



## **MOIST WOUND HEALING AND MOIST EXPOSED THERAPY**

***Professor Bishara S. Atiyeh and Dr Shady N. Hayek  
American University of Beirut Medical Center, Beirut, Lebanon***

### **Introduction**

Wound healing is a complex and highly regulated process that can be compromised by both endogenous and exogenous factors.<sup>1</sup> In both primary and secondary healing it consists of a series of events characterized by inflammation, epithelialization, connective tissue deposition and contraction. The contribution of each event varies according to the type of wound.<sup>2</sup> At any rate, the longer it takes for spontaneous wound healing to be completed, the worse the outcome usually is, with increasing likelihood of developing hypertrophic scarring and unsightly alterations in pigmentation. Moreover, under unfavorable conditions, the self-perpetuating inflammatory cascade may result in increasing tissue destruction and necrosis rather than healing.<sup>3,4</sup> On the other hand, understanding the concept of occlusion has been fundamental to the evolution of our knowledge about wound healing leading to the development of new wound dressings and has created a paradigm shift in the management of wounds.<sup>6,7,8,9,10</sup> Before this understanding, wounds often were kept dry, as advocated by Pasteur to keep them 'germfree'.<sup>6</sup> There is now growing evidence of improved healing of full- and partial-thickness cutaneous wounds in wet and moist environments. Retention of biologic fluids over the wound prevents desiccation of denuded dermis or deeper tissues and allows faster and unimpeded migration of keratinocytes over the wound surface. It allows also the naturally occurring cytokines and growth factors to exert their beneficial effect on wound contracture and re-epithelialization. Enthusiasm generated by these results has been, however, tempered by concerns over tissue maceration and infection following prolonged cutaneous water exposure.<sup>2,11</sup> These concerns may not be justified.<sup>2,12,13</sup> Nevertheless, despite mounting evidence and appreciation of the biologic beneficial factors of moist environments, applying the moist healing principles to large surface areas, in particular to large burns and skin graft donor sites, is hindered by the major impracticality and technical handicap of creating and maintaining a sealed moist environment over these areas.<sup>5,14,15</sup>

Dressings have been used since antiquity to facilitate the healing process. More recently many sophisticated dressings have become available to the wound care practitioner. These newer materials and agents supplement older dressing materials, such as gauze, which still are commonly used.<sup>6</sup> Wound dressings provide several important functions including protection, prevention of infection, promotion of healing through keeping the wound moist and warm, reduction of pain, absorption of exudate, comfort, stability and reduction of wound motion. Dressings should also be easy to apply and remove without causing further trauma. Although there is not one ideal dressing capable of providing all these functions, and not every wound requires every attribute, yet a wound may need a different dressing as it progresses through the healing process.<sup>6,7,8</sup> Different dressing materials, devices and agents provide different functions to greater or lesser degrees, and the attributes of each need to be matched to the specific wound on which it is placed.<sup>6</sup>

### **Moist Exposed Burn Ointment**

Since recent evidence suggests that moist environment favors more optimal healing, and since currently available moisture retentive devices cannot be universally applied, clinical trials were conducted to evaluate the efficacy of a newly introduced moisture retentive ointment, MEBO (Moist Exposed Burn Ointment) (Julphar Gulf Pharmaceutical Industries, UAE), on primary healing of surgically repaired wounds and on re-epithelialization of partial thickness wounds. The ointment is capable of providing an optimal moist environment without the need of an overlying occlusive dressing. MEBO is a Chinese burn ointment with a USA patented formulation since 1995. The active component of the ointment is b-sitosterol in a base of beeswax, sesame oil and other components. Clinical and experimental studies reported in the Chinese literature have demonstrated that it reduces markedly evaporation from the wound surface.<sup>15</sup> Though MEBO does not have any demonstrable in vitro bacteriostatic and bactericidal activity probably due to its oily composition that does not allow proper diffusion in a watery culture medium,<sup>16,17, 26,27</sup> it has been shown that in vivo, it had similar action to 1% Silver Sulfadiazine in controlling burn wound sepsis and systemic infection with *P. aeruginosa*.<sup>18,28</sup> It has also been demonstrated experimentally that MEBO exhibited a statistically significant wound healing potential on rabbit corneal epithelium as compared to saline, homologous serum, Vitamin A and dexamethasone.<sup>19</sup> The ointment produces good analgesia and has a good debriding effect, moreover, it drastically reduces water loss and exudation from the open wound surface. The required frequent application of the ointment is easy and can be performed by the patient himself or a member of his family. The most remarkable practical advantage of MEBO over other types of dressings is that it provides an effective wet environment favorable for optimal wound healing without the need of any covering or occlusive dressing. In some cases, however, particularly when the patient is not confined in bed or at home, a simple covering dressing may be more convenient.

