What's New in Burns and Metabolism

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"What's New in Surgery" evolves from the contributions of leaders in each of the fields of surgery. In every instance the author has been designated by the appropriate Council from the American College of Surgeons' Advisory Councils for the Surgical Specialties. This feature is now presented in issues of the Journal *throughout the year.*

It would be difficult to set forth the variety of physical and moral . . .
—Surgeon Daniel Drake MD, describing his own hand burns in 1830[1]

Burn surgery is a young specialty in an environment rich with organizational and technical innovation.[2] New modes and techniques of care are being constantly explored, challenging the ability of even its most active practitioners to clearly define best practices. Although clinical outcomes are vastly better than they were 50 years ago, important questions remain.

EVOLUTION OF THE FIELD

Until surprisingly recently, burn care was a depressing field, in which terrible suffering and tragic outcomes were the general expectation.[3-5] Patients died after burning from burn shock during the first few postinjury days. If they survived this period, death came from wound sepsis during the first few postinjury weeks. Respiratory insufficiency killed those who escaped these two most common problems. These issues were understood poorly, if at all, in the early part of the 20th century.

The casualties of disastrous accidents and wars promoted innovation in burns. Clinical observations of victims of the Rialto Concert Hall fire in 1930[6] and the Coconut Grove fire in 1942[7] made surgeons aware of the vastly increased fluid requirements of burn patients during the first 1 to 2 days after injury. This led to the development of the Moore Burn Budget Formula.[8] At the end of World War II, stimulated by burn injuries seen in armored and aerial warfare and in the fire bombings of cities, the United States Army Institute of Surgical Research was established to ensure an adequate understanding of burn injury on which to base the management of future casualties. This group refined clinical observations and developed weight- and burn size−based resuscitation formulas, such as the Evans, Brooke, and modified Brooke.[9]

In the early 20th century, burn wounds were managed by application of any number of topical preparations. Septic death was still the lot of most patients with large injuries. In the 1970s, early excision of small deep burns and immediate autografting was reported to result in shortened hospital stays, reduced patient suffering, and better functional outcomes.[10] To do these operations in patients with larger injuries, particularly children, surgeons required sophisticated intensive care and blood banking technologies that were then in their infancies. But surgeons, notably at the Army Institute of Surgical Research and at the Massachusetts General Hospital, were successful in exploring these strategies in patients with large wounds. They demonstrated improved survival in patients with burns that were previously routinely lethal.[11,12] These operations have evolved over the intervening years, so that near total early excision is now possible and patients with very large wounds have excellent survival probabilities.[13,14]

Respiratory failure, induced by inhalation injury or by systemic inflammation[15] is the final common killer of burn patients who follow the natural history of their injuries. Development of positive pressure ventilation, lung protective ventilation strategies,[16-18] general critical care techniques, and innovative modes of support[19-22] have contributed to markedly enhanced survival in these patients, but respiratory failure remains a serious problem in the burn intensive care unit.

Although burn injury continues to cause great suffering, survival and outcomes quality have steadily im-

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Abbreviations and Acronyms

ABA	=	American Burn Association
ACS	=	American College of Surgeons
BST	=	Burn Specialty Teams
IGF	=	insulin-like growth factor
PTSD	=	posttraumatic stress disorder
r-HGH	=	recombinant human growth hormone

proved since Dr Drake's description of his own injury.[14,23-25] The field has seen recent changes in both systems and surgical techniques.

SYSTEMS ISSUES

Like most aspects of medicine, burn care has evolved both organizationally and technically. But the multidisciplinary personnel and unique physical infrastructure required to manage serious burns have driven marked organizational changes in burn care.

Volume-outcomes linkage and the burn center concept

As the field has evolved, an increasingly complex and expensive infrastructure of personnel and equipment has been required to generate outcomes consistent with a rising standard of care. It is not cost effective to maintain this infrastructure unless clinical volumes are high, and individual practitioner skill cannot be maintained if clinical volumes are low. These pressures, and demonstration of reduced costs associated with burn center care when compared with nonburn center care, have driven increasing regionalization.[26] Patients with large injuries are now usually transported to regional burn programs for care, rather than being cared for in general hospitals close to home, because any inconvenience is more than compensated for by enhanced outcomes.

A rapidly growing body of data supports a strong link between clinical volumes and outcomes quality.[27-29] These analyses have been applied to both individual surgeon performance and overall program volume.[30-32] Burn-specific data exist that suggest not only shortened hospital stays and enhanced clinical outcomes, but also lower costs, when complex burns are managed in burn center programs.[26] Quality of life of burn survivors has been statistically significantly linked to longterm participation in burn center—based aftercare programs.[25]

The result of regionalization has been the evolution of the burn center from an isolated intensive care unit and operating room to a place where the full range of burn care is provided in one location. Such centers are able to attract and retain a multidisciplinary group of providers with particular interest and expertise in burns. The range of services provided is large, including initial acute care, rehabilitation services, and reconstructive surgery.[33,34]

Burn center verification

Almost 20 years ago, the American College of Surgeons (ACS) recognized that seriously injured patients fared better when managed by experienced teams with proper equipment. This realization evolved into the Trauma Center Verification Program, which has so profoundly molded trauma care, with emergency medical services directing patient flows only to ACS-verified trauma centers.[35] Shortly thereafter, the American College of Surgeons, in collaboration with the American Burn Association (ABA), began the Burn Center Verification Program, in recognition of the unique needs of the seriously burned. This program has reached maturity. Verification must be renewed every 3 years. Verified centers can be relied on to provide competent comprehensive care to burn patients.[36] Burn centers have not been uniform in accepting the ACS-ABA verification process; to date there has been little financial benefit associated with verification.

