Tissue-engineered temporary wound coverings. Important options for the clinician

M. Ehrenreich and Z. Ruszczak

SUMMARY

Finding an ideal temporary wound dressing is challenging. Although TransCyte®, built on Biobrane®, offers many of the characteristics of the ideal wound dressing, and may have added benefits from the delivery of extra-cellular matrix (ECM) and growth factors to the wound, the downside of high cost and less convenient storage and usage are considerable barriers to its broader adoption. The low cost and established clinical utility of Biobrane sets the bar high for new products.

KEY WORDS

Biobrane, TransCyte, acute wounds, burns, tissue-engineering

Overview of burns

When the famous bank robber Willie Sutton was asked why he robbed banks, he simply replied, "Because that's where the money is" (1). It is not surprising then that the earliest focus for tissue-engineered skin products was in burns, because it was thought "that's where the skin is needed." Although the most obvious of uses, it is also the smallest of contemplated applications today.

Burns have traditionally been classified as first, second or third degree, depending upon depth. However, a more recent schema is as follows. Injury restricted to the epidermis is termed superficial (previously first degree). Burns involving the dermis are classified as partial thickness (previously second degree), and can be superficial or deep. Superficial partial thickness burns involve the papillary dermis, while deep partial thickness burns involve both the papillary and reticular dermal layers.

Burns extending through all layers of the dermis and through to subcutaneous tissue are termed full-thickness (previously third degree). A burn extending to muscle is termed full thickness with injury to underlying muscle (sometimes call fourth degree).

Deep partial-thickness and full-thickness burns invariably require autografting to achieve healing. In the case of severe burns, a temporary covering is often employed as a bridge to autografting. Allograft from cadaver skin has been the traditional choice for the temporary dressing of severe burns*. Any new product intended as a temporary dressing must be compared to

** Porcine xenografts are sometimes used as temporary wound coverings. Xenograft is rejected more quickly than allograft and otherwise has the same deficiencies as allograft*

this standard. The immune suppression observed in severely burned patients prevents rapid rejection of allograft, but rejection ultimately occurs, typically within days to weeks, necessitating repeat allografting if the patient is not yet ready for autografting. It is important to note that the immunosuppressed state of the burn patient makes it impossible to generalize the use of allograft skin to other applications requiring temporary skin coverage. The advantages of allograft are tempered by variable supply, the possibility of disease transmission — though careful screening of donors substantially reduces this risk — and bleeding provoked upon removal.

A tissue-engineered biological dressing or other temporary covering as efficacious as cadaver skin would eliminate these problems, allowing delay of definitive autografting until sufficient graft is available. Even more desirable is a product that eliminates the need for autografting. In many applications, limited autograft availability necessitates maximizing the available resource in the form of thinner grafts in which the donor site can be reharvested sooner, meshing of the graft, and using cultured epidermal cells. If the method chosen (e.g. a very thin split-thickness-skin-graft) does not supply a solid dermal layer, wound contraction, scarring, and long-term disability can result.

Under best of circumstances, autografting creates a donor site, which is itself a site of potential infection and fluid loss. The donor site is generally a partial-thickness wound, but sometimes extends no deeper than the epithelium. Donor wounds are associated with pain, discomfort, fluid collection, and the ever-present possibility of infection. The use of tissue-engineered biological dressings may help eliminate or reduce donor site wounds, lead to more rapid donor site healing, and require fewer donor site recropping procedures. This can ultimately result in reduced length of hospital stay and more rapid patient rehabilitation. The use of these products can also eliminate the cost of allograft and, in some cases, the nursing costs associated with repeated dressing changes. A tissue-engineered product that can replace or complement autograft may result in improved functional and cosmetic outcomes, and reduced morbidity by elimination of the donor site. Tissue-engineered products may also be used in conjunction with meshed autograft, where it may result in reduced scarring and improved functionality.

