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SOME DERMATOLOGICAL HAZARDS OF TO-DAY*

BY

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When the Chadwick Trustees paid me the honour of inviting me to deliver the Malcolm Morris Lecture they suggested that its subject should be related to skin hazards of to-day. It is indeed most appropriate to reflect in this way the great interest which Morris at all times showed in preventive medicine both in relation to dermatology and in wider fields. One's first thought, therefore, was to ask what had been the outstanding changes in recent times in relation to which dermatological risk may arise; and it is not merely because of the association with St. Mary's Hospital and Medical School that the development of antibiotics springs to mind as a major advance in human progress in our time.

I wonder whether there is any drug or method of treatment which is entirely free from the drawback of some undesired effect. Penicillin has proved to be, as it seems, completely without toxicity in ordinary therapeutic doses, but it has become familiar to dermatologists as an antigen inducing allergic sensitivity which manifests itself in the skin more often than in other ways.

Penicillin Urticaria

I think the experience of most of us is that urticaria is the most common cutaneous eruption to occur in patients who are receiving penicillin. Most often it appears four or five days after the beginning of treatment, and its duration is very variable. Although in most cases the eruption is of short duration—clearing up after a few days, as might be expected—it is common for the rash to last for two to three months or even longer, although penicillin treatment has of course been stopped. This is a strange feature of penicillin urticaria, and one which urgently requires some explanation. When one remembers the rapid excretion of penicillin this prolongation of urticaria for several weeks or for a few months, as is often observed, is not easy to understand. It is axiomatic that an allergic reaction does not take place in the absence of the allergen. Four possible explanations come to mind: first, that penicillin or some secondary product which is the allergen may be very slowly eliminated, perhaps from a depot injection; second, that penicillin is still being encountered from other continuing sources; third, that the urticaria is not due to penicillin but to some other antigen; and fourth, that the urticaria is not based upon an allergic mechanism at all.

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As regards the first possibility, the extreme solubility and the rapid absorption and excretion of penicillin at one time constituted a disadvantage. Delayed absorption which may be brought about by the use of slow-absorption vehicles or by combination with procaine will usually maintain measurable quantities of penicillin in the body up to 24 to 48 hours, but the rate of fall of detectable blood levels makes it highly improbable that any penicillin would remain in the body for weeks or months after injection (Florey *et al.*, 1949).

Penicillin Reactions from Milk

The second possibility, of continuing exposure to penicillin from less obvious or from non-therapeutic sources, brings to mind particularly the production of penicillin reactions by milk, to which Vickers *et al.* (1958) drew attention in this country. It has been known for ten years that when penicillin is used for the treatment of mastitis in cows some of the antibiotic enters the milk. In recent years, however, the amount of penicillin reaching milk in England is diminishing, partly because penicillin treatment is not so widely used as formerly, and partly because mass treatments of cows, which were popular at one time, are now seldom given.

Zimmerman (1959) mentions a concentration of penicillin in milk of 550 units/quart—that is, about $\frac{1}{2}$ unit/ml. In the first case described by Vickers *et al.* the patient was consuming milk with a concentration of 4 units/ml. Even with less concentration than this it is easy for several hundred units to be drunk daily, and there is no doubt that this would be enough to evoke urticaria or more serious reactions in a hypersensitive subject. In fact, when penicillin is encountered in milk at all in this country the quantity in pooled milk is not likely to exceed 1 unit/ml.

The published cases—for example, those of Vickers *et al.* and of Zimmerman—indicate sufficiently that when allergy is initiated by penicillin in ordinary therapeutic doses the reactions may be prolonged or produced anew by consumption of these much smaller doses, and that this effect may continue indefinitely. But there is a further point of considerable importance: granted that milk may provide enough penicillin to elicit an allergic response, is the dose sufficient to initiate sensitization and to give rise to penicillin allergy in a person who has never received penicillin in therapeutic doses? I am not aware of any case in which this has been known to occur; but presumably

the possibility exists, for the quantity of some allergens required to induce allergic sensitivity in the first instance can be extremely small. If we accept the possibility that penicillin allergy may thus arise without penicillin treatment having been given, it means that before giving penicillin treatment we must inquire not only into previous reactions which may have followed the known use of penicillin but into any allergic reaction the cause of which was not identified and which might therefore have been produced by penicillin unwittingly taken in milk or milk products. It is evidently going to be very easy to overlook this type of case.

