

# Evaluating Therapeutic Hypothermia

## *Parental Perspectives Should Be Explicitly Represented in Future Research*

**T**HE SYSTEMATIC REVIEW OF RANDOMIZED controlled trials by Tagin et al in this issue of the *Archives*<sup>1</sup> confirms therapeutic hypothermia, or cooling, as a major advance for infants with hypoxic ischemic encephalopathy (HIE). The evidence, achieved during 2 decades of international collaboration, reflects great credit on the neonatal community, parents, researchers, funding agencies, and providers of health care.

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Many questions about cooling remain to be answered, such as whether xenon and erythropoietin are indicated, and the role of cooling in mild HIE. Could future research be enhanced by greater efforts to represent the perspectives of parents? In 2007, a Cochrane review of cooling<sup>2</sup> included a plain language summary:

There is evidence that induced hypothermia . . . reduces death or disability, without increasing disability in survivors. This means that parents should expect that cooling will decrease their baby's chance of dying, and that if their baby survives, cooling will decrease his/her chance of major disability. The results of ongoing trials may or may not confirm these favourable results.

The review concluded that cooling reduced mortality or major disability by one quarter for those up to 18 months of age ( $P = .00063$ ).<sup>2</sup> Contemporaneous systematic reviews reached comparable conclusions.<sup>3,4</sup> Whether it was still ethical to randomize infants not to receive cooling was widely discussed,<sup>5-8</sup> but parental perspectives and contributions were notably absent from the debate. Some experts recommended that no new patients be recruited to ongoing trials.<sup>5,7</sup> Others were hesitant,<sup>9</sup> partly because the data were considered inadequate to show whether cooling was indicated in subgroups of infants with either moderate or severe HIE.<sup>1</sup> Subsequent evidence has confirmed that cooling reduces death or major disability at 18 months<sup>9</sup> both in moderate and severe encephalopathy.<sup>1</sup> Parents and clinicians who opted for hypothermia outside clinical trials can thus be reassured that they made the right decision.

### SHOULD PARENTAL PERSPECTIVES BE EXPLICITLY REPRESENTED?

Cochrane plain language summaries provide one opportunity to address the perspectives of parents when assessing completed research.<sup>2</sup> This is part of a broad in-

ternational effort, exemplified by the UK Department of Health, which since 2006 has required that "patients and the public must be involved at all stages of the research process."<sup>10</sup> There are several potential benefits for future trials in HIE.

First, greater involvement of parents in the design and conduct of trials may enhance not only how parents and consumers perceive these studies but also their participation in them. Parents may help inform whether a particular study is worth conducting, and they may suggest patient-centered outcomes and whether it is likely to achieve recruitment targets. Parents may contribute as members of data monitoring committees. They may sometimes provide a more subjective, emotional viewpoint. Their perceptions about issues that are important and whether a trial would be ethical are sometimes subtly, and sometimes radically, different from those of health care professionals.

Next, information statements for research trials are sometimes dense and unwieldy and may not present a balanced perspective on the evidence.<sup>8</sup> Parents of critically ill infants can struggle to make sense of this information and decide whether to take part, often relying instead on their trust in their child's clinicians. Involving consumers can result in patient information that is more relevant, readable, and understandable to patients, without affecting their anxiety. Shorter information leaflets may be better understood than longer ones.<sup>11</sup>

Parent participation may help researchers understand barriers to recruitment. Parents hold great respect for the research process and are aware that their own children have benefited from decisions by parents before them to support research. Reasons considered important by parents for participating include (1) that they would be helping other babies and families, (2) no perceived risk to their baby, or (3) a perceived benefit to their baby's health. Despite this, parents often deal with strong emotions such as fear, guilt, anxiety, and shock and may struggle with making an informed decision when invited to participate in a study.<sup>12</sup> Decisions often come from a heart-over-head position. Studies deemed too invasive, experimental, or potentially harmful are often declined.

Finally, once research is completed, parents may also have an important role in informing how best to communicate results sensitively to participants as well as to the wider community. This phase of research often receives relatively little attention, but it can raise ethical challenges. For example, researchers may have concerns about distressing families of children who have died or who had an adverse outcome. Participants may want

to be provided with aggregate results even if they have not benefited from the research. Increasingly, trials in HIE will require longer follow-up of perhaps 5 to 10 years. Successful engagement with parents will be important to maintain high rates of follow-up as well as the power and validity of future trials.

Without strong partnerships based on trust, transparency, and mutual education, as well as adequate funding and support,<sup>13,14</sup> there remains the potential for conflict and disillusionment. However, greater lay involvement in research decision making could help to develop a lobby of well-informed lay people to press for the resources needed to resolve the many remaining uncertainties in protecting the health of infants at risk for HIE and of all newborns.<sup>15</sup>

### HOW CAN PARENTAL AND LAY PERSPECTIVES BE SUCCESSFULLY INTEGRATED INTO FUTURE RESEARCH?

Governments are placing greater emphasis on the need to develop stronger partnerships between clinicians, patients, and parents. One approach toward this goal is illustrated by the development of the James Lind Alliance, which was begun in 2004. This UK government-funded initiative brings patients, caregivers, and clinicians together to identify and prioritize, for various conditions, the top 10 uncertainties, or unanswered questions, about the effects of treatments that they agree are most important to guide those who fund health research.<sup>13</sup> In the United States, the recently established Patient-Centered Outcomes Research Institute will disburse more than \$3 billion of federal funding before 2019 to support its aim of promoting "research guided by patients, caregivers, and the broader health care community."<sup>14</sup> The aims and methods of both organizations have been described.<sup>13,14</sup> One major goal to aim for in HIE will be participation by parents and lay representatives in priority-setting consensus workshops and in the design and conduct of future trials.

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