Effects of Occlusion (II): Wound Healing

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This is the second article in a series discussing effects of occlusion on skin. (The series opened in November 2003 with a focus on percutaneous absorption.) The present article focuses on the effects of occlusive and semipermeable membranes on wound healing and summarizes related data.

Skin occlusion is a complex issue that includes altering epidermal lipids, DNA synthesis, epidermal turnover, pH, epidermal morphology, sweat glands, Langerhans cells stresses, etc.[1-17] Occlusion usually means the skin is covered directly or indirectly by impermeable films or substances such as diapers, tape, chambers, gloves, textiles garments, wound dressings, transdermal devices, etc.;[1] but certain topical vehicles that contain fats and/or polymer oils (petrolatum, paraffin, etc.) may also generate occlusive effects.[2]

A broad selection of occlusive or semi-occlusive dressings has been long employed to speed the healing processes in acute and chronic wounds.[18] They keep healing tissues moist and increase superficial wound epithelialization.[2,18-22] However, occlusive or semiocclusive dressings can increase microorganisms and hence induce wound infections.[2,23-25] Significant increases in the density of *Staphylococcus aureus* and lipophilic diphtheroids were observed after 24 h occlusion in eczematous and psoriatic skin.[14]

Effects of Occlusive and Semipermeable Membranes on Wound Healing

Superficial wounds in domestic pigs: Alvarez et al.[21] compared the effects of several types of occlusion on superficial wounds in domestic pigs. The occlusion types were: two different occlusive dressings; non-occlusive wet to dry gauze dressings; and air exposure. Collagen synthesis and re-epithelialization were increased in the wounds treated with occlusive dressings. Re-epithelialization was increased beneath both the oxygen-impermeable and the oxygen-permeable dressing. When removed, the wet to dry gauze dressing and one of the occlusive dressings often damaged the new epidermis.

Biopsy punch in rabbits: Surinchak et al.[26] monitored healing process by measuring water evaporation. In the first study two wounds were created with a 2-mm biopsy punch on the backs of each of 15 rabbits and covered with occlusive and semiocclusive dressings. Water loss increased from a preoperative value of 6 $g/m^2/hr$ to 55 $g/m^2/hr$ after biopsy. Water loss from the occluded site returned to baseline values in 9 days as opposed to 17 days for the semioccluded sites ($p < 0.05$).

Full-thickness 4 x 4 cm wounds in rabbits: A second study by Surinchak et al.[26] followed the healing of full-thickness 4 x 4-cm wounds in five rabbits treated with fine-mesh gauze and five treated with a human amnion dressing.[26] Wound area and water loss were observed during the repair process. In visual evaluations of the wound area, the injuries appeared 100% healed on day 30. However, the evaporimeter detected significantly increased water loss up until day 45 when original baseline values were reached. No differences were observed between the gauze and amnion groups.

The evaporimeter presents a simple yet accurate, noninvasive tool for measuring the wound healing endpoint based on regeneration of the epidermal water barrier.

Human dermabrasion wound: Pinski[27] compared a series wound dressing utilizing a human dermabrasion wound healing model. Occlusive dressings hastened healing time as much as 50% over air-exposed sites.

Acetone-induced wounds in hairless mice: Grubauer et al.[28] treated hairless mice with acetone that removed stainable neutral lipids from the stratum corneum (SC) and compared the rate of repletion of stainable lipids, barrier recovery, and epidermal lipogenesis in animals covered with occlusive membranes or vapor-permeable membranes versus uncovered animals. Acetone treatment perturbed epidermal barrier

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function, which returned to normal in uncovered animals in parallel with the reappearance of SC lipid; when animals were covered with an occlusive membrane, barrier function did not recover normally. In contrast, occlusion with vapor-permeable membranes allowed barrier function to recover normally.

They concluded that occlusive membranes prevented the increase in epidermal lipid synthesis while a vapor-permeable membrane increased epidermal lipid synthesis in animals.

Wounds produced in human subjects: Silverman et al.[29] examined the effects of occlusive dressings on the reestablishment of the cutaneous barrier to transepidermal water loss (TEWL) after standardized skin wounds produced in human subjects. Wound repair occurred more quickly under occlusive or semiocclusive dressings than when it was allowed to proceed exposed to the environment. However, no significant improvement in the rate of reestablishment of the barrier to TEWL was measured between the covered test or uncovered control sites in each subject.

Suction blister wound model in humans: Levy et al.[30] utilized a suction blister wound model to assess drug effects on epidermal regeneration with 20 healthy volunteers. Four suction blisters were produced on the volar aspect of the forearm. Then the epidermis was removed to create a standardized subepidermal wound. Thereafter, the wounds were treated topically for 6 h daily during 14 days. The following treatments were compared: a topical clobetasol 17-propionate preparation under occlusion; a corticoid-free cream under occlusion; no treatment and occlusion (aluminium chamber); no treatment and no occlusion.

Daily measurement of TEWL above the wounds was performed. The 0.05% clobetasol 17-propionate preparation caused a dramatic delay in TEWL decrease, whereas the untreated unoccluded field showed a continuous decrease over 14 days. Occlusion and corticoid-free treatment led to a weak but significant delay of TEWL decrease when compared to the untreated unoccluded test field.

Tape stripping wound in humans: Visscher et al.[31] evaluated the effects of semipermeable films on human skin following a standardized tape stripping wound by measuring of TEWL, skin hydration, rate of moisture accumulation, and erythema. Wounds treated with semipermeable films underwent more rapid barrier recovery than either unoccluded wounds or wounds under complete occlusion. Barrier films that produced intermediate levels of skin hydration during recovery produced the highest barrier repair rates.

Conclusions

Occlusion dressing may hasten the healing time[2,18-22,27,29] but complete occlusion dressings have some disadvantages,[21,26,28,30] particularly when compared to semiocclusion dressings. Therefore, an ideal wound dressing would require a compromise between occlusion and nonocclusion. It should absorb exudate, thus decreasing bacteria; permit fluid evaporation; and either avoid incorporation into the eschar or be sufficiently fragile to allow its removal without compromising the healing wound.

Advanced dressings attempt to specifically maintain a moist wound environment. Natural, pure, and non-woven dressings from calcium alginate fibers can rapidly absorb and retain wound fluid to form an integral gellified structure, thereby maintaining an ideal moist wound healing environment.[32] It can also trap and immobilize pathogenic bacteria in the network of gellified fibers. And it can stimulate macrophage activity and activate platelets, resulting in homeostasis and accelerated wound healing.

The biologic effects of dressings remain a complex science: at a minimum, clinical relevance for man requires a multifaceted interpretation based on our current knowledge of "validation for man." When can we extrapolate from rodents to man, what is the overlying "Rosette Stone" that might relate the more "superficial" (stripping and/or solvent extraction) knowledge to split and full thickness wounds? What can be learned from other factors (O_2, CO_2, and electrolytic transport)? These represent but a few of the challenges for wound dressing developers.

Today, with the rapid development of new technologies in bioscience, we can expect greater efficacy and optimal dressings or materials that can absorb excess water in accelerating the healing of wounds without the unfavorable effects of occlusion.

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