In most cases of penicillin urticaria the eruption ceases spontaneously after a few months and does not continue or relapse indefinitely as one might expect if milk penicillin were responsible. Because of this, and of the comparatively uncommon presence of penicillin in our milk nowadays, I do not suppose that this factor is often present, though the possibility should evidently not be forgotten.

Role of Impurities

My third suggestion was that penicillin itself may not indeed be the allergen: the precise identification of penicillin as a cause of urticaria is not easy. We have for a long time known how common it is for patients to attribute urticaria to a certain food on the basis of a single attack and how often this is afterwards disproved. In most cases when patients tell us they are allergic to penicillin and when hospital notes are emblazoned with this warning, the diagnosis is based on exactly the same kind of single observation and is equally tenuous. The incidence of penicillin urticaria varies considerably in relation to the disease under treatment; this may depend upon factors such as dosage, but it should make us pause also to ask whether the nature of the disease may not play some part. Further, even if we are correct in assuming that urticaria appearing in these circumstances is due to penicillin injections we must still not overlook the possible part played by impurities and by the vehicle. Reactions were more common with the beeswax-based slow-absorption vehicle, probably due to allergy to beeswax or to some material such as pollens which it contains. More modern vehicles, and the combination of penicillin with procaine, are less allergenic but not altogether free from this possibility.

Leaving aside allergy to the vehicle, however, Florey (1952) was able to say that there was yet no clear-cut proof that penicillin rather than impurities was the cause of penicillin reactions. She draws attention to the much greater frequency of reactions and of positive intradermal tests obtained with amorphous (impure) penicillin than with the more pure crystalline product; even different batches of crystalline penicillin give variable skin-test results, suggesting that these depend upon the presence of unidentified contaminants. This may explain the unreliability of skin tests in the diagnosis of individual cases, which is generally accepted. It is conceivable that the impurities are more slowly absorbed or more slowly excreted, and that this may account for the strange chronicity of some cases.

The value of skin tests—scratch tests or intradermal—in the diagnosis of subacute or chronic urticaria is in general notoriously little. After the first onset in relation to exposure to the possible antigen the diagnosis has to be confirmed by the reappearance of urticaria

after another exposure. In the case of suspected penicillin allergy re-exposure does not usually occur, since we know that in these circumstances dangerous anaphylactoid reactions are possible, but it may nevertheless happen accidentally. I expect many of us have met cases—I have seen three or four—where patients thought to be allergic to penicillin because of urticaria which followed treatment have mistakenly been given penicillin again, and without the slightest reaction. From what we know of true allergic urticaria, spontaneous desensitization is not a likely explanation of this, and it is more likely that the presumptive diagnosis was wrong. Zimmerman (1959) has reviewed the use of penicillinase in diagnosis, a cessation of symptoms after the administration of penicillinase indicating penicillin as the responsible agent. This depends, of course, upon the assumption that the penicillinase in question has no action upon the impurities and is quite specific for penicillin. Since the impurities have not been identified, it is presumably impossible to justify this assumption.

We must conclude, on consideration of these various facts, that if the urticaria which follows penicillin treatment is truly allergic then the allergen is not necessarily always penicillin itself; indeed, as Florey said, we do not even know for certain whether any of these cases are based upon specific allergy to penicillin alone. The idea that these impurities may linger in the body for weeks and months after an injection and thus prolong urticaria, however, is difficult to accept.

Is the Allergen a Metabolite?

There remains the possibility that this kind of urticaria is not based upon an allergic mechanism at all; or that the allergen is not a foreign substance but is a metabolite normally produced in the tissues.

In cholinergic urticaria there exists a hypersensitivity to acetylcholine which is transferred by the Prausnitz-Küstner method, and which may therefore be accepted as depending upon an allergic mechanism. Factitious urticaria produced by stroking the skin or by other physical stimuli may depend upon allergy to some substance which is normally released from the tissues under the appropriate stimulus. Since this allergen has not been identified, this remains an assumption, which is supported by the fact that this wealing can be passively transferred by injecting the serum of the patient into a normal person. Pillsbury *et al.* (1956), however, regard this type of urticaria as non-allergic. How factitious urticaria arises is completely unknown.

