# Evaluation and Management of Suspected, Medical and Surgical Necrotizing Enterocolitis Clinical Pathway

JOHNS HOPKINS
All Children's Hospital

Johns Hopkins All Children's Hospital

# Evaluation and Management of Suspected, Medical and Surgical Necrotizing Enterocolitis Clinical Pathway

**Table of Contents**

Updated: 12/08/2022

Owner & Primary Author: Sandra Brooks, MD, MPH

*This pathway is intended as a guide for physicians, physician assistants, nurse practitioners and other healthcare providers. It should be adapted to the care of specific patient based on the patient's individualized circumstances and the practitioner's professional judgment.*

# Evaluation and Management of Suspected, Medical and Surgical Necrotizing Enterocolitis Clinical Pathway

**Rationale**

To optimize the diagnostic evaluation of infants with suspected necrotizing enterocolitis (NEC), with goals of earlier confirmation of a NEC diagnosis, avoidance of unnecessary treatment in the absence of NEC, administration of patient and condition- specific antibiotics and provision of additional information to guide decisions regarding the need for surgical intervention.

To establish and operationalize an abdominal ultrasound protocol specific for necrotizing enterocolitis assessment that can be obtained as part of the diagnostic evaluation of neonates with suspected necrotizing enterocolitis. This imaging exam will be referred to in this document as "abdominal doppler ultrasound" (ADUS).

**Background / Published Data and Levels of Evidence**

Necrotizing enterocolitis (NEC) is an inflammatory disease of the gastrointestinal tract characterized by ischemic necrosis of the intestinal mucosa, mostly affecting premature neonates. Its pathogenesis is incompletely understood and is thought to be multifactorial in nature. Predisposing factors include intestinal immaturity, microbial dysbiosis and impaired intestinal oxygen delivery (1-4).

***Clinical Presentation:***
The clinical diagnosis of NEC is often a challenge, as the presentation may vary considerably among affected infants, is frequently nonspecific, and may be indistinguishable from neonatal sepsis. The initial presentation can range from 1) non-specific signs and symptoms of lethargy, temperature instability, feeding intolerance or apnea; 2) classical form with abdominal distension, bloody stool and / or bilious aspirates/emesis; 3) Fulminant onset with shock and circulatory collapse.

Abdominal tenderness and discoloration are highly suggestive of NEC. Pneumatosis intestinalis and/or portal venous gas are pathognomonic radiographic findings. Even though timely and accurate diagnosis is key as the mortality rate is higher after intestinal perforation, the challenge remains as the most common presentation of non-specific clinical findings (including gastric residuals and gaseous abdominal distention) is not diagnostic of the disease and most of the affected infants will not have a subsequent diagnosis of NEC (5).

### Modified Bell's Classification:
The Bell's classification system was developed to stratify patients with NEC by disease severity to aid standardization of management in each category. The original classification was subsequently modified with sub classifications proposed within stages II and III by Walsh and Kleigman in 1986 (Table 1). A prospective cross-sectional survey of 158 level 2 and 3 UK NICUs found that 45% of infants with NEC initially presented as modified Bell's I, 21% modified Bell's II, and 33% modified Bell's III (6,7).

Table 1. (Adapted from Kleigman)

| STAGE | SYSTEMIC SIGNS | INTESTINAL SIGNS | RADIOLOGIC SIGNS |
|---|---|---|---|
| IA—Suspected NEC | Temperature instability, apnea, bradycardia, lethargy | Elevated pre-gavage residuals, mild abdominal distention, emesis, guaiac-positive stool | Normal or intestinal dilation, mild ileus |
| IB—Suspected NEC | Same as above | Bright red blood from rectum | Same as above |
| IIA—Definite NEC Mildly ill | Same as above | Same as above, *plus* absent bowel sounds, +/− abdominal tenderness | Intestinal dilation, ileus, pneumatosis intestinalis |
| IIB—Definite NEC Moderately ill | Same as above, *plus* mild metabolic acidosis, mild thrombocytopenia | Same as above, *plus* absent bowel sounds, definite abdominal tenderness, +/− abdominal cellulitis or right lower quadrant mass | Same as IIA, *plus* portal vein gas, +/− ascites |
| IIIA—Advanced NEC Severely ill, bowel intact | Same as IIB, *plus* hypotension, bradycardia, severe apnea, combined respiratory and metabolic acidosis, disseminated intravascular coagulation, neutropenia | Same as above, *plus* signs of generalized peritonitis, marked tenderness, and distention of abdomen | Same as IIB, *plus* definite ascites |
| IIIB—Advanced NEC Severely ill, bowel perforated | Same as IIIA | Same as IIIA | Same as IIB, *plus* pneumoperitoneum |

