

Local Guideline



Health
Hunter New England
Local Health District

Necrotising Enterocolitis (NEC): Diagnosis and management in NICU

Sites where Local Guideline applies	Neonatal Intensive Care Unit JHCH
This Local Guideline applies to:	
1. Adults	No
2. Children up to 16 years	No
3. Neonates – less than 29 days	Yes Approval gained from the Children Young People and Families Network on 28 th September 2017
Target audience	Clinicians caring for infants in NICU and SCN
Description	Provides information on assessment and management of an infant with NEC
National Standard	Standard 3: Preventing & Controlling Healthcare Related Infections

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Keywords	Gastrointestinal, GIT, Necrotising Enterocolitis, NEC, Preterm, Sepsis, Neonatal, NICU, JHCH
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Related Legislation, Australian Standard, NSW Ministry of Health Policy Directive or Guideline, National Safety and Quality Health Service Standard (NSQHSS) and/or other, HNE Health Document, Professional Guideline, Code of Practice or Ethics:	
<ul style="list-style-type: none"> NSW Health Policy Directive 2014_032 Clinical Procedure Safety NSW Health Policy Directive 2017_013 Infection Prevention and Control Policy 	
Prerequisites (if required)	N/A
Local Guideline note	This document reflects what is currently regarded as safe and appropriate practice. The guideline section does not replace the need for the application of clinical judgment in respect to each individual patient but the procedure/s require mandatory compliance . If staff believe that the procedure/s should not apply in a particular clinical situation they must seek advice from their unit manager/delegate and document the variance in the patient's health record.
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Note: Over time links in this document may cease working. Where this occurs please source the document in the PPG Directory at: <http://ppg.hne.health.nsw.gov.au/>

PURPOSE AND RISKS

This local clinical procedure has been developed to provide instruction to the health clinician and to ensure that the risks of harm to the infant associated with NEC are prevented, identified and managed.

The risks are:

- Preterm infant with immature GIT*
- Ischaemic injury during pregnancy, intra partum or post-partum*

The risks are minimised by:

- Understanding of the importance and relevance of clinical history taking*
- Clinicians having knowledge of signs and symptoms of NEC to recognise early*
- Clinicians seeking assistance if the infant is displaying symptoms outside the normal limits*
- Following the instructions set out in the clinical procedure*
- Awareness of the consequences of the risks to the infant e.g. preterm infant and not receiving breast milk*

Risk Category: *Clinical Care & Patient Safety*

GLOSSARY

Acronym or Term	Definition
CRP	C-reactive protein
NEC	Necrotising enterocolitis
N-Pass	Neonatal Pain and Sedation Score

Necrotising Enterocolitis (NEC): Diagnosis and management in NICU

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GUIDELINE

This Guideline does not replace the need for the application of clinical judgment in respect to each individual patient.

Staff Preparation

It is mandatory for staff to follow relevant: “Five moments of hand hygiene”, infection control, moving safely/safe manual handling, documentation practices and to use HAIDET for patient/carer communication: **H**and hygiene **A**cknowledge, **I**ntroduce, **D**uration, **E**xplanation, **T**hank you or closing comment.

Rationale

Necrotising enterocolitis (NEC) is the most common gastrointestinal emergency in neonates, occurring mainly in preterm infants, and can result in significant morbidity and mortality.

Introduction

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It is a disease of unknown etiology with multifactorial pathogenesis.

Incidence

The incidence of NEC is between 0.3 and 3 per 1000 live births. The risk of developing NEC is inversely related to gestational age at birth with the extremely premature infant at greatest risk. It is estimated 10% of very low birth weight infants develop NEC. NEC also occurs in term infants at a rate of 0.05/1000 live births.

The incidence of NEC for neonates born at less than 32 weeks gestation in the neonatal intensive care unit at JHCH has been ~2.4% over the past 10 years (~10% for neonates < 28 weeks gestation). The mortality related to NEC requiring surgical intervention has been over 50% and is much higher in extremely low birth weight (ELBW, < 1000 g birth weight) neonates in the JHCH cohort.

