CHAPTER 29

# Therapeutic Hypothermia as Potential Intervention on Acute Encephalopathy

GEORGE IMATAKA, MD, PHD, BA, PGDBA

## INTRODUCTION

The use of brain hypothermic therapy (BHT) for acute encephalopathy occurring in childhood may be very valuable and promising, but to date the medical evidence for efficacy is still very small.[1,2] There are few institutions worldwide where this treatment is currently conducted. However, presently in Japan, this state-of-the-art treatment is actively performed in more than 20 facilities specialized in pediatric emergency center.

## HISTORY AND EXPERIMENTAL EVIDENCE

There are various stories stating that BHT may have a life-saving impact on accidental hypothermia. One of the most popular incidents occurred in 1963 in which a young boy drowned in a cold river in Norway.[3] Through careful warming of his body, he was successfully brought from the verge of death due to hypothermia to a complete recovery. Afterward, some of the animal experiments in the 1980s reported that 34 °C provides some degree of cerebral cell protection.[2]

In the 1990s, BHT was applied in human trial studies. Since 2000, it has been shown to be effective against cardiac arrest in adults.[4] In 2010, BHT was endorsed in the American Heart Association guideline for adult cardiac arrest,[5] as well as in the guideline for Hypoxic Ischemic Encephalopathy (HIE) in newborns.[6] The following reasons were indicated in the BHT guidelines for adults and newborns. In adults, BHT prevents cerebral edema, inhibits cerebral metabolism to reduce the amount of oxygen consumption, and improves homeostasis of intracerebral $Ca^{2+}$ to reduce cerebral nerve damage. In newborns with HIE, BHT is said to preserve oxygen supply through cerebral ischemia and also prevent ATP deficiency in neuronal cells. In addition, BHT protects against increased free radicals and prevents irreversible nerve cell apoptosis.[5,7] However, there is still very little evidence for the effects of BHT against acute encephalopathy in children.[1,2]

## GENERAL PRACTICE FOR BRAIN HYPOTHERMIC THERAPY

Based on the evidence for BHT for adults and newborns, we introduced in children the use of BHT to cytokine storm–related encephalopathy, with a primary symptom status epilepticus. Moreover, we applied it in near-drowning based on the evidence, introduced by its use in hypoxic ischemic encephalopathy in neonates.

In our treatment strategies for acute encephalopathy and status epilepticus, we enforced the management of central nervous system together with the treatment of the whole body organ systems.[1] Central nervous system management may prevent irreversible cerebral nerve cell apoptosis. Therefore, it is for this reason that the BHT team was combined with the ICU and related members of the patient transport systems.

In Japan, the emergency doctor heads off in a helicopter after receiving word of a child with an emergency. They massage the heart and give respiratory care while administering a midazolam nasal spray and intravenous solution as first-line anticonvulsants. BHT is introduced in cases with predicted poor neurologic prognosis, including drowning, cardiac arrest, serious respiratory failure, and status epilepticus lasting 30–45 min. The specialized pediatric ICU always has a prepared bed that is laid with a cooling blanket to introduce BHT promptly.

General management with BHT, anesthetic management, respiratory care, circulation, and body temperature control are all taken care of in the ICU. Intracranial pressure is also controlled as per the requirement with a neurosurgeon. Cooling is done simultaneously for the body's cooling blanket and the head cooling system.

Commonly, the classification of clinical hypothermia is divided into 4 degrees (Table 29.1). We currently use "mild hypothermia" defined between the 35 and 32°C. To maintain body temperature, the temperature of the urinary bladder is brought to 34.5°C. Hypothermia persists for 48 h, and then the body temperature increased at a pace of 0.5° every 12 h. Steroid pulse therapy is administered together with the concomitant use of other drugs including anesthetics and mannitol.[1] Fig. 29.1 is a diagram of the process for BHT. BHT is performed in three stages. The first one is the introduction stage, the next is the cooling stage, and the final stage is the rewarming stage. The target is to keep the body temperature of the urinary bladder at 34.5°C for 48 h. Concomitant monitoring during BHT includes respiration, an ECG, CVP, and oxygen saturation. A portable electroencephalogram (EEG), with a scalp skin oxygen saturation device (INVOS), a Bispectral index (BIS) monitor, and an intracranial pressure monitor are available when necessary.

EEGs undergo dramatically rapid changes during the three stages of BHT (Fig. 29.2).

In the introduction stage, we see irregular high-voltage slow wave activity. During the cooling stage, this changes to "suppression and burst pattern." At that time, the body temperature is retained at 34.5°C. Rewarming stage of the body begins by suspending the use of anesthetics. In recovery examples, there is a gradual appearance of basic background waves in the EEG. For useful EEG managing "suppression and bursts" during the cooling stage, a BIS monitor is placed on the forehead by an anesthesiologist when administering general anesthesia.

