The Effect of Gas Permeability of Film Dressings on Wound Environment and Healing

Larry M. Sirvio, M.S., and Duane M. Grussing

3M Biosciences Research Laboratory, St. Paul, Minnesota, U.S.A.

We have determined the effect of oxygen and carbon dioxide permeability of thin film dressings on wound exudate $P O_2$, $P CO_2$, pH, and epithelialization in shallow wounds on domestic pigs. Three kinds of films were compared: polyvinylidine chloride, a low gas permeability film; polyurethane, a medium gas permeability film; and poly(dimethyl silicone), a high gas permeability film. Exudate under the silicone film had the highest $P O_2$ and the lowest $P CO_2$; exudate under the polyurethane had intermediate $P O_2$ and $P CO_2$; and exudate under the polyvinylidine chloride had the lowest $P O_2$ and highest $P CO_2$. Values for pH under the films correlated inversely with $P CO_2$. The gas tensions and pH are a reflection of the ability of the films to control the diffusion of oxygen into and the loss of carbon dioxide from the wound exudate.

Mean epithelialization values at 2 and 3 d were not significantly different under polyvinylidine chloride and polyurethane, but both were higher than under the silicone film. We infer from the data that the use of oxygen and carbon dioxide impermeable film dressings do not affect epithelialization in well-perfused, shallow wounds. The use of the silicone film (highly permeable to both oxygen and carbon dioxide) led to a loss of carbon dioxide. The resulting relatively high pH may have been responsible for the reduced rate of epithelialization which occurred beneath the silicone film. *J Invest Dermatol 93:528–531, 1989*

The use of vapor permeable membranes as wound dressings has been shown to decrease the time required to achieve healing as defined by various epithelialization measurements [1–4]. The possibility of further reducing the time required for epithelialization was tested by Winter using hyperbaric oxygen [5] and by varying the oxygen permeability of the film being used [3]. In these studies the direct measurement of the environment under the dressing was not undertaken. Studies by Silver [6,7] measured the effect of film oxygen permeability on the corresponding wound $P O_2$ without determining the effect of these differences on epithelialization. Hunt et al [8,9] and Niinikoski et al [10] studied gas tensions and pH in implanted stainless steel mesh cylinders in rabbits and showed that collagen synthesis was directly related to oxygen tension in a subepidermal wound model.

Alvarez et al [11] showed that epithelialization of shallow wounds on pigs under an oxygen-permeable polyurethane film and under an oxygen-impermeable hydrocolloid dressing were both increased relative to gauze covered or air exposed wounds.

Varghese et al measured $P O_2$ and pH under polyurethane and hydrocolloid dressings [12] on chronic full thickness dermal ulcers in humans. They showed a surprisingly low $P O_2$ under the polyurethane film dressing in spite of the relatively high permeability of the polyurethane dressing to oxygen.

In our studies, we measured the effect of gas permeability of film dressings on the environment of a superficial wound as well as the effect on wound healing. We considered two critical questions which should be addressed regarding the effects of film permeability on wound healing: 1) Can the gas permeability (specifically to oxygen and carbon dioxide) of the film influence the physiologic conditions under the dressing? 2) If so, does this permeability influence the rate of epithelialization?

We approached these questions by monitoring wound exudate oxygen and carbon dioxide tensions and pH under film dressings applied over shallow excisional wounds on the backs of domestic pigs. Three different films covering a wide range of gas permeabilities were studied: Polyvinylidine chloride (Saran*), low oxygen and CO_2 permeability; a polyurethane film with an acrylate based adhesive (Tegaderm*), intermediate oxygen and CO_2 permeability; and a medical grade silicone film (cross-linked polydimethylsiloxane), high oxygen and CO_2 permeability (see Table I).

MATERIALS AND METHODS

Dressings Standard Tegaderm (3M Medical Products Div.-Product No.1626) was used as the polyurethane dressing. Polyvinylidine chloride (0.0025 cm thick; Saran Wrap - Dow) was rinsed thoroughly with distilled water and dried before use. This was done to remove possible surface contaminants which may have been present from the manufacturing process. It was cut to 5 × 5 cm and fixed to the adhesive side of Tegaderm in which a 2.5 × 2.5 cm cut-out had been made. Medical grade silicone film (0.0025 cm thick polydimethylsiloxane- McGhan Medical) was cut to 3.75 × 3.75 cm. In order to facilitate adherence of this film to a similar Tegaderm cut-out, the silicone film was treated by oxygen-Rf glow discharge before use. The latter two dressing materials were also sterilized with ethylene oxide prior to use.

