East Midlands Neonatal
Operational Delivery Network

NETWORK GUIDELINE

Guideline:	**Investigation and Management of the Hydropic Infant**
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Distribution:	**Neonatal units with EMNODN**
Risk Managed:	**Managing the baby born with hydrops** **Investigation of hydrops**

This document is a guideline. Its interpretation and application remains the responsibility of the individual clinician, particularly in view of its applicability across the different Trusts in the East Midlands Neonatal Operational Delivery Network. Please also consult any local policy/guideline document where appropriate and if in doubt contact a senior colleague.

Caution is advised when using guidelines after a review date.

REVIEW AND AMENDMENT LOG

Version	Type of Change	Date	Description of Change
1	-	May 20	-

Key Points

- ANY anticipated case of hydrops antenatally should be referred to a tertiary NICU and in-utero transfer or planned delivery at the tertiary NICU will usually be planned. In the mildest cases, delivery in the LNU be may more appropriate

- Anticipate the need for complex or advanced resuscitation at birth in the case of infants with hydrops; their transition can pose a significant challenge

- A consultant should be present at delivery wherever possible and must be contacted in or out of hours

- Antenatal counselling should by a senior neonatal clinician in light of the significant mortality and morbidity

- Parallel planning should be considered early and might include a special baby plan as appropriate to the family's wishes

Abbreviations

ANNP	Advanced neonatal nurse practitioner
CTG	Cardiotocography
G6PD	Glucose 6 Phosphate Dehyrogenase
IUGR	Intrauterine growth restriction
NIFH	Non-immune fetal hydrops
OOPC	Operation on placental circulation
PIP	Peak inspiratory pressure
QIS	Qualified in Specialty
ST	Specialty Trainee
UAC	Umbilical arterial catheter
UVC	Umbilical venous catheter

Contents

1. Background

Fetal hydrops describes abnormal accumulation of fluid in 2 or more fetal compartments [1, 2]. This may include pleural effusion, pericardial effusion, abdominal ascites, soft tissue oedema and others. Where fluid accumulation is 1 compartment only, this is not classified as hydrops. Hydrops results from altered fluid homeostasis and implies overload in total body fluid. Fetal hydrops is traditionally divided into immune and non-immune in origin.

This guideline will refer predominantly to non-immune fetal hydrops (NIFH) which accounts for 85 – 90% of all cases of hydrops [2-7].

1.1 Immune Fetal Hydrops

This is now a rare diagnosis due to antenatal Rhesus D immunoglobulin prophylaxis “Anti-D”. Antibodies generated by maternal red cell alloimmunisation may cross the placenta leading to red cell haemolysis, anaemia and fetal hydrops. The specific additional haematological management of this aetiology is beyond the scope of this guideline.

1.2 Non- Immune Fetal Hydrops (NIFH)

The estimated prevalence of NIFH is 0.3 – 2.4 per 1000 live births[2,4,6,8,9]. NIFH is the end stage of a process that may result from a variety of aetiologies[3, 9] and should be viewed as a symptom rather than disease in its own right. **Management, therefore, should focus upon diagnosis of the underlying causative factor or factors and symptomatic control of fluid dysregulation in the meantime.**

Three primary mechanisms result in NIFH: Anaemia, cardiac failure and hypoproteinaemia. The most commonly reported underlying causes of NIFH are outlined below[2,4,5,9–11]. Specific examples can be found in Table 1.

- Cardiac 17 – 35%
- Idiopathic 15 – 29%
- Chromosomal / Syndromic 6 – 17%
- Haematological / oncological 4 – 12%
- Pulmonary / Thoracic 2 – 12%
- Renal / urogenital 1 – 12%
- Placental / Twin to Twin 3 – 10%
- Lymphatic 5 – 9%
- Infection 5 – 7 %
- Gastrointestinal 0.5 – 9%
- Metabolic 0.2 – 2%

2. Management

Management will depend on the degree of hydrops but **ANY anticipated case antenatally should be referred to a tertiary NICU.** In-utero transfer or planned delivery at the appropriate tertiary NICU will usually be planned following a multidisciplinary discussion regarding place and timing of delivery. In the mildest cases, delivery in the LNU be may appropriate.

