The modern management of burns

Heather J Cleland

Abstract

- The risk of dying as a result of a burn injury has decreased significantly in the past 50 years.
- Although the pathophysiology of burns shock and the need for large volumes of fluid resuscitation in major burn injuries has been recognised since the 1940s, there is ongoing debate regarding the ideal fluid for resuscitation and the best determinants of rates of administration.
- The oral route for fluid resuscitation has been largely ignored in the literature, despite potential advantages of this approach in many situations.
- The principles of partial and full thickness burn wound management in modern burn care largely focus on early radical debridement of necrotic tissue and early wound closure.
- Various skin substitutes are in clinical use, although none yet developed has the attributes of the ideal replacement. The promotion of healing and recovery by modulation of the local and systemic inflammatory responses is the subject of ongoing research.

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THE CHANCES OF SURVIVING a major burn injury have increased significantly in the past 50 years, because of the combination of a number of advances in the care of the burn-injured patient. These are:

- an understanding of the acute physiology of the response to the burn injury, so that appropriate and timely resuscitation is instituted;
- improvements in supportive intensive care of the critically burnt patient;
- an ability to control and treat infection; and
- early surgical burn wound excision and closure.

Today, patients aged 15–44 years have at least a 50% chance of surviving a 70% total body surface area (TBSA) burn when treated in a specialist burns unit.

Burns comprise up to 30% of combat injuries, depending on the nature of the conflict. However, a significant proportion — up to half — of burn injuries sustained by military personnel may not be combat-related, and are amenable to preventive strategies.[1]

The logistical difficulties in delivering adequate acute burn care in resource-poor environments have long been recognised: extremely large amounts of fluids, topical antimicrobials and dressings are required to treat extensive burn injuries. Various strategies have been examined in relation to these difficulties, such as the use of oral fluid replacement for resuscitation rather than intravenous fluids,[2] and identification of patients most likely to benefit from topical antimicrobials.[3]

Although combat-related burns are frequently the result of blast injuries, and specific kinds of burns may be more likely to occur in military environments (eg, white phosphorus burns), this article concentrates on the resuscitation and management of patients with thermal burn injury, with particular reference to surgical management of the burn wound.

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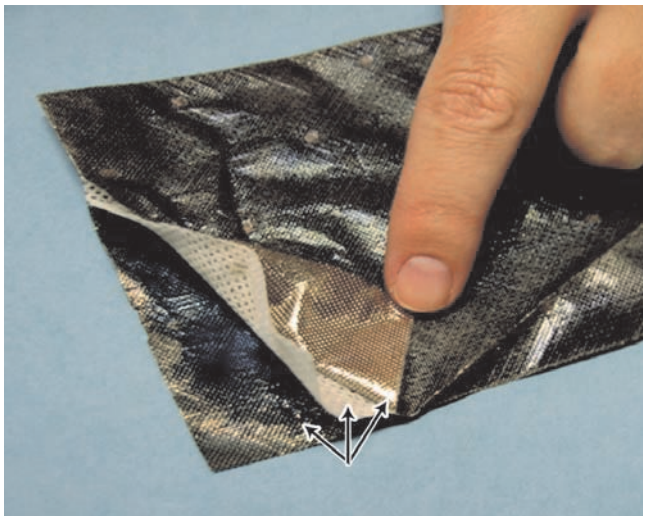
Resuscitation

Without administration of fluids, patients with greater than a 15%–20% TBSA burn will develop hypovolaemic shock. Many formulas to calculate fluid needs and types of fluid have been proposed and used over many years.

The most widely used of these formulas is the Parkland formula: 4 mL/kg/% TBSA burn given in the first 24 hours after a burn, with half given in the first 8 hours. This formula was devised after experiments in monkeys using Ringer's lactate.[4] Many reports, including from my own centre,[5] demonstrate that the actual amounts of fluid infused are often greater than the amount predicted by the Parkland formula when clinical parameters are used as a guide to the adequacy of resuscitation.