The American Burn Association

The American Burn Association was founded almost 40 years ago to foster communication of clinical strategies in the evolving field of burn care. But the organization itself has evolved, and activities of the ABA are diverse and are now supported by a full-time staff, with headquarters in Chicago. ABA activities range from clinical teaching through legislative advocacy.

The Advanced Burn Life Support Course, modeled on the American College of Surgeons Committee on Trauma Advanced Trauma Life Support Course, is administered by the ABA. Its mission is to disseminate standardized management strategies relevant to the early care of serious burns to practitioners who manage such injuries infrequently. This is particularly important as regionalization of burn care has evolved and seriously injured patients commonly spend many important hours in transport before reaching the site of definitive burn care. The course has been well received and has been translated into Spanish. Several thousand students attend courses worldwide each year.

The ABA has been active in coordinating lobbying efforts at the national level for flame-retardant sleepwear and the fire-safe cigarette.[37] It has played an important role in burn disaster preparedness, helping to support staffing of the Burn Specialty Teams of the National Disaster Medical System.[38] It has sponsored development of practice guidelines in burn care, convening an expert committee that developed a now popular set of practice guidelines that address the first hours after injury.[39]

Disaster preparedness

Mass casualty situations, caused by structural fires, terrorist attack, or war, can generate large numbers of burn patients.[40-42] A high incidence of deep and complex fourth-degree burns and severe inhalation injury has been noted in survivors of mass casualties related to structural fires.[43,44] The rising threat of domestic terrorism has prompted the National Disaster Medical System to create Burn Specialty Teams, designed to augment its Disaster Medical Assistance Teams in event of a mass casualty situation involving burns. There are now four Burn Specialty Teams (BST) nationally, made up of volunteers from regional burn programs who become federal employees on deployment. These specialists can augment a deployed Disaster Medical Assistance Team, general hospital, or regional burn unit overwhelmed with volume or complexity of burn casualties. The deployed Disaster Medical Assistance Team members can assist with initial evaluation and resuscitation, surgery, critical care, triage, and transportation. To date, BSTs have been deployed for two burn disasters. Boston-based BST-1 was deployed on the afternoon of September 11, 2001, to assist in the aftermath of the World Trade Center attack. In the following week, additional BSTs provided staff to augment New York Hospital's burn unit. After the Rhode Island nightclub fire in February 2003, in which 187 people were injured and 100 killed, BSTs provided staff to facilitate care of these patients. This system is now an important and quickly responsive resource able to augment burn care facilities facing sudden surges in census caused by natural or manmade disasters.

Nonburn conditions

Burn units have a unique set of resources, critical care and surgical wound expertise, that can be very useful in several nonburn conditions. These conditions are increasingly referred to burn programs for definitive care.[45]

Perhaps most common of these conditions is toxic epidermal necrolysis. Although the pathophysiology of toxic epidermal necrolysis remains unclear, the clinical consequences are well described, with a diffuse slough at the dermal-epidermal junction, involving both cutaneous and mucosal surfaces. These patients have been shown to have improved clinical outcomes in burn units.[46-49] Their longterm care needs are often best met in the multidisciplinary environment of a burn aftercare program.[50-53]

Other disease and injury processes commonly referred to burn units are purpura fulminans and major mechanical soft tissue injuries and avulsions. These patients fall well within the expertise and practice patterns of burn center multidisciplinary staff.[54,55] There is some evidence that the incidence of certain soft tissue infections is increasing, and these are also well managed with the unique resources available in burn units.[56,57]

Workforce issues

Burn care has become increasingly complex over the past few decades. Burn surgery has evolved into a surgical subspecialty that focuses on the comprehensive needs of burn patients throughout injury and recovery, including both acute and reconstructive needs. Burn surgery encompasses elements of general, trauma, plastic, pediatric surgery, and surgical critical care. No single basic training program encompasses all of these requirements. Increasingly, practitioners at a high level seek added training in burn surgery,[2] burn-focused physical and occupational therapy, and burn nursing.

In the United States, most burn surgeons come from the ranks of general-trauma surgeons, many also trained in critical care and having additional training or experience in burn surgery. Special training requirements, long hours, relatively low reimbursement, and the challenging patient population make it probable that it will be increasingly difficult to staff burn and trauma programs with adequate numbers of properly trained surgeons as the current active generation ages.[58,59] It is likely that we will see increased use of nurse practitioners and physician assistants in future years. Programs specializing in high-acuity patients are increasingly difficult to keep funded.[60-62] It is probable that the common practice of combining burn, trauma, and urgent general surgery programs will continue, given the similarity in practice patterns (unpredictable surgical needs and critical care) and the greater efficiency of higher-volume programs.[63] Additional training opportunities are needed for surgeons to receive combined burn surgical and surgical critical care training.

