STUDIES OF SWEATING

I. Preliminary Report with Particular Emphasis on a Sweat Retention Syndrome*†

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A good deal of attention has been devoted to skin diseases associated with plugging of the orifices of the sebaceous glands. Acnes, comedones, milia, some furuncles, folliculitides, lichen spinulosus, and keratosis pilaris are common examples of affections in which keratotic plugs in the openings of the pilosebaceous apparatus have been recognized as an intimate part of the pathogenetic happenings. In contrast, but little attention has been accorded the role of plugging of the *sweat gland orifices* as an important part of the pathology of certain cutaneous diseases. Recent findings have made us feel that sweat gland-obstruction deserved further consideration and more intensive study. The principal stimulus to the present studies was given by recent observations in the tropics (1, 2, 3). These observations confirmed those of S. Pollitzer (4) in that it could be shown that horny plugs in the openings of the sweat ducts occurred in prickly heat, and played a substantial part in the pathogenesis of this disease. It was further shown that the outflowing of sweat was very much reduced or absent in and around the affected zones; and that this reduced or absent sweating could persist for some time after the acute clinical manifestations of ordinary miliaria were no longer in evidence.

It was also demonstrated that the syndrome described by Allen and O'Brien (5) as *tropical anidrotic asthenia* and by Wolkin, Goodman and Kelley (6) as *thermogenic anidrosis* was associated with horny plugging of the openings of the sweat pores with an inhibition of outpouring of sweat; and with histologic and clinical cutaneous pictures (e.g. papulation, vesicle formation on exposure to elevated environmental temperatures) quite analagous to those found in the end stages of ordinary prickly heat. In the most recent studies from Guam (1, 2, 3) it was emphasized that prickly heat and tropical anidrotic asthenia might well be related to one and the same fundamental mechanism, namely occlusion of the sweat ducts, and consequent local cutaneous effects. It was inferred that when extensive areas were involved, the plugging of the pores, and the consequent failure to pour out (and evaporate) sensible perspiration when needed, could lead to profound disturbances of the heat-regulating mechanisms and systemic aberrations of great significance.

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The present report confines itself to two groups of cases evidencing signs and symptoms referrable to failure of sensible perspiration. In Group I the failure to pour out fluid is thought to be connected with the plugging of glandular orifices; in Group II failure to sweat rests on a different basis, namely on atrophy of the ducts.

GROUP I

Failure of Sensible Sweating, Associated with Plugging of Ducts

Our investigations of patients in temperate zones, namely New York City and vicinity, have, during the last 1½ years brought to light a number of cases with findings resembling those in tropical prickly heat and in tropical anidrotic asthenia.

It is the purpose of this presentation to sketch a few of these findings and submit the following hypotheses as a basis for further study and discussion:

Plugging of the sweat ducts occurs in a variety of conditions which do not present the classic picture of ordinary prickly heat, or tropical anidrotic asthenia. It has thus far been demonstrated in cases resembling or actually presenting the picture of ordinary atopic dermatitis (disseminated neurodermatitis); mild forms of ichthyosis or ichthyosiforme erythroderma; and dry forms of seborrheic dermatitis. It is logical to suppose that such plugging may occur in other, common cutaneous diseases e.g. certain "dysidrosiforme" eczemas (see for example Gougerot), (7, 8) hydroadenitis, tropical bullous impetigo, and perhaps even some cases of lichen planus, nummular eczemas, and psoriasiform dermatoses. Further studies must be directed toward the elucidation of this supposition. Almost regardless of the exact appearance or classification of the dermatoses, when a sufficient number of the sweat glands are firmly plugged, the affected patients present a syndrome having the following characteristics:

1) *Rapid elevations* of environmental temperature accompanied by high humidity bring on attacks of pruritus. Various degrees of systemic malaise may accompany the attack.
2) Almost immediately upon sudden experimental elevation of environmental temperature, various types of objective skin changes appear. These may include shiny papules, minute papulo-vesicles and vesicles.
3) The pouring out of sweat is reduced or absent in large or small areas, as shown in our cases by the starch iodine tests, by tests with dibromfluorescein ("Bromo-Acid") paper[1], by electrohygrometric studies, and by consistent elevation of the pH on the skin surface. Stimuli which ordinarily produce sensible perspiration do so only in certain areas which are sometimes small in number and extent, and are inclined to be fixed (i.e. in repeated tests approximately the same areas either sweat or do not sweat).

[1] Skin prints are made on absorbing paper which has been soaked for 10 minutes in a 0.5% solution of "Bromo-Acid" (= di-brom fluorescein) in acetone, and dried; any presence of water-sweat droplets produces a bright, golden fluorescence on inspection of the paper under "filtered" ultraviolet radiation (Wood's light).

