Therapeutic Protocol for Thermally Injured Animals and Its Successful Use in an Extensively Burned Rhesus Monkey

Lee M. Cera, DVM
John P. Heggers, PhD, MT(AMT)
William J. Hagstrom, MD
Martin C. Robson, MD

A therapeutic protocol that included topical and systemic administration of a thromboxane inhibitor was used to successfully treat a burned Rhesus monkey. Accidental exposure of the animal to steam and water (180C) for five minutes had caused full-thickness dermal injury to its entire body surface area (BSA). Animals with full-thickness burns involving more than 50% BSA are generally regarded as having remote chances of recovery. Based on the favorable outcome obtained, the therapeutic protocol that was used for this monkey is advocated for general use.

Introduction

Thermal injury is a nonuniform, dynamic injury. In 1953, Jackson[5] noted a zone of vascular stasis in which progressive vascular occlusion took place in the first 24 hours after burning. Reversal of this process seems particularly important in deep partial-thickness burns where the zone of stasis extends through the dermis into the subcutaneous tissue. If progressive vascular occlusion can be prevented, then deep partial-thickness wounds heal by regeneration of the spared epidermal elements harbored near the dermal appendages. If stasis is not prevented, full-thickness injury requiring a skin graft results.

The concepts revolving around the pathophysiology of burns are complex and by no means completely understood. Treatment of burned animals is based on the percentage of BSA affected. The prognosis for burns greater than 40% of BSA is poor, and most frequently euthanasia is recommended.

After the initial injury, local and regional vasculature and capillary beds undergo marked dilation, followed by edema. Recent studies suggest that the edematous phase results directly from white cells sticking together and blockage of dermal microcirculation.[3] As the volume of inflammatory tissue fluid increases, the concentrations of biochemical constituents in the circulatory system and tissues increases. The sodium:potassium balance is severely altered. Protein loss is usually severe.

Investigators have also reported elevated levels in either serum or tissue, or both, of catecholamines, prostaglandins, and thromboxanes. The liberation of these substances has recently been implicated as mediators of dermal ischemia.[2,6] These may contribute in covering the zone of stasis to nonviable tissue. Robson *et al* recently demonstrated that through pharmacologic manipulation, the zone of stasis could be preserved, and they confirmed that dermal ischemia was mediated by thromboxanes.[7,8] The major important factors in the standard therapeutic approach in treating a severe thermal injury begins with fluid replacement, relief of pain and prevention of infection.

Based on the concept that dermal ischemia is mediated by thromboxanes, the management of major and minor burns in animals was modified to include an additional pharmacologic therapeutic ap-

From the University of Chicago Hospitals and Clinics, 950 East 59th Street, Chicago, IL 60637.

Dr. Cera is director of Animal Care for the University, director, A.J. Carlson Animal Research Facility, and assistant professor, Division of Biological Sciences; Dr. Heggers is director, Basic Science Laboratory University of Chicago Burn Center; Dr. Hagstrom is associate professor, Plastic and Reconstructive Surgery Section and Dr. Robson is chief, Plastic & Reconstructive Surgery Section and director, University of Chicago Burn Center.

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Figure 1— Upper trunk, head, and neck area, 10 minutes post-burn of the thermally injured animal.

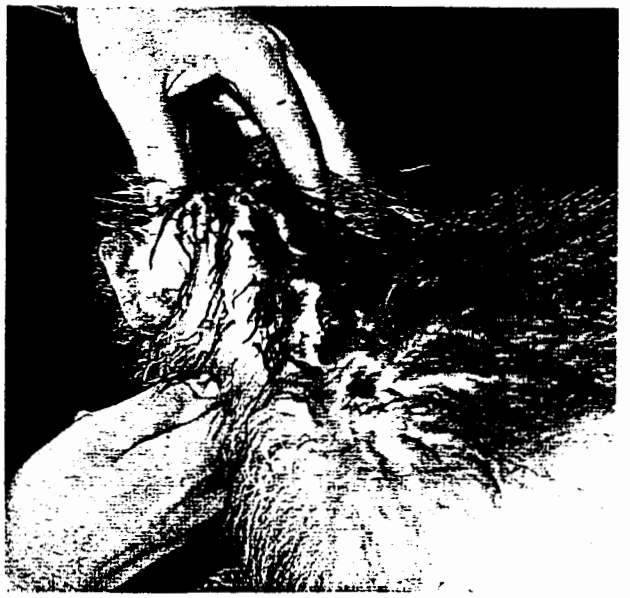

Figure 2— Posterior aspect of the left ear, 10 minutes post-burn.