Patients with major burns develop significant generalised oedema, which may produce secondary complications, such as compartment syndrome, peripheral ischaemia, and airway compromise. Anecdotal reports that the low incidence of airway obstruction in patients evacuated to Australia from Bali after the bombings in 2002 was due to lack of fluid resuscitation[6] should not lead clinicians to delay resuscitation of patients requiring transfer: the primary determinant of mortality in burnt patients is the timing and adequacy of fluid replacement.[2] However, the dangers of over-resuscitation are also recognised,[7] and precise minimal volumes necessary in

1 Acticoat 3-ply dressing



initial resuscitation are not clearly defined. Resuscitation based on the Parkland formula and modified according to clinical parameters such as urine output, while demonstrated to be safe and effective in preventing renal failure, is associated with the need for infusion of large volumes of fluid, which results in widespread oedema, and the complications of fluid overload. It is conceivable that, if more accurate and sensitive methods of determining optimal fluid volumes and types were generally available, lower volumes could be administered and the incidence of complications minimised. Use of colloids (eg, albumin or dextran) and hypertonic saline has been associated with lower required volumes for resuscitation, and less oedema formation in some studies;[8,9] however, there is a need for further clinical trials to establish best infusion regimens for colloid use and for the use of hypertonic saline resuscitation in major burns.[10]

Finally, there is evidence that enteral resuscitation alone, or in combination with intravenous fluids, is safe and effective for larger burn injuries up to 40% TBSA, although its utility may be limited by vomiting,[11] and variable absorption. The ideal composition of an oral fluid replacement for burns shock is as yet undetermined.[2]

Antimicrobial dressings

Immediately following injury, the burn wound surface is sterile, but it soon becomes colonised with the patient's normal endogenous skin flora. Gram-positive bacteria (eg, *Staphylococcus*) in the sweat glands and hair follicles may survive the injury, and will colonise the wound within 48 hours unless a topical antimicrobial is used.

After 5–7 days, other organisms colonise wounds: gram-negative and gram-positive bacteria from the host (gastrointestinal and respiratory) and from the environment.[12]

Topical antimicrobials decrease morbidity and mortality due to burn wound infection in situations where early (ie, before significant microbial colonisation occurs) burn wound excision is not practised. They decrease bacterial counts and control infection, and therefore decrease the incidence of conversion of partial thickness to full thickness wounds.

Most topical antimicrobials contain silver. Silver-containing products are bacteriocidal because of interaction between the silver and thiol groups in the respiratory enzyme in the cell. Silver also binds with DNA bases to inhibit replication, and interacts with structural proteins. It is well recognised that silver is toxic to regenerating keratinocytes, and delays healing of partial thickness burn wounds. Silver-containing products are not the dressing of choice for partial thickness burns at low risk of infection. Although there are reports of organisms that have developed resistance to silver, this occurs with much less frequency than with the use of topical antibiotics.

Silver sulfadiazine (SSD) with chlorhexidine cream (Silvazine, Smith & Nephew Pty Ltd, Melbourne, Vic) has been the most commonly used topical antimicrobial for burns in Australia for many years.

More recently, however, Acticoat (Smith & Nephew Pty Ltd, Melbourne, Vic) has replaced SSD as the standard of care in most Australian burns units. This is a 3-ply dressing (Box 1); the outer layers are a silver-coated polyethylene mesh. The silver is in the un-ionised nanocrystalline form (formed by a process of physical vapour deposition). Unlike normal silver, nanocrystalline silver dissolves in water. Un-ionised silver is less rapidly deactivated and the silver is released gradually from the dressing.[13]

Acticoat releases silver onto the wound for 3 days if kept moist. A 7-day formulation is also produced. In contrast to SSD, which must be reapplied once or twice daily for efficacy, Acticoat requires dressing changes only at 3-day intervals for ongoing antimicrobial efficacy. It is considerably less bulky and lighter than creams, and therefore poses fewer logistical difficulties in transport and storage. Heavily contaminated burn wounds should be adequately cleaned before Acticoat is applied.

Skin substitutes and burns

Cutaneous burn injuries may be partial or full thickness. Partial thickness injuries have surviving dermis with dermal epithelial elements that can proliferate to produce wound healing with varying degrees of scarring. Full thickness injuries will not heal spontaneously, and require skin replacement.

