SYMPOSIUM ON PSORIASIS*

A FAULT OF EPIDERMAL PROTEIN METABOLISM IN PSORIASIS: A BIOCHEMICAL REVIEW

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During 1958 an American award of $1,000 was made to three workers at the Berne dermatological clinic for their outstanding research on psoriasis. I shall present here some particulars from their prize-winning articles.

Paschoud, Schmidli and Keller, the three investigators, started their work by improving the way of recovering amino acids and certain peptides from the skin. They worked throughout with small fresh razor-shavings of the skin, which seemed mostly to include all the epidermis and a little of the upper corium. By prompt fixation in chilled absolute alcohol, autolysis and the loss of water-soluble components were prevented, and after this the skin slice was cut fine, homogenized and dried to a powder. This dry powder was the standard from which hot aqueous extracts were made. In these extracts the total content of amino acids and of water-soluble peptides was determined. The former was done by Folin's aminonitrogen method, and the latter by the increase in amino-nitrogen after hydrolysis of the peptides by acid digestion in a sealed tube.

In normal skin a fairly stable level of amino acids was found, with a noteworthy presence of acidic amino acids (aspartic and glutamic acids) in the paper chromatograms made of them. In contrast, the hydrolysed water-soluble polypeptides showed a wider range of amino acids in them and contained cystein and

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some basic amino acids (lysine, argine, histidine) which were not characteristic of the free amino-acid mixture.

The polypeptide fraction being rather unstable was less constant in amount and composition than the amino-acid fraction, but a normal range could nevertheless be established. Its exact constitution was not further analysed; high-voltage paper electrophoresis may ultimately help in doing this.

The workers repeated these determinations on the unaffected and the affected skin in patients with psoriasis. The unaffected skin was found to resemble the normal values from non-psoriatic individuals, and in the lesions themselves the amino-acid level was also normal. However, the psoriasis lesion itself showed a statistically highly significant diminution in water-soluble peptides. The value was about half that of the normal average value. Two explanations for this were considered, namely a dilution effect due to the scales, and a non-specific inflamatory decrease in the peptides. A few control tests were made on scale-free lesions and various inflammatory conditions, but the decrease in water-soluble peptides was found to be confined to the lesions of psoriasis, and was not due to the presence of scale or inflammation.

A possible reason for reduced peptide concentration in psoriasis may be a lack of the enzymes causing protein and peptide breakdown. Since little is known about the properties and activity of epidermal peptidases, the Swiss investigators prepared some dialysed fresh skin homogenates uncontaminated with therapeutic metals to investigate their lytic activity on some simple peptide substrates. The assay of enzyme activity was again made by determining the rise in aminonitrogen by Folin's method as the substrates were hydrolysed.

A marked reduction in the activity of certain dipeptidases was established beyond question. Although this may naturally have little direct bearing on the low polypeptide values, it is nevertheless suggestive besides being interesting in itself. Further study of the enzyme activity in psoriasis material showed that these enzymes were not in fact lacking, but were functionally inhibited, and that the activity could be made to approach normal by removing this brake. Other inflammatory skin disorders, as was the case with the soluble peptide levels, did not show any similar disturbance in peptidase activity, thus making the enzyme inhibition a characteristic of the psoriatic lesion.

Some studies were made into the nature of this enzyme inhibition. It was noted that cobalt exerted its normal activating influence on glycylglycine dipeptidase. Also, the flocculation of an unknown substance after storage of the psoriasis skin homogenates led to a rise in their dipeptidase activity to near normal. Lastly it was found that by preparing a homogenate from scale-stripped lesions, the pure Malpighian layer gave near-normal values of enzyme activity. The workers therefore suggested that some inhibitory substance was possibly formed in the Malpighian layer which was stored in concentrated form in the scales. Whole-epidermis homogenates would therefore be relatively inhibited. This last conclusion is difficult to integrate with the histochemical findings of Braun-Falco, who, using a synthetic histochemical substrate, noted an inhibited aminopeptidase activity in the Malpighian layer in psoriasis. Here the contamination with scale material could not affect the reaction as it does in a biochemical technique, and if the results can at all be compared, the activity should also have been nearly normal histochemically.

Confirmation and extension of these studies will be eagerly awaited, as they indicate a fruitful biochemical approach to the understanding of psoriasis.

