Fifteen-minute consultation: Therapeutic hypothermia for infants with hypoxic ischaemic encephalopathy—translating jargon, prognosis and uncertainty for parents

Paul Cawley, Ela Chakkarapani

ABSTRACT
Hypoxic ischaemic encephalopathy may lead to death or severe long-term morbidity. Therapeutic hypothermia (TH) increases survival without impairments in childhood, but prognostic uncertainty may remain for years after birth. Clear and accurate communication is imperative but challenging. This article explores the predictive value of routinely performed assessments during TH, as well as the qualitative research relating to parental experience. This article will benefit paediatric trainees, consultants and nurse practitioners in providing: (1) the background information needed for initiating a conversation with parents regarding outcome and (2) optimising their communication with parents in translating jargon, prognosis and uncertainty.

Neonatal hypoxic ischaemic encephalopathy (HIE) is a potentially devastating condition, which may progress to moderate to severe short-term morbidity, long-term disabilities or death.1–3 Controlled reduction of an encephalopathic infant’s core temperature, known as therapeutic hypothermia (TH), increases survival without impairment in childhood. TH is the standard care in developed countries.1 2

TH is indicated in newborn infants with evidence of perinatal asphyxia resulting in moderate to severe encephalopathy. Grade of encephalopathy is determined clinically (based on Sarnat score) and/or with amplitude-integrated electroencephalography (aEEG; moderate or severely abnormal pattern). Criterion for perinatal asphyxia typically includes meeting any one of1 4 5:

► Acidosis on blood sample from cord or within 1 hour of age: pH <7.0 or base excess ≤−16 mmol/L.
► Apgar score ≤5 at 10 min.
► Need for resuscitation at 10 min after birth (such as endotracheal or mask ventilation).

During TH, core temperature is reduced to 33°C–34°C for 72 hours, using a servo-controlled (automatic feedback) cooling wrap, mattress or cap. Infants require intensive care support and monitoring and are therefore frequently transferred to a tertiary neonatal intensive care unit, away from their parents.

Clear and accurate communication is imperative in order to minimise parental distress, but this can be difficult. Clear and effective communication can be achieved if:

1. Clinicians are aware of the accuracy of the prognostic tests they have performed, together with the level of uncertainty that exists.
2. Clinicians have an appreciation of the turbulent parental experience and are able to filter the frequency, volume and detail of their communications to meet the needs of the parents in a stepwise fashion.
3. Clinicians are able to translate medical terms relating to the current condition of the baby, and the future implications of this, into plain/simple language.

This paper will explore each of these three points in turn. First, by considering what prognostic information is available, and what weighting a clinician should place on this when considering certainty of outcome.
**DETERMINING PROGNOSIS AND UNCERTAINTY**

Determining prognosis for an infant undergoing TH is a challenge for the attending clinician for many reasons:

- The initial working diagnosis of HIE may be incorrect (e.g., encephalopathy due to sepsis or metabolic conditions) and could be associated with other comorbidities (e.g., cardiac or surgical problems).
- Pharmacological sedation may limit assessment.
- No test is 100% predictive of infant outcome.
- TH modifies the prognostic value of clinical and aEEG assessment.
- The prognostic value of many predictive markers may not be apparent until several days into the evolution of the infant’s abnormal neurological state.
- Clinical trials report the composite outcome of ‘death and major neurodisability’, whereas clinicians must pragmatically try to separate these two entities.
- Clinical trials and observational studies of cooled infants divide outcome into severe (death or disability) versus non-severe (survival without disability). Disability is often defined as the developmental scores being 1–2 SD (Standard Deviations) below the population mean, whereas a spectrum of neuromotor, cognitive and behavioural impairment may present through childhood.

**Death**

Death following HIE is the most imminent outcome to prognosticate as this has immediate ramifications for both clinicians and parents. Accurate prognostication of death helps to: (1) avoid futile but potentially distressing medical interventions, (2) offer appropriate palliative care with amelioration of pain and distress in the infant and (3) prepare parents for palliative care and/or death as much as possible (including attention to wider family, social support and cultural or religious requirements).

