

Recent Advances in the Management of Burns

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Burn injuries represent a major cause of mortality and morbidity, as well as a significant drain on limited health care resources. Advances in resuscitation, critical care, protective ventilatory strategies and early debridement complemented by more aggressive treatment of burn wound sepsis have reduced mortality due to thermal injuries worldwide. A focus on community education and prevention campaigns has reduced the incidence of burns in the paediatric population. Burn care, once a Cinderella specialty, has become a well focused multi-disciplinary specialty in its own right. The critical care specialist involved in the care of the burn patient has a central role in the co-ordination of the multi-system disease state that burns represent.

This review will summarise some of the more significant changes that have occurred in the field of burn care. These have resulted in improved survival and functional status. It highlights innovative fields of research which may be responsible for further improvement in outcome.

Changing epidemiology of burns

WHO estimates that fire-associated burns alone directly resulted in over 320,000 deaths in 2002. In the USA, approximately one million children sustain burns each year. Mortality in these patients follows a bimodal pattern of early and late deaths. Causes of early death include refractory shock, inability to obtain a safe airway or

provide adequate oxygenation, co-existent trauma, non-survivable carbon monoxide poisoning and decisions that injuries are non-compatible with recovery, leading to therapy withdrawal. With improved resuscitation strategies, 95% of patients survive the early resuscitation phase. Late deaths are secondary to sepsis, usually associated with wound infection, and multiple organ failure.^{1,2}

Aetiology varies with the patient population and specific at-risk groups. Young children and the elderly are specifically at risk, which is partly explained by their poor co-ordination. The at-risk paediatric population also has a bimodal distribution. Toddlers are unaware of risks posed by “extinguished” campfires, barbeque plates, hot water and similar heat sources, whilst older children (particularly boys) are knowingly involved in risk-taking behaviour associated with flames. In the elderly population (>65 yrs) contact with flame is the main cause of injury, followed by cooking accidents. Many of these injuries are a reflection of declining physical and psychological ability.³ Age is well recognised as an independent predictor of mortality in this group.⁴

Advances in fluid resuscitation

The capillary leak associated with an acute burn, compounded by loss of the skin barrier, causes a vast deficiency of intravascular fluid in the first 24 hours after a burn injury. Delay in resuscitation can lead to a secondary injury to the burn penumbra, extending both the depth and size of burn. Both of these are major contributors to eventual mortality.

Burn shock was first described by Underhill in the 1930s following his study of the Rialto Theatre fire, and modern principles of burn resuscitation had their origins in the Coconut Grove Disaster in the USA. In the early 1940s, Cope and Moore developed a fluid resuscitation protocol called “body-weight burn budget formula” after their involvement in the Coconut Grove disaster.⁵ This was followed by the Evans formula, subsequently modified to what is now known as the Brooke formula. Baxter and Shires, following original work on a canine model, developed the Parkland formula. This is the most commonly used burn resuscitation formula guiding fluid therapy in the first 24 hours post burn injury. The attraction of the Parkland formula lies in its simplicity, ease of use in the community and delivery of an adequate amount of salt, fluid and free water therapy. It must be remembered however, that these formulae exist as a framework and other injuries, such as presence of smoke inhalation, other trauma and inadequate response to resuscitation may necessitate deviation from the suggested fluid requirements. These formulae are summarised in Table 1.

In the first 16 hours following the burn, fluid therapy is solely of crystalloid, with colloids introduced after this period. Colloids have no advantage over crystalloids in

Table 1
The commonly used crystalloid formulas

Crystalloid formulas	Infusate	Formula	First 24 hours	Second 24 hours
Parkland	Ringer's Lactate	4 ml/kg/ % burn	½ total volume given in first 8 hours and ½ over the next 16 hours	5% Dextrose and 0.5 ml/kg/% burn Colloid supplementary infusion
Modified Brooke	Ringer's Lactate	2 ml/kg/ % burn	½ total volume given in first 8 hours and ½ over the next 16 hours	0.3-0.5 ml/kg/% burn colloid and 5% dextrose

