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# DECLARATION OF ACCURACY AND PRECISION

Re: Translation from Portuguese

ARticle by Peixoto and Santos," Biofill. Use and clinical evaluation of a cellulose membrane in cutaneous lesions"

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This declaration certifies the accuracy and precision of the translation from Portguese into English of the above material and is an accurate reflection of the text as it appeared in Portuguese.

For the translator:

Translator

11/11/96

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# BIOFILL. USE AND CLINICAL EVALUATION OF A CELLULOSE MEMBRANE IN CUTANEOUS LESIONS

by

R. Peixoto* and D.L.N. Santos*

SUMMARY

*It is reported the experience with a new skin substitute (BIOFILL) in 52 cases of burns, dermabrasion or skin donor sites. BIOFILL is a cellulose pellicle obtained through bacterial biosynthesis. The membrane is semi-transparent, homogenous and has a selective permeability. It is easy to apply and molds itself well to fit the wound. The relief of pain, the diminution of both contamination and proliferation of microbes, hemostasis and shortening of cicatrization time are all direct results of this adherence. These properties were well confirmed in the study.*

KEY WORDS: skin substitutes; biological dressing

Superficial skin lesions take on clinical importance on account of the great frequency of their occurrence, the suffering they produce, the bacterial proliferation verified in a significant number of cases, and also the high cost of the treatments being administered at present. Among such lesions , burns, graft-donor areas, and dermal abrasions must be cited. Owing to the clinical importance mentioned, innumerable investigations have been developed over the last decades, for the purpose of finding products, of organic or synthetic origin, that can be used as a substitute for injured skin, with aggregation or not to the patient's organism.

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Three lines of products deserve mention:

a) substitutes of animal origin, such as homologous graft, amniotic membrane, pig skin, bovine embryo skin, and collagen;

b) substitutes developed on the basis of synthetic substances, such as silicone, polyurethane, and "hidron";

c) substitutes in which organic material and a synthetic membrane, such as collagen and silicone, are combined.[1-9]

Up until now, these products have not reached high levels of use, owing to their high cost and the difficulty of obtaining and stocking them, as well as to specific deficiencies noted.

The purpose of the present article is to report the results of the use of a new product, called BIOFILL, which consists of a membrane of pure cellulose, produced through a biotechnological process. It is a matter of a substitute for skin and quite similar to it, which is applied as a prosthesis or temporary implant.

## MATERIAL AND METHODS

The cellulose membrane, called BIOFILL (biological fill-in), consists of a microfibrillar net of cellulose, obtained through biosynthesis carried out by the reproduction of bacteria in a favorable culture medium. The membrane resulting from this synthesis, after processing, is endowed with selective permeability, permitting the passage of water vapor, but impeding the passage of microorganisms. It is semitransparent, homogeneous, with an average thickness of 0.05 mm, and is visually very similar to human skin. It does not contain adhesives.[10]

As it consists basically of cellulose, an inert substance, resistant and insoluble in all organic solvents, it has specific characteristics, such as: definite permeability to liquids and gaseous substances, tensile strength, elongation, characteristic weight and molecular structure.

After epidermal regeneration, the membrane comes loose, retaining the same characteristics that it had at the time of its

application. What is involved, therefore, is a prosthesis or temporary implant.

BIOFILL is packed in disposable packages, varying in shape and size. Its sterilization is accomplished with ethylene oxide, in accordance with the strictest technological standards, its efficacy being evaluated by inherent quality control. Sterilization is guaranteed for 24 months. Shipping and storage are effected without any special conditions, and it keeps at room temperature with unlimited durability.

The patient was put into a comfortable position, one capable of permitting easy handling of the injured area by the operator. Step by step, the following procedure was followed:

a) perfect asepsis of the hands and the wearing of sterilized gloves;

b) asepsis all around the injured area, with iodinated alcohol or polyvinylpyrrolidone-iodine (PVP-I) [povidone-iodine];

c) debridement of the lesion, with removal of devitalized tissues and foreign bodies (in dermal abrasions);

d) copious washing of the lesion with physiological salt solution, at room temperature;

e) removal of the BIOFILL membrane from its package, bringing it close to the lesion in order to calculate the ara to be covered. The membrane must cover the lesion and another 1 cm beyond its edges. If the surface requires for its coverage two or more membranes, they must be placed in such a way that there is a 1-cm overlap at the site of the seam;

f) fitting of the membrane over the bloody bed and, with the aid of moistened gauze, perform manual movements over the surface of the membrane. The object of doing so is to get rid of air bubbles or excess exudation, in order to permit tight adhesion of the membrane to the bloody bed.