Risk factors

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Prematurity and intrauterine growth restriction are found consistently to predispose to NEC. NEC is associated with conditions that reduce mesenteric blood flow that may lead to intestinal ischaemia/hypoxia and injury.

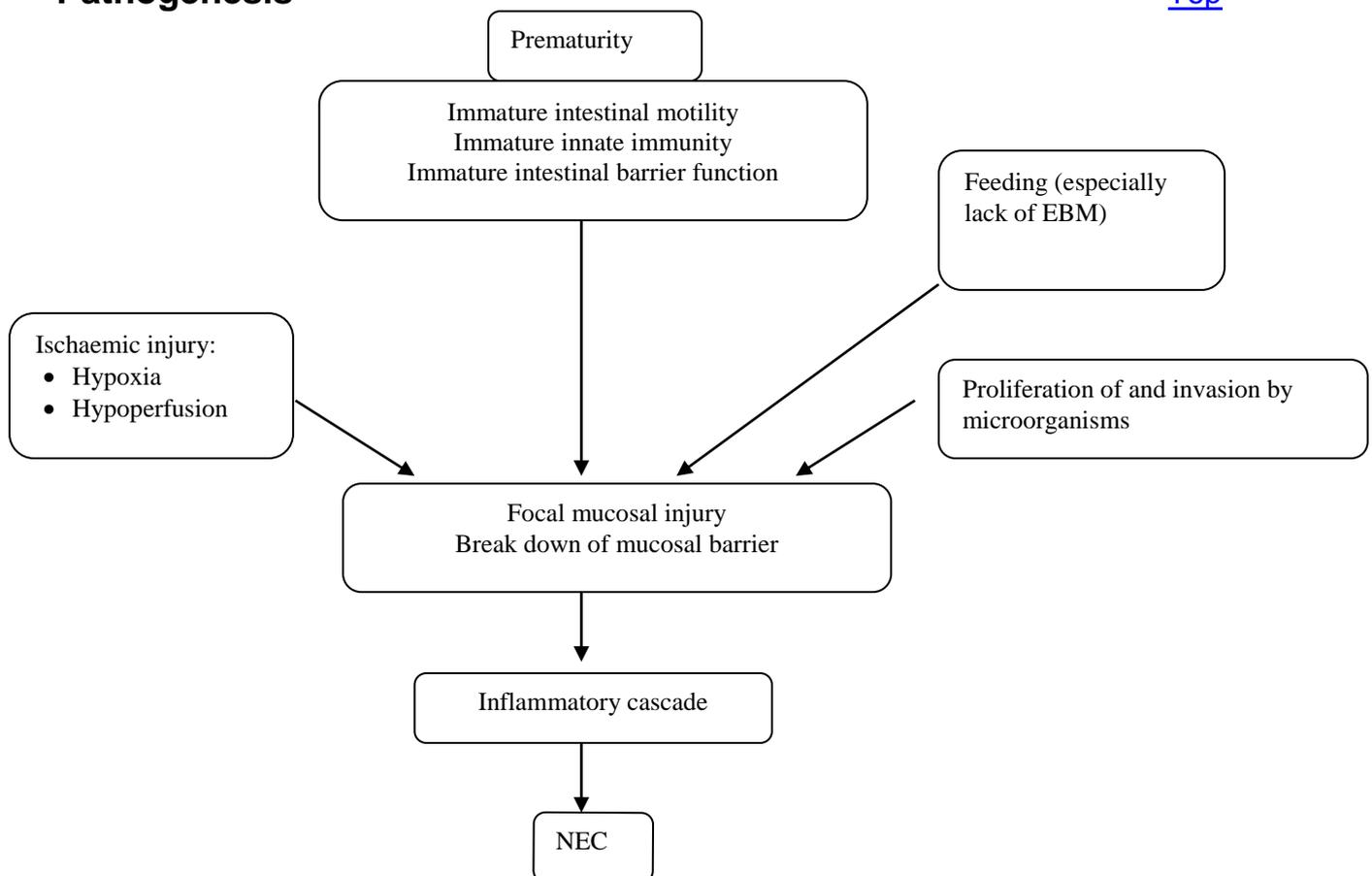
1. **Gestational age:** Prematurity is the main risk factor with > 90% of infants who develop NEC born prematurely.
2. **Enteral feeding:** The majority of infants (> 90%) that develop NEC have received enteral feeds. However, NEC can occur in infants who have never been fed.
3. **Type of feed:** NEC is rare in infants fed exclusively with breast milk. Prospective, non-randomised studies have shown NEC to be 6–10-times more common among formula fed babies and 3 times more common in formula plus breast milk, compared to those fed breast milk alone⁸.