Moist exposed burn ointment (MEBO) has been used traditionally in China for topical burn injuries treatment and was explored by Xu Rongxiang<sup>20</sup> from the Beijing Chinese Burn Center. It has been popularized outside China only two and a half decades ago. Reports about its properties and functions have been published in the Chinese literature; there was, however, a need to independently document the claimed benefits of this ointment in wound healing. Chinese traditional medicine (CTM) is quite different from the type of medicine and approach to disease as practiced in the west. Amongst our frenetic drive to develop more and more sophisticated and active wound healing devices and treatment modalities, it is wrong, however, to totally disregard CTM and its empirically time proven practices and remedies. It is difficult though to accept CTM without somehow adapting it to our ways of scientific analysis and documentation.<sup>21</sup>

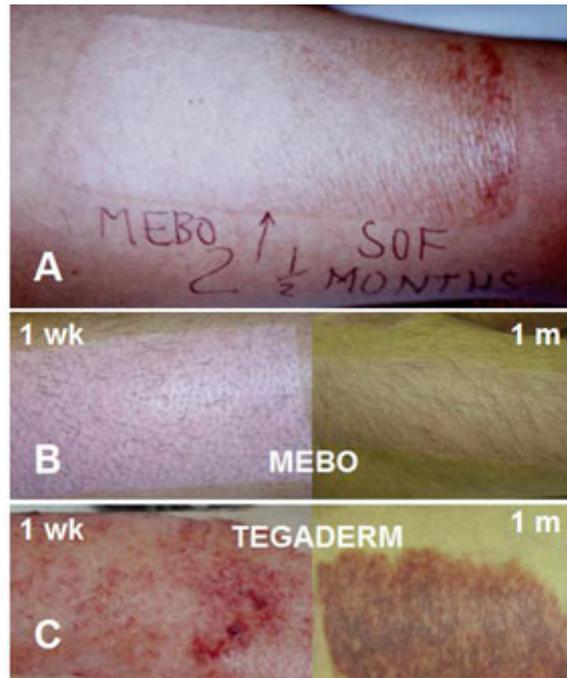


FIG. 1

Figure 1: (A) Healed STSG donor site at 2.5 months.

Note better cosmetic result of the area treated with moist exposed burn ointment (MEBO®).

Note also epidermal sliding present in the area treated by Sofra-Tulle®.

Demarcation zone between the two treatment areas indicated by arrow.

(B and C) STSG donor sites treated by MEBO® and Tegaderm®.

Better healing with better cosmetic result observed with MEBO®.

## Clinical Trials

We as well as others have already validated the claim that the ointment effectively preserves moisture at the surface of partial thickness wounds by both experimental studies and clinical trials. Results have already been published documenting better re-epithelialization.<sup>21,22,23,24,25,26,27,28</sup> When compared to the classical split thickness skin graft donor site dressing consisting of an antibiotic impregnated Vaseline gauze (Sofra Tulle®, Roussel Laboratories Ltd., Uxbridge, England) covered by a bulky gauze dressing, moist exposed burn ointment promoted speedy healing with excellent cosmetic outcome.<sup>23,24,25</sup> Re-epithelialization of donor sites with ointment application was also better than dressing the donor sites with Tegaderm® (3M Health Care, St Paul, MN), a moisture retaining semi-permeable adhesive film<sup>27,28</sup> (Figure 1). MEBO treatment resulted in earlier anatomical healing with significantly superior cosmetic appearance of the resultant scars over six months follow-up. The study demonstrated also significantly faster functional healing with restoration of cutaneous barrier function with ointment application. The observed positive correlation between improved scar quality and early physiologic recovery indicated that better cosmesis and improved function are closely linked.

When evaluating primary healing using the visual analogue scale,<sup>29</sup> cosmetically better scars consistent with lower scores are observed following prophylactic MEBO application for a period of six weeks after wound primary suturing at one, three, and six months when compared to a control no treatment group and another group treated with topical antibiotic application (Fucidin®, Leo Pharmaceutical, Denmark)<sup>30,31</sup> (Figure 2). Though significant differences in scores for colour, contour, distortion, and aspect between the three groups were observed with more favorable scores for the

MEBO treated group, only colour scores exhibited significant changes over time. At six months, the observed colour difference among the three groups becomes nonsignificant. It is, however, extremely significant at one and three months indicating that the permanent scar colour may be expected at an earlier stage whenever the scar is managed prophylactically with MEBO. Of all the parameters, only differences in texture values reflecting deeper dermal healing became extremely significant at six months while these were less significant at one and three months, indicating a net divergence in fibroblastic and scar remodeling activity between the treatment groups in favor of moist exposed burn ointment.