### Serologic markers of NEC:
As in many neonatal infections, infants with NEC may present with non-specific indicators of infection such as thrombocytopenia or elevated lactate levels.

C Reactive protein (CRP) is an early phase reactant that becomes abnormal in stage II and stage III NEC and as such is a sensitive but non-specific marker for NEC. Persistently elevated CRP after initiation of appropriate medical management suggests associated complications which may require surgical intervention, while normal serial CRP values would not be consistent with NEC and therefore discontinuation of antibiotic therapy and early resumption of feedings would be indicated.

To date, there are no "ideal" biomarkers for screening or early diagnosis of NEC. Non-specific biomarkers like IL-6 and neutrophil CD64 are good "early warming" indicators, but cannot differentiate between systemic infection and NEC.

Platelet-activating factor and intestinal fatty acid binding protein were both sensitive and specific and could be potentially useful, although their use must be further tested in larger prospective studies.

Gut-associated proteins like plasma or urinary L-FABP, I-FABP and TEF3 are specific for acute intestinal injury and NEC. These biomarkers and the LIT score can predict severe cases of NEC witch subsequently require surgery. They are, however, unable to diagnose mild or early cases of intestinal injury.

Enhanced inflammatory biomarkers like fecal calprotectin and S100A12 are relatively specific mediators for intestinal injury. However, the intra- and inter-individual variability in concentration and the source of the specimen render the tests inconsistent, unreliable, and difficult to use in the acute clinical situation.

A systemic review concluded that most serologic markers of NEC have been used in too few studies to evaluate their use (8-10).

### *Antimicrobial coverage:*
Antimicrobial therapy is universally prescribed to manage NEC and is primarily geared toward preventing bacteremia and potential complications of peritonitis or abscess formation caused by translocation of organisms through a compromised intestinal barrier. However, there is no clear evidence-based consensus on either antimicrobial selection or duration of therapy.

A 2012 Cochrane review and a 2021 systemic review found that most antibiotic regimens used included broad-spectrum coverage for enteric gram-negative organisms (e.g. *E.coli, Klebsiella spp*.), *Enterococcus spp.*, and anaerobic organisms consisting of a combination of ampicillin, gentamicin and clindamycin/metronidazole were effective in decreasing mortality and preventing clinical deterioration. However, there was insufficient evidence to recommend a particular antibiotic regimen for the treatment of NEC.

There are some studies that link the addition of anaerobic therapy with later intestinal stricture formation. However, a large multicenter cohort study noted that this association is most likely a consequence of survival bias.

The addition of Vancomycin is institution-specific and is dictated by the prevalence of methicillin-resistant Staphylococcus aureus (MRSA) in the NICU.

Because there are limited evidence-based recommendations for cessation of antimicrobials, short courses of antimicrobial coverage may be indicated when evidence of intestinal

inflammation has remitted (11-16).

### *Resumption of feeds after NEC:*
Duration of bowel rest after resolution of acute signs of NEC remains controversial.

