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Joint Trust Guidelines for the Management of Necrotising Enterocolitis in Neonates and Infants

A clinical guideline recommended for use

For Use in	Neonatal Intensive Care Unit
By:	Neonatal and Paediatric medical, surgical and nursing staff
For:	Neonates and infants admitted to NICU
Key words:	Necrotising enterocolitis, enteral feeds
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Objective/s

Ensure best practice in suspected and confirmed cases of Necrotizing enterocolitis (NEC).

Rationale

This guideline has been developed to aid medical and nursing staff to recognize and diagnose NEC at an early stage and take appropriate action to limit the progress of the illness and complications. The decisions regarding feeding and other aspects of prevention and treatment will be based on available evidence and/or best practice. The guidelines are based on a review of medical literature to March 2012.

Clinical audit standards

Appropriateness of investigations, surgical referral and duration of treatment.

Summary of development and consultation process undertaken before registration and dissemination

The authors listed above drafted the guideline. During its development it was discussed at a multidisciplinary guideline meeting of the Paediatric Medicine and Surgical Departments and the Neonatal Unit, changes suggested were discussed and incorporated. It was subsequently circulated for comment to the Paediatric Medicine and Surgical Departments and the Neonatal Unit (Consultants, Specialist Registrars, Advanced Neonatal Nurse Practitioners, Sisters and Senior Staff Nurses. Suggestions for further improvement were incorporated; consensus was reached for non-evidence based treatment (advised according to current expert opinion/best practice). There is little good quality evidence on treatment for this condition.

Distribution list dissemination method

Neonatal Intensive Care Unit and NNUH Intranet.

References / source documents

See page 10

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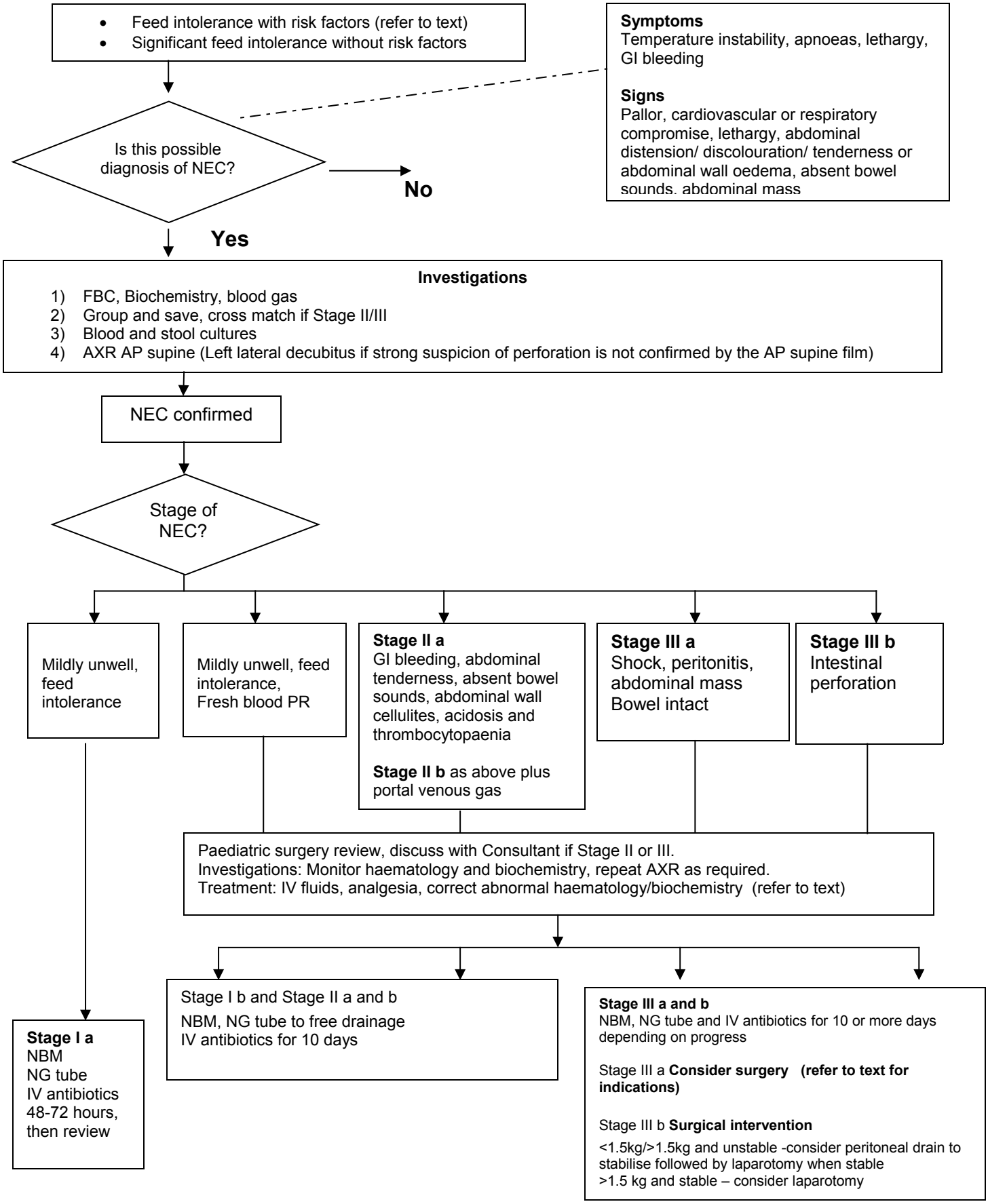
Quick Reference Guideline