The role of skin substitutes in the case of partial thickness burns is to provide temporary wound cover while the wound regenerates.

In deep burns, skin substitutes may potentially act either as a definitive skin substitute or — in extensive burns when there

is a paucity of donor sites — be used to achieve temporary wound closure while autograft donor sites regenerate for further harvesting. Currently, no skin substitute product performs as well as autologous split skin graft for closure of full thickness burns, so skin substitutes are generally reserved for extensive injuries where there are limited donor sites for autologous grafting. In addition, the use of skin substitutes entails significantly more expense than use of autologous skin.

The characteristics of the ideal skin substitute are that it:

- is readily available in a timely fashion;
- acts as a barrier to moisture;
- acts as a barrier to microorganisms and resists infection;
- is mechanically robust and elastic;
- is adherent to or integrates into the wound for as long as required;
- produces physiological wound closure, so that ongoing inflammation in the wound is minimised and healing promoted; and
- is non-antigenic, and does not carry a risk of disease.[14]

Currently, an ideal skin substitute is not available; however, various (non-ideal) alternative and adjunctive products are available for use in treatment of patients who have suffered significant burn injury. These may be classified as biological skin replacements (including allografts and xenografts), and bioengineered skin substitutes (including autologous cultured and non-cultured products, and biosynthetic skin substitutes).

Biological skin replacements

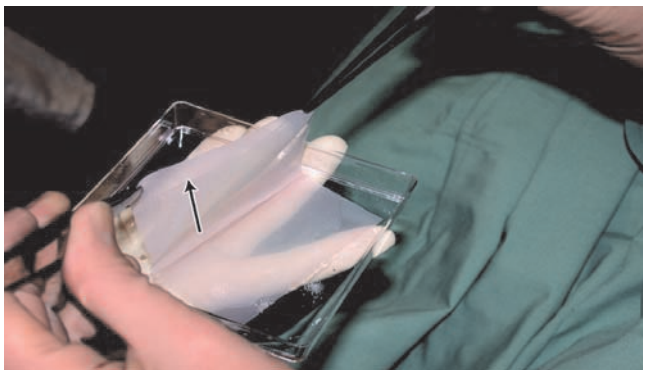
Allografts are allogenic, and following engraftment are rejected after a period that depends mostly on the immune status of the individual. In unwell, immunocompromised patients, allograft skin may be tolerated for some weeks, but this is unusual in modern burn care, and allograft skin is frequently sloughed within a few days of engraftment. The dermal component of an allograft is much better tolerated than the epidermal, which is mostly responsible for rejection. Hence, the dermal element may persist, and act to minimise wound contracture and scar formation after autologous grafting. Commercial preparations of human dermis are also available in some countries for use in this way (eg, Alloderm, LifeCell Corporation, Branchburg, NJ, USA), but are not commercially available in Australia.

Allograft skin is used for temporary wound closure after full thickness burn excision, or as a biological dressing to promote healing of partial thickness burns. Cryopreserved allografts remain viable, in contrast to glycerol preserved allograft.

The Donor Tissue Bank of Victoria supplies frozen allograft skin to Australian burns units. There is a need for extension of the activities of the Victorian Donor Tissue Bank to encompass harvesting of donor skin in all Australian states and territories, if a true "bank" of skin is to be available and contain adequate supplies for mass casualty burn events. Currently, a proposal to enable the establishment of this service has been submitted to an intergovernmental subcommittee of the Australian Health Ministers' Advisory Council.

Xenografts are commercially available in many countries, but not in Australia. They are commonly of porcine origin, and supplied as a processed, de-epidermised product used as a biological dressing.

