PERSPECTIVE

Hypothermia to Protect the Brain

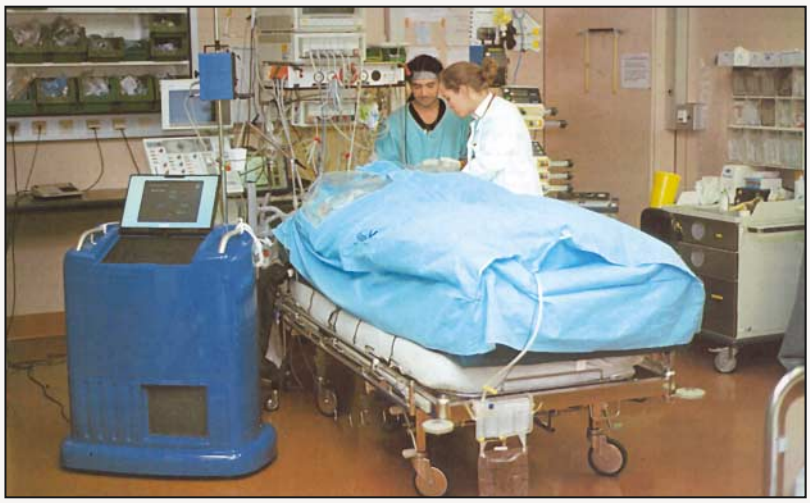

Figure 1. Cooling Device Used in the Hypothermia after Cardiac Arrest Study, Which Operates by Circulating Cool Air over the Patient.

For decades, cooling the body below the normal physiologic temperature has been used as a therapeutic tool. Hypothermia is used most often during cardiac surgery with cardiopulmonary bypass, as a means of protecting the brain from ischemic injury. Hypothermia is also used during some neurosurgical procedures and is being investigated as a treatment for ischemic stroke and traumatic brain injury. In this issue of the *Journal*, two groups of investigators report on the use of therapeutic hypothermia to prevent neurologic injury in comatose survivors of cardiac arrest.

Out-of-hospital cardiac arrest claims some 225,000 lives each year in the United States and a similar number in Europe, accounting for about half of all deaths due to cardiovascular disease. Even when resuscitation efforts are successful, recovery is too often limited by anoxic encephalopathy. The risk of this complication increases with the delay in resuscitation, and the prognosis for comatose survivors of cardiac arrest — albeit not hopeless — is poor. In an international study, less than a third of comatose survivors of out-of-hospital cardiac arrest awakened within seven days; the others either died or remained unconscious. Even if patients do regain consciousness, persistent neurologic or cognitive deficits are common. We urgently need better methods to protect the brain in victims of cardiac arrest.

The reports by the Hypothermia after Cardiac Arrest Study Group and by Bernard et al. (see pages 549–56 and 557–63) in this issue of the *Journal* represent an important first step toward reaching this goal. Working independently on two continents (Europe and Australia), both research groups found that lowering the body temperature to 33°C for 12 or 24 hours in comatose survivors of cardiac arrest resulted in an impressive improvement in the neurologic outcome. The larger European study also showed significant improvement in overall survival. The methods used for cooling were remarkably simple — placement of ice packs on the patient's torso, or use of a device that circulates cool air over the patient (Fig. 1). It is surprising that the induction of brief, mild hypothermia led to such meaningful improvement in the clinical outcome.

The simplest biologic explanation of how hypothermia may provide protection against anoxic brain injury is that it reduces the cerebral oxygen requirement. However, as Safar and Kochanek discuss in an accompanying editorial (page 612), the mechanisms involved are likely to be much more complex. An array of cellular pathways participate in the genesis of anoxic brain injury, and hypothermia may interrupt one or more of them, preventing free-radical injury, membrane damage, and injury due to the release of neurotransmitters, as well as other types of damage.

The encouraging findings reported by these two groups of investigators should not necessarily be diminished by the contradictory results of studies of therapeutic hypothermia in patients with traumatic brain injury. Although one study (N Engl J Med 1997;336:540-6) reported a benefit in patients with nonpenetrating head trauma, a more recent study (N Engl J Med 2001;344:556-63) failed to confirm this observation. Traumatic and anoxic brain injuries differ in important ways, and it is possible that injury due to trauma is less easily reversed than anoxic injury after circulatory arrest.

The two studies of therapeutic hypothermia are mutually confirmatory. The findings, which may have profound clinical implications, are applicable to current resuscitation practice. Still, given the magnitude and complexity of the clinical problem, further studies of the efficacy and safety of therapeutic hypothermia in survivors of cardiac arrest should be given a high priority.

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