Neonatal Encephalopathy Management

Guideline Responsibilities and Authorisation

Department Responsible for Guideline	NICU
Document Facilitator Name	Claire West
Document Facilitator Title	Neonatologist
Document Owner Name	Jutta van den Boom
Document Owner Title	Clinical Director - NICU
Target Audience	Neonatologists; Midland Region Paediatricians and Registrars; NICU Registrars, Nurse Practitioners, Clinical Nurse Specialists and Nurses
Disclaimer: This document has been developed by Waikato District Health Board specifically for its own use. Use of this document and any reliance on the information contained therein by any third party is at their own risk and Waikato District Health Board assumes no responsibility whatsoever.	

Guideline Review History

Version	Updated by	Date Updated	Summary of Changes
3	Claire West	May 2014	
4	Claire West	July 2020	Reformatted, updated, flow diagram added

Neonatal Encephalopathy Management

Contents

1 Overview

1.1 Purpose

To provide guidance around the identification and management of neonates with neonatal encephalopathy (NE).

To guide the assessment and management of newborn neonates who may benefit from cooling / therapeutic hypothermia for presumed hypoxic-ischaemic encephalopathy.

This is to be read in conjunction with the Neonatal Encephalopathy Consensus Statement from the Newborn Clinical Network.

1.2 Scope

Neonatal and Paediatric SMOs and RMOs, Clinical Nurse Specialists and Neonatal Practitioners caring for neonates in the Waikato DHB, and Midland Region.

1.3 Patient / client group

Infants born in the Midland Region with potential / definite neonatal encephalopathy.

1.4 Exceptions / contraindications

Babies who are moribund or have severe life limiting congenital abnormalities are believed not to benefit from cooling.

Coagulation abnormalities may be exacerbated by the effect of lower temperature on the clotting cascade and must be aggressively corrected PRIOR to initiation of cooling.

Consideration of cooling for infants with subgaleal haemorrhage need decisions made on a clinical basis as there is some evidence of worse outcome, and one author has recommended cooling to only 35^{o}C.

Pulmonary hypertension may also be exacerbated by hypothermia and clinicians may consider warming by one or two degrees to improve oxygenation.

1.5 Definitions

aEEG	Amplitude-integrated electroencephalography (aEEG) is a method for continuous monitoring of brain activity. In its simplest form, aEEG is a processed single-channel electroencephalogram that is filtered and time-compressed.
Neonatal Encephalopathy (NE)	Disturbed neurological function in the first week of life in a (near) term infants manifested by difficulty with initiating and maintaining respiration, depression of tone and reflexes, sub-normal level of consciousness and often seizures
Hypoxic-Ischaemic Encephalopathy (HIE)	A specific form of neonatal encephalopathy related to a significant hypoxic-ischaemic insult. Most trials have attempted to select infants for therapeutic hypothermia that have a moderate to severe hypoxic- ischaemic encephalopathy.
Therapeutic Hypothermia / Cooling	The use of specific devices, or cool packs, to reduce the core temperature of an infant with moderate to severe neonatal encephalopathy to 33.5-34.5^{o}C and maintain it at this level for 72 hours.
NICU	Neonatal Intensive Care Unit (Waikato Hospital for level 3 regional care)

2 Clinical Management

2.1 Equipment

- Criticool Cooling blanket, or cool packs if necessary.
- Continuous core temperature monitoring.
- Amplitude Integrated EEG (aEEG) monitor (for Level 3 NICU).
- Ultrasound machine (for head ultrasound).
- Medication as indicated and prescribed e.g. morphine for sedation, inotropes and anticonvulsants.

3 Guideline

The terminology NE is preferred to HIE as it is not always possible to document a significant hypoxic-ischaemic insult and there are potentially several other aetiologies.

Other conditions such as metabolic disease, infection, drug exposure, nervous system malformation and neonatal stroke may present as a NE.

The requirement for investigation to exclude these possibilities will depend on the presentation, history and clinical features of the individual case.