2 A cultured epithelial autograft



Bioengineered skin substitutes

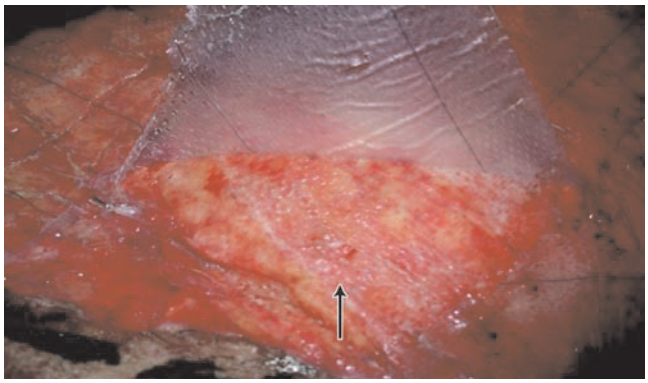
Autologous cultured and non-cultured products

The technique of keratinocyte culture was described more than 30 years ago,[15] and since then cultured epithelial autografts (CEA) have been used in many clinical centres. The main disadvantages of CEA, especially in relation to their use in burn-injured patients, are well recognised. They take weeks to produce, are destroyed easily by infection, and, in the absence of intact dermis, lack structural integrity (Box 2). However, in individual clinical situations, they may be a useful adjunctive treatment.

Because of the delay and other disadvantages entailed in production and use of sheets of CEA, there has been interest in the application of preconfluent keratinocytes (cultured or non-cultured) to wound beds. These cells are less differentiated, and theoretically may have a higher proliferative and wound-healing potential than CEA sheets. However, they cannot be expected to heal a full thickness wound in which there is no dermis. Therefore, they have been used in association with meshed skin grafts, or applied to partial thickness wounds to promote healing. Solid clinical evidence of their efficacy is lacking.[16]

The problem of combining living cells and a supporting dermal substitute matrix to produce a living skin equivalent is not yet solved. In-vitro construction of artificial "skin", consisting of a scaffold or matrix and keratinocytes and/or fibroblasts, has been pursued in several centres. None is generally available for routine use in burn patients. Revascularisation of these constructs is a major issue, and a vasculature may need to be incorporated into their structure if these products are to behave as predictably as autologous skin grafts.[14]

3 Integra



The arrow indicates the vascularised dermal template after the silicone "epidermal" layer has been removed.

Biosynthetic skin substitutes

Various products are currently available to produce physiological wound closure until the epidermal layer of a partial thickness burn wound has repaired or, after extensive deep burn excision, until autologous skin is available for skin grafting of a full thickness wound.

Of these, Integra (Integra LifeSciences Corporation, Plainsboro, NJ, USA), Biobrane (Smith & Nephew Pty Ltd, Melbourne, Vic) and TransCyte (Advanced BioHealing Inc, La Jolla, Calif, USA) are available in Australia, and in clinical use in many burns units. TransCyte production has recently ceased, and at this stage it is not clear if it will continue to be manufactured for commercial use.

Integra is designed to incorporate permanently into the wound bed and produce a neodermis, which is able to support an epidermal graft or thin split skin graft. It consists of a dermal replacement layer of bovine collagen and glycosaminoglycan, and a sialastic epidermal replacement layer, which is removed after the dermal layer has revascularised (Box 3) and can then be grafted. It is used in the management of extensive acute burns, when there is insufficient donor skin immediately available. There is a considerable learning curve associated with its successful use, and it is much more susceptible to infection and failure to adhere than autologous skin.

Biobrane is a dressing that consists of a semipermeable silicone membrane which has been mechanically bonded to knitted nylon fabric. Embedded in the structure are peptides derived from porcine dermal collagen. This produces a dressing that tends to adhere to the wound and acts to control water vapour loss across the dressing (Box 4). Its main use is as a dressing for extensive partial thickness burns.

TransCyte consists of a nylon mesh coated with porcine dermal collagen bonded to a silicone polymer membrane. Neonatal human fibroblasts are cultured on the nylon mesh. The fibroblasts secrete dermal collagen matrix proteins and growth factors. The product is supplied frozen, and no viable cells remain in the dressing.

It adheres to the wound, contains growth factors, and suppresses inflammation, producing physiological wound closure. It can be used as a dressing for partial thickness burns, and will reliably adhere to full thickness excised wounds, for weeks if necessary, until donor sites are available for grafting and it can be replaced (Box 5).