A 2018 review of the literature found that initiating early enteral feeding, within 5 days of NEC diagnosis, was not associated with adverse outcomes, including NEC recurrence. In addition, catheter-related sepsis and post-NEC stricture rates were unchanged between early and delayed enteral feeding groups after NEC. However, the quality of the evidence was suboptimal. (17)

Another systematic review and meta-analysis in 2020 had 3 studies that met inclusion criteria and no randomized trials. Bell's Stage I infants were not included. The early refeeding group was defined as <5-7 or median 4 days and later refeeding group as ≥5-7 or median 10 days. There was no increase in negative outcomes with earlier refeeding after NEC. Earlier initiation of enteral feeds resulted in a significantly lower risk for the combined outcome of recurrent NEC and/or post-NEC stricture. (16)

Conversely, duration of bowel rest may be longer than duration of antibiotic therapy depending on clinical assessment of patients' readiness to feed.

### *Radiologic diagnostic dilemmas:*
The current and absolute indication for surgery for infants with NEC is intestinal perforation. However, more than 50% of infants who receive surgery for NEC or die have no sign of perforation as evidenced by the presence of pneumoperitoneum on plain abdominal films (KUBs). The timing of surgical intervention in these Infants remains unclear.

KUBs are the gold standard for NEC diagnostic imaging. However, such testing has several known limitations that include difficulty in assessing the amount of intraabdominal fluid, difficulty in interpretation of findings in the face of a gasless abdomen, and a reported relatively high incidence of neonates with NEC and demonstrated bowel perforation who had a non-diagnostic abdominal radiograph.

Abdominal and doppler Ultrasonography (ADUS) has become a useful diagnostic adjunct in recent years. Like KUBs, US can depict intramural gas, portal venous gas, and free intraperitoneal gas. However, the major advantages of US over KUBs are that it can detect intestinal motility, intraabdominal fluid, impaired bowel wall thickness, and decreased bowel wall perfusion. Thus, non-specific and inconclusive findings on KUBs can be better delineated by US prompting earlier suspicion of necrotic or non-viable bowel and prompting earlier intervention

A retrospective evaluation of 238 infants with confirmed NEC who had no radiological evidence of pneumoperitoneum identified a combination of several independent predictors of surgical intervention that were seen on abdominal ultrasonography and radiography. These included persistent dilation of the bowel loops and evidence of portal venous gas which were detected

by radiography, and bowel wall thickening, absent peristalsis and echogenic-free fluid or focal fluid collection which were detected by ADUS. (1, 18-22).

The use of ADUS may be limited by variability of operator expertise, lack of 24-hour availability, and insufficient data to accurately apply findings for management decisions (e.g. surgery).

### *Indications for surgical intervention:*
Evidence of pneumoperitoneum on abdominal imaging indicates intestinal perforation due to severe necrosis. This finding is a clear indicator that surgical intervention is warranted. However, detecting intestinal perforation is not straightforward, as perforation can occur without evidence on abdominal radiographs.

Surgery is also appropriate for infants with severe irreversible necrosis who are at high risk for perforation or other severe complications of NEC. However, in clinical practice, it is difficult to identify such infants. Based on clinical experience, it is presumed these patients have continued clinical deterioration despite maximal medical support.

### *Comparison of surgical interventions*:
Surgical NEC is managed with a peritoneal drainage (PD) insertion or initial laparotomy (IEL). There remains no clear support of one intervention over the other.

Two large multicenter and prospective RCTs (the North America NET trial and the predominantly European NECSTEPS) attempted to address the issue. The NET trial concluded that PD did not improve survival and was limited in its utility as definitive treatment for NEC as 74% of neonates treated with PD required delayed EL.  Further analysis of the data in 2010 showed no improvement in the immediate clinical status of patients treated with PD and it did not support the use of PD as a stabilizing or temporizing measure. NECSTEPS concluded that the type of operation performed did not influence survival nor the early outcomes. A 2011 Cochrane review combined the results of the two studies and concluded that no significant benefits or harms of PD over IEL could be identified.

