A Silver-Sulfadiazine-Impregnated Synthetic Wound Dressing Composed of Poly-L-Leucine Spongy Matrix: An Evaluation of Clinical Cases

Yoshimitsu Kuroyanagi,* Eikichi Kim, Makoto Kenmochi, Kenji Ui, Hiromi Kageyama, Motonobu Nakamura, Akira Takeda, and Nobuyuki Shioya

*Department of Biomedical Engineering and Department of Plastic Reconstructive Surgery, School of Medicine, Kitasato University, Sagamihara, Kanagawa, Japan

The management of severe burns requires the suppression of bacterial growth, particularly when eschar and damaged tissue are present. For such cases, silver sulfadiazine (AgSD) cream has been traditionally applied. This antibacterial cream, however, cannot be used in conjunction with a temporary wound dressing that is needed to promote healing. The authors developed a synthetic wound dressing with drug delivery capability for clinical use by impregnating a poly-L-leucine spongy matrix with AgSD, which is released in a controlled, sustained fashion. In general, the dressing adhered firmly to the wound in the case of superficial second-degree burns, and during the healing process it separated spontaneously from the re-epithelialized surface. In the management of deep second-degree burns where eschar and damaged tissue were present, the dressing had to be changed at intervals of 3 to 5 days until it adhered firmly to the wound. Once the dressing had firmly attached to the wound, it was left in place until it separated spontaneously from the re-epithelialized surface. Dressing changes were fewer than with other treatments and the pain was effectively reduced. Cleansed wounds were effectively protected from bacterial contamination. Of 52 cases treated with this wound dressing, 93% (14/15) of superficial second-degree burns, 75% (3/4) of deep second-degree burns, 85% (6/7) of superficial and deep second-degree burns, and 75% (12/16) of split-thickness skin donor sites were evaluated as achieving good or excellent results.

INTRODUCTION

Many types of temporary wound dressings have been developed, both nonmedicated and medicated, and some have been successful clinically.[1-6] Commercially available synthetic wound dressings consisting of a polyurethane membrane are capable of minimizing evaporative water loss from the wound and preventing bacterial invasion and thus are useful in the management of superficial second-degree burns. They are of no use, however, in the treatment of deep second-degree and third-degree burns.

The ideal structure of a bilaminate dressing consists of an outer membrane and an inner three-dimensional matrix of fabric or sponge. The outer membrane prevents body fluid loss, controls water evaporation, and protects the wound from bacterial invasion; the inner matrix encourages wound adherence by tissue growth into the matrix.

One such dressing developed by Woodroof[2] is Biobrane®, a silicone membrane, bonded to a nylon fabric, with a small amount of collagen peptide. The silicone membrane functions as a barrier, controlling evaporative water loss and preventing bacterial invasion; the nylon fabric provides a rough surface that promotes tissue ingrowth and adherence. Another example developed by Yannas and Burke[7-9] is a biosynthetic bilaminar wound dressing composed of a silicone membrane and a collagen-GAG spongy matrix. Although the silicone membrane can effectively control water loss from a superficial second-degree burn, it cannot control water loss from deep second-degree and third-degree burns (a loss estimated to range from 3500 to 4500 $g/m^2/day$[10]).

In the management of deep second-degree or third-degree burns, the drainage of exudate must be taken into account. Therefore, the silicone membrane must be made porous, yet its integrity must be maintained to prevent bacterial invasion. To resolve this inconsistency, the concept of the drug delivery system has been introduced to burn care, and antibacterial drug-impregnated wound dressings are proving effective in controlling bacterial invasion even through a porous matrix (Fig. 1).

Several such wound dressings have been developed. One is an AgSD-impregnated porcine skin that has a meshlike structure capable of suppressing bacterial growth and preventing exudate buildup.[11-13] Another type is an AgSD-impregnated polymer gel composed of poly-2-hydroxyethylmethacrylate (poly-HEMA) and polyethyl-

Requests for reprints should be sent to Dr. Yoshimitsu Kuroyanagi, Department of Bioengineering, School of Medicine, Kitasato University, Sagamihara, Kanagawa 228, Japan.

Journal of Applied Biomaterials, Vol. 3, 153–161 (1992)
 CCC 1045-4861/92/020153-09$4.00

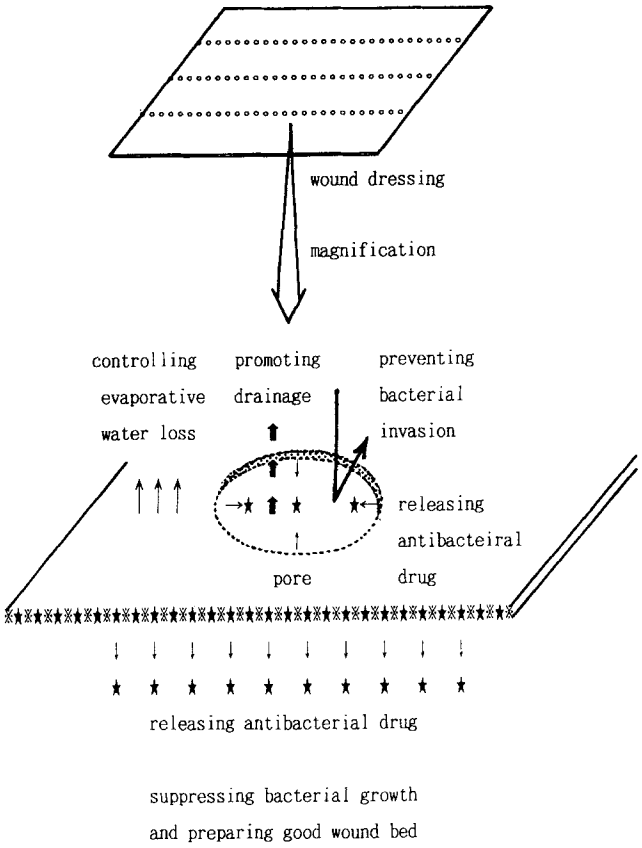


Figure 1. Functions of the wound dressing with drug-delivery capability.

englycol containing a small amount of dimethylsulfoxide and with a fabric backing (DIMAC).[14]

The present paper focuses on the development of a synthetic wound dressing with a drug delivery capability and reports on a clinical evaluation of this wound dressing.

