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THE EFFECTS OF SOME LOCALLY APPLIED MEDICATIONS ON THE
HEALING OF SECOND DEGREE BURNS

by

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ABSTRACT

The possibility of evaluating experimentally the effects of locally applied medications on the rate of burn healing was explored. Twenty or 24 small burns were produced on each of eight anesthetized Chester White pigs by an exposure of 10 calories per square centimeter delivered in 3 seconds. In earlier studies it had been found that lesions from this exposure are moderate second degree burns which, if untreated, are completely covered with new epithelium in 14 days. Nine days after injury, less than half of them exhibit this degree of healing.

The five medicated ointments tested were applied to randomized burns once a day for five days. After four days without treatment, the burns were biopsied. The degree of epithelial coverage was evaluated microscopically, and the results in treated and untreated areas were compared.

None of the medications significantly promoted or delayed epithelial regeneration. Variations in healing rate from one animal to another and in different anatomical locations on the same animal were noted. These findings should affect the design of any experiment to determine the effects of treatment on healing.

The method used has definite limitations. No assessment of alleviation of pain or of incidence of secondary infection is permitted. Possible benefits from the analgesic or antiseptic properties of the ointments

cannot, therefore, be considered. On the other hand, mildly deleterious effects would escape notice, and it cannot be stated that a medication which does no great harm when applied to a small burn would be equally innocuous if applied to a larger area.

INTRODUCTION

It is understandable that the medical profession greets each new panacea for the local treatment of burns with something less than unrestrained enthusiasm. Although testimonials of the efficacy of various ointments and oils are readily available, no preparation has so far been demonstrated to promote healing. When some medication or bland ointment is applied to a burned area, it is done with the intention of alleviating pain or of decreasing mechanical abrasion from a dressing. It is hoped that the treatment will do no harm, and, if the agent used possesses some antibacterial property, that it might lessen the chance of secondary infection. Even with meddlesome care, a mild burn usually heals rapidly and completely. For centuries this restorative power of nature has been attributed to one preparation or another. When the full thickness of the skin is injured in such a way that all the epithelial elements are lost, repair will proceed slowly from the undamaged periphery. A claim that some medication promotes the epithelial repair of a third degree burn without subsequent scarring makes little sense; it would be as likely to lead to the restoration of an amputated limb. Such testimonials quite naturally produce skepticism concerning the other supposed attributes of the product.

Over the years we have been asked to test many compounds, some reasonable and others bizarre, to determine their effect on the healing of burns. These requests have always been declined because our experimental methods did not lend themselves particularly well to this type of procedure and we were much more interested in exploring the factors which govern burn severity. However, as our experimental methods and designs became more refined, we began to wonder about the feasibility of evaluating local therapeutic agents on the skin of laboratory animals. This report records our results with five medications.

By the nature of the experiment, only gross differences in rates of epithelial coverage of treated and untreated burns can be detected, and any possible benefits from alleviation of pain or from prevention of infection cannot be discovered in this way. It is also fair to say that evidence of severe toxicity only would be observed, and more subtle deleterious effects would go unnoticed. With these limitations, because it is possible to produce a number of similar burns with the carbon arc source, the value of locally applied medications can be investigated.

MATERIALS AND METHODS

Young Chester White pigs, anesthetized with intraperitoneal Dial with urethane (Ciba), were used as the experimental animals because their skin resembles human skin in thickness and composition and reacts similarly to thermal injury (1, 2). Surface contamination does not lead to infection of small burns on pigs. It is, therefore, possible to evaluate the direct effect of medication on epithelial coverage without regard to a secondary effect due to suppression of infection. Since the animals, anesthetized at the time of injury, show no evidence of pain on awakening, whether treated or not, pain relief from medication cannot be observed.

Evaluation of the following preparations was requested by their manufacturers or distributors:

1. Salcolan ointment, manufactured by the Rich Company, Inc., Houston, Texas. Content: Cod liver oil, lanolin, caraway oil, olive oil, and phenyl salicylate.
2. Skincuo, an ointment prepared for Vincent Viscuso, 414 1/2 W. 5th Ave., McKeesport, Pennsylvania. Content: "Mineral Oil, Cente Herbe, Sulfur, Boric Oxide, Etc."

3. Epital, made and supplied by A. Farkas, Chemical Research Laboratories, 425 NE 173rd St., North Miami Beach, Florida. Described as "a glucosid type compound, composed of carbon, hydrogen and oxygen only," obtained from plants of the Liliacea family.

In addition to these three, two other medications were studied. Furacin (Eaton Laboratories) was chosen because it is commonly used as a dressing for burns. Perazil 2% (Burroughs Wellcome and Company) was selected as representative of a water soluble antihistamine cream.