Burn aftercare organization

High-quality burn survivals are not generally reached at initial discharge, but commonly require a monitored scar management program, physical and occupational therapy, and staged reconstructive operations spaced out over several years. Until relatively recently, these predictable aftercare needs were either not met, or were found by patients in a haphazard way, among unrelated practitioners. These needs are most effectively met in a coordinated multidisciplinary setting,[64] and, increasingly, these services are being delivered within comprehensive burn care programs.[25,65]

Emotional distress is a predictable part of many burn injuries.[66-68] Posttraumatic stress disorder (PTSD) is reported to occur in up to 30% of burn patients and may be especially difficult in the presence of preinjury psychiatric illness.[69,70] Newer tools are being developed to anticipate and prevent PTSD in burns.[71,72] There is some evidence that early pharmacologic treatment may reduce subsequent PTSD incidence and severity, although data are not sufficient to recommend this as routine therapy.[73-76] Effective pain control measures may also have a favorable impact on PTSD rates. Recent data revealed a strong inverse relationship between opiate dosing during acute care and ultimate PTSD severity.[77] Acknowledgment of this reality fosters early intervention and seems to enhance the rapidity and quality of recovery.[78,79]

Longterm outcomes

Longterm outcomes are assuming an increasingly important role in burn research programs; there remain many unexplored aspects of burn recovery. This work is particularly important in light of the increasing survival of patients with very large burns. Available data seem to support the contention that most survivors of large burns have satisfying longterm quality of life.[80-82] A study of 80 adult survivors of massive burns as children, an average of 15 years earlier, revealed that most had very satisfying outcomes quality.[25] This study revealed that strong family support and participation in a coordinated burn aftercare program were strongly associated with enhanced outcomes quality, findings confirmed by other studies.[80,83-85] A collaboration under the auspices of the American Burn Association is pursuing additional studies with newly developed outcomes quality tools to examine factors related to outcomes quality in greater detail.[86]

SURGICAL TECHNIQUES

Burn care has become an increasingly technical field, crossing several traditional disciplinary boundaries. Progress in multiple fields has major impact in burn care.

Initial evaluation and resuscitation

Burn patients are often injured in ways that are consistent with nonburn trauma.[87] A through initial evaluation is essential to exclude concurrent nonthermal trauma that might complicate management and result in morbidity through nontreatment.[88] As in trauma, helical CT scanning has become increasingly useful to evaluate patients at risk for blunt injuries of the head, neck, chest, abdomen, or pelvis. Single-pass scanning protocols, from the vertex of the head to the pelvis, have been devised. With properly timed dye injections, such scans can include CT angiograms and abdominal visceral evaluation and can be completed in as little as 3 minutes. After taking the patient from the radiology suite, data can be reformatted so one can visualize the facial skeleton and spine, eliminating the need for many time-consuming conventional radiographs.[89]

The early capillary leak and consequent fluid resuscitation requirements of burn patients are unique and remain poorly understood. Current thinking is that mediators released from the injured tissue cause this leak through unknown mechanisms.[90,91] The resulting soft tissue edema is a major source of morbidity, associated with airway instability, respiratory failure, limb ischemia, and compartment syndromes of the extremities and torso.[92] Patients with particularly deep burns, inhalation injury, or delayed resuscitation have predictably increased volume requirements for resuscitation. The increased requirements of those in whom resuscitation has been delayed is in some ways suggestive of a whole-body ischemia-reperfusion reaction. Because the pathophysiology is so poorly understood, intervention has been confined to careful fluid replacement guided by fomula, although most common formulae are inaccurate in individual patients.[93] There is good evidence suggesting that antioxidants may be able to modify immediate postburn physiology so that such fluid administration is not needed.[94] One animal trial of vitamin E did not reveal any benefit,[95] but subsequent animal and clinical projects with various antioxidants and high-dose vitamin C demonstrated reduced resuscitation volumes.[96-100] These benefits remain unconfirmed, and early antioxidant use is not considered the standard of care in burn resuscitation.

Current burn resuscitation practices are not evidence based,[101] but morbidity related to excessive soft tissue edema associated with burn resuscitation is widely acknowledged.[92,102] Three percent hypertonic saline was advocated in the 1970s to address this issue,[103,104] but its use has been abandoned because of associated technical difficulties.[105] Initial administration of 7.5% saline-dextran solution has been explored with cautiously encouraging initial results.[106] The concept of oxygen delivery limited resuscitation and the potential benefit of hyperdynamic resuscitation guided by pulmonary artery catheter has been advocated, but not generally adopted.[107,108]

Colloid is not advocated during the first 24 hours after injury by most formulae because it has been feared that the administered colloid will leak out into the interstitium.[109] Although criticized for methodologic problems,[110] a metaanalysis of albumin use in critical illness suggested no benefit.[111,112] But many practitioners administer 5% human albumin during the first post-injury hours in patients with very large burns in whom massive crystalloid volume is otherwise needed,[113] even while tolerating low serum albumin levels in the post-resusciation period.[114,115] The role of colloid in fluid resuscitation is an important area needing quality prospective investigation.

Monitoring the adequacy of fluid resuscitation is generally done by observing blood pressure, pulse, and urine output.[116] Pulmonary artery catheters have less benefit than previously thought, even in elderly high-risk patients[117] and are generally reserved for exceptional cases. Intrathoracic blood volume[118] and thermodilution[119] have been investigated recently, with encouraging preliminary results. The ultimate goal of burn resuscitation is tissue oxygen delivery, and several direct tissue oxygenation monitoring techniques are being developed. Near infrared spectroscopy[120] and direct tissue oxygen measurements[121] have been looked at, again with cautiously encouraging initial results. Further data are awaited.

