East Midlands Neonatal
Operational Delivery Network

NETWORK GUIDELINE

Guideline:	**Management of Neonatal Encephalopathy (South Hub)**
Version:	**Version 1**
Date:	**July 2020**
Review Date:	**July 2023**
Approval:	**EMNODN Clinical Governance Group**
Authors:	**Tim Syche** **Dr Joanna Behrsin**
Consultation:	**EMNODN Clinical Governance Group**
Distribution:	**Neonatal unit within EMNODN South Hub**
Risk Managed:	**Parental distress and concerns, risk of failing to diagnose and appropriately manage encephalopathy**

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 – South Hub. 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	-	Jul 2020	-

Abbreviations used within this document

aEEG	Amplitude Integrated Electroencephalograph, also known as CFM
AKI	Acute Kidney Injury
CFM	Cerebral Function Monitor
CSF	Cerebrospinal fluid
HIE	Hypoxic Ischaemic Encephalopathy
HSV	Herpes Simplex Virus
LNU	Local Neonatal Unit
nCPAP	nasal continuous positive airway pressure
NICU	Neonatal intensive care unit
NIV	Non-invasive ventilation
PCR	Polymerase Chain Reaction
SCU	Special Care Unit

Introduction

General definition of encephalopathy

Encephalopathy may arise from many pathologies[1] and consideration should be given to non-HIE aetiology if features of hypoxic-ischaemia are not present. HIE may also co-exist with other pathologies.

Neonatal encephalopathy is a clinical syndrome of abnormalities in level of consciousness, tone, primitive reflexes, autonomic function and sometimes seizures[2], graded mild, moderate or severe (I-III)

Patient Selection

TOBY treatment criteria[3]

A. Infants ≥36 completed weeks gestation admitted to the neonatal unit with <u>at least one</u> of the following:

- Apgar score of ≤5 at 10 minutes after birth
- Continued need for resuscitation, including endotracheal or mask ventilation, at 10 minutes after birth
- Acidosis within 60 minutes of birth (defined as any occurrence of umbilical cord, arterial or capillary pH <7.00)
- Base Deficit ≥ 16 mmol/L in umbilical cord or any blood sample (arterial, venous or capillary) within 60 minutes of birth

Infants that meet criteria A should be assessed for whether they meet the neurological abnormality entry criteria (B):

B. Seizures or moderate to severe encephalopathy, consisting of:

- Altered state of consciousness (reduced response to stimulation or absent response to stimulation) **<u>and</u>**
- Abnormal tone (focal or general hypotonia, or flaccid) **<u>and</u>**
- Abnormal primitive reflexes (weak or absent suck or Moro response)

Infants who meet criteria A and B may be considered for treatment with cooling.

Infants of **≥36 completed weeks** gestation and **less than 6 hours of age** with evidence of perinatal hypoxic ischaemic risk factors (**any** of the risk factors in 'TOBY A'), and are encephalopathic (**all** of the criteria in 'TOBY B') may be considered for treatment with therapeutic hypothermia.

For babies meeting these criteria in a LNU or SCU, contact the transport service where a conference call will be held between the referring, transport and NICU receiving clinicians, ideally these should be at Consultant grade.

For babies outside this criteria where there is consideration that cooling may be beneficial a discussion should be had with Consultant Neonatologist covering Leicester Royal Infirmary (lead NICU for South Hub).

Contraindications & dilemmas

Therapeutic hypothermia is contra-indicated if:

- The infant is likely to require surgery during the first 3 days after birth
- There are other abnormalities indicative of poor long term outcome

Therapeutic hypothermia may not be appropriate if the infant appears moribund or has a persisting extremely severe encephalopathy such that further treatment is likely to be futile.

This scenario should be discussed with a conference call held between the referring, transport and receiving Consultants.

If the referring clinician is unsure if a baby is suitable for therapeutic hypothermia this should initially be discussed with the relevant tertiary centre but can be discussed in a conference call between the referring, transport and receiving clinicians if necessary.

Babies with evidence of encephalopathy (criteria B) but not fulfilling criteria A can be discussed with the local service/on call consultant to establish whether therapeutic hypothermia may still be appropriate. It may be appropriate to transfer these infants for further management.