The heat source was a modified Army Carbon arc searchlight (3). All burns were produced by the delivery of ten calories per square centimeter during a three second exposure time. In earlier experiments (4) it had been found that most burns resulting from this exposure-exposure time combination will be of moderate second degree severity. In addition, it had been determined that, although all are covered by new epithelium fourteen days after injury, half or more of them are not completely covered nine days after burning. The size of the burns was controlled by a port 1.7 cm. in diameter.

Twenty-four burns were placed on the sides of each of three animals. Of the twenty-four, four exposure sites were not treated and four were treated with each of the selected medications. The seventy-two burns in this part of the experiment were randomized in such a way that there was equal probability of any one site being untreated or treated with any of the five ointments or creams. On each of five additional animals, twenty burns were produced. Half of the burns on each animal were treated with one of the medications, the other half were left untreated. Randomization assured equal probability of any one exposure site on a given animal being treated or untreated; in these five animals, comparable sites were treated with the different medications and comparable sites were left untreated. On all animals, treatment consisted of the application of the ointment once a day,

beginning with the day of injury, for five days. On the ninth day after injury, after four days without treatment, each burn was biopsied in such a way that normal tissue was included on each side of the healing lesion. The tissues were placed in 10% formalin and sections were stained by a method for the differentiation of burned and normal tissues (5).

On microscopic examination of the sections it was noted whether or not new epithelium completely covered the tissue beneath the slough, or whether coverage was far advanced, moderately advanced, or very incomplete.

RESULTS

The results are summarized in Tables I, II, III, and IV which are arranged so that the following comparisons can be made: 1) the effect of each treatment versus no treatment, 2) the rates of healing in different animals, and 3) the influence of the sites of the burns on the rate of epithelial coverage.

Table I shows the degree of epithelial coverage of the burns on the three pigs on which the sites of injury were treated by one of the five medications or were not treated. This table, by itself, would seem to indicate the superiority of no treatment since only two of twelve such burns showed very incomplete coverage while at least half of each group of treated burns showed poor epithelialization. Again, if this table alone is considered, Perazil, for example, would seem to have a deleterious effect. Table II, which gives the results on the five animals, each of which had half its burns treated with one of the preparations and the other half left untreated, conveys a different impression. If the untreated burns in these five pigs are considered, a variation in the rate of epithelialization from animal to animal can be seen. In the pig treated with Perazil, none of the untreated burns shows a delay in coverage, while in the others from half to three-fourths of the twelve have very incomplete epithelial coverage. Comparison

TABLE I

EPITHELIAL COVERAGE NINE DAYS AFTER PRODUCTION OF MODERATE
SECOND DEGREE BURNS. RESULTS IN THREE ANIMALS
IN WHICH ALL FIVE OINTMENTS WERE TESTED

Treatment	Number of Burns Showing			
	Complete Epithelial Coverage	Far Advanced Coverage	Moderately Advanced Coverage	Very Incomplete Coverage
None	2	3	6	2
Skincuo	0	2	3	7
Salcolan	3	1	0	8
Epital	1	3	2	6
Furacin	1	0	5	6
Perazil	0	0	4	8

TABLE II

EPITHELIAL COVERAGE NINE DAYS AFTER PRODUCTION OF MODERATE
SECOND DEGREE BURNS. RESULTS IN FIVE ANIMALS
IN EACH OF WHICH A DIFFERENT OINTMENT WAS TESTED

Treatment	Number of Burns Showing			
	Complete Epithelial Coverage	Far Advanced Coverage	Moderately Advanced Coverage	Very Incomplete Coverage
Skincuo	0	1	0	9
None	0	0	1	9
Salcolan	0	0	3	7
None	1	0	0	9
Epital	1	0	0	9
None	0	2	2	6
Furacin	0	0	1	9
None	1	0	2	7
Perazil	5	4	1	0
None	3	4	3	0

of each group of treated and control burns fails to demonstrate either definite benefit or harm from any of the treatments.

Tables III and IV illustrate an effect of the anatomical location of a burn on its rate of epithelial coverage. Row A consisted of five or six burns along the side of the animal about two inches ventral to its spine. Row B contained five or six burns located about three inches nearer the belly. Whether treated or not, the burns in the dorsal row tended to show more advanced epithelial regeneration than did the ones in the ventral row. It can also be seen that no treatment hastened epithelial coverage in the more sluggish Row B. Likewise, no treatment definitely enhanced or delayed healing in the Row A burns. The seemingly harmful effect of some medications shown by the data in Table I is probably due to the distribution of burns treated by these preparations (Table III).