Patients with large burns, particularly those in whom resuscitation has been delayed, are at risk for abdominal compartment syndrome.[122-124] This presents with increasing abdominal distention, decreasing urine output, hypotension, and worsening pulmonary compliance. Diagnosis is by serial examination supported by a bladder pressure over 25 mmHg. Although more common in multiple-trauma patients, it is increasingly described in patients with serious burns, particularly in those in whom resuscitation has been delayed. Treatment is by decompressive laparotomy with temporary abdominal closure using a variety of prosthetic materials.[125] Subsequent abdominal closure is accomplished after visceral edema has resolved. Burns of the abdominal wall can make this a technically challenging exercise, sometimes requiring component release of the abdominal wall for closure.[126] In some cases, large amounts of intraperitoneal fluid are the cause of abdominal compartment syndrome, and simply tapping this can improve the situation enough to avoid laparotomy.[127]

Unique burn critical care issues

Seriously burned individuals can only recover with definitive wound closure. They can be sustained through wound closure only with sophisticated critical care. Most burn programs have embedded intensive care units designed for the unique needs of burn patients,[34] and increasingly sophisticated critical care capabilities are an expected part of burn programs. Although many maneuvers are neither new nor unique to burn patients, some are, and these will be discussed now.

Deep venous thrombosis and thromboembolic complications were thought to be rare in burn patients in the past,[128,129] despite protracted immobility, hypercoagulability, and common need for femoral vascular access. Routine prophylaxis of deep venous thrombosis was not justified.[130] This supposition is coming into question with the advent of higher index of suspicion prompted by experience with trauma patients,[131] and the increasing availability of portable ultrasonic screening methods.[132] Several authors have described a higher incidence of thrombotic complications in burn patients than previously reported.[133-135] Currently, there is no consensus on the advisability or technique of routine thrombosis prophylaxis in burn patients. But some form of prophylaxis is increasingly being prescribed for adult burn patients during periods of protracted critical illness or immobility, including selective use of vena cava filters in very high risk patients.[136] This is an area ready for a quality prospective study.

Tight control of serum glucose in the critically ill has been associated with a reduced incidence of infectious complications and enhanced survival.[137,138] Although it is not clear if this effect will be seen in burn patients, tighter glucose control is being practiced more commonly. Tight glucose control is not without risk; interruption of glucose administration during the high-dose insulin infusions typically required by burn patients poses some risk of hypoglycemia.[139] This may be moderated by adherence to insulin protocols.[140] This is another area of burn critical care ripe for quality study.

Maintenance of serum albumin levels in the post-resuscitation period has been debated for many years. Albumin production is decreased in the hypermetabolic patient.[141,142] Quite low serum albumin concentrations are well tolerated, probably because the overproduction of acute phase proteins maintains colloid oncotic pressure.[115] A 1998 metaanalysis suggested albumin administration may be harmful, but these data are relatively flawed and the conclusions are unlikely to apply to very sick burn patients with profound hypoalbuminemia.[111] The bulk of opinion supports maintenance of serum albumin concentrations at least above 1.0 g/dL, and higher in the face of enteral feeding intolerance or pulmonary dysfunction.

Recombinant Activated Protein C (r-APC) is now available and data suggest it may have some benefit in selected patients with systemic sepsis and sudden organ failures.[143] It should be used judiciously because it is expensive and associated with potential bleeding complications.[144] In properly selected patients, it is probably cost effective.[145] Data in burn patients are only anecdotal, but r-APC seems unlikely to be generally useful in this population with relatively chronic organ dysfunctions and large wounds.

Burn surgery has been a bloody business historically, but this has changed dramatically in recent years.[146] Increasing efforts have been made to minimize exposure to blood products. Transfusion practices still vary between programs to some extent, but are becoming more consistent as the rate of blood loss, particularly in the operating room, becomes more controlled.[147] Transfusion practices in burns are an area where more research is needed.

Topical agents play an important adjunctive role in burn care. There are an increasing number of agents available. The major agents used for patients with larger injures remain silver sulfadiazene, aqueous 0.5% nitrate, and 11.1% mafenide acetate cream. A 5% aqueous mafenide acetate preparation is now widely available, after limited use for many years.[148-151] Like the 11.1% cream, it is particularly useful against resistant Pseudomonas species, but is also a strong carbonic anhydrase inhibitor, making it difficult to use in patients with respiratory failure being managed with permissive hypercapia.[16] Its use also may predispose to fungal growth.[152] It has an important role in wounds colonized or infected with resistant gram-negative species. Innovative nonpharmacologic wound therapies, such as antimicrobial peptides,[153] are being actively explored, as are a number of recently available silver-releasing membranes.[154-156]

The role of tracheostomy in burn intensive care remains unclear. This issue has been debated for more than 30 years[157] and remains unresolved, with recent publications urging both aggressive[158,159] and conservative[160,161] approaches. Given the higher incidence of clinically important airway morbidity in young children after tracheostomy, an individualized approach is advised.

Inhalation injury and respiratory failure

Inhalation injury remains a major cause of morbidity, prolonged ICU and hospital length of stay, and mortality in burn patients.[162] A large variety of toxic substances are inhaled, generally products of incomplete combustion attached to smoke particles. Burning composite materials are replete with potential toxins.[163] Very fine smoke particles will result in an alveolar injury; coarse smoke will deposit primarily in the upper tracheobronchial tree. Injury pattern will differ with the type of smoke and variety of toxins inhaled. In most patients, early problems consist primarily of upper airway edema and bronchospasm; initial chest radiographs are generally normal.[164-166] In the days that follow, the injured endobroncial epithelium will slough to a variable extent, resulting in diffuse small airway obstruction. Very distal injuries will cause alveolar flooding and derecruitment.

Diagnosis of inhalation injury remains a clinical guess, despite efforts to develop tools to measure its presence and severity and thereby compare therapies and predict outcomes. Diagnostic tools have included bronchoscopy, bronchoalveolar lavage, technitium scanning, and a variety of serum tests.[164,167-172] None has proved able to stratify the severity of subsequent clinical course.