MATERIALS AND METHOD

The authors' wound dressing consists of a hydrophobic poly-L-leucine spongy matrix impregnated with AgSD, which is released in a sustained fashion. The proportion of AgSD in the wound dressing is 0.4 mg/cm^2, to provide adequate support for testing its efficacy, a fine nylon mesh was incorporated as a middle layer of the matrix. This type of wound dressing has been shown to suppress bacterial growth in an *in vitro* test and in tests of experimentally infected animals.[15-18] The dressing was packaged and sterilized in sealed bags and stored at room temperature before testing on burn patients.

The protocol governing the use of this wound dressing is substantially the same as that for commercially available wound dressings. For partial-thickness burns, the dressing was applied directly to the wound and secured with sterile gauze. Twice a week the gauze was changed and the dressing was examined for absorption of exudate, drying, and adherence to the wound bed.

The wound dressing was left in place until it separated spontaneously from the re-epithelialized surface. In cases where the wound dressing did not adhere to the wound—for whatever reason, including cases of eschar and/or damaged tissue—the dressing was changed 3 or 4 days after application. When infection was present, the dressing was changed at intervals of 2–3 days, until it adhered firmly to the wound. Adherence is an indicator that the bactericidal properties of the dressing are having a beneficial effect. In severe burn cases manifesting necrotic skin, all eschar and damaged tissues were removed by chemical, mechanical, or surgical debridement before application of the wound dressing.

CASE REPORTS

Case 1

A 21-year-old male received a superficial second-degree burn of the right hand from a gasoline flame. Initially, he was treated with a commercially available 1% AgSD cream in an emergency room; he was referred to the authors 2 days later. A broken blister from the burn was removed, and the burn area was gently cleansed before an AgSD-impregnated wound dressing was applied and secured with sterile gauze to absorb exudate [Fig. 2(a–c)]. Three days later, the sterile gauze left was changed. Seven days after start of treatment, the wound dressing was changed. Except for a small area, the wound was found to be healing well, and a new AgSD-impregnated wound dressing was applied for another 7 days. This second dressing adhered firmly to the wound and subsequently fell off 14 days after application [Fig. 2(d–e)]. The wound was found to be completely healed. One month later, the patient had no problems with his motor movements and showed no scarring.

Case 2

A 22-year-old male received a superficial second-degree burn of the right foot from hot water. A broken blister from the burn was removed, and the burn area was gently cleansed before an AgSD-impregnated wound dressing was applied and secured with sterile gauze [Fig. 3(a–b)]. Three days later, the sterile gauze was changed. The wound dressing adhered firmly to the wound and subsequently fell off 9 days after start of treatment [Fig. 3(c)]. The wound was found to be completely healed.

Case 3

A 2-year-old male received a superficial second-degree burn of the right knee from hot water. The wound area was gently cleansed before the application of an AgSD-impregnated wound dressing and a commercially avail-

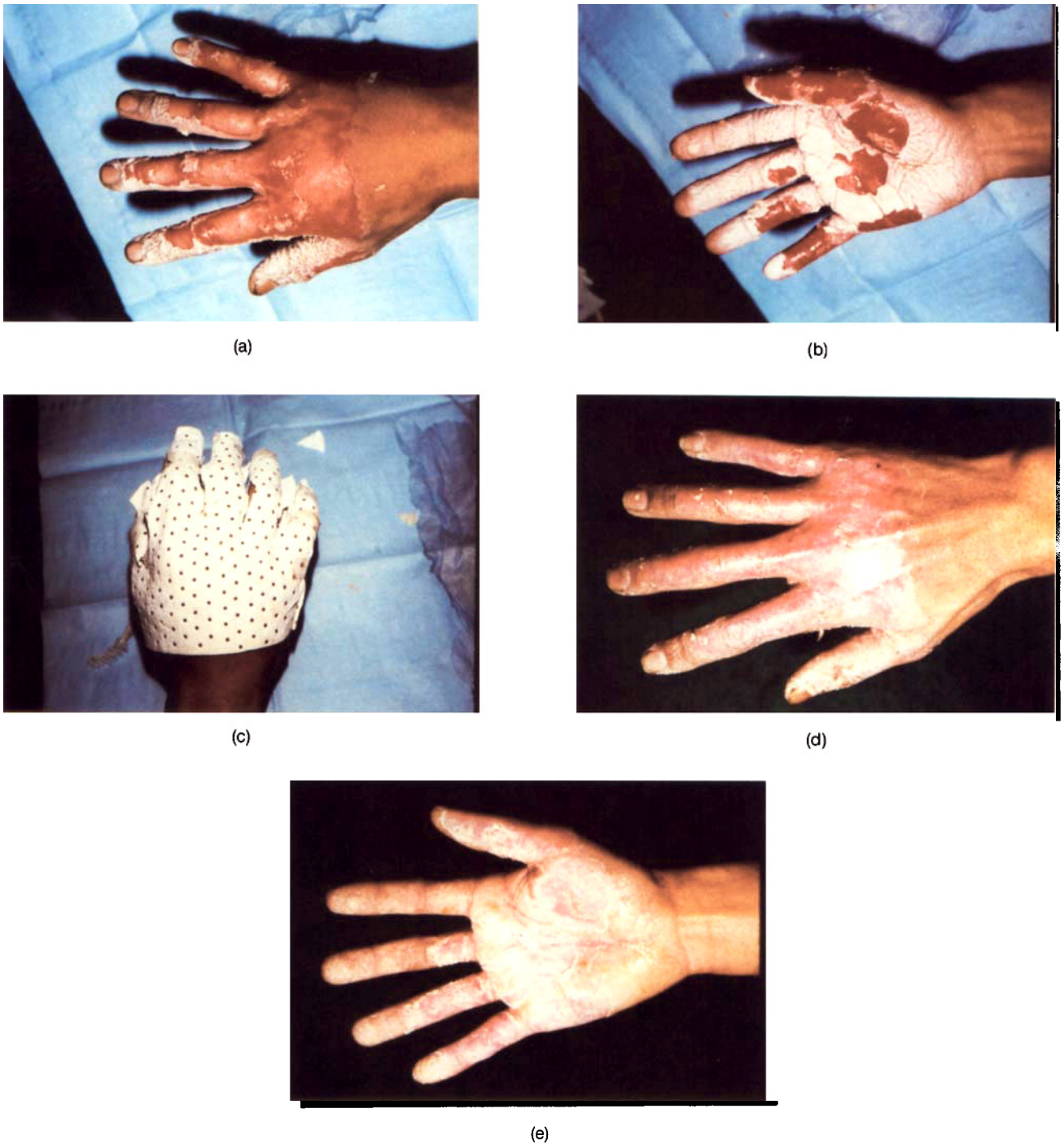
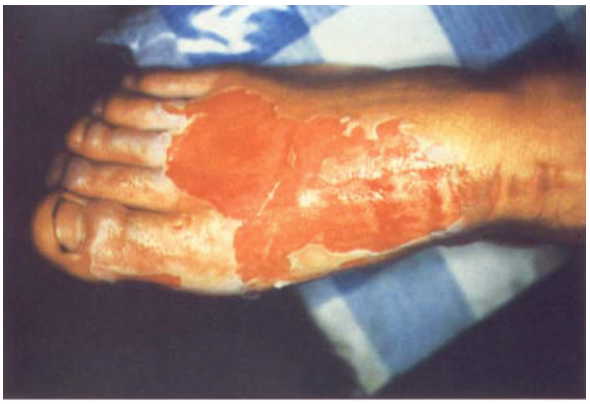


