

*Current Concepts***INITIAL MANAGEMENT OF BURNS**

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**T**HE incidence of burn injury has declined steadily over the past several decades in the United States and in some other developed countries. In-hospital fatality rates have also declined and are now only about 4 percent among patients with major injuries who are treated in specialized burn units.<sup>1,2</sup> Despite this declining incidence, about 1.25 million persons are still treated for burns annually in the United States, and 50,000 are hospitalized each year for the treatment of burns.<sup>3</sup> Seventy-five percent of those hospitalized have burns covering less than 10 percent of the body-surface area.<sup>1</sup> Such burns rarely cause hemodynamic problems or death except in the elderly or in those with smoke inhalation. But these common small injuries cause major, persistent morbidity because burn injury to the reticular dermis is associated with the development of unsightly, restrictive, and uncomfortable hypertrophic scars.<sup>4</sup> The lack of understanding of the biologic basis of these scars and therefore of their effective prophylaxis or treatment is a major unresolved problem. The present alternatives for the management of such scars include wearing of elastic garments or applying silicone-gel sheeting over the scars, but these are not very effective.<sup>4,5</sup>

**BURN SHOCK****Pathophysiology**

After a burn, fluid accumulates rapidly in the wound and, to a lesser extent, in unburned tissues. If the burns involve at least 15 to 20 percent of the body-surface area, hypovolemic shock will develop unless there is effective and rapid intervention. Edema formation is most rapid in the first 6 to 8 hours after injury but continues for 18 to 24 hours.<sup>6,7</sup> Inflammatory mediators are elaborated locally in part from activated platelets, macrophages, and leukocytes and contribute to local and systemic hyperpermeability of the microcirculation (Fig. 1).<sup>8</sup> Histologically, gaps appear in the venular and capillary endothelium; the

wound capillary-protein reflection coefficient falls by 50 percent or more. Regional blood flow increases and is accompanied by an early increase in capillary pressure.<sup>9</sup> Physicochemical alterations in the extravascular, extracellular matrix, such as degradation and unraveling of the collagen triple helix due to its partial denaturation from loss of cross-linking, may further increase wound edema by forming osmotic and hydrostatic gradients.<sup>10</sup> Erythrocytes also are invariably extravasated, but substantial early loss of blood is rare, and transfusion is not required or desirable.

The many factors involved in the formation of edema in burns are still incompletely understood. At present the risks of clinical trials of pharmacologic blockade of mediators that are efficacious in animal models or hypothetically beneficial may outweigh the potential advantages.<sup>11-15</sup>