In 12 cases of this kind which I investigated very thoroughly no other physical abnormality could be detected, but in all of them there was considerable psychological stress though no uniform psychiatric pattern. This finding conforms with the commonly held view that factitious urticaria is often psychogenic, an assumption which has been criticized, and I believe very rightly, by Rothman and Walker (1950). In this connexion the observations of Kalz and Prichard (1952) are of the greatest interest. They examined the cutaneous vascular response to stroking the skin before and after the administration of penicillin. In only 15 of their 100 subjects did this remain unchanged. 9.7% of those tested actually developed factitious urticaria; 21% produced a peculiar papular follicular response which may have been urticarial but may have been due to pilomotor action. The remainder gave an

erythematous response, normal in type but of greater degree than before penicillin treatment. Kalz and Prichard suggest that penicillin may have some cholinergic action.

Florey *et al.* (1949) mention the suggestion that in guinea-pigs penicillin may have a toxic action on capillaries and venules, but no such effect has been observed in man. Among the occasional reactions to penicillin they mention flushing of the skin: its cause is obscure, and it seems less common since purer penicillin has become available. The observations of Kalz and Prichard do, however, suggest either that penicillin has some direct action on cutaneous vascular response or that it somehow promotes the development of allergy to autogenous metabolites. It may be significant that seven of their patients developed epidermal contact sensitivity (to substances other than penicillin) during the 12-months follow-up period; these authors point out that no conclusions can be drawn from that isolated observation, but it is at least suggestive that penicillin may have the property of promoting the development of allergy to unrelated substances.

Chronic Urticaria

What I have said about factitious urticaria may or may not apply to ordinary chronic urticaria. In most of these cases specific sensitivity cannot be identified. If the eruption is produced by an autogenous antigen then the nature of this and the stimulus which causes its release are quite unknown. It may be that chronic urticaria does not always depend upon an antigen-antibody reaction at all, but upon some other mechanism which leads to transient vasodilatation and increased capillary permeability; and that penicillin, just as it provokes factitious urticaria, may lead to the development of chronic urticaria which, once established, does not need the continuance of an exogenous antigen. This suggestion implies that in those cases where penicillin urticaria continues for some weeks or longer there is not, and never has been, penicillin allergy; but that penicillin has the property of inducing a state of chronic urticaria, the mechanism of which may not be different from that of ordinary chronic urticaria of obscure origin. The conclusion which I favour is that in at least a goodly proportion of cases the action of penicillin has been to induce the condition of ordinary chronic urticaria in which an allergen cannot be convincingly identified, which is suppressed with antihistamine drugs, and which eventually clears up spontaneously.

The results of skin tests are confusing and unreliable, and we can clearly place no confidence in them. Dangerous anaphylactoid reactions may result in highly sensitive subjects, and otherwise, whether tests are positive or negative, they give no final indication in diagnosis nor guide to procedure. There must be many patients to whom penicillin is denied because of the fear of severe allergic reactions, particularly atopic subjects, who appear to suffer more severely in this respect. In many cases penicillin could almost certainly be given without any reaction following, but by present methods it is very difficult to distinguish genuine penicillin sensitivity from presumed, and wrongly presumed, sensitivity. The development of penicillin allergy has proved to be a troublesome drawback, and if this antibiotic is to retain its prominent place further investigation must indicate a way in which this complication may be avoided or minimized.

Sensitivity to Epoxy Resins

The synthetic resins, because of several remarkable properties, have already made for themselves a secure place in a considerable variety of industries. Since they are very potent epidermal sensitizers an important place as a cause of industrial dermatitis seems to be equally assured. The subject of epoxy-resin dermatitis has been fully dealt with by Grandjean (1957) and by Calnan (1958). In spite of this the awareness of these dangers is slow to be realized in industry.