Another RCT comparing IEL to PD among ELBW infants included 992 eligible infants, 310 were randomized and 96% had primary outcome assessed. Death or NDI occurred in 69% of infants in the laparotomy group versus 70% with drainage (adjusted relative risk [aRR] = 1.0; 95% confidence interval [CI]: 0.87–1.14). With a preoperative diagnosis of NEC, death or NDI occurred in 69% after laparotomy versus 85% with drainage (aRR=0.81; 95% CI: 0.64 to 1.04).  For preoperative diagnosis of IP, death or NDI occurred in 69% after laparotomy versus 63% with drainage (aRR, 1.11; 95% CI: 0.95 to 1.31). There was no overall difference in death or NDI rates at 18–22 months corrected age between initial laparotomy versus drainage. However, the preoperative diagnosis of NEC or IP modified the impact of initial treatment (23).

A 2022 meta-analysis of five case series, five retrospective cohort studies, and three randomized controlled trials (RCT) (that included the NET trial) with a total of 1062 patients, found no significant difference in mortality between PD and EL as initial surgical intervention. Their results suggest that either intervention could be used in selected patients.

Similar findings were found in a 2020 systematic review when only observational studies and RCTs with high quality of reporting based on the STROBE checklist (Strengthening the Reporting of Observational Studies in Epidemiology) were included (24-31).

***NEC complications:***
Complications are related to the stage of the disease.

A- Short term complications may include:
- Infectious complications – Sepsis, meningitis, peritonitis, and abscess formation
- Disseminated intravascular coagulation
- Respiratory and cardiovascular complications – Hypotension, shock, and respiratory failure
- Metabolic complications – Hypoglycemia and metabolic acidosis


B- Long-term complications may include:
- Gastrointestinal strictures and adhesions
- Cholestasis
- Short bowel syndrome with or without intestinal failure
- Failure to thrive (32)


***Long-term outcomes:***
 Complications of NEC include gastrointestinal problems of strictures and adhesions, cholestasis from long-term parenteral nutrition, short bowel syndrome with or without intestinal failure. It is also associated with significantly worse neurodevelopmental outcome than prematurity alone. Presence of advanced NEC and need for surgery increase the risk of neurological impairment including a higher risk of cerebral palsy (1.5 (1.2 to 2.0), p = 0.001), visual (2.3 (1.0 to 5.1), p = 0.04), cognitive (1.7 (1.4 to 2.2), p<0.0001) and psychomotor impairment (1.7 (1.3 to 2.2), p<0.0001). The odds ratio of neurodevelopmental impairment was found to be 2.3 times higher in neonates with Bell's stage III disease or requiring surgery ((1.5 to 3.6), p = 0.0001) (33).

Follow-up examinations at 18 to 22 months in infants who had undergone surgery for NEC showed a significantly reduced risk of death or neurodevelopmental impairment among those who had undergone a EL as compared with those who had undergone PD. These studies indicate that once surgery is required, the outcome may be poor, a finding that underscores the need for effective prevention (23).

**Clinical Management**

*Physical Assessment:*
a) Vital signs, cardiac/respiratory/neuro status
b) Hemodynamic status (capillary refill, blood pressure (BP), urine output)
c) GI function and exam (bowel sounds, distension, color, girth)

*Diagnosis per Modified Bell's Staging (Table 2)*

| Stage | Classification* | Systemic and Laboratory signs | Intestinal signs | Radiological signs |
|---|---|---|---|---|
| **Ia** | **Suspected NEC**\*\* | - Temperature instability<br>- Apnea/bradycardia<br>- Lethargy | - Gastric residuals<br>- Mild abdominal distension<br>- Emesis<br>- *Hemoccult positive stool* | Normal or mild ileus |
| **Ib** | | | - *Hematochezia* | |
| **IIa** (mildly ill) | **Confirmed Medical NEC** | Same as above | Same as above, *plus:*<br>- Absent bowel sounds<br>± abdominal tenderness | - Intestinal dilation<br>- Ileus<br>- Pneumatosis intestinalis |
| **IIb** (moderately ill) | | Same as above, *plus:*<br>- Mild metabolic acidosis<br>- Mild thrombocytopenia | Same as above, *plus:*<br>- Definitive abdominal tenderness<br>± abdominal cellulitis or right lower quadrat mass | Same as above *plus:*<br>- portal venous gas<br>± ascites |
| **IIIa** (severely ill) | | Same as above *plus:*<br>- Hypotension<br>- Bradycardia<br>- Severe apnea<br>- Combined respiratory and metabolic acidosis<br>- Disseminated intravascular coagulation<br>- Neutropenia | Same as above, *plus:*<br>- Signs of generalized peritonitis<br>- Marked tenderness<br>- Abdominal distention | Same as above, *plus:*<br>- Definitive ascites |
| **IIIb** | **Confirmed Surgical NEC** | Same as above | Same as above | Same as above, *plus:*<br>- Pneumoperitoneum |