4) The reduction of surface sweat is not due to reduction of sweat secretion by the acini of the glands, but apparently to plugging of the ostia of their ducts which prevents the delivery of sweat to the surface. This is shown by a series of pertinent findings among which are: (a) histologic findings of acini, which appear normal in structure and distribution; (b) the clinical and histologically demonstrated vesicles which—on the stimulus of heating—form in the epidermis, sometimes at, or near the sweat gland orifices; and which on pricking deliver a fluid which does not have the characteristically high pH of inflammatory fluid, but the low pH of sweat.
5) More or less prompt subjective relief and objective improvement follow consistent reduction of environmental temperature and humidity; and benefits follow local procedures which will cause a peeling and casting out of the orificial plugs, and measures which bring about a reduction of the load on the sweat mechanism.

Short summaries of some selected cases will illustrate the 5 points just enumerated.

CASE 1

(Atopic Dermatitis) An example presenting many of the gross clinical features of *atopic dermatitis* was that of B.A., a 29 year old white man. This patient had suffered from a severely itching skin disease since infancy. His mother had "eczema" and attacks of sneezing. On intracutaneous skin testing the patient had moderate to marked urticarial reactions to fish and some other foods. Clinically there were distinct exacerbations on ingestion of fish.

The patient stated that he perspired very little, even on hot summer days, and that only the face, armpits, groins and popliteal fossae became moist.

Clinically, he presented essentially the picture of atopic dermatitis with scratch marks and moderate lichenification with lichenoid papules, preponderantly on face, cubital and popliteal fossae.

Bromo-Acid paper tests, starch-iodine tests, and electrohygrometric readings showed that the sensible perspiration was confined to patches in cubital and popliteal fossae, in the axillae, on lower chest, and between the toes. After exposure to heat, an increase in sensible perspiration was demonstrable, but essentially limited to circumscribed areas on the forehead, neck, chest, both axillae, arms, dorsa of hands, popliteal fossae, and between the toes. The larger papules and their immediate surroundings, in particular on the dorsa of the hands, remained free from any dark coloration under the starch-iodine test, and thus contrasted as light "islands" with the darkening surroundings (Fig. 1 and 2).

Histologic findings of serial sections of skin from the right upper back:

There are occasional areas of parakeratosis, many foci of spongiosis, intracellular edema, and even rarefaction of the epidermis where the latter is also infiltrated by inflammatory cells from the underlying papillae. There is a conspicuous perivascular inflammatory infiltrate of lymphocytes, fibroblasts, and histiocytes. Plugging of follicles by horny material, and inflammation in the surrounding corium are observed. There is an occasional irregular penetration of horny epidermal plugs into the corium. Although the sweat glands

as a whole show no significant changes, one sees occasional sweat ducts in the cutis which have hyalinized basement membranes, and which are atrophic. Numerous sweat pores contain plugs of cornified material, or are lined by a horny layer. In a number of instances these plugs seem to be perforated centrally by slit-like lumina. The total number of sweat pores is perhaps decreased.

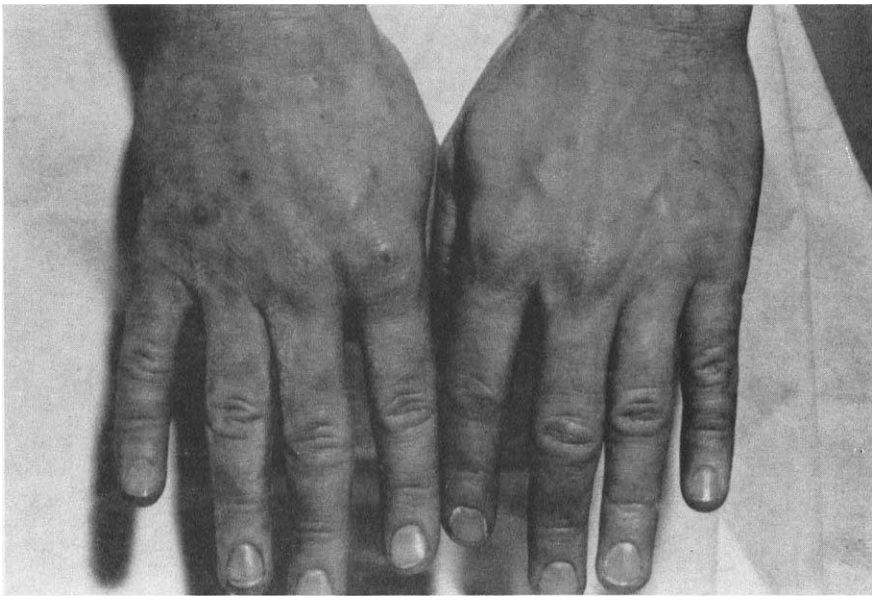

FIG. 1. GROUP I, CASE 1 (B.A.)
Papular lesions. Starch-iodine test, before exposure to heat. No sweat excretion manifest on the skin surface.