Between 1985 and 1996, in the United States, age-specific fire and burn death rates declined 27-42 percent across all age groups (3). In 1997, fire-related deaths numbered 3,961, down 24% from 5,189 in 1989. This improvement is due largely to the decline in residential property fires, which fell 21% during this period, from 513,500 to 406,500 (4). Advances in care are thought to have contributed little over the past two decades. LA_{50} the percentage of total body surface area burned at which half of the patients survive, improved only modestly between 1980 and 1990, and this trend is believed to have continued into the present (5). Most of the improvement in burn care observed over the past half century occurred between 1970 and 1980. During this period, LA_{50} improved from under 40% to over 65%, due primarily to the introduction of early eschar excision, skin banks, total parenteral nutrition, and improved antibiotics. These improvements in burn and fire mortality should not obscure the major unresolved problem in burn care today — the unsatisfactory cosmetic and functional outcomes following full-thickness burn injuries.

Each year in the United States, 696,000** people visit the emergency room due to burns (7), resulting in 50,000 hospitalizations (8). The majority of these cases in which the burns are not extensive, do not pose a clinical challenge. These patients usually have sufficient healthy skin from which autograft can be harvested. However, often sufficient healthy material is unavailable for autograft or the added trauma of creating a donor wound cannot be tolerated.

According to the American Burn Association (9), the average size of a burn injury admitted to a burn center is about 14 percent of total body surface area (TBSA). Burns of 10 percent TBSA or less account for 54 percent of cases, while burns of 60 percent TBSA or greater account for just four percent of admissions. The subset of severely burn patients represents the most compelling application in burns for a tissue-engineered biological dressing that can serve as either permanent coverage or a bridge to autografting. There are also certain rare skin disorders, such as toxic epidermal necrolysis (TEN) and epidermolysis bullosa (EB), which conditions resemble those that result from severe burns. These, too, may benefit from the application of tissue-engineered biological dressings.

The ideal synthetic wound dressing or biologic skin substitute should have the following characteristics, enumerated for the most part by Pruitt and Levine more than twenty years ago (10) and added to by ourselves and others (11):

- absence of antigenicity
- tissue compatible
- absence of local or systemic toxicity
- impermeable to exogenous microorganisms
- water vapor transmission similar to normal skin
- rapid and sustained adherence to wound surface
- conformal to surface irregularities
- elastic to permit motion of underlying tissue
- resistant to linear and shear stresses

*** A more recent publication (McCaig LF,BurtCW.National Hospital Ambulatory MedicalCare Survey:2002 Emergency Department Summary. Advance data from vital and health statistics;no340.*

- tensile strength to resist fragmentation
- inhibition of wound surface flora and bacteria
- long shelf life, minimal storage requirements
- biodegradable (for permanent membranes)
- low cost
- minimize nursing care of wound
- minimize patient discomfort
- translucent properties to allow direct observation of healing
- reduce heal-time
- not increase rate of infection
- patient acceptance

Some products which are often thought of as dermal replacements, such as Biobrane® (see below), are indicated for partial-thickness wounds that do not require skin grafts. Though this patient population is larger than that of full-thickness injuries in terms of number of patients, it is also far more price sensitive as a number of alternative wound dressing are available. Expensive tissue-engineered products, such as TransCyte® and Integra Bilayer Matrix Wound Dressing® (Integra Life Sciences, Plainsboro, NJ), are far too expensive for this market, and regardless of clinical and technical attributes are unlikely to have a role in this indication.

In most cases, it is difficult to argue for the use of expensive products on donor sites when cheap and effective alternatives, such as conventional wound dressings and Biobrane, are readily available. In extensive burns, where donor sites must be harvested multiple times, a tissue-engineered biological dressing that promotes faster, higher-quality healing may be justified.

