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DECLARATION OF ACCURACY AND PRECISION

Re: Translation from Italian

Article by Grisolia, et al., "The use of a new skin substitute in deep second-degree pediatric burns. Preliminary observation.

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

for the translator:

Translator

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The Use of a New Skin Substitute in Deep Second-degree Pediatric Burns. Preliminary Observation

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THE USE OF A NEW SKIN SUBSTITUTE IN DEEP SECOND-DEGREE PEDIATRIC BURNS. PRELIMINARY OBSERVATION

by

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SUMMARY

Skin substitutes are today playing an important role in the treatment of burns, above all of superficial second-degree ones and deep second-degree ones. We are convinced that lesions of this type, if treated in timely fashion, usually do not require an autologous graft in order to obtain healing and do not cause significant outcomes of an esthetic or functional nature.
From this perspective, we recently started to use a new bio-synthetic skin substitute. (Commercial name: BIOPROCESS, distributed by Farmitalia Carlo Erba).
We adopted this material in 20 children suffering from deep second-degree burns and in one patient with Lyell's syndrome.
We then compared the results obtained by us with those in which use was made of other skin substitutes or of the traditional medication, the subject of an earlier article of ours.
The data obtained, although not altogether comparable with those of the previous study, because of the smaller number of cases observed and the more limited follow-up, already strike us as significant enough to induce us to extend our study in the future to a larger number of patients.

INTRODUCTION

Accepted by now by all burn specialists is the important role played by skin substitutes in the topical treatment of burns, particularly superficial second-degree and deep second-degree burns.

They constitute, in fact, the best wound medication, reducing the loss of fluids, protecting the wound against external infective agents, stimulating its spontaneous re-epithelialization, and decreasing the number of medications.[1-3]

The industry, for its part, is producing ever more sophisticated skin substitutes suitable for the therapeutic requirements, with the ultimate objective of obtaining the ideal substitute for skin. For about 14 years now, we have been making use in our pediatric surgery unit of skin substitutes of various types, with very satisfactory results.[4,5]

The successes obtained, above all in deep second-degree burns which, if not properly treated, may become deeper and result in scarring that is significant at least from the esthetic standpoint, have always let us look favorably on the use of this type of medication. For about 10 months now, our protocol has included the use of a newly conceived skin substitute based on cellulose (BIOPROCESS), in order to test its efficacy and compare it with those [products] we used before.[6-8]

MATERIAL AND METHODS

BIOPROCESS is a transparent, homogeneous membrane, 0.05 mm thick, nonporous, with a structure made up of cellulose microfibrils. It is obtained with a biotechnologic process through biosynthesis by the bacterium Acetobacter. It has a structure altogether similar to that of the skin, is flexible, but not elastic, adapts itself very well to the body surface to be covered, to which it adheres perfectly without the need for using any other type of fixation. It keeps for an indefinite period of time at room tem-

perature, but has a higher unit cost as compared with other skin substitutes.

We have treated with this biotechnologic skin substitute a group of 20 patients (12 of them male and 8 female) ranging in age from 2 months to 9 years (mean age 4 years and 2 months), all of them suffering from deep second-degree and third-degree burns over an area varying from 1% to 25% of the body surface; Bioprocess was applied to a limited extent to lesions judged to be deep second-degree ones (Table 1). In the same period, we also treated, with excellent short- and long-term (5 months) results, a 10-year-old male patient with Lyell's syndrome with more than 50% of the body surface de-epithelialized; the latter is not considered in the present study, however.

TABLE 1 TREATMENT OF BURNS WITH BIOPROCESS

CASE MATERIAL

NO. PATIENTS	20 (12 M, 1 F)
MEAN AGE	4 yr 2 mo (min 2 mo, max 9 yr)
EXTENT OF BURNS	min 1%, max 25%
DEPTH OF BURNS	DEEP IInd DEGREE

The 20 patients were subdivided into three groups according to the time elapsed from the thermal trauma to the application of BIOPROCESS (Tables 2, 3, and 4).

The first group comprises the patients treated within 4 days, the second, those treated between day 5 and day 8, and the third, those treated after 8 days following the trauma. This last group includes 4 children coming under our observation late because they had been medicated in various ways at another location and were sent to us after they had exhibited a cessation of the

healing process, and 4 children who had been treated by us with a different type of medication without satisfactory results.