DISCUSSION

It is well to point out the limitations of this type of experiment as an evaluation of the local treatment of burns. Possible benefits from the alleviation of pain and the prevention of secondary infection cannot be assessed in this way. Since small, partial thickness burns heal rapidly even under adverse circumstances, it is just as difficult to detect any but the gravest deleterious effects of treatment. Only striking benefit or harm from a medication would become obvious. Neither effect was seen in this study.

The natural variations in healing rates from animal to animal and from one site to another on the same animal, demonstrated well by this experiment, make clear certain pitfalls to be avoided in attempting an experimental assessment of local treatment for burns. If different animals are used for each treatment, only differences which seem statistically significant should be seriously considered. If different medications are tested on different

TABLE III

CONTRAST IN HEALING RATES OF BURNS IN DORSAL AND VENTRAL ROWS
(SAME ANIMALS AS THOSE IN TABLE I)

Treatment	Number of Burns Showing			
	Complete Epithelial Coverage	Far Advanced Coverage	Moderately Advanced Coverage	Very Incomplete Coverage
Skincuo				
Row A*	0	2	2	3
Row B**	0	0	1	4
Salcolan				
Row A	3	0	0	2
Row B	0	1	0	6
Epital				
Row A	1	2	0	3
Row B	0	1	2	3
Furacin				
Row A	1	0	1	2
Row B	0	0	4	4
Perazil				
Row A	0	0	2	2
Row B	0	0	2	6
None				
Row A	1	2	4	2
Row B	1	1	1	

*Row A - Nearer the spine

**Row B - Nearer the belly

TABLE IV

CONTRAST IN HEALING RATES OF BURNS IN DORSAL AND VENTRAL ROWS
(SAME ANIMALS AS THOSE IN TABLE II)

Treatment	Number of Burns Showing			
	Complete Epithelial Coverage	Far Advanced Coverage	Moderately Advanced Coverage	Very Incomplete Coverage
Skincuo				
Row A*	0	1	0	4
Row B**	0	0	0	5
None				
Row A	0	0	1	4
Row B	0	0	0	5
Salcolan				
Row A	0	0	2	3
Row B	0	0	1	4
None				
Row A	1	0	0	4
Row B	0	0	0	5
Epital				
Row A	0	0	3	2
Row B	1	0	0	4
None				
Row A	0	1	1	3
Row B	0	1	1	3
Furacin				
Row A	0	0	1	4
Row B	0	0	0	5
None				
Row A	1	0	2	2
Row B	0	0	0	5
Perazil				
Row A	3	2	0	0
Row B	2	2	1	0
None				
Row A	2	2	1	0
Row B	1	2	2	0

*Row A - Nearer the spine

**Row B - Nearer the belly

injury sites on the same animal, the effect of location of the lesion must be carefully evaluated.

It is probable that the velocity of the healing process is maximal under ordinary circumstances. There has never been any proof that it could be consistently accelerated. Infection, drying or therapeutic agents may retard it. The question at issue is often not if the compound applied speeds healing but rather how much does it delay repair in return for the comfort or satisfaction it gives.

The kindness of nature in providing us with a mechanism for the rapid repair of minor injuries will continue to lead, just as it has in the past, to extravagant praise for various burn ointments, oils, lotions and creams. This is regrettable only in that if a truly beneficial preparation is ever discovered (or if it is now available to us) our ears, long accustomed to so many misleading claims, will be nearly deaf. In selecting a preparation for the local treatment of a minor burn, there are many from which to choose. Most do no great harm, many add to the comfort of the patient, and some may decrease the chance of infection. The acceptance of these preparations for the treatment of small burns should not mean that they are also to be used when a larger proportion of the body surface area has been injured. Here, only a treatment which has been demonstrated to have no toxic effect can be permitted.

Our primary objective, the use of carefully controlled laboratory experiments for judging the effect of locally applied agents on the healing of burns, has been accomplished. However, it should be clearly understood that such a method evaluates the healing process alone and does not give insight into the many ancillary factors which may result when patients are treated by the application of some impressive looking substance.

SUMMARY AND CONCLUSIONS

1. The possibility of evaluating, on experimental animals, the effects of different medications on the rate of burn healing was explored. The method used was satisfactory for the detection of differences in epithelial recovery, but it gave no indication of analgesic or antiseptic properties.
2. Five ointments were tested for their efficacy in the treatment of small, moderate second degree burns. None was found to promote or delay healing to a significant degree.
3. Variations in the rates of epithelial regeneration from animal to animal and from one site of injury to another on the same animal were noted. The necessity of considering these variations in any attempt to assess local burn therapy is discussed.
4. The fact that a medication may do no noticeable harm when used on a small burn does not imply that it is equally innocuous when applied to a larger injured area.

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