THERAPEUTIC HYPOTHERMIA

# Protecting the newborn brain—the final frontier in obstetric and neonatal care

For newborns with encephalopathy, therapeutic hypothermia can improve brain function and long-term developmental outcomes. For ObGyns, being a part of joint care discussions is important as this therapy is used more frequently.

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During the past 40 years neonatologists have discovered new treatments to improve pulmonary and cardiovascular care of preterm newborns, resulting in a dramatic reduction in newborn mortality and childhood morbidity. Important advances include glucocorticoid administration to mothers at risk for preterm birth, surfactant and nitric oxide administration to the newborn, kangaroo (or skin-to-skin) care, continuous positive airway pressure, and high-frequency ventilation.[1] In 1960, only 5% of 1,000-g newborns survived. In 2000, 95% of 1,000-g newborns survive.[1]

The successes in pulmonary and cardiovascular care have revealed a new frontier in neonatal care: the prevention of long-term neurologic disability by the early treatment of newborn encephalpathy with therapeutic hypothermia. This novel undertaking is an important one; approximately 1 in 300 newborns are diagnosed with encephalopathy.[2]

Until recently there were no proven treatments for newborns with encephalopathy. However, therapeutic hypothermia now has been proven to be an effective intervention for the treatment of moderate and severe encephalopathy,[3,4] and its use is expanding to include mild cases.

This increased use can lead to more complex situations arising for obstetricians, for when a neonatologist decides to initiate therapeutic hypothermia of a newborn the parents may wonder if the obstetrician's management of labor and delivery was suboptimal, contributing to their baby's brain injury.

## Instant Poll

In your practice have any newborns you delivered been treated with therapeutic hypothermia? What was your experience with the process of initiating therapeutic hypothermia for the baby you delivered?

Tell us at **rbarbieri@frontlinemedcom.com** Please include your name and city and state.

## Therapeutic hypothermia: The basics

First, we need to define therapeutic hypothermia. Both head hypothermia and whole-body hypothermia are effective techniques for the treatment of newborn encephalopathy.[3,4] Most centers use whole-body (**FIGURE**, page 12) rather than head, hypothermia because it facilitates access to the head for placement of electroencephalogram (EEG) sensors.

The key principles of therapeutic hypothermia include[5,6]:

1. Initiate hypothermia within 6 hours of birth.
2. Cool the newborn to a core temperature of 33.5° to 34.5°C (92.3° to 94.1°F). Some centers focus on achieving consistent core

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**TABLE Cochrane systematic review of beneficial and adverse effects of therapeutic hypothermia for newborns with presumptive encephalopathy[4,*]**

| Newborn outcome | Beneficial effect of therapeutic hypothermia on risk of outcome, RR (95% CI) | Number of newborns treated to avoid 1 adverse outcome (95% CI) |
|---|---|---|
| Death | 0.75 (0.64–0.88) | 11 (8–25) |
| Major neurodevelopmental disability | 0.77 (0.63–0.94) | 17 (10–100) |
| Neuromotor delay | 0.75 (0.59–0.94) | 11 (6–50) |
| Developmental delay | 0.75 (0.58–0.94) | 11 (6–50) |
| Cerebral palsy | 0.66 (0.54–0.82) | 8 (6–17) |
| Abnormal brain MRI | 0.73 (0.6–0.89) | 6 (4–17) |
| Blindness | 0.62 (0.38–1.01) | – |
| Deafness | 0.66 (0.35–1.26) | – |
| | **Adverse effect of therapeutic hypothermia on risk of outcome, RR (95% CI)** | **Number of newborns treated resulting in 1 adverse outcome (95% CI)** |
| Sinus bradycardia | 11.6 (4.9–27.2) | 11 (9–14) |
| Thrombocytopenia | 1.21 (1.05–1.40) | 17 (10–50) |

*Meta-analysis included 11 randomized trials with 1,505 newborns with moderate/severe encephalopathy. Many of the newborn outcomes were assessed based on 8 trials with 1,344 newborns.

Abbreviations: CI, confidence interval; MRI, magnetic resonance imaging; RR, relative risk.

temperatures of 33.5°C (92.3°F).

3. Monitor core temperature every 5 to 15 minutes.
4. Cool the newborn for 72 hours.
5. Obtain head ultrasonography to detect intracranial hemorrhage.
6. Initiate continuous or intermittent EEG monitoring.
7. Treat seizures with phenobarbital, lorazepam, or phenytoin.
8. Obtain blood cultures, a complete blood count, blood gas concentrations, alactate coagulation profile, and liver function tests.
9. Sedate the newborn, if necessary.
10. Minimize oral feedings during the initial phase of hypothermia.
11. Obtain sequential magnetic resonance imaging (MRI) studies to assess brain structure and function.
12. For all newborns with suspected encephalopathy, the placenta should be sent to pathology for histologic study.[7]

## The data on therapy effectiveness

Two recent meta-analyses independently reported that therapeutic hypothermia reduced the risk of newborn death and major neurodevelopmental disability.[3,4] The Cochrane meta-analysis reported that the therapy reduced the risk of neuromotor delay, developmental delay, cerebral palsy, and abnormal MRI results (**TABLE**).[4] The study authors also reported that therapeutic hypothermia reduced the risk of blindness and deafness, although these effects did not reach statistical significance.[4] Therapeutic hypothermia did increase the risk of newborn sinus bradycardia and thrombocytopenia.[3,4] Compared with usual care, the therapy increased the average survival rate with a normal neurologic outcome at 18 months from 23% to 40%.[3] It should be noted that even with therapeutic hypothermia treatment, many newborns with moderate to severe encephalopathy have long-term neurologic disabilities.