Surgical Procedures The animals used were young, female, Yorkshire-cross swine (Sus scrofa), weighing approximately 35 kg. They were housed at least 1 week prior to use and were visited daily to acclimate them to handling. Three days prior to surgery the back of each animal was clipped with an electric clipper and a protective

Table I. Gas Transmission Rates of Film Dressings

Dressing	Oxygen transmission[a] (L/M²/24 h)	CO₂ transmission[b] (L/M²/24 h)
Polyvinylidine chloride	0.028	0.40
Polyurethane (Tegaderm)	2.74	125
Silicone	> 20	> 375

[a] Test conditions: Oxygen gradient 21.33 kPa (160 mm Hg) at 37.8°C and 50% relative humidity.

[b] Test Conditions: Carbon dioxide gradient 98.64 kPa (740 mm Hg) at 37.8°C and 0% relative humidity.

cage was strapped to its back. On the day of surgery the animal was anesthetized with Halothane, nitrous oxide, and oxygen through a face mask. Anesthesia was continued through an endotracheal tube with 1% Halothane (balance; oxygen/nitrous oxide; 50/50). The site for surgery was scrubbed with a Povidone-iodine solution and closely shaved with a safety razor. All surgery was done under sterile surgical conditions. The surgical site was scrubbed twice alternately with solutions of Povidone-iodine and 70% ethanol. Twelve partial thickness wounds (2.5 × 2.5 × 0.0375 cm) were made on the back of each animal using an air-powered dermatome (Howe Medica). The skin surrounding each wound was wiped with ether and painted with tincture of benzoin. The last two steps were found to be essential in order to prevent leakage of exudate and/or exposure of the wound to the outside atmosphere due to adhesive failure of the dressing. In addition, the last step standardized the area of the dressings exposed to wound exudate.

Four each of the three dressing types were applied to six animals. They were placed on wounds in a manner designed to distribute the various film types evenly. After the dressings were applied, the protective cage was replaced over the back of the animal to protect the dressings from disturbance [13], and the animal was returned to its run.

Analysis of Wound Exudate Wound exudate was withdrawn and analyzed at 2 d (three animals) and 3 d (three animals). Biopsy samples of the wound area were also taken at those times for histologic evaluation and measurement of epithelialization. Data were collected only from wounds in which there was no evidence of leakage for the duration of the experiment. Samples of exudate were withdrawn with a 1 mL syringe by inserting a needle through the Tegaderm, taking extreme care not to expose the sample to the atmosphere. The exudate samples were analyzed immediately for pH, P O₂, and P CO₂ using an Instrumentation Laboratories System 1303 Blood Gas Analyzer. Results of blood gas analyses are reported in kilo Pascals (kPa).

Histology Full thickness biopsy specimens were obtained from the middle ⅓ of each wound (cut dorsal to ventral). Each specimen was cut into quadrants prior to routine processing into paraffin. Five sections from each quadrant were cut, mounted, and stained with hematoxalyn and eosin. Sections were cut at 500-μm intervals and were started from non-adjacent faces of the quadrants in order to obtain sections from four different areas of the biopsy. Epithelialization was measured on approximately 20 cm of total wound length (four sections per quadrant; equivalent to eight full width sections per wound) using a Zeiss Video Plan Image Analyzer. The technique microscopically measures wound length and new epidermis on each section, allowing calculation of the percent epithelialization. The use of a limited number of tissue sections to determine the epithelialization over shallow wounds in the back of the pig has been described by Chvapil et al [14].

RESULTS

Analysis of Exudate Volumes of exudate from 2 and 3 d wounds under all dressing types ranged from 1 to 3mL. There was no relationship between exudate volume and blood gas values obtained, indicating that adequate convective mixing had occurred beneath the dressing and that the values obtained represented equilibrium
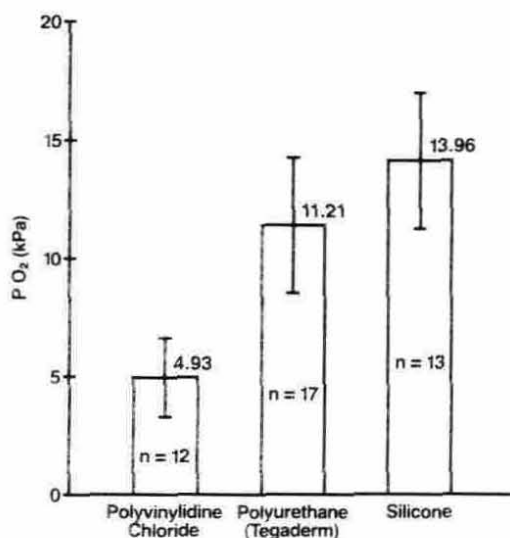

Figure 1. P O₂ under film dressings. Combined data from 2 and 3 d partial thickness wounds on domestic pigs.

values between the tissue and exudate. In seven of the 72 wounds (two under polyvinylidine chloride, five under the silicone films) exudate P O₂ values were found to be near zero. All data from such wounds were excluded from the results (healing of these wounds did not appear to be affected). The phenomenon of low P O₂ has been reported by Hunt et al [15] and was attributed to the activity of neutrophils in the presence of bacteria in the wound fluid. Similarly, the presence of bacteria in wound exudate may be responsible for the low P O₂ values seen here.