maintaining circulatory volume in the early resuscitative phase. Concerns about the use of colloids were raised following the publication of a meta-analysis. (Cochrane Injuries Group Albumin Reviewers, *Br Med J* 1998; 317:235-240.) This led to patients receiving fluid volumes greater than the Parklands formula. This “fluid creep” has the potential for significant consequences, including abdominal and extremity compartment syndromes, severe pulmonary insults and extension of burn depth.⁵ It has now been recognised that this meta-analysis was flawed, being based on very diverse and old studies. A recent double-blinded randomized control trial comparing the use of albumin and crystalloid in the treatment of general ICU patients, confirmed that there was no detrimental effect associated with 4% albumin, when it was used appropriately in the general ICU population.⁶ Whilst the study excluded burns, there is no good data which supports the exclusion of albumin-based fluid as part of a balanced fluid resuscitation protocol following initial resuscitation.

There has been a resurgence of interest in oral resuscitation in the treatment of moderate burns (<40% TBSA) in the wake of terrorist induced mass burn situations such as 9/11 and the Bali disaster.⁷ In the 1960s, Sorensen et al managed all patients admitted to a burns unit over a 16 month period by oral salt containing fluids. They reported successful resuscitation of patients with up to 45% TBSA burns with oral fluids in the majority of patients.⁸ Unfortunately, details on the volumes required are limited in the paper, and the incidence of ileus in larger burns may diminish the applicability of this simple technique in the pre-hospital or mass casualty situation. This technique may be of use in younger patients with smaller TBSA burn, allowing more aggressive IV resuscitation of more critically injured patients who are at greater risk of tissue ischaemia and end organ dysfunction.

Resuscitation with hypertonic saline has been trialled by a number of groups. Purported benefits include sustained reduction in peripheral and visceral oedema, improved myocardial function, better organ perfusion and possibly a reduction in the incidence of compartment syndromes.⁹⁻¹¹ However, the potential for renal dysfunction, increase in intestinal permeability and the lack of a clear positive impact on outcome have limited the adoption of this form of resuscitation in burns.^{12,13} In those studies that have demonstrated a successful use of hypertonic saline without hypernatraemia, silver nitrate soaked dressings are often employed. These possibly leach away sodium through the eschar.¹⁴

End points of resuscitation

The optimal end points for burns resuscitation continue to generate much debate. Despite the administration of fluid therapy according to prescribed guidelines, problems frequently noted at the end of the burn resuscitation are generalized oedema, decreased efficiency of pulmonary gas exchange, hypoalbuminaemia and intermittent episodes of hypotension and oliguria. Some problems may indicate over resuscitation, whereas others are suggestive of ongoing hypovolaemia. Clinical examination, together with assessment of end organ perfusion (urine output $\frac{1}{2}$ to 1 ml/kg/hr; intact sensorium), is the minimum assessment possible to guide burn resuscitation. Pulmonary artery catheters and other more invasive forms of monitoring of haemodynamic parameters have not been shown to improve outcome in surgical, medical or burns patients.

Both subcutaneous and splanchnic oxygenation are sensitive indicators of evolving haemorrhagic shock, and have been used in burn care to monitor tissue oxygenation

indices during burn shock and resuscitation.¹⁵ Recently, Rivers et al investigated the use of central venous oxygen saturation (ScvO₂) as part of a package to guide therapy for severe sepsis, and showed an improvement in outcome when it was used in a single centre.¹⁶ However, the role of ScvO₂ to guide resuscitation of burn shock is not established. A single centre Australasian study is planned.

Smoke Inhalation

Inhalation injury is a major contributor to mortality in burns. The presence of inhalation injury is a greater contributor to overall mortality and morbidity than either percentage BSA burn or age. Smoke inhalation is present in approximately 22% of all burns and increases to greater than 60% when a central facial burn is sustained. Isolated smoke inhalation injury is uncommon. Whilst the mortality associated with cutaneous burns has fallen dramatically, a similar trend has not been reflected in inhalation injury. Difficulties in diagnosis and quantification of the injury and delay in symptom presentation account for some of these problems.