## Indications for therapeutic hypothermia are expanding

In the initial clinical trials of therapeutic hypothermia, newborns with moderate to severe encephalopathy were enrolled. Typical inclusion criteria were: gestational age ≥35 or 36 weeks, initiation of therapeutic hypothermia within 6 hours of birth, pH ≤7.0 or base deficit of ≥16 mEq/L, 10-minute Apgar score <5 or ongoing resuscitation for 10 minutes, and moderate to severe encephalopathy

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Whole-body cooling wrap to induce therapeutic newborn hypothermia.

on clinical examination.[3,4] Typical exclusion criteria were: intrauterine growth restriction with birth weight less than 1,750 g, severe congenital anomalies or severe genetic or metabolic syndromes, major intracranial hemorrhage, sepsis, or persistent coagulopathy.

Given the success of therapeutic hypothermia for moderate to severe newborn encephalopathy, many neonatologists are expanding the indications for treatment. In some centers current indications for initiation of hypothermia include the following:

- gestational age ≥34 weeks
- *suspicion* of encephalopathy or a seizure event
- *any obstetric sentinel event* (including a bradycardia, umbilical cord prolapse, uterine rupture, placental abruption, Apgar score ≤5 at 10 minutes, pH ≤7.1 or base deficit of ≥10 mEq/L or Category III tracing, or fetal tachycardia with recurrent decelerations or fetal heart rate with minimal variability and recurrent decelerations).

Suspicion for encephalopathy might be triggered by any of a large number of newborn behaviors: lethargy, decreased activity, hypotonia, weak suck or incomplete Moro reflexes, constricted pupils, bradycardia, periodic breathing or apnea, hyperalertness, or irritability.[8]

## Coordinate neonatology and obstetric communication with the family

Given the expanding indications for therapeutic hypothermia, an increasing number of newborns will receive this treatment. This scenario makes enhanced communication vital. Consider this situation:

**CASE Baby rushed for therapeutic hypothermia upon birth**

**A baby is born limp and blue without a cry. Her hypotonia raises a concern for encephalopathy, and she is whisked off to the neonatal intensive care unit for 72 hours of therapeutic hypothermia. Stunned, the parents begin to wonder, "Will our baby be O.K.?" and "What went wrong?"**

When neonatologists recommend therapeutic hypothermia for the newborn with presumptive encephalopathy, they may explain the situation to the parents with words such as brain injury, encephalopathy, hypoxia, and ischemia. Intrapartum events such as a Category II or III fetal heart rate tracing, operative vaginal delivery, or maternal sepsis or abruption might be mentioned as contributing factors. A consulting neurologist may mention injury of the cerebral cortex, subcortical white matter, or lateral thalami. The neonatologists and neurologists might not mention that less than 50% of cases of newborn encephalopathy are thought to be due to the management of labor.[2]

The obstetrician, as stunned by the events as the parents, may be at a loss about how to communicate effectively with their patient about the newborn's encephalopathy. Obstetricians can help assure the parents of their continued involvement in the care and reinforce that the hospital's neonatologists are superb clinicians who will do their best for the baby.

**Challenges exist to effective communication.** It is often difficult to optimally coordinate and align the communications of the neonatologists, neurologist, nurses, and obstetrician with the family. Communication with the family can be uncoordinated because interactions occur between the family and multiple specialists with unique perspectives and vocabularies. These conversations occur in sequence, separated in time and place. The communication between family and neonatologists typically occurs in the neonatal intensive care unit. Interactions between obstetrician and mother typically occur in the postpartum unit. The neonatologists and obstetricians are assigned to the hospital in rotating coverage shifts, increasing the number of hand-offs and physicians involved in the hospital care of the mother and newborn dyad.

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A joint family meeting with the neonatologists, obstetrician, and family early in the course of newborn care might be an optimal approach to coordinating communication with the parents. Conflicting obligations certainly may make a joint meeting difficult to arrange, however.

Reducing the risk of permanent injury to the central and peripheral nervous system of the newborn is the goal of all obstetricians and neonatologists. Many authorities believe that therapeutic hypothermia can reduce the risk of death and major neurodevelopmental disorders in newborns with encephalopathy. Initial data are promising. If long-term follow-up studies prove that this therapy reduces neurologic disability, the treatment represents a major advance in maternal-child care. As we learn more about this novel, and potentially effective therapy, it should be on the minds of those involved with newborn care to involve the ObGyn in coordinated communication with the family and other medical staff.

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