or SIP) only at surgery or postmortem examination.<sup>13</sup> This lack of a universal definition for NEC has greatly limited our understanding of the pathogenesis and outcomes of NEC. It hinders ongoing clinical trials.<sup>14</sup>

In this month's issue of the Journal of Perinatology, Murthy et al.<sup>15</sup> may have given us the definition of surgical NEC going forward. Using the database of the Children's Hospitals Neonatal Consortium (CHNC), the authors evaluated 753 cases of surgical NEC in 27 centers across 3 years. All but two cases were out born and subsequently referred to one of the centers, although not necessarily for NEC (50%). In this large cohort, they found that hospital mortality (34.4%) and short bowel syndrome (22.7%) were extremely prevalent. The combined outcome measure of death or short bowel syndrome was not different if infants were < 28 weeks (50.2%) or between 28 to 36  $\frac{6}{7}$  weeks (49.2%). Over 10% of the cohort developed NEC totalis and of these, only 7% survived. The cohort also had high rates of other morbidities including: failed hearing screens (14.4%), retinopathy of prematurity (39%; 15% with stage 3 or greater), and abnormal neuroimaging studies (grade III or IV intraventricular hemorrhage—15%; periventricular leukomalacia—9.7%).

What makes this study unique, however, is its case-definition of surgical NEC. In order to develop a 'clean' dataset, the authors removed all of the confounding diagnoses that they could, prior to analyzing the data. Of the over 55 000 infant records in the CHNC database, 1052 had surgical NEC (898 with closed records available to be analyzed). They then excluded infants with congenital heart disease, volvulus, and gastroschisis (subgroups who have NEC-like disease, but have widely divergent origins of pathogenesis and strategies for prevention).<sup>16,17</sup> In addition, the authors note that there were an additional 742 infants with SIP who did not have surgical NEC, although they do not specify how these cases were defined. I look forward to reading that paper in the future.

Despite the removal of confounding diagnoses, the authors still retained a large cohort of infants acquired from a nationally representative sample. In short, they managed to build a clean, big and relevant dataset that will undoubtedly be of value to every neonatal intensive care unit that cares for infants with surgical NEC. Having this resource available for counseling prior to surgery will be invaluable for providing accurate and realistic expectations for families whose children have NEC. In addition, using such a clean definition without the potential of dataset contamination of confounding diagnoses should be required for NEC research going forward.

Murthy *et al.* should be commended. They have provided the fields of neonatology and surgery a better definition and thus a better understanding of surgical NEC.

## CONFLICT OF INTEREST

The author declares no conflict of interest.

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## REFERENCES

- 1 Bell MJ, Ternberg JL, Feigin RD, Keating JP, Marshall R, Barton L et al. Neonatal necrotizing enterocolitis: therapeutic decisions based upon clinical staging. Ann Surg 1978; 187: 1–7.
- 2 Kliegman RM, Walsh MC. Neonatal necrotizing enterocolitis: pathogenesis, classification, and spectrum of disease. *Curr Probl Pediatr* 1987; 17(4): 243–288.
- 3 Neu J. Necrotizing enterocolitis: the search for a unifying pathogenic theory leading to prevention. *Pediatr Clin North Am* 1996; **43**(2): 409–432.
- 4 Gordon PV, Swanson JR, Attridge JT, Clark R. Emerging trends in acquired neonatal intestinal disease: is it time to abandon Bell's criteria? J Perinatol 2007; 27(11): 661–671.
- 5 Aschner JL, Deluga KS, Metlay LA, Emmens RW, Hendricks-Munoz KD. Spontaneous focal gastrointestinal perforation in very low birth weight infants. *J Pediatr* 1988; **113**(2): 364–367.
- 6 Wadhawan R, Oh W, Hintz SR, Blakely ML, Das A, Bell EF et al. NICHD Neonatal Research Network. Neurodevelopmental outcomes of extremely low birth weight infants with spontaneous intestinal perforation or surgical necrotizing enterocolitis. J Perinatol 2014; 34(1): 64–70.
- 7 Moss RL, Dimmitt RA, Barnhart DC, Sylvester KG, Brown RL, Powell DM et al. Laparotomy versus peritoneal drainage for necrotizing enterocolitis and perforation. N Engl J Med 2006; 354: 2225–2234.
- 8 Gordon PV. Treatment of necrotizing enterocolitis. N Engl J Med 2006; 355: 846-847.
- 9 Moss RL, Kalish LA, Duggan C, Johnston P, Brandt ML, Dunn JC et al. Clinical parameters do not adequately predict outcome in necrotizing enterocolitis: a multi-institutional study. J Perinatol 2008; 28(10): 665–674.
- 10 Swanson JR, Attridge JT, Gordon PV. Potential confounder of NEC clinical trials. *J Perinatol* 2009; **29**: 256–257.
- 11 Schmidt B, Roberts RS, Davis P, Doyle LW, Barrington KJ, Ohlsson A *et al.* Caffeine therapy for apnea of prematurity. *N Engl J Med* 2006; **354**: 2112–2121.
- 12 Kinsella JP, Cutter GR, Walsh WF, Gerstmann DR, Bose CL, Hart C *et al.* Early inhaled nitric oxide therapy in premature newborns with respiratory failure. *N Engl J Med* 2006; **355**: 404–406.
- 13 Vermont Oxford Network. 2014 Manual of operations: Part 2. Release 18.0. November 2013.
- 14 Battersby C, Santhakumaran S, Costeloe K, Modi N. The UK neonatal collaborative necrotizing enterocolitis (NEC) study: development of an evidence-based casedefinition of NEC. Arch Dis Child Fetal neonatal Ed 2014; 99(Suppl 1): A41.
- 15 Murthy K, Yanowitz TD, DiGeronimo R, Dykes FD, Zaniletti I, Sharma J *et al*. Shortterm outcomes for preterm infants with surgical necrotizing enterocolitis. *J Perinatol* 2014 (this issue).
- 16 Gordon PV, Swanson JR. Necrotizing enterocolitis is one disease with many origins and potential means of prevention. *Pathophysiology* 2014; 21(1): 13–19.
- 17 Gordon P, Christensen R, Weitkamp JH, Maheshwari A. Mapping the new world of necrotizing enterocolitis (NEC): review and opinion. *EJ Neonatol Res* 2012; 2(4): 145–172.