A recent systematic review of the use of bioengineered skin substitutes for the management of burns revealed a paucity of clinical trials.[17] The efficacy and safety of these products is at present undetermined. Although several are available for clinical use, and seem to be valuable adjunctive treatments in many situations, there is little good quality clinical evidence to confirm indications for their use and establish their effectiveness for improving outcomes. Their use should be confined to specialist centres, in the context of defined clinical pathways or clinical trials.

Management of the burn wound

Deep burns

Modern burn wound management is now well established on the base of early excision and grafting of deep burns.

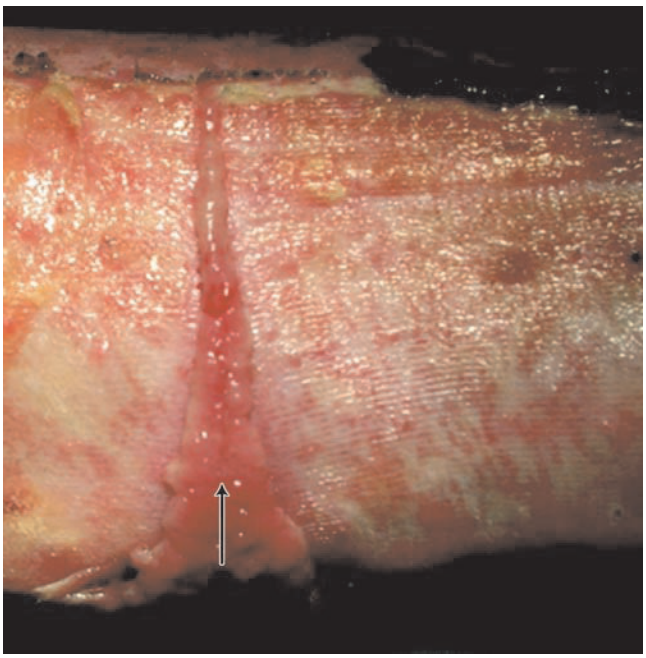
The policy of surgical management in our burns unit is based on early surgical excision of the burn. In fit, stable patients with major burns (> 30% TBSA) who are transferred acutely to the unit, immediate excision is performed. In effect, the policy is one of immediate transfer to the operating theatre from the emergency department. The patient is resuscitated pre- and intraoperatively by anaesthetic staff. The main challenge in pursuing this surgical strategy is maintaining body temperature.

The excised burn wounds are closed temporarily with cadaver skin or a synthetic skin substitute (eg, Biobrane), or else dressed with Acticoat. Depending on autologous skin

4 Biobrane

The arrow indicates the Biobrane, applied to an acutely debrided partial thickness burn. A meshed split skin graft to an excised deep burn is adjacent to the Biobrane.

5 TransCyte



TransCyte on an excised burn wound 3 weeks after application. The TransCyte is adherent, and the wound is quiescent and physiologically "closed", as evidenced by lack of granulation tissue except in the area between the two pieces of TransCyte (arrow).

availability, definitive wound closure should occur around 48 hours post-excision.

Unstable patients and those with significant comorbidities generally do not undergo acute excision of burns, but are operated on once stabilised; usually 24–48 hours after transfer. The literature suggests that early surgery is associated with a lower mortality in patients without inhalation injury;[18] however, the definition of "early" varies from unit to unit.

Partial thickness burns

The appropriate management of partial thickness (mid-dermal) wounds is less clear, in part because of the difficulty of assessing the depth of these burns in the first day or two after injury. This difficulty has led to the tendency to adopt a wait and see attitude — dressing the burn until it becomes clear whether it is going to heal within a couple of weeks. It is well recognised that burns that acutely appear to be perfused often show delayed healing and require grafting.

This phenomenon is known as burn wound progression, and the histopathological correlate is the Jackson burn wound model, which describes three zones of a burn wound:

- a central zone of coagulation, where everything is dead;
- a mid-zone of stasis, which tends to progress to tissue necrosis in non-superficial wounds (ie, the deeper dermal burns); and
- a surrounding zone of oedema and inflammation.