CASE 2

Ichthyosis, with extensive inflammatory changes which somewhat resemble atopic dermatitis

S. F., a 17 year old white school girl, who had never been outside of New York City, complained of an almost generalized, severely itching eruption which had recurred every summer for 15 consecutive years. Itching was unbearable during periods of warm weather, and was absent in cold weather. The patient and her mother thought the disease was due to hypersensitivity to sunlight. The patient stated that, with the exception of her armpits, no part of her skin surface showed perspiration when all other people perspired profusely. When exposed to heat she complained of headaches and nausea, irritation of the skin and severe itching.

FINDINGS

The entire skin, except for some patches on forehead and in both axillae, presented rhomboid or polygonal, adherent fine scales and accentuation of the normal skin markings; the palms and volar aspects of the fingers showed moderate hyperkeratosis, the soles presented greatly thickened, cornified plaques.

There was extensive papulation and lichenification, most pronounced on cubital and pop-

liteal fossae, on neck, upper back and face. The entire picture resembled *atopic dermatitis in combination with a moderate generalized ichthyosis.*

On numerous occasions we tested this patient by exposure to dry heat for periods of 10 minutes. In normal persons this stimulus produces an appreciable increase in sensible perspiration.

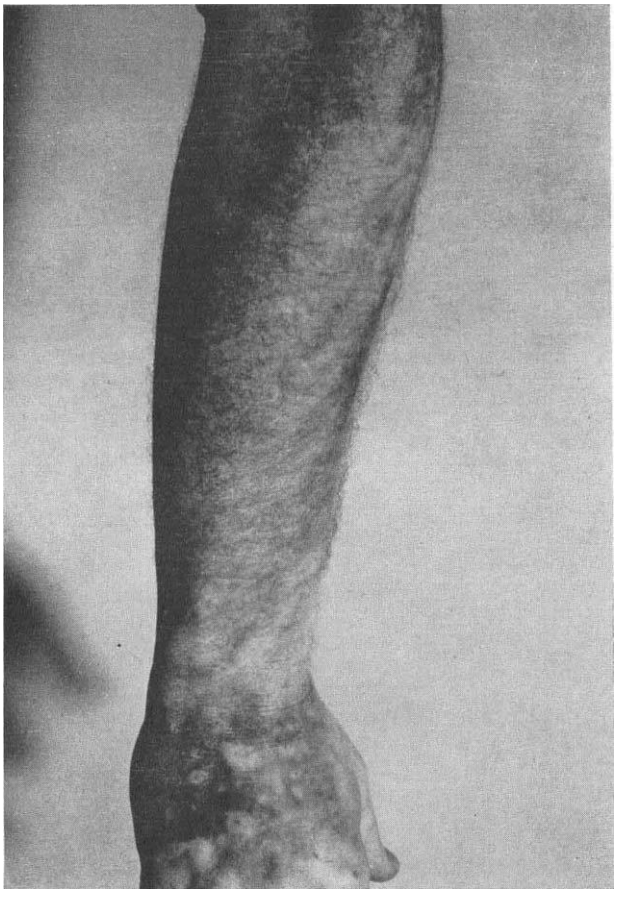

FIG. 2. GROUP I, CASE 1 (B.A.)
Starch-iodine test, after exposure to heat. Absence of darkening shows that the surface of the papular lesions and their immediate surroundings remained free from sweat.

This patient (S.F.) presented the following manifestations: The skin remained dry, but many of the papules became more pronounced (especially on upper trunk and both arms). Unbearable itching set in, accompanied by headaches, general malaise and nausea. The high pH findings (7.1 to 8.5), the sweat pattern tests, and electrohygrometric readings—all showed absent or reduced sweating in all areas except for the centers of both axillae.

The following histological findings of skin tissue taken from symmetrically

situated sites before and after exposure to heat may perhaps throw some light on the causes of the absent sensible sweating.