Table 2 - Group I; application of Bioprocess by day 4

Pt. No.	Wound depth	% burn	Dermal abras.	Days in hosp.	H.T.T., days	H.T.A., days	Prein-fection	Postin-fection	Cicatr. out-comes
1	Deep IInd	7	Yes	13	9	5	No	No	No
2	Deep IInd	3	Yes	13	10	7	No	No	No
3	Deep IInd	2	Yes	11	12	8	No	No	No
4	Deep IInd	11	Yes	13	20	17	Yes	No	No
5	Deep IInd	3	No	8	13	10	No	No	No
6	Deep IInd	5	No	35-	7	6	No	No	No
7	Deep IInd	1	No	4	10	9	No	No	No
8	Deep IInd	1	No	26-	10	9	No	No	No

H.T.T. = healing time from trauma
H.T.A. - healing time from application
- concomitant IIIrd-degree lesions

In each group, then, we distinguished the children to whom Bioprocess had been applied without any other previous surgical treatment, except for complete removal of the blisters, from those in whom it had been deemed advisable, because of the extent and depth of the lesions, to effect the application of Bioprocess by dermal abrasion. This procedure was undertaken in a total of 10 patients and always under general anesthesia obtained with various techniques (i.v. or i.m. ketamine, inhalation anesthesia with endotracheal intubation, regional local anesthesia).
All the patients were subjected to remote clinical monitoring with a follow-up period varying from a minimum of 3 months to a maximum of one year as of last April 30 (Table 5).

The results were compared with those of a previous study conducted by us on 2 groups of 37 patients in whom we compared the results achieved with the use of biosynthetic skin substitutes (Biobrane) and/or synthetic ones (polyurethane sponge) and those obtained with the traditional medication.[5]

Table 3 - Group II: application of Bioprocess between the 5th and the eighth day

Pt. No.	Burn depth	% Burn	Dermal abras.	Days in hosp.	H.T.T., days	H.T.A., days	Prein-fection	Postin-fection	Cicatr. out-comes
1	Deep IInd	3	Yes	12	14	7	No	No	No
2	Deep IInd	5	Yes	17	16	8	Yes	No	No
3	Deep IInd	1	Yes	12	30	23	No	No	No
4	Deep IInd	1	No	5	16	11	No	No	no

H.T.T. = healing time from trauma
H.T.A. = healing time from application

Table 4 - Group III: Application of Bioprocess after the eighth day

Pt. No.	Burn depth	% Burn	Derm. abras.	Days in hosp.	H.T.T., days	H.T.A., days	Prein-fection	Postin-fection	Cicatr. out-comes
1	Deep IInd	3	Yes	16	18	6	Yes	No	No
2	Deep IInd	7	Yes	23	23	7	Yes	No	No
3	Deep IInd	1	Yes	15	25	12	Yes	No	Yes
4	Deep IInd	1	No	9	20	11	Yes	No	No
5	Deep IInd	1	No	10	30	17	Yes	No	Yes
6	Deep IInd	1	No	17	26	16	Yes	No	Yes
7	Deep IInd	1	No	21	19	8	No	No	No
8	Deep IInd	1	No	7	38	18	No	No	No

H.T.T. = healing time from trauma
H.T.A. = healing time from application

Table 5 - Follow-up

Min. 3 mo	Max 12 mo
Mean F-U time:	14 mo 19 d

RESULTS

Tables 6 and 7, which summarize the main data from our study, warrant the following remarks:

a) the HEALING TIME of the lesions, both from the trauma and from the application of the Bioprocess membrane, increases appreciably from the 1st to the 3rd group of children in relation to the time the treatment is given (Table 6);

b) after careful disinfection of the burned surface and the subsequent application of Bioprocess, we never isolated pathogenic germs from any secretions that may have been evacuated below the membrane on the days succeeding its application. This result was also verified in 8 patients (1 from the 1st, 1 from the 2nd, and 6 from the 3rd group) in whom positive cultures were obtained from the burned surface on the days before the application (Table 6);

c) cicatricial outcomes were shown in 3 patients (15%), all from the 3rd group; and

d) DERMAL ABRASION does not seem to have exerted a favorable effect on the healing process, except in the 3rd group of patients treated late (Table 7).

Table 6 - Comparison between groups treated with Bioprocess

Patient group	No. patients	Mean hospitalization	M.H.T post-trauma	M.H.T. post-application	Post-infection	Cicatric. outcomes
I	8	15.5	11.0	8.5	No	0/8
II	4	11.5	19.0	12.0	No	0/4
III	8	15.5	22.0	14.0	No	3/8
I+II+III	20	14.4	17.5	11.5	No	3/20

M.H.T. = mean healing time

Table 7 - Influence of dermal abrasion on healing time from application

Patient group	Dermal abras.	No. of pts.	M.H.T. post-application	Variance, days
I	Yes	4	9	....
I	No	4	8.5	-0.5
II	Yes	3	12.5	....
II	No	1	11	-1.5
III	Yes	3	9	....
III	No	5	17.5	+8.5

Table 8 - Comparison with other methods of medication

Patient group	No. of pts.	Mean hospi-talization	M.H.T., days	Cicatric. outcomes
A	37	17	28	81%
B	37	11	23	13%
C	20	14	17.5	15%

Table 8, on the other hand, compares the main data from the present study with those from a prior one that took into consideration and compared the results obtained in the treatment of deep 2nd-degree burns by means of traditional medication (group A) and with the use of other skin substitutes (Biobrane and Syspur derm) (group B). We can notice that the mean healing time from the trauma obtained with Bioprocess (group C) was considerably decreased, not only in comparison to the children in group A, but also to that in group B. The mean hospital stay was reduced in comparison to that in group A, but not to that in group B. That is influenced by the fact that the first patients treated with Bioprocess remained hospitalized until healing was attained, on account of the need to follow directly the whole process of re-epithelialization, thus prolonging hospitalization.