The main contributor to the pathophysiology of smoke inhalation is the particulate matter. Carbonaceous particles, impregnated with a variety of toxins, are carried to the alveolar level. These particles and associated chemicals induce pulmonary oedema, can precipitate bronchospasm and induce degranulation and autolysis of pulmonary macrophages, which rapidly result in hypoxaemia. They can in isolation result in systemic inflammatory response syndrome (SIRS). Combustion of organic material in oxygen-depleted environments, such as enclosed spaces, can also result in poisoning by products of incomplete combustion including carbon monoxide and cyanide, both of which can be fatal if the diagnosis is missed.

New therapies in smoke inhalation

Smoke inhalation may result in a requirement for mechanical ventilation. Formation of casts composed of proteinacious exudates and necrotic cellular debris results in heterogeneous lungs, with some bronchi almost completely occluded and some normal. Atelectasis, raised airway pressures, shunt and ventilator induced lung injury occur. Airway and ventilatory management (including indications for tracheostomy) of these patients are similar to the management of acute lung injury from other aetiologies. Wide bore tracheostomy tubes, bronchoscopy and airway toilet are needed more frequently in the smoke inhalation group because of the possible presence of large airway casts. Some groups have used high frequency oscillatory ventilation in patients with refractory hypoxaemia following smoke inhalation and have reported some success, but no randomised studies exist.

A pro-coagulant tendency has been identified in animal models of smoke inhalation.¹⁸ This is consistent with previous studies which show there is some benefit from nebulised heparin.¹⁹ At present, many studies evaluating the use of both fibrinolytics and endogenous anticoagulants administered systemically and through inhalation are underway in animal smoke-inhalation models. Pending the results of these trials, some recommend the use of nebulised heparin.

Management of the Burn wound

Topical treatments

Patients with major burns are at risk from both cutaneous and extra-cutaneous

infection. Prior to the routine use of topical antimicrobial agents (TAAs), burn wound sepsis was causative in 60% of all burns patient deaths. The routine application of topical silver nitrate in 1965²⁰ rapidly reduced this figure to 28%. This was further diminished by the addition of mafenide acetate and silver sulphadiazine (SSD) to the therapeutic armamentarium. Despite these interventions and more potent systemic antibiotics, infection remains a leading cause of morbidity and mortality in burns patients.

The rise of multi-resistant and pan-resistant bacteria, such as the *Acinetobacter* species, in the burns population has seen the demise of topical antibiotics. Hence a variety of silver dressings are the mainstay of topical antimicrobials. Silver has broad antimicrobial gram-negative and positive activities, as well as antifungal properties. Development of bacterial resistance to silver is uncommon. Topical silver therapy has limited side effects; silver toxicity or argyrosis is uncommon and resolves with cessation of the therapy.

The most commonly used antimicrobial in the developed world is SSD. In Australasia, SSD is combined with chlorhexidine. This improves its anti-microbial efficacy, but at the expense of a significantly increased cytotoxic profile.²¹ However, the pain induced by SSD, the potential for inadvertent dislodgement of the newly developed keratinocytes with daily dressing changes and the potential delay in wound closure from its cytotoxic effects have led to a waning of enthusiasm for SSD. Nanocrystalline silver dressings are now utilised in many countries.²² This unstable silver is released from a moist fabric mesh, does not have to be washed or scrubbed off and has an adequate antibacterial and anti-fungal profile. Cerium dressings are popular in the United Kingdom and there are some reports that their application may allow chelating of toxic products of the burn wound, diminishing the development of SIRS in large burn wound.²³

Skin substitutes

Early excision of burn wound and provision of skin cover have been shown to improve mortality in adult burn patients, improve cosmesis and potentially reduce infection.^{24, 25} Improved infection control and better anaesthesia and critical care have allowed surgeons to debride the complete wound in one sitting. However, this predicates that adequate skin cover is available to cover the wound and, frequently, there is not enough donor skin to be harvested to cover this newly debrided area. In this context, biotechnology and skin substitutes have greatly assisted. Although techniques of very thin donor skin can be applied to allow repeated harvesting from the same site, frequently wound coverage cannot be achieved immediately. Allograft (preserved cadaveric skin) is an effective temporary covering, which reduces wound colonisation, induces neovascularisation and improves subsequent graft uptake, until it is rejected.