3.1 Initial Care

- Call for help early.
- Routine resuscitation should be provided, if NE is considered think about turning off radiant heater on resuscitate.
- Ensure resuscitation efforts are recorded by a clinician to assist documentation.
- Obtain cord gases.
- Ask for placenta to go to pathology.
- Note time until spontaneous ventilation, and return of heart rate.
- Note the presence of meconium staining, and evidence of recent weight loss of infant.
- Perform a neurological assessment as soon as possible.

3.2 Entry Criteria for Therapeutic Hypothermia (see figures 1 and 2)

Current trials provide strong evidence for improved long-term outcomes in infants having evidence of **both** asphyxia **and** moderate to severe encephalopathy.

See Figure 1 - Neurocritical Care Pathway.

3.2.1 Strong Evidence base exists for the following criteria

- ≥ 36 weeks gestation.
- ≥ 1800g birth weight.
- Age ≤ 6 hours.

OR

1. ***Evidence of asphyxia*** as defined by the presence of at least **ONE** of the following criteria:
   - Apgar <5 at 10 minutes or continued need for assisted ventilation for at least 10 minutes.
   - Any acute perinatal event that may result in HIE e.g. placental abruption, cord prolapse, severe FHR abnormality.
   - Any cord pH ≤ 7.0 or base deficit ≥12 mmol/L
   - Any blood gas within 60 minutes of birth with pH ≤ 7.0 or base deficit ≥12 mmol/L.

AND

2. ***Evidence of Moderate / Severe Encephalopathy*** (see Figure 2 - Modified Sarnat Criteria)
   - Seizures **OR**
   - AT LEAST **THREE** signs from the Sarnat Criteria (either moderate OR severe), see Figure 2 - Simplified Sarnat Criteria examination. Repeated examinations are required over the first 6 hours if baby has evidence of asphyxia, but has not yet shown clinical signs of moderate / severe encephalopathy. Consider talking to NICU SMO in these situations.

     In these infants, cooling should be started as soon as an infant fulfils entry criteria, ideally within the first 60 minutes after delivery.

3.2.2 The Evidence Base for the following is weaker, or based on expert opinion (from around the globe)

a. Infants born between 34 and 36 weeks gestational age.

b. Growth restricted near term / term infants with birth weight <1800g.

c. Postnatal collapse.

d. Infants between 6 and 24 hours of age.

e. Infants with mild encephalopathy.

f. Alternative evidence of a substantial insult may include:
   - At least **TWO** of the criteria for asphyxia outlined above, with evidence of mild encephalopathy.

   OR

   - **ONE criteria for asphyxia PLUS an abnormal aEEG trace**, including:
     i. Abnormal background voltage - lower margin <5μV.
     ii. Electroencephalographic seizures (**NOTE:** the presence of clinical seizures put infants in the moderate HIE category and they should be cooled if seizures within 6 (-12) hours of delivery).

There are no / minimal research data available yet to support therapeutic hypothermia for infants in these categories. Therefore it would be recommended to document the family discussion regarding therapeutic hypothermia prior to initiating treatment.

3.3 Notes

If cooling has been commenced then it is recommended that the 72 hours of cooling is completed rather than rewarming early as residual injury has been reported.

All infants potentially eligible for cooling should be discussed with the on-call Neonatologist as early as possible (see Figure 1, Neuroprotection Care Pathway).

As the clinical features of neonatal encephalopathy often evolve over time so serial observation and documentation of evolution is important (see Figure 2, Simplified Sarnat Criteria Examination).

aEEG can be useful (where possible), but **do not** delay cooling to obtain aEEG in an infant who meets the criteria outlined above. See Figure 3 for potential reporting format for aEEG.

Common aEEG abnormalities occurring in NE include:

- Abnormal background voltage (lower margin <5μv).
- Seizure activity.

However, the aEEG may be normal in an infant that fulfils cooling criteria, and in such a case the infant should still be cooled.

As neonatal encephalopathy evolves over time it may be appropriate to initiate cooling in an infant with mild encephalopathy (hyper-alert; hyper-reflexic; myoclonus may be present; normal-to-increased tone; dilated pupils; normal posture and Moro reflex; no seizures) who has evidence of a significant asphyxial insult that may cause progressive encephalopathy over the next 48 hours (see Figure 1, Neuroprotection Care Pathway). These infants should be discussed with the on-call Neonatologist early. If a decision is made for cooling this should be maintained for the full 72 hours.

