HYPOXIC ISCHAEMIC ENCEPHALOPATHY (HIE) INCLUDING PREPARATION FOR ACTIVE COOLING
Supporting information

This guideline has been prepared with reference to the following:

Gale C, Longford NT, Jeyakumaran D et al. Feeding during neonatal therapeutic hypothermia, assessed using routinely collected National Neonatal Research Database data: a retrospective, UK population-based cohort study. Lancet Child Adolesc Health. 2021;5:408-16

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8131202/

British Association of Perinatal Medicine. Therapeutic Hypothermia for Neonatal Encephalopathy: A Framework for Practice. 2020. BAPM

https://www.bapm.org/resources/237-therapeutic-hypothermia-for-neonatal-encephalopathy

In neonates with HIE, is MRI, EEG, or cranial ultrasonography the most useful technique in predicting outcome?

A study in 46 infants (Rutherford, 1994) found that, although ultrasonography adequately identified those with a poor prognosis, MRI was better at detecting the precise site and extent of the lesion. A resistive index </= 0.55 had a PPV of 71% in predicting adverse outcome in a case-control study in 212 patients (Jongeling, 2002).

In a study comparing 47 neonates undergoing CT (n=26), MRI (n=24) or both (n=3) with ultrasonography (Blankenberg, 2000), CT and MRI revealed 25 instances of hypoxic-ischaemic injury compared to 13 identified by ultrasonography. Intraparenchymal haemorrhage was also identified twice as often (10 instances vs 5) by CT and MRI compared to ultrasonography.

A small study in 16 infants (Malik, 2002) found that MR spectroscopy was more sensitive than MRI in detecting the insult due to HIE.

A study of combined standard EEG with MRI in 25 infants (Biagioni, 2001) found that the presence of any EEG background abnormality early in the course of the illness predicted 94% of cases that resulted in an abnormal outcome (mild to severely abnormal). This compared with 85% for MRI. The authors advocate early EEG to distinguish those infants likely to have an abnormal outcome, followed by MRI to provide further information on the nature of the outcome. However, an accompanying editorial (Baumgart, 2001) suggests that focusing on the moderate-to-severely abnormal outcomes results in 100% accuracy for MRI, with little extra benefit from EEG.

Standard EEG may be difficult to obtain in the first hours following birth, but amplitude integrated EEG (aEEG) has been developed to monitor cerebral electrical background activity in the intensive care unit. A study of the technique in 47 infants (Hellstrom-Westas, 1995) found that it predicted outcome correctly in 43 (91.5%). Similar results were obtained from a study of 73 infants (Toet, 1999).

Baumgart S, Graziani LJ. Predicting the future for term infants experiencing an acute neonatal encephalopathy: electroencephalogram, magnetic resonance imaging, or crystal ball? Pediatrics 2001;107:588-90

Biagioni E, Mercuri E, Rutherford M, et al. Combined use of electroencephalogram and magnetic resonance imaging in full-term neonates with acute encephalopathy. Pediatrics 2001;107:461-8

Blankenberg FG, Loh NN, Bracci P, et al. Sonography, CT, and MR imaging: a prospective comparison of neonates with suspected intracranial ischemia and hemorrhage. AJNR Am J Neuroradiol 2000;21:213-8
http://www.ajnr.org/content/21/1/213.long

Eken P, Toet MC, Groenendaal F, et al. Predictive value of early neuroimaging, pulsed Doppler and neurophysiology in full term infants with hypoxic-ischaemic encephalopathy. Arch Dis Child Fetal Neonatal Ed 1995;73:F75-80
http://fn.bmj.com/content/73/2/F75.long

Hellstrom-Westas L, Rosen I, Svenningsen NW. Predictive value of early continuous amplitude integrated EEG recordings in outcome after severe birth asphyxia in full term infants. Arch Dis Child 1995;72:F34-38
http://fn.bmj.com/content/72/1/F34.long

Jongeling BR, Badawi N, Kurinczuk JJ, et al. Cranial ultrasound as a predictor of outcome in term newborn encephalopathy. Pediatr Neurol 2002;26:37-42