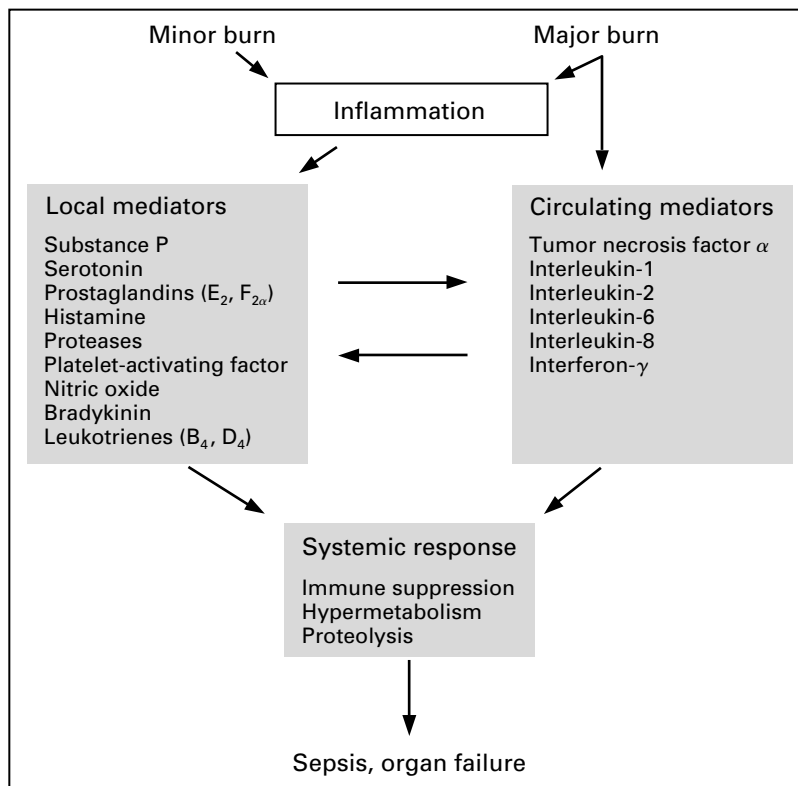
**Fluid Resuscitation**

Sodium-salt solutions (crystalloids) are the essential component of fluid resuscitation. Lactated Ringer's solution has been the most widely used of these solutions. The volumes required vary greatly, from a minimum of about 2 ml per kilogram of body weight multiplied by the percentage of body-surface area burned during the first 24 hours to an amount that can exceed 6 ml per kilogram multiplied by the percentage of body-surface area burned, with a mean of about 4 ml per kilogram multiplied by the percentage of body-surface area burned.<sup>16,17</sup> Fluid requirements are greater if resuscitation has been delayed, in children with large burns, and in patients with smoke inhalation.<sup>18</sup> Large volumes are needed because only 20 to 30 percent of the crystalloid administered remains with the vascular system.<sup>19</sup> About half the fluid must be given during the first eight hours after the injury, coincident with the period of rapid edema formation. In most patients the hourly rate of urine flow, a reasonable indicator of organ perfusion, is the principal guide used to alter the rate of fluid administration. In adults an hourly urine output of 0.5 ml per kilogram is adequate; in children who weigh less than 25 kg, an output of 1.0 ml per kilogram is necessary. Urine outputs appreciably in excess of these values increase wound edema and may necessitate otherwise unneeded escharotomies. Abrupt weight gains of 30 percent or more of body weight can result from resuscitation in patients with massive injury; early endotracheal intubation and multiple limb and truncal escharotomies are commonly required in these circumstances. Pulmonary-artery catheters are not routinely used but are helpful in elderly patients and in those with limited cardiac reserves.

Survival after near-total burns is no longer uncommon, provided that early organ failure is avoided.<sup>20</sup> Vigorous resuscitative measures should there-

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**Figure 1.** Response to Minor and Major Burns.

Major burns precipitate a systemic inflammatory response that if overly prolonged or exaggerated can lead to organ dysfunction, sepsis, or both. The local mediators listed appear within minutes to hours after the injury. Among the systemic mediators, plasma levels of interleukin-1, 2, and 8 are elevated very early. Increases in the level of interleukin-6 occur with sepsis. Transient elevations of tumor necrosis factor  $\alpha$  are associated with a poor prognosis. Interferon- $\gamma$  levels tend to peak about 10 days after the burn. Arturson<sup>8</sup> has reviewed this process in detail. Many factors in addition to the extent of the burn, especially age, determine the severity of injury. A burn involving 20 percent of the body-surface area involves a 30 percent risk of mortality in a 70-year-old patient but is not lethal in a 20-year-old patient.

fore be pursued in previously healthy patients with injuries that inexperienced observers might judge to be lethal.

The crystalloid requirement during the second day of treatment is about half that of the first day. Within 48 to 72 hours after the burn injury, the hematocrit begins a progressive fall due to such factors as intravascular resorption of edema, lysis of thermally injured cells, and the onset of the anemia that is characteristic after burn injury. Crystalloid administration should be discontinued at the earliest possible time. A reasonable goal is for the patient to have returned to his or her preinjury weight within one week after the burn; the elderly tend to retain excess water and may require diuretics.<sup>21</sup>

#### Adjuvant Colloid

Resuscitation using fluids containing solutes with plasma-like oncotic properties has intuitive appeal,

since these fluids resemble what is being lost and protein sieving is still at least partially operative in unburned tissues. Nevertheless, the adjunctive use of colloid in burn shock has decreased, mainly because the controlled trials that have been done have shown no clear advantage to its use.<sup>22,23</sup> One trial found potentially harmful effects: increased accumulation of water in the lungs and an increased rate of clinical pulmonary complications were both associated with the administration of 5 percent albumin in lactated Ringer's solution.<sup>22</sup>