Histology (biopsy specimen taken from left forearm (flexor surface) *before heating*; serial sections:

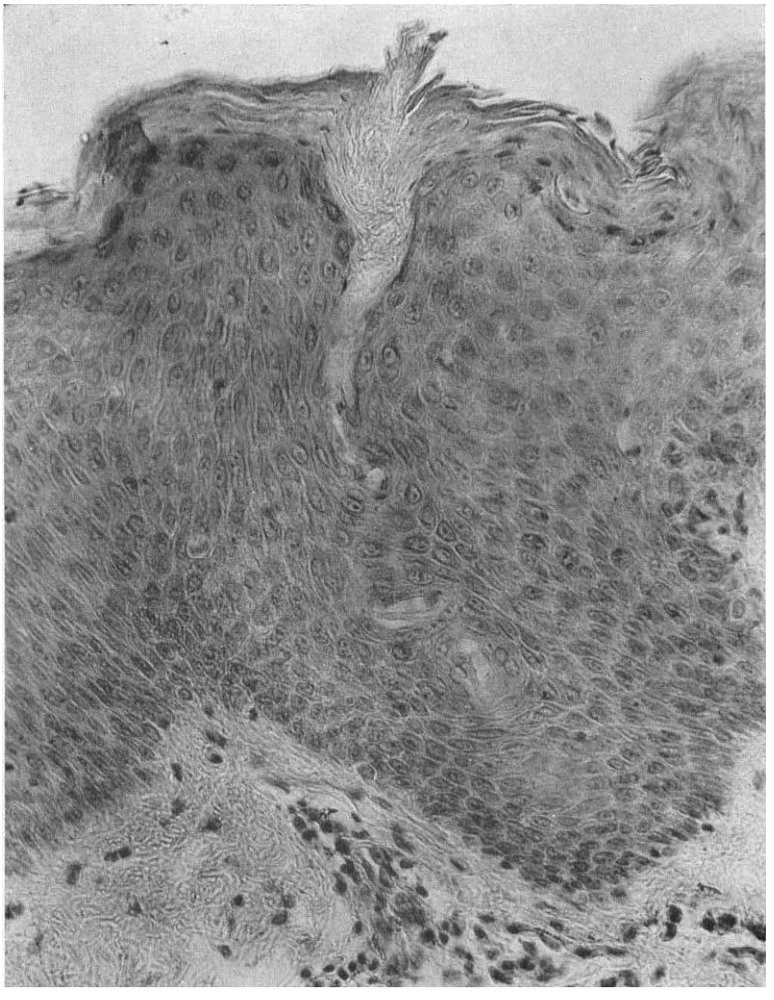

FIG. 3. GROUP I, CASE 2 (S.F.)
Funnel shaped sweat pore filled with horny plug. 484×

There is acanthosis with thickening of the entire epidermis. Moderate hyperkeratosis and parakeratosis are present. Many sweat pores appear plugged by horny material (Fig. 3), though a number of them seem to have slit-like lumina in these plugs. There is a cellular infiltrate in the papillae, and around the vessels of the corium, which consists of lymphocytes, fibroblasts, and histiocytes. Focal intercellular edema and exocytosis are present, leading in one instance to an epidermal bleb. An intraepidermic abscess seen in one instance may have arisen from such a bleb. A few "corps ronds"-like cells are observed.

There is a peculiar, granular, brown pigment (iron-free) which appears to be located in the outer portion of the cell bodies of the myoepithelial elements, if indeed it is not in the basement membrane (Fig. 4).