Figure 1 - Neuroprotection Care Pathway

Adapted from https://bebop.nhs.uk/wp-content/uploads/EoE-HEALTH-FOUNDATION-NCP1.pdf)

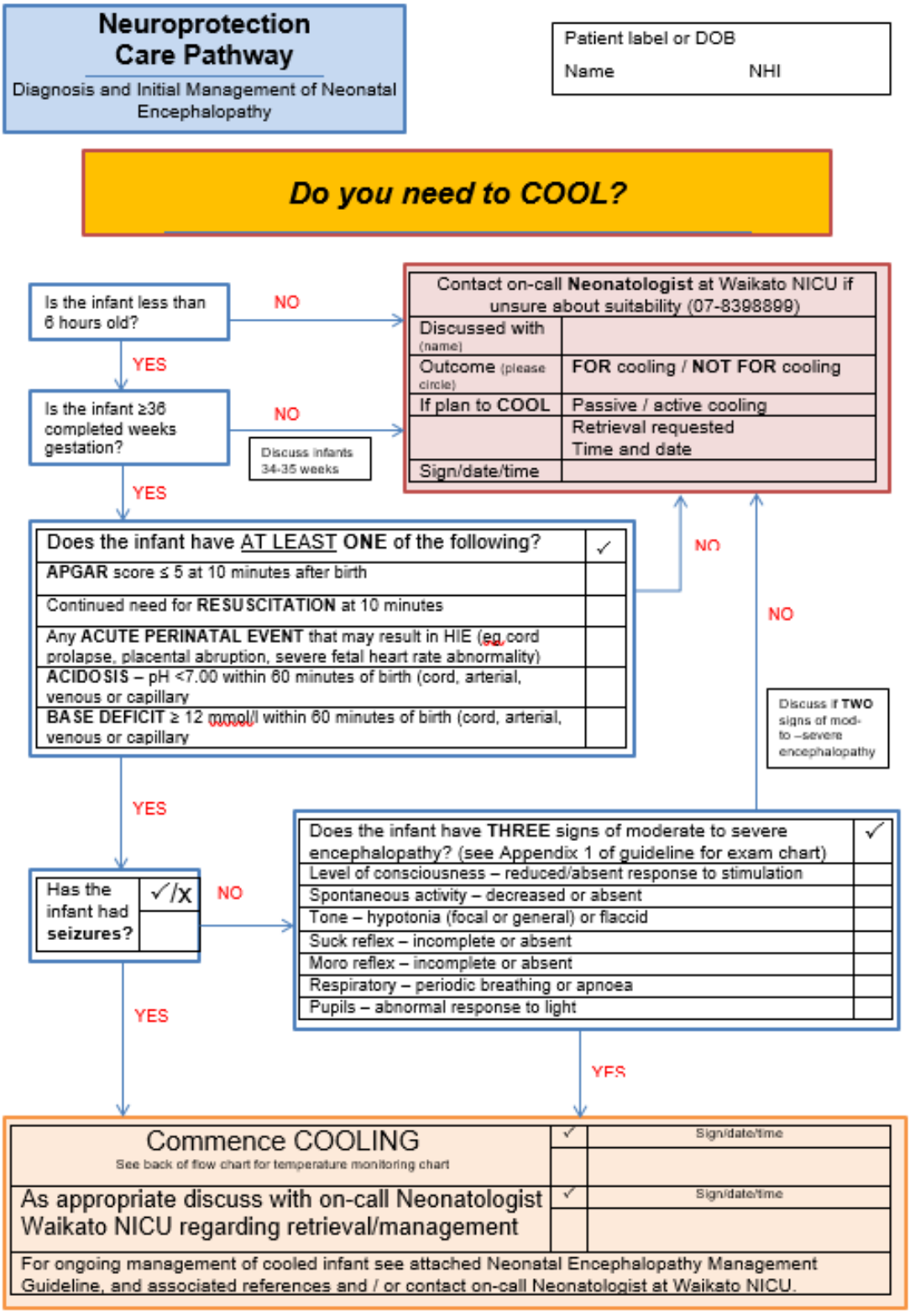

Figure 2 - Simplified Sarnat Assessment Form

SIMPLIFIED SARNAT CRITERIA (Assess as many signs as possible)									
SIGN	**SEVERITY**			***Circle to indicate whether the sign is consistent with normal, or mild, moderate or severe neonatal encephalopathy***					
	Mild encephalopathy	**Moderate encephalopathy**	**Severe encephalopathy**	**1 hr**	**2 hr**	**3 hr**	**4 hr**	**5 hr**	**6 hr**
Level of consciousness	Hyper alert	Decreased = reduced response to non-painful stimulation ("lethargic")	Absent = only responds to painful stimuli ("stupor"); or no or minimal response to pain ("coma")	Normal Mild Moderate Severe	Normal Mild Moderate Severe	Normal Mild Moderate Severe	Normal Mild Moderate Severe	Normal Mild Moderate Severe	Normal Mild Moderate Severe
Spontaneous activity	Normal or increased	Decreased	None	Normal Mild Moderate Severe	Normal Mild Moderate Severe	Normal Mild Moderate Severe	Normal Mild Moderate Severe	Normal Mild Moderate Severe	Normal Mild Moderate Severe
Tone	Normal or increased in trunk AND extremities	Hypotonia = reduced trunk OR extremity tone OR both	Flaccid = no tone	Normal Mild Moderate Severe	Normal Mild Moderate Severe	Normal Mild Moderate Severe	Normal Mild Moderate Severe	Normal Mild Moderate Severe	Normal Mild Moderate Severe
Suck reflex	Normal or incomplete	Incomplete	Absent	Normal Mild Moderate Severe	Normal Mild Moderate Severe	Normal Mild Moderate Severe	Normal Mild Moderate Severe	Normal Mild Moderate Severe	Normal Mild Moderate Severe
Moro reflex	Strong, low threshold	Incomplete	Absent	Normal Mild Moderate Severe	Normal Mild Moderate Severe	Normal Mild Moderate Severe	Normal Mild Moderate Severe	Normal Mild Moderate Severe	Normal Mild Moderate Severe
Respiratory abnormality	Normal	Periodic breathing	Apnoea	Normal Mild Moderate Severe	Normal Mild Moderate Severe	Normal Mild Moderate Severe	Normal Mild Moderate Severe	Normal Mild Moderate Severe	Normal Mild Moderate Severe

