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Review

Congenital heart disease (CHD) and necrotizing enterocolitis (NEC)

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ABSTRACT

The incidence of necrotizing enterocolitis or NEC is higher in infants with congenital heart disease. A heightened awareness and early surgical consultation is needed in order to optimize outcome.

1. Nutrition

There are three important factors related to the initiation of enteral feeding in infants at risk for NEC [1]. First, trophic feeds or "gut priming" at 10–20 ml/kg/day for a set period of time, usually 5 days, has been demonstrated to provide a protective benefit in preterm infants. The presence of an umbilical artery catheter does not pose risk for enteral feeding. Second, establishing a standardized feeding protocol with objective criteria for withholding feeds has been shown to reduce the risk of NEC (Fig. 1). Third, the use of human breast milk, whether maternal or donated, is the most significant enteral feed strategy used to decrease the incidence of NEC in high risk infants.

Probiotics and enteral supplementations have been advocated to reduce the incidence of NEC. The 2017 Cochrane review of enteral lactoferrin supplementation in preterm infants reported a reduction in the risk of NEC by about 60% [2]. However, the included trials were small and contained design and methodological flaws. This led to the performance of a large adequately powered randomized control trial, the ELFIN (Enteral lactoferrin supplementation for very preterm infants) Trial [3]. However, the ELFIN Trial contradicted the Cochrane review. This trial involved over 2200 patients and found that lactoferrin supplementation did not decrease NEC. In fact, there were 2 serious adverse events reported; one death after intestinal perforation probably associated with NEC and one case of blood in stool also thought to be related to trial intervention. Data from this trial do not support the routine use of probiotics to decrease morbidity and mortality in preterm infants.

2. Necrotizing enterocolitis (NEC) presentation

Despite vigilance, NEC continues to be the most common surgical emergency in neonatal intensive care units. NEC is fundamentally a disease of prematurity (< 32 weeks gestation), affecting 5 to 10% of preterm infants born < 1500 g.

The initial presentation of NEC may be nonspecific, with initial signs such as apnea and bradycardia, temperature instability, feeding intolerance, and lethargy. The most common specific presenting sign is abdominal distention, while other physical findings include tenderness, guarding, palpable loops/abdominal mass, crepitus and erythema or dusky discoloration of the abdominal wall (Fig. 2A).

The actual diagnosis of NEC is based on both clinical and radiologic features. Radiologic findings suggestive of NEC involves pneumatosis intestinalis, portal venous gas, and in the event of frank intestinal perforation, pneumoperitoneum. Pneumatosis results from the accumulation of hydrogen gas bubbles in the bowel wall (Fig. 2B). Most commonly the small and large bowel are both affected; the next most frequent location of disease involvement is the small bowel. In infants with congenital heart disease and NEC, the colon is most commonly affected.

3. NEC management

NEC management is primarily supportive. Bowel rest with gastric decompression, cessation of enteral feeds, and the administration of intravenous antibiotics are the mainstay of management, with fluid replacement and correction of hematologic and metabolic abnormalities as required. In cases complicated by hemodynamic derangement and shock, intubation and mechanical ventilation as well as the administration of intravenous inotropes may be required. The average duration of intravenous antibiotic treatment ranges from 7 to 14 days, and culture-proven bacteremia is present in roughly 25% of cases.

Serial physical and radiologic exams are of critical importance, particularly during the first 24 to 48 h after a diagnosis of NECC is suspected. Clinical examination and 2-view supine and decubitus x-rays should be performed every 6 to 8 h during this initial period of observation, and may be spaced to longer intervals in babies whose