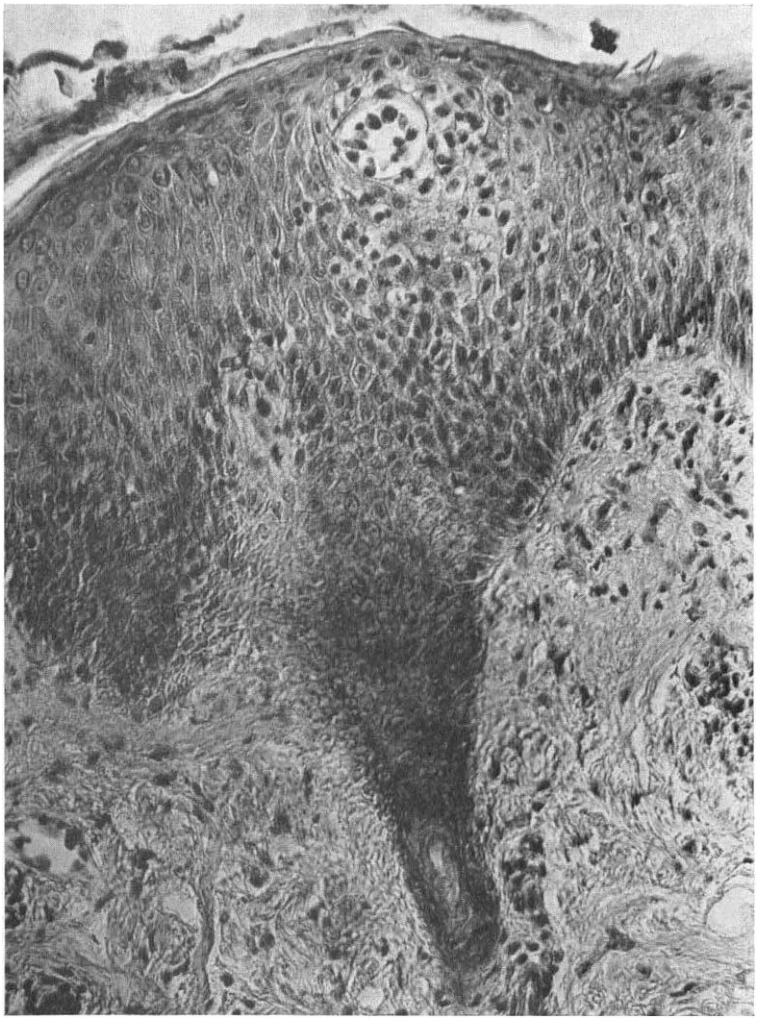

FIG. 4. GROUP I, CASE 2 (S.F.)
Small intraepidermic vesicle next to sweat duct. The latter may be seen at the bottom of rete peg. 383×

Histology after exposure to heat (biopsy specimen from right forearm-flexor surface i.e. from site symetrically situated to that on left forearm which was excised before exposure to heat; serial sections):

When compared with the findings before heating, the inflammatory process, particularly the formation of vesicles, is intensified (Fig. 5). The blisters arising from exocytosis and

exocrosis appear to have more relation to blood vessels in the papillae than to sweat ducts, since most of them are not in the vicinity of sweat ducts. However, there is one sweat duct which shows disintegration of the adjacent epithelium, caused by escaping fluid (Fig. 6).

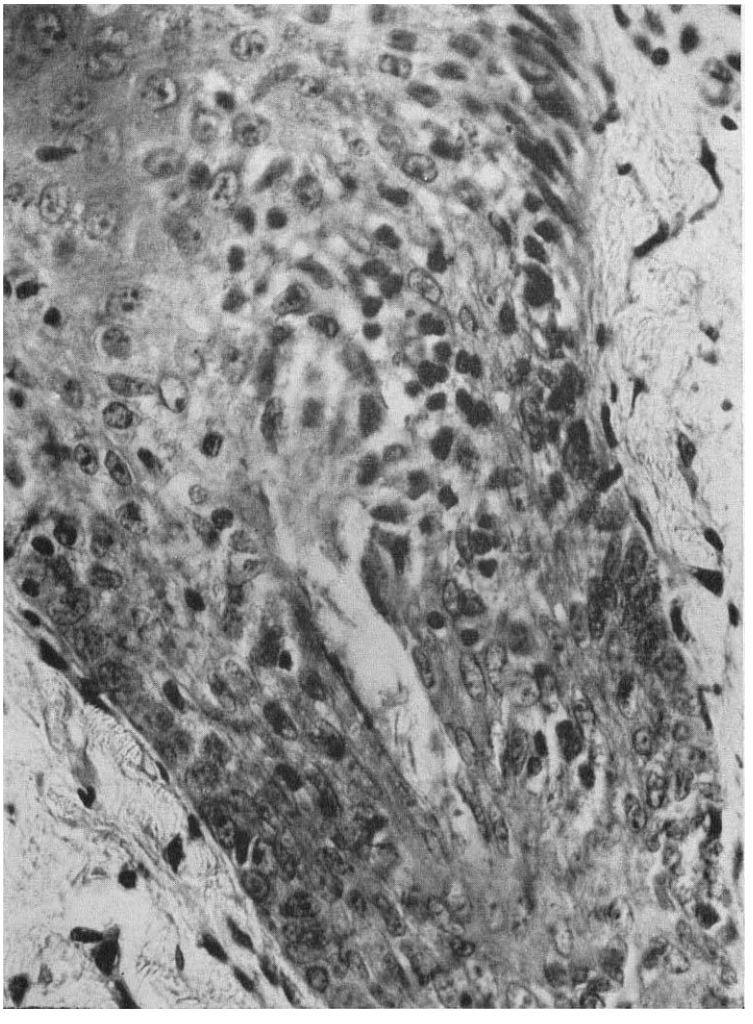

FIG. 5. GROUP I, CASE 2 (S.F.)
Sweat duct in rete peg with distintegration of its wall and inflammatory cells near its right upper margin 900×

A small epidermal vesicle conta ning red cells speaks in favor of the vascular origin of some of the blebs.

It appears permissible to infer that the plugging of the sweat ducts and consequent retention of the secreted sweat may have led to the rapid formation of vesicles and increased inflammation. This inference is in accord with all the clinical and other gross findings.

CASE 3

(Ichthyosis) A. P., a white woman, 31 years old, could be observed for only short time. This patient presented the clinical picture of a moderate, but quite widespread *ichthyosis*. Her mother and one brother have similar skin changes.