Intriguing early animal work with CT to stratify injury severity during initial evaluation awaits clinical confirmation.[173] The increased need for resuscitation fluid caused by inhalation injury has now been roughly quantitated as 30 mL/kg.[174]

The 1980s were called a "decade without progress" in inhalation injury management.[175] But more recently, there have been additional alternatives, if not real progress, available for inhalation injury management.[176] Active animal projects are exploring a number of potential therapeutic strategies. Ketorolac has been shown to attenuate mircovascular changes after inhalation injury in sheep.[177] Surfactant and partial liquid ventilation with perflubron have shown efficacy in a piglet model of inhalation injury.[178] Perflubron partial liquid ventilation, although conceptually ideal for improved pulmonary toilet and mechanical recruitment needs of inhalation injury patients,[179] was ineffective in a swine model of inhalation injury.[180] Nebulized dimethyl sulfoxide improved inhalation injury physiology in a sheep model.[181,182] Nitric oxide synthase inhibition reduced pulmonary dysfunction after inhalation injury in sheep,[183] as did poly (ADP ribose) synthetase inhibition,[184] although P-selectin blockade did not.[185] Nebulized heparin has been investigated in sheep with inhalation injury, with recent studies showing no benefit,[186,187] although an earlier study had suggested utility,[188] and antithrombin-3 attenuated pulmonary inflammation and improved function after inhalation injury in sheep.[189]

Human trials of inhalation injury salvage techniques have been much more limited. In respiratory failure trials, prone positioning transiently improved oxygenation, but did not impact survival.[190,191] Use of volumetric diffusive (percussive) ventilation has been reported to improve outcomes in inhalation injury,[192,193] although other studies have shown improved oxygenation but no change in rates of pneumonia or survival.[194] Inhaled nitric oxide has improved oxygenation in inhalation injury,[19,20] but outcomes improvement has not been demonstrated. Oscillatory ventilation has been used effectively in young children with primary oxygenation failure, with limited use reported in pediatric inhalation injury.[195] Compared with historic controls, nebulized heparin has benefited inhalation injury patients,[196] and confirmatory data are awaited. Extracorporeal support has been reported, but is rarely advised in most burn patients because of associated bleeding complications.[22,197,198]

Perhaps the only therapy that has shown clear benefit in human patients with respiratory failure is low-volume ventilation.[16,18,199] Most patients with inhalation injury who require mechanical ventilation are best managed with a strategy that includes pressure controlled ventilation, which limits inflating pressures and concentrations of oxygen to nonharmful levels and effective pulmonary toilet. Innovative and experimental methods of support are reserved for those few in whom this approach fails.

Carbon monoxide poisoning

Carbon monoxide poisoning is common in burn patients, and the role, if any, of hyperbaric oxygen has been debated for years.[200-203] Although serum carboxyhemoglobin is commonly used to track the severity of exposures, CO binds to other heme-containing enzymes and can interfere with oxygen use and delivery. After decades of anecdotal case series, two important prospective trials have recently been published, unfortunately with conflicting results. In a randomized, controlled, double-blind trial, which included neuropsychologic testing and sham treatments in a multiplace hyperbaric chamber, hyperbaric oxygen did not benefit, and may have worsened, the outcomes of patients with CO poisoning.[204] In a second double-blind randomized trial, which included sham chamber treatments and neuropsychiatric testing, cognitive sequelae at 6 weeks were less frequent in the hyperbaric-oxygen group.[205] Both articles have been criticized for methodologic flaws, so the role of hyperbaric therapy in CO poisoning remains an open question, and judgment must still be used to decide who should be treated with hyperbaric oxygen. A reasonable compromise is to consider for treatment those with severe CO poisoning (otherwise unexplained loss of consciousness or documented very high carboxyhemoglobin level) who can be safely treated. In a monoplace chamber, this often precludes treatment of hemodynamically tenuous patients or those who are wheezing, febrile, or have thick endobronchial secretions and are at risk of air-trapping and gas embolism.[206,207] If intubated patients are to be treated, they should undergo myringotomy to eliminate the possibility of tympanic membrane rupture, and endotrachael tube balloons should be filled with saline rather than air.

Nutritional support of hypermetabolism

Postresuscitation physiology is characterized as hypermetabolic, with fever, increased muscle catabolism, and a hyperdynamic circulation.[208] Traditionally, this physiology is supported by providing adequate nutrients while the process is truncated through wound closure. Realization that this physiology will continue for some months after wound closure,[209] and that there may be adverse consequences of inadequately supported catabolism in some patients,[210-212] has led to increasing interest in modifying the physiology, rather than simply supporting it.[213] But nutritional support remains the essential cornerstone of management of the hypermetabolic burn patient.

Nutritional targets have remained static in recent years, with most programs striving for protein goals of 2 to 3 grams per kilogram per day and caloric targets of 1.5 times a calculated basal metabolic rate or 1.2 times the resting energy expenditure measured using indirect calorimetry.[214,215] Glucose is ideally not the only fuel because high levels are not oxidized in this hormonal milieu.[216] Additionally, adequate amounts of micronutrients and vitamins are essential.[217]

Nutritional support is generally monitored by serial physical examination, urinary nitrogen excretion and nitrogen balance, and indirect calorimetry.[218] Urinary nitrogen balance is not accurate as a predictor of protein accretion when compared with stable isotopic studies, so monitoring of muscle mass by other means is desired.[219] Measurement of extracellular water by corrected bromide space has recently been shown to be an accurate way of determining lean body mass in acutely burned patients, and might be a way to track changes in lean body mass.[220] Three-methylhistidine is an amino acid unique to skeletal muscle, and its urinary excretion may be a more accurate alternative to urinary urea nitrogen in tracking muscle catabolism.[221]