*\* Patients may progress through the different stages of NEC. Status should be re-evaluated and treated according to the treating physicians' judgement.*
*\*\*These patients invariably end up not having a diagnosis for NEC. Their symptomatology could have been non-specific related to prematurity or secondary to non-intestinal etiology*

## *Management per Diagnosis* (Table 3)

| Classification | Stage | Interventions | Laboratory Testing[1] | Suggested Radiographic Imaging Frequency[2,3,4] | Antibiotic Choice and Duration[5,6] | Bowel Rest Duration | Pediatric Surgery Consult |
|---|---|---|---|---|---|---|---|
| **Suspected NEC** | Ia | Serial examinations | CBC CRP | KUB Q12H for 24-48 hours | Ampicillin Tobramycin for 48 hours | Variable, up to 48 hours | No |
| | Ib | | | | | | |
| **Confirmed Medical NEC** | IIa | Same as above, *plus:* Replogle to LIS[7] Hemodynamic stabilization | Same as above | Q12H for 48 hours, then prn | Piperacillin-Tazobactam for 7 days | 5-7 days | Yes |
| | IIb | Same as above, *plus:* Acid-base correction | Same as above *plus:* Blood gas CMP | Q8H for 48 hours, then prn | Piperacillin-Tazobactam for 10 days | 7-10 days | |
| | IIIa | | Same as above, *plus:* Lactate | Q6H for 48 hours, then Qday until stable, then prn | | 7-14 days | |
| **Confirmed Surgical NEC** | IIIb | Interventions per surgical team | Same as above | Pre-op and post-op, then prn | Piperacillin-Tazobactam for 14 days | To be determined by surgical team | Yes |

1. Testing frequency will be based on clinical status / derangements present with correction done as indicated

2. To ensure all images are assessed immediately, order as "stat" and select "wet read" option to ensure that images are sent to VRad (virtual radiology) when applicable.

3. Frequency and types of radiographs may vary based on patient disease progression.
**Radiographs include plain KUBs, left lateral decubitus or a combination.** Cross-table lateral and orthogonal views may be used if recommended by the radiological team.
**KUBs**: assess the pattern of bowel gas (moving, fixed, absent), presence/persistence/resolution of pneumatosis, and portal venous gas. It also allows to assess placement/depth of OGT for gastric decompression
**Left lateral decubitus views**: optimal for detecting free air
Cross-table lateral view: can aid in seeing tiny foci of free air.
Orthogonal views: may help in visualizing pneumatosis

4. May consider obtaining an ADUS in a patient with symptoms concerning for NEC and a gasless or equivocal KUB, or in patients with an abnormal KUB to confirm findings and rule-out evidence of necrotic or perforated bowel

5. **Add Vancomycin for 48 hours (or replace ampicillin in stage Ia/Ib) in patients with central venous lines, MRSA colonization, or history of previous MRSA infections.** Monitor and manage drug levels with pharmacy
- In patients with concomitant use of Zosyn and Vancomycin, monitor serum creatinine Q24H for 48 hours

6. **Consider ID consult for bacteremia, persistent/worsening symptoms after 48 hours, anticipated extended use of vancomycin beyond 48 hours and/or use of alternative antibiotics such a meropenem**