Figure 2. Case 1: A 21-year-old male received a superficial second-degree burn of the right hand from a gasoline flame. (a), (b) The burn area was cleansed; (c) the wound was covered with an AgSD-impregnated wound dressing; (d), (e) the wound was healed 14 days after application.

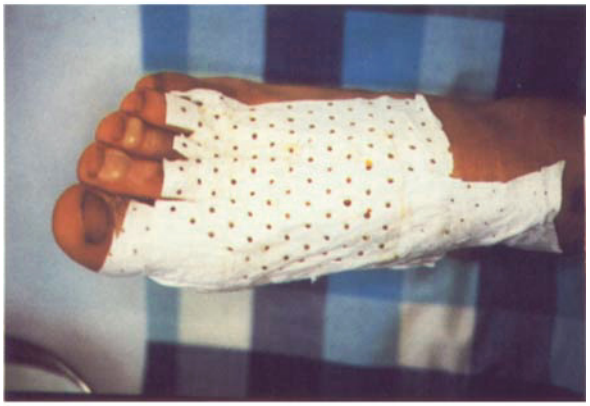
able lyophilized porcine skin as a half side test [Fig. 4(a)]. Sterile gauze used to secure both wound dressings and absorb exudate was left on and changed 3 days later. Six days after start of treatment, although the AgSD-impregnated wound dressing had adhered firmly to the wound, the porcine skin was partially dissolved [Fig. 4(b)]. A second AgSD-impregnated wound dressing was applied on the wound surface and secured with sterile gauze. This wound dressing was left on the wound until it fell off spontaneously and the wound was found to be completely healed 19 days later [Fig. 3(c)].

Case 4

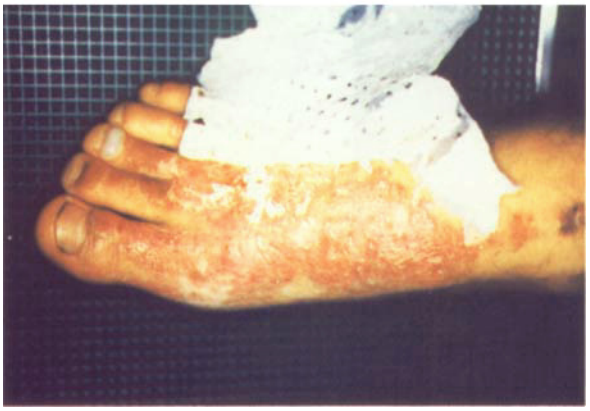
A 37-year-old female received a deep second-degree burn from hot oil that involved most of the first webspace of the right hand. She initially had been treated with an ointment and gauze dressing at another hospital before



(a)

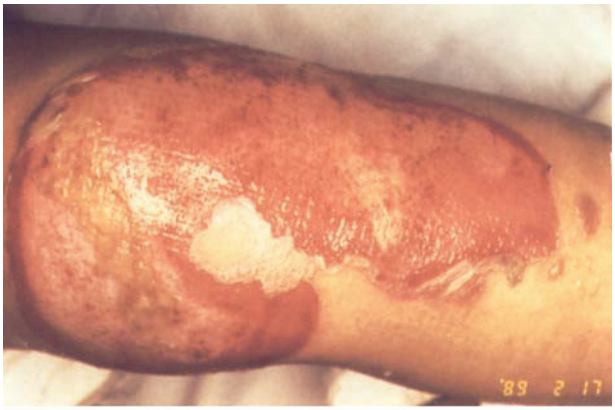


(b)