The area of the lesion, already covered with BIOFILL, can remain exposed, provided that:

1) the patient allows the lesion to remain exposed;

2) the injured area is not articular;

3) the hygienic conditions in the place where the patient is staying are good; and

4) the age of the patient permits rest, as far as the area of the lesion is concerned.

In the cases of injury in a joint area, it is advisable to leave it immobilized during the first 10 days.

**Use in graft-donor area**

In this case, the following sequence of procedures was followed:

a) anesthesia of the patient;

b) asepsis and antisepsis, with washing of the previously selected and trichotomized donor area. Use of an antimicrobial solution of povidone-iodine, removed later with physiological salt solution;

c) demarcation of area and lubrication with liquid vaseline;

d) removal of skin layers with Blair's knife;

e) compressive hemostasis of the donor areas by means of compresses impregnated with physiological salt solution;

f) with all due care to ensure asepsis, the membrane is removed from the package and drawn near to the lesion for calculation of the area to be covered, which will comprise the injured surface plus another 1 cm beyond its edges. Should use of more than one membrane be necessary, one will be superimposed over the other, going 1 cm beyond it, at the site of the seam;

g) application of the membrane, gently, over the bloody area. With the aid of gauze moistened in physiological salt solution, or of rod-shaped compresses, execution of gentle movements over the membrane, with the aim of removing the excess bloody secretion and air bubbles (which may make its adhesion difficult); and

h) protection of the area with a compress and bandage, so as to permit removal of the patient to his room, where the dressing will be exposed over a protective arch; and

i) keep the patient at rest and, if possible, with the donor area elevated. Use heating lamp in order to accelerate the dehydration of the clot.

The hospitalized patients had daily evaluations of the following parameters: pain, odor, fever, heat, local reddening, adhesion of the membrane, epithelialization, secretion, bleeding, and patho- logic appearances.

The out-patients had their return set for every 3 days, for an identical evaluation. In the cases where infection was suspected, material was taken for bacteriologic examination, culturing, and determinations of susceptibility to antibiotics.

## RESULTS

**In dermal abrasion** (Figs. 1 - A,B,C,D,E)

The 10 cases studied had the membrane applied within the first 12 hours after the accident. Through clinical examination, all of them were determined to have superficial lesions. The mean body surface covered with BIOFILL was 1.5%.

It was observed that the membrane was easily applied, exhibiting tight adhesion to the bleeding bed, with a clear hemostatic effect.

The patients reported a burning sensation when the membrane was applied over the bed, a symptom which varied in intensity and disappeared within minutes. Painful symptoms in the course of the treatment were observed only at the time when the lesion was palpated more deeply. In spite of prescriptions, there was no need to use systemic analgesics.

It was not necessary to change the dressing. In all 10 cases, there was only one application of the membrane. Signs of infection did not appear. All the cases progressed with dehydration of the clot within the first 48 hours and scab formation, which varied in color and thickness.

Fig. 1A

Fig. 1B

Fig. 1C

Fig. 1D

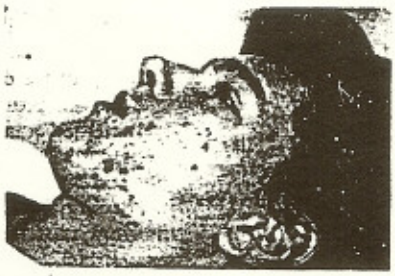

Fig. 1E

Figs. 1(A-E) - Dermal abrasion:
1 (A) after debridement; 1(B)) after application of BIOFILL;
1C) 24 hours afterwards;
1D) 7 days afterwards;
1E) after 10 days.