THE TREATMENT OF PSORIASIS: CONSULTING ROOM ASPECTS

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I feel that I can best use the time at my disposal by avoiding any attempt at a wide review of my subject and by confining myself to a few challenging and perhaps controversial statements, largely in the hope that they will stimulate discussion. Consequently, much of what I shall say will probably be proved incorrect, none of it will have statistical backing, but in all of it there will be, I believe, some basis of truth.

Chronic psoriasis *en plaques* in the adult seems to me to be as far removed from the acute guttate psoriasis of the child as chronic nephritis is from acute nephritis. Both occur chiefly in the young, and both sometimes follow an upper respiratory infection. Are they not both allergic responses to coccal infection, differing only in the shock organ affected? Cases of arthropathic psoriasis would appear to have a similar pathogenesis, which leads me to the conclusion that the secret of this common disease lies in such a mechanism and not in some obscure biochemical upset.

Why is the pate spared in psoriatics who also show male baldness? It is some years since the lie was given to the statement that psoriasis does not occur in the non-European. It is therefore unlikely that this statement, that I have never seen involvement of the scalp in association with this kind of baldness, will survive this afternoon's meeting. I have never had the opportunity of examining tribal Natives in large numbers. Could not the psoriasis that we see in those attending our Transvaal clinics have been introduced amongst them by miscegnation as porphyria seems to have been. That there is a hereditary predisposition to the disease, I have no doubt. There must in addition be several external causes which act as precipitating factors. Bacterial allergy, I have mentioned. Trauma can also act in this way, and an injury can determine the site of the original lesion, as well as producing a Koebner effect when dissemination is occuring. I have under my care at present a meter reader who cut off the electrical supply of a family who had not paid their account, whereupon the irate housewife threw stones at him and hit him on the leg. His psoriasis started at the site of the injury and has since spread.

There are many atypical forms of the disease and for a survey of some of those which are commonly recognized I cannot do better than refer you to Michelson's recent article in the *Archives*.[1] I would go further and say that anything which seems to a dermatologist to be psoriasis (and a dermatologist is not likely to be mistaken about Bowen's disease or anything similar if consideration is given to all the factors) probably is psoriasis; and will certainly respond to treatment in the manner of psoriasis. The position approximates to what the teachers of the last generation had to say regarding the diagnosis of syphilis—an awareness of its possible presence is of great help and importance in its detection.

As far as treatment goes, my nihilism of former years is being replaced by a feeling that sometimes something can be done. Triamcinolone is part of that something. Apart, however, from the cost, which worries everyone, almost all of those on an effective dose complain of headaches, and a peculiar flatness or lack of energy. Many have stomach pain and polyuria, the latter even when they have not previously been on steroids. One or two suffer loss of libido. These side-effects are so much more noticeable with this drug than with prednisone that, apart from cases of psoriasis, I have now returned to prescribing meticorten as my steroid of choice. The two cases which I have recently had in hospital on aminopterin have not improved even by 1% and the same might be said of those to whom I have given riboflavine. As a local application I have not found anything better than ½% dithranol in Lassar's paste rubbed in well twice a day with a toothbrush and used in combination with tar baths, ultraviolet light and vitamin B_{12} in my own modification of Joeckerman's regime. It is unfortunate that the non-staining chrysocreme appears to be as ineffective as it is inconspicuous. Superficial radiotherapy, in the 40-70 KV range of which my apparatus is capable, is of value chiefly in hitherto untreated cases of recent onset. Even if improvement follows a first course of therapy, repeat treatment at a later date seems much less effective and I therefore await with great interest the remarks of Dr. Loewenthal to whom I now give the floor, on his experience with grenz rays.

1. Michelson, H. E.: A.M.A. Arch. Dermat. 78, 9. (1958).

TREATMENT OF PSORIASIS WITH GRENZ RAYS AND ULTRA-SOFT RAYS

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X-rays have been used in the treatment of psoriasis for over 50 years and in most types the immediate results are satisfactory. Unfortunately psoriasis is well known for its tendency to recur in previously affected areas and these recurrences usually happen relatively quickly, i.e. before the tissues have had time to recover from irradiation. Further X-ray therapy then entails risking permanent damage to the skin. The use of ultra-soft and grenz rays in psoriasis is recommended, not because their beneficial effect is greater, or even as great. at the same surface dosage, but because the danger of producing permanent damage to the skin and subcutaneous tissues is far less.

