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## Wound Coverage Technologies in Burn Care: Established Techniques

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### Abstract

Major advances in burn care have reduced post-burn morbidity and mortality. The development and incorporation of new wound healing modalities into the clinical arena have contributed to this improvement by allowing standard-of-care regimens to be established. These regimens range from early excision to the use of cultured epithelial autograft. Here, we review the wound care options that are now well established and used by many burn surgeons.

### Keywords

burn; burn care; wound coverage

## INTRODUCTION

Burn trauma is one of the worst forms of trauma and has a worldwide incidence that has risen to approximately 2 million cases annually.<sup>1</sup> Over the past decade, progress in the treatment of severe burn injuries has significantly decreased morbidity and mortality.<sup>2</sup> Improvements in survival have been most notable in severely burned pediatric patients.<sup>3, 4</sup> Burn care has seen four major areas of advances: 1) fluid resuscitation and early patient

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management, 2) control of infection, 3) modulation of the hypermetabolic response, and 4) surgery and wound care.

## BURN WOUND CARE

Extensive burn injuries are marked by chronic exposure to inflammatory mediators released by immune cells infiltrating the wound and to toxins produced by microorganisms colonizing the wound. One of the clinician's main goals is to close the wound rapidly to prevent the development of burn wound sepsis. The current surgical approach to burn care entails early excision of full-thickness burn tissue followed by early wound coverage, preferably with autologous skin graft. With the now routine incorporation of early burn wound excision and coverage,<sup>3</sup> the risk of serious systemic infection originating from the burn wound has been reduced.<sup>4</sup> Early excision performed once the patient is resuscitated and stabilized, usually within 48 to 72 hours post-burn, significantly reduces blood loss and reduces post-burn morbidity and mortality.<sup>5, 6</sup> In large burns, sufficient temporary wound coverage can be achieved by using allograft to provide protection for many weeks until enough donor sites are available for grafting. In addition, widely meshed autografts have been used with allograft overlay (i.e., sandwich technique) to provide adequate coverage. Donor sites can be used repeatedly following healing, which typically occurs within 7 to 14 days.<sup>7-9</sup> At high-volume burn centers, donor site reharvest has occurred around 7 days over the last quarter century, though many surgeons treating fewer burn injuries opt to wait for donor reharvest until approximately 14 days. However, during this time, new approaches and devices have been introduced: the use of dermal substitute Integra<sup>®</sup>,<sup>10</sup> cultured epidermal autografts (CEA) and cultured skin substitute,<sup>11, 12</sup> and human amniotic membrane as stand-alone coverage or overlay.<sup>13</sup> Here, we review the established methods used for modern day burn wound care.

## PARTIAL-THICKNESS BURNS

Partial-thickness burns are classified as superficial or deep based on the depth of injury. Superficial partial-thickness burns often form blisters, are moist, have normal capillary refill, and are painful. These wounds spontaneously re-epithelialize within 7 to 28 days from retained epidermal structures in the rete ridges and more likely, stem cells in hair follicles and sweat glands. After the wound has re-epithelialized, secondary scar maturation takes place, and this may result in long-lasting hypo- or hyper-pigmentation.

Deep dermal burns involving the reticular dermis have a pale and/or mottled appearance, have poor or no capillary refill, and are dry and less sensate. Because of the loss of the dermis, complete re-epithelialization of these burns can take up to 4 weeks. Re-epithelialization occurs through cells residing in the hair follicles, often resulting in severe scarring.

Exposed nerve endings can make these partial-thickness burns quite painful. Historically, these burns have been treated conservatively by removing the damaged epidermis and applying topical medications once or twice daily.<sup>14, 15</sup> Severe pain and anxiety may result from these procedures even when narcotics are administered.

In general superficial and full thickness burns can be treated with various burn wound dressings (Table 1). Each agent has advantageous and disadvantageous and therefore every institution has their own protocols and preference. At our burn centre we use all of these agents where appropriate. The goal is either to prevent infection/contamination or treat infection/contamination.