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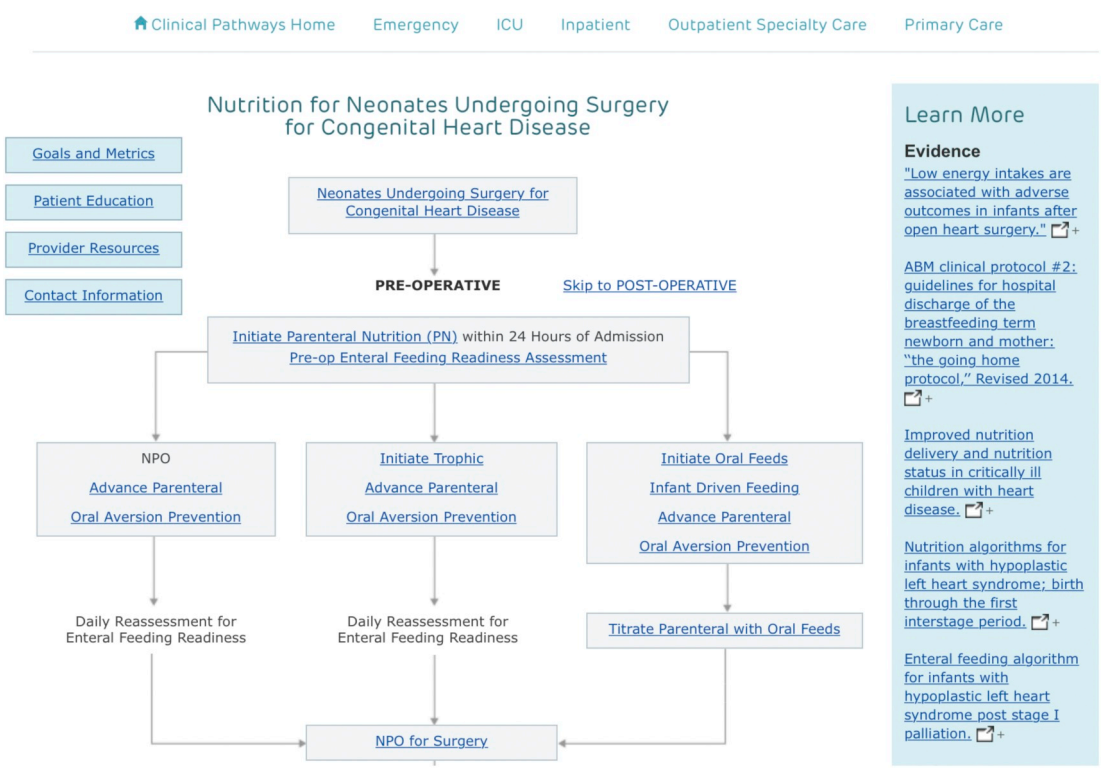

Fig. 1. Children's Hospital of Philadelphia pre-operative nutrition guidelines.

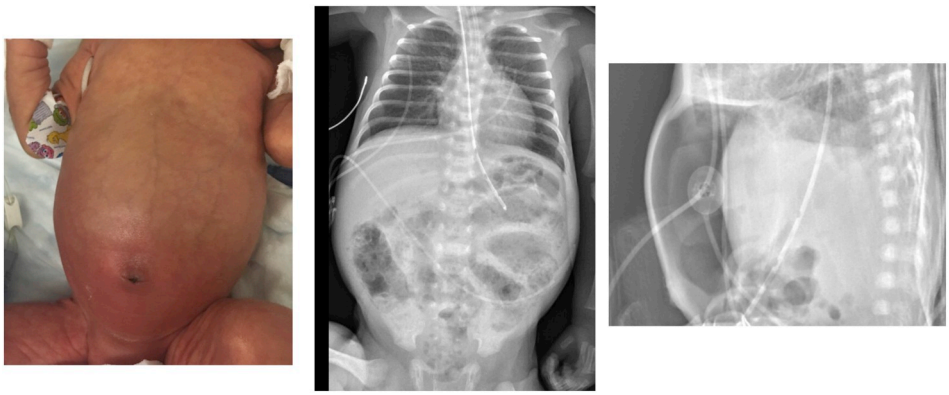

Fig. 2. Clinical and radiographic findings of NEC.
A - abdominal distention and discoloration; B - pneumatosis intestinalis; C pneumoperitoneum

examinations remain reassuring. The role of ultrasound is not well defined, but a recent meta-analysis suggested this imaging modality may provide additional insight into bowel perfusion, peristalsis, and thickening, as well as the demonstration of pneumoperitoneum in cases of intestinal perforation.