Figure 3 - aEEG Reporting Template

aEEG	Normal	Abnormal			
Lower border	≥ 5µV □	< 5µV □	***aEEG assessed - Date:***		
Upper border	≥ 10µV □	< 10µV □	***Time:***		
			By (Name, position)		
Seizures	No □	Yes □	Status epilepticus □	Clinical seizures □	Only aEEG algorithm □
Background pattern (circle)	Continuous normal voltage	Discontinuous normal voltage	Continuous low voltage	Burst suppression	Flat trace
Cyclicity	Yes □	No □	Unsure □		
Medication (circle all currently used)		Morphine Phenobarbital Phenytoin Midazolam Levetiracetam Other _____			

3.4 Whole Body Cooling

3.4.1 Inborn (Waikato Hospital)

Nurse on radiant warmer with warmer off.

a. Cool infant with CritiCool cooling blanket (refer to 'How to use CritiCool System' guide sheet attached to the cooling unit)

- Adjust set core temperature to **33.5° C** (see figure 4)
- Cooling blanket should be applied to baby wrapping legs and trunk if this does not compromise infant's care. Place bubble wrap under head to minimise temperature fluctuations.
- Cardiopulmonary monitoring including blood pressure should be continued.
- Change the position every 4-6 h during care: flat- supine, right or left side to avoid pressure sores on cold oedematous skin. Cyanosis of the hands and feet is common and usually transient.
- Re-warming - leave cooling blanket and bubble wrap in place:
  - Start 72 hours after reaching target temperature (not after delivery) unless specified by on-call Neonatologist.
  - Increase set temperature by 0.1° C every 30 minutes to slowly re-warm **- see figure 3.**
  - **The automatic warming programme has been set to warm the baby at 0.2° C every 60 mins** (i.e. the same speed at recommended above) but requires careful monitoring and if automatic warming is faster than 0.2° C per hour the warming should be changed to manual.
  - Criticool system may be turned off when core temperature reaches 36.5° C.