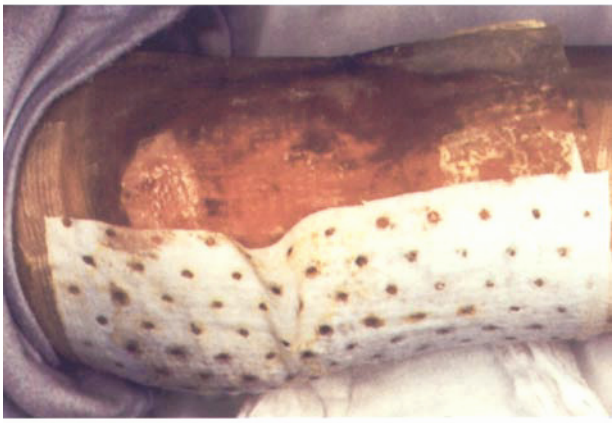


(c)

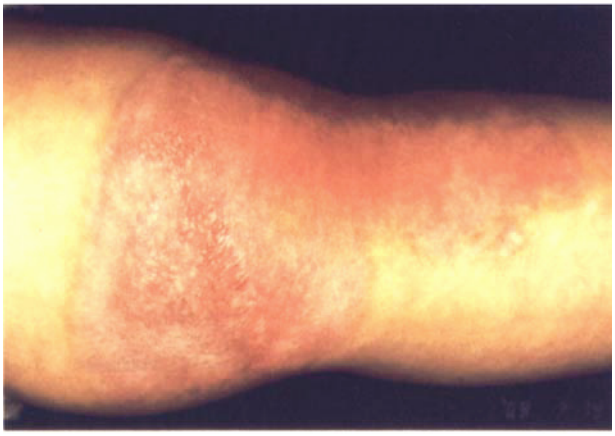
Figure 3. Case 2: A 22-year-old male received a superficial second-degree burn of the right foot from hot water. (a) The burn area was cleansed; (b) the wound was covered with an AgSD-impregnated wound dressing; (3) the wound was healed 9 days after application.



(a)



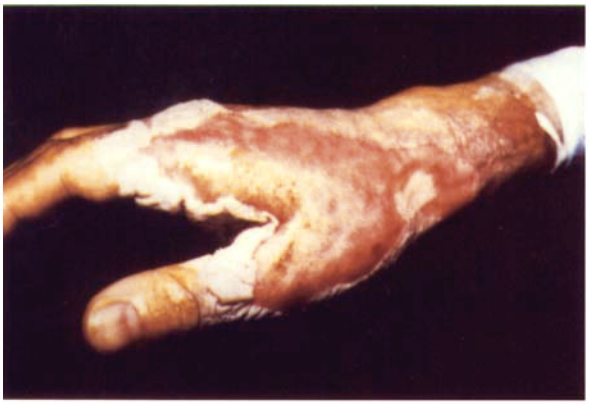
(b)



(c)

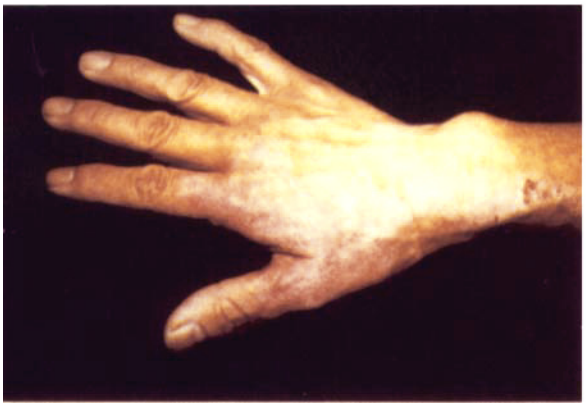
Figure 4. Case 3: A 2-year-old male received a superficial second-degree burn of the right knee joint from hot water. (a) The burn area was cleansed; (b) each half of the wound was covered with an AgSD-impregnated wound dressing and lyophilized porcine skin; (c) the wound was healed 19 days after application.

being referred to the authors 3 days later after experiencing considerable pain. The wound was gently cleansed, and an AgSD-impregnated wound dressing was applied and secured with sterile gauze. Application of the dressing immediately helped alleviate the pain. The gauze was changed 3 days later [Fig. 5(b)], and the initial wound dressing was changed 7 days after application. The dressing had adhered firmly except in a small area of the web-space. A second AgSD-impregnated wound dressing was applied and secured with sterile gauze. This wound dressing was left on the wound until it fell off spontaneously; by that time (4 weeks postinjury) the wound had completely healed [Fig. 5(c)]. Healthy re-epithelialization was



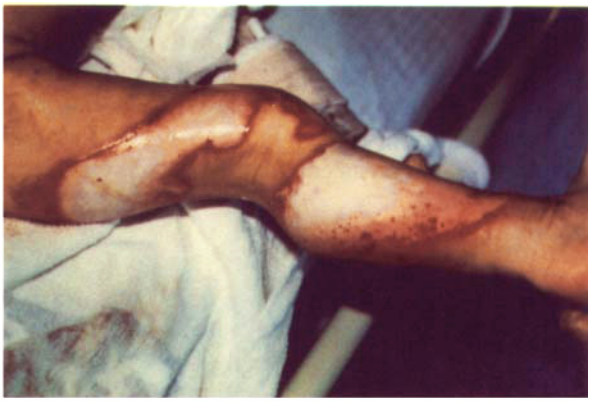
(a)

(b)

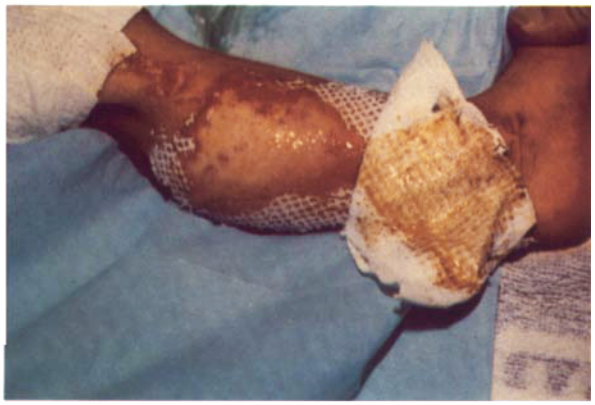


(c)