Some centers defer colloid administration for 12 to 24 hours after the injury — a time when capillary permeability has partially returned to normal but plasma volume may be subnormal. This practice has no demonstrated clinical benefit, however, and recent data suggest that it may be deleterious. The administration of albumin to patients in stable condition after 24 hours of clinically satisfactory crystalloid

resuscitation resulted in a significant decrease in the glomerular filtration rate below the normal range despite an increase in plasma volume.<sup>24</sup>

#### Hypertonic Saline

The administration of crystalloid with a sodium concentration of 250 mmol per liter can reduce volume requirements, presumably by mobilizing water from cells that are overhydrated as a consequence of the injury.<sup>17</sup> This therapy is useful in patients with limited cardiopulmonary reserves but demands careful monitoring and clearly has a much narrower therapeutic margin than does the use of isotonic crystalloid.<sup>25</sup> A recent study reported that the use of hypertonic saline in burn shock increased the incidence of renal failure and death.<sup>26</sup>

### INHALATION INJURY

Injuries to the airways and lungs are principally the result of exposure to chemicals during building or vehicular fires. Direct thermal injury below the larynx is rare because the humid airway gas transfers heat poorly. A variety of toxic incomplete products of combustion are inhaled. Carbon monoxide is commonly inhaled and thus can serve as a useful diagnostic marker. The airway mucosa becomes inflamed and usually contains carbon particles. Fiberoptic laryngobronchoscopy is indicated if the diagnosis is in doubt. The incidence of inhalation injury increases with the increasing extent of the burn, so that it is present in two thirds of patients with flame burns that exceed 70 percent of the body-surface area. Unless laryngeal edema is present, clinical evolution can require 12 to 24 hours or more as mucosal slough and secretions accumulate and airway obstruction and atelectasis progress. If signs of laryngeal edema appear — hoarseness, brassy cough, or stridor — immediate endotracheal intubation is indicated. There is no method of quantitating the severity of injury, but measurement of arterial carboxyhemoglobin levels, extrapolated to the time of injury, provides a reasonable estimate of the severity of exposure.

The simplest and probably the best treatment for carbon monoxide poisoning is ventilation with 100 percent oxygen, which decreases the half-life of carboxyhemoglobin from 4¼ hours to about 50 minutes.<sup>27</sup> Hyperbaric-oxygen therapy has been recommended, but credible evidence of its superiority is sparse. Moreover, the logistics of initiating and delivering care to patients with extensive burns within the confines of most hyperbaric-oxygen chambers are formidable.<sup>28</sup>

Inhalation injury is rarely limited to the upper airway; endotracheal intubation alone may be required for several days until edema subsides. In diffuse injury, airway infection is often severe or recurrent, but in less severe cases, healing requires about three weeks. The development of tachypnea with the re-

cruitment of accessory muscles of respiration or hypoxemia (partial pressure of arterial oxygen, <70 mm Hg; ratio of partial pressure of arterial oxygen to fraction of inspired oxygen of less than 200; or both) are signs of impending respiratory failure requiring endotracheal intubation and the institution of mechanical ventilation. Rigid bronchoscopy may be necessary to clear voluminous or tenacious secretions or casts. Corticosteroids and prophylactic antibiotics are ineffective.<sup>29</sup>

#### Newer Treatments

High-frequency percussive jet ventilation might be superior to conventional, volume-controlled mechanical ventilation, presumably because barotrauma is minimized. Survival was better in patients so treated than in historical controls.<sup>30</sup> Permissive hypercapnia (pressure-targeted ventilation) and nitric oxide inhalation have also been used with at least transient apparent benefit.<sup>31,32</sup> Burned children with severe respiratory failure from various causes have survived after receiving extracorporeal membrane oxygenation. This technique has been the least successful in patients with flame burns and inhalation injury, in whom major wound hemorrhage is an additional problem, because full anticoagulation is required.<sup>33</sup> Topical therapy with an aerosolized mixture of heparin and acetylcysteine may reduce mortality.<sup>34</sup>