4. **Associated organisms:** The most frequently isolated bacteria are gram negative: *Klebsiella*, *E coli*, *Enterobacter* (these 3 are isolated in over half of cases); anaerobes: *Clostridia*, *Bacteroides*; gram positive: *Staph. epidermidis*, *Enterococci*. Virus and fungi, especially *Candida spp.*, have also been implicated.
5. **Blood flow abnormalities:** Absent or reversed umbilical artery flow on antenatal ultrasound scans and low systemic blood flow and hypotension requiring inotropes in the neonatal period are associated risk factors. Babies with severe IUGR are also at risk of antenatal blood flow abnormalities.
6. **Perinatal asphyxia:** It has been shown to be a risk factor mainly for NEC occurring in infants > 32 weeks.
7. **No antenatal steroids:** Antenatal steroids given for preterm labour with rupture of membranes significantly decrease the incidence of NEC (by 50%).
8. **Polycythaemia**
9. **Congenital heart disease**
10. **Exchange transfusion**

About 10% of NEC cases can occur in term babies. Infants who are at risk of bowel hypoperfusion (e.g. congenital heart disease) or infants with perinatal asphyxia are at risk. On rare occasions, NEC can develop in infants with **no identifiable risk factors**.

Pathogenesis

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Pathology

NEC can affect all portions of the gastrointestinal tract (GIT) but most commonly the jejunum, terminal ileum and proximal colon. An infant's GIT with NEC shows mucosal and transmural necrosis, haemorrhage, inflammation, ulceration and reparative changes.

Consequences

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Mortality

Mortality rate of NEC is high – 20 to 40% (higher in extremely low birth weight infants). At JHCH NICU, the overall mortality rate from NEC has been 35% rising to 65% for ELBW infants and 50% for infants with Stage III NEC.

Intestinal sequelae

At discharge, many infants have a high prevalence of adverse intestinal sequelae and remain at significant risk of undernutrition, recurrent illness, gastrointestinal complications, poor growth and recurrent hospitalisation. These are associated with:

- **Strictures:** The most common long-term GIT complication, present in up to 35% of infants who have had NEC. They occur in both surgically and medically treated NEC. The most common site is at the junction of the descending and sigmoid colon. Potential indicators of stricture formation are failure to thrive, feeding intolerance, altered stool pattern or bowel obstruction.
- **Short bowel syndrome:** Seen in 25% of infants that undergo surgery.
- **Bowel obstruction:** In 5% of patients who have had surgery for NEC.
- **Cholestasis:** Secondary to prolonged TPN
- **Uncommon sequelae:** Fistula, abscess, recurrent NEC, malabsorption, enterocyst formation

Neurodevelopmental sequelae

NEC is significantly associated with increased neurodevelopmental morbidity independent of other factors and is more common in infants who have required surgery compared with medically-treated infants with NEC.

Growth

Normal catch-up growth is seen in infants with NEC who were managed conservatively. There is an increased incidence of growth failure in infants who required surgery, developed short bowel syndrome and/or were on prolonged TPN.

