ATOPIC DERMATITIS*

II. Role of the Sweating Mechanism

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Attention recently has been directed toward a syndrome of abnormal reaction to high temperature and humidity. This condition has been called tropical anidrotic asthenia by Allen and O'Brien (1) and thermogenic anhidrosis by Wolkin, Goodman and Kelley (2). In it, horny plugging of the openings of the sweat pores was shown to be the mechanism by which the outpouring of sweat is inhibited. More recently, Sulzberger and Zimmerman (3) showed that this situation is also responsible for the very common condition of prickly heat. In a later report, Sulzberger, Herrmann and Zak (4) showed the same phenomenon in a case of atopic dermatitis. In discussing this paper, Sulzberger called attention to the possibility that the sweating mechanism might be one seat of the difficulty in some instances of atopic dermatitis. Sulzberger believes that as a result of the blockage of the pores, the sweat may pour into the subcutaneous tissues and thus carry with it the fluid antigens to which the patient may be sensitive.

Our interest in this phase of the problem was stimulated by our observations in an experimental clinical study of a case of atopic dermatitis recently reported elsewhere (5). While attempting to reproduce the lesions of atopic dermatitis, we deliberately exposed the patient to inhalant allergens. After each trial, the patient volunteered the information that profuse sweating had followed immediately after the inhalation of the alternaria powder. We decided, therefore, to investigate this phenomenon further by more detailed means. These observations, as well as those on an additional patient, form the basis of the present report.

EXPERIMENTAL OBSERVATIONS AND RESULTS

We made use in these studies of the same technic employed by Sulzberger, Herrmann and Zak (4) in their study of the prickly heat problem. A 2% mixture of powdered iodine in soluble starch was used as the indicator. This was carefully dusted onto the affected areas in a thin and relatively uniform layer. If water comes in contact with the mixture, a blue color is developed by the familiar reaction of iodine on starch.

The materials used for inhalation were alternaria powder and ragweed pollen granules. The former was prepared by growing the mold on a suitable medium and powdering the resultant killed growth pad. The ragweed powder was obtained commercially.

Two patients are described in this report. The first patient was a 29-year old veteran with atopic dermatitis of long duration who was extensively studied at

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Temple University Hospital during the period of January 17, 1949, to December 3, 1949. The details of his history have been given in the previous report, (5) but as already indicated, during this study we were able to reproduce the dermatitis repeatedly, both by the inhalation of house dust and alternaria spores. In the course of the latter experiments, the patient complained of profuse sweating after the nasal test. On April 12, 1949, when the lesions were disappearing, the patient inhaled alternaria into the left nostril in an amount sufficient to cover the flat end of the conventional toothpick. Within five minutes, marked rhinorrhea and lacrimation of the left eye began. The patient complained that the chest, antecubital and popliteal areas were itching. He also called attention to the droplets of sweat which had begun to form in these areas and in no others.

This sweating phenomen was considered of little consequence at that time, but a control test was carried out in order to check the accuracy of these observations and to rule out psychogenic influences. Accordingly, while the patient was intent upon a game of cards on the ward and without any prior knowledge of the proposed test, powdered talc was instilled into the same nostril by inhalation. The patient was observed from a distance at first and then asked about his reaction. No sweating occurred with this procedure. In the same manner, alternaria powder was substituted for the talc and on this occasion, sweating was again produced in the same areas. Another control test performed with pine pollen gave no reaction.

In order to picture more succinctly the sweating changes, the method of starch iodine powder application then was used. The starch iodine powder was dusted on the entire body of the patient. The first experiment showed the effect of exercise. The patient was instructed to step up and down from a chair for two minutes. An immediate blue color developed but was localized solely to the neck and antecubital skin which formerly were the sites of dermatitis.

Another test was carried out the next day with inhalation of pine pollen and without exercise. No blue color occurred.

The following day, again without exercise, alternaria powder was inhaled after dusting the skin with starch iodine powder. Within five minutes, itching of the back of the neck began. This was followed by color change to deep blue on the neck, antecubital fossae and beneath the nipples bilaterally.

Several days later, after the mild reaction had subsided, an attempt was made to note the effect upon this phenomenon of Benadryl, administered intramuscularly. Accordingly, a solution containing 30 mgm. of Benadryl was injected. An hour later the patient's skin was dusted with starch iodine powder. Alternaria powder then was inhaled in the usual manner, and the patient observed for some period of time for the development of symptoms. These, however, did not occur; neither did any blue color develop in the dusted areas, thus indicating a lack of sweating.

With this data as a basis, similar studies were carried out upon a second patient, a 31-year old male accountant who had had "eczema" since infancy. The lesions were in the antecubital fossae, popliteal fossae, neck, and thighs. They persisted almost without change and despite all the usual forms of dermatologic

therapy until the patient was at an army hosptial in 1942. He attributed the improvement to a course of histamine injections; however, the relief lasted only four months and the lesions returned in more severe form. No relief was obtained after two subsequent courses of histamine. Under close questioning, this patient revealed that an increase in his symptoms occurred on or about September 4, 1949, with increase in sneezing and rhinorrhea. The nasal symptoms were present for the previous year in mild form. Flare-up in the skin condition occurred in the fall of both 1947 and 1948, and the 1949 increase was considered much worse than the previous ones. This clinical evidence of possible ragweed sensitivity was supported by a positive urticarial skin reaction to ragweed pollen extract.

