C.S. MOTT CHILDREN'S HOSPITAL
MICHIGAN MEDICINE

DIAGNOSIS AND MANAGEMENT OF SUSPECTED AND DEFINITIVE NECROTIZING ENTEROCOLITIS

I. Applicability

a) Inclusion criteria: Intended for use in preterm infants with clinical concern for necrotizing enterocolitis (NEC) (see II below)

b) Exclusion criteria: Congenital GI anomalies, Term or near term infants

II. Clinical Presentation

Infants may present with a classical form of necrotizing enterocolitis (NEC) with abdominal distension (75%), bloody stool (28%) and bilious aspirates/emesis (18%).[1] Pneumatosis intestinalis and/or portal venous gas are pathognomonic radiographic findings.[2] NEC can present with a fulminant onset with shock and circulatory collapse, but can also present insidiously with non-specific signs (lethargy, temperature instability, or apnea). As infants with non-specific signs are more likely *not* to have NEC, this type of presentation offers a challenge to the clinician. For example, increased gastric residuals can be a hallmark of NEC, but can also be a normal finding in the premature infant. A significant overlap in the volume of residuals among infants with and without a subsequent diagnosis of NEC precludes it use as a marker for the disease.[3] [Please review the Brandon NICU feeding intolerance algorithm for more information]. Infants with other abdominal processes or sepsis may also present with these non-specific signs.

The possible cost of intervention (withholding of feedings, laboratory testing, x-rays, and antibiotics) must be weighed against the benefit of early treatment of those who will prove to have NEC. Using epidemiology to take into account the underlying a priori probability of NEC may help guide the clinician. Infants who are growth restricted (IUGR), whose mothers received multiple doses of prenatal steroids, who have underlying reasons for low cardiac output and ischemia, who received indomethacin, H2 blockers, and > 5 days of empirical antibiotic therapy may be at increased risk for NEC and non-specific signs taken more seriously.

III. Physical assessment of infants suspected of having NEC

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

IV. Interventions if NEC remains highly suspected:

a) Hold enteral feedings
b) Gastric decompression: Replogle to continuous suction
c) Radiographic evaluation: anterior-posterior and left lateral decubitus x-rays (cross table if unable to tolerate)
   i) Refer to "radiologic signs" in Table 1
d) Serologic tests
   i) If NEC is suspected but not definitive, consider sepsis evaluation (blood, urine, CSF), stool for guaiac, CBCPD, CRP, and basic metabolic panel
   ii) If definitive or advanced NEC based on x-ray and clinical presentation: blood gas, CBCPD, CRP, basic metabolic panel, blood culture

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e) Volume resuscitation
i) Infants with changes in hemodynamic status or severe illness may need up to 2x volume replacement in severe disease[1]
ii) Since VLBW infants do not tolerate excessive fluids well, meticulous attention to intravascular water content should be made
f) Pediatric surgery consultation for infants with stage II or III NEC
  i) With serious and/or advancing disease, decisions regarding the need for operative intervention require surgical consultation
  ii) To assist in making such decisions, earlier consultation (prior to the infant requiring critical care), will help the surgical team follow the progression of disease

g) For NEC requiring surgical intervention[5]
  i) Infants ≤1000 grams: primary drain placement
  ii) Infants >1500 grams: exploratory laparotomy
h) Pediatric infectious disease consultation:
  i) In cases of bacteremia or if no improvement/worsening within 48 hours of illness
  ii) Antibiotic choice is provided in Table 1 based on University of Michigan Health System antibiogram and in consultation with Pediatric Infectious Disease[5, 6]

