Guidelines for the management of Necrotising Enterocolitis

- Necrotising enterocolitis (NEC) is common in both preterm and IUGR infants; affecting 3-7% of neonates weighing <1500g.
- 90% of cases occur in pre-term babies who have been fed, however around 10% of cases occur in term infants usually secondary to a known insult i.e. perinatal asphyxia, polycythemia, congenital heart disease, sepsis, post exchange transfusion, intrapartum infection or maternal cocaine abuse.
- Mortality following NEC is 15-30%. There is substantial long-term morbidity in survivors, especially those with BW<1500g; namely intestinal failure and functional neurodevelopmental delay, which contribute significantly towards increased health costs.
- Prematurity, formula feeding and a significant PDA increase the risk of NEC, whereas antenatal steroids and breast milk are protective. Mothers of high-risk babies should be actively encouraged to express breast milk.

Pathology
Aetiology is multifactorial with interaction of gut hypoxia, poor mucosal integrity, bacterial flora and presence of metabolic substrate. NEC is a transmural disease characterised by mucosal oedema and haemorrhage, transmural necrosis and ulceration and development of subserosal gas collections. It can affect any part of the bowel, but predominantly involves terminal ileum, caecum and ascending colon. As the gut heals the bowel wall often thickens and can form areas of adhesions and strictures.

Clinical presentation
Clinical presentation can be classical with the triad of abdominal distension, blood in the stools and bile stained aspirates/vomits. However it can also present insidiously with non-specific signs e.g. lethargy, temperature instability, change in feed tolerance and apnoeic episodes, or with a fulminant onset with shock, respiratory failure and collapse.

Diagnosis
Diagnosis of NEC is based on Bell's staging criteria, which combines clinical and radiological features. Please see table on next page for a summary.

NB: X-rays can be normal in NEC and intramural and portal gas is seen less in preterm babies.
<table>
<thead>
<tr>
<th>Stage</th>
<th>1A</th>
<th>1B</th>
<th>II A</th>
<th>IIB</th>
<th>III A</th>
<th>III B</th>
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<tbody>
<tr>
<td><strong>Classification</strong></td>
<td>Suspected NEC</td>
<td>Confirmed NEC, Mildly ill</td>
<td>Confirmed NEC, Moderately ill</td>
<td>Severe/ Advanced NEC Bowel intact</td>
<td>Severe/ Advanced NEC Bowel perforation</td>
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<td><strong>Systemic Features</strong></td>
<td>Non specific signs e.g. Temperature instability, apnoea, feed intolerance, lethargy, bradycardia</td>
<td>As for stage I</td>
<td>Mild metabolic acidosis, thrombocytopenia</td>
<td>Stage IIB plus clinical deterioration/ evidence of septic shock e.g. hypotension, bradycardia, apnoeas, severe acidosis, DIC, neutropaenia</td>
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<td><strong>Abdominal Signs</strong></td>
<td>Poor feeding, increased gastric aspirates, bilious vomiting, mild distension, abdominal tenderness, faecal occult blood.</td>
<td>As for IA plus frank bloody stools</td>
<td>Stage I plus: Abdominal tenderness and/or guarding. Marked abdominal distension. Periumbilical flare. Blood or mucus in the stool.</td>
<td>Marked GI haemorrhage. Abdominal wall discolouration.</td>
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<tr>
<td><strong>Radiological Signs</strong></td>
<td>AXR within normal limits or evidence of simple ileus. Note similar appearance to “CPAP belly”</td>
<td>Distended and featureless bowel loops, bowel wall oedema, persistent or fixed loops Pneumatosis intestinalis (blue arrow) Portal venous gas. (red arrow)</td>
<td>Widespread pneumatisos (blue arrow) and portal air (red arrow)</td>
<td>As for stage II No free air</td>
<td>As for stage II plus free air. Pneumoperitoneum. (“Football sign” – blue arrows) Note falciform ligament outline by free air (red arrow)</td>
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Management

**Stage I: Suspected NEC with normal x rays:**
1. Stop enteral feeds and insert NGT for gastric decompression. Start IV fluids/Parenteral nutrition.
2. FBC, U&Es, blood gas, blood culture and CRP. Consider full septic screen if presenting with non specific signs. If neutropaenic or thrombocytopaenic perform clotting screen and G +S and consider more severe stage.
3. AXR, usually AP but to consider lateral decubitus if worried about perforation. During normal working hours please consider discussing with and/or view AP films with Radiology before proceeding to further views.
4. Start triple antibiotics, as per local policy, however this will vary depending on the recent antibiotic usage. 20-30% of patients with NEC have been reported to have a concomitant bacteraemia.
5. Consider giving paracetemol and/or morphine for analgesia.
6. Repeat bloods and AXR if clinical concerns persist.
7. If signs and symptoms resolve, stop antibiotics after 48-72 hours and recommence feeds.