### **Synthetic and Biosynthetic Membranes—Biobrane<sup>®</sup>, AWBAT<sup>®</sup>, and Suprathel<sup>®</sup>**

The need for improved patient comfort, infection control, and rate of re-epithelialization has led to the development of various alternative treatments for partial-thickness burn wounds over the course of the past three decades. Semi-occlusive and synthetic membranes are the most important clinically applicable devices to have emerged in recent times. The need for frequent dressing changes is eliminated as re-epithelialization continues underneath partially occlusive dressings. As a standard of care for selection or use of these dressings has not yet been established, we discuss only the substitutes that we most frequently use in our hospitals.

The biosynthetic wound dressing, Biobrane<sup>®</sup> (Bertek Pharmaceuticals, Morgantown, WV, USA), is constructed by chemically adhering collagen to nylon fabric embedded in a silicone film. Sera and blood clot within this matrix, forming a tight bond with the wound so that the fabric adheres until epithelialization occurs and the Biobrane<sup>®</sup> falls off. Biobrane<sup>®</sup> controls water vapor transfer and maintains a moist healing environment. Since 1982, numerous studies have shown that it is useful for the treatment of partial-thickness burns, particularly in pediatric patients.<sup>16–22</sup>

A newer biosynthetic product, AWBAT<sup>®</sup> (Aubrey Inc., Carlsbad, CA, USA), became commercially available following FDA approval in 2009. AWBAT<sup>®</sup> has many similarities to Biobrane<sup>®</sup>. Both incorporate a thin, porous medical-grade silicone membrane and have elasticity facilitating easy application. In addition, they both have a structure that enables the egress of excess wound exudate through the skin substitute into a sterile outer wrap, where it is absorbed. Finally, both incorporate collagen peptides, which improve adherence to the wound by binding to fibrin. The main difference between the two membranes is the pore size. AWBAT<sup>®</sup> is about 500% times more porous than Biobrane<sup>®</sup>. The greater porosity of AWBAT<sup>®</sup> may improve transfer of exudate from the wound surface, possibly resulting in better acute adherence and a shorter healing time. Nevertheless, clinical experience with this new membrane is limited.<sup>23, 24</sup>

Suprathel<sup>®</sup> (Wound Source, Allentown, PA, USA) is a synthetic copolymer comprised of >70% DL-lactide polymerized with methylenecarbonate and  $\epsilon$ -caprolactone to yield a membrane with pore sizes ranging from 2 to 50  $\mu\text{m}$  and an initial porosity of over 80%. It also boasts high plasticity and water permeability. After application to the wound bed with an overlay of paraffin or non-adherent gauze, the Suprathel<sup>®</sup> peels off within approximately 2 weeks as the re-epithelialization of the wound bed progresses.<sup>25</sup> Prospective randomized clinical studies of partial-thickness burns and split-thickness donor sites have shown that use of this membrane is associated with reduced pain, though wound healing times and long-term scar qualities are comparable to those seen with the use of other commercially available membranes.<sup>25–27</sup>

## Biological Covering—Amnion

The use of the human amnion as a bio-dressing has endured for centuries but was not embraced by western medicine until the beginning of the last century. Following Davis' incorporation of amniotic membrane into skin transplantation in 1910, Sabella used amnion to treat burn wounds.<sup>28</sup> However, the lack of suitability of amnion as a permanent skin substitute was soon realized, leading to its use as a temporary wound dressing. As a temporary biological dressing, amnion is effective due to its ability to reduce pain, accelerate wound healing, and reduce infection.<sup>28–34</sup> By 1952, the protocol for applying amnion as a temporary skin substitute to burn wounds was published.<sup>35</sup> Since this time, amnion has primarily been used to treat partial-thickness burns. Because amnion is particularly easy to manipulate, it is especially useful for treating second-degree facial burns.<sup>32, 34, 36, 37</sup>

The use of amnion in burn patients has expanded over the past 20 years. Processing techniques have been standardized so that they are reliable and improve the quality and safety of amnion. The establishment of amnion banks in cooperation with already existing tissue banks has enabled provision of safe, sterile amnion in several countries.<sup>38–40</sup>

Basic properties of amnion, such as its thinness, pliability, moldability, durability, and ability to be easily removed, make amnion especially attractive for use in the pediatric burn population. Branski et al.<sup>13</sup> found that infection rates associated with use of amnion were no higher than those seen with standard dressings and that the rate of wound healing was similar in both groups. Moreover, long-term cosmesis was not impaired by amnion use. The advantage of this treatment was that significantly fewer dressing changes were required.