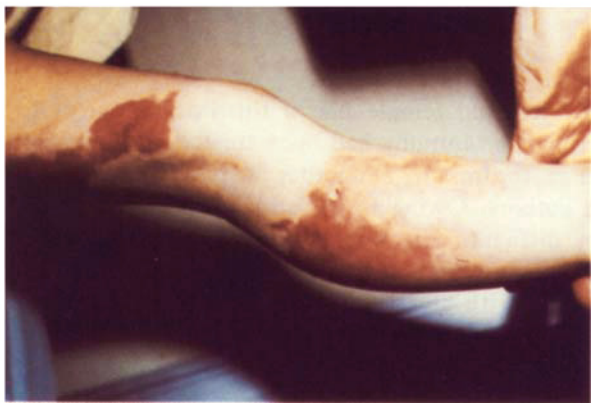
Figure 5. Case 4: A 37-year-old female received a deep second-degree burn of the right hand from hot oil. (a) The burn area was cleansed; (b) the wound was covered with an AgSD-impregnated wound dressing; (c) the wound was healed 25 days after application.



(a)



(b)



(c)

Figure 6. Case 5: A 3-year-old male received a deep second-degree burn of the right calf from hot water. (a) The wound area was cleansed; (b) 2 weeks after application, the wound appeared to be healing slowly; (c) the wound was healed 6 weeks after application.

seen, and the patient had no problem with her hand movements and showed no scarring.

Case 5

A 3-year-old male received a deep second-degree burn of the right calf from hot water, resulting in a small area of necrotic skin. He was initially treated with 1% AgSD cream in an emergency room before being referred to the authors 5 days later [Fig. 6(a)]. After gentle cleansing of the wound, an AgSD-impregnated dressing was applied and changed at intervals of 3–5 days until the dressing had adhered firmly to the wound [Fig. 6(b)]. At this point, 2 weeks after start of treatment, the wound appeared to be healing slowly; consequently, the wound dressing was changed at intervals of 5–7 days thereafter.

The sterile gauze was changed twice a week. Four weeks after start of treatment, the wound had healed except for a small area. At 6 weeks, the wound had completely healed and manifested a moderate pigmentation change but healthy re-epithelialization [Fig. 6(c)]. The wound dressing was no longer needed, although a pressure dressing was continued.

Case 6

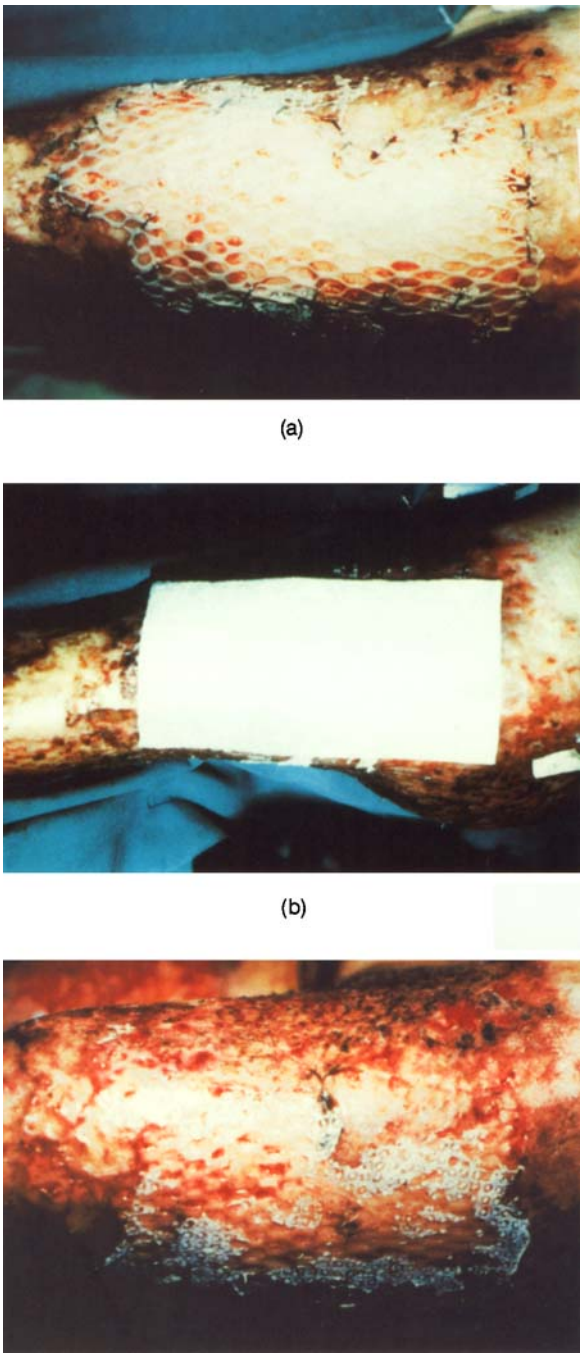
A 60-year-old female received a third-degree burn to the right thigh from a fire. Initially, she was treated with 1% AgSD cream for 10 days; at the end of this period, the necrotic skin had been debrided and a mesh autograft was applied. Owing to infection, the autograft did not take, and so the wound was again debrided and covered with an AgSD-impregnated wound dressing. This dressing was left in place for 1 week in an attempt to free the wound bed from infection before applying a second autograft; the sterile gauze securing the wound dressing was changed twice during that week. After autografting [Fig. 7(a)], the mesh autograft was covered with an AgSD-impregnated wound dressing and sterile gauze to suppress bacterial growth [Fig. 7(b)]. This wound dressing was removed 8 days after autografting, at which time the mesh autograft was noted to be taking well [Fig. 7(c)]. An AgSD-impregnated wound dressing was again applied to the wound and secured with sterile gauze for another 7 days, at which time the wound showed healthy re-epithelialization.