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Malik GK, Pandey M, Kumar R, et al. MR imaging and in vivo proton spectroscopy of the brain in neonates with hypoxic ischemic encephalopathy. Eur J Radiol 2002;43:6-13

Pressler RM, Boylan GB, Morton M, et al. Early serial EEG in hypoxic ischaemic encephalopathy. Clin Neurophysiol 2001;112:31-7

Rutherford MA, Pennock JM, Dubowitz LM. Cranial ultrasound and magnetic resonance imaging in hypoxic-ischaemic encephalopathy: a comparison with outcome. Dev Med Child Neurol 1994;36:813-25

Toet MC, Hellstrom WL, Groenendaal F, et al. Amplitude integrated EEG 3 and 6 hours after birth in full term neonates with hypoxic-ischaemic encephalopathy. Arch Dis Child Fetal Neonatal Ed 1999;81:F19-23
http://fn.bmj.com/content/81/1/F19.long

Evidence Level: IV

Normal body temperature (36.5 – 37.2°) should be maintained?

A Cochrane review (Jacobs 2013) found that hypothermia, resulted in a statistically significant and clinically important reduction in the combined outcome of mortality or major neurodevelopmental disability to 18 months of age (typical RR 0.75 95%; CI 0.68 to 0.83; typical RD -0.15, 95%; CI -0.20 to -0.10; number needed to treat for an additional beneficial outcome 7, 95% CI 5 to 10 (8 studies, 1344 infants).

An earlier systematic review (Shah, 2007) also found that hypothermia, in 4 studies including 497 infants, resulted in a reduced combined outcome of death or neurodevelopmental disability compared with normothermia (RR 0.76, 95% CI 0.65-0.88, NNT 6, 95% CI 4-14).

There have been conflicting opinions in the US in the past as to whether or not the strength of the existing evidence warrants a change in practice (Perlman, 2008; Kirpalani, 2007).

Jacobs SE, Berg M, Hunt R et al. Cooling for newborns with hypoxic ischaemic encephalopathy. Cochrane Database of Systematic Reviews 2013, Issue 1. Art. No.: CD003311
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003311.pub3/full

Kirpalani H, Barks J, Thorlund K, et al. Cooling for neonatal hypoxic ischemic encephalopathy: do we have the answer? Pediatrics 2007;120:1126-30

Perlman M, Shah P. Time to adopt cooling for neonatal hypoxic-ischemic encephalopathy: response to a previous commentary. Pediatrics 2008;121:616-8

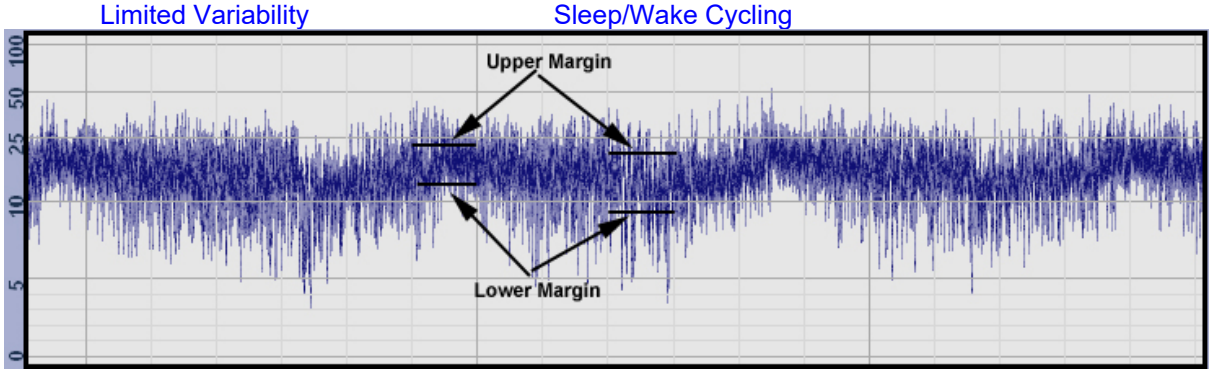
Shah PS, Ohlsson A, Perlman M. Hypothermia to treat neonatal hypoxic ischemic encephalopathy: systematic review. Arch Pediatr Adolesc Med 2007;161:951-8
http://archpedi.jamanetwork.com/article.aspx?articleid=571322

Evidence Level: I

What are the normal, moderately abnormal, severely abnormal and seizure CMF traces?