Following establishment of amnion banks, there has been a push towards commercial availability of amniotic membrane. Commercially available amniotic membranes can now be found in either fresh-frozen form (Grafix™, Osiris Therapeutics, Inc., Columbia, MD) or glycerol-preserved form. However, use has been limited, and these products have not become the standard of care.

Another benefit of using amnion is that it may harbor live cells, including stem cells, which release growth factors that improve wound repair. The use of these stem cells to augment wound healing has tremendous potential but is still in early investigative stages.

## FULL-THICKNESS BURNS

Full-thickness (third-degree) or deep-dermal burns, which will not heal within approximately 14–21 days, are best managed by immediate full excision followed by autograft coverage. In use since the 1970's, early excision and grafting has become the standard of burn care. In the extensively burned patient, coverage with autograft is sometimes not possible, necessitating the use of homograft (allograft) or dermal substitutes.

### Skin Grafting

If the burn affects only a small area, there are options how this area can be covered: sheet split thickness vs. meshed split thickness vs. full thickness sheet. The gold standard for large burns is meshed (1:2 or 1:4) split thickness autograft. Sheet split thickness is used for small

burns or cosmetically important areas such as face, neck, hands, fingers and possibly feet/toes. Full thickness skin grafts are not widely used for acute burn surgeries but often used for burn reconstruction. In burn reconstruction, split thickness and full thickness skin grafts are used and their indication depends mainly on the thickness of the area that requires grafting. Upper eyelid and ear are thin, while scalp, trunk, lower eyelid, palm of the hand and feet are thick and require a full thickness skin graft.

For completeness, we would like to mention the Meeks technique. This technique is used for massive burns and can expand skin to a maximum of 9:1 covered by allograft and can be a lifesaving approach.

### **Dermal Analogs**

The goal of many research groups around the globe is to develop a fully functional composite graft that has the durability and utility of autograft or homograft, can replace the dermis and epidermis, and is immediately available for coverage of an excised burn. Creation of the dermal analogs was the first efforts in this direction. Integra™ (Integra LifeSciences Corporation, Plainsboro, NJ, USA) was developed by John Burke from the Massachusetts General Hospital in collaboration with Ionnas Yannas from the Massachusetts Institute of Technology. Following full excision of devitalized tissue, Integra™ is placed over the wound where fibrovascular ingrowth is facilitated by the bovine collagen and glucosaminoglycans that form Integra™. Within approximately 3 weeks, the matrix is fully incorporated into the wound bed and a split-thickness autograft is placed over it. The long-term use and outcomes of Integra™ are favorable, despite a theoretical increase in infection risk.<sup>10, 41</sup> Another dermal analog available for the treatment of full-thickness burns is Alloderm® (LifeCell Corporation, Branchburg, NJ, USA), which is made from cadaveric dermis devoid of cells and epithelial elements. Alloderm® is very similar to other dermal analogs and has shown favorable results.<sup>42, 43</sup>

### **Keratinocyte Coverage**

CEAs have become an important tool in managing patients with massive burn injuries. In cases where full-thickness burns involve 90% or more of the total body surface area, this may be the only option given that procurement of unburned skin will not be sufficient to cover the patient's body, even when extensive expansion techniques are employed. Cultured epithelial autografting involves obtaining two 2 × 6 cm full-thickness specimens of unburned skin very early in the patient's hospitalization, preferably upon admission. The skin is then processed and cultured *ex vivo* in the presence of murine fibroblasts, which promote growth. The final product takes approximately 3 weeks to be ready for grafting and consists of sheets of keratinocytes that are 5 × 10 cm in size, 2–8 cells thick, and mounted on a petrolatum gauze.

While the CEA is made available, these critically ill patients' wounds need to be excised and temporarily covered with allograft. Complications like wound infections and multiorgan failure must be aggressively treated to maximize chances of survival and eventual graft take.