Death may occur due to global multiorgan injury or following reorientation of care due to severe brain injury. The ability to determine which infants are at highest risk of severe brain injury, in order to consider reorientation of care, is, however, limited. Likewise, clinical trials are limited in their ability to provide prognostic markers of death of any cause. Nearly 75% of deaths reported in the TH clinical trials are following withdrawal or withholding of life-sustaining treatment and are thus subject to bias. This is reflected by the variable death rates in the contemporary cohorts of TH (6%–23%).

Clinicians should be alert to:
- **Iniminent or inevitable death** in infants with severe encephalopathy and multiorgan failure who are deteriorating despite maximal intensive care support.
- **Infants in whom TH is futile and death highly likely.** These infants may only be identified with time, as sequential evidence of a severe hypoxic-ischaemic insult and absence of neurological recovery is required:
  - Severe asphyxia: Apgar score <3 at 10 min and/or need for epinephrine (adrenaline) during resuscitation and/or an umbilical cord or first newborn blood gas pH <6.8.

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**Table 1 Neurodevelopmental outcomes of infants aged 18–24 months treated with therapeutic hypothermia for hypoxic ischaemic encephalopathy**

| Outcome measure                                                                 | Percentage of Infants |
|---------------------------------------------------------------------------------|-----------------------|
| Major neurodisability at 18–24 months in survivors                             | 29–32                 |
| Infants with moderate encephalopathy at baseline                               | 20–27                 |
| Infants with severe encephalopathy at baseline                                 | 37–71                 |
| Infants with moderately abnormal aEEG at baseline                              | 12                    |
| Infants with severely abnormal aEEG at baseline                                | 58                    |

Component outcomes within ‘major neurodisability’ (definitions are provided in brackets)

| Neuromotor delay in survivors (Bayley Scales of Infant Development – PDI >2 SD below mean) | 26 |
|-----------------------------------------------|----|
| Developmental delay in survivors (Bayley Scales of Infant Development – MDI >2 SD below mean) | 25 |
| Cerebral palsy in survivors (Range of movement difficulties affecting posture and motor function and often associated with difficulties of vision, hearing, intellect, communication and feeding) | 11–23 |
| Blindness in survivors (Vision <6/60 in both eyes) | 6 |
| Deafness in survivors (Sensorineural deafness requiring amplification) | 4 |

Other outcomes not included in ‘major neurodisability’

| NG feeds at discharge | 11 |
| Seizures/anticonvulsant treatment at follow-up | 9–12 |

Data extracted from refs.\textsuperscript{1, 10, 11, 14}

aEEG, amplitude-integrated electroencephalography; MDI, Mental Development Index; NG, nasogastric; PDI, Psychomotor Development Index; SD, standard deviation.
Figure 1  Risk of death or major disability (moderate to severe disability as defined in tables 1 and 2); routinely available prognostic markers from birth to discharge in infants treated with therapeutic hypothermia for hypoxic-ischaemic encephalopathy. Only markers with outcome data at >12–24 months included. *Caution: small number of participants; †combined hypothermia/normothermia group data; ‡major MRI abnormality=moderate/severe basal ganglia or thalamic lesions, severe white matter lesions or an abnormal posterior limb of the internal capsule. aEEG, amplitude-integrated electroencephalography; NG, nasogastric; MRI, magnetic resonance imaging; NICHD, National Institute of Child Health and Human Development; NPV, negative predictive value; PPV, positive predictive value.
Best practice and Fifteen-minute consultations

Spectrum of prognostic uncertainty in Hypoxic Ischaemic Encephalopathy

Clinical Example:
Infant A, B & C all met identical entry criteria for cooling, their subsequent risk of severe disability may be estimated by the evolution of their encephalopathy, as assessed clinically and using aEEG:

Infant A
- Normalisation of aEEG voltage by 6 hours
- Sleep-Wake Cycling at 24 hours
- Grade 0 encephalopathy on day 4

Infant B
- Normalisation of aEEG voltage by 48 hours
- Sleep-Wake Cycling by 60 hours
- Grade 2 encephalopathy on day 4

Infant C
- Severely abnormal aEEG at 72 hours
- Did not demonstrate sleep-wake cycling
- Grade 3 encephalopathy and seizures on day 4

Outcome:
Severe disability highly unlikely
While outcome is not certain, severe disability would be highly unlikely. Overstating ‘uncertainty’ to parents would be unnecessarily non-reassuring for parents.

Severe disability highly likely
Whilst outcome is not certain, disabilities are expected; purely reporting ‘Uncertainty’ would be falsely reassuring for parents.