Biobrane

Biobrane, a product of Mylan Laboratories, Inc., is a biosynthetic wound dressing constructed of a silicone film bonded to a porcine collagen cross-linked nylon fabric. Developed by Woodroof (12), it has been commercially available since 1979. Blood and sera in the wound clot within the nylon matrix, biologically fixing the dressing in place until epithelialization occurs. Importantly, the outer silicone membrane acts to reduce water loss from the wound by evaporation. After healing, Biobrane must be removed, but as healing progresses the dressing naturally separates from the wound. It is available in various sizes ranging from 5 x 5 to 15 x 20 inches, as well as in a glove format (13, 12). Biobrane-L is, according to the manufacturer, a less complex nylon fabric for use when less aggressive adherence is required (14). It utilizes a lower weight monofilament thread resulting in a less complex matrix, thereby reducing adherence to the wound, as compared with the trifilament thread of Biobrane (15).

Most often, Biobrane is used to treat patients with partial-thickness burns, typically on an outpatient basis (16, 17). It is best reserved for relatively fresh wounds (<24-48 hours), with low bacterial counts, and without eschar or debris, as Biobrane does not debride dead tissue (15,18,19). In a controlled, non-blinded, 52-subject clinical trial in partial-thickness burns, Biobrane was shown to decrease total healing time by 29% (10.6 days vs. 15.0 days), lower treatment cost ($434 vs. $504), and reduce patient pain (1.6 vs. 3.6 out of 5) and use of pain medication (0.6 vs. 3.0 tablets) at 24 hours, with no significant change in the rate of infection as compared with the twice daily use of 1% silver sulfadiazine, an antimicrobial, covered with dry gauze and elastic wraps (15). In a controlled, non-blinded, 30-subject clinical study in patients with partial-thickness scald burns the use of Biobrane was also associated with decreased pain, reduced hospital stay, and reduced days of physical therapy (20). But not all studies are positive. A controlled, non-blinded, 49-subject clinical trial in partial-thickness burns failed to show an advantage to Biobrane versus silver sulfadiazine in reducing length of hospital stay (9.1 days vs. 9.2 days) or costs ($360 vs. $310), (21). Twelve percent of the Biobrane treated patients required early removal of the product, one case due to increasing burn depth and three cases for infection.

There has been some concern that Biobrane use is associated with an increased risk of infection. In one 21-subject donor site study the infection rate was 57% with Biobrane versus 9.5% with Scarlet Red, the standard for treatment in the 1980's (22). Others trials did not find an increased rate of infection. In a controlled, non-blinded 89 patient study in pediatric patients with superficial burns of less than 25% TBSA, its use was not associated with a greater incidence of infection when applied within 48 hours of injury (23). As in other studies, Biobrane use resulted in shorter hospitalizations and decreased healing time versus topical antimicrobials and dressing changes. In a 20-subject pediatric study in patients with partial-thickness burns presenting within 24 hours of injury, Biobrane was superior to 1% silver sulfadiazine and standard wound care on measures of length of hospital stay (1.5 vs. 3.6 days), time to complete wound healing (9.7 vs. 16.1 days), and use of pain medication (0.5 vs. 1.9 doses/person/day), also with no difference in the rate of infection (zero in both groups) (24).

Although some early studies concluded that as a temporary dressing Biobrane is as effective as frozen allograft in freshly excised full-thickness burn wounds (25), it is now considered that accurate diagnosis of wound depth and careful wound selection is considered critical as deep wounds interfere with Biobrane adherence (16, 17, 26). Often it is difficult to judge initially the depth of the wound, leading to nonadherance (27).

Out of a series of 201 Biobrane applications in four different clinical indications, 124 (61.7%) were left in

place until healing occurred, but the rates varied considerably by wound type, from 100% for shallow wounds awaiting epithelialization to 21.7% for deep wounds after eschar excision (28). Biobrane has little utility in deep partial-thickness and full-thickness burns other than as a dressing for meshed autograft (29), with removal at 5-7 days to allow for reepithlialization (24). But others consider it inferior to allograft for this application (30). The use of Biobrane-L, with less adherence, may be preferred for covering meshed autograft (13). Misuse may also contribute to infection, likely secondary to partial nonadherance and resultant bacterial proliferation. In a series of 141 pediatric scald burn patients, of which 106 were treated with Biobrane, there was a 22.6% infection rate which the authors attribute to indifferent application of Biobrane to both superficial and deep partial-thickness burns (31). The authors were nevertheless satisfied with its performance.