Introduction

Necrotizing Enterocolitis is a significant cause of morbidity and mortality affecting 5-15% of premature newborns and up to 7% of term newborns. The classic histological finding is one of coagulative necrosis. It is postulated that there are three contributing factors - intestinal ischaemia, colonization by pathogenic bacteria and excess protein substrate in lumen. [1]

Prematurity is the most significant risk factor. Other risk factors implicated include any cause for compromised splanchnic blood flow in the foetus/infant i.e. maternal toxaemia, maternal cocaine use (poor umbilical artery Doppler's on antenatal ultrasound scan), asphyxia and Patent Ductus Arteriosus. The following factors relating to enteral feeding have been described: high osmolality of formula feeds, early timing of feeds, high volumes and rapid rate of advancement of feeds. However, the question of fast versus slow and early versus delayed feedings remains unanswered. Several randomized trials have shown no effect on the incidence of NEC.[2-4] It has been observed that giving babies minimal enteral feeds reduces the number of days needed to reach full enteral feeds and the duration of hospital stay. Giving minimal enteral feeds have not been conclusively shown to reduce the incidence of NEC.[5,6] The presence of infective pathogens may also be significant. Organisms isolated in blood cultures include *Klebsiella, Staph epidermidis* and *Staph aureus*. Positive stool cultures include *Klebsiella, E coli* and *Staph sp*. [7] The use of Indomethacin has also been implicated as this is postulated to reduce mesenteric blood flow. [8] This has not been confirmed in studies. NEC can recur after medical or surgical treatment.[9]

In term infants anomalies of the cardiovascular, gastrointestinal, musculo-skeletal and multiple systems are risk factors associated with NEC.[7]

Clinically, the signs may range from very subtle to severe depending on the stage of NEC. The course of the disease similarly varies from mild to fulminant.

Risk factors

- Prematurity
- Compromised blood supply to fetus (maternal PET, poor umbilical artery dopplers)
- Birth asphyxia, PDA
- Anomalies of the cardiovascular, gastro-intestinal and musculoskeletal systems in term infants
- Feeds -Early and rapid advancement, hyper osmolar and high volume feeds (evidence inconclusive)

Differential diagnoses to be considered are:
Primarily abdominal symptoms: Isolated intestinal perforation, ascites, volvulus, umbilical sepsis.
Systemically unwell: sepsis/meningitis, urinary tract infection.

Prevention
Commence and advance feeds judiciously in babies with risk factors. Minimal enteral feeding should be considered prior to advancing feed volumes in preterm babies and babies with risk factors. [6]

Probiotics may have a role in prevention of NEC [17].