The application of CEA can be difficult because of the fragility of the grafts, which have been described as having the consistency of wet tissue paper. CEAs applied to areas like the

back, buttocks, posterior lower extremities, and other dependent areas are prone to shearing and possible loss. Once healed, the skin has a better cosmetic result than healed 4:1 meshed autograft, but this approach is associated with a longer hospital stay and more reconstructive procedures.<sup>44</sup> Recent studies have shown very variable results of CEA application. A single-center retrospective cohort study with over 30 severely burned patients with burn sizes exceeding 75% of the total body surface area showed excellent survival and permanent coverage, although no control group was provided.<sup>11</sup> CEA used in conjunction with an allograft base was reported to result in a graft take of over 72%.<sup>45</sup>

## CONCLUSION

Progress in the acute treatment of burn patients within the last decades has been a success story, with significant improvements being seen in ICU mortality and the long-term survival of severely burned patients. However, this development has led to a new set of challenges for burn researchers—reducing scarring, improving skin graft quality, and creating a pluri-stratified dermal or epidermal construct for the coverage of an excised burn wound. The design of new molecular methodologies and animal models for the study of underlying pathophysiological mechanism can allow us to manipulate disease pathology with the goal of improving patient outcome. Future wound healing modalities will build upon the basics described here. A summary of products and techniques are shown in Table 2.

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**Table 1**

Common partial-thickness or full-thickness burn wound dressings

Dressing Agent	Active Substance	Presentation	Main Use	Advantages	Disadvantages
Bacitracin	Bacitracin	Ointment	Superficial burns, skin grafts	Gram (+) coverage	No G(-) or fungal coverage
Polymyxin	Polymyxin B	Ointment	Superficial burns, skin grafts	Gram (-) coverage	No G(+) or fungal coverage
Mycostatin	Nystatin	Ointment	Superficial burns, skin grafts	Good fungal coverage	No bacterial coverage
Silvadene	Silver sulfadiazine	Ointment	Deep burns	Good bacterial and fungal coverage, painless	Poor eschar penetration, sulfa moiety, leucopenia, pseudoeschar formation
Sulfamylon	Mafenide acetate	Ointment and liquid solution	Deep burns	Good bacterial coverage, good eschar penetration	Painful, poor fungal coverage, metabolic acidosis
Dakin's	Sodium hypochlorite	Liquid solution	Superficial and deep burns	Good bacterial coverage, inexpensive and readily available	Very short half life
Silver	Silver nitrate, silver ion	Liquid solution, dressing sheets	Superficial burns	Good bacterial coverage, painless	Hyponatremia, dark staining of wounds and linens
Acetic Acid 2%	Acetic acid	Liquid solution, dressing	Superficial and deep burns	Good gram negative coverage	Painful, vinegary smell

**Table 2**

Products and solutions mentioned in this article

<b>Product</b>	<b>Description</b>	<b>Presentation</b>	<b>Main Use</b>	<b>Advantages</b>	<b>Disadvantages</b>
AlloDerm	Human cadaveric acellular matrix	Membrane	Full thickness deep burn in cosmetically important areas	Dermal substitute	<b>Expensive</b>
Amnion	Biological dressing	Membrane	Partial thickness face burn	Moldable, pliable, monitoring of wound, contains growth factors	<b>Allogenic, expensive</b>
AWBAT					<b>Off the market</b>
Biobrane	Biosynthetic collagen matrix	Membrane (large sheets, hands)	Superficial burns	No dressing change if adherent for 2 weeks; reduced pain; monitoring of wound;	<b>If not adherent risk of infection</b>
Cultured Epithelial Autograft (CEA)	Keratinocytes	Thin sheet of skin	Large burns	Large coverage with small donor	<b>Fragile, expensive, long-time to grow in-vitro</b>
Integra	Bovin collagen matrix with silicon layer on the surface	Membrane with silicon layer	Deep full thickness burn, burn in cosmetically important areas, large burns	Good cosmetic outcome, dermal substitute	<b>Infection risk, expensive</b>