7. Duration of Replogle to be determined by surgical team

*Additional Considerations:*

*Infectious considerations:*
- Oxacillin is not recommended in stage I given concerns for Enterococci prevalence in the pathogenesis of NEC and the high likelihood of UTI in patients with ileus
- Fluconazole is not indicated for routine use and should not be added without ID recommendations
- Consider obtaining an ID consult for complicated cases
- Duration of antibiotics for complicated cases to be done in consultation with the ID team
- Please refer to NICU "Late Onset Sepsis" clinical pathway for further details on sepsis evaluation approach

*Hematologic considerations:*
Hematologic abnormalities to be corrected as needed with optimal platelets counts goal of > 100,000 during the acute phase of the illness and coagulation studies within therapeutic range for age

**Glossary**

ADUS- abdominal doppler ultrasound
AP- anterior-posterior KUB
BMP - Basic metabolic panel
CBC - Complete blood count with differential
CD64- Cluster of differentiated 64
CRP - C reactive protein
CSF - Cerebrospinal fluid
CVL – central venous line
EP- exploratory laparotomy
IEL – Initial exploratory laparotomy
IL-6 – Interleukin 6
I-FABP – Intestinal fatty acid binding protein
KUB- Kidney, ureter and bladder XRay
L-FABP – Liver fatty acid binding protein
LIS- low intermittent suction
MRSA – methicillin resistant staphylococcus aureus
NEC- Necrotizing enterocolitis
RCT- randomized controlled trial
S100A12 – S100 calcium binding protein
TEF3 – Transcriptional enhanced factor 3
UK- United Kingdom
PD - Primary drain placement

**References**

1- Neu J, Walker WA. Necrotizing enterocolitis. *NEJM*. 2011;364(3):255-264

2- Pammi M, Cope J, Tarr PI, Warner BB, Morrow AL, Mai V, Gregory KE, Kroll JS, McMurtry V, Ferris MJ, Engstrand L, Lilja HE, Hollister EB, Versalovic J, Neu J. Intestinal dysbiosis in preterm infants preceding necrotizing enterocolitis: a systematic review and meta-analysis. Microbiome. 2017 Mar 9;5(1):31. doi: 10.1186/s40168-017-0248-8. PMID: 28274256; PMCID: PMC5343300

3- Lin PW, Stoll BJ. Necrotising enterocolitis. Lancet 2006;368:1271-83

4- Parker LA, Weaver M, Murgas Torrazza RJ, Shuster J, Li N, Krueger C, Neu . Effect of Gastric Residual Evaluation on Enteral Intake in Extremely Preterm Infants: A Randomized Clinical Trial. JAMA Pediatr. 2019;173(6):534.

5- Cobb B, Carlo W, Ambalavanan N. Gastric residuals and their relationship to necrotizing enterocolitis in very low birth weight infants. *Pediatrics (Evanston)*. 2004;113(1):50-53.

6- Walsh M, Kliegman R. Necrotizing enterocolitis: treatment based on staging criteria. *Pediatr Clin North Am*. 1986;33(1):179-201.

7- Bell MJ, Ternberg JL, Feigin RD, Keating JP, Marshall R, Barton L, Brotherton T. Neonatal necrotizing enterocolitis. Therapeutic decisions based upon clinical staging. Ann Surg. 1978 Jan;187(1):1-7. PubMed PMID: 413500; PubMed Central PMCID: PMC1396409.

8- Pourcyrous M, Korones S, Yang W, Boulden T, Bada H. C-reactive protein in the diagnosis, management, and prognosis of neonatal necrotizing enterocolitis. *Pediatrics (Evanston)*. 2005;116(5):1064-1069.

9- Evennett NN, Alexander N, Petrov M, Pierro A, Eaton S. A systematic review of serologic tests in the diagnosis of necrotizing enterocolitis. *J Pediatr Surg*. 2009;44(11):2192-2201.

10- Ng PC. Biomarkers of necrotising enterocolitis. Semin Fetal Neonatal Med. 2014 Feb;19(1):33-8

11- Shah D, Sinn J. Antibiotic regimens for the empirical treatment of newborn infants with necrotising enterocolitis. *Cochrane Database Syst Rev*. 2012(8):CD007448.

