also reacts with hydroxyl radicals (7), leukocyte-generated hypochlorous acid (8), and nitric oxide (9).

A limitation of the present report is that the dogs were studied only during 5 to 7 hrs of treatment. Even in controls, there was no mortality within that time. Anti-inflammatory agents can transiently alleviate manifestations of sepsis but not necessarily prevent death (10). Maxwell Finland (10) saw that phenomenon in the 1950s when bacterial pneumonias were “treated” with the then-new drug cortisone. As related by Lewis Thomas (11), there was “what seemed at first a miraculous clinical cure. Within a few hours the fever, malaise, prostration, chest pain, and cough vanished, and the patients felt themselves to be restored to abundant good health, asking for dinner and claiming to be able to be up and around. At the same time, however, the radiograph evidence of pneumonia showed an alarming extension of the process, and the experiment was promptly terminated.” Accordingly, it will be interesting to see if ethyl gallate can increase survival in a lethal model of sepsis.

REFERENCES

Therapeutic hypothermia for acute severe spinal cord injury: Ready to start large clinical trials?*

I read with great interest the article by Dr. Maybhate and colleagues entitled, “Potential Long-Term Benefits of Acute Hypothermia: Assessments With Somatosensory-Evoked Potentials” (1). In that study, the authors reported that early systemic hypothermia (32°C) in a model of spinal cord injury (SCI) provided significant neuroprotection weeks after injury and improved sensory electrophysiological signals in rats. Electrophysiological improvement was accompanied by higher motor behavioral scores and more spared tissue in acute and postacute periods after injury. As the authors emphasized, the potential use of hypothermia in experimental models of SCI is well established in the literature (2, 3). Various laboratories throughout the world have shown that moderate levels of cooling (32–33°C) for extended durations of time improve motor function in terms of both lower and upper extremities (4–10). Also, this improvement in function is commonly associated with reductions in both gray and white matter damage and targets multiple pathomechanisms activated by trauma (3).

In a study by Yu and colleagues (4), mild systemic hypothermia was reported to improve outcome after thoracic SCI. In a subsequent study, Lo and colleagues (5) showed that systemic hypothermia improved functional and histopathological outcome after cervical SCI in rats. The recent study by Maybhate and colleagues (1) is important because it provides electrophysiological information regarding the beneficial effects of hypothermia in terms of motor-evoked potentials and somatosensory function. Long-term functional benefits as measured by somatosensory electrophysiological measurements as well as increased motor behavioral scores were reported. Although this study is important to the field, there are certain limitations in terms of the experimental design. For example, the authors only tested a relatively limited duration of cooling (2 hrs) followed by gradual rewarming. Previous studies from the cerebral ischemia and trauma literature have demonstrated that the duration of cooling is extremely important in terms of promoting long-term benefits and histopathological outcome (3). Thus, the lack of long-term improvements in pathology in this particular study may relate to that factor. Indeed, recent clinical studies have shown that patients with acute cer-

*See also p. 573.

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vical SCI can be cooled relatively safely up to 48 hrs using endovascular catheters (11). Levi and colleagues reported that in a relatively small group of severely injured patients with cervical SCI, mild cooling did not lead to greater incidence of potential risk factors, including cardiac arrhythmias, deep vein thrombosis, or episodes of pneumonia compared with noncooled patients (11). Most importantly, encouraging results have now been published showing that 1 yr after injury, some patients that started out as American Spinal Injury Association A or B converted to American Spinal Injury Association C or D (12). These encouraging findings would suggest that therapeutic hypothermia may be an experimental treatment that could benefit patients with severe SCI.

Currently, there have been no multicentered trials that have tested the efficacy and safety of therapeutic hypothermia in large numbers of severely injured patients with SCI (13, 14). The Congress of Neurologic Surgeons has commented that although there are some clinical studies showing efficacy, at present, there are limited data to support the use of hypothermia as a standard of care (13). Thus, it is critical that a well-designed, randomized multicentered trial is conducted to test whether this therapy can provide clinically significant improvements in people’s lives. The Miami Project to Cure Paralysis and Department of Neurologic Surgery at the University of Miami Miller School of Medicine has commented on the potential risk factors, including cardiac arrhythmias, deep vein thrombosis, or episodes of pneumonia compared with noncooled patients (11). Most importantly, encouraging results have now been published showing that 1 yr after injury, some patients that started out as American Spinal Injury Association A or B converted to American Spinal Injury Association C or D (12). These encouraging findings would suggest that therapeutic hypothermia may be an experimental treatment that could benefit patients with severe SCI.

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