Clinical Presentation

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- NEC varies greatly. Infants may have a sudden onset with rapid clinical deterioration or it may evolve slowly over a few days. Consider NEC if any of the following signs are present:
 - **–Nonspecific for GIT:** Feed intolerance, abdominal distension, occult blood in stool

- **Specific for GIT:** Increased abdominal distension with tenderness, abdominal wall oedema, decreased or absent bowel sounds, bile-stained gastric aspirates, bloody stool.
- **Systemic:** Temperature instability, apnoea, persistent acidosis, thrombocytopenia, anaemia, neutropenia and cardiovascular compromise such as hypotension, oliguria, shock

Differential diagnosis

- Sepsis with ileus
- Bowel obstruction, volvulus and malrotation
- **TPN peritonitis:** Make sure the umbilical venous catheters are in the right position on abdominal X-rays. TPN peritonitis can mimic NEC and rapidly progress to abdominal compartment syndrome. If in doubt, get an abdominal US done. A diagnostic peritoneal tap might have to be performed after surgical referral. Refer to CPG for details. [Umbilical lines in NICU NICU 10.03](#)
- **Spontaneous intestinal perforation:** This appears to be a distinct clinical entity in the VLBW infant, differentiated from NEC surgically by isolated perforation often at the terminal ileum with normal bowel. AXR shows no evidence of pneumatosis intestinalis. The infant usually presents early within the first week of life with minimal systemic signs. However, despite extensive literature on the subject, there has been an ongoing debate on whether this condition represents a mild form of necrotising enterocolitis or a distinct entity
- **Systemic candidiasis:** Clinical signs are often similar to NEC with abdominal distension seen in half these infants; metabolic disturbances, hypotension and thrombocytopenia also occur

Objective staging criteria developed by Bell have been widely adopted or modified to help tailor therapy according to disease severity.[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 and Kliegman RM, Walsh MC. Neonatal necrotizing enterocolitis: pathogenesis, classification, and spectrum of disease. *Curr Probl Pediatr* 1987]

Stage	Systemic signs	Intestinal signs	Radiographic signs	Management
I – Suspected NEC	<ul style="list-style-type: none"> Mild, nonspecific, systemic signs such as apnoea, bradycardia, and temperature instability are present 	<ul style="list-style-type: none"> Mild intestinal signs such as increased gastric residuals and mild abdominal distension are present 	<ul style="list-style-type: none"> Radiographic findings can be normal or can show some mild nonspecific distension 	<ul style="list-style-type: none"> Treatment is keep on a diet of nothing-by-mouth (NPO) with antibiotics for 3 days Intravenous (IV) fluids, including total parenteral nutrition (TPN)
IIA – Mild NEC	<ul style="list-style-type: none"> Patient is mildly ill Diagnostic signs include the mild systemic signs present in stage I 	<ul style="list-style-type: none"> Intestinal signs include all of the signs present in stage I Infant also has absent bowel sounds and abdominal tenderness 	<ul style="list-style-type: none"> Radiographic findings show ileus and/or pneumatosis intestinalis 	<ul style="list-style-type: none"> Treatment includes support for respiratory and cardiovascular failure, including fluid resuscitation, NPO, and antibiotics for 14 days. Surgical consultation should be considered. After stabilisation, TPN should be provided during the period that the infant is NPO
IIB – Moderate NEC	<ul style="list-style-type: none"> Patient is moderately ill. Diagnosis requires all of stage I signs plus the systemic signs of moderate illness, such as mild metabolic acidosis and mild thrombocytopenia 	<ul style="list-style-type: none"> Abdominal examination reveals definite tenderness, perhaps some erythema or other discoloration, and/or right lower quadrant mass 	<ul style="list-style-type: none"> Radiographs show portal venous gas with or without ascites in addition to pneumatosis intestinalis. 	<ul style="list-style-type: none"> Treatment includes support for respiratory and cardiovascular failure, including fluid resuscitation, NPO, and antibiotics for 14 days. Surgical consultation should be considered. After stabilisation, TPN should be provided during the period that the infant is NPO

