

Necrotizing Enterocolitis (NEC) — Pathophysiology and Management

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Necrotizing enterocolitis is a life-threatening inflammatory condition of the bowel that is characterized by mucosal injury, bowel necrosis or perforation. The condition is more common in pre-term infants. Bowel ischemia is believed to play a key role in the pathology of the condition, especially in full-term infants.



Overview

Necrotizing enterocolitis usually occurs in premature infants that are formula-fed and is **characterized by intestinal mucosal injury to full-thickness intestinal tract necrosis and even perforation**. The condition carries a high rate of mortality, 50%, especially in more severe cases in young neonates who weigh less than 1500 grams.

Epidemiology of Necrotizing Enterocolitis

The estimated **annual incidence of necrotizing enterocolitis is around 0.3 to 2.4 per 1000 live births**. Newborns who develop perinatal asphyxia, or have severe congenital heart disease, are prone to a severe form of necrotizing enterocolitis.

Epidemic cases of necrotizing enterocolitis have been shown to occur in nurseries over

time. This finding suggests a possible **infectious** etiology of necrotizing enterocolitis; however, a specific causative organism is yet to be identified.

Necrotizing enterocolitis has similar incidence in newborns of different ethnicities and races. Additionally, the condition has been reported to have an **equal incidence in boys and girls**.

The single most important risk factor for necrotizing enterocolitis is **premature birth**. The estimated incidence of necrotizing enterocolitis in infants born before 32 weeks of gestation is 6.4%. In addition to prematurity, a very low birth weight of 1000 grams or less is a risk factor for severe necrotizing enterocolitis.

The average age at time of diagnosis of necrotizing enterocolitis is largely dependent on the gestational date at birth. The average age of onset for infants born before 30 weeks of gestation is around 20 days, whereas the average age of onset in infants born at 31 to 33 gestational age is 14 days, and after 34 weeks' gestation is 5.4 days. **Full-term babies usually develop necrotizing enterocolitis within the first 48 hours of life.**

Pathophysiology of Necrotizing Enterocolitis

Necrotizing enterocolitis is believed to be an inflammatory disease caused by poorly understood etiologies. The damage to the intestinal tract can range between mucosal injury to full-thickness necrosis. Necrotic segments of the bowel might perforate. The most commonly affected site with necrotizing enterocolitis is the **terminal ileum**.

Our current understanding of the pathophysiology of necrotizing enterocolitis is limited, but it seems to be **multifactorial**. **Ischemic bowel** and **reperfusion** injury combined with the activation of the proinflammatory mediators seem to play a key role in the pathology of necrotizing enterocolitis. The possibility of an infectious trigger of the pathology has been suggested because of several reasons.

The epidemic nature of the distribution of the cases of neonatal necrotizing enterocolitis, the isolation of gram-positive or gram-negative bacteria in a significant proportion of the cases, and the isolation of fungi or viruses in other rarer cases of necrotizing enterocolitis all point towards a possible **infectious etiology**. Unfortunately, a clear causative relationship has not been established between any of the isolated organisms and the disease.

The most commonly identified organisms from blood cultures of infants with necrotizing enterocolitis are **Escherichia coli** and **Klebsiella pneumoniae**. Other less common organisms that have been isolated from patients with necrotizing enterocolitis include **Proteus species, Staphylococcus aureus, Streptococcus epidermidis, Enterococcus species, and Pseudomonas species**.

An important risk factor for necrotizing enterocolitis is **formula-feeding** instead of using breastmilk. It is hypothesized that the increased incidence of necrotizing enterocolitis in infants who are formula-fed might be related to the loss of exposure to protective secretive immunity from breastmilk, exposure to milk contaminated by Cronobacter species or loss of protective bacteria and alterations in the normal flora of the bowel.

Several maternal risk factors have been identified to be associated with an increased risk of necrotizing enterocolitis in the offspring. **Maternal hypertension, preeclampsia** and **cocaine exposure** are the most established maternal risk factors for neonatal necrotizing enterocolitis. These conditions and exposure to cocaine are believed to cause

compromised placental blood flow and subsequent bowel ischemia.

Clinical Presentation of Necrotizing Enterocolitis

The symptoms of necrotizing enterocolitis are **non-specific** and include vomiting, diarrhea, feeding issues, abdominal distention and the presence of blood in the stools. Abdominal wall edema, erythema, crepitans and palpable bowel loops are signs of severe and late necrotizing enterocolitis.

In addition to the localized signs and symptoms of necrotizing enterocolitis, infants can also have **systemic features** such as apnea, bradycardia, lethargy, body temperature changes or go into shock.



“Clinical Presentation Necrotizing Enterocolitis” Image created by Lecturio

Risk factors for necrotizing enterocolitis in full-term babies include birth asphyxia, respiratory distress, congenital heart disease, restricted intrauterine growth and metabolic derangements. Maternal risk factors such as hypertension or diabetes are also possible risk factors of necrotizing enterocolitis in full-term babies.

Pre-term babies usually do not have any other risk factor for necrotizing enterocolitis, except for prematurity and low birth weight. The use of **indomethacin** has been associated with an increased risk of necrotizing enterocolitis in pre-term babies. Pre-term babies who are recently switched to enteral feeding are at an increased risk of necrotizing enterocolitis.

On physical examination, the treating physician might notice **abdominal distention**, visible intestinal loops, decreased bowel sounds, presence of diarrhea with or without blood in stools, and the presence of systemic features such as respiratory failure, and increased capillary refill time. Premature infants who have severe necrotizing enterocolitis might develop shock.