V. Additional Considerations:
a) Laboratory testing frequency will be based on the trend and derangements present. For moderate to severe disease, derangements can be sudden and severe, especially with advanced disease.[1]
b) A systematic review of serological tests in the diagnosis of NEC reported: CRP was a "relatively sensitive but nonspecific marker for NEC", thrombocytopenia occurs in many neonatal systematic disease states, and nadir platelet counts typically occur after a diagnosis is made and hence are less useful in diagnosis.[7] CRP has been shown to be abnormal in infants with stage II and III NEC by 24-48 hours but may also be positive in other disease states (e.g., sepsis).[8]
c) Progression and/or perforation is most likely to occur within 48 hours of disease onset.[1, 9]
d) Abdominal ultrasound may be used as an adjunct study for infants with IIB or IIIA disease with inconclusive radiographs.[10]
e) Nasogastric suction may be discontinued when output is <3 ml/kg/shift (opinion)
f) Contrast studies are <u>not</u> indicated routinely before re-starting enteral feeds and should be performed if evidence of feeding intolerance and the suspicion of stricture.[11]
g) Antibiotic levels must be monitored closely to minimize toxicities.[1, 12]

VI. References
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VII. Related Policies/Guidelines/Standards/Procedures
a) Feeding intolerance algorithm

VIII. Author(s), Consultant(s)
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Table 1: Staging and Management of Necrotizing Enterocolitis

STAGE	ILLNESS SEVERITY	SYSTEMIC SIGNS	INTESTINAL SIGNS	RADIOLOGIC SIGNS	SURGERY CONSULT	X-RAYS FREQ.	ANTIBIOTICS[2,3] (see notes below)	DURATION
I. Suspected – No radiographic evidence. Differential includes ileus, fissure, other systemic infections, etc.								
Ia & Ib	Suspicious, mildly ill	- Temperature instability - Apnea/bradycardia - feeding intolerance	Residuals, mild distension, occult blood (1a), gross blood (1b)	Normal or mild ileus	No	Q12 x 24-48 hours	**Ampicillin**, or **vancomycin** if central line or MRSA colonized and **gentamicin**	48 hours
II. Medical NEC – MUST HAVE RADIOGRAPHIC DIAGNOSIS								
IIa.	Mild medical NEC	- Same as Ia - may (or may not) see some minor electrolyte or platelet changes	- Same as stg I - +/- bowel sounds - +/- abdominal tenderness	- Pneumatosis intestinalis (PI) - or fixed dilated loops	Yes	Q12 x 48 hours	**Ampicillin**, or **vancomycin** if central line or MRSA colonized (change to ampicillin if cultures negative at 48hrs) and **gentamicin**	7 days
IIb.	Moderate medical NEC	- Same as Ia, plus some lab changes (mild metabolic acidosis, mild thrombocytopenia) - often needs more support (resp or CV)	- Abd tenderness - Abd distension - Absent bowel sounds - +/- abdominal cellulitis	- Same as IIa - often portal venous gas - ± ascites	Yes	Q8 x 48 hours	**Vancomycin** (discontinue if cultures negative at 48hrs) and **piperacillin-tazobactam**	10 days
IIIa	Severe medical NEC (very sick like IIIb)	- ***Mod-severe* metabolic and/or respiratory acidosis** - electrolyte & CBC abnormalities - **shock**	- As above - + peritonitis, - marked tenderness	- Same as IIb - May see persistent ileus or absent bowel gas	Yes	Q8 x 48 hours	**Vancomycin** (discontinue if cultures negative at 48hrs) and **piperacillin-tazobactam**	10 days
III. Surgical NEC								
IIIb	Surgical NEC	- Same as IIIa	- Same as IIIa	Pneumoperitoneum	Yes	X-rays prn	**Vancomycin** (discontinue if cultures negative at 48hrs) and **piperacillin-tazobactam** and **fluconazole**	14 days

1. Systemic and intestinal signs are provided for your reference but generally reflect the illness severity (with moderate NEC, the systemic signs will be more deranged than with mild NEC). Not all signs will be present and crossover between stages may occur. Choose the stage that overall best fits the severity of illness.
2. If bacteremia present OR persistent symptoms/worsening at 48 hours, consult Pediatric Infectious Disease
3. Surgical intervention may be warranted if no clinical improvement after 48-72 hours and abdominal exam/X-rays remain concerning. Consider drain or paracentesis/ultrasound as a diagnostic study if NEC diagnosis unclear.

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