No randomized trials of any of these treatments have yet been performed. Inhalation injury remains an important cause of death in patients with burns. In one large cohort the mortality rate was 29 percent when inhalation injury was present and only 2 percent in its absence.<sup>1</sup>

### BURN-WOUND MANAGEMENT

#### Topical Therapy

Microorganisms proliferate rapidly in burn wounds, especially in those severe enough to impair immune function. Topical antimicrobial agents have an important role. They delay the interval between injury and colonization and maintain low levels of the wound flora. A variety of antibiotics and antiseptics are used for topical therapy in minor burns, but only three agents have proven efficacy for major burns: 11.1 percent mafenide acetate cream, 1 percent silver sulfadiazine cream, and 0.5 percent silver nitrate solution. Silver sulfadiazine is the mostly widely used of the three for routine prophylaxis because of its relatively low toxicity and ease of use. Treatment with silver sulfadiazine can cause leukopenia during the first week after injury, due in part to bone marrow toxicity, but it nearly always resolves within a period of several days despite continuation of the drug.<sup>35</sup> A solution of 0.5 percent silver nitrate, although an effective antimicrobial agent, leaches elec-

trolytes from open wounds and stains everything that it touches. Mafenide, unlike the other two agents, penetrates the burn eschar rapidly, but it is a carbonic anhydrase inhibitor and is associated with metabolic acidosis and increased minute ventilation when applied continuously to large burns. Mafenide is useful, however, in treating invasive burn-wound infections, which are fortunately now infrequent.<sup>36</sup>

**Care of Shallow Burns**

Shallow burns are treated with daily dressing and local wound care until epithelialization occurs. Full functional recovery is the rule (Table 1). They can also be treated effectively by covering the denuded wound with a skin allograft or xenograft or one of several commercially available synthetic membranes.<sup>37,38</sup> If adherent, these materials reduce pain and eliminate the need for dressing changes with the patient under heavy sedation or general anesthesia, which may otherwise be necessary, especially in infants and children or uncooperative patients.

**Surgical Treatment of Deep Burns**

About 20 years ago, it became possible to excise extensive deep burns safely and close the wounds with autologous split-thickness skin grafts. The introduction of effective topical therapy, ongoing innovations in surgical technique and instrumentation, and improved intensive and anesthetic care together permitted this important advance.<sup>39,40</sup>

Full-thickness burns — those covering about 25

percent of the body-surface area or less in young or previously healthy patients — have a low mortality rate. Such injuries should be treated as soon after resuscitation as is feasible by excision of the eschar and skin grafting. There is no benefit in delay. Sufficient autologous skin grafts should be available to close the wounds at the same operation, particularly if the grafts are meshed and expanded. Excision and skin grafting are bloody procedures, however, especially if they are prolonged. An experienced surgical and anesthetic team and adequate amounts of blood matched to the patient's blood type are essential.

Some deep partial-thickness burns are also treated surgically as soon as their depth can be estimated.<sup>41-46</sup> Advocates believe that this approach results in better joint function and less severe hypertrophic scar than more conservative management, which requires a period of at least three weeks for wound epithelialization. Although surgical therapy clearly results in earlier return of function and a shorter convalescence, its long-term results are probably similar to those of expectant therapy.<sup>42</sup>

Grafting skin on established, granulating wounds from which the eschar has sloughed (a phenomenon due primarily to bacterial proteases) was once the norm, but it is currently the poorest surgical option. This approach is sometimes necessary, however, in the presence of severe illnesses or systemic complications.

