injury to the original mechanical disruption. Current research is aimed at neutralizing these secondary effects as early as possible after injury to preserve function in undamaged tissue. The administration of high-dose methylprednisolone sodium succinate has been shown to improve the outcome after spinal cord injuries. The use of tirilazad mesylate and GM_1 ganglioside is being studied.

In initial trials, methylprednisolone was not effective in improving the outcome. In the second National Acute Spinal Cord Injury Study (NASCIS II), methylprednisolone was given in a dosage of 30 mg per kg of body weight within 8 hours of injury, followed by the administration of methylprednisolone, 5.4 mg per kg per hour, for 24 hours. This regimen produced significant neurologic improvement on six-month and one-year follow-up tests when compared with placebo. As a result the methylprednisolone protocol has become the standard of care. The beneficial effects of methylprednisolone seem to result not so much from the anti-inflammatory effects seen at much lower doses, but rather from an ability to scavenge free oxygen radicals and to block "lipid peroxidation," a rancidification of the fatty acid chains that make up neuron cell membranes.

The search for steroids with less anti-inflammatory and more antioxidant activity led to a group of compounds retaining the tetracyclic steroid nucleus but being able to profoundly suppress lipid peroxidation. So far their success has been so great that the agents have been given the name "lazeroids" (after Lazarus). The use of the most promising of these, tirilazad mesylate, greatly improved walking ability in cats if given within four hours of injury. At eight hours after injury, tirilazad was no longer effective even at triple the dose.

Third NASCIS Trial

Tirilazad has been included in one of the three treatment arms in the NASCIS III trial. Treatment arm 1 consists of current methylprednisolone treatment; treatment arm 2 consists of the current methylprednisolone treatment extended for two days; and treatment arm 3 consists of the administration of methylprednisolone, 30 mg per kg, followed by tirilazad, 2.5 mg per kg every 6 hours for 24 hours. The study is intended to determine the best time for starting the methylprednisolone regimen, the optimal duration of therapy, and the benefits, if any, of substituting tirilazad mesylate for methylprednisolone after the initial dose.

GM_1 Ganglioside

Unlike methylprednisolone and tirilazad, which can be thought of as "preservative," GM_1 ganglioside is the first seriously studied agent that could be considered "regenerative." When normal GM_1 turnover is blocked by an enzyme (hexosaminidase) deficiency, GM_1-lipid storage disease results (GM_2-lipid storage disease is Tay-Sachs disease). After central nervous system neurons of a cat with GM_1 storage disease were found to have axonal sprouting of most neurons, many GM_1 studies, including a human clinical trial, were undertaken. One study showed that patients receiving GM_1 ganglioside achieved a higher level of functioning than those given a placebo.

Although methylprednisolone, tirilazad, and GM_1 ganglioside are the major agents currently being studied, other agents are being developed. In the future, we can envision paramedics or trained police officers carrying drugs and administering them before a patient is evacuated. In this way, we might see an increase in the percentage of patients with incomplete instead of complete spinal cord injuries.

PETER C. WERNER, MD
San Jose, California

REFERENCES

Baffour R, Achanta K, Kaufman J, Berman J, Garb JL, Rhee S, et al. Synergistic effect of basic fibroblast growth factor and methylprednisolone on neurological function after experimental spinal cord injury. J Neurosurg 1995 Jul; 83:105–110

Gerhart KA, Johnson RL, Menconi J, Hoffman RE, Lammertse DP. Utilization and effectiveness of methylprednisolone in a population-based sample of spinal cord injured persons. Paraplegia 1995 Jun; 33(6):316–321

Savitsky E. Role of glucocorticosteroids in treatment of acute spinal cord injury. West J Med 1996 Jan; 164:69-70

Perez-Espejo MA, Haghighi SS, Adelstein EH, Madsen R. The effects of taxol, methylprednisolone, and 4-aminopyridine in compressive spinal cord injury: a qualitative experimental study. Surg Neurol 1996 Oct; 46:350–357

Management of Suffering in Patients With Severe Burn Injury

BURN INJURIES are a frequent, painful, and often disabling form of trauma. Such trauma is estimated to account for 731,000 of emergency department visits and 60,900 hospital admissions annually in the United States. The quality of burn care over the past few decades has improved dramatically, resulting in a consistent increase in the number of survivors requiring rehabilitation. Three important challenges in the treatment of burn patients remain: pain control, emotional adjustment, and physical rehabilitation.