In these instances it is advised to commence therapeutic hypothermia at the earliest opportunity before further discussions occur. A cooled baby can always be warmed if it is not indicated, whereas a warm baby cannot be cooled if it is too late. Acceptable methods of cooling in the EMNODN are passive cooling following the TOBY guideline (Appendix 1) or servo-controlled active cooling where the unit has been approved to deliver this service for stabilisation by the EMNODN team. Ongoing intensive care of babies with HIE will be in a tertiary NICU.

Transport Management (See Appendix 2)

Cooling is TIME CRITICAL if the infant is NOT in cooling temperature range at the time of referral AND IS NOT in an active cooling centre. The transport service will aim to dispatch a team within 1 hour of referral once the decision for cooling is made.

Multi-organ dysfunction often accompanies encephalopathy following an hypoxic-ischaemic delivery[4,5] but may also be a feature of other causes of encephalopathy. Initial management is directed at preventing secondary injury from reduced cerebral oxygen delivery. Later management is aimed at treating the underlying cause, associated other organ injury or neuroprotective brain therapeutic hypothermia.

A systematic approach to clinical care will ensure the most appropriate supportive management is identified.

Airway & Breathing
There may be no associated lung injury and so the infant may not require intubation and ventilation.

nCPAP, High Flow, and other forms of NIV are **not** appropriate for this group of babies.Intubation and ventilation should be initiated if there are any concerns regarding an unstable airway or respiratory compromise.

Aim to maintain normocarbia ($PaCO_2$ between 5-7kPa) with careful ventilation to avoid any resulting hypocarbic cerebral vasoconstriction.

Muscle relaxation and an appropriate analgesic infusion are indicated for ventilated transfers. Non-ventilated babies will require a low dose analgesic infusion, see neurology below.

Circulation
Invasive monitoring is indicated for cooling transfers, and maintaining a mean arterial blood pressure >40mmHg will help to preserve cerebral, renal and cardiac oxygenation.

Owing to the potential impairment to cardiac contractility, fluid bolus resuscitation should be kept to a minimum of 2x 10ml/kg bolus' (unless there is objective evidence of hypovolaemia). Early implementation of inotropic support may be indicated to avoid fluid overload. Central venous catheterisation is the preferred route for inotropes, however, Dobutamine can be infused peripherally in an emergency.

Coagulopathy is not uncommon and a clotting screen should be checked to exclude this and managed appropriately if abnormal.

Fluids
Fluid restriction to 40ml/kg/day is advisable due to the likelihood of renal impairment (acute kidney injury) from acute tubular necrosis. An increase in glucose concentration may be indicated.

Urinary catheterisation may be beneficial.

Neurology
Early application of amplitude integrated electroencephalohram (aEEG) monitoring by the referring unit (if available) can help assess the level of electrophysiological disturbance whilst also identifying electrical seizure activity. The aEEG record can be categorised into normal, moderately abnormal, suppressed or seizure patterns. Table 1 below contains details of criteria for each category.

Category		**Upper margin**	**Lower margin**
Amplitude	Normal	>10 µV	>5 µV
	Moderately abnormal	>10 µV	<5 µV
	Suppressed	<10 µV	<5 µV often accompanied by burst suppression
Seizures		Periods of sudden increase in voltage accompanied by narrowing of the band of activity followed by a brief period of suppression	

Table 1 Categorical features of aEEG

Pictorial examples of these traces can be found in the TOBY CFM handbook.

Careful neurological examination must be performed and clearly documented, including abnormalities of **tone and reflexes (primitive, deep tendon and pupillary).** Evidence of skull fractures may suggest traumatic injury to the brain.

At referral the transport team will complete a proforma (Appendix 3) documenting a detailed rationale for cooling and the neurological status at referral. It is essential that the baby has had a full neurological examination prior to referral so that this can be completed appropriately and used as a reference point for later examinations and assessment of neurology.

A cranial ultrasound may be of use in looking for mass lesions causing midline shift such as intracranial haemorrhages and congenital brain parenchymal abnormalities.

Sepsis
Infection may play a role in the development of encephalopathy even in the presence of hypoxic ischaemic markers[6]. A septic screen should be performed and investigations for bacterial sepsis sent including a sample of CSF. If features of hypoxic ischaemia are absent or inconsistent then samples of blood, urine and CSF should be sent for viral PCR including HSV, and the infant started on acyclovir.