In 1959 I saw two french-polishers who had developed dermatitis of the hands and fingers. They were both between 40 and 50 years of age, and had been working as french-polishers for over 25 years. During the previous two years or so they had been engaged in polishing wooden doors and panelling on the outside of a building for which they used a special material which was described as a weather-proof polish. I found upon inquiry that the polish they had been using, instead of being the relatively harmless shellac mixture, contained an amino-resin which in both cases had produced the dermatitis. These men may well return to ordinary french-polishing in due course, but, clearly, if they are to handle amino-resins they should take greater precautions than when they are handling the ordinary materials of their trade. Another patient whom I saw last year worked as a transformer-core builder. In assembling the transformer cores he mixed an epoxy resin to apply to them. He mixed the resin with hardener on a slab with his bare hands, kneading a mass the size of a football, as a baker kneads dough, for about half an hour, afterwards moulding it by hand around the core. He developed an allergic dermatitis due to the resin.

In none of these cases, as in many others we still see, had the workers been given any warning of the risk of dermatitis, and they were consequently handling the resins with the indifference that is natural in ordinary work. In preventing this sensitization dermatitis, the only sure safeguard is avoidance of contact. When these substances are being used it is imperative that the skin is not brought into contact with them. Implicit in this also is the proviso that the resins must not be allowed to contaminate benches, door-handles, and machinery, in order that accidental and unnoticed contact may not occur. Grandjean found that atmospheric contamination was so slight as to be unmeasurable, so that risk other than by direct contact is negligible. Sometimes much is made of protection with barrier creams, and Grandjean believes that they offer a certain amount of protection.

Barrier Creams

In general, the idea of applying to the hands a protective layer before starting work is not new. Prosser White (1915) mentions the use of a fatty application to protect the skin, mostly against water-soluble irritants.

Barrier creams acquired their real lease of life when they received official support from a Ministry of Labour pamphlet in 1946. In the years that have followed, the use of these preparations has increased enormously, and has received support from dermatologists far beyond what is justified by the evidence. In theory the conception of a barrier cream is excellent; it is to form an invisible, impalpable, inodorous, and innocuous layer on the skin, flexible and unbreakable, which will allow

perspiration and evaporation to take place from the skin, but which is, above all, impermeable from the outside. It resists removal during work but is easily removable in ordinary washing. To believe in a substance so nearly bordering on the miraculous requires either a naive credulity or the most conclusive scientific evidence. The latter certainly does not exist.

The properties chiefly claimed for an efficient barrier cream are: (1) effective barrier against irritants and sensitizers; (2) after application it becomes invisible and impalpable; (3) it does not, by greasiness or otherwise, interfere with the work; (4) it is easily removed with ordinary washing, but it is not removed by work exposure over a period of at least a few hours; and (5) it is non-irritating to the normal skin.

Tests of various kinds have been proposed. First, there is the purely laboratory test such as that used by Sadler and Marriott (1946). They smeared barrier cream on to paper and then observed the transmission of various substances through this layer. Their results were very variable, and the authors themselves do not appear to place much reliance on them.

Schwartz *et al.* (1946) elaborated a method by which a continuous layer of cream of standard thickness was sandwiched between two layers of paper; the layer of cream was of uniform thickness—about 0.13 mm., or 5/1000 in. On the upper layer of paper they placed caustic soda or hydrochloric acid solution, and on the lower an indicator. They measured the time taken for the indicator to show transmission of alkali or acid through the layer of cream. In order to study the passage of liquid paraffin they stained the liquid paraffin with Sudan red. Among their results they found, first, that ordinary soft paraffin and anhydrous lanolin were as good as any of the 27 barrier creams they tested, and indeed better than most. Second, that the creams were not as the makers claimed; for example, some creams claimed to be water-repellent showed themselves to be more effective against oil than against water. A third point of considerable importance was the influence of humidity and temperature. As these rose above normal laboratory levels the efficiency of the creams fell off—in other words, they had less barrier effect as conditions came closer to those of the skin surface.

Porter (1959) attempted to make Sadler and Marriott's method more realistic by using an apparatus which subjected the paper on which the cream was smeared to a repeated bending movement. His results also were disappointing, and, like Schwartz *et al.*, he found that such value as a cream might have was not always that claimed by the maker. In general, he found little to support the effectiveness claimed for the 11 creams he examined.