If delivery is imminent, or circumstances contraindicate transfer to a tertiary centre, the case should still be discussed with the relevant NICU Neonatologist at the earliest opportunity. In all cases, liaison between obstetric and neonatal teams will be required to facilitate a safe delivery.

2.1 Antenatal Planning

Parents should be counselled appropriately by the most senior clinician available and should be aware of the potential for a poor outcome, or death of their baby. Risks of IUGR and stillbirth are increased for hydropic infants. Parallel planning with involvement of family care and/or bereavement teams should be considered early, with discussion about **special baby plans** with the parents as appropriate [see ODN Pathway for potentially Life-limiting or Life-threatening conditions]. Where available, the obstetric/antenatal alert for the baby should be consulted and a comprehensive assessment of the antenatal investigations, management and any existing diagnoses made. The USS findings on growth, liquor volume, cardiac structure, rate and rhythm and any anatomical abnormalities should be reviewed. **Clinical genetics** should be involved if there is a suspicion of a genetic cause. Antenatal investigations that may have been completed by the obstetric team include:

- Haemoglobin
- ABO, rhesus group, haemolysins, minor blood group antibodies
- Hb electrophoresis
- Kleihauer Test
- Maternal autoimmune antibody screen
- Lupus anticoagulant
- VDRL
- TORCH and parvovirus serology
- G6PD screen
- Random blood glucose or glucose tolerance test
- Alpha fetoprotein

Fetal investigations which may have been taken antenatally include:

- Karyotype/ Array CGH
- Viral studies
- Hb concentration and electrophoresis
- 24hour CTG in the case of tachyarrhythmia
- Specific genetic testing

2.2 Preparation for Delivery

The decision for elective caesarean section versus spontaneous vaginal delivery should have been considered by the multidisciplinary team, alongside the optimal time and place of delivery for both maternal and infant wellbeing. The size of the baby, allied risk of dystocia and hypoxia should be taken into consideration [12,13].

Specific requirements around delivery:

- An experienced neonatal team should be present for delivery, where possible led by a consultant, and including a middle grade doctor, ANNP (middle grade or SHO level), ST1 – 3 doctor and ideally 2 neonatal nurses (QIS trained for checking drugs). If out of hours/short of staff, it may be appropriate to request assistance of general paediatric, anaesthetic or other team members.
- The **local consultant on call should be contacted** both in and out of hours.
- It is very useful to discuss roles of different team members before delivery, for example in case of antenatal severe hydrops with bilateral pleural effusions: consultant leading stabilisation, registrar/experienced ANNP providing airway support, second ANNP/middle grade ready to insert chest drain/s, trainee prepared for vascular access and 2 nurses ready with emergency drugs.
- Placental examination (**sent as fresh, not formalin specimen**) should be requested if not already planned.
- Blood bank should be consulted and suitable blood requested for urgent transfusion in the event this is necessary (maternally cross matched or O negative – **always** CMV negative and irradiated).
- Equipment should be prepared for difficult intubation, pleural effusion aspiration and drainage, abdominal ascites aspiration/drainage and UVC insertion as a minimum.
- Emergency drugs should be readily available.

2.3 Delivery and Stabilisation

This is likely to be challenging due to pulmonary hypoplasia and soft tissue oedema. Team members should be allocated clear roles and a leader identified to oversee resuscitation. Emergency drugs should be readily available and nursing staff present to check and prepare. Consideration should be given to the possibility of resuscitation at mother's side with cord intact. This can provide up to 6 minutes for effective stabilisation with placental oxygenation.

Airway

The majority of infants with hydrops will require early intubation in the delivery room. This may be technically difficult due to laryngeal and soft tissue oedema.