Moderate likelihood of severe disability

Figure 2  Schematic demonstrating the spectrum of prognostic uncertainty in hypoxic ischaemic encephalopathy. Clinicians must balance the predictive value of prognostic markers with the level of reassurance/uncertainty reported to parents. aEEG, amplitude-integrated electroencephalography.

- Initial severe encephalopathy: abnormal aEEG background (continuous low voltage or flat trace) at 6–12 hours after birth.\(^{12}\)
- Persistent abnormal aEEG background pattern at 24 hours of TH without improvement.\(^{12}\)
- Early brain lesions on MRI: presence of basal-ganglia/thalami predominant lesions at 48–72 hours of TH.\(^{13}\)

In all decisions relating to end-of-life care, the burden of treatment must be considered (eg, are medical interventions causing non-ameliorable harm or discomfort without reciprocate benefit). In addition, clinicians must carefully examine their primary diagnosis of HIE to ensure potential reversible causes are not missed.

Disability
Neurodevelopmental disabilities in survivors include cerebral palsy, developmental delay or intellectual impairment, blindness and deafness (definitions and incidences of neurodisability are provided in table 1).\(^{14}\)

Prognostic markers
Published studies typically reference the predictive value of prognostic markers relative to the composite outcome of death and major neurodisability. Based on data from these studies, many routinely performed assessments may be used to help further stratify ongoing risk of mortality and long-term disability. TH reduces the positive predictive value of many of these assessments:

Early markers of newborn condition
TH decreases ongoing brain injury following HIE. The predictive values of early markers of infant condition, such as the Apgar score, early blood pH and base excess and admission Sarnat stage, are therefore reduced, with the exception of infants at the very extremes of poor condition.\(^{6,15–19}\)

Serial clinical neurological assessment using modified Sarnat staging
Impairment of renal and liver function and reduced core temperature during TH prolong the effect of sedatives. The evolution of an infant’s encephalopathic state, reflected by their Sarnat stage, is therefore modified. In addition, intensive care procedures, such as tracheal intubation, present barriers to clinical neurological examination. Neurological examinations performed after rewarming, and at discharge, have a lower false positive rate for death and disability, when
### Table 2  Outcomes at 6–7 years in children who received therapeutic hypothermia (TH)

| Outcomes at 6–7 years following TH | Percentage of infants |
|-----------------------------------|-----------------------|
| Survival                          | 71–72                 |
| Neurodisability in survivors  2 3 (definitions are provided in brackets)* | 14–16 |
| Severe disability 
  (IQ <55 (<3 SD), GMFCS 4 or 5 (needs adaptive seating or has severely limited mobility) or no useful vision) | 8–19 |
| Moderate disability  
  (IQ 55–69 (2–3 SD), GMFCS 2 2 or 3 3 (minimal ability to perform gross motor skills or requires assistance with walking), moderately reduced vision, bilateral deafness or epilepsy requiring anticonvulsant therapy) | 10–25 |
| Mild disability  
  (IQ 70–84 (1–2 SD), GMFCS 1 2 or 2 3 (able to walk independently but may have some gait abnormalities) or abnormality in one or both eyes with normal or nearly normal vision) | 41–68 |
| No disability  
  (IQ ≥85 (≥1 SD), with no cerebral palsy, hearing or visual deficits or epilepsy) | 11–21 |
| Cerebral palsy                  | 1–1.5                 |
| Bilateral blindness             | 4–5                   |
| Hearing impairment              | 10–13                 |
| Seizures or confirmed epilepsy  | 48                    |
| Special educational needs in survivors 2 3 11: | 48 |
| Parental reported behavioural problems | 7  |
| Mainstream school with academic or behavioural educational support | 31 |
| Special educational needs school | 14                  |

**Table Footnotes:**

* Differences in trial definitions are individually referenced.

GMFCS, Gross Motor Function Classification System; IQ, intelligence quotient; SD, standard deviation.

Neurodevelopmental abnormalities may still occur, however, in infants with no obvious, or only minor brain tissue, diffusion-weighted or spectroscopy MR abnormalities. Accurate neurological examination and aEEG pattern interpretation are essential for achieving the stated prognostic values. Adequate training is essential for trainees to achieve competence in these skills. Normalisation of aEEG within 48 hours of cooling, mild or no encephalopathy after rewarming or at discharge and normal brain MR imaging increase the chances of a good prognosis.