Clinical features

Any baby with feed intolerance and risk factors or significant feed intolerance without risk factors **must** have an early medical review and reassessment.

Abdominal signs: feed intolerance (increased naso/orogastic tube aspirate), vomiting (feeds, bile or blood), abdominal distension +/- "loopy abdomen", discolouration, tenderness, abdominal wall erythema, abdominal mass, decreased bowel sounds and blood in stools.

Systemic signs: temperature instability, lethargy, irritability, apnoeas, respiratory distress, poor capillary refill, decreased urine output, increasing metabolic acidosis. In ventilated infants a respiratory prodrome of NEC consisting of decreased oxygenation, increased respiratory rate or increased pCO_2 may be seen.

Bell staging (modified by Walsh and Kleigman) [11, 12]

	Stage I a and b Suspected NEC	**Stage II a and b Definite NEC**	**Stage III a and b Advanced NEC**
Systemic symptoms	Mildly unwell, temperature instability, apnoeas, bradycardias, lethargy	Moderately unwell	Severely unwell, severe apnoeas, shock, bradycardias
Abdominal symptoms	Increased prefeed residue, vomits (**Stage Ib** fresh rectal bleeding)	Gastrointestinal bleeding	
Signs	Abdominal distension	Abdominal tenderness/ abdominal wall cellulitis, absent bowel sounds	Marked abdominal distension, tenderness/ mass
Haematology and Biochemistry	Initial investigations may be within normal limits	Thrombocytopenia, mild metabolic acidosis	May have anaemia, abnormal electrolytes, deranged coagulation, marked metabolic acidosis with lactic acidosis
Radiology	Findings of ileus	Intestinal pneumatosis **Stage IIb** portal venous air with/without ascites	Ascites **Stage IIIb** pneumoperitoneum

Initial investigations

Investigations	Findings
Full blood count and coagulation	Leucopoenia/ leucocytosis, anaemia, thrombocytopenia and deranged coagulation
CRP, renal, liver and bone profiles	Raised CRP, hyponatraemia, hypoalbuminaemia
Blood gas analysis including serum lactate	Metabolic or mixed acidosis, high serum lactate
Group and save, cross match	Cross match 4 Paediatric packs (1 Unit) packed red cells if Stage I b/II/III
Blood culture	
Stool culture	
Abdominal X-ray supine, consider left lateral decubitus (right side up) Left lateral if strong suspicion of perforation is not collaborated by the AP supine film (discuss need for left lateral decubitus x-ray with consultant)	Multiple gas filled bowel loops, pneumatosis intestinalis, persistent dilated loops, portal venous gas. Gasless abdomen, gas filled loops occupying the centre of the abdomen and increased haziness may be seen in ascites. Pneumoperitoneum (best seen in left lateral decubitus) and “football sign”: air outlining the falciform ligament, umbilical artery or urachal remnant may be seen in the presence of intestinal perforation.[10]
Abdominal ultrasonogram	May be useful to identify portal venous gas or ascites.[13] Discuss with consultant.

Initial management

1) Cardio-respiratory – may need additional ventilatory, volume and inotropic support depending on clinical condition.

2) Stop enteral feeds.

3) Nasogastric/ orogastric tube (size 6-8) free drainage with hourly aspiration.

4) Antibiotics - Commence Penicillin, Gentamicin and Metronidazole. If the baby is already on Penicillin and Gentamicin or has a long line; commence Cefotaxime, Vancomycin and Metronidazole. If already on these antibiotics; discuss with Neonatal Consultant.

5) Fluids –

    a) Resuscitation: Normal saline bolus 10 mLs/kg, to be repeated as required.

    b) Ongoing losses: replace nasogastric tube aspirates mL for mL (0.9% normal saline with Potassium Chloride 2 mmol/100mLs). May need additional volume due to third space and gastrointestinal losses.

    c) Maintenance fluids: as per guidelines according to age of baby.

    d) Ensure any additional supplements - (e.g. Sodium, Potassium) - are added to IV fluid or TPN prescription chart.

    e) Maintain strict fluid balance chart. Monitor urine output, catheterize if poor output.