These tests are of course highly artificial. They take no account of friction and sweating, and it seems improbable that a layer of cream 5/1000 in. (0.13 mm.) thick will lie on the skin invisible but persistent during some hours of work. Many of the creams tested by Schwartz *et al.* penetrated even this substantial layer in less than half an hour. How long would an invisible layer on the hands provide a barrier? One may conclude that a cream which does not pass such a test with a very high performance cannot be expected to have any practical value, and, even on this lax criterion alone, many present-day barrier creams must be rejected.

A more realistic type of test is that devised by Cruickshank (1948). He applied barrier creams to the skin in the prescribed fashion, and then applied mineral oil. After a given time he washed off the oil, and by examination under ultra-violet light estimated the degree to which the oil had penetrated to the skin surface. As Cruickshank himself pointed out, this test takes no account of friction and sweating, which are very important factors under normal working conditions, and would therefore tend to give optimistic results. Nevertheless, Cruickshank concluded that no barrier cream gave satisfactory protection. His best result was with a soap-based cream very thickly applied; but, as I shall indicate later, the use of soap-based creams at any time is of doubtful wisdom for other reasons, even if they do provide a better barrier than alternative formulae. Cruickshank concluded from his tests that reliance could not be placed on protective applications—this in spite of the fact that his tests were admittedly less stringent than conditions of use.

Morris and Maloof (1953) made a similar test, applying cutting-oil to a skin surface prepared with barrier cream. They found that, of 24 barrier creams tested, 20 were penetrated within three minutes. Of the four which resisted three minutes' exposure, two were later tested again with 30 minutes' exposure and found to be penetrated. This seems an astonishingly poor performance for creams which are supposed to give substantial protection for several hours at a time.

Skin-cleansing—a Complex Problem

I may at this juncture mention one argument often put forward in support of barrier creams—namely, that their use before work facilitates cleaning the skin afterwards. In some cases this claim is obviously untenable. Morris (1954) quotes a maker's claim that a certain cream protects against soap and household cleansers and yet is easily removed with soap and water when desired. Cruickshank, in the experiments referred to, paid attention to this point, and concluded that soap-based barrier creams did not facilitate the removal of mineral oil, although such a cream is particularly the kind which might be expected to have this effect.

The problem of cleansing the skin is a complex one, and clearly depends to a considerable extent on the nature of the dirt to be removed. What is meant here is presumably the removal of ground-in solid or oily particles which have entered the hair follicles and possibly the sweat-duct ostia and the minute interstices of the corneous layer during prolonged exposure and aided by friction—under conditions, that is, which were not reproduced in Cruickshank's experiments. Presumably, this kind of contamination can be prevented by filling the pores and fissures first with solid particles—for example, kaolin—or with soap or with some fatty material. This is an acceptable practice only if we know that the substances we apply are less harmful and more easily removed than the dirt to which the skin is afterwards exposed. Otherwise the state will arise where visible dirt is removed but a persistent layer of barrier cream remains to produce the consequences of follicular blockage, sweat-duct occlusion, and irritation of the skin surface. When Morris and Maloof (1953) were testing the effectiveness of barrier creams they found that, of 24 barrier creams they examined, five could not be washed off the skin with any ordinary skin-cleanser. This may well be what happens with silicone

creams, which appear to resist very strongly removal with soap and water (Suskind, 1955). Although workmen often say that barrier creams make cleaning the hands easier, I have not been able to find any evidence of exactly how this is achieved or how thoroughly in these circumstances the barrier cream itself has been removed.

Practical Aspects of Use of Barrier Creams

Turning to the more practical aspects, many writers, in general terms, give support to the use of barrier creams. For example, Schwartz (1955) lists the properties which a barrier cream should possess, but does not explicitly say which, if any, products actually have these qualities. Horner (1950) supports the use of barrier creams, but without seeming enthusiastic; she considers that their value in certain circumstances must be acknowledged, but I am not certain that these circumstances are easily achieved or likely to be realized in ordinary working conditions in the average factory.

Given favourable conditions a barrier effect can no doubt be obtained. Talbot *et al.* (1951) used a silicone barrier cream for the treatment of napkin rash, of skin irritation around colostomy openings, and comparable situations where the skin needs to be protected against discharges and secretions. They obtained satisfactory protection in 58 out of 61 cases. In this kind of use there is not the same tendency for the cream to be rubbed off the skin as there is with a workman's hands, and a comparatively thick layer can usually be kept on the skin surface for several hours, covered with a dressing if need be.