b. If CritiCool system is not available use 'ICE' protocol as below

- Do not dress - leave nappy unfastened.
- Insert continuous rectal temperature probe and tape to upper inner aspect of thigh.
- Set alarm limits for rectal temperature at 33.5 - 34.5° C
- Apply cold packs (never frozen) if initial rectal temperature >35.5° C. Apply with appropriate cloth coverings to both sides of the trunk. If necessary additional cold packs may be used around the top of the head and on the anterior abdomen to reach the cooling temperature. Generally the temperature can be maintained with cooling packs applied to each side of the trunk. As the packs warm up they need to be changed for new cold packs. Regularly inspect skin integrity.
- When rectal temperature <34°C, set radiant warmer on manual and gradually adjust heater output to maintain rectal temperature at 33.5 - 34.5°C.
- Note: severely encephalopathic infants may require active WARMING to maintain core body temperature.
- Maintain cooling for 72 hours (replacing cool packs as required).
- Re-warming procedure:

- Remove cooling pack, if in place.
- Apply skin temperature probe and turn radiant warmer on if switched off.
- Set servo at 34.5°C
- Increase servo temperature by 0.5°C every 2 hours until rectal temperature 36.5°C
- Re-warm no faster than 0.5°C/hour, aim to rewarm slowly i.e. 0.2°C/hour.
- Avoid hyperthermia (>37°C)

Figure 4 - CritiCool adjusting set core temperature

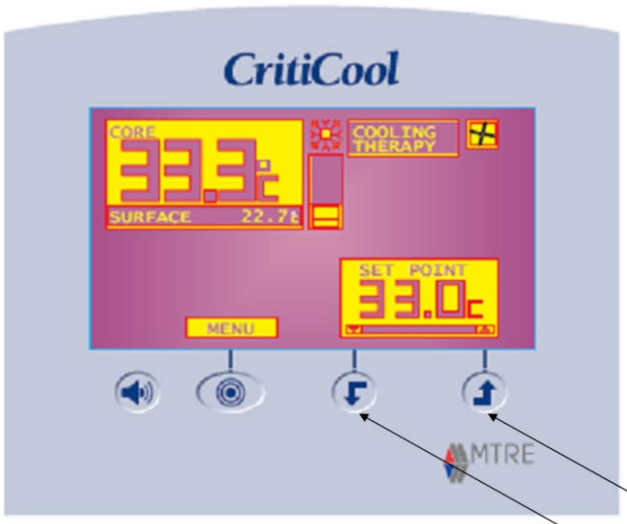

Figure – Regulation of core temperature

3.4.2 Outborn

- Nurse on radiant warmer with warmer off.
- Resuscitate as required, follow 'Initial Care' recommendations.
- See Waikids Neuroprotection Care Pathway, Appendix 1. Aim is to stabilise and transfer.
- Liaise with Waikato Neonatologist on call regarding diagnosis, management and transfer.
- Nurse on radiant warmer or incubator with heater set to "Skin Servo Control" set at 34°C
- Do not dress - leave nappy unfastened.
- Measure core temperature at least every 30 minutes.
- Aim for rectal temperature 33.5°C - 34.5° C - see 'ICE' protocol above for active cooling if required while awaiting transfer.

  Note: severely encephalopathic infants may require active WARMING to maintain core body temperature
- Set low alarm for rectal probe at 34°C and heart rate low alarm at 75bpm.
- Obtain baseline bloods: full blood count, blood gas (including glucose and lactate), blood culture and where possible coagulation screen.
- Ensure continuous monitoring and hourly recording of: heart rate, respiratory rate, pulse oximetry, blood pressure, fluid balance and where possible rectal temperature.
- Please send as much information as available regarding antenatal care, labour and delivery with the infant, including names of GP / Practice, LMC and obstetrician if possible.
- During transport to Waikato NICU careful core temperature monitoring is essential.