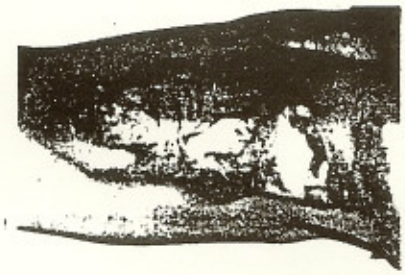

Fig. 2A

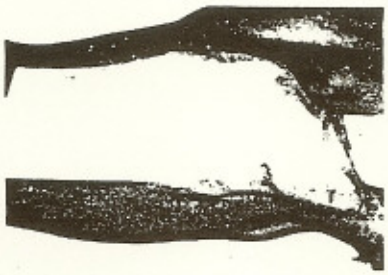

Fig. 2B

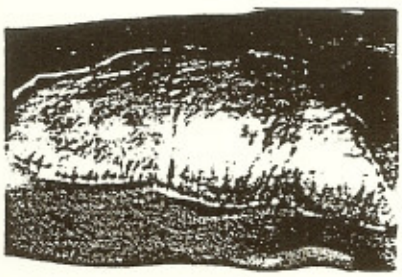

Fig. 2C

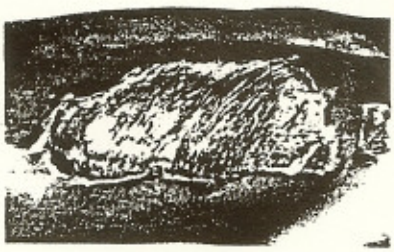

Fig. 2D

Fig. 2E

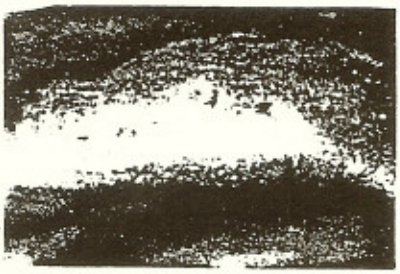

Fig. 2F

Figs. 2(A-F) - Second-degree burns in potentially infected areas;
2A) before debridement; 2B) after application of BIOFILL;
2C) 24 hours afterwards; 2D) 5 days afterwards; 2E) after 8 days;
2F) 15 days afterwards.

Fragmentation of the scab began, on the average, on the fifth day, reaching the edges and articular areas. It was observed that the time taken for elimination of the scab fragments depended on its greater or lesser thickness. The average total shedding time, with exposure of the scar tissue, was 11 days; the tissue appeared uniform, with a rosy color, smooth and shiny.

After scab formation, the patients were directed to take brief shower baths. After the bath, the scab and the BIOFILL membrane remained adherent and moistened. After spontaneous dehydration, they reacquired their previous characteristics.

Sensitivity reactions were not observed in any of the patients, and there was no interruption of the treatment.

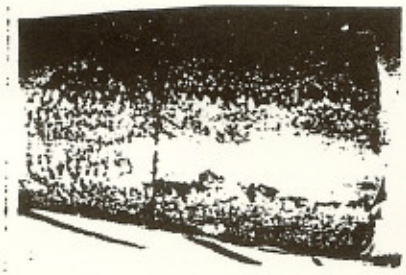

Fig. 3A

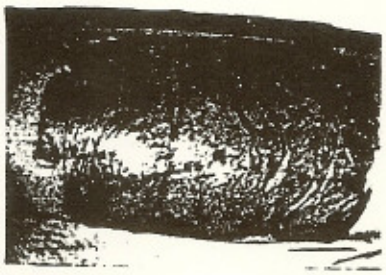

Fig. 3B

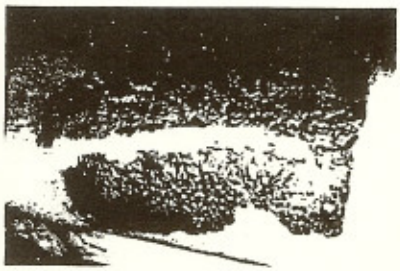

Fig. 3C

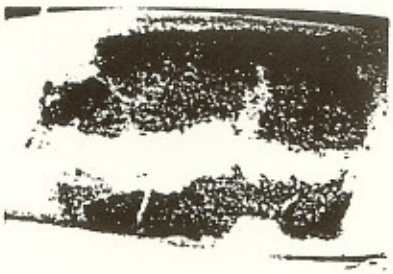

Fig. 3D

Fig. 3E

Fig. 3(A-E) - Graft-donor area: 3A - immediately after the application of the BIOFILL; 3B 24 hours after application; 3C) 7 days afterwards; 3D) after 11 days; 3E) 15 days afterwards.

**In superficial burns** (Figs. 2 - A,B,C,D,E,F)

Of the 33 patients studied, the membrane was applied in six within the first 12 hours, in 10 after 24 hours, and in 17, after 48 hours.

In 26 cases, the lesions were of second degree, superficial; in seven cases, there were small areas of second degree, deep. The average body surface covered with the membrane was 4%.

It was observed that the product was easily applied, adhering to any surface.

The patients reported a burning sensation at the time of application of the membrane over the lesion, a symptom that varied in intensity and then disappeared. Let it be noted that, in the cases in which the membrane was applied right after the injury, there was very intense burning and, in those in which the application took place after 48 hours, it was not very intense or else absent.

In the course of the treatment, the rare painful symptoms were reported in the following situations:

a) appearance of bubbles under the membrane from excess exudation, causing loss of the membrane's adhesion;

b) occurrence of exposure of the bloody area; and

c) development of infection.

In 30.3% of the cases, infection was verified and, in our hospitalized patients, the culture revealed that the etiologic agents were *Staphylococcus aureus* and *Pseudomonas aeruginosa*. The rate of infection was higher in the cases in which the application of BIOFILL was effected 24 hours after the accident.