The route of support is ideally enteral, reserving parenteral support for periods of ileus, often induced by sepsis. Most patients tolerate gastric feedings without difficulty,[222] but the postpyloric route is required by some,[223] although this route is more difficult to monitor and is not without serious potential complications.[224] When properly used for moderate periods, properly administered parenteral nutrition has not been associated with morbidity and can have an important protective effect on lean body mass.[222]

The nonessential amino acids, glutamine and arginine, have critical roles in the burn patient. A significant body of animal data suggests that these may be relatively deficient in the hypermetabolic state.[225] Using stable isotope tracer techniques, this is being evaluated in burn patients.[226] The implications of this work are important, in that certain patients may benefit from supplemental administration of these otherwise nonessential amino acids; clinical data to date have been mixed.[227-229] Multiple projects are looking at infectious and other complications with and without provision of nonessential amino acids, and these data are eagerly awaited. Nutritional support is a complex area with much basic information still missing.[230]

Modification of hypermetabolism

Before modern medical care, hypermetabolic physiology probably had survival value because it was so well retained across mammalian species. But it was now widely assumed that certain aspects of this physiology are maladaptive and may actually impair recovery. First among these is muscle catabolism, which has become the principal target of efforts to modify hypermetabolic physiology.

The research group at Galveston has done extensive pioneering work in this area, using a combination of animal models and clinical protocols to evaluate recombinant human growth hormone (r-HGH), insulin, insulin-like growth factor-1 (IGF-1), propranolol, clenbuterol, and oxandrolone, both during acute care and in the months after initial hospital discharge.[231,232]

The use of r-HGH as a daily intramuscular injection during acute burn care has favorably influenced the hepatic acute phase response,[233,234] increased IGF-1 expression,[235] decreased tumor necrosis factor expression,[236] improved protein kinetics,[237] maintained growth,[238] prevented intestinal epithelial atrohpy,[239] and decreased donor site healing time by 1.5 days.[240] Concerns about safety and longterm scarring have been unfounded, despite unfavorable results in nonburn adult critical illness.[241-244] Administration of r-HGH can be continued in the outpatient setting by self-injection,[245] and 1 year of such treatment has been reported to decrease muscle catabolism and osteopenia,[246] although vitamin D depletion may have a role in the latter.[210]

Recombinant human growth hormone (r-HGH) can lead to hyperglycemia, which increases mortality,[247] but can be well controlled by insulin infusion.[248] Insulin infusion prevents muscle catabolism after burn,[249] and prolonged euglycemic insulin infusion through acute burn care prevents muscle catabolism and preserves lean body mass.[250]

A combination of IGF-1 and its binding protein, IGFBP-3, attenuates muscle catabolism in children with serious burns.[251] Local IGF-1 gene transfer within wounds decreases inflammatory cytokine expression.[252] IGF-1 has a general anabolic effect and improves gut mucosal integrity.[253,254]

Beta blockade with propranolol has anabolic actions,[255,256] decreasing cardiac work,[257] lowering peripheral lipolysis,[258] decreasing extremity blood flow,[259] and increasing expression of anabolic substances in the muscle of burned children.[260] The beta agonist Clenbuterol improves protein kinetics in burn animal models[261,262] and in nonburn patients.[261,263]

Oxandrolone improves lean body mass in burn patients,[264,265] especially those who were emaciated after delayed treatment;[266] these effects are not age dependent.[267] Anabolic gene expression in the muscle of burned children was enhanced with oxandrolone treatment.[268] When compared with r-HGH, fewer complications were noted with oxandrolone.[269] Although anabolic agents can increase lean body mass, exercise is essential to developing strength.[270]

Our lack of detailed understanding of the cellular and subcellular biology of injury physiology has limited the ability to modify it. But it seems likely that burgeoning research efforts in the molecular mechanisms behind this physiology of injury will lead to an enhanced ability to control it. Notable among these research efforts is the National Institutes of Health–sponsored "Glue Grant" project, in which a diverse group of basic scientists and surgeons have been brought together in an ambitious attempt to describe these molecular mechanisms in human patients. This project, already in multicenter clinical trials involving both burn and trauma patients, is likely to be a landmark contribution leading to major improvements in clinical care of the injured.

Interestingly, early burn wound excision has also recently been shown to favorably influence the hypermetabolic response and reduce catabolism,[271] confirming earlier work that demonstrated decreased energy needs with early wound excision.[272] Prompt wound closure and effective elimination of infection remain a most potent tool to limit the hypermetabolic state.

Burn surgery

At the heart of the improved outcomes in burn patients are changes in the breadth, indications, and techniques of burn surgery, with perhaps the greatest recent change being its breadth. As a field of specialization, burn surgery brings together components of plastic, general, trauma, and pediatric surgery. Operations fall into four general categories: decompression procedues (escharotomies and fasciotomies), excision and closure operations, reconstructive operations, and supportive general surgical procedures (tracheostomy, gastrostomy, cholecystectomy, bronchoscopy, vascular access procedures).