Normal CFM

Upper Margin > 10 µVolts
Lower Margin > 5 µVolts
Limited Variability
Sleep/Wake Cycling



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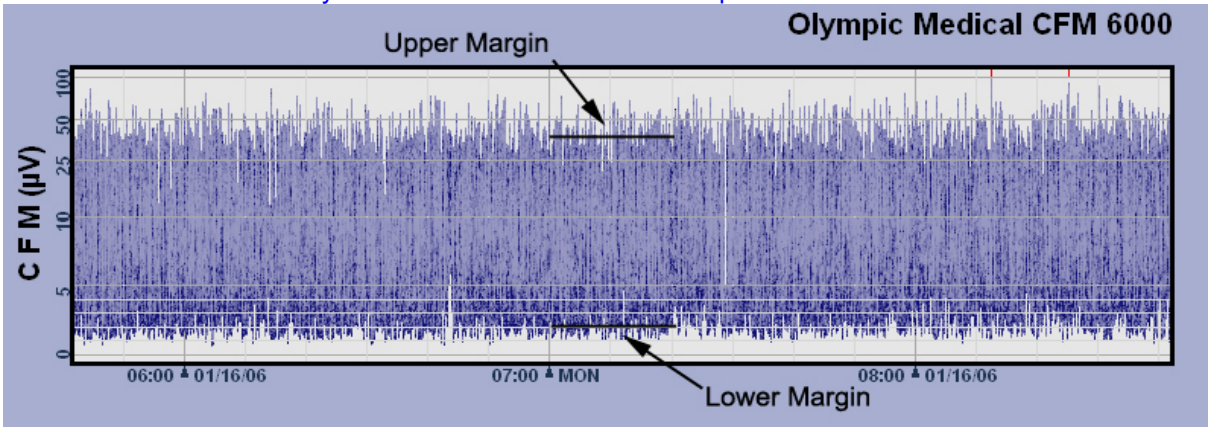
Moderately Abnormal