Case 7

A 57-year-old female had a third-degree ulcer to the sacrum. She initially had been treated with an ointment and gauze dressing at another hospital before referred to the authors. Owing to infection, wound care had been very difficult. The wound was gently cleansed, and an AgSD-impregnated wound dressing was applied and secured with sterile gauze [Fig. 8(a, b)]. The wound dressing and the gauze were changed at interval of 2–3 days until exudate buildup beneath the wound dressing was effectively reduced. Two weeks after start of treatment, the wound was found to be free from infection, and accumulation of exudate was not observed. After then, the wound dressing was changed at interval of 5–7 days. Eight weeks after start of treatment, the wound was found to be completely healed [Fig. 8(c)].

Case 8

A 62-year-old female had a third-degree ulcer to the sacrum. She initially had been treated with an ointment and gauze at another hospital before referred to the authors. Owing to excessive accumulation of exudate, the dressing had been changed twice a day. The wound was gently cleansed, and an AgSD-impregnated wound dressing was applied and secured with sterile gauze [Fig. 9(a, b)]. After 3 weeks of treatment, during which time the wound dressing was changed at interval of 2–3 days, accumulation of exudate was effectively reduced. After then, the wound dressing was changed at interval of 5–7 days. Eight weeks after start of treatment, the wound conditions were found to be much improved [Fig. 9(c)]; subsequently, an autograft was applied.

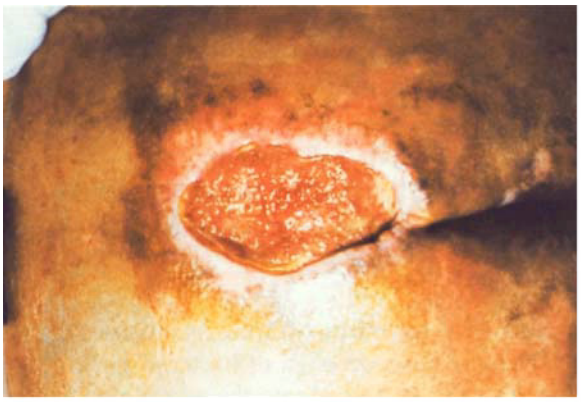


(a)

(b)

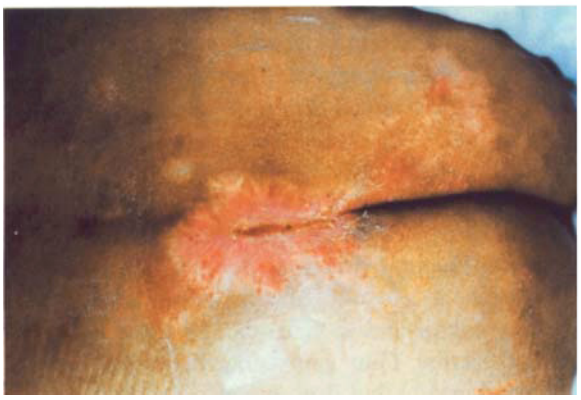
(c)

Figure 7. Case 6: A 60-year-old female received a three-degree burn to the right thigh from a fire. (a) Second mesh autograft was applied; (b) the mesh autograft was covered with an AgSD-impregnated wound dressing; (c) the mesh autograft was noted to be taking well.



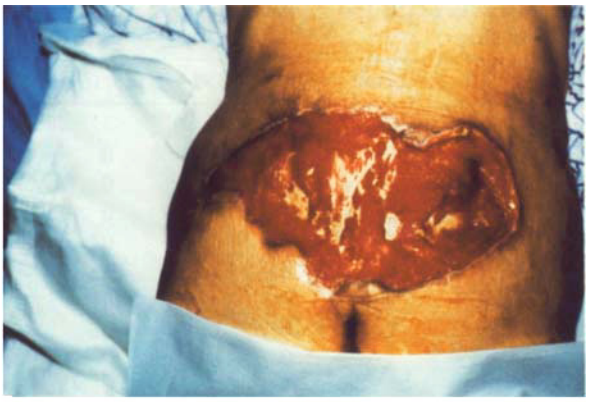
(a)

(b)

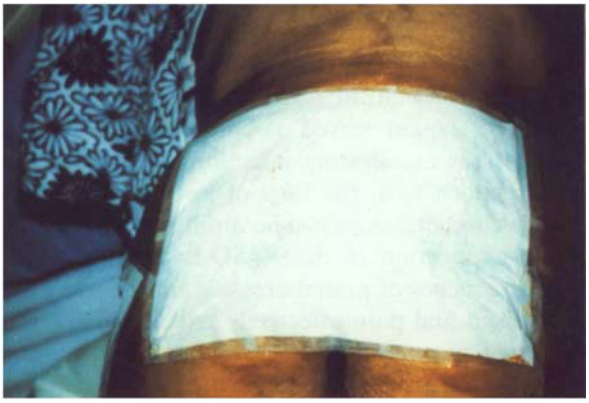


(c)

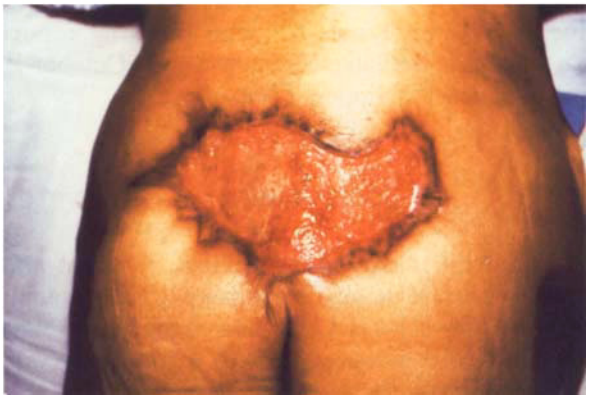
Figure 8. Case 7: A 57-year-old female received a third-degree ulcer to the sacrum. (a) The wound area was cleansed; (b) the wound was covered with an AgSD-impregnated wound dressing; (c) the wound was healed 8 weeks after application.