Biobrane is suitable for use on donor sites and has been used extensively in this capacity (32). The use of Biobrane on donor site wounds is associated with decreased pain and reduced exudate compared with Scarlet Red impregnated gauze (33). However, others have concluded that Scarlet Red is superior to Biobrane in extensive burns (20). One negative study found that the use of Biobrane, when applied to donor sites, was associated with increased healing time, greater infection rates, and higher costs versus xeroform gauze (34). The site of application is important. In a series of 108 applications of Biobrane to 95 pediatric patients with donor site wounds, 43 early removals were necessary due to lack of adherence (35). The back and hip region had the highest early removal rates of 43 and 80 percent, respectively. In the chest and thigh area, Biobrane provided full-term coverage in greater than 90% of the cases. Surprisingly, early removal did not affect donor site healing time.

Biobrane has also been used successfully to treat dermal ulcers and other difficult wounds (36), but controlled trials are lacking. Other disorders that mimic characteristics of partial-thickness burn wounds, such as toxic epidermal necrolysis (TEN), (37-42) have also been treated successfully with Biobrane. TEN is a rare idiosyncratic exfoliative disorder resulting in the loss of sheets of epidermis at the dermal-epidermal junction. Recently, extensive erosions secondary to paraneoplastic pemphigus, an automimmune blistering disorder, in a 77 year old woman were reported to have been dressed with Biobrane with good results (43). There has been a few case reports of Biobrane being used as a dressing in toxic shock syndrome developing in a scald patient (44, 45). It has also been used in a series of 85 patients to reduce erythema or discomfort following carbon dioxide laser resurfacing following laser facial resurfacing (46) and similarly following dermabrasion (47). Furthermore, Biobrane is often used in non-burn skin deficits, such as may result from trauma, where temporary coverage may be required prior to grafting or a flap procedure. It has even been used to cover an open sternotomy wound (48), and to provide wound coverage and stoma appliance support following a colostomy perforation (49). Biobrane is not indicated for chemical or electrical burns, though some have used it in this context (50).

Biobrane offers many of the characteristics of the ideal wound dressing described above. Importantly, wound desiccation is prevented and pain is decreased. Since dressing changes are performed less frequently, outpatient care is sometimes made possible, reducing hospital costs. It is also transparent, allowing direct wound observation. It is highly effective as a dressing for superficial partial-thickness burns, donor sites, and TEN. It is equivalent to or superior to silver sulfadiazine or xeroform gauze on most parameters and far preferred for patient comfort (24). Biobrane has no special storage requirements and a long shelf life. It handles well, with high elasticity and 100% elongation in any direction (9), but may be difficult to use in areas of irregular topography or on joint surfaces, though some have reported good results using meshed Biobrane even in these challenging areas (51). The risk of infection in inappropriately chosen wounds is the largest concern, followed by non-adherance, though initial non-adherance in a non-infected wound can be addressed with aspiration or reapplication. Although reported, hypersentivity reactions to Biobrane have occurred on repeat application (52).

At Biobrane's price of approximately £0.48 per sq. cm (53), it does not seem likely that any of the newer biological skin substitutes will prove more cost-effective or provide better outcomes in superficial partial-thickness burns.

TransCyte

TransCyte, originally termed Dermagraft-TC, was commercialized by Advanced Tissue Sciences, Inc. and is now a product of Smith & Nephew. It is composed of human neonatal fibroblasts cultured under aseptic conditions onto the nylon mesh component of Biobrane (54). The fibroblasts secrete into the mesh extracellular matrix components, such as fibronectin, type I collagen, decorin and matrix bound growth factors, but are themselves no longer viable in the final product (52). The presentation of the ECM components and the bound growth factors are thought to promote wound healing. The product must be stored between -20° and -70° C, and thawed at 37° C prior to use. It has a shelf life of 18 months at the proper temperature.