Figure 1 provides a chronological reference of predictive values of death and major disability, before, during and after TH. Accurate neurological examination and aEEG pattern interpretation are essential for achieving the stated prognostic values. Adequate training is essential for trainees to achieve competence in these skills. Normalisation of aEEG within 48 hours of cooling, mild or no encephalopathy after rewarming or at discharge and normal brain MR imaging increase the chances of a good prognosis.

Prognostic certainty therefore increases with time, as more clinical, neurophysiological (aEEG) and neuroimaging information becomes available. Nevertheless, a degree of uncertainty will persist; clinicians should be open with parents regarding uncertainty. The degree of uncertainty portrayed is a fine balance; overstating or understating uncertainty may unfairly give parents an unrealistic perception of their child’s risk of long-term impairment (see figure 2). Parents should be aware that no test or assessment is 100% predictive for death or severe disability.
Box 1  Key learning from qualitative studies investigating parental experiences following admission of an infant with hypoxic ischaemic encephalopathy for therapeutic hypothermia (TH)16–28

(1) Consistent and frequent communication:
► Brief update by the neonatal team prior to transfer to the neonatal unit.
► Senior member of the neonatal team should update parents as soon as possible after admission.
► If the mother is unable to come to the neonatal unit, the neonatal team should go to the mother (or direct telephone call where in a different hospital).
► Medical updates should be provided at least daily or after any significant event.
► Ideally both parents, or alternatively an additional supporting family member, should be present for significant updates.
► Summary discussions should be provided to clarify parents’ total understanding of event.
► Obstetric debrief, before the mother’s discharge, will be beneficial for parental understanding of delivery events.

(2) Avoid jargon and acknowledge prognostic uncertainty:
► Use simple lay language; explain jargon if used.
► TH within guideline criteria is not experimental; parents should be reassured it is well researched and ‘proven’.
► Be honest regarding uncertainty; this is inevitable.
► Share what prognostic information is known openly and honestly.
► Ensure postdischarge follow-up is offered with sufficient time to address parental anxiety and questions.

(3) Address barriers to attachment:
► Parents should see, and by preference have physical contact with, baby prior to transport from delivery room.
► Maximise opportunities for parental physical contact and involvement (eg, stationary holding of infant’s hand, scheduled cares/nappy changes and feeding if started).
► Ensure pain is monitored and attended to; reassure parents of this.
► Provision of parent room on unit or patient hotel, if distance from home is barrier to parental visiting.
► Explain the function of monitoring equipment used in basic terms.
► Ensure early parental orientation to hospital facilities and unit routines (including coffee room/vending machines/restaurant, ward round/hand over times, visiting hours for extended family and parking).

Later childhood outcomes
Follow-up data from TH trials, in children aged 6–7 years, are supportive that the neuroprotective benefits of TH continue into school age. Benefits extend to both motor and cognitive domains, with increased survival with IQ ≥85, reduced rates of cerebral palsy and better gross motor function and manual ability and better gross motor function and manual ability.

Box 2  Stages of parental communication

1. Immediate parental update (ideally in delivery room)
Address the infant by name if parents have chosen one for their baby. Explain that:

a. Infant has been unwell and has required help/resuscitation at birth.

b. Ongoing support if required (eg, ventilation).

c. It is possible that the baby has had a period of reduced blood flow and oxygen to the whole body. This may lead to injury to the baby’s brain and other vital organs including the kidney, liver and heart.

d. It is too early to know how severely the baby has been affected.

e. The infant will be admitted to the neonatal unit for further assessment and may need a treatment called ‘cooling’ to protect the brain from ongoing injury.

2. Parental update following admission and therapeutic hypothermia (TH) commenced (undertaken by both medical and nursing team member looking after the infant)

a. Ascertain parental understanding.

b. Provide explanation of general condition of baby (including multiorgan support if relevant) and reiterate support they needed after birth (explain ventilation, chest compressions and medications).

c. Explain what hypoxic ischaemic encephalopathy is (including risk of death or major disability).

d. Explain role and duration of TH and need for transfer to ‘cooling centre’ (if relevant).

e. Explain TH improves survival and reduces the number of babies with severe long-term disability.

f. Explain prognosis is uncertain but that over the next week it will become clearer how severely the baby has been affected, as response to TH is observed and results of investigations are available.

g. Reassure infant will be kept comfortable and monitored by experienced staff.

h. When at cotside: briefly explain the role of monitoring leads connected to baby (pulse-oximeter, ECG and amplitude-integrated electroencephalography (aEEG)).

i. Summarise discussion at end, clarify parental understanding, offer time for questions and sign-post when next update is expected and what further information may be known at that time.

j. Ensure parents will be given tour of neonatal unit and that visiting rules, parking and hospital facilities will be explained.