(a)



(b)



(c)

Figure 9. Case 8: A 62-year-old female received a third-degree ulcer to the sacrum. (a) The wound area was cleansed; (b) the wound was covered with an AgSD-impregnated wound dressing; (c) the wound conditions were much improved 8 weeks after application.

RESULTS

Clinical results were evaluated as excellent, good, or bad by considering efficacy in promoting wound healing, exudate buildup beneath the wound dressing, adherence to wound bed, frequency of wound dressing changes, and pain reduction. In the 52 cases treated with the authors' wound dressing, 93% (14/15) of superficial second-degree burns, 75% (3/4) of deep second-degree burns, 85% (6/7) of superficial and deep second-degree burns, and 75% (12/16) of split-thickness skin donor sites were evaluated as achieving good or excellent results (Table I). Commercially available wound dressings, including lyophilized porcine dermis (Alloask D^{R}, Kohtai

TABLE I. Results of Clinical Cases Using an AgSD-Impregnated Wound Dressing

Type	Excellent	Good	Bad	Exceptions	Total
SDB	8	6	0	1	15
DDB	0	3	1	0	4
SDB & DDB	1	5	1	0	7
DB	0	1	0	0	1
Mesh-graft[a]	1	2	0	0	3
Donor	6	6	4	1	17
Full-thickness	1	0	1	0	2
Split-thickness	1	0	0	0	1
Deep ulcer	2	0	0	0	2
Total	20	23	7	2	52

SDB, superficial dermal burn; DDB, deep dermal burn; DB, dermal burn.
[a]Covered with mesh graft.

Kasei, Japan), collagen nonwoven dressing (Meipac^R, Meiji, Japan), and chitin nonwoven dressing (Beschitin-W^R, Unitika, Japan) served as controls. In severe burn and ulcer cases manifesting infection, controls were not tested, inasmuch as at the time of testing, commercially available wound dressings had no antibacterial properties.

In the application of the AgSD-impregnated wound dressing, frequency of wound dressing change was eventually decreased and pain effectively reduced. This wound dressing had proven quite effective for the management of burn injuries. In the management of severe ulcers, the AgSD-impregnated wound dressing promoted reconstruction of granulation tissue and suppressed bacterial growth, thereby encouraged wound healing.

The AgSD-impregnated wound dressing reported herein was made available commercially in October 1991 in Japan (Epicuel^R, Nippon Zeon, Japan).

DISCUSSION

In patients with massive burn wounds, it is not always possible to achieve immediate closure of the wound by autografting. In such cases, excision of the burn wound is routinely followed by coverage with a temporary wound dressing or homograft. In Japan, however, where homografts are not readily obtained because donor sources are limited and a skin bank has yet to be established, temporary wound dressings must be used until previously harvested donor sites have re-epithelialized for reharvesting. Temporary wound dressings also have proven useful in allowing partial-thickness wounds to re-epithelialize. Although certain commercially available wound dressings are effective in inhibiting further water loss and promoting burn wound healing, if infection is present, the beneficial effects of these wound dressings are limited.

To overcome these limitations, the authors focused on developing a wound dressing that could provide the following capabilities:

1. Inhibition of water loss through evaporation.
2. Inhibition of body fluid loss.
3. Promotion of drainage and prevention of exudate buildup.
4. Protection from external contamination.
5. Sufficient bactericidal effect to inhibit infection.
6. Preparation of an optimum wound bed for autografting.

In treating severe burns with necrotic tissue, the most important issue is suppression of bacterial growth. Antibacterial drugs impregnated into the wound dressing have been shown to provide potent bactericidal effect when the dressing is directly applied to the wound. To enhance the efficacy of this approach, however, the bacteriacide must be released in a controlled, sustained manner. Because release rate depends largely upon the physical-chemical properties of the matrix, selection of a suitable matrix is paramount. Because an impregnated drug is released more rapidly from a hydrophilic matrix than from a hydrophobic matrix, a hydrophobic matrix makes it possible to extend the period of drug release and thus sustain its antibacterial action. On the basis of its inherent properties, we therefore decided to use hydrophobic poly-L-leucine as the matrix for our dressing.

DIMAC[14] is composed of hydrophilic synthetic polymers, poly-2-hydroxyethylmethacrylate (poly-HEMA) and polyethylenglycol. Therefore, AgSD-impregnated polymer gel dressing,[14,19] does not appear to be suitable for a controlled, sustained drug release. Another commercially available wound dressing with a drug delivery capability is AgSD-impregnated porcine skin,[11-13] which uses a matrix of biological origin that is regarded as being hydrophilic.

In addition to the physical-chemical properties of the matrix, such other factors as biodegradability and histocompatibility must be taken into consideration in developing an ideal wound dressing. Some kinds of synthetic materials present no problems with histocompatibility, and certain poly(α-amino acid) can be designed to have no such problems. Thus poly-L-leucine was selected for the matrix of our wound dressing also on the basis of its molecular design.

In a previous paper by the authors[20] using animal experimentation, data on the value of a nonmedicated poly-L-leucine wound dressing were shown, wherein commercially available wound dressings like Alloask®, Meipac®, vaseline gauze (Sofratulle®, Roussel, England), and Biobrane® (Woodroof Lab., Inc., U.S.A.) served as controls.

Clinically, the drainage of the exudate is also very important, especially in the management of severe burns where necrotic tissue is present, since an accumulation of exudate beneath the dressing promotes bacterial growth. Therefore, our wound dressing was designed to have

small pores throughout the spongy matrix, thereby eliminating exudate buildup.

The poly-L-leucine spongy sheet was designed to be very soft, so as to ensure adherence to irregular wound surfaces. A fine nylon mesh was incorporated as a middle layer in the wound dressing to provide adequate mechanical support, thereby improving manipulation in clinical application.