Eventually, I suggest, it comes to this—that the only evidence that will really indicate the practical value of a barrier cream must be derived from testing and observing in actual work, the cream being used over a prolonged period by real workmen. A comparison must then be made between the incidence of skin disease with and without the cream, other conditions being of course kept constant.

Silicone Cream

Suskind (1954) made an evaluation of a silicone cream in a factory where aircraft engines were being made. Exposures to oils, solvents, and irritants were many and various. The comparison here was made of the condition of the workers' skin before and during the use of a barrier cream. The conditions of work before the experiment had apparently given rise to a good deal of minor skin irritation, and this was observed to clear up when the barrier cream was brought into use. Simultaneously with the cream, however, a special cleanser (sodium lauryl sulphoacetate) was introduced, presumably replacing ordinary soap and other cleansing agents. No controls were run during the time of the experiment, and Suskind's promising and apparently favourable results are therefore not easy to interpret.

Morris (1954), on the other hand, could observe very little protection from the use of a silicone cream. He used a cream of this type in patients known to have allergic epidermal sensitivity. Patch tests were applied to skin which had been previously treated with barrier cream and the results compared with patch tests on untreated skin. No significant effect could be seen; in five cases there was no difference, in seven the prepared skin reacted less, but in six the treated skin reacted

more strongly—an important observation to which I shall refer later. Three patients with specific contact sensitivity to a substance encountered at work were returned to work after their eruption had healed with the use of a barrier cream. Their dermatitis relapsed at once, the cream apparently affording not the slightest protection.

Lack of Experimental Evidence

Evidence of the effect of barrier creams in actual use is in fact extremely difficult to obtain. From time to time, no doubt, a high incidence of industrial dermatitis in a factory has led to the introduction of barrier creams and the incidence of skin disease may have fallen afterwards. Almost always there are, however, several other factors involved—altered methods of work, medical supervision, improved washing facilities, and the like—and it is seldom that these are carefully kept constant so that the effect of barrier cream can be isolated and assessed.

Great care would have to be taken to ensure that groups of workers using different creams were matched in age, sex, and other relevant factors, and that their work, washing facilities, and other circumstances were precisely the same. The experiment would need to be carried out with a sufficiently large number of people and for a sufficiently long time, for the irregular and unpredictable incidence of industrial dermatitis could lead to false conclusions. The few experiments of which I have read in which barrier creams have been assessed in the factory have not taken account of all these factors, and the statistical validity of results has been difficult to assess because of the confusion by other methods which have been introduced at the same time. For this reason I do not feel satisfied that clear-cut evidence of their effectiveness is available. Such evidence as exists is fragmentary, contradictory, and inconclusive.

The B.P. Codex Revision Committee (1954) published a report from its Barrier Substances Subcommittee. At this time four formulae for barrier creams were suggested as being likely to afford some protection from industrial hazards. The subcommittee recommended that before these formulae were included in the *Codex* an opportunity should be given for wider experimental use and comment by interested parties. Whether or not these formulae have been subjected to the examination suggested, or to what extent, I cannot say. It appears to have been intended at the time that the secretary of the Barrier Substances Subcommittee should in due course be informed of experiments and of their results. A recent inquiry I made revealed that no information had been forthcoming. These four formulae, like many other proprietary creams whose composition is secret, remain insufficiently tested and assessed.

Irritancy

There remains the question of irritancy. The Barrier Substances Subcommittee to which I have referred recommended four formulae. One of these was an "oil and solvent barrier," and it contained 12% of hard soap. It is, of course, very well known that soap is a primary skin irritant, and that if 48-hour patch tests are carried out with soap in a concentration even as low as 1% a substantial number of positive results are obtained. It is not surprising that patch tests carried out by Dr. Elaine Donoghue and me on 29 normal

subjects using this recommended barrier cream gave 25 positive results indicating primary irritancy. Although it is usually harmless to use soap for washing when a concentration of about 5% remains in contact with the skin for only a few moments, it is doubtful whether 12% soap can be applied in the form of a barrier cream without a serious risk of primary irritation. Particularly is this so if the cream remains on the skin, as it is supposed to, throughout the working day.