Statistical analysis of the data included an F-test for variance ratio of the two populations followed by Student's t-test of the means. Data reported are mean ± one standard deviation. Analysis of blood gas data from wound exudates on days two and three were combined because there were no differences in the data that could be attributed to the day of analysis.

The analysis indicated that film permeability (see Table I) did influence wound P O₂, P CO₂, and pH (see Figs 1–3). The P O₂ under polyvinylidine chloride (mean 4.93 kPa) was significantly lower (p < 0.0001) than under polyurethane (mean 11.21 kPa) and
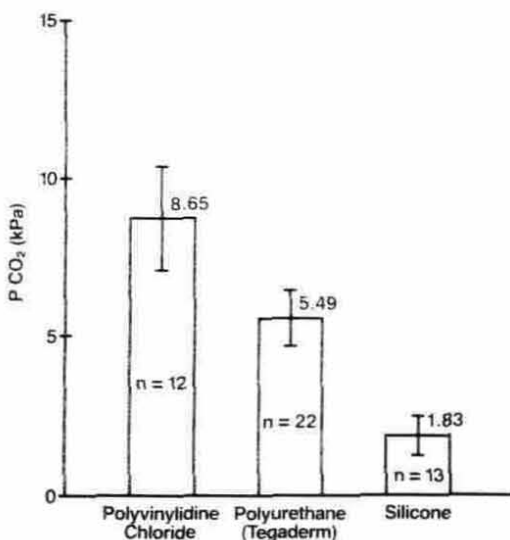

Figure 2. P CO₂ under film dressings. Combined data from 2 and 3 d partial thickness wounds on domestic pigs.
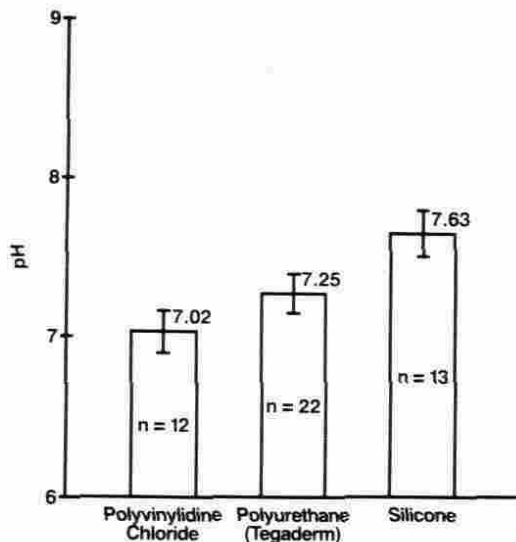
Figure 3. pH under film dressings. Combined data from 2 and 3 d partial thickness wounds on domestic pigs.

silicone (mean 13.96 kPa). While the difference in mean $P\,O_2$ under polyurethane and the silicone film was statistically significant ($p = 0.012$), the difference was not as great as we had expected considering the large difference in oxygen permeability between the two films.

Mean $P\,CO_2$ and pH values were all significantly different from each other ($p < 0.001$; see Figs 2 and 3) with polyvinylidine chloride at one extreme (mean $P\,CO_2$ 8.65 kPa, mean pH 7.02), followed by polyurethane (mean $P\,CO_2$ 5.49 kPa, pH 7.25), and silicone (mean $P\,CO_2$ 1.83 kPa, pH 7.63).