3. Updates day 1–3 (in TH centre, preferably as a multidisciplinary team with nurses, family worker or psychologist):

a. Update at least daily:

i. Overall clinical condition (eg, lung/heart/kidney function).

ii. Level of encephalopathy and interpretation of aEEG if this aids with assessment of prognosis.

iii. Seizure management if required.

iv. Explain timeline for rewarming and prewarn of

Continued
Parents experience uncertainty that may persist years into their child’s development.26–27 The combined use of unexplained jargon and medical acronyms, as well as potentially contradictory statements by medical personnel risking augmenting parental confusion and their distress.26

Understanding parental experience and expectations
Clinicians must be sensitive to the extreme stress parents are placed under, following the delivery and neonatal admission of an infant with suspected HIE. Parents are presented with an unexpected, rapidly emergent, adverse event that may threaten the life of their newborn child. Parents will have little control and little understanding, while the actions of the perinatal teams may appear chaotic.26–27

Information given in the early stages of an infant’s admission may be forgotten or misconstrued. Qualitative research identifies that parents often feel they are provided with infrequent and fragmented updates. Parents struggle to retain and organise information into logical thought processes.26 Conceptualising ongoing uncertainty is then very difficult to achieve and, critically, involvement in complex decision making is compromised.26–27

Optimal communication with parents
Clinicians may lessen the burden of communication in several ways. Parents benefit from frequent updates, use of plain English and regular sign-posting to the next step in their infant’s assessment and treatment. Summary discussions that review the infant’s progress from admission provide a vital opportunity to correct misunderstandings.26–28 Communication to parents who cannot understand or speak the English language must include use of a qualified medical translator.

Parental–infant attachment is challenged due to early and prolonged separation. TH apparatus, ventilator tubing and monitoring present both physical and psychological barriers.27–28 Opportunity to be involved in infant cares from an early stage, milk expression and normalisation of infant handling following rewarming may help.27

Parents face ongoing uncertainty about their child’s future following neonatal discharge. This is a significant source of distress. A clear postdischarge follow-up plan should be offered.27

Box 1 lists some of the key learning points that have been identified by qualitative research studies into parental experiences.

**TRANSLATING JARGON AND PUTTING IT ALL TOGETHER**
Medical jargon related to TH and HIE will be novel, daunting and difficult for parents to recall. Use of clear language is important for parental understanding, and this is the immediate priority. It is, however, inevitable that parents will read or overhear medical terms during the course of their infant’s neonatal admission. For this reason, key medical terminologies should be explained to parents once their baseline understanding has been established. Common medical terms relating to HIE, with examples of lay explanations that parents may find helpful, are provided in the online supplementary figure 1.

Vague/ambiguous terms should be avoided, even in the presence of uncertainty. For example, ‘Developmental Delay’ is commonly used but can be interpreted in many ways and should be avoided unless further clarification is provided. Parents may infer that their child will eventually attain all their milestones, whereas there may be significant risk that the...
infant’s ability to walk, see, hear, communicate and learn will be permanently impaired. Communication with parents should progress through several stages (box 2). Each stage may need to be adapted if infant condition is critical, worsening and ongoing treatment considered futile. Communication should be delivered in conjunction with multidisciplinary support, including the nursing team, family worker or perinatal psychologist. See also parental communication flow chart (figure 3). Further written parental guidance may be sought from the Bliss Patient Information Leaflet: ‘HIE (hypoxic ischaemic encephalopathy) information for parents’.29

Worked examples of using this paper to construct parental communication are provided in the online supplementary file 2. This may be used for personal reflection or for supervised group education.

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ORCID iDs
Paul Cawley http://orcid.org/0000-0002-4353-0656
Ela Chakkarapani http://orcid.org/0000-0003-3380-047X

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