Stage	Systemic signs	Intestinal signs	Radiographic signs	Management
IIIA – Advanced NEC	<ul style="list-style-type: none"> • Patient has severe necrotising enterocolitis with an intact bowel • Diagnosis requires all of the above conditions, with the addition of hypotension, bradycardia, respiratory failure, severe metabolic acidosis, coagulopathies, and/or neutropenia 	<ul style="list-style-type: none"> • Abdominal examination shows marked distension with signs of generalised peritonitis 	<ul style="list-style-type: none"> • Radiographic examination reveals definitive evidence of ascites 	<ul style="list-style-type: none"> • Treatment involves NPO for 14 days, fluid resuscitation, inotropic support, and ventilator support • Surgical consultation should be obtained • TPN should be provided during the period of NPO
IIIB – Advanced NEC	<ul style="list-style-type: none"> • Patient is severely ill with all of above signs 		<ul style="list-style-type: none"> • Radiographic examination reveals pneumoperitoneum 	<ul style="list-style-type: none"> • Treatment similar to recommendations for IIIA

Investigations

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Laboratory

- **FBC: Thrombocytopenia** is often seen. There can be associated anaemia and neutropenia
- **C-reactive protein (CRP)**
- **Blood film:** Haemolysis and toxic changes
- **Electrolyte abnormalities** especially hyponatraemia
- **Arterial, venous or capillary blood gas:** For evidence of acidosis, hypoxia or hypercarbia
- **Coagulation profile:** If there is active bleeding.
- **Blood cultures:** Positive blood cultures are found in less than 1/3 of cases. Bacterial and fungal cultures may be helpful in management

Imaging

Both a supine AP abdominal and left-lateral decubitus X-ray are essential for the diagnosis of suspected NEC. It is important to note that radiological findings associated with NEC are not seen in all infants. Infants with suspected/established NEC require serial abdominal X-rays (6–8th hourly – check with Neonatal consultant).

For examples of X-rays on NEC please follow the link: [Teaching Resources-radiology](#)

X-ray findings include:

- Dilated and thickened bowel loops ± air-fluid levels
- Pneumatosis intestinalis (intramural gas); the radiological hallmark of NEC
- Pneumoperitoneum: Best seen under the diaphragm in the left-lateral decubitus AXR. Less commonly, on the AP film it is seen as a central collection of free air ('football sign')
- Persistently distended loop of bowel
- Portal venous gas
- Gasless abdomen

Contrast studies: These are best avoided during the acute illness as there is a high risk of gastrointestinal perforation.

Treatment guideline

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Treatment is directed towards prevention of further injury and recognition and removal of gangrenous bowel. Serial physical examinations and investigations should be done to guide duration of treatment.

Principles of treatment

- Bowel rest and nutrition
- Intravenous antibiotics
- Fluids and cardiovascular support
- Respiratory support
- Correction of acidosis
- Analgesia
- Surgery

Bowel rest and nutrition

- Stop enteral feeding. Conventionally the duration of no enteral feed is 7–14 days. This is empirical with no available evidence to support it. Consider earlier recommencement of feed if gut function has returned to normal, i.e. soft, non-distended, non-tender abdomen with normal bowel sounds and minimal gastric residuals
- Gastric decompression with a large bore 8–10F orogastric tube placed on free drainage
- Commencement of intravenous fluids
- TPN should be commenced unless there is severe acidosis
- Correction of electrolyte disturbances

Gradual reintroduction of feed: Rate – no more than 20 mL/kg/day increments; type – ideally, expressed breast milk. Following the reintroduction of feeds, up to 10% of infants show increased gastric residuals and abdominal distension.