Considerations:

- Have difficult airway box/equipment present
- Consider need and availability of video laryngoscopy
- Consider preparing longer endotracheal tube than expected for gestation (or uncut tube) to account for oedema

Breathing

Commence ventilation at pressures of 30/5 for term infants or 20-25/5 for infants under 28 weeks gestation. Higher pressures may be needed due to pulmonary hypoplasia. Titrate PIP in increments of 2-4cm of H_2O according to saturations and heart rate, or until good chest movement achieved.

It is likely early thoracocentesis will be required unless good chest movement is easy to achieve. This may be undertaken using a butterfly needle or pink cannula with 3-way tap connected (See appendix 1 for equipment list). **Deeper than anticipated needle insertion will likely be required to reach pleural spaces due to oedema.** Following this, definitive chest drains are likely to be necessary either in the delivery room or on the neonatal unit. In the presence of massive ascites, abdominal drainage may also be necessary to facilitate effective chest movement.

Circulation
An emergency UVC should be sited at delivery if any suspicion of vascular access being required. Peripheral access is likely to be difficult due to oedema. If significant anaemia is known or suspected at delivery and the baby is unwell, **5 – 10ml/kg of maternally cross matched or O negative blood** can be considered during initial resuscitation.

Rarely, pericardiocentesis may be necessary in the case of frank cardiac tamponade secondary to a very large pericardial effusion.

Additional factors to pay careful attention to include temperature control, glucose homeostasis, management of acidaemia and oxygenation parameters. The infant should be promptly transferred to the neonatal unit once sufficiently stable.

2.4 Early Management on the Neonatal Unit

Additional nursing staff may be required, and significant nursing care levels required. This should be discussed with the nurse in charge and arrangements made appropriately alongside preparation for transfer to a tertiary NICU should the baby be born outside this setting. Referral to CenTre for transfer should be made at the earliest opportunity.

Examination
Detailed physical examination may reveal dysmorphic features suggestive of a unifying diagnosis and their presence or absence should be carefully documented. Around 40% of cases will have another congenital abnormality.

Weight
For the purposes of early management, a working weight should be considered; this may be significantly lower than the birth weight. The **50th centile for gestation may be an appropriate starting point.** This will need ongoing review depending on the clinical status

Ventilation
Ventilation should proceed as clinically indicated. Though high pressures may be required initially to achieve oxygenation, as the pulmonary pressures decrease a reduction in ventilation pressures may paradoxically improve oxygenation.

Access and fluid administration
Aseptic umbilical catheterisation should be performed early on the neonatal unit and arterial blood pressure monitoring commenced. Infants may require fluid restriction especially in first 24-48 hours. Consider the risk of hypoglycaemia with fluid restriction, using higher concentration dextrose (or parenteral nutrition). IV diuretics may be appropriate following discussion with the tertiary Neonatologist.

Cardiovascular support
Inotropic support may be required to improve cardiac output and is generally preferable to giving fluid volume/boluses. The choice of inotrope should follow discussion with the tertiary Neonatologist and may be guided by echocardiographic assessment if available locally. A reasonable first choice is Dopamine at 5microgram/kg/min whilst discussions are commenced. If anaemia is significant, partial exchange transfusion may be indicated also.

Coagulopathy
Coagulation studies should be **checked on admission** as significant coagulopathy is common. Treatment of any abnormal results should be considered in the context of any active bleeding and the infant's current fluid status.

3. Post-natal Investigations

Following stabilisation, ongoing management will be assisted by seeking to identify an underlying cause for hydrops. Investigations (see Table 2) can be considered by the organ systems[4,8,11,14-16]. Please **see Appendix 3 for a proforma** that can be used to record the results in the primary centre.

4. Prognosis

Overall prognosis at antenatal diagnosis is poor but some aetiologies will be amenable to treatment. Mortality after live birth with hydrops is quoted to vary from 6% (isolated congenital chylothorax), to 58% (in presence of congenital anomalies)[9].