The recommendation in support of barrier creams made by the Ministry of Labour and National Service (1946) says that preparations with a pH much above or below 5.5 to 6.5 are apt to be irritating. The "oil and solvent barrier" formula when diluted 25% gave a pH of 9.2. Sadler and Marriott (1946) examined eight barrier creams and immediately rejected three because their pH was over 9. Two proprietary barrier creams on sale at present which I have tested give a pH over 9 in 10% solution, and thus it seems very probable that the inclusion of soap in oil-resistant barrier creams is still fairly common practice. If such a cream is thoroughly applied and remains on the skin throughout the working day, it seems probable that it will give rise to some degree of primary skin damage. This primary irritation may of course be mistaken for industrial dermatitis.

A minor degree of primary irritation of this sort may give rise to a condition somewhat resembling chapping, and may in itself give no great trouble. It is probable, however, that small fissures which form in the corneous layer may allow the entry of dirt and of irritants, and thus pave the way for the production of a more severe dermatitis by some other irritant or by a sensitizer. The other formulae mentioned by the subcommittee may be non-irritant, but the inclusion of triethanolamine is of doubtful wisdom, since this substance has been suspected of irritating the skin. Regarding proprietary barrier creams, one cannot speak in this respect as their formulae are secret. One may observe, however, that Tas (1957) obtained primary irritant reactions by patch-testing with several barrier creams; in the case of some creams, over 50% of subjects gave positive reactions. The problem of primary irritancy in barrier creams seems clearly not to have received sufficient attention from the makers.

Sensitization

Quite apart from visible and obvious signs of primary irritancy and damage to the epidermis, we must consider also the possible influence of barrier creams on the permeability of the skin to other substances. It is easy to appreciate that increased penetration into the epidermis increases the likelihood of sensitization to a substance applied on the surface (Rothman, 1954). Treatment of the skin with lipoid solvents, detergents, and emulsifiers is apt to increase absorption through the transepidermal barrier. This effect has been observed and proved in a number of ways. Skog (1958) determined the results of patch-testing with dinitrochlorbenzol on normal skin and on skin which had been pretreated with 2% soap. After treatment with soap increased reactions were obtained, a potentiation of the irritant effect of DNCB.

Kvorning and Svendsen (1956) showed that the addition of "teepol" to a chromium or nickel patch test lowered the threshold of reaction in sensitive subjects, presumably because teepol enables the metallic salt to

reach the Malpighian layer more readily. A similar effect was noticed by Nilzen and Wikström (1955), in which lauryl sulphate appeared to increase the permeability of the skin to dichromate. Rabeau and Malangeau (1947) discuss the effect of wetting agents in promoting contact eczema, and suggest that this may be because the permeability of the epidermis is increased by these substances. Laug *et al.* (1947) also found that the addition of a wetting agent to an emulsified ointment increased its penetration, but they attributed this not to an alteration in the epidermis but to a diminution of particle-size in the ointment that was being applied.

Horner (1950) drew attention to the need for care in the choice of cream in the presence of toxic substances, and she mentioned that lanolin contained in a barrier cream may increase absorption. Jenkins (1948) found that the use of lanolin as a protective application actually increased the "smarts"—the acquired light sensitivity which results from contact of tar with the skin. He attributed this to the solubility of tar in lanolin bringing the tar into more intimate contact with the skin. In the case of tar this was easily recognized, since the smarts is a well-known symptom which appears soon after exposure. May I at this point recall that Morris (1954), in patch-testing known hypersensitive subjects, found that a proportion of them reacted more strongly if a barrier cream had been first applied? How often, one may ask, is the same mechanism in action when the effects are less immediately obvious? Consideration of these various aspects leads one to suppose that emulsifiers and wetting agents are all liable to have the effect of increasing absorption through the skin in appropriate circumstances. The modern formulation of barrier creams is, of course, not revealed, but it seems reasonable to surmise that many of them contain substances belonging to this category. Whether they are really diminishing the risks of dermatitis or whether they are adding to them remains unknown. In view of this complete uncertainty, it is unfortunate that barrier creams should have received such measure of support from doctors. The legal consequence of this has been that in many industries a failure to provide barrier cream is *prima facie* negligence of the employer to his employee, for which damages may be awarded.