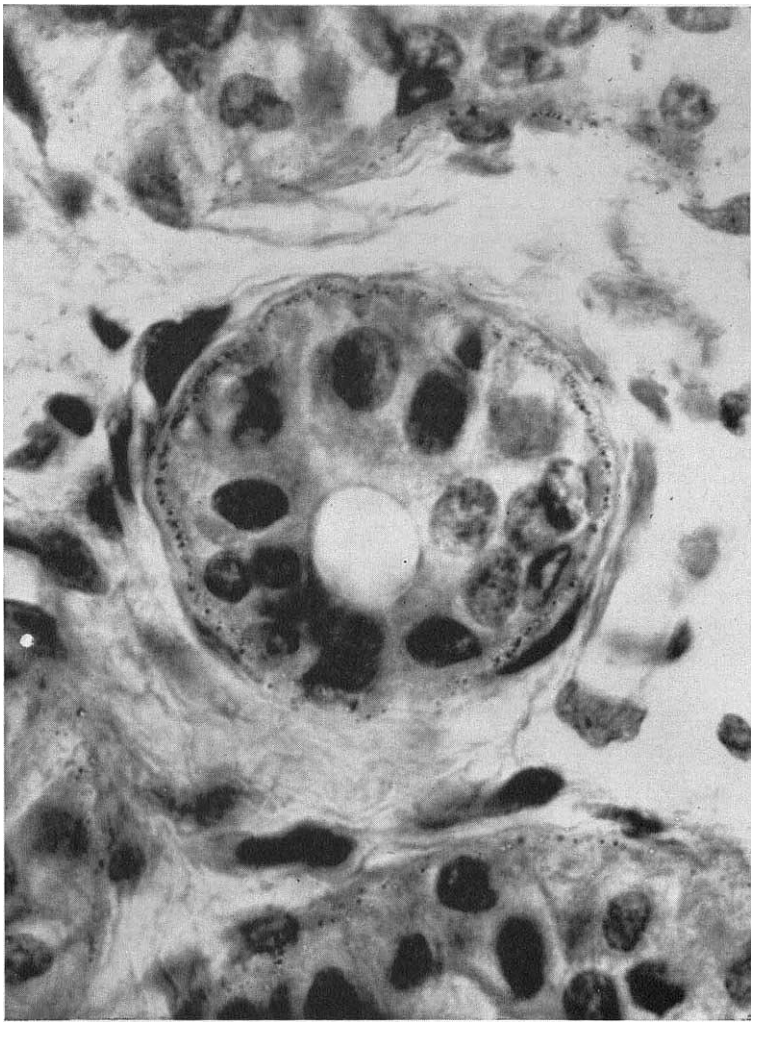

FIG. 6. GROUP I, CASE 2 (S.F.)

Pigment granules inside basement membrane of sweat gland—resembling the findings in argyria. A constant feature of this case. 2070×

The patient stated that she perspired very little, even on hot summer days, and only on the face, while even the axillae remain dry. On hot and damp summer days, especially under physical strain (such as fast walking) she often feels dizzy and had painful sensations "about the heart". She attributed this to "high blood pressure".

FINDINGS

The skin presented distinct generalized scaliness, except for the palms and soles. The skin markings were accentuated. There was some lichenification and diffuse bluish discoloration on the distal half of the extremities. Net-like, reddish streaks were present between the larger scales on the extremities, and scratch marks on the back, forearms and legs. Papules resembling those of pseudoxanthoma elasticum were present on the anterior and lateral surfaces of the neck, and in the axillae.

The elevated pH of the entire surface (all areas 6.8 to 7.6) as well as the electrohygrometric readings and sweat patterns indicated practically complete absence of sensible perspiration.

Unfortunately no biopsy could be obtained.

CASE 4

(Seborrheic Dermatitis and Prickly Heat.) B. S., a white man, 34 years of age, suffered from an itching skin eruption on trunk and arms during the last 10 summers. His skin remained almost normal during the cool season.

Here the clinical picture presented features suggestive of *prickly heat* as well as of a dry scaly form of *seborrheic dermatitis*. There were scaly, erythematous, oval patches behind the ears, on back, chest, abdomen and upper arms. On close inspection some of these lesions presented closely set, millet-seed-sized papules. In addition there were outlying pinhead-sized, discrete, reddish papules in the vicinity of the plaque-like lesions.

Experimental exposure to "dry heat" not only produced a great intensification of itching and of the erythema in all lesions originally present, but also numerous new, itchy, erythematous macules and patches on face, trunk, abdomen and arms. During the heating, we were able to observe a papulo-vesicle of about pea-size develop on the flexor surface of the right upper arm. The patient stated that such lesions commonly appeared "throughout the hot summer season".

The fluid content of this vesicle was released by pin-prick and had a pH of 5.3 (characteristic of *sweat*, rather than *inflammatory exudate*).