**Stage II and III: Confirmed and Advanced NEC.**

**As Stage I plus**
1. Consider transferring the baby to a surgical centre. Always discuss with the on-call consultant before referring to the surgical team.
2. Consider need for early respiratory support by intubation and ventilation as increasing abdominal distension can cause diaphragmatic splinting. CPAP may worsen abdominal distension. Insert NGT for gastric decompression.
3. Give early volume expansion if signs and symptoms suggest shock. Often these babies have a high volume requirement due to capillary leak syndrome. Start inotropic support promptly if hypotensive. (Please see hypotension guideline for more information)
4. Correct electrolyte abnormalities, monitor urine output and consider catheterisation.
5. Start morphine infusion to provide analgesia. NEC is painful and these patients will often need more than 20 micrograms/kg/hour.
6. Haematology: aim for Hb>120g/l and platelet>50x10^9/l (please see RBC and platelet transfusion guidelines for more information). Check clotting, if abnormal and/or actively bleeding consider FFP.
7. Monitor blood tests regularly ~12 hourly and blood gases/lactates ~ 4-6 hourly.
8. Repeat the AXR if clinical deterioration. Pneumatosis intestinalis is pathognomonic of NEC; can be linear or curvilinear if subserosal and foamy if submucosal similar to the appearance of stool. Consider if stool in a fully fed baby.
9. Consider lateral decubitus or right side up view if worried about perforation. During normal working hours please consider discussing and/or view AP film with Radiology before proceeding to further views. Inform the consultant urgently if the X-ray reveals a perforation. Surgical team to also be informed, as surgical intervention may be needed.
10. When stabilised insert a percutaneous long line early as these infants will be NBM for many days and will require prolonged PN.
11. If improving with medical management, continue antibiotics for 7-10 days and NBM for 10 days. Start enteral feeds when abdomen is soft, non-tender, non-distended with normal bowel sounds and no aspirates. If a baby suffers a second episode of NEC and breast milk is not available commence baby on appropriate formula (DEBM, low birth weight formula or nutrient enriched post discharge formula). If there are further concerns consider peptijunior.

**Surgery**

50% of neonates with confirmed or advanced disease will require surgical intervention. Usually a laparotomy is performed, however some patients will be too sick for theatre and these patients may undergo peritoneal drainage on the unit. Most common indications for surgery include failure to respond to maximal medical therapy, perforation, fixed intestinal loop and abdominal mass with obstruction. Please see Stoma guideline for management of babies who have been to theatre and required resection and stoma.

**Probiotics**

Probiotics are live non-pathogenic microbial preparations that colonise the intestine and provide benefit to the host. They act by preventing colonisation of the gut with pathogenic bacteria and promoting beneficial bacterial colonisation. They also modulate the immune system to the advantage of the host. Although available evidence has suggested probiotics reduce the risk of NEC; there has been large variability in quality of the data and heterogeneity between studies plus a lack of evidence for an optimal strain and dosing. In addition there is an absence of quality control regulation to ensure consistency and safety of available product. Please follow your unit’s policy on probiotics.

**Prevention of NEC:**

- Current evidence suggests that neither slow advancement of feeds nor delay in introduction of enteral feeds to over day 4 of life reduces the risk of NEC; and are associated with delay in regaining birth weight and establishing full enteral feeds. Minimal enteral/trophic feeds have not been demonstrated to increase incidence of NEC – please see enteral feeding guideline for guidance on enteral feeds in premature/high risk babies. Small studies have suggested increased risk of NEC with feed thickeners so these should be used sparingly and starting H2 receptor blockers (e.g ranitidine) is a senior decision.
- Empiric antibiotic use >5 days has been associated with increased risk of NEC – it is vital that antibiotics are reviewed daily and rationalised accordingly.
- Recent papers have questioned the association of NEC and PRBC transfusion and suggested a possible association between anaemia and development of NEC. The Transfusion of prematures (TOP) trial is currently ongoing and recruiting until Dec 2019. Currently we recommend transfusion of high-risk neonates remains a consultant-led decision and please consult the service-consultant to discuss feeds during transfusion.
- There is an on-going clinical trial into oral lactoferrin to reduce risk of NEC (ELFIN trial – due to complete in March 2017). Small trials have suggested possible benefit.
- Evidence shows that having a unit feeding guideline lowers the risk of NEC.

References

1. AlFaleh K et al, Probiotics for prevention of NEC in preterm infants; Cochrane Database of Systematic Reviews 2011, Issue 3. Art. No.: CD005496