The incidence of remote cicatricial outcomes (not yet definitive because of the limited follow-up time) was 15%, little better than for group B. The fact that the outcomes occurred only in patients in group III seems to tend to emphasize the need for early application of the membrane in order to obtain the best remote results as well.

DISCUSSION

At the end of this preliminary study we cannot, obviously, formulate definitive judgments on how good this newly conceived therapeutic defense is or is not for the local treatment of burned children. The number of subjects studies and the limited follow-up to which they were subjected forces us to be cautious. It can already be firmly asserted, however, that Bioprocess exhibits undoubted qualities, like its excellent adhesion to the burned surface, good manageability, despite its poor elasticity, good transparency (better than that of other skin substitutes), surprising protection from exogenous infections, painless application and removal, good stimulation of spontaneous re-epithelialization, problem-free storage, and maintenance on third-degree lesions, once the eschar is removed, of an excellent granulation tissue (Table 9).

In addition, we were able to show, too, some defects connected with the type of skin substitute, with the method of application, and with the particular patient of pediatric age, of a quite special nature:

a) The membrane is not elastic and can be easily torn;

b) the scab which forms at times under it hampers accurate checking of the healing process;

c) in children it is almost always impossible to keep the medication uncovered with Bioprocess, as it is advised to do after the first 24 hours, unless with coercive immobilization, to which we resorted only in case of absolute necessity (e.g., in a 2-month-old patient with a burn of the buttocks and perineum);

d) the higher cost than for other, similar skin substitutes (Table 10). Added to this must also be the lack of smaller-size products for covering the openings made for evacuating the secretions present under the membrane or its spontaneous tears. It also has to be pointed out that we did not note any appreciable improvement in the pain component as compared with other, similar products.

If we proceed to consider the results obtained with respect to healing time, we can assert that so far we have noted a shortening of the healing time in comparison to the previously used skin substitutes--and that the extent was greater the earlier the application of Bioprocess occurred. We have found a shorter healing time in burns treated after dermal abrasion limited to the third group of patients.

As far as cicatricial outcomes are concerned, these appeared exclusively in patients treated late with Bioprocess, but already at a higher percentage, even if slight, than with the previously used skin substitutes. However, this finding requires more exhaustive analysis and checking.

Considering the cost-benefit ratio, the price of the membrane turned out to only appear high, since the number of applications necessary was greatly reduced (a single application was generally sufficient) and the costs might be even less if smaller-sized products became available for the above specified uses.

Table 9 - Advantages of Bioprocess

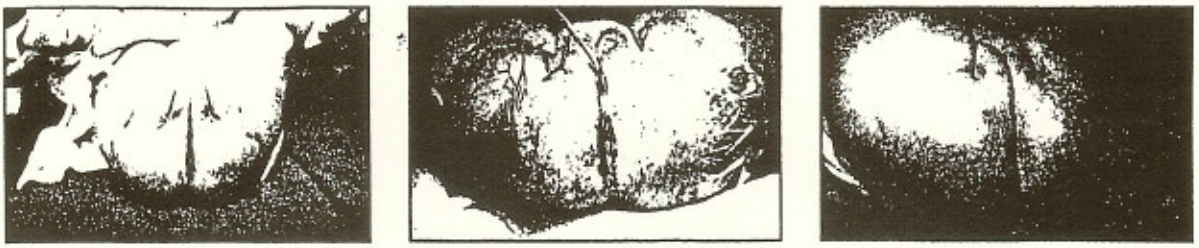
•EXCELLENT ADHESION	•PAINLESS REMOVAL
•GOOD MANAGEABILITY	•GOOD STIMULATION OF SPONTANEOUS RE-EPITHELIALIZATION
•GOOD TRANSPARENCY	•MAINTENANCE OF GOOD GRANULATION TISSUE
•EXCELLENT PROTECTION FROM INFECTIONS	•PROBLEM-FREE KEEPING
•PAINLESS MEDICATION	

Table 10 - Drawbacks of Bioprocess

•INELASTIC	•	NEED FOR COVERED MEDICATION IN SMALLER CHILDREN
•SCAB FORMATION	•	HIGH COST

CONCLUSION

We can assert in conclusion that the results obtained, judged as a whole, and the qualities exhibited by Bioprocess encourage us to continue the study undertaken and to extend its use to other therapeutic indications, notwithstanding the good successes achieved by us previously with the use of other skin substitutes.



D.M.G., 3 mo old, burn of the perineum and buttocks from boiling liquid

P.T., 1 year old, burn on the face from boiling liquid

B.E., 3 years old, burn of the right hand from red-hot surface

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