Pain control is crucial during acute and intensive phases of burn care. The treatment of partial- and full-thickness burns typically requires frequent dressing changes, debridement, and excision and grafting. Burn wound care is often done daily and may cause more pain than sustaining the burn itself. The use of opioid drugs is the most effective treatment of burn pain, and they should be given immediately and aggressively because virtually no opioid addictions occur in burn patients through treatment. The fear of addiction should not interfere with abating suffering through the appropriate use of opioids. Effective strategies for treating background burn pain include using intravenous morphine sulfate, patient-controlled analgesia, or long-acting orally administered opioids (such as time-release morphine or methadone hydrochloride). Procedural pain is more intense and difficult to control. Morphine or hydromorphone hydrochloride given in a bolus is often effective for dressing

changes. Synthetic morphines (fentanyl citrate, alfentanil hydrochloride, sufentanil) are more powerful forms of analgesia but require more careful supervision. If opioid drugs are not effective, a variety of adjunctive interventions should be systematically introduced. These include the use of ketamine hydrochloride, inhalant therapies (such as nitrous oxide), nonsteroidal drugs (such as ketorolac tromethamine), and benzodiazepines. Hypnosis, behavioral interventions, and cognitive-behavioral techniques have been cited as effective nonpharmacologic interventions.

Challenges in emotional adjustment take different forms during each phase of care. When patients are in the intensive phase of care, two of the most common problems reported are anxiety and delirium. Treatment with benzodiazepines and neuroleptic drugs is often warranted, and psychological interventions often focus on survival and supporting family members. As patients improve and become more energetic and lucid, grief reactions, posttraumatic stress disorder, and depression are more prevalent. Brief psychological counseling and a steady flow of information about burn care are useful. Patients often fare well emotionally when their pain is controlled and they see a steady progression in their care. Most patients with burns adjust well in the long run, but a notable proportion report many problems after discharge. Patients showing such difficulties often have burns that result in visible cosmetic effects, amputations, or the restriction of joint function. Returning to work becomes an important issue for many patients. Burn injuries resulting from abuse or assault are unfortunately common.

More attention should be given to the physical rehabilitation of patient with burns. Some of the problems that can seriously affect outcome are scars and contractures, heterotopic ossification, peripheral neuropathy, muscle weakness, and amputations. The goal of treatment of scars conventionally is to minimize hypertrophic scarring through the use of pressure garments made to fit tightly, providing pressure to the skin. The tendency of skin and tissue scarring to cause contractures and joint deformities is counteracted through range-of-motion exercises, stretching, and splinting. Splinting can be either static to place the joint in a position of maximal range and function, or it can be dynamic. Dynamic splinting uses rubber bands or other devices to provide continuous stretching while the splint is being worn. The skin has to be monitored closely for any pressure areas during the wearing of a splint, and the time of splint wearing should be gradually increased as tolerated. Periarticular heterotopic ossification frequently occurs, especially at the elbows. The rate of heterotopic ossification may be slowed with the use of medications such as indomethacin and range-of-motion exercises with stretching to prevent further loss of joint motion. Surgical resection or manipulation may be necessary to restore the range of motion and should be followed by aggressive range-of-motion exercises to prevent recurrence of contracture.

Persons with severe burn injuries will often have generalized muscle weakness from inactivity or due to a peripheral neuropathy. Treatment involves strengthening exercises, but restoring function may also require bracing areas not burned, such as providing ankle-foot orthoses to stabilize the ankle and knee. A final common secondary complication after burn injury involves amputations of the upper or lower extremities. Proper prosthetic fitting and training are essential to ensure the best functional outcome for these patients.

DAVID R. PATTERSON, PhD
Seattle, Washington
JOHN T. PTACEK, PhD
Lewisburg, Pennsylvania
PETER C. ESSELMAN, MD
Seattle, Washington

REFERENCES

Ashburn MD. Burn pain: the management of procedure related pain. J Burn Care Rehabil 1995; 16(3 pt 2):365–370

Hurren JS. Rehabilitation of the burned patient: James Laing Memorial Essay for 1993. Burns 1995; 21(2):116–126

Patterson DR, Everett JJ, Bombardier CH, Questad KA, Lee VK, Marvin JA. Psychological effects of severe burn injuries. Psychol Bull 1993; 133 (2):362–378