12- Donà D, Gastaldi A, Barbieri E, Bonadies L, Aluvaala J, English M. Empirical Antimicrobial Therapy of Neonates with Necrotizing Enterocolitis: A Systematic Review. Am J Perinatol. 2021 Jun 14. doi: 10.1055/s-0041-1730364. Epub ahead of print. PMID: 34126646

13-Zani A, Eaton S, Puri P, Rintala R, Lukac M, Bagolan P, Kuebler JF, Hoellwarth ME, Wijnen R,

Tovar J, Pierro A; EUPSA Network. International survey on the management of necrotizing enterocolitis. Eur J Pediatr Surg. 2015 Feb;25(1):27-33

14- Faix RG, Polley TZ, Grasela TH. A randomized, controlled trial of parenteral clindamycin in neonatal necrotizing enterocolitis. J Pediatr. 1988 Feb;112(2):271-7

15- Autmizguine J, Hornik CP, Benjamin DK Jr, Laughon MM, Clark RH, Cotten CM, Cohen-Wolkowiez M, Benjamin DK, Smith PB; Best Pharmaceuticals for Children Act—Pediatric Trials Network Administrative Core Committee. Anaerobic antimicrobial therapy after necrotizing enterocolitis in VLBW infants. Pediatrics. 2015 Jan;135(1):e117-25. doi: 10.1542/peds.2014-2141

16- Patel EU, Wilson DA, Brennan EA, Lesher AP, Ryan RM. Earlier re-initiation of enteral feeding after necrotizing enterocolitis decreases recurrence or stricture: a systematic review and meta-analysis. J Perinatol. 2020 Nov;40(11):1679-1687

17- Hock AM, Chen Y, Miyake H, Koike Y, Seo S, Pierro A. Initiation of Enteral Feeding After Necrotizing Enterocolitis. Eur J Pediatr Surg. 2018 Feb;28(1):44-50

18- Bohnhorst B, Kuebler J, Rau G, Gluer S, Ure B, Doerdelmann M. Portal venous gas detected by ultrasound differentiates surgical NEC from other acquired neonatal intestinal diseases. *Eur J Pediatr Surg*. 2011;21(1):12-17.

19- Faingold R, Daneman A, Tomlinson G, Babyn PS, Manson DE, Mohanta A, Moore AM, Hellmann J, Smith C, Gerstle T, Kim JH. Necrotizing enterocolitis: assessment of bowel viability with color Doppler US. Radiology. 2005 May;235(2):587-94.

20- He Y, Zhong Y, Yu J, Cheng C, Wang Z, Li L. Ultrasonography and radiography findings predicted the need for surgery in patients with necrotising enterocolitis without pneumoperitoneum. Acta Paediatr. 2016 Apr;105(4):e151-5

21- Epelman M, Daneman A, Navarro OM, Morag I, Moore AM, Kim JH, Faingold R, Taylor G, Gerstle JT. Necrotizing enterocolitis: review of state-of-the-art imaging findings with pathologic correlation. Radiographics. 2007 Mar-Apr;27(2):285-305

22- Silva CT, Daneman A, Navarro OM, Moore AM, Moineddin R, Gerstle JT, Mittal A, Brindle M, Epelman M. Correlation of sonographic findings and outcome in necrotizing enterocolitis. Pediatr Radiol. 2007;37(3):274.

23- Blakely ML, Tyson JE, Lally KP, et al. Laparotomy versus peritoneal drainage for necrotizing enterocolitis or isolated intestinal perforation in extremely low birth weight infants: outcomes through 18 months adjusted age. Pediatrics 2006;117:e680-e687

24-van Heesewijk AE, Rush ML, Schmidt B, Kirpalani H, DeMauro SB. Agreement between study designs: a systematic review comparing observational studies and randomized trials of surgical treatments for necrotizing enterocolitis. J Matern Fetal Neonatal Med. 2020 Jun;33(12):1965-1973

25- Elm Ev, Altman DG, Egger M, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. BMJ (Clin Res Ed). 2007;335(7624):806–808