4. Indications for surgery

Pediatric surgical evaluation is required in all cases of NEC, as decision making regarding surgical intervention requires integration of radiologic and clinical evidence as well as surgical judgement. Pneumoperitoneum is a radiologic finding that in most instances mandates prompt surgical intervention (Fig. 2C), while evolving abdominal wall erythema and the presence of radiologically or clinicallypalpable fixed intestinal loops may also prompt exploratory surgery.

Surgical management involves either an exploratory laparotomy or peritoneal drainage. Exploratory laparotomy allows for resection of the affected bowel segment, creation of an ostomy, and reanastamosis in a delayed interval fashion. Confluent areas of necrosis involving the distal ileum and right colon are seen in Fig. 3. Peritoneal drainage involves placement of a penrose drain and is typically performed in extremely low birth weight infants (typically < 800 g) (Fig. 4). Some infants with clinical decompensation despite maximal medical management may also require surgical intervention, and a significant number of patients initially treated with peritoneal drainage will progress to requiring a laparotomy (32% in a recent retrospective cohort study) [4]. Approximately 33–50% patients with classic NEC will require surgery, and overall mortality in babies requiring operative intervention is approximately 30%.

Controversy persists regarding the optimal surgical intervention in NEC, with multiple retrospective studies reporting higher survival rates associated with both peritoneal drainage as well as laparotomy. The results of the muchanticipated randomized controlled NEST trial [Laparotomy vs Drainage for Infants with Necrotizing Enterocilitis] are expected to be reported later this year, and may yield important insights on the relative pros and cons of these management approaches.