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Diagnostic Workup for Necrotizing Enterocolitis

Whenever the diagnosis of necrotizing enterocolitis is suspected, one should obtain **abdominal radiographs**. Other laboratory tests can help in supporting the diagnosis of necrotizing enterocolitis but cannot confirm the diagnosis or exclude it reliably.

Complete blood count and blood cultures

Note: A complete blood count should be repeated every six hours, especially if the infant's condition is getting worse. Leukocytosis or leukopenia, thrombocytopenia and anemia should be excluded. Severe neutropenia is a very strong sign of neonatal sepsis.
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Before starting antibiotic therapy, blood cultures should be obtained in infants with necrotizing enterocolitis. The purpose of blood cultures is to exclude sepsis, not to

confirm the diagnosis of necrotizing enterocolitis, because the frequency of a negative blood culture is very high.

Checking serum electrolytes

Serum electrolytes should be checked in infants with necrotizing enterocolitis.

Hyponatremia is a worrisome sign. If present, hyponatremia should be corrected aggressively. **Metabolic acidosis** is usually seen in infants with necrotizing enterocolitis.

Lactic acidosis is a marker of cardiovascular collapse and ischemic bowel injury.

Radiology

X-Ray



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The best modality to establish the diagnosis of necrotizing enterocolitis is an **abdominal X-ray**. An anteroposterior abdominal X-ray and a left lateral decubitus view should be obtained. Abdominal X-rays should be repeated every 6 hours. Abnormal gas pattern, dilated and thickened bowel loops are the most commonly seen signs of necrotizing enterocolitis on abdominal X-rays. Fixed dilated loops and absence of intestinal gas are more worrisome signs of necrotizing enterocolitis on abdominal X-rays.

The presence of **pneumatosis intestinalis** is pathognomonic of necrotizing enterocolitis. The bowel appears to have a train-track lucency on abdominal X-ray. This finding is caused by the entrapment of air within the intramural bowel walls due to gas forming bacteria.

The presence of free air on an abdominal X-ray in an infant suspected to have necrotizing enterocolitis is a very worrisome sign that is indicative of bowel necrosis and perforation.

Ultrasonography

Ultrasonography has been also used in establishing the diagnosis of necrotizing enterocolitis. The main advantages of ultrasonography over abdominal X-rays are the availability of ultrasonography at the bedside and the decreased exposure to ionizing

radiation. Recent studies have shown that increased peak flow velocity of more than 1 in the celiac and superior mesenteric arteries is an accurate sign of early necrotizing enterocolitis.

Staging of Necrotizing Enterocolitis

Infants with mild non-specific systemic signs, mild intestinal signs such as abdominal distension and mild abdominal radiographic findings of bowel dilatation are diagnosed with Stage IA necrotizing enterocolitis. If gross blood is observed in the stool, then stage IB is used.

If the infant has all the previously mentioned signs in addition to radiographic features of ileus or pneumatosis intestinalis, Stage IIA necrotizing enterocolitis is diagnosed. The presence of portal venous gas with or without ascites is indicative of stage IIB disease.

When the patient also has hypotension, severe metabolic acidosis, cardiovascular and respiratory failure, and neutropenia, the diagnosis of Stage IIIA advanced necrotizing enterocolitis is made. Stage IIIA patients usually require surgical intervention. If the bowel is perforated, the designation stage IIIB is used.

Treatment of Necrotizing Enterocolitis

Infants with an extremely low birth weight should be started on enteral feeding using the standardized slow enteral feeding protocol rather than early enteral feeding. The risk of necrotizing enterocolitis is lower when enteral feeding from start to full feeds ranged between 44–52 days for babies weighing under 750 grams and 32–36 days for babies weighing between 750 and 1000 grams at birth.

Infants who develop stage II necrotizing enterocolitis should be kept on a diet of nothing by mouth for one week up to 10 days. Parenteral hyperalimentation is usually indicated in these patients. The placement of a central venous catheter is usually indicated due to the difficulty of obtaining a sustainable peripheral venous line.

Antibiotics are indicated for three days in infants with stage I disease and for two weeks in children with stage II disease. Surgical consultation is indicated in any infant with stage II disease.

Infants with stage IIIA disease should be kept on a nothing by mouth diet for two weeks. These children are usually in shock and adequate fluid resuscitation, inotropic support and ventilator support is usually needed. Surgical consultation should be obtained as early as possible.

Infants with necrotic intestine or a perforated intestine, stage IIIB disease, require surgical intervention. Infants with a perforated intestine usually go straight to surgery, whereas those with a necrotic intestine are usually referred for surgical intervention if they fail medical treatment. Signs of failure of medical treatment of necrotizing enterocolitis include the presence of peritonitis, worsening or intractable metabolic acidosis, severe and persistent thrombocytopenia, rising leukocytosis or declining leukopenia and intractable hemodynamic instability.

Primary anastomosis is not recommended in surgical patients. Different surgical approaches have been used in the management of necrotizing enterocolitis. Patching perforations, placement of intra-abdominal drains and initiation of long-term parenteral nutrition is the more conservative approach to treat surgical cases of necrotizing

enterocolitis.

More drastic approaches of resection of the multiple necrotic segments and placement of multiple stomas are no longer recommended. Instead, primary anastomosis of the distal resected segments with the placement of a single stoma at the end of the proximal segment is recommended. Enterostomy closure is typically performed 1 to 2 months after the first operation.

References

Springer SC. Necrotizing Enterocolitis. Practice Essentials, Background, Etiology. <http://emedicine.medscape.com/article/977956>. Published January 6, 2017. Accessed April 26, 2017.

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