Family
Clinicians should always discuss therapeutic hypothermia treatment with parents and seek parental **assent** as soon as practically possible. Details of all discussion with parents about their baby's treatment with therapeutic hypothermia should be documented in the patient record.

Avoid commenting on the midwifery or obstetric management of the delivery and direct parents towards the appropriate professional if they have questions about the perinatal period.

Rewarming after passive hypothermia

If no features of encephalopathy are identified by 6 hours after birth then the baby may be re-warmed by turning on the incubator and setting the incubator air temperature to 30°C. This decision must be discussed with receiving NICU **and** Transport Consultants.

Clinical Observations

Babies with this condition should have ECG monitoring and saturation monitoring and BP measured at a minimum of 2 hourly.

Any baby being cooled (active or passive) requires rectal temperature monitoring to avoid overcooling.

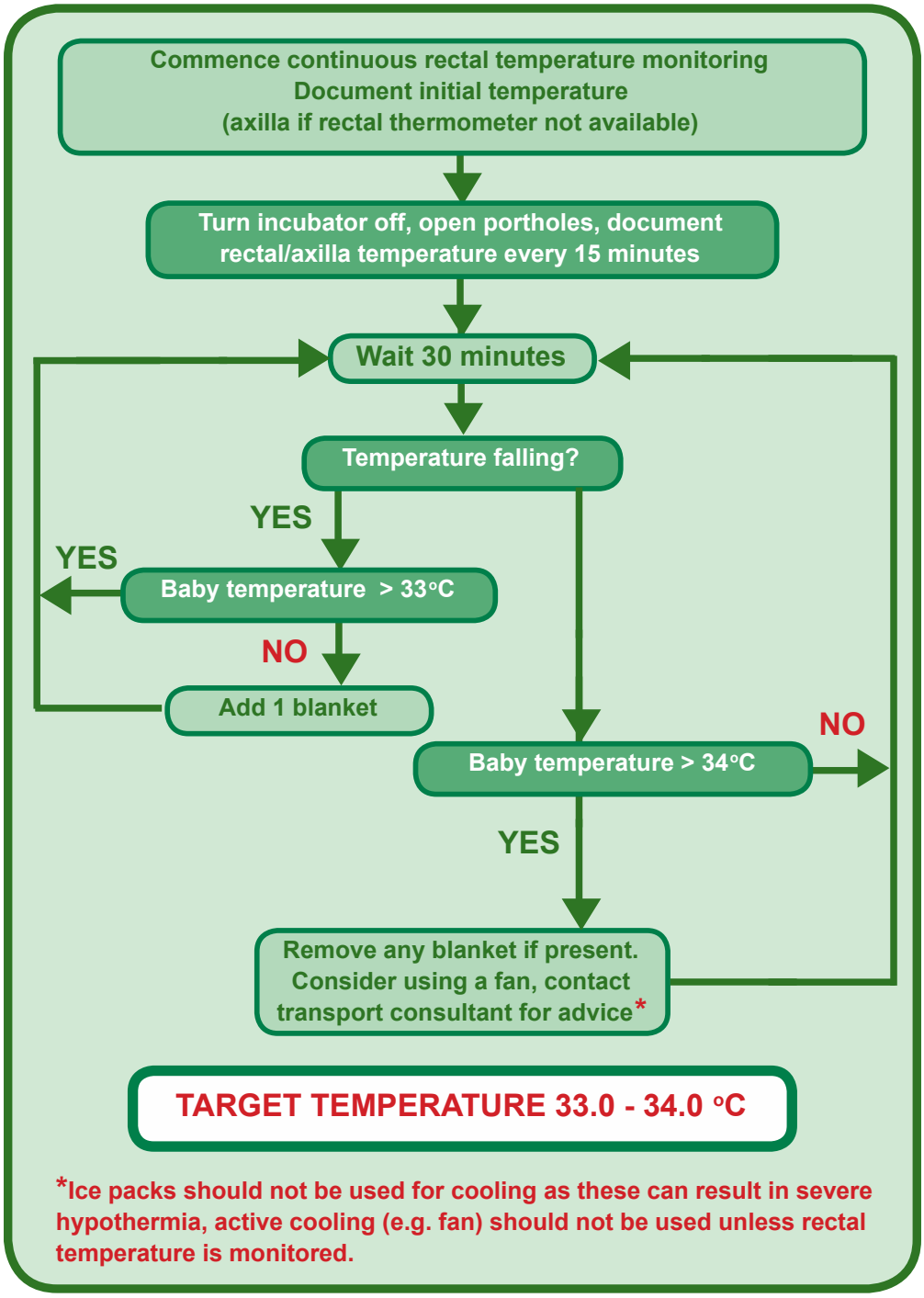
4-6 hourly gases at a minimum – it is likely that more frequent assessment of acidosis will be required in most cases.