Upper Margin > 10 µVolts
Increased variability

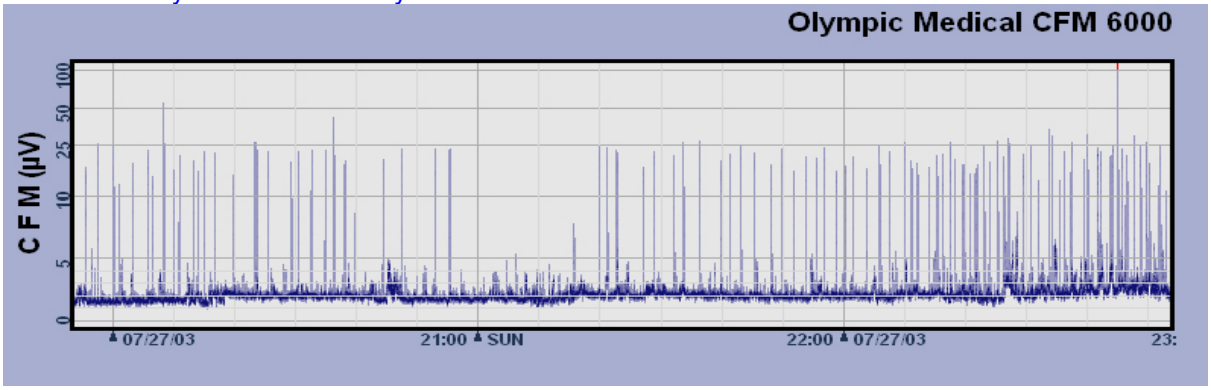
Lower Margin < 5 µVolts
No Sleep/Wake



Severely Abnormal

Upper Margin < 10 µVolts
Greatly reduced variability

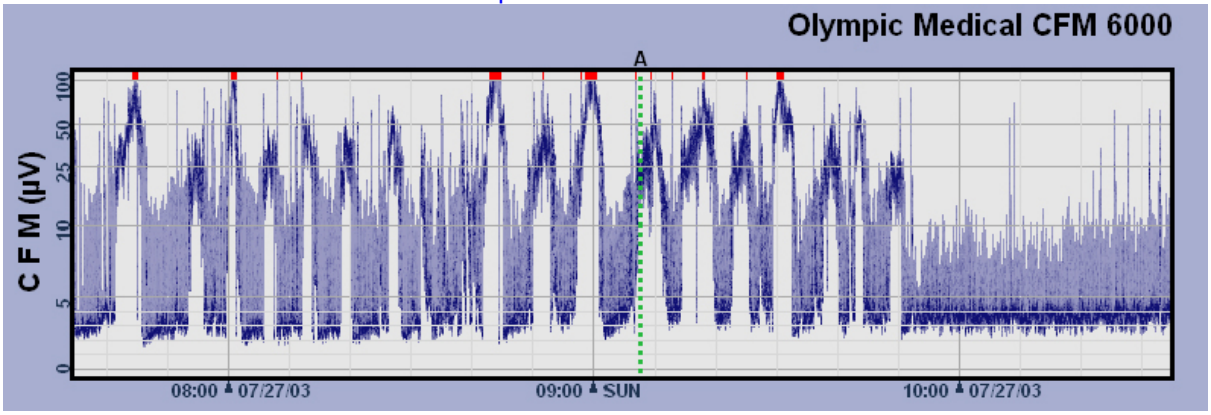
No Sleep/Wake



Seizure

Injured brain has increased variability
Causes CFM to narrow and rise up

Onset of seizure > continuous, high activity



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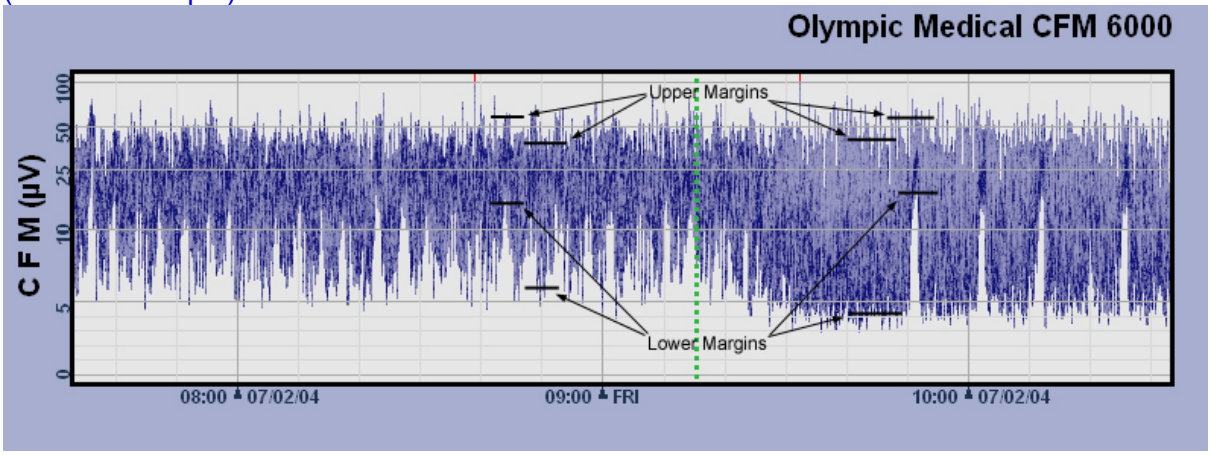
Seizure
(second example)



Olympic Medical. Olympic Medical CFM 6000: Infant aEEG Cerebral Function Monitor with CFM Insight.

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