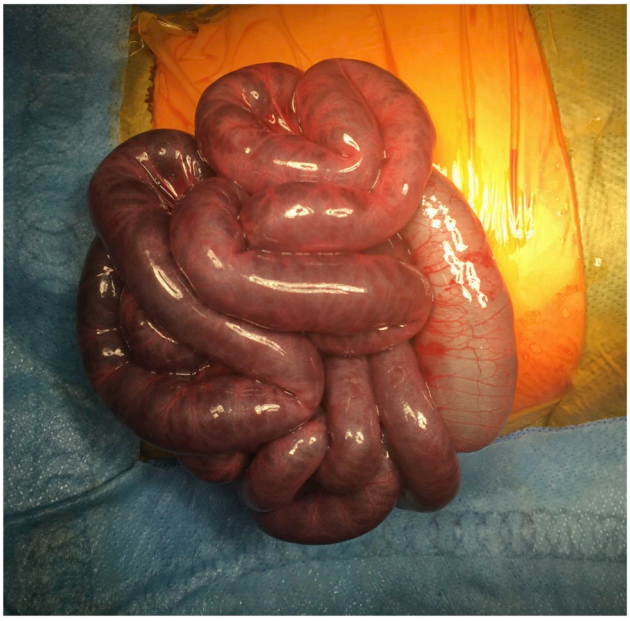

Fig. 3. Intraoperative finding of bowel necrosis

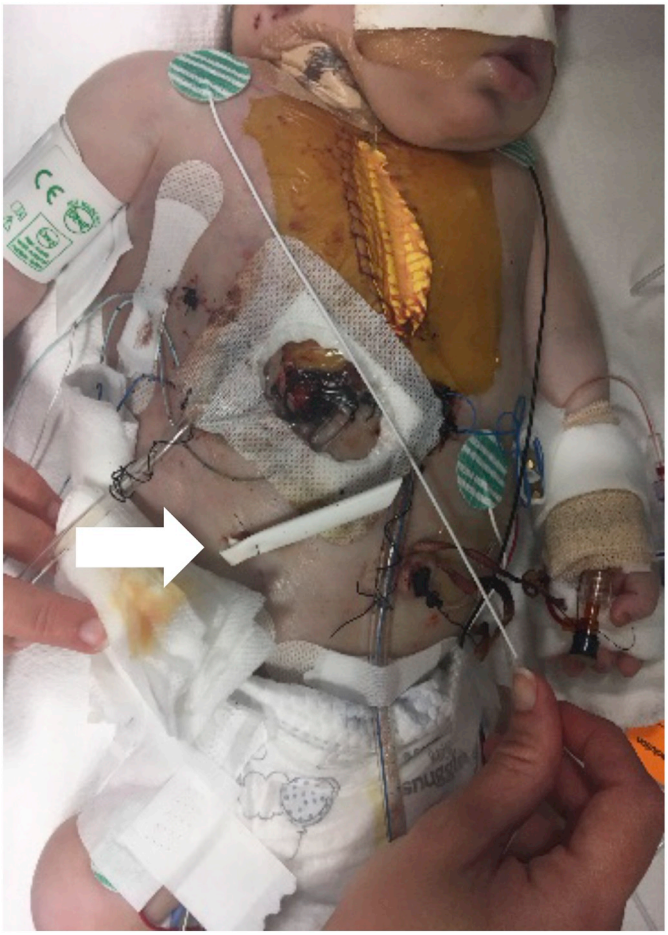

Fig. 4. Penrose drain

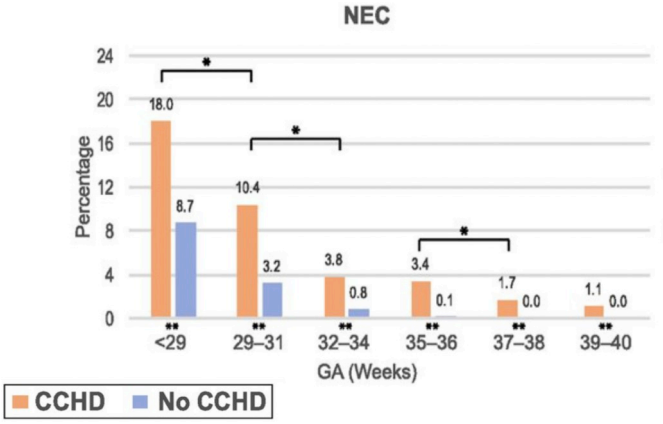

Fig. 5. NEC with and without CHD
Excerpted from Steurer et al. Pediatrics (2017) [7]

5. Congenital heart disease (CHD) and necrotizing enterocolitis (NEC)

The pathophysiology of cardiogenic NEC is likely different than classic NEC, which is thought to result from a mixture of inflammatory and vascular injury involving areas of infarction and necrosis. Cardiac NEC is more of a vascular phenomenon involving mesenteric hypoperfusion from diastolic steal and flow reversal in the abdominal aorta.

In a recent meta-analysis by Siano et al. [5] the incidence of NEC was shown to be higher in babies with CHD, occurred at an older age and was associated with higher overall mortality [4]. Interestingly, fewer babies with CHD required surgical intervention, and cardiogenic NEC was observed at equal frequency before versus after cardiac repair. Another group did not find that the incidence of NEC was increased with enteral feeds, thus supporting the practice of enteral feeds in babies with duct dependent CHD at all gestations [6].

The incidence of NEC is greater in premature infants with CHD than in those without (Fig. 5), suggesting an additive effect of classic risk factors in preterm babies as well as the hemodynamic changes observed in congenital heart disease.

6. Conclusion

Caring for premature infants with congenital heart disease requires particular vigilance for the development and management of NEC. Early consultation from pediatric surgery, regular clinical and radiographic examinations, and interventions ranging from bowel rest and supportive care to surgical intervention optimize chances of survival and protection of long-term potential for tolerance of enteral nutrition. Continued study regarding the optimal approach to surgical intervention in these patients is required.

Declaration of competing interest

The authors confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

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