The studies of sweat excretion (Bromo-Acid paper) and of pH of the skin surface showed a failure of sensible perspiration involving large areas of the skin of face, both upper- and forearms, dorsa of hands, chest, back, and abdomen.

Biopsies were made of three areas after exposure to heat and presented these histologic findings (serial sections):

Abdomen: The epidermis shows focal parakeratosis and occasional inflammatory cells. The follicles are plugged by horny material and covered by a parakeratotic scale. Inflammation is seen around the hair follicles and sebaceous glands, but not around the ducts of the sweat glands. There is a perivascular cellular infiltrate of lymphocytes, fibroblasts, plasma cells, and occasional segmented neutrophils. Many sweat pores appear plugged by horny material which in numerous instances has slit-like central lumina.

Back: In addition to the above-described findings, the sections show features of focal intercellular edema and atypical cells in epidermis. The sweat pores are often dilated by horny lamellated material.

Axilla: There is a cyst, lined by epidermis and filled with horny debris. The apocrine and ekkrine glands are abundant. There are numerous sweat pores, and some of these are plugged.

Discussion of Cases of Group I

These four cases presenting in their aggregate features of *atopic dermatitis, ichthyosis, atypical seborrheic dermatitis* and *patchy prickly heat*—all evidenced findings indicating retention of sensible perspiration and consequent faulty dissipation of heat from the skin's surface. The histologic findings suggest *plugging* of the *orifices* or the *sweat ducts* as a cause of contributing factor in preventing the outpouring of sweat. The skin changes, including both the subjective pruritus and the appearance of papules, vesicles, and lichenification, as well as the constitutional symptoms could all be the result of sweat retention.

Many features of these cases seen in New York City are very similar to the findings recently observed in the tropics (1, 2, 3); and also similar to the observations of R.D.G.Ph. Simons (9) in "Miliaria erythematosa et papulosa tropica". The narrow, slit-like lumina found in many of the horny plugs in the sweat pores of cases 1) and 4) are in effect analogous to the "smallness of the sweat gland ducts" which Simons reports in "white immigrants" and which he considers the cause of sweat stagnation, and hence of the tropical condition, rarely seen in natives.

The beneficial effect of selected therapeutic procedures tend to support the outlined assumption. Vitamin A and peeling therapy with salicylic acid solutions appeared useful in three of the described cases. Moreover in this connection it appears of great significance that three of our patients (Case 2, 3, and 4) were invariably free from complaints and lesions during the cool seasons, and suffered only during the hot and damp periods of the summer.

It is, of course, a well established fact that striking improvements or "cures" are often observed in atopic dermatitis and some other chronic lichenoid and pruritic dermatoses (as well as psoriasis and even asthma, arthritis, etc.) *after transfer of the patients to "a different climate or environment. Our findings may perhaps provide some explanation as to why the "cures" are often best obtained precisely in those climates where evaporation is facilitated through constant, extremely low relative humidity, with elevated temperatures (sunny deserts, etc.).*

GROUP II

Post-Atrabrine Atrophy of Sweat Ducts

There are two patients in this group, both Navy men who had suffered from severe lichenoid eruptions due to atabrine. The history, clinical description and tissue specimens of Case A were kindly put at our disposal by Lt. W. K. Hall (MC) U.S.N.R.:

CASE A

This patient (a white male, 38 years old) had suffered from a typical lichenoid atabrine-dermatitis contracted while on duty in the Pacific Theater of war in 1945. Though the acute eruption gradually regressed, the patient continued to complain of severe itching and aggravation of skin lesions in warm weather, whereas subjective and objective improvement was distinctly noticeable in cool climate. Disappearance of the rash in hairy parts of scalp, pubic region, and lower legs was followed by spotty loss of hair.

Abstracts from the records of U.S.Naval Hospital, National Naval Medical Center, Bethesda, Md.:

(April 1945) "There is a blotchy rash over the entire body, and it is confluent about lower legs. . . . The individual lesion is raised, and dark brown in color. There is quite a bit of lichenification and the legs actually appear silvery."

(July, 1945) "The residual lesions are disfiguring and continue to give discomfort in the presence of heat and perspiration."

Miliaria on abdomen, observed for 3 days.

Lt. W. K. Hall excised skin tissues for biopsy in *October 1946*, when active lesions of atabrine dermatitis had long disappeared, and only some degenerative skin alterations were present clinically. Two specimens were excised; the first in a cool room (left leg); and the second after "patient had been lying under a heat cradle in a hot room—long enough to develop sweating of unaffected skin" (right leg).