26- Raval MV, Hall NJ, Pierro A, Moss RL. Evidence-based prevention and surgical treatment of necrotizing enterocolitis-a review of randomized controlled trials. Semin Pediatr Surg. 2013 May;22(2):117-21

27- Sola JE, Tepas JJ III, Koniaris LG. Peritoneal drainage versus laparotomy for necrotizing enterocolitis and intestinal perforation: a meta-analysis. J Surg Res 2010;161:95-100

28- Li W, Tang J, Zhu Z, Tang W. Initial surgical treatment of necrotizing enterocolitis: a meta-analysis of peritoneal drainage versus laparotomy. Eur J Pediatr. 2022 Jul;181(7):2593-2601

29- Rees CM, Eaton S, Kiely EM, Wade AM, McHugh K, Pierro A. Peritoneal drainage or laparotomy for neonatal bowel perforation? A randomized controlled trial. Ann Surg. 2008 Jul;248(1):44-51

30- Rees CM, Eaton S, Khoo AK, Kiely EM; Members of NET Trial Group, Pierro A. Peritoneal drainage does not stabilize extremely low birth weight infants with perforated bowel: data from the NET Trial. J Pediatr Surg. 2010 Feb;45(2):324-8

31- Downard CD, Renaud E, St Peter SD, Abdullah F, Islam S, Saito JM, Blakely ML, Huang EY, Arca MJ, Cassidy L, Aspelund G; 2012 American Pediatric Surgical Association Outcomes Clinical Trials Committee. Treatment of necrotizing enterocolitis: an American Pediatric Surgical Association Outcomes and Clinical Trials Committee systematic review. J Pediatr Surg. 2012 Nov;47(11):2111-22

32- Bazacliu C, Neu J. Necrotizing Enterocolitis: Long Term Complications. Curr Pediatr Rev. 2019;15(2):115-124.

33- Rees CM, Pierro A, Eaton S. Neurodevelopmental outcomes of neonates with medically and surgically treated necrotizing enterocolitis. Arch Dis Child Fetal Neonatal Ed. 2007 May;92(3):F193-8
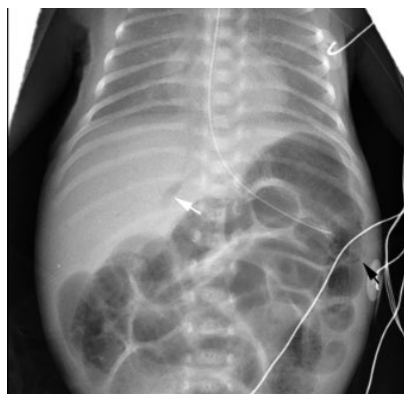
**Outcome Measures**

- Compliance with guidelines on antibiotics choice and duration of treatment

- Clinical complications of NEC recurrence / intra-abdominal abscess formation / short bowel syndrome

**Appendix**

**Pneumatosis Intestinalis**



**Portal venous gas**



**Pneumoperitoneum**

Clinical Pathway Team

Evaluation and management of suspected, medical and surgical Necrotizing enterocolitis Clinical Pathway

*Johns Hopkins All Children's Hospital*

Primary author: Sandra Brooks, MD, MPH, Chair NICU Clinical Pathway Council

Guideline Review Panel: (alphabetical order)

Fernando Bula, MD, Division of Pediatric Infectious Diseases

Nicole Chandler, MD, Chief, Division of Pediatric Surgery

Megan Charlton, PharmD, NICU clinical Pharmacist

Jane Cook, MD, Division chief, Pediatric Diagnostic Radiology

Katie Namtu – PharmD, Co-director, Antimicrobial Stewardship Program

Noura Nickel, MD - Neonatology

Kyle Thompson, MD, Fellow, Pediatric Surgery

Clinical Pathway Management Team: Joseph Perno, MD; Courtney Titus, PA-C

Date Approved by JHACH Clinical Practice Council: N/A

Date Available on Webpage: December 16, 2022

**Disclaimer**