TransCyte received FDA approval in March 1997 for use as a temporary wound covering for surgically excised full-thickness and deep partial-thickness ther-

mal burn wounds in patients that require a covering prior to autograft placement.

Early studies in 10 adult burn patients indicated that TransCyte was at least equivalent to human cadaver allograft skin (55). The initial approval was based upon a 66-patient trial in which comparable full-thickness or deep partial-thickness burn sites on each patient were randomized to receive either TransCyte or cadaver allograft. TransCyte sites, when evaluated 14 days post-autograft, were equivalent to or superior to allograft with regard to ultimate autograft take: 94.7% vs. 93.1% (56). TransCyte also performed better than control on secondary endpoints such as ease of removal, degree of excision required, amount of bleeding upon excision, and overall satisfaction rating by investigators (54). TransCyte was equivalent to control on the secondary endpoints of adherence, wound closure, and infection (54).

In October 1997, TransCyte's label was expanded to include partial-thickness burns that are mid-dermal to indeterminate depth and that may be expected to heal without autografting. In a 14-subject, randomized, within-patient paired comparison study, the one-time application of TransCyte resulted in a 39% decrease in time to 90% or greater epithelialization versus silver sulfadiazine cream applied with once or twice-daily dressing changes: 11.1 days vs. 18.1 days (57, 58). The use of TransCyte also resulted in significantly less hypertrophic scarring, as defined by the Vancouver Burn Scar Scale, versus control (55). It is little surprise that the TransCyte performed better than a silver sulfadiazine control in partial-thickness burns. Biobrane, the nylon mesh base of the product, itself performed better than silver sulfadiazine in clinical trials (see above).

In a 21 patient study comparing TransCyte with standard topical antibiotic management in adult patients with mid-dermal facial burns, there was a decrease in wound care time (0.35 vs. 1.9 hours), pain (2 vs. 4), and time for reepithelialization (7 vs. 13 days) in the TransCyte group (59).

In a series of 20 pediatric burn patients treated with TransCyte, compared with an historical control of 20 pediatric patient treated with antimicrobrial ointments and hydrodebridement, only one child (5%) in the TransCyte group required autografting as compared with seven children (35%) in the control group. The TransCyte treated group had decreased hospital length of stay versus control: 5.9 vs. 13.8 days (60).

In a randomized 33 patient, 58 wound site study directly comparing the effectiveness of TransCyte, Biobrane, and Silvazine cream (silver sulphadiazine and 0.2% chlorhexidine) in treating children with partial-thickness burns, the mean time to 90% of greater reepithelialization was 7.5 days for TransCyte versus 9.5 days for Biobrane and 11.2 days for Silvazine. The percentage of wounds ultimately requiring autografting were only 5% for TransCyte as compared with 24% for Silvazine, and 17% for Biobrane. TransCyte-dressed wounds required fewer dressing changes (1.5) than either Biobrane (2.4) or Silvazine (9.2) (59).

At £7.87/sqr. cm TransCyte is 16-times more expensive than Biobrane, 2.3 times more expensive than Integra Bilayer Matrix Wound Dressing, and 13 times more expensive than allograft (51). It is also more difficult to store and handle than either of the above synthetic products. This higher cost versus allograft may be justified based upon the latter's limited availability, the risk of viral transmission by cadaver skin, and TransCyte's advantages on the secondary endpoints described above (54).

TransCyte, in its pivotal clinical trial (54), was used in full-thickness and deep partial thickness wounds, in contrast to Biobrane which is used for the most part in more superficial wounds (see above). Although one author (58) observed that TransCyte may not adhere well to deeper burns, he still felt that its use was warranted in those cases due to the delivery of bioactive substances to the wound, and that TransCyte, early in the course of the injury, may serve to "seal the wound". These deeper burns may prove the niche where the higher cost of TransCyte can be justified.