Intravenous antibiotics: (for drug dosage see NICU Drug protocols)

- Broad-spectrum, intravenous antibiotic cover against gram positive and negative organisms should be commenced as soon as the diagnosis is considered. Because of the prominence of anaerobic bacteria, the routine inclusion of –an anti-anaerobic drug is suggested. Clinical trials of definitive management regimens are lacking, but therapy should be determined by the sensitivity of local organisms
- The recommended antibiotic regimen is [ampicillin](#) and [gentamicin](#) with anaerobic cover using [Metronidazole](#). [Vancomycin](#) (instead of ampicillin) may sometimes be used in infants < 28 weeks gestation due to their higher susceptibility to nosocomial coagulase negative staphylococci sepsis.
- The duration of antibiotic treatment is usually 7–14 days. Again this is convention without evidence to support it. Stopping earlier may be considered if the baby is tolerating oral feeds and is clinically improved

- Infectious disease consult should be obtained for further guidance regarding antibiotic cover depending on blood culture results

Cardiovascular support

Many infants will be hypovolaemic as a result of capillary leak, third spacing and hypoalbuminaemia and may require aggressive fluid resuscitation. Volumes starting from 20 mL/kg up to 60 mL/kg may be required. To assist in management, assessment of cardiac haemodynamics should be considered.

Haematological support

Any haematological abnormalities (e.g. anaemia, thrombocytopenia and coagulopathies) should be corrected appropriately (washed RBCs if T-activation is present)

- [FFP](#)
- [Platelets](#)
- [Cryoprecipitate](#)

Respiratory support

Mechanical ventilation may be required if there are increasing oxygen requirements, apnoea or acidosis. Infants with NEC may continue to receive CPAP unless contraindicated (suspected intestinal perforation; tense abdominal distension).

Correction of acidosis

The acidosis in NEC is mixed. Correct the respiratory component (hypercarbia and acidosis from hypoventilation) with appropriate ventilatory support. The initial metabolic component is usually from hypoperfusion and requires fluid support.

Analgesia

Assessment of pain should be recorded using The Neonatal Pain and Sedation Score (N-Pass). Follow link to CPG [Assessment and Management of pain in the Neonate](#). If required, commence [morphine](#) infusion at 10–20 microgram/kg/hr.

Surgery

Early consultation with a paediatric surgeon is essential once the diagnosis has been considered. The decision for surgery is based on taking into account both the clinical context of the presentation as well as the acute problem itself.

Indications for surgery:

- Definitive indication: Perforation of the gut as evidenced by free air on X-ray or US
- Relative Indications: Failure of medical management with
 - 1) Abdominal mass
 - 2) Refractory acidosis
 - 3) Refractory thrombocytopenia
 - 4) Portal venous gas
 - 5) Fixed loop on serial X-ray
 - 6) Positive paracentesis
 - 7) Ascites with gasless abdomen

Long term management of NEC

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- Parents must be instructed about the signs of bowel obstruction
- Medical and surgical follow-up after discharge
- Contrast studies for strictures should be done if clinically indicated
- Appropriate developmental follow-up

Prevention

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Probiotics are live microorganisms that increase natural intestinal defences by regulating inflammatory responses, cellular proliferation and apoptosis. Several studies have demonstrated the efficacy and safety of prophylactic, enteral probiotic administration in the prevention of necrotising enterocolitis in infants with very low birth weight. A Cochrane review on this topic analysed 24 trials and demonstrated that enteral [probiotics](#) supplementation significantly reduced the incidence of severe necrotising enterocolitis and associated mortality.

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25/06/2017
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IMPLEMENTATION, MONITORING COMPLIANCE AND AUDIT

1. Following approval of the guideline it will be communicated to staff via the HUB and email and placed on the PPG.
2. Incident investigations associated with this Guideline and Procedure will include a review of process.
3. The Guideline and Procedure will be amended in line with the recommendations.
4. The person or leadership team who has approved the Guideline and Procedure is responsible for ensuring timely and effective review of the Guideline and Procedure.
5. Evaluation will include a review of the most current evidence as well as a consideration of the experience of Neonatal staff at JHCH in the implementation of the Guideline and Procedure.

FEEDBACK

Any feedback on this document should be sent to the Contact Officer listed on the front page.