An essential element of excisional surgery is an ability to accurately determine the burn depth or, more importantly, the ability of a burn to heal. Multiple variables influence the ability of a cutaneous burn to heal, including burn depth, skin thickness, anatomic area, density of skin appendages, age, and quality of resuscitation. There is a rich history, spanning several decades, of efforts to develop tools to answer this common clinical question.[273] These efforts have included reflectance of colored light from the burn wound, helium-neon laser Doppler flowmeters to measure microvascular blood flow, thermography, direct temperature measurement, high-resolution ultrasonography, fluorescence of intravenously administered fluoresecein dye with ultraviolet excitation, nonfluorescent intravenous dyes, burn wound biopsy, nuclear magnetic resonance imaging, and fluorescence of intravenously administered indocyanine green dye. Most recently, scanning laser Doppler has been advocated.[274] But at present, the eye of an experienced examiner can most accurately integrate the multiple variables that influence the ability of a burn to heal.

A major change in excisional burn surgery in recent years has been a marked reduction in blood loss. Blood product use in burn programs is now as much as 10-fold less than it was 2 decades ago.[148] This has come about largely through adoption of a number of simple operative techniques. Principal among these are subeschar and subcutaneous epinephrine clysis, extremity exsanguination, pneumatic tourniquet use, and maintenance of intraoperative euthermia.[275-277] Although high-energy carbon dioxide laser ablation of burn eschar has been proposed as a way to reduce bleeding in these patients,[278,279] progress with simpler techniques has made complex laser use much less attractive.

A practical alternative to staples and suture material for skin graft fixation remains elusive;[280-282] cyanoacrylic glues have a limited role,[283] as have various fibrin glues.[284-286]

Skin substitutes

Gauze dressings remain the standard of care for temporary cover of partial-thickness burns, and split-thickness autograft remains the standard of care for definitive coverage of full-thickness burns, but both have significant imperfections. There has been a great deal of work done in recent years attempting to address these imperfections through development of a number of membranes designed for temporary and permanent application to wounds.[287] This is a rapidly moving area and significant additional changes are likely in the next few years.

Temporary skin substitutes are useful as dressings on donor sites, as coverage of clean superficial wounds, to provide temporary physiologic closure of deeper wounds after excision while awaiting autografting, and occasionally to test the viability of questionable wound beds. Fresh or cryopreserved split-thickness human allograft is the only temporary membrane that vascularizes, and it remains the optimal temporary skin replacement.[288,289] The risk of viral disease transmission with allograft is minimal, because transplant screening techniques are universally used by tissue banks.[290,291] Increased regulation by the Food and Drug Administration has led to closure of many single-tissue banks with increased regionalization of these resources into larger multiple-tissue facilities.[292-294]

Fresh human amniotic membrane has been extensively used all over the world as a temporary skin substitute.[295,296] Difficulty screening for viral diseases limits its use in developed countries. Porcine xenograft, or processed porcine dermis, is the only xenograft currently in common use.[297] Several single- and double-layer semipermeable synthetic membranes are available as are several hydrocolloid dressings; all are useful, and none has emerged as clearly superior.

To address the common issue of submembrane infection, several silver impregnated membranes or dressings have been developed and marketed.[154-156,298] Impregnated partially occlusive and hydrofiber dressings are being increasingly used for coverage of burns and other wounds within programs of wound care. Clinical protocols vary widely, but there clearly seems to be a place for well-monitored membrane treatment of partial-thickness burns.

There are some laboratory data suggesting that application of growth factors to wounds may improve healing.[299,300] To date this has been most practically done by applying allogeneic cells rather than isolated growth factors, which are expensive to produce with current techniques. Substances secreted by allogeneic cells, or released upon their dissolution, are thought by many investigators to enhance wound healing. Clinical examples of this concept include allogeneic keratinocytes applied to superficial wounds and donor sites,[301,302] topical application of recombinant platelet-derived growth factor,[303] cultured keratinocytes and fibroblasts seeded onto opposite sides of a bilaminar bovine collagen matrix,[304] and by culture of neonatal fibroblasts into the inner layer of a bilayer skin substitute.[305] None has emerged as clearly superior.

During the next few years, it seems probable that we will see greater use of membrane dressings for many wounds, particulaly "active" membranes that either provide antibacterial activity, growth factor activity, or both. With further development of viral transfection techniques, keratinocytes genetically modified to overexpress growth factors may be incorporated into dressings.[306-309]

A reliable permanent skin substitute, most likely an autologous composite, will profoundly change the field of burn care. Several membranes have become available, including epidermal, dermal, and composite substitutes. Although all are useful, none yet meets the need for a reliable composite skin replacement. In the mid 1970s, Rheinwald and Green[310] developed autologous epithelial cell membranes. These are used clinically, despite suboptimal engraftment and fragility, in patients with massive injuries.[311,312] The fragility of wounds closed with epithelium led investigators to develop dermal replacements. This has taken three general directions: retention of vascularized allograft through excision of the overlying antigeneic epithelium,[313,314] engraftment of acellular dermis,[315] and incorporation of synthetic dermal analogs.[316]

Integra (Integra LifeSciences Corporation) was initially approved by the US Food and Drug Administration for use in life-threatening burns. The inner layer of this material is a 2-mm thick combination of bovine collagen and chondroitin-6-sulfate, which has a 70- to 200-micrometer pore size to allow fibrovascular ingrowth. The outer layer is 0.009-inch polysiloxane polymer to provide a physiologic vapor barrier. It can be placed on freshly excised full-thickness burns, allowed to vascularize for 2 weeks, and the outer silicone membrane replaced with a thin epithelial autograft. Postmarketing trials of Integra have shown favorable results in highly experienced hands,[317] but the membrane must be carefully monitored for infectious complications.[318] It has been used with some success in experienced hands for burn reconstruction.[319-321] Incorporation of epithelial cells by centrifugation has been tried in animals,[322] and, if successful, will potentially eliminate the two operations now required to use this membrane.