In cases where an autograft is expected to be required, Integra Bilayer Matrix Wound Dressing may be superior in that it requires only an epidermal autograft or a very thin split-thickness skin graft as opposed to the split-thickness graft required with TransCyte.

Although TransCyte, built on Biobrane, offers many of the characteristics of the ideal wound dressing, and may have added benefits from the delivery of ECM and growth factors to the wound, the downside of high cost and less convenient storage and usage are considerable barriers to its broader adoption.

Conclusion

Both Biobrane and TransCyte have a strong body of evidence supporting their use in acute wounds. The most important clinical advantages of both products are prevention of wound dessication, reduction in pain, reduced dressing changes, and, in most reported studies, an acceleration in healing. TransCyte is considerably more expensive than Biobrane and more difficult to store, as it must be stored at -20° to -70° C, and thawed at 37° C prior to use. Its applications must, therefore, be well-considered. TransCyte may be justified in full thickness and deep partial thickness injuries, whereas Biobrane is more appropriate for more superficial wounds.

REFERENCES

1. Available at: http://www.fbi.gov/libref/historic/famcases/sutton/sutton.htm

2. National Center for Health Statistics. Health, United States, 1996-1997 and Injury Chartbook. Hyatsville, MD: 1997. pg. 28.

3. National Fire Data Center. FEMA/United States Fire Administration. http://www.usfa.fema.gov/nfdc/

4. Mann R and Heimbach D. Prognosis and treatment of burns. West J Med 1996; 165: 215-20.

5. Nourjah P. National Hospital Ambulatory Medical Care Survey: 1997 emergency department summary. Advance data from vital and health statistics; no. 304. Hyatsville, MD: National Center for Health Statistics. 1999. pg. 17.

6. Brigham PA and McLoughlin E. Burn incidence and medical care use in the United States: estimates, trends, and data sources. J Burn Care Rehabil. 1996; 17: 95-107.

7. Available at: www.ameriburn.com

8. Pruitt BA and Levine NS. Characteristics and uses of biologic dressings and skin substitutes. Arch Surg 1984; 119: 312-22.

9. Smith DJ Jr. Use of Biobrane in wound management. J Burn Care Rehabil. 1995; 16: 317-20.

10. Available at: www.uspto.gov. Bio compatible and blood compatible materials and methods. Patent nos: 4,828,561; 4,820,302; and 4,725,279. All continuation-in-part of Ser. No. 005,319 filed 1/22/79, now abandoned.

11. Smith DJ, McHugh TP, Phillips LG, et al. Biosynthetic compound dressings—management of hand burns. Burns, Including Thermal Injury. 1988; 14: 405-8.

12. Available at: http://www.bertek.com/burnandwound/frameset_productguide.php?id=6

13. Rodeheaver GT, Hartsell ML, Faulkner BC, et al. Influence of Biobrane construction on adherence. J Burn Care Rehabil. 1995; 16: 321-3.

14. Klein RL, Rothmann BF, Marshall R. Biobrane—a useful adjunct in the therapy of outpatient burns. J Pediatr Surg. 1984; 19: 846-7.

15. Gerding RL, Emerman CL, Effron D, et al. Outpatient management of partial-thickness burns: Biobrane versus 1% silver sulfadiazine. Ann Emerg Med. 1990; 19: 121-24.

16. Gerding RL, Imbembo AL, Fratianne RB. Biosynthetic skin substitute vs. 1% silver sulfadiazine for treatment of inpatient partial-thickness thermal burns. J Trauma. 1988; 28: 1265-9.

17. Phillips LG, Robson MC, Smith DJ, et al. Uses and abuses of a biosynthetic dressing for partial skin thickness burns. Burns. 1989; 15: 254-6.

