Current status of hypothermia as a treatment modality

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INTEREST in hypothermia is longstanding; early laboratory experiments were done more than 70 years ago and the effects of cooling on whole body and brain metabolic rates have been known since the early 1940's. Only in 1943 did Temple Fay report his initial experience with the use of hypothermia in head injured patients but in spite of exceptionally positive results (100% recovery!), the neurosurgical community showed little interest. In contrast, the growth of cardiac surgery - first closed and then open - created a demand for techniques that made procedures easier and safer, and by 1950, the use of hypothermia was widespread. Even after the introduction of cardiopulmonary bypass, hypothermia remained a routine component of cardiac surgery until very recently - although more for "cardiac preservation" than for anything else.

Outside of cardiac surgery, the clinical use of hypothermia was sporadic. For example, in the 1960's there was a transient surge in the use of cooling (often with some kind of circulatory arrest) during the early days of intracranial aneurysm surgery. This disappeared largely due to the introduction of better operative tools (and the microscope). However, in the late 1980's, a laboratory observation changed the landscape. Prior to the late 1980's, it had been assumed that since CMRO_2 fell in a curvilinear fashion with cooling, the degree of central nervous system (CNS) protection was directly proportional to temperature. However, in the late 1980's, Busto and colleagues in Miami demonstrated that even small reductions in temperature could have dramatic protective benefits in animal models of cerebral ischemia. The importance of such work was the fact that protection could be achieved with temperatures that were relatively easy to achieve.

This triggered a marked resurgence of interest in clinical hypothermia and within a few years, hypothermia had, for example, become routine in neurovascular operating rooms. In 1992, a survey of neuroanesthesiologists by Rosemary Craen and

Adrian Gelb suggested that nearly a third cooled their intracranial aneurysm patients. A recent survey in Great Britain indicated that this number had risen to nearly 60%. This enthusiasm has persisted - a 2003 British survey suggests that as many as 60% of neuroanesthesiologists used hypothermia during vascular surgery - in spite of: a) a lack of any controlled data indicating the benefits of hypothermia in humans; and b) a body of evidence suggesting that hypothermia may result in increased risks for wound infection, pneumonia, hemorrhage, and myocardial ischemia.

With this background, I will present and discuss the existing data concerning the clinical use of mild hypothermia in five areas:

- I. Cardiac surgery (not circulatory arrest);
- II. Head trauma;
- III. Stroke;
- IV. Cardiac arrest;
- V. Intracranial vascular surgery.

A more detailed discussion of the individual studies will be presented at the meeting; I will only summarize the material here.

I. Cardiac surgery

While moderate hypothermia (temperatures between 28 and 32°C) was long used primarily for the purpose of myocardial preservation, there was a general assumption that it had beneficial CNS effects as well. This was based on existing animal data and on the well known protective effects of deep hypothermia during circulatory arrest. The shift away from systemic hypothermia triggered the first formal clinical trials examining the neurologic impact of cooling during bypass. There have now been several such trials - and the general consensus, as summarized by the Cochrane group, is that there are no advantages to cooling.

II. Head trauma

Soon after the Busto studies appeared, laboratory work appeared demonstrating the beneficial effects of

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cooling applied after head injury in rats. Initial human studies suggested that hypothermia could be useful in controlling intracranial pressure. This quickly led to a small clinical trial, which seemed to show a benefit, which led in turn to a large definitive trial. However, that large trial convincingly demonstrated that hypothermia did not improve outcome and several smaller trials in the last two years seem to confirm this. One major problem is logistical; it is very difficult to cool patients quickly after their injuries. There is, hence, a new trial now in progress, which is enrolling ONLY patients who are cold on arrival in the emergency room, randomizing them to either continued cold or to rewarming. If the cold group has a better outcome, it will serve as an impetus to the development of more efficient methods for rapidly cooling patients, perhaps even in the field or during transport.

III. Stroke

In spite of a great deal of publicity, no controlled trials of cooling in stroke have been published at the time of this writing.

IV. Cardiac arrest

The animal work that triggered our modern interest in hypothermia involved models of global cerebral ischemia - the same form of insult encountered in cardiac arrests. Multiple animal studies confirmed both the protective effects of cooling (started before arrest) and its therapeutic benefit (started after resuscitation). Last year, the results of two human studies were reported, both demonstrating a rather strong beneficial effect of post-resuscitative cooling in patients who had suffered from ventricular fibrillation (VFib). While the work is only directly applicable to a small fraction of cardiac arrest victims, the American Heart Association has now recommended that cooling be used in successfully resuscitated VFib patients.

V. Intracranial vascular surgery

As noted above, hypothermia remains popular among neuroanesthesiologists. This popularity, combined with the risks noted above, led to the development of a large clinical trial entitled "Intraoperative Hypothermia for Aneurysm Surgery Trial (IHAST)." This was a prospective randomized trial of 1,000 patients undergoing open aneurysm surgery following subarachnoid hemorrhage, with half of the patients being cooled to a target of 33°C during surgery. Enrollment and follow-up was completed in September of 2003 and results will be presented in February 2004. These results and their implications will be presented.

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