References

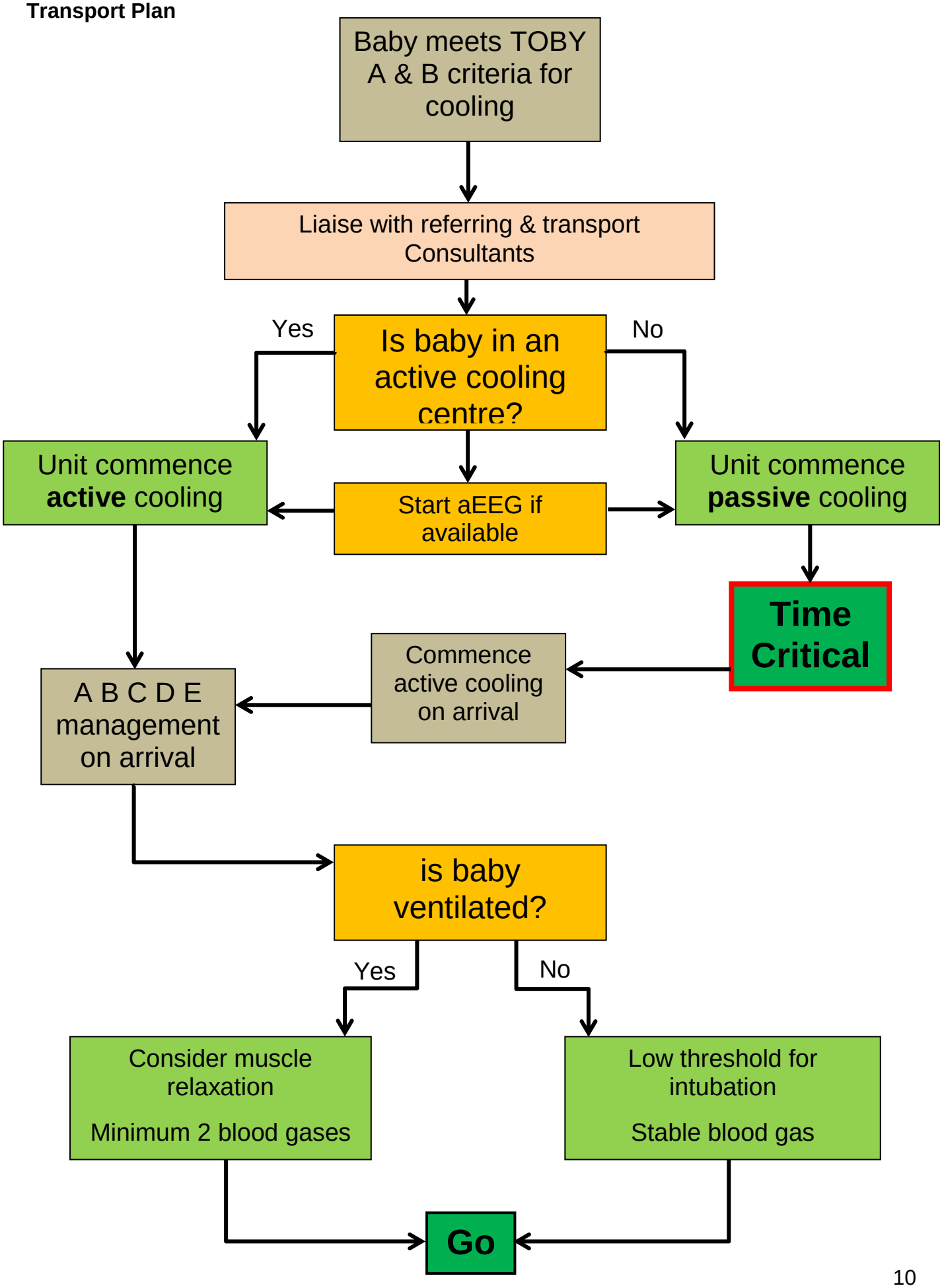
1. Martinello K, Hart AR, Yap S, *et al.* **Management and investigation of neonatal encephalopathy**: 2017 update. *Arch Dis Child - Fetal Neonatal Ed* 2017;**102**:F346–58. doi:10.1136/archdischild-2015-309639
2. Leviton A, Nelson KB. **Problems with definitions and classifications of newborn encephalopathy**. *Pediatr Neurol* 1992;**8**:85–90.
3. National Perinatal Epidemiology Unit. **UK TOBY Cooling Register Clinician's Handbook**. Oxford: NPEU 2010. https://www.npeu.ox.ac.uk/downloads/files/tobyregister/Register-Clinicans-Handbook1-v4-07-06-10.pdf
4. Martín-Ancel A, García-Alix A, Gayá F, *et al.* Multiple organ involvement in perinatal asphyxia. *J Pediatr* 1995;**127**:786–93.http://www.ncbi.nlm.nih.gov/pubmed/7472837
5. Shah P, Riphagen S, Beyene J, *et al.* Multiorgan dysfunction in infants with post-asphyxial hypoxic-ischaemic encephalopathy. *Arch Dis Child Fetal Neonatal Ed* 2004;**89**:F152-5