Alternative Wound coverings

Temporary skin substitutes provide physiological cover, reducing all the physiological perturbations associated with loss of part of the skin, the largest body organ. This can assist with fluid balance, analgesia and infection control, as well as better wound bed preparation. There are a number of permanent skin substitutes, derived from both animal and human tissue. These include Integra™, a combination of bovine collagen and shark chondroitin 6 sulphate, which can create a new dermis onto which

thin autograft can be placed, and Transcyte™, a sheet of freeze dried neonatal foreskin fibroblasts.

Cultured epithelial autograft (CEA) requires a biopsy of the patient's skin as soon as possible post-injury. The resultant cells are cultured in the laboratory prior to their application in a sheet or spray to the same patient. Whilst there are a number of very keen enthusiasts, no studies have shown an improved outcome with these techniques. The spray cell technique is not used widely in Australasia.

The hypermetabolic response

Pathophysiology

The initial response post burn injury is a brief period of reduced metabolism, with low cardiac output, coupled with low extraction fractions of oxygen and impaired glucose tolerance. This is a classical pattern seen in early shock states. Following the immediate resuscitation period, this hypometabolic phase converts to a hypermetabolic one — the so-called “Ebb and Flow”. The process of healing wounds, heat losses from denuded skin and replacement of growing tissue, together with a co-ordinated immune response combined with the endogenous catecholamine excess, all require huge calorific requirements. The degree of hypermetabolism is proportional to the surface area of the burn, presence or absence of sepsis and extent of debridement carried out.²⁶

The vast majority of increased metabolism occurs in liver and muscle and this is associated with an alteration of ATP utilisation in pathways including proteolysis and gluconeogenesis. These pathways are partially responsible for the rise in body temperature of up to 2°C, seen in many patients. Protein loss is prolonged and significant, continuing for up to a year post injury. Alterations in gut permeability resulting in a protracted protein losing enteropathy have been described.²⁷ The aims of the team treating a major burn should include optimisation of the local environment, appropriate support of the hypermetabolic phase and correction of modulators of further hypermetabolism, such as burn wound sepsis and endogenous catecholamine excess.

a) Environmental modification

The body uses large amounts of energy to maintain normothermia, a problem compounded by the attempt of the body to raise the temperature to almost 39 degrees. In large burns, maintenance of a thermoneutral environment dramatically reduces energy use by the body from 2 to 1.4 times resting energy expenditure.²⁶ Defence of normothermia should be one of the goals during the initial resuscitation management in ICU and whilst being optimally and aggressively debrided in theatre. Simple dry wound dressings such as “Glad Wrap” in the field, warmed fluid resuscitation, single room temperature control to a thermoneutral environment and cover of all extremities as soon as possible following dressing changes can achieve the majority of these aims.

b) Dietary support of hypermetabolism

The degree of hypermetabolism varies depending on size of injury, extent of debridement and the presence or absence of SIRS. A patient with a burn of 40% BSA can lose up to 25% total body weight within three weeks, if not optimally supported.²⁸ Whilst catabolism is increased, excess feeding can be deleterious. Excess glucose administration (>5 mg/kg/min) results in fatty liver, increased CO₂ production and

resultant work of breathing. Attempts at equalling the derived metabolic rate using a combination of enteral and parenteral nutrition resulted in increased mortality, diminished immune function and impairment of liver function.²⁹ Optimal practice includes the commencement of enteral feeds as soon as practically possible with available enteric formulation. A delay in commencement of feeds increases the risk of gastroparesis.³⁰ Attempts should still be made to provide the patient's calculated caloric requirements, with balanced protein and carbohydrate contents. Carbohydrate enhances insulin production and hence muscle protein synthesis. Protein catabolism is approximately 50% higher in burn patients compared to fasting healthy individuals. On that basis, increasing the protein input from the normal recommendations of 1 g/kg to 1.5 g/kg may be beneficial. Even higher ratios have been used in burned children, but this resulted in increased urea production and no improvement in muscle mass.

c) Closure of Wound

One of the main engines driving the hypermetabolic response is the burn wound. Maximising early excision, minimising cutaneous sepsis and early skin cover dramatically reduce the degree of hypermetabolism.³¹

d) Endocrine manipulation of hypermetabolism

The cytokinaemia from burn injury contributes to SIRS and hypermetabolism. Their effects are heightened by the presence of infection and the cytokines which leach from necrotic cells in the non-debrided wound. There are a number of evidence based strategies modulating the endocrine response to burn injury, which have been shown to improve these situations.