3.5 Supportive Care

- Ventilation support as required.
- Arterial and venous access, aim for UAC and UVC - take initial FBC, coagulation screen, blood culture and blood gas at time of placement if not already obtained.
- Initial fluids should be restricted to 40ml/kg/day (in anticipation of renal impairment and oliguria) beware of increased potential for hypoglycaemia. Initial fluids are usually 10% dextrose, with EBM oral immune therapy. Oral feeds should be cautiously introduced from the rewarming phase. TPN may be considered when the infant is stabilised and renal/liver dysfunction has resolved.
- Careful attention to fluid balance. Infant may need in-dwelling catheter placed.
- Morphine infusion (10mcg/kg/hr).
- Regular blood testing – full blood count for evidence of anaemia, thrombocytopenia or infection; biochemistry including electrolytes, renal and liver function tests, haematology (thrombocytopenia), blood sugars, blood gases; coagulation screen.
- aEEG monitoring and serial neurologic assessment (use report template - Figure 3, to assess).
- Consideration of entry into trials e.g. PAEAN.
- Consider investigation for other aetiologies of NE (for example metabolic disease, infection, drug exposure, neonatal stroke or nervous system malformation) as indicated by presentation, history and clinical features. Recommend sending urine for 'URINE METABOLIC SCREEN' to LabPlus, Auckland City Hospital (urine organic and amino acid testing with tandem mass spectometry) if there is any indication that the case is not a 'textbook hypoxic-ischaemic' neonatal encephalopathy.
- Echocardiography is helpful to rule out structural cardiac disease and will assist with assessment of cardiac function.
- Treat clinical or electrographic seizures with anticonvulsants (phenobarbitone, leviteracetam, midazolam, phenytoin). Monitor for seizure activity throughout cooling and rewarming.
- Assess pain and sedation score and sedation management is appropriate, according to Waikato DHB Clinical management NICU Nursing guideline: Neonatal pain and sedation: Assessment and nursing management (1684).If there is consideration of withdrawal of intensive care for any infant after cooling has been commenced the infant should ideally be re-warmed before intensive care is withdrawn.
- Infants undergoing cooling should have a medical review by Registrar / CNS/NNP if there is:
  - Difficulty maintaining core temperature at set point.
  - Persistent bradycardia <75bpm or abnormal rhythm - may need increased temperature.
  - Persistent hypoxaemia despite appropriate support - may need increased temperature.
  - Persistent hypotension despite appropriate management - may need increased temperature.
  - Break-through seizures on re-warming - may need to review rewarming speed (to be discussed with on-call Neonatologist).

3.6 Neuroimaging

- EARLY Cranial ultrasound.
- MRI once clinically stable, discuss with Paediatric Neuroradiologist regarding timing.

3.7 Follow up

- Nurse on radiant warmer with warmer off.
- Dubowitz neurological examination before discharge and/or General Movement Assessment, with Visiting Neurodevelopmental Therapy or other community support as indicated.
- Ideally the discharge and follow up plan is discussed with the parents in a multi-disciplinary meeting including an appropriate Senior Medical Officer or their delegate.
- Neonatal Home Care Nursing follow-up as indicated.
- Outpatient appointment with nominated Paediatrician ~6 weeks after discharge.
- Ideally a 2 year neurodevelopmental assessment is performed.
- Referral to Ophthalmology Department for all infants with moderate or severe Neonatal Encephalopathy.
- Cases should be reported to ANZNN and PMMRC NEWG.
- Ensure local DHB multi-disciplinary (Obstetric, midwifery, paediatric) review of circumstances around development of moderate / severe Neonatal Encephalopathy to determine any local quality improvement initiatives (PMMRC 8th report 2014: All DHBs should review local incident cases of NE. The findings of these reviews should be shared a multidisciplinary local forums and form the basis of quality improvements as appropriate).
- There should be a multidisciplinary discussion regarding whether the infant should be referred to ACC for potential cover as a treatment injury.

3.8 Potential complications

Localised (particularly excessive) hypothermia can result in focal subcutaneous fat necrosis and potential scarring, and should be avoided.

Cooling for longer than 72 hours or deeper than 33.5°C may have potential for increased mortality[1].

Careful attention to communication with families, and appropriate family integrated care is important to facilitate parent-infant bonding

See also 1.4, contraindications.

3.9 After care

See 3.6 Neuroimaging and 3.7 Follow up.