6. Nelson KB, Penn AA. Is infection a factor in neonatal encephalopathy? *Arch Dis Child - Fetal Neonatal Ed* 2015;**100**:F8–10. doi:10.1136/archdischild-2014-306192

Appendix 1
TOBY passive cooling guidelines



Appendix 2
Transport Plan



Appendix 3

CenTre 2 Person Record, page 3

Name of baby:					**DOB:**			
Complete for COOLING transfers ONLY								
Time when 6 hours of age		Hr	mins	Passive cooling started		YES	NO	
Current temperature		degrees C		Rectal temp monitoring Y / N / Advised				
Details of pregnancy, delivery & resuscitation								
Any concerning features in the history to suggest this is not HIE e.g. scalp swelling, possible inborn error of metabolism								
Apgars	1min		5min		10min			
Age at 1st gasp		mins	Reg breathing by		mins			
Age intubated		mins	Cardiac compressions Y/N		mins			
TOBY A Assessment			pH		BE		LAC	
Cord Gas ART								
Cord Gas VEN								
Worst gas ART VEN CAP								
Most recent gas ART VEN CAP								
TOBY B Neuro Assessment age in mins			mins		mins		mins	
Level of consciousness - record if alert, irritable, poorly responsive or comatose								
Tone - focal, generalised, hypotonia, flaccid								
Reflexes - suck, gag, moro, tendon reflexes (normal, hyperreflexic, hyporeflexic, absent)								
Seizures/abnormal movements - none, suspected, confirmed, clinical seizure								
Is baby encephalopathic Y / N			**CFM available** Y / N		Normal / Abnormal			
Breathing Apnoea Y / N				Respiratory support Y / N				
CVS Low B/P				Prolonged Capillary refill time Y / N				
Renal / Hepatic	Urine output	Oliguria	Anuria	Liver enzymes elevated Y / N				
Criteria A - Infants >36 completed weeks gestation with at least 1 of following:								
Apgar < 5 @ 10mins after birth				Ongoing resus, ET / mask vent @ 10mins				
pH <7.00 in 1st hr- CORD /ART / CAP				BE >16mmol/l in1st hr or LAC > 14				
Criteria B: Seizures or moderate to severe encephalopathy consisting of								
Abnormal primitive reflexes - weak or absent suck, moro or gag response						YES	NO	AND
Altered level of consciouness - reduced or absent response to stimulation						YES	NO	AND
Hypotonia - focal or general, flaccid						YES	NO	
Meets A + B criteria - Decision to cool Y / N				**If not cooled is tertiary unit aware Y / N**				
ACTIVE cooling started		**DATE**				**TIME**		
Age 1st in temperature range of 33-34C					**HRS**			**MINS**