Some time ago I learnt of a case where a man in contact with paraffin oil (kerosene) had good conditions of work and washing facilities which were acknowledged excellent, yet because this man developed a mild dermatitis lasting for two or three weeks—without later relapse—damages were awarded against his employer on the sole grounds that no barrier cream had been provided. Medical evidence in this case was largely non-committal, and the support given for barrier cream was lukewarm; the strong support came from the evidence of the technical director of a firm of barrier-cream manufacturers. This is in spite of the doubtful effectiveness of barrier creams against oil and solvents in general and against paraffin oil in particular; none of the recorded tests I have seen, even the favourable results of Suskind, show any protection against paraffin oil.

Conclusion

The courts of law can make judgment only on the evidence presented to them. I believe it should be our

task to make clear that the protection afforded by barrier creams is questionable, and that it has not yet been scientifically substantiated; we should demand that the experts employed by manufacturers publish the evidence on which their views are based in such a form and in such detail that it can be critically assessed; and we should insist that the formulae of these products are made known. The claims of those who make and sell these preparations are specious and their literature voluminous, but I have shared Porter's experience that these firms yield little information when one seeks the precise evidence on which their claims are based, and when one tries to find out the composition of their products.

I am not saying that all barrier creams are completely useless; only that we do not know and at present have no means of knowing. If this conclusion is correct, then no employer should be blamed or held negligent for failing to provide them. The present unsatisfactory situation is partly our fault, and we should reconsider our position. First, we should actively advocate the use of barrier cream only when we know that the proof of its value is soundly based (at the present time I suggest this means never); anything short of this should be regarded as an experiment and should be planned accordingly. Second, we should adhere to the general principle that we cannot recommend the use of an application whose exact composition is not made known to us. At the present time proprietary barrier creams are secret remedies.

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OLIGURIC RENAL FAILURE OF SURGICAL ORIGIN

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Renal failure, an omnibus term used to describe events which follow inadequate renal control of the internal environment of the body, may develop as an acute phenomenon in patients with previously normal kidneys or in patients with overt or occult antecedent renal disease. In its acute oliguric form it is a relatively rare complication of major surgical and traumatic conditions, and, perhaps for this reason, may be temporarily overlooked. While a high fatality rate may be inevitable as a direct result of the primary condition, delayed recognition and inadequate treatment of the secondary acute renal failure makes the overall prognosis significantly worse.

Acute oliguric renal failure has been well documented during the years since the second world war (Legrain, 1951; Swann and Merrill, 1953; Aoyama and Kolff, 1957; Hamburger *et al.*, 1958; Salisbury, 1958; Parsons and McCracken, 1959), but, apart from the wartime experiences recorded by Smith *et al.* (1955), Balch *et al.* (1955), and others, the surgical aspect of the problem, in the main, has received little specific attention. This despite the fact that a significant proportion of all cases of acute oliguric renal failure have a "surgical" basis.

Moreover, conclusions drawn from experience gained in the management of "medical" and "obstetric" patients with acute renal failure are not necessarily applicable: not only is the prognosis significantly worse in the surgical patients but their detailed management is often much more complicated and difficult. Oral feeding may be impracticable. Abdominal distension or vomiting may require prolonged use of an indwelling gastric tube with risk of pharyngo-oesophageal irritation, ulceration, bleeding, and the development of chest infection. Repeated gastro-intestinal aspiration may add to the difficulties of fluid and electrolyte management. Poor wound-healing, wound dehiscence, infection, secondary haemorrhage, and the development of intestinal fistula may occur. Incontinence may develop, and it may be virtually impossible to prevent the development of pressure sores.

The so-called "conservative" management of patients with acute oliguric renal failure (Borst, 1948; Bull *et al.*, 1949), by fluid and protein restriction, administration of carbohydrate, insulin, and calcium (Meroney and Herndon, 1954), ion-exchange resins (Evans *et al.*, 1953), and sodium lactate, as a rule easily applicable to "medical" and "obstetric" cases, is used whenever possible: there are, however, some potential difficulties in the "surgical" cases. It may not be easy to assess extrarenal fluid and electrolyte losses from fistulae, skin burns, or skin and intestinal ulceration: oral ion-exchange resins may not be effective in cases of ileus (they may even be dangerous because gastric casts