Figure 3— Plantar surface of the animal's right foot, 10 minutes post-burn.

Figure 4— Posterior view of the thermally injured monkey, 10 minutes post-burn.

proach utilizing a medicated cream known to be bactericidal as well as a thromboxane inhibitor. To date, two dogs with burns on greater than 20% BSA were successfully treated[1] and of particular interest is the primate case report which follows.

Case Report

An adult male Rhesus monkey (*Macaca mulatta*) was presented to the Carlson Animal Research Facility 10 minutes after sustaining a severe burn. The monkey had been exposed to 180 C steam and water, with detergent, for five minutes. The monkey appeared to have full-thickness burns over approximately 70% of BSA, with severe burns on the face, hands, feet and scrotum [Figures 1-4]. It was presumed that tracheal and lung injury had occurred from steam inhalation. Inspiratory and expiratory rales were present, vital signs were erratic, rectal temperature was off the scale (44 C), and the acute clinical picture was one of shock. Although the prognosis was poor, treatment with intermittent cold water baths was started, pending a consultation with members from the University of Chicago Burn Center. The initial examinations from both the emergency room and the Burn Center gave a poor prognosis; the burn injury was consid-

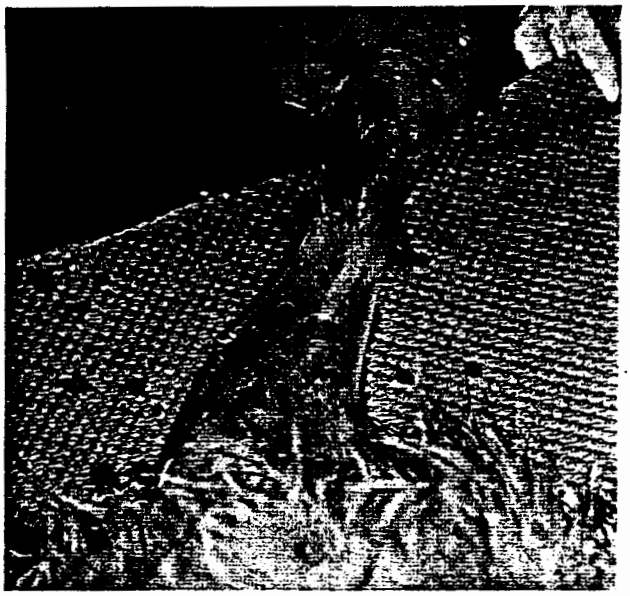

Figure 5— Lateral side of right forearm untreated—18 hours post-burn.

ered severe and the areas involved were sites usually active in metabolic heat transfer. However, because of the monkey's value as part of a research project, the decision was made to initiate burn therapy and to evaluate progress hourly.

Therapy involved sedation (ketamine HCL), 5% dextrose in lactated Ringer's solution given IV at a rate of 5ml/kg per hour, cool compresses, wound debridement, and irrigation with sterile saline solution, topical application of Dermaide Aloe[3] cream (80% concentration of *Aloe vera*) every two hours, and oral administration of Dermaide Aloe tablets (1 mg/kg). The eyes were irrigated with boric acid and kept lubricated with ophthalmic ointment.[2] After six hours the monkey's condition had stabilized, and all vital signs were within normal limits. The treatment was continued. There was not enough viable skin to consider early excision and grafting.