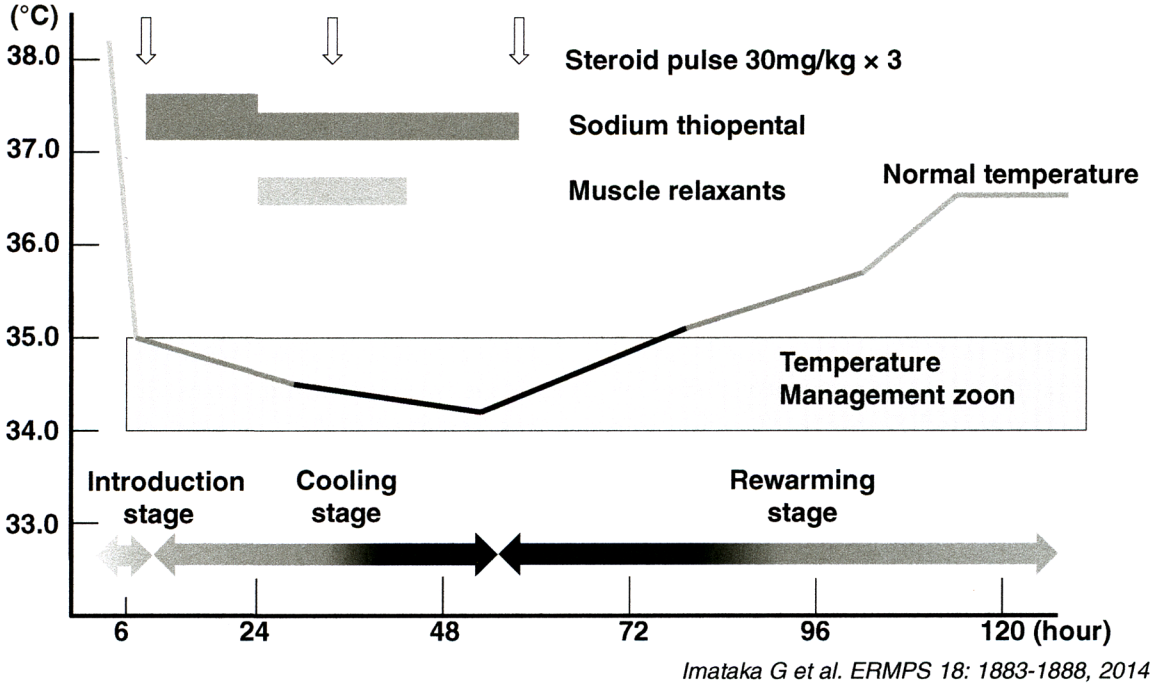
There are concerns with the use of hypothermia as adverse events such as cardiac arrhythmia, low blood pressure, coagulation abnormalities, severe infection, and abnormalities in hematopoiesis. The more severe the degree of hypothermia, the greater the chance that adverse effects may occur but may still happen with mild hypothermia.

**TABLE 29.1**
**Classification of Clinically Hypothermia**

| | |
|---|---|
| Normothermia | 35.0–37.0°C |
| Mild hypothermia | 35.0–32.0°C |
| Moderate hypothermia | 32.0–28.0°C |
| Severe hypothermia | Below 28.0 |

## CONCLUSION

We anticipate that in the future there will be additional evidence that will help establish the role of BHT in the treatment of acute encephalopathy in childhood,




*Imataka G et al. ERMPS 18: 1883-1888, 2014*

**FIG. 29.1** Clinical process for mild brain hypothermia therapy. (From Imataka G, wake H, Yamanouchi H, et al. Brain hypothermia therapy for status epilepticus in childhood. *Eur Rev Med Pharmacol Sci.* 2014;18:1883–1888.)

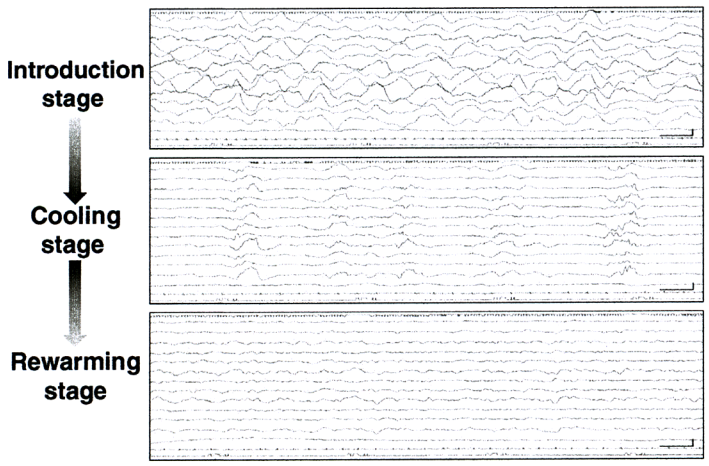



FIG. 29.2 Electroencephalogram changes during three stages of brain hypothermic therapy.

by developing criteria how to be safely used and an understanding of the possible outcomes separating the potential injury stemming from the cause of the underlying etiology as well as the symptoms i.e., status epilepticus.

## REFERENCES

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