Growth hormone

Growth hormone is frequently deficient post burn injury.³² Its effect, directly and through IGF-1 in health, is to increase appetite, reduce nitrogen losses and speed up wound healing, decrease respiratory quotient and increase oxygen utilisation. Furthermore, the anabolic benefits seen in GH administration are largest in catabolic patients. Data on treatment of paediatric and adult patients with critical illness and burns are confusing and contradictory. Studies in which critically ill patients without burns show increased mortality are not reflected in the burns literature.^{33, 34}

Anabolic steroids

Oxandrolone, a synthetic steroid analogue of testosterone with a much diminished side effect profile, has been shown to improve weight gain and urinary nitrogen balance. In a recent RCT, the lean body mass and regained weight which occurred with oxandrolone treatment were maintained at 6 months following cessation of the drug, whereas lost lean mass had not yet been regained in the control group.³⁵ Other studies in similar patient groups have shown no increase in liver dysfunction.³⁶

e) Beta adrenergic blockers

The hypermetabolic phase of burn injury is associated with vast increases in circulating catecholamines. Attempts have been made to modify the hypermetabolic response through the use of beta blockers. Their benefits include a reduction in thermogenesis, tachycardia and resting energy expenditure. In a recent study, 25 paediatric patients with large burns (>40%) were randomised to control or oral

propranolol groups, aiming for a decrease in HR by 20%. Net protein balance increased by >80% in the experimental group ($p=0.002$), as opposed to a drop by >20% in the control group ($p=NS$). A reduction in resting energy expenditure and HR was also noted.³⁷

Whilst total blockade of beta adrenoreceptors has been shown to reduce hypermetabolism in laboratory animals, it also increased the mortality. Acute beta receptor blockade has been shown to reduce appearance of free fatty acids (FFA), which raises concerns as FFA is an important substrate in the stressed burn patient. Furthermore, catecholamines have been shown to induce a direct anabolic effect, so it is possible that blocking their action could lead to increased protein loss.

In practice, beta blockers should be considered in burns patients who, after the initial resuscitation phase, remain tachycardic in the face of appropriate fluid replacement. Many clinicians aim for a drop of approximately 20% in the basal heart rate as an appropriate response to therapy.

f) Insulin

Insulin may be used as an anabolic agent. Its use, combined with carbohydrate and aiming for normoglycaemia, resulted in a reduction in wound healing times and induced muscle protein synthesis.^{38, 39} Smaller doses of insulin have been shown to induce anabolism.

g) Glutamine

Enteral glutamine administration has been an area of research in trauma patients, and has shown promising results. There is increasing literature supporting its use in patients with severe burns. A recent small single-centre double-blinded randomised trial showed a significant reduction in infectious complications and mortality ($p<0.05$) in patients with severe burns.⁴⁰

Conclusion

Burn injury continues to be a major cause of morbidity and mortality in the paediatric and adult population in both developed and developing countries. There has been a reduction in the incidence of early deaths, due to improved critical care and surgical techniques. Late deaths have also declined, due to improved antimicrobial therapies and dressings. Minimal improvements have been seen with respect to smoke inhalation, despite many promising animal studies. The chronic morbidity associated with scar formation, frequently a massive burden in a patient surviving a large burn injury, continues to be an area of huge research effort. The advent of synthetic biological membranes and cell culture shows great promise.

The cost of treating burn injury remains huge and beyond the resources of all but the most advanced countries. Education, prevention campaigns and smoke detector usage will continue to be the most cost-effective way to treat these devastating injuries — to prevent rather than to cure.

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