4 Patient information

https://bebop.nhs.uk/families/information/treatment-options/

5 Audit

5.1 Indicators

- Appropriate cooling management for inborn infants:
  - Time of NE recognition.
  - Time to core temperature 33.5ºC
  - Length of time at core temperature 33.5ºC
  - Lowest serum/cap gas sodium level, and time since birth.
- Interpretation of first 24 hours of aEEG.
- Documentation of neurologic examinations:
  - Within first hour.
  - Until decision to cool.
  - Daily during cooling.
  - Before discharge.
- Follow up arrangements for cooled infants at the time of discharge.
- Results of ophthalmologic and neurodevelopmental assessments at 2 years of age.

6 Evidence base

6.1 References

Neonatal Encephalopathy Consensus Statement from the Newborn Clinical Network. Published 30/10/2019. https://www.starship.org.nz/guidelines/neonatal-encephalopathy-consensus-statement-from-the-newborn-clinical (accessed 28/4/20)

Thoresen M. Who should we cool after perinatal asphyxia? Semin Fetal Neonatal med 2015;20(2):66-71.

Austin T et al. To cool or not to cool? Hypothermia treatment outside trial criteria. Arch Dis Child Fetal Neonatal Ed 2013;98(5):F451-3.

Jacobs SE et al. Whole-Body Hypothermia for Term and Near-Term newborns with Hypoxic-Ischaemic Encephalopathy. A Randomised Controlled Trial. Arch Pediatr Adolesc Med 2011;165(8):692-700.

https://bebop.nhs.uk/wp-content/uploads/EoE-HEALTH-FOUNDATION-NCP1.pdf (accessed 28/4/20)

6.2 Additional Reference Material

- aEEG interpretation, An Atlas of Amplitude-Integreated EEGs in the Newborn. L Hellstrom-Westas, L de Vries, I Rosen.
- Natus / Olympic website.https://partners.natus.com/asset/resource/file/newborncare/asset/2018-04/013154B_CFM%20Olympic%20Brainz%20Monitor%20BPc%20Datasheet_EN%20A4_lo-res.pdf (accessed 9/5/20)

6.3 External Standards

PMMRC NEWG recommendations 2019:

Neonatal encephalopathy:

- The PMMRC recommends that DHBs provide interdisciplinary fetal surveillance education for all clinicians involved in intrapartum care on a triennial basis. This is to be provided free for staff and at no cost to lead maternity carers (LMCs). The PMMRC encourages the Midwifery Council, the New Zealand College of Midwives (NZCOM) and Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) to work with DHBs in the implementation of this recommendation.
  a. This education includes risk assessment for babies throughout pregnancy as well as intrapartum observations.
  b. The aims include strengthening of supervision and support to promote professional judgement, interdisciplinary conversations and reflective practice.
- All neonatal encephalopathy (NE) cases need to be considered for a Severity Assessment Code (SAC) rating. Neonatal hypoxic brain injury resulting in permanent brain damage (or permanent and severe loss of function) should be rated as SAC 1. Those who received cooling with as yet undetermined outcome should be rated as SAC 3.

  Justification - SAC reviews can be a useful tool for identifying systems issues that can be modified to reduce the chance of further harm. Having a third-party assessment of the quality of the review will help DHBs to fully utilise this opportunity for improvement.

- All babies with NE, regardless of severity, should have a multidisciplinary discussion about whether to refer to the Accident Compensation Corporation (ACC) for consideration for cover as a treatment injury, using ACC's *Treatment Injury Claim Lodgement Guide*.7 Parents should be advised that not all treatment claims are accepted.

  Evidence - Currently there is little consistency as to which babies with NE are notified to ACC for assessment of a treatment injury claim.

  Justification - Quality of life for the baby and their family or whānau may differ considerably depending on whether their condition is covered by ACC.

6.4 Associated Waikato DHB Documents

- Waikato DHB NICU Drug Manual.
- Waikato DHB Nursing Guideline: Neonatal pain and sedation: Assessment and nursing management (1684).
- Waikato NICU Nursing Procedure: Admission to Level 3 intensive care nursery (4571).
- Waikato Nursing Procedure: CritiCool Device for Infants in Newborn Intensive Care Unit (1639).