In total, among newborns with NIHF the observed survival rate is around 50%[7, 9, 13], with preterm birth below 34 weeks and low serum albumin two significant poor prognostic predictors[7,9,12]. Variable prognosis should be **fully discussed with parents by the consultant** responsible, parallel planning considered, and a resuscitation plan agreed as soon as possible. This should be clearly documented in the notes and communicated to the medical and nursing teams.

UK follow-up suggests reasonable neurodevelopmental outcomes for survivors of NIFH with two thirds exhibiting normal development beyond 1 year of age[17]. All survivors should be followed up as standard.

Table 1: Post-natal investigations in hydrops fetalis

System	Investigations	Potential findings
Cardiac	• Postnatal echo • 12 lead ECG	Structural anomalies Arrhythmias
Chromosomal / syndromic	• Karyotype and array • Careful examination • Cranial ultrasound	Trisomies Noonans Syndrome Turners Triploidy
Haematological	• FBC • Film • Newborn blood spot • DCT • Maternal Kleihaur (to look for feto-maternal haemorrhage)	Anaemia Thalassaemia Leukaemia Feto-maternal haemorrhage (rhesus disease) G6PD anaemia
Thoracic / Pulmonary	• CXR • Examination of pleural fluid (cytology, lipids and MC+S) • *Consider CT / MRI*	CCAM CDH Chylothorax Atresia of right main bronchus Tracheo-oesophageal fistula
Gastrointestinal	• AXR • *Consider abdomen USS* • Examination of ascitic fluid (cytology and MC+S) • Albumin	Intrauterine perforation Meconium peritonitis Obstruction Hepatic vascular malformation
Infection	• TORCH screen • LFTs • Placental pathology	Toxoplasmosis CMV Rubella

	• Hepatitis screen	Syphilis HSV Parvovirus Varicella Hepatitis
Renal / urogenital	• Renal function • Consider USS • Urine protein: creatinine ratio	Obstructive uropathy Congenital nephrotic syndrome Polycystic kidneys Renal vein thrombosis
Metabolic	• Urine inborn errors • G6PD levels • Plasma amino acids	Lysosomal disorders Storage disorders
Twin – Twin Transfusion / placental	• Placental examination – will need to request feedback from obstetric team	True knot Placental chorioangioma Umbilical Artery aneurysm TTTS Umbilical vein thrombosis

5. Postmortem Management

In the case of a foreseeable unavoidable death, or a planned reorientation to palliative care, it is desirable for as many investigations as possible to be undertaken antemortem after detailed discussion with the lead tertiary consultant.

Postmortem examination should be offered and recommended in the case of neonatal death, both to determine underlying cause if possible and to aid future pregnancy counselling. Please refer to the care pathway for management of neonatal death. A limited post-mortem may be offered if the family do not wish for a full post-mortem. Clinical photography may be a useful adjunct. In the case of a family declining any postmortem examination, consent could be sought for skin biopsy (cytogenetics for fibroblast culture, sterile container, **notify and liaise with local laboratory at earliest opportunity**) and aspiration liver biopsy (freezing and histopathology, **notify and liaise with local laboratory at earliest opportunity**).

Useful Investigations:

- Skin biopsy and culture of fibroblasts after discussion with the laboratory
- DNA storage for future analysis
- Skeletal survey
- Post mortem examination

6. Audit points

- Delivery in NICU for hydropic infants
- Placental examination requests for hydropic infants
- Team composition at deliveries for hydropic infants
- Use of the designated proforma to collate investigations and results in the medical notes

7. Allied Guidelines

- EMNODN Care pathway for the Unborn Child, Neonate or Infant with potentially Life Threatening or Life Limiting Conditions
- EMNODN Guideline Transport Stabilisation

8. References

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Appendix 1 - Staff and Equipment List for Delivery of the Hydropic Infant

Team Members as local availability allows:

1. Neonatal Consultant - Team leader
2. Middle grade allocated to airway (consider anaesthetic support dependent on local set up)
3. Middle grade allocated to needle aspiration / chest drain
4. (If available), second person (experienced SHO / ANNP) allocated to contralateral needle aspiration / chest drain
5. Competent Middle grade / ANNP / SHO allocated to emergency UVC insertion
6. Neonatal Nurse 1 (preferably QIS)
7. Neonatal Nurse 2 (preferably QIS)
8. Scribe

Ideally this team will consist of 5 medical staff, 2 nursing staff and a scribe of any background. It may be necessary to enlist help from general paediatrics or anaesthetics if adequate neonatal professionals are not available.