Animal models suggest that progression of the burn wound, with increasing tissue ischaemia and tissue death, occurs for at least 48 hours after injury. Its basis seems to be the development of oedema and vascular occlusion due to vasoconstriction and thrombosis.[19]

In addition, the burn wound is increasingly conceptualised as an injury characterised by an exaggerated inflammatory phase, which persists beyond that required for optimal healing outcomes. The ability to influence these processes (oedema formation and inflammation) is particularly relevant when dealing with extensive injuries, when promotion of spontaneous healing may be lifesaving; not only by promoting earlier spontaneous wound closure, but also by preventing the development of a systemic inflammatory response.

Several strategies are theoretically attractive: pharmacological treatment, hyperbaric oxygen, and topical negative pressure.

Pharmacological treatment

Experimentally, there has been a mostly pharmacological approach to trying to minimise oedema, dermal ischaemia and inflammation.

Catecholamines, oxygen free radicals, prostaglandins, and various cytokines (eg, tumour necrosis factor and interleukin 1) have all been targeted for manipulation. Although laboratory studies have frequently been promising, positive effects in the clinical situation have not been demonstrated.[20]

Hyperbaric oxygen

Hyperbaric oxygen was first suggested as a treatment for burns more than 40 years ago, when it was noted that burnt miners being treated for carbon monoxide poisoning healed more quickly than initially expected.

Experimentally, hyperbaric oxygen has been shown to decrease burn wound oedema, improve microcirculation, and reduce the inflammatory response, resulting in faster re-epithelialisation and healing.

Various mechanisms for these effects have been postulated:

- gross hyperoxia decreases microvascular obstruction by inhibiting the leukocyte activation that occurs with endothelial injury (this effect persists for some hours);
- an osmotic effect of oxygen may enhance oedema resolution; or
- various immune and healing functions may be improved (eg, enhanced phagocytosis).

A Cochrane review in 2004 revealed a paucity of high level clinical data. Although it seems that there is an effect on the pathophysiology of burns, this did not translate into definite evidence of decreased length of stay, mortality, or number of surgical procedures, in the only two randomised controlled trials found. Nevertheless, various comparative studies and case series lend support to the idea that hyperbaric oxygen may be a useful adjunctive therapy. There is a need for a multicentre trial to get a series with enough power to detect clinical differences.[21]

Topical negative pressure

Topical negative pressure is another theoretically attractive way to promote burn wound healing, by reducing oedema, and perhaps by a direct effect on cellular activity.[22]

We recently conducted a systematic review of the topic of negative pressure treatment in burns. Three clinical studies were identified, but all had serious methodological shortcomings. Nevertheless, topical negative pressure potentially results in increased blood flow, decreased oedema, and fewer grafting procedures. Again, there is a need for well designed studies with appropriate controls.

Recommmended treatment for partial thickness burns

In the absence of any proven therapies to promote healing of partial thickness burns, the approach should be to remove necrotic tissue and dress the wound with a non-cytotoxic dressing that will provide protection from infection, have an anti-inflammatory effect, and promote healing.

Significant mid to deep dermal burns require acute aggressive surgical debridement, generally under general anaesthetic, to remove as much dead tissue as possible, while preserving potentially viable tissue. In general, tangential excision is not suitable for these wounds in the first few hours, as it is not accurate enough to preserve all potentially viable elements. Dermabrasion to bleeding tissue is preferable. Enzymatic debridement has also been described. The recently developed Versajet Hydrosurgery System (Smith & Nephew Pty Ltd, Melbourne, Vic) may prove to be suitable for more acute accurate debridement of partial thickness burns.

Once all frankly necrotic tissue has been removed, the wound must be dressed. The traditional silver sulfadiazine dressing no longer constitutes the standard of care for these wounds after debridement, as it is cytotoxic, does not suppress inflammation, and delays healing. TransCyte or Biobrane are preferable dressings.

If an antibacterial dressing is required, Acticoat may be used alone or in conjunction with these products.

Conclusion

The modern approach to burns management has focused beyond prevention of infection and grafting of deep burns to an approach that emphasises prevention of burn wound progression and modulation of inflammation, to promote rapid healing with minimisation of scarring.

Competing interests

None identified.

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