After 18 hours, vital signs continued to remain stable; temperature was 37 C and the prognosis was changed to guarded. Dermal ischemia with tissue necrosis was minimal. One severely discolored area that appeared on the right forearm was an untreated site not initially recognized as a burn area [Figure 5]. Oral mucosa, tongue, and trachea appeared edematous, and it was decided to continue parenteral alimentation for an additional 24 hours. During the next 24 hours the monkey was given an analgesic (Talwin) every six hours and was anesthetized twice daily with ketamine for fluid administration (5% dextrose in lactated Ringer's with B and C vitamins), debridement of wounds, topical and oral Dermaide Aloe administration, ocular irrigation and lacrilube administration.

At 42 hours the monkey's condition was remarkably improved. Aside from the one area that had not been treated until 18 hours postinjury, dermal necrosis had been negligible. Skin discoloration was minimal [Figures 6 and 7].

For the next five days the monkey was anesthetized twice daily for an hour (8:00 am to 9:00 am; 4:00 pm to 5:00 pm) for therapy fluid and Dermaide Aloe applications. Additional therapy, which included continuation of Talwin for pain (every six hours), oral Dermaide Aloe administration, oral high protein, and high caloric supplementation was provided as well.

At seven days, re-epithelialization of the burned areas was well underway and the monkey appeared to be free of pain. All therapy except oral protein supplementation was discontinued, and the monkey was returned to the colony 15 days later. Recovery was complete within 30 days [Figures 8 through 11].

Discussion

Fluid therapy as part of the treatment of thermally injured animals is similar to that for maintenance of human therapy. The purpose of reviewing the following study by Drs. Fox and Lasker is to acquaint the reader with their mortality rate for a smaller burn in the same animal species. Their experimental data can serve as a historical control for a comparative evaluation of our approach. Fox and Lasker,[4] in evaluating the requirement for fluid therapy in scalded and flash-burned monkeys, found that monkeys scalded at 85 C for 30 seconds died in 10 hours if the trunk and two limbs were involved. If the temperature was reduced 10 degrees and immersion in steam/water did not exceed 10 seconds, a 55% BSA injury would occur. Skin necrosis was evident in seven to 10 days, and all monkeys died in 10 days. Survival time was not prolonged even when fluid therapy (dextran and electrolyte solution) was used. If the time was increased to 15 seconds, mean survival time was 3.14 days. However, the mortality of the animals involved was comparable to that of the controls by the fourth day.

Figure 6— Full face view 42 hours post-burn, treated.

Figure 7— Posterior view, 42 hours post-burn, treated.

Therefore, based on the successful resuscitation of the Rhesus monkey using a new therapeutic approach, we suggest the following for the management of severe thermal injuries in animals.

1. Establish a patent airway and assist ventilation as needed.
2. Complete a physical examination; obtain baseline biochemical parameters (CBC, Chem 17).
3. Install an intravenous catheter and maintain fluid therapy as indicated for species treated (suggest 5% dextrose in lactated Ringer's), catheterize and record urine output (approximate 30cc per one hour output).
4. Immersion in water, cool saline or ice if necessary, to decrease both temperature and pain (approximately 30 minutes).
5. Debride loose flesh and remove foreign material. Cleanse wound with 5% saline. Assess the burn injury and appply an 80% Dermaide Aloe compound every six hours. (Dermaide Research Corporation, Chicago, Illinois.)
6. Initial oral (systemic) Dermaide Aloe administration (1 mg/kg).
7. Initiate pain relief (suggest narcotic or narcotic derivative).
8. Re-evaluate patient hourly until vital signs are stable; reassess every six hours thereafter.
9. Oral and topical Dermaide Aloe therapy should continue until biopsy of the burned area shows complete thromboxane inhibition (six to 10 days of therapy have proven effective to date).
10. Patient must be monitored at least every four hours through the first 48-hour period.