Epithelialization data were analyzed separately for days two and three and were also found to be influenced by film type on both days. There was no significant difference in healing on either day two or three between polyurethane and polyvinylidine chloride in spite of the differences in $P\,O_2$ in wound exudates. Epithelialization under the silicone film was significantly less than the other dressings on both days ($P = 0.003$, see Fig 4).
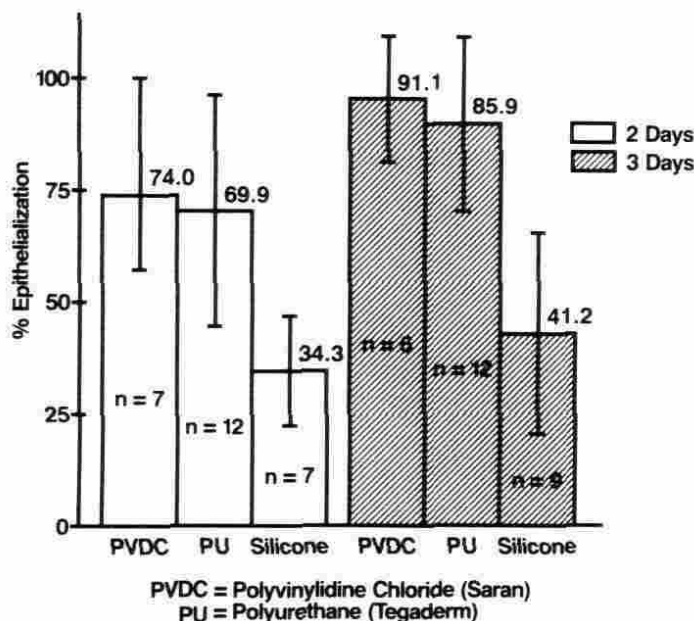

Figure 4. Epithelialization of partial thickness wounds on domestic pigs at 2 and 3 d under film dressings.

DISCUSSION

Our results demonstrate that the gas permeability of thin film dressings can influence the local environment under the dressing. We have also shown that healing is adversely affected by a dressing with high permeability to oxygen and carbon dioxide, possibly due to the loss of carbon dioxide and the resulting high pH. Such inhibition due to high pH/low $P\,CO_2$ was not seen by Winter [3]. This may have been due to the fact that the most permeable film used in that study (polyethylene) was several orders of magnitude less permeable than the silicone used here. High pH values (pH 8 to 9) have been observed in air exposed wounds by Leveen et al [16] who also found that failure to heal surface wounds was correlated with alkaline pH. They also demonstrated that serum exposed to air will lose CO_2 and approach pH 8. Similarly, the pH of pig wound exudate collected from our experiments was found to go from pH 7.2 to 8 to 8.5 when exposed to air. $P\,O_2$ quickly equilibrated to about 20.66 kPa under these conditions.

The reason for the relatively small difference in oxygen tension between the silicone and polyurethane films despite the large difference in gas transmission rates (see Table I) is not clear. One possibility considered was that a layer of protein had been adsorbed on the wound side of the silicone film and was limiting the diffusion oxygen. We eliminated this possibility by noting the very low $P\,CO_2$ under the silicone film and the fact that oxygen and carbon dioxide permeabilities, as shown in Table 1 and elsewhere [17], are always related.

Silver [7] has also reported a relatively small difference in $P\,O_2$ under films with large differences in permeability. He measured a $P\,O_2$ of 18.00 kPa in human wound exudate under a Teflon film and 16.40 kPa under polyethylene. The ratio of oxygen permeabilities of these two materials is approximately 500 [17].

Microscopically, it appeared that the delayed epithelialization under the silicone film was often associated with areas where epidermal cells failed to migrate from the edges of hair follicles. This was never seen under the urethane or polyvinylidine chloride films.

In a typical urethane or polyvinylidine chloride film covered wound the migrating epidermal sheet was one to three layers thick.

In the silicone film covered wounds the migrating epidermis was almost always more than three layers thick. These observations suggest that, perhaps because of the high pH, epidermal cells failed to migrate in a "normal" manner.

The failure to observe any difference between epithelialization under polyurethane and polyvinylidine chloride is not consistent with the observations of Winter [3]. Epithelialization under polyvinylidine chloride ($P\,O_2 = 4.93$ kPa) occurs at the same rate as under polyurethane ($P\,O_2 = 11.36$ kPa). This indicates that in this "well-perfused" wound model, oxygen delivery across the film dressing is not necessary to obtain the enhanced rate of epithelialization seen under occlusive dressings. A similar conclusion was also reached by Alvarez et al [11] in their study of oxygen-permeable and oxygen-impermeable dressings.

Our results suggest that dressings with high permeability to CO_2 (such as silicone) may be inappropriate for wound dressings. However, these results do not preclude the possibility that topical delivery of oxygen without increasing wound pH could enhance epithelialization. This could be done, for example, by topical oxygen application where excessive loss of carbon dioxide was avoided by including it in the applied gas. These results also do not preclude the possibility that dressing permeability to oxygen could play a role in healing of less well-perfused wounds, because under those conditions, wound oxygen tension may fall below that needed for normal epidermal cell function.

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