FIG. 2

Figure 2: Improved scar quality of primarily healed facial lacerations.

## Conclusion

Our investigation of this new moisture retentive ointment indicates so far that it has a definite positive effect on wound healing. The nature of the studies and their limited clinical scope, allow us, however, only to speculate on its mechanism of action as well as on its effect on the various phases and components of the wound healing cascade. Further research is still required to explore the bio-cellular mechanisms involved and its action on the different cytokines and metalloproteinases proven lately to be essential in determining the final outcome of healing. These reported studies as well as another prospective clinical trial of this ointment in topical treatment of chronic ulcers<sup>32,33</sup> have demonstrated the extreme ease of application and practicality of this ointment in providing the necessary moist conditions for optimal healing as compared to currently available labor intensive and time consuming moisture retaining products and devices. Though it is not an antibiotic and definitely not suitable for the treatment of established wound sepsis, adequate local antibacterial action of the ointment maintaining open wounds in a healthy 'none infected' condition has also been demonstrated. Even when used for prolonged periods of time, emergence of resistant strains was not observed.<sup>32,33</sup>

## References

1. Bowler PG. Wound pathophysiology, infection and therapeutic options. *Ann Med* 2002; 34: 419–427.
2. Grinnel F. Fibroblasts, myofibroblasts, and wound contraction. *J Cell Biol* 1994; 124: 40–44.
3. Grossman PH, Grossman AR. Treatment of thermal injuries from CO2 laser resurfacing. *Plast Reconstr Surg* 2002; 109: 1435–42.
4. Spence RJ, Wong L. The enhancement of wound healing with human skin allograft. *Surg Clin North Am* 1977; 77: 731–745.
5. Atiyeh BS, El-Musa KA, Dham R. Scar quality and physiologic barrier function restoration after moist and moist-exposed dressings of partial-thickness wounds. *Dermatol Surg* 2003; 29: 14–20.
6. Lionelli GT, Lawrence WT. Wound dressings. *Surg Clin North Am* 2003; 83: 617–38.
7. Thomas DR, Kamel HK. Subacute care for seniors, *Clin Geriatr Med* 2000; 16: 783–804.
8. Pearson AS, Wolford RW. Management of skin trauma. *Dermatology* 2000; 27: 475–92.
9. Mostow EN. Wound healing: A multidisciplinary approach for dermatologists. *Dermatol Clin* 2003; 21: 371–387.
10. Brem H, Nierman D, Nelson JE. Pressure ulcers in the chronically critically ill patient. *Critical Care Clin* 2002; 18: 683–694.
11. Winter GD. In: Epidermal regeneration studied in the domestic pig. Maibach HI, Rovee DT (eds). *Epidermal wound healing*. Year Book Medical Publishers, Inc. Chicago 1972, 71–112.
12. Vogt PM, Andree C, Breuing K, Liu PY, et al. Dry, moist, and wet skin wound repair. *Ann Plast Surg* 1995; 34: 493–499.
13. Reuterving CO, Agren MS, Soderberg TA, Tengrup I, et al. The effects of occlusive dressings on inflammation and granulation tissue formation in excised wounds in rats. *Scand J Plast Reconstr Surg* 1989; 23: 89–96.
14. Jonkman MF, Hoeksma EA, Nieuwenhuis P. Accelerated epithelialization under a highly vapor-permeable wound dressing is associated with increased precipitation of fibrin(ogen) and fibronectin. *J Invest Dermatology* 1990; 94: 478–84.
15. Wang GS, Zhang YM, Liu RS, et al.: Experimental study of the Effect of MEBO on blood rheology in the treatment of burned rabbits. *Chinese J Burns Wounds Surf Ulcers* 1993; 5 (4): 30–32.
16. Qu YY, Wang YP, Qiu SC et al.: Experimental research on the anti-infective mechanism of MEBO. *Chinese J Burns Wounds Surf Ulcers* 1996; 8 (1): 19–23.
17. Xing D: Experimental study on the actions of the moist burn ointment on promoting healing of skin wound and anti-infection. *Chinese J Burns Wounds Surf Ulcers* 1989; 1 (1): 75–76.
18. Geng XL, Bu XC, Gao FQ, Liu YL: Study on the bacterial count in the subeschar living tissues of burn wounds. *Chinese J Burns Wounds Surf Ulcers* 1989; 1 (1): 49–50.
19. Huang QS, Zhou G, Su BP, Huang EX: A comparative study of fibronectin and MEBO in the treatment of experimental rabbit corneal alkaline burn. *Chinese J Burns Wounds Surf Ulcers* 1995; 7 (1): 18–9
20. Xu R: the medicine of burns and ulcers, a general introduction. *Chinese J Burns Wounds Surf Ulcers* 1989; 1 (1): 68
21. Atiyeh BS, Ioannovich J, Magliacani G, Masellis M, Costagliola M, Dham R, Al-Musa K A. A new approach to local burn wound care: moist exposed therapy, a multi-phase, multicenter study. *J Burns & Surg Wound Care* [serial online] 2003; 2:18. Available from: URL: <http://www.journalofburns.com>
22. Ioannovich J, Tsati E, Tsoutsos D, Frangia K, et al. Moist exposed burn therapy: evaluation of the epithelial repair process (an experimental model). *Ann Burns Fire Disast* 2000; 8: 3–9.
23. Atiyeh BS, Ioannovich J, Al-Amm CA. Pansements de sites donneurs de greffe de peau mince: resultats preliminaires d'une etude clinique limitee comparative de 'MEBO' et de 'sofra-tulle'. *Brûlures, Revue Française de Brûlologie* 2000; 1: 155–61.
24. Atiyeh BS, Ghanimeh G, Kaddoura IL, Al Amm C, Ioannovich J. Split thickness skin graft donor site dressing:

- preliminary results of controlled clinical comparative study of MEBO and sofra-tulle. Letter-to-the-editor. *Ann Plast Surg* 2001; 46: 88–89.
25. Atiyeh BS, Al-Amm CA, Nasser AA. Improved healing of split thickness skin graft donor sites. *J Applied Research* 2002; 2: 114–21.
26. Ang ES, Lee ST, Gan CS, See P, et al.: The role of alternative therapy in the management of partial thickness burns of the face – experience with the use of moist exposed burn ointment (MEBO) compared with silver sulphadiazine. *Ann Acad Med Singapore* 2000; 29: 7–10.
27. Atiyeh BS, Al-Amm CA, El-Musa KA, Sawwaf A, Dham R. Scar quality and physiologic barrier function restoration following moist and moist exposed dressings of partial thickness wounds. *Dematol Surg* 2003; 29: 14–20
28. Atiyeh BS, Al-Amm CA, El-Musa KA, Sawwaf A, Dham R. The effect of moist and moist exposed dressings on healing and barrier function restoration of partial thickness wounds. *Eur J Plast Surg* 2003; 26: 5–11.
29. Beausang, E, Floyd, H, Dunn, KW, Orton, GI et al. A new quantitative scale for clinical scar assessment. *Plast Reconstr Surg* 1998; 102: 1954–61.
30. Atiyeh, BS, Ioannovich, J, Al-Amm, CA, El-Musa, KA, Dham, R. Improving scar quality: A prospective clinical study. *Aesth Plast Surg*. 2002; 26: 470–6.
31. Atiyeh BS, Amm CA, El Musa KA. Improved scar quality following primary and secondary healing of cutaneous wounds. *Aesth Plast Surg* 2003; 27: (in press).
32. Atiyeh BS, Ioannovich J, Magliacani G, Masellis M, Costagliola M, Dham R. The efficacy of moisture retentive ointment in the mangement of cutaneous wounds and ulcers: a multicenter clinical trial. *Indian J of Plast Surg* 2003; 36: 89–98.
33. Atiyeh BS, Ioannovich J, Magliacani G, Masellis M, Costagliola M, Dham R. The efficacy of MEBO (moist exposed burn ointment) in the management of cutaneous wounds and ulcers: a pilot study. Letter-to-the-editor, *Ann Plast Surg* 2002; 48: 226–7.

***Bishara S. Atiyeh, MD, FACS***

Clinical Professor

Division Plastic and Reconstructive Surgery

American University of Beirut Medical Center

Beirut, LEBANON

***Shady N. Hayek, MD***

Chief Resident

Division Plastic and Reconstructive Surgery

American University of Beirut Medical Center

Beirut, LEBANON

Responsible Author and Reprint Requests:

***Bishara S. Atiyeh, MD, FACS.***

Clinical Professor

Division of Plastic and Reconstructive Surgery

American University of Beirut

Beirut, Lebanon

Tel: (916) 3 340032

Fax: (961) 1 363291

E-mail: [aata@terra.net.lb](mailto:aata@terra.net.lb)