Recently, in an attempt to prove or disprove the therapeutic value of *Aloe vera* (Dermaide Aloe) in thermal injury, we noted an interesting response: thermally injured tissue treated with this Mexican cactus extract showed no evidence of injury three weeks postburn. Another yet more important finding was the equal distribution of PGF_{2a} and PGE_2 (prostaglandins F_{2a} and E_2) and the absence of TxB_2 (thromboxane B_2) in the treated tissue. One may postulate then that the steriochemical configuration of the *Aloe vera* plant products (anthraquinone-like) are similar to each other and the presence of the appropriate carboxyl, hydroxyl,

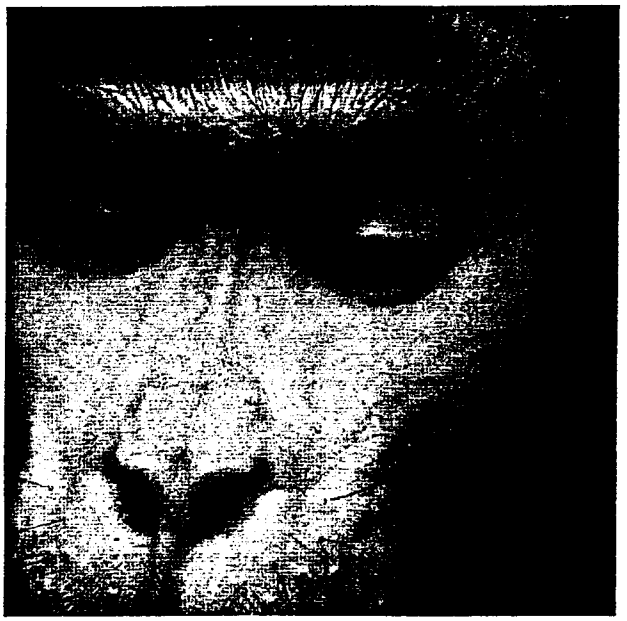

Figure 8— Full face view 30 days post-burn, treated.

Figure 9— Plantar surface right foot 30 days post-burn, treated.

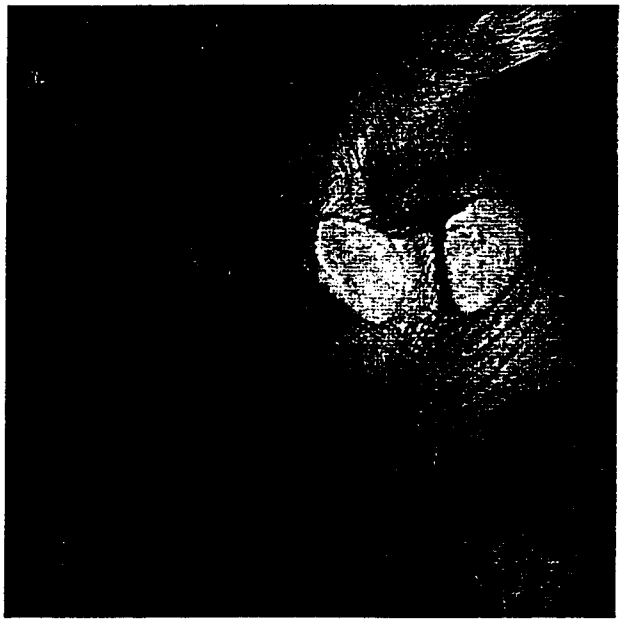

Figure 10— Posterior view 30 days post-burn, treated.

Figure 11— Lateral side right arm, 30 days post-burn, treated.

or oxygen molecules combine to create a false substrate inhibitor. This, therefore, may be one of its beneficial effects in preventing the synthesis of TxA_2, a most potent and devastating vasoconstrictor.

Aloe vera, therefore, has three major properties which are most beneficial in thermal injury: (1) Either due to the aspirin-like effect or the high Mg++ content or possibly by both acting synergis-

tically it can potentiate an anesthetic effect; (2) it has a broad spectrum antimicrobial effect especially against those agents frequently responsible for burn wound sepsis; and (3) its antiprostanoid, or more specifically, its anti-thromboxane effect.

[a]Dermaide Aloe®, Dermaide Research Corporation, 400 North Michigan Avenue, Chicago, IL 60611

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