In the management of severe burns with necrotic tissue, the application of 1% AgSD cream is a traditional therapy,[21,22] although this antibacterial cream cannot be used in conjunction with a wound dressing because when applied beneath the wound dressing it inhibits the adherence of that dressing to the wound bed. It has recently been established that 1% AgSD cream in fact inhibits epithelial growth and may even result in cell death.[17,18] Therefore, a hydrophobic wound dressing that releases AgSD in a controlled, sustained manner is more effective for both inhibiting bacterial growth and promoting healing. The antibacterial properties of this type of dressing are effective in decontaminating even grossly infected wounds and in protecting clean wounds from adjacent infected areas and/or external infection. This wound dressing is especially useful in treating deep burns. The extended bactericidal effect of this dressing permits healing by epithelialization from the wound edges in certain cases where autografting would previously have been required. Should autografting still be necessary, the wound dressing can ensure the preparation of an optimum wound bed.

In the management of severe ulcers with contaminated and/or damaged tissue, application of an ointment and a gauze dressing is the traditional therapy. Such dressings have to be changed twice a day. By contrast, the authors' AgSD-impregnated wound dressing requires less frequent dressing changes, thus making it preferable in the management of troublesome ulcers.

REFERENCES

1. Park, G. B. Burn wound coverings: a review. Biomater. Med. Devices Artif. Organs. 6:1–35; 1978.
2. Tavis, M. J.; Thornton, J.W.; Bartlett, R. H.; Woodroof, E. A. A new composite skin prosthesis. Burns. 7:123–130; 1980.
3. Chvapil, M. Considerations on manufacturing principles of a synthetic burn dressing: a review. J. Biomed. Mater. Res. 16:245–263; 1982.
4. Davies, J.W. L. Synthetic materials for covering burn wounds: progress towards perfection. Part I. Short-term dressing materials. Burns. 10:94–103; 1984.
5. Davies, J.W. L. Synthetic materials for covering burn wounds: progress towards perfection. Part II. Long-term substitutes for skin. Burns. 10:104–108; 1984.
6. Queen, D.; Evans, J. H.; Gaylor, J. D. S.; Courtney, J. M.; Reid, W. H. Burn wound dressings: a review. Burns. 13:218–228; 1987.
7. Burke, J. F.; Yannas, I.V.; Quinby, Jr., W. C. Successful use of a physiologically acceptable artificial skin in the treatment of extensive burn injury. Ann. Surg. 194:413–428; 1988
8. Yannas, I.V.; Burke, J. F.; Orgill, D. P.; Skrabut, E. M. Wound tissue can utilize a polymeric template to synthesize a functional extension of skin. Science. 215:174–176; 1982.
9. Heimbach, D.; Luterman, A.; Burke, J. F.; Cram, A.; Herndon, D.; Hunt, J.; Jordan, M.; McManus, W.; Solem, L.; Warden, G.; Zawacki, B. Artificial dermis for major burns. Ann. Surg. 208:313–320; 1988.
10. Lamke, L. O.; Nilsson, G. E.; Reithner, H. L. The evaporative water loss from burns and the water–vapour permeability of grafts and artificial membranes used in the treatment of burns. Burns. 3:159–165; 1977.
11. Ersek, R. A.; Denton, D. R. Silver-impregnated porcine xenograft for damaged or missing skin. Contemp. Surg. 23:83–93; 1984.
12. Ersek, R. A.; Denton, D. R. Treatment with electrocautery and silver-impregnated porcine xenograft. Plast. Reconstr. Surg. 74:269–273; 1987.
13. Ersek, R. A.; Denton, D. R. Silver-impregnated porcine xenografts for treatment of meshed autografts. Ann. Plast. Surg. 13:482–487; 1984.
14. Miller, L.; Hansbrough, J.; Goldfarb, I.W.; Kealey, P.; Saffle, J.; Slater, H.; Silverstein, P. Efficacy and safety of DIMAC with silver sulfadiazine as compared to silvadene cream in the treatment of full thickness thermal injury. Abstract of 20th Annual Meeting of American Burn Association, Seattle. 1988:89.
15. Kuroyanagi, Y.; Koganei, Y.; Shioya, N. Development of wound dressing II. Evaluation of poly-L-leucine wound dressing containing antibacterial drug. J. Jpn. P.R.S. 7:526–537; 1987.
16. Kuroyanagi, Y.; Koganei, Y.; Shioya, N. Suppression of bacterial growth by a new temporary wound dressing containing antibacterial drug. J. J. Burn Inj. 13:206–212; 1987.
17. Kim, E.; Shioya, N.; Kuroyanagi, Y. Evaluation of a new temporary wound dressing containing antibacterial drug. J. Jpn. P.R.S. 9:676–686; 1989.
18. Kuroyanagi, Y.; Kim, E.; Shioya, N. Evaluation of synthetic wound dressing capable of releasing silver sulfadiazine. J. Burn Care Rehabil. 12:106–115; 1991.
19. Fox, C. L.; Modak, S.; Stanford, J.W.; Bradshaw, W. Silver sulfadiazine poly-hydroxylethylmethacrylate (PHEMA) dressing. Burns. 7:295–297; 1981.
20. Kuroyanagi, Y.; Koganei, Y.; Shioya, N. Development of wound dressing I. Comparison of poly-L-leucine wound dressing with others. J. Jpn. P.R.S. 7:515–525; 1987.
21. Sagar, I. K.; Nagesha, C. N.; Rao, P. G. Effectiveness of zinc sulphadiazine, zinc sulphate and silver sulphadiazine in the topical therapy of Pseudomonas infection in burn. Burns. 6:131–133; 1979.
22. Fox, C. L. Silver sulphadiazine, a new topical therapy for Pseudomonas in burns. Arch. Surg. 96:184–188; 1968.