Hospitalization of the patient at Temple University Hospital was followed within a short period by marked improvement in the dermatitis. In order to ascertain, and if possible prove, the effect of the ragweed pollen, the patient's skin was dusted with iodine powder and he was subjected to inhalation of ragweed pollen. A measure of pollen sufficient to cover the flat end of a toothpick was inhaled. Immediate sneezing and rhinorrhea began, and this was followed by color change in the areas of the cutaneous lesions. There was sweating of the neck as shown by the blue coloration, as well as sweating in both antecubital fossae and both popliteal fossae. This was of special interest to the patient, since he stated that he rarely sweated, even during the summer, but of course this was at a time when his dermatitis was rather marked.

Because Sulzberger, Herrmann and Zak reported plugging of the sweat ducts in the histologic section in their case of atopic dermatitis, a biopsy study of the first patient was done. A piece of tissue was taken from the right antecubital fossa in the region of exacerbation of the atopic lesion. The biopsy was obtained when a flare-up due to inhalation of alternaria powder was in progress. The comment on the biopsy report, studied in serial section by Dr. Franz Herrmann and Dr. Stephen Brunauer[1] of the Skin and Cancer Unit of New York University Hospital, is as follows:

"The histology is mainly that of a neurodermatitic lesion, the changes of the arterioles being compatible with a 'neurodermatic reaction'.

The described changes in, around or on top of several of the sweat ducts are highly suggestive of abnormal imbition of the epidermis with sweat, under the influence of horny plugging. In view of the limited number of ducts indicating features of this process—as compared to the total number of visible ducts, no conclusion can be drawn from the microscopic findings in this case as to the magnitude of the clinical significance of such defect in sweat delivery.

Several of the histologic findings, e.g., the focal infiltration, the thickened vascular walls, and the plasma cells would seem compatible with a diagnosis of distinctive exudative discoid lichenoid chronic dermatitis (Sulzberger-Garbe). However, none of these features, in particular the number of plasma cells, are sufficiently excessive to warrant this diagnosis on histologic grounds only; rather than that of the much more common picture of an atopic dermatitis (disseminated neurodermatitis)."

This histologic report tends to support the existence of atopic dermatitis. Although there was some evidence of horny plugging of some of the sweat ducts,

[1] This is to acknowledge our great appreciation to Drs. Herrmann and Brunauer for their courtesies in this study.

not many of the latter were affected compared with the total number of visible ducts present.

DISCUSSION

In the experimental studies previously reported, we were able to demonstrate that the inhalation of specific allergens in susceptible patients can induce the lesions of atopic dermatitis. The demonstration in the two cases herein reported of localized sweating in the affected areas prior to the outbreak of these lesions suggests that disturbance of the sweating mechanism may in some way be concerned in the mechanism of production of the dermatitis. As originally mentioned, from Sulzberger's study of his patient with atopic dermatitis, he felt that plugging of the sweat ducts might be responsible for the dermatitis through internal sweating. This is not demonstrated by our studies, since both our patients sweated in the areas in which the lesions were most pronounced. It is entirely possible, of course, that the amount of plugging and of its resultant interference with sweating will depend upon the degree of involvement of the affected skin. Thus if only part of the glands are involved, sweating still may be brought about by the unaffected glands under proper stimulation. Such stimulation might be provided by the active allergenic excitant brought to the sweat glands through the circulating blood after inhalation through the nasal mucosa. It is hoped that future studies will lead to further clarification of this point.

For the present, it seems apparent that, at least in some cases of atopic dermatitis, the sweating mechanism is in some way concerned with the production of the dermatitis. This would seem to be confirmed by the fact that in both our patients sweating was evident in the areas only mildly involved by the dermatitis, whereas these same areas, when markedly affected by the dermatitis, did not show any sweating upon provocation. Furthermore, the prevention of the sweating and of the outbreak of dermatitis by the preliminary injection of Benadryl also indicated that the localized sweating was in some way related to the inhalation of the specific allergen and its subsequent local effect. It suggests also the possibility that any beneficial effects obtained in atopic dermatitis patients from the antihistaminics might be due, perhaps even in large measure, to prevention of the inhalation of the specific allergen rather than to a direct local effect on the skin.

CONCLUSION

Evidence is presented from experimental studies of two patients with atopic dermatitis that the production of the dermatitis by the inhalation of specific allergens is in some way associated or concerned with disturbances in the sweating mechanism. Localized increased sweat and also, in more severe and later stages plugging of the sweat ducts, (Sweat Retention Syndrome) may both play a role.

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