Infection is easily diagnosed, once a yellowish-greenish, copious and foul-smelling secretion appears at the site, accompanied by pain, hyperemia, edema, and local hyperthermia. Once infection was verified, the patients were treated with systemic antibiotics and daily changing of the BIOFILL at the infected site. It is worth noting that the infectious process

is restricted to certain regions, dissemination throughout the whole area not occurring.

In the cases that progressed with a single application of the membrane, the exudate underwent dehydration, turning into a gelatinous secretion of a yellow color and, later on, into a chestnut-colored scab.

From the seventh day on, in the less extensive lesions, fragmentation of the scab began, a good-quality scar tissue arising. In the extensive lesions, fragmentation began on the ninth day. The average cicatrization time was 13 (± 3) days.

Once the burn is protected by a resistant scab, the patients were directed to take a shower bath and carry out their activities in a normal fashion. No intercurrent condition was observed.

For various reasons, 9% of the treatments were interrupted. In none of the patient was there any sign of sensitization.

**In graft-donor area** (Figs 3 - A,B.C,D,E)

In the nine cases studied, the patients received the application of the membrane during the autografting procedure. The thickness of the skin layers removed left exposed a superficial bloody area. The application of BIOFILL reached 0.4%, on the average, of the body area.

No difficulty was experienced in applying the product. To aid hemostasis, compresses with physiological salt solution were applied over the membrane.

Painful symptoms were reported when the patients were moved into the bed or on the occasion of deep palpations. All this before the scab had been formed or in the cases in which there was infection.

Infection occurred in three patients, twice with *Staphylococcus aureus* and in one case with *Proteus mirabilis*, and it has to be reported that these pathogenic agents were already inhabiting the main lesion before grafting. Such infectious foci

were easily diagnosed, owing to the transparency of the membrane and to the associated signs and symptoms (secretion, heat, reddening, and pain). The infections remained restricted to these foci, complete infection of the donor bed not occurring in any of the cases. The treatment included systemic antibiotics and removal of BIOFILL only at the site of the focus, cleansing of the area, and application of a new membrane over this area. The procedure was repeated until remission of the picture.

In our cases which developed without complications, coagulum dehydration occurred within 48 hours, and a thick crust formed, the color of which varied from chestnut to black.

From the ninth day on, fragmentation of the scab began, commencing along the edges of the lesion. The exposed scar tissue was of good quality, 15 days being the mean cicatrization time.

In the formed crust phase, too, there was a report of pain and tightening, on the occasions when the patients were walking. Rest led to the cessation of the symptom.

Sensitization reactions were not observed in any of the patients.

In one case, the treatment was not concluded.

## CONCLUSIONS

In view of the results obtained, it can be concluded that the BIOFILL membrane protects the injured tissue physiologically, affording the organism the conditions for promoting, within an abbreviated period of time, epithelial regeneration of excellent quality. Contamination and the proliferation of germs are significantly diminished, thereby reducing the coefficients of labor and medications employed.

As far as the psychosocial aspects are concerned, the patients reported a sensation of comfort, a consequence of:

a) relief or cessation of the pain;

b) generally a single application of the membrane;

c) early resumption of normal activities;

d) lower incidence of cases of infection; and

e) reduction of the number of cases in which there is a need for hospitalization and for systemic medication.

According to Tavis et al.,[8] the ideal properties of a temporary skin substitute are: adhesion, permeability to water vapor, elasticity, durability, bacteriological barrier function, lack of toxicity, non-antigenic properties, hemostasis, ease of application and removal, and low cost.

We verified that the new product, BIOFILL, fits these requirements, with the exception of one: that having to do with elasticity. The cellulose membrane is semi-elastic.

In any case, however, the results of the application of BIOFILL are surprising and with nothing similar to the products existing on the market.

We conclude that BIOFILL is a biological dressing that is easy to apply and to follow up clinically, the results of which indisputably surpass those of traditional treatments. Its application affords striking advantages as far as patients, doctors, nurses, and hospital establishments are concerned.

We also believe that various biomedical investigations must be carried out with a view to evaluating the possibility of applying BIOFILL in a number of situations, such as deep burns, surgical scars, ulcerated tumors, radiodermatitis, ulcers of different etiologies, bedsores, fractures with excoriations, dermatitides, lesions of the tympanic membrane, lesions of the mucosae, internal surgery, etc.

From the financial standpoint, a survey of the costs of treatment with BIOFILL made it possible to conclude that, on the average (with consideration of cases hospitalized or not), they are approximately 70% lower than those found with traditional treatment.

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