The advantages of grenz and ultra-soft X-ray therapy derive from the following 3 facts:

1. A quality of radiation can be used of which 50% is absorbed in the upper layers of the skin. The precise depth at which this 50% absorption occurs can be selected from a depth of 0·3 mm. to one of 3·5 mm., according to varying kilovoltage (10-30) and qualities of filtration. Below this 50% level falling-off proceeds at such a rate that at a depth of 3·5 mm. only 10% of the original quantity of radiation emitted at 10 kv. survives; this is reduced to 4% at a depth of 6 mm.[1]

2. It is generally agreed that serious permanent sequelae do not follow unless the necessary quantity of radiation has reached a depth of 3 mm.

3. Whether the initial lesion of psoriasis is in the epidermis or in the capillaries of the upper corium[2] is of little practical importance, because it is certainly to be found in the outer half millimetre of skin, according to either theory.

Thus a form of radiation which exerts its maximum effect in the upper half millimetre of skin, and falls off rapidly in the deeper layers, would appear to be ideal. Rays emitted between 10 and 30 kv. will thus be appropriate for all forms of psoriasis, the latter being used where surface scaling is marked, or where the presence of hair (as on the scalp) forms a barrier to the softer rays.

METHOD

My own experience comprises relatively few cases who could be followed up; it must be remembered that to treat widespread psoriasis is time-consuming and that in practice one treats only those lesions which are a social handicap. In the 14 cases reviewed here, lesions of the hands were treated in 8, elbows in 6, face and ears in 3, ankles and scalp in 2 and legs or knees in 1 each. Grenz rays (10 - 14·5 kv.) were used in 17 instances and ultra-soft rays (29 kv.) in 4. For lesions whose apparent thickness suggested that grenz rays would not penetrate sufficiently, a filter of 1 mm. of cellon was added; where the scalp was to be treated 29 kv. with a filter of 0·3 mm. of aluminium was used. With grenz rays the dosage varied from 160 to 200 r. weekly to a total of 880 to 1,840; with 29 kv. the usual dosage was 66 r. weekly to a total from 266 to 1,056 r. These schedules are similar to those used in chronic hyperkeratotic eczema,[3] but slightly higher than those used by Baer and Witten.[4] Nevertheless, I have rarely had to exceed their maximum *annual* recommended dose of 1,600 r. of grenz rays. Simultaneous topical therapy has been limited to an occasional application of soft paraffin at night in hyperkeratotic lesions, and the regular use of a shampoo in cases where the scalp was involved.

RESULTS

Immediate results have been most gratifying and only one lesion—on the elbow—has proved refractory to 1,840 r., though lesions on the hands of the same patient cleared with 1,060. Relapses are of course frequent and may begin as soon as 6 weeks after the end of treatment, though in most cases 3-6 months' complete freedom is obtained. I have the impression that relapses occur sooner with the more superficial types of radiation, i.e. soonest after treatment at 10 kv. and latest after 29 kv. One encouraging and unexpected finding is that the response to second and subsequent courses of grenz-ray therapy is more rapid than to the original course, so that fewer treatments are needed with each course and the intervals of freedom are longer. Thus one patient needed 1,525 r. at 10 kv. to clear the elbows in February 1957. He reported an early recurrence in June 1957, which cleared after 675 r. The second recurrence in November 1957 was treated at 14·5 kv. and responded to 830 r; there was then a period of 10 months' complete freedom followed by a relapse, which responded rapidly to 660 r. He has therefore received a total of 3,690 r. to the elbows in just under 2 years.

No unwanted sequelae have been seen in the admittedly short period of 3 years during which I have used this treatment, and I have the feeling that it is possible in most cases to continue suppressing the more noticeable manifestations of psoriasis without incurring the risk of such sequelae. Thus a statement recently made,[5] 'There is nothing a dermatologist can do with grenz rays that a radiologist cannot do with X-rays', does not apply, *inter alia*, to the treatment of psoriasis, for I think most radiologists would hesitate to use X-rays generated at 70 kv. or more, in effective doses, to the same area of skin, repeated as often as is permissible with grenz rays.

1. Graul, E. H. (1953): Z. Haut- u. Geschl.-Kr., **15**, 3.
2. Shelley, W. B. and Arthur, R. P. (1958): AMA Arch. Derm., **78**, 14.
3. Bohnstedt, R. M. (1955): Strahlentherapie, **98**, 1.
4. Baer, R. L. and Witten, V. H. (1956): *Year Book of Dermatology and Syphilology* p. 32. Chicago: Year Book Publishers.
5. Weinbren, M. (1958): S. Afr. Med. J., **32**, 565.