The impediments to early surgical closure increase in parallel with the increasing extent of the burn. In trials comparing early with delayed surgical therapy

**TABLE 1.** TREATMENT ALGORITHM FOR THE THREE CLINICALLY IMPORTANT BURN DEPTHS.\*

| BURN DEPTH†                   | LEVEL OF INJURY                           | CLINICAL FEATURES  | TREATMENT   | USUAL RESULT  |
|-------------------------------|---|--|---|---|
| Superficial partial thickness | Papillary dermis                          | Blisters<br>Erythema<br>Capillary refill<br>Intact pain sensation  | Tetanus prophylaxis<br>Cleaning (e.g., with chlorhexidine gluconate)<br>Topical agent (e.g., 1% silver sulfadiazine)<br>Sterile gauze dressing‡<br>Physical therapy<br>Splints as necessary | Epithelialization in 7–21 days<br>Hypertrophic scar rare<br>Return of full function   |
| Deep partial thickness        | Reticular dermis                          | Blisters<br>Pale white or yellow color<br>No capillary refill<br>Absent pain sensation   | As for superficial partial-thickness burns<br>Early surgical excision and skin grafting an option   | Epithelialization in 21–60 days in the absence of surgery<br>Hypertrophic scar common<br>Earlier return of function with surgical therapy |
| Full thickness                | Subcutaneous fat, fascia, muscle, or bone | Blisters may be absent<br>Leathery, inelastic, wrinkled appearance over bony prominences<br>No capillary refill<br>Thrombosed subcutaneous vessels may be visible<br>Absent pain sensation | As for superficial partial-thickness burns<br>Wound excision and grafting at earliest feasible time   | Functional limitation more frequent<br>Hypertrophic scar mainly at graft margins  |

\*Epidermal (first-degree) burns present clinically with cutaneous erythema, pain, and tenderness; they resolve rapidly and generally require only symptomatic treatment.

†There is no clinically useful objective method of measuring burn depth; classification depends on clinical judgment.

‡Sterile gauze dressings are frequently omitted on the face and neck.

at the same institution, the hospital stay was reduced with early surgery only when the burn area averaged 6 percent of the body-surface area. The incidence of other problems, such as the frequency of septic episodes, was lower with early surgical therapy, however.<sup>43,44</sup>

### Treatment of Extensive Deep Burns

For deep burns too extensive to be closed in one procedure, wound excisions can be staged — typically at intervals of about one week — as sufficient autologous skin grafts become available to close the excised wound. Alternatively, the burns can be completely excised within the first several days after injury, and a temporary skin substitute used to close the wound remaining after all available autologous skin has been harvested and grafted. Fresh or cryopreserved allogeneic skin from cadavers is the most reliable wound cover, although its use has a small risk of disease transmission.<sup>45</sup> In severely burned children the systemic administration of recombinant human growth hormone can speed reepithelialization of skin-grafting sites and permit earlier reharvest.<sup>46</sup>

### Alternatives for Wound Closure

The skin substitute Integra<sup>47</sup> is a bilaminar membrane composed of a porous lattice of cross-linked chondroitin 6-sulfate engineered to induce neovascularization as it is biodegraded. An outer layer of silicone serves to close the wound while permitting water-vapor transfer. This layer is peeled off after about 14 days and replaced with ultrathin (0.01 to 0.015 cm [4/1000 to 6/1000 of an inch]) autologous skin grafts. These donor sites can be reharvested after about one week.

Autologous keratinocytes cultured in vitro from a small (2 cm<sup>2</sup>) biopsy of unburned skin obtained shortly after injury offer another option for the treatment of extensive burns. Culture of the keratinocytes for three weeks results in multilayered epithelial sheets, which are then applied on freshly excised burns. The rates of permanent engraftment of these cells have been poor in most centers, however, and the technique is extraordinarily expensive. In patients with burns involving more than 70 percent of the body-surface area, there was an engraftment rate of only 31 percent and only 4.6 percent of the body-surface area burned was closed, at a mean cost of \$60,000 per patient.<sup>48</sup>

It remains unclear whether the early total excision of extensive burns (those involving more than 40 percent of the body-surface area) improves survival and so is preferable to staged excision. In the most recent randomized trial, early total excision was associated with a marginal increase in survival in burns involving at least 40 percent of the body-surface area, but only in young adults without inhalation injury.<sup>49</sup> However, the increasingly rapid pace of devel-

opment of skin substitutes<sup>50</sup> and of transplantation biology increases the likelihood that early total excision of the burn accompanied by one or more means of permanent, reliable wound closure will soon become routine in the care of patients with extensive deep burns.

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