Freeze-dried acellular allogenic dermis simultaneously engrafted with a thin epithelial autograft (AlloDerm, LifeCell Corporation) is another approach to dermal replacement.[318,323] Clinical experience with this material in acute and reconstructive burn wounds is limited.[324]

Presence of both dermal and epidermal elements enhances epithelial maturation and graft performance.[325] Ideally, both dermal and epidermal layers would be provided in an autologous composite. Human fibroblasts cultured into a collagen-glycosaminoglycan membrane with overlying epithelial cells have been successful in animal models.[326-331] Exciting clinical trails are in progress with this material. Autologous keratinocytes cultured into acellular allogeneic split-thickness dermis has also been successful in an animal model and in pilot human trials.[311,332] Addition of fibroblasts into this composite has demonstrated enhanced performance in a nude mouse model.[333] Maturation of the composite substitute concept will have a profound impact on the acute and reconstructive care of burn patients.

Pain and anxiety management

Tremendous progress has been made in dealing with the inevitable pain and anxiety associated with burn injury and its management.[334] Most burn programs have evolved highly specific protocols that provide for objective assessment and specific interventions.[335] Aggressive management of these problems may reduce longterm emotional sequalae.[77] Reducing pain associated with burn care has a major positive impact on patient[336] and caregiver[337] experience, and increasing work is being done with assessment and treatment of pain and anxiety in young children with burns.[338] Burn-specific assessment tools have been lacking, a problem that is being actively addressed.[339] The strong synergy between opiates and benzodiazepines has become more widely appreciatated in burn programs,[340,341] and although pharmacologic management is the cornerstone of pain control, the efficacy of adjuncts such as hypnosis and virtual reality are being explored in an objective way.[342,343]

Hypertrophic scarring

Hypertrophic scarring remains a terrible clinical problem. Hypertrophic scars can be described with a standardized rating system,[344,345] but understanding the pathophysiology and developing effective treatment strategies have been hindered by the absence of an animal model. Healed wounds typically show involution of neovasculature about 9 weeks after epithelialization.[346] Wounds destined to become hypertrophic do not demonstrate this normal physiology, but become increasingly vascular at this time; the physiology behind this clinical observation remains unclear, despite significant new understanding.[347,348] Recently, successful transplantation of human hypertropic scars onto nude mice has been reported,[349] and is hoped that this model can be used to develop innovative treatment strategies.

Current treatment methods are empirically derived and include early wound closure, pressure garments, injectable steroids, topical silicone, and massage regimens.[350,351] The multiple recommendations for treatment are confusing and are not generally evidence based.[352] Recently, judicious use of vascular lasers has been explored,[353,354] but more work needs to be done before vascular laser treatment can be endorsed.

Pruritis remains a very difficult problem during the first year after injury;[355,356] it is thought to involve local release of histamine and other local mediators.[357] Traditional treatment strategies have been based on systemic antihistamine treatment.[358] Recently, doxepin, an antidepressant with strong antihistamine properties, has been approved for topical use for pruritis,[76,359-361] and additional experience with burn pruritis is awaited. Neuropathic pain in scars and healed burns can be a problem in some patients. This can be addressed with a variety of supportive treaments. Occasional patients will benefit from the use of gabapentin, an anticonvulsant thought to stabilize nerves;[362] more data would be valuable. Custom clear face masks, using a digital map created by scanning with a helium-neon laser, are new devices that are improvements over older technologies.[363]

Reconstruction and rehabilitation

The standard of successful burn care is no longer simply survival, but the quality of that survival, which demands a great deal of the burn occupational and physical therapy staff. This staff involvement transcends the entire spectrum of care from the intensive care unit through the outpatient clinic.[364] In the critical care setting, rehabilitation priorities include ranging, splinting, and antideformity positioning. These activities will prevent the otherwise inevitable capsular contraction and shortening of tendon and muscle that complicate recovery. Ideally, these activities can be scheduled so they coincide with medications administered for dressing changes.[34] As patients are weaned from intensive care, therapy efforts increase markedly. Priorities during this phase are continued passive ranging, increasing active ranging and strengthening, reduction of edema, and preparation for work or school. Resisted range of motion, isometric exercises, active strengthening, and gait training are important objectives. After discharge, rehabilitation priorities include progressive ranging and strengthening, evaluation of evolving problem areas, postoperative therapy after reconstructive operations, and scar management.[365] Directed exercise programs may shorten the time to full recovery of preinjury strength.[273,366]

In the past, burn reconstruction was often delayed until scars were fully mature, and it was often performed by scattered practitioners not associated with the acute burn care team. These factors could lead to significant delays and lack of coordination in performing needed operations, resulting in potentially correctable soft tissue contractures becoming fixed deformities. Current data demonstrate that outcomes quality is enhanced by long-term followup with a multidisciplinary burn program.[25] Increasingly, burn reconstruction has become part of the package of comprehensive care offered by burn programs. Functionally limiting deformites are corrected early in recovery, and important esthetic deformities are given a high priority because they may help foster successful reintegration.

In conclusion, despite recent progress, there are a number of important organizational and technical issues that remain in burn care. These include maintenance of the burn workforce, burn center verification, disaster preparedness, maintenance of capillary integrity during resuscitation, restraint of hypermetabolism and muscle catabolism, support of inhalation injury, understanding of molecular biologic changes with injury, and control of scar hypertrophy. Nevertheless, in no other area of trauma care are multidisciplinary teamwork and comprehensive care from injury through recovery so evident as in burns. Although the field is replete with unresolved problems, care of the seriously burned can be incredibly rewarding.

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