18. Demling RH. Use of Biobrane in management of scalds. J Burn Care Rehabil. 1995; 16: 329-30.

19. Bauman LW, Hawkins ML, Howdieshell TR, et al. Bilaminate synthetic dressing for partial thickness burns. Lack of cost reduction for inpatient care. Am Surg. 1991; 57: 131-33.

20. Prasad JK, Feller I, Thomson PD. A prospective controlled trial of Biobrane versus scarlet red on skin graft donor areas. J Burn Care Rehabil. 1987; 8: 384-6.

21. Lal S, Barrow RE, Wolf SE, et al. Biobrane improves wound healing in burned children without increased risk of infection. Shock. 2000; 14: 314-8.

22. Barret JP, Dziewulski P, Ramzy PI, et al. Biobrane versus 1% silver sulfadiazine in second-degree pediatric burns. Plast Reconstr Surg. 2000; 105: 62-5.

23. Purdue GF, Hunt JL, Gillespie RW, et al. Biosynthetic skin substitute versus frozen human cadaver allograft for temporary coverage of excised burn wounds. J Trauma. 1987; 27: 155-7.

24. Bishop JF, Demling RH, Hansbrough JF, et al. Summary [of conference proceedings]. J Burn Care Rehabil. 1995; 16: 341-2.

25. Bishop JF. Pediatric considerations in the use of Biobrane in burn wound management. J Burn Care Rehabil. 1995;16: 331-3; discussion 333-4.

26. McHugh TP, Robson MC, Heggers JP, et al. Therapeutic efficacy of Biobrane in partial- and full-thickness thermal injury. Surgery. 1986; 100: 661-4.

27. Frank D, Wachtel T, Frank N. Comparison of biobrane, porcine and human allograft as biologic

dressings for burn wounds. Surg Forum. 1980; 31: 552-8.

28. Hartford CE, Wang XW, Peterson VM, et al. Healing characteristics of expanded autografts on wounds covered with homograft and Biobrane temporary wound dressing. J Burn Care Rehabil. 1989; 10: 476-80.

29. Ou LF, Lee SY, Chen YC, et al. Use of Biobrane in pediatric scald burns-experience in 106 children. Burns. 1998; 24: 49-53.

30. Hansbrough JF. Use of Biobrane for extensive posterior donor site wounds. J Burn Care Rehabil. 1995; 16: 335-6.

31. Zapata-Sirvent R, Hansbrough JF, Carroll W, et al. Comparison of Biobrane and Scarlet Red dressings for treatment of donor site wounds. Arch Surg. 1985; 120 :743-5.

32. Feldman DL, Rogers A, Karpinski RH. A prospective trial comparing Biobrane, Duoderm and xeroform for skin graft donor sites. Surg Gynecol Obstet. 1991; 173: 1-5.

33. Housinger TA, Wondrely L, Warden GD. The use of Biobrane for coverage of the pediatric donor site. J Burn Care Rehabil. 1993; 14: 26-8.

34. Kirwan L. Management of difficult wounds with Biobrane. Conn Med. 1995; 59: 523-9.

35. Kucan JO. Use of Biobrane in the treatment of toxic epidermal necrolysis. J Burn Care Rehabil. 1995; 16: 324-7; discussion 327-8.

36. Bradley T, Brown RE, Kucan JO, et al. Toxic epidermal necrolysis: a review and report of the successful use of Biobrane for early wound coverage. Ann Plast Surg. 1995; 35: 124-32.

37. Bannasch H, Kontny U, Kruger M, et al. A semisynthetic bilaminar skin substitute used to treat pediatric full-body toxic epidermal necrolysis: wraparound technique in a 17-month-old girl. Arch Dermatol. 2004; 140: 160-2.

38. Arevalo JM and Lorente JA. Skin coverage with Biobrane biomaterial for the treatment of patients with toxic epidermal necrolysis. J Burn Care Rehabil. 1999; 20: 406-10.