Equipment:

- Laryngoscopes – various sizes
- Prepared ET tubes – anticipated size, sizes above and below
- ET Tube fixation device
- Difficult airway equipment including bougie
- *Consider video laryngoscopy if available*

- NG tube and fixation
- Enteral syringes

- Butterfly needle / pink cannula x 2
- Three way tap x 2
- Large volume syringe x 2
- *Consider chest drains and chest drain insertion kit*
- *Consider underwater drain set up*

- Scalpel
- UVC
- Cord tie
- Tape for securing emergency UVC
- Saline flush
- 5ml syringes for sampling
- Cannulas and flushes

- Drug card with emergency drugs prescribed (**use 50th centile for gestation as emergency working weight**)
- Emergency drugs box
- Saline flushes

Appendix 2 - Relevant Technical Procedures Overview

Thoracocentesis

The necessary depth of insertion for thoracocentesis and definitive drain will be greater than anticipated due to oedema in the chest wall - Ensure this is accounted for.

Ventilation is briefly stopped once ready to perform the procedure. A 21 gauge butterfly needle attached to a three way tap and large volume syringe is inserted in the midaxillary line, fourth intercostal space, immediately above the rib and aspirated while being advanced, until fluid is obtained.

Ventilation is then promptly recommenced. Aspiration can be continued until no further fluid is obtained **HOWEVER** bradycardia and/or haemodynamic instability may occur if fluid is removed too quickly. Fluid volume aspirated, and infant heart rate should be regularly and frequently re-evaluated. The volume aspirated is noted and *fluid saved* for further investigation (see guideline Table 1, postnatal investigations). Pneumothorax may occur if the lung is injured during this procedure. A formal intercostal drain may be required at this stage, or later.

Abdominal paracentesis

Lower borders of both the liver and spleen should be determined by palpation if possible. A 21 gauge butterfly needle is inserted at the **midpoint of a line drawn from - the umbilicus to the LEFT anterior superior iliac spine**. The volume of fluid aspirated is noted and the *fluid saved* for investigation as noted (guideline Table 1).

Pericardiocentesis

This is rare, and only necessary in the case of frank tamponade.

A 25 gauge needle, attached to a 3 way tap and syringe, is inserted immediately under the xiphisternum and advanced upward, backward, and left laterally - aiming for the tip of the left shoulder. It should be continually aspirated during insertion. The pericardial sac should be entered within 1-2 cm. This procedure can be done under ultrasound guidance. The *fluid should be saved* and sent for investigation as outlined (guideline Table 1).

Appendix 3 - Results of Investigations for the Infant with Hydrops

Name:

Unit No.:

DOB:

	Specimen date	**Result**	**Expected date of result if not yet available**
Blood			
Urea, Cr, electrolytes			
Total protein, albumin, electrophoresis			
Liver Function			
CK			
Bilirubin (direct and indirect)			
Osmolality			
FBC			
Blood film			
Group and Direct Coomb's Test			
Hb electrophoresis			
Newborn blood spot			
G6PD			
Karyotype and array			
Plasma amino acids			
Toxoplasma immunoglobulins			
Rubella immunoglobulins			
CMV			
VZV			
Parvovirus			
VDRL			
Hepatitis screen			

Urine			
Urine Protein:Creatinine ratio			
Inborn errors screen			
Urine CMV			

Pleural/ascitic fluid			
Biochemistry			
Microscopy			
Microbiology			
Viral studies			
Cytogenetics			

Imaging / physical Ix			
Echo			
CXR			
AXR			
CrUSS			
12 lead ECG			