6) Nutrition – Commence total parenteral nutrition as soon as baby's condition is stable.
7) Correct abnormal coagulation (urgently in case of significant bleeding or impending surgical intervention). Refer to Guideline no: CA 2045 (v1) on the use of blood products in new born infants.

8) Metabolic – correct abnormal electrolytes and blood glucose.

9) Analgesia as required. Intravenous Morphine bolus/ infusion. Do not give rectal analgesics. Minimal handling.

10) Request paediatric surgical consultation (contact surgical middle grade via bleep 1047) from Stage Ib onwards. Stage II onwards should be discussed with Neonatal Consultant and Neonatal Surgeon.

Subsequent investigations and management

Monitor FBC, coagulation, biochemistry every 12 to 24 hours and blood gases every 4 to 6 hours until clinically stable.
Abdominal X-rays – the frequency of repeat x-rays should be guided by the stage of NEC and the clinical course of the patient. Consultant Neonatal Surgeon/Neonatologist for advice regarding further x-rays.

Duration of antibiotic treatment and NBM depends on staging

Stage Ia: 48 – 72 hours; then review, to be guided by clinical course.
Stage Ib and Stage II: 10 days.
Stage III: May need more than 10 days, depends on individual baby's progress.

Re-feeding

Refer to Appendix A

Surgical management[14, 18]

Absolute indications for surgical intervention

Pneumoperitoneum (i.e.; evidence of intestinal perforation)

Ensure coagulation profile is satisfactory before surgical intervention, arrange platelet/FFP transfusion if necessary. Give fluid resuscitation if required pre-operatively.

The choice of surgery is dependent on the baby's weight and clinical condition.

<1500 gms/ unstable clinical condition – consider peritoneal drain which may be a temporising measure). Give adequate analgesia if procedure is performed on NICU. Assess response to drainage and then plan laparotomy if indicated.

>1500 gms/ stable baby - consider laparotomy

Relative indications for surgical intervention

In case of deterioration of clinical condition despite optimal medical management (oliguria, hypotension and metabolic acidosis unresponsive to medical treatment, thrombocytopenia, leucopenia, leucocytosis, ventilatory failure) or a failure to improve / presence of complications such as portal venous gas, fixed abdominal mass/loops, signs of unresolving intestinal obstruction and abdominal wall erythema.

Communication to parents

A true estimate of survival following NEC is not possible because of the difference in patient population. Prognosis varies depending on gestation, weight and severity of illness. Poor prognostic features include extreme prematurity, Stage III NEC, acidosis, hyponatraemia, coagulopathy, severe thrombocytopenia, neutropenia, high blood lactate, hyperglycaemia, the presence of portal vein air on abdominal radiograph and multiple organ failure.[14,15,16]

It differs markedly with a very poor prognosis in infants <1000 gm to a much better prognosis in larger babies. Very low birth weight infants who are <1000 gm and less than 28 weeks gestation are more likely to have pan-involvement of the gut and are more likely to require surgical treatment. Pan-involvement of the gut is associated with 100% mortality. If cases with pan-involvement are excluded, the survival rate in surgically treated infants should reach 80-90%. An overall mortality of 25% is a reasonable guess.[10]

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APPENDIX A

Restarting feeds – a guide

To follow High Risk Feeding Regime from the "East of England Pernatal Networks Clinical Guideline for Feeding preterm infant on the neonatal unit " [19].

The regime is as follows:

Day 1 10 mls/ Kg/ day 2 hrly trophic feeds

Day 2 advance feeds if tolerated as follows:

Increase 10 mls /kg twice in 24 hrs as 1- 2 hrly feeds

Day 3 continue to increase 10 /kg twice in every 24hrs as tolerated until 180 mls /kg. Further increases to be guided by assessment of growth.

The above plan is strictly guided by the tolerance to feed and clinical condition of the baby. If not sure consult neonatal / gastroenterology / neonatal surgery consultant.

TPN and Lipids to be weaned as feeds tolerated. Lipids may be discontinued when feeds have reached half the total daily requirement.