39. Peters W et al. Toxic epidermal necrolysis: a burn-centre challenge. CMAJ. 1991; 144: 1477-80.

40. Sowder LL. Biobrane wound dressing used in the treatment of toxic epidermal necrolysis: a case report. J Burn Care Rehabil. 1990; 11: 237-9.

41. Vun YY, Lun K, Strutton G.. Use of biosynthetic dressings in paraneoplastic pemphigus. Australas J Dermatol. 2004; 45: 133-5.

42. Weinzweig J, Gottlieb LJ, Krizek TJ. Toxic shock syndrome associated with use of Biobrane in a scald burn victim. Burns. 1994; 20: 180-1.

43. Egan WC and Clark WR. The toxic shock syndrome in a burn victim. Burns Incl Therm Inj. 1988; 14: 135-8.

44. Levy PM and Salomon D. Use of Biobrane after laser resurfacing. Dermatol Surg. 1998; 24: 729-34.

45. Pinski JB. Dressings for dermabrasion: new aspects. J Dermatol Surg Oncol. 1987; 13(6): 673-7.

46. Snow N, Gerding R, Horrigan TP, et al. Coverage of the open sternotomy wound with Biobrane dressing. J Thorac Cardiovasc Surg. 1987; 94: 914-6.

47. Gomez ER and Rosenthal D. Management of a subcutaneous colostomy perforation. The role of a new synthetic skin. Dis Colon Rectum. 1984; 27: 651-3.

48. Erdmann D, Hussmann J, Kucan JO. Treatment of a severe alkali burn. Burns. 1996; 22: 141-6.

49. Phillips LG, Jarlsburg C, Mathoney K, et al. Meshed Biobrane: a dressing for difficult topography. J Burn Care Rehabil. 1990; 11: 347-51.

50. Reed BR, Zapata-Sirvent RL, Kinoshita JR, et al. Contact dermatitis to Biobrane. Plast Reconstr Surg. 1985; 76: 124-5.

51. Jones I, Currie L, Martin R. A guide to biological skin substitutes. Br J Plast Surg. 2002;55:185-93.

52. Hansbrough JF. Development of a temporary living skin replacement composed of human neonatal fibroblasts cultured in Biobrane, a synthetic dressing material. Surgery. 1994; 115: 633-44.

53. Hansbrough JF, Mozingo DW, Kealey GP, et al. Clinical trials of a biosynthetic temporary skin

replacement, Dermagraft-Transitional Covering, compared with cryopreserved human cadaver skin for temporary coverage of excised burn wounds. J Burn Care Rehabil. 1997; 18: 43-51.

54. Purdue GF, Hunt JL, Still JM Jr., et al. A multicenter clinical trial of a biosynthetic skin replacement, Dermagraft-TC, compared with cryopreserved human cadaver skin for temporary coverage of excised burn wounds. J Burn Care Rehabil. 1997; 18: 52-7.

55. TransCyte Label.

56. Noordenbos J, Dore C, Hansbrough JF. Safety and efficacy of TransCyte for the treatment of partial-thickness burns. J Burn Care Rehabil. 1999; 20: 275-81.

57. Demling RH and DeSanti L. Management of partial thickness facial burns (comparison of topical antibiotics and bio-engineered skin substitutes). Burns. 1999; 25: 256-61.

58. Lukish JR, Eichelberger MR, Newman KD, et al. The use of a bioactive skin substitute decreases length of stay for pediatric burn patients. J Pediatr Surg. 2001; 36: 1118-21.

59. Kumar RJ, Kimble RM, Boots R, et al. Treatment of partial-thickness burns: a prospective, randomized trial using TransCyte. ANZ J Surg. 2004; 74: 622-6.

AUTHORS' ADDRESSES

Michael Ehrenreich MD, Dermatology, New Jersey Medical School, 185 Orange Avenue, Newark 07193, USA. Telephone 917 869 7755. Corresponding author, e-mail: ehrenrmi@umdnj.edu

Zbigniew Ruszczak MD, PhD, same address