Histology (serial sections)

There is slight thinning of the epidermis. The horny layer is widened and loose. An occasional patch of parakeratosis is seen. Mild intracellular edema is abundant. The stroma of the papillae is dense and eosinophilic. The subpapillary layer and the upper cutis contain perivascular infiltrates of lymphocytes, fibroblasts, histiocytes and occasional polymorphonuclear neutrophilic leukocytes. Chromatophores are numerous in upper corium. There is an occasional focus of spongiosis and exocytosis adjacent to inflammation in the uppermost cutis. The tubules of the sweat glands are chronically inflamed, dilated[2] and atrophied. There are nowhere any straight sweat ducts or sweat pores.

There is no significant difference between the biopsies taken before and after heating.[3]

The clinical picture and course, as well as the histologic findings in this patient show a striking similarity with the findings in the following patient who has been and still is under our own observation at the New York Skin and Cancer Unit.

CASE B

M. R. a white male, 36 years old, suffered 3 years ago from a lichenoid atabrine eruption, acquired while in the Pacific theater of war. For some time after the onset he continued his activity as a *cook*, and during this period there was a severe aggravation of the disease. During the next twelve months the patiet was treated in various military hospitals outside of the continental U. S. A. but was finally returned to this country.

At the beginning there were noted countless small nodules, which gradually merged with a generalized, diffuse inflammation. Itching was "unbearable". On return to the United States there was only very slow improvement of the redness, inflammation, etc. Eventually, at the time of final dismissal from the hospital, there remained "scarlike" alterations, bald patches on the hairy scalp, and dryness and scaliness of almost the entire skin surface.

During the last two summers (spent in New York City) the patient suffered from frequent

[2] In this connection it appears interesting that Donald J. Wilson found keratotic plugging of sweat ducts, and dilatation and atrophy of sweat glands in lichenoid dermatitis caused by atabrine.

[3] We are indebted to Dr. Chas. S. Sims for his assistance in these histologic studies.

attacks of severe pruritus on hot, damp days. These attacks were accompanied by *palpitations, dizziness, and nausea.* During the attacks many *dark-red patches appeared on his skin,* each time at exactly the same sites. These sites could be clearly defined and predicted by the patient. Likewise, certain *fixed areas* were always moist from sweat on these occasions, whereas large parts of the skin surface remained completely dry. Occasionally, there was fainting during these attacks. The patient found out that his best means for overcoming periods of "damp heat" was frequent ice cold showers—day and night—and staying undressed.

During the winter and cool seasons of the last two years he was free from complaints.

FINDINGS

Slightly scaly and reddish patches of atrophic skin, of quarter to silver-dollar size, somewhat resembling lupus erythematosus, were present on crown of hairy scalp, forehead, both cheeks, around the ears, and on chin.

The skin markings were accentuated on neck, chest, upper abdomen, back, extremities, chiefly on the extensor surfaces of both upper- and fore-arms, on the palms, and the thighs. There was fine, dry scaliness and a slight bluish-red discoloration over these areas.

Bluish-red atrophic spots and fine scaliness were present on both palms; there was marked hyperkeratosis of the soles.

The skin of the lower abdomen showed a slight, diffuse atrophy, and scattered patches of brownish pigmentation.

The nails of fingers and toes were thin, friable, and the finger-nails dotted with fine, dark groves.

Brown patches of pigment and bluish-white streaks were seen on the mucosae of lips and cheeks.

Responses to Experimental Elevation of Environmental Temperature

During and after each of our repeated experimental exposures to heat, the patient complained of palpitations, weakness, dizziness, and feelings of nausea.

The skin showed a peculiar erythematous reaction which persisted for $2\frac{1}{2}$ to 3 hours: very sharply demarkated, dark-red patches of quarter to silver dollar size, chiefly on face, neck, and chest, less pronounced on hands, abdomen and extensor surfaces of the thighs.

The intervening areas were apparently ischemic and pale. The red plaques reappeared in exactly the same sites after each heating. Moreover, on back and thighs (extensor aspects) several, about lentil sized, rather deep-seated vesiculopapules developed—within 20 to 30 minutes.

Sensible perspiration was noticeable in these experiments only in certain, always identical areas, which did not coincide with either the erythematous or the pale zones.

pH tests, electrohygrometric examinations, and the patterns of sweat excretion with starch-iodine or on Bromo-Acid paper, revealed that sensible perspiration was present, without preceding exposure to heat as well as thereafter, in a number of sites immediately adjoining areas without any demonstrable presence of sweat. The number and extent of the perspiring sites, and the degree of sweat production were increased after the heating (Fig. 7), but large areas even then failed to show any appreciable quantity of sensible perspiration. These areas included the entire back, abdomen, arms, and thighs.

Thorough medical examination[4] and blood analyses (CO_2, Ca, phosphates, chlorides, pH, etc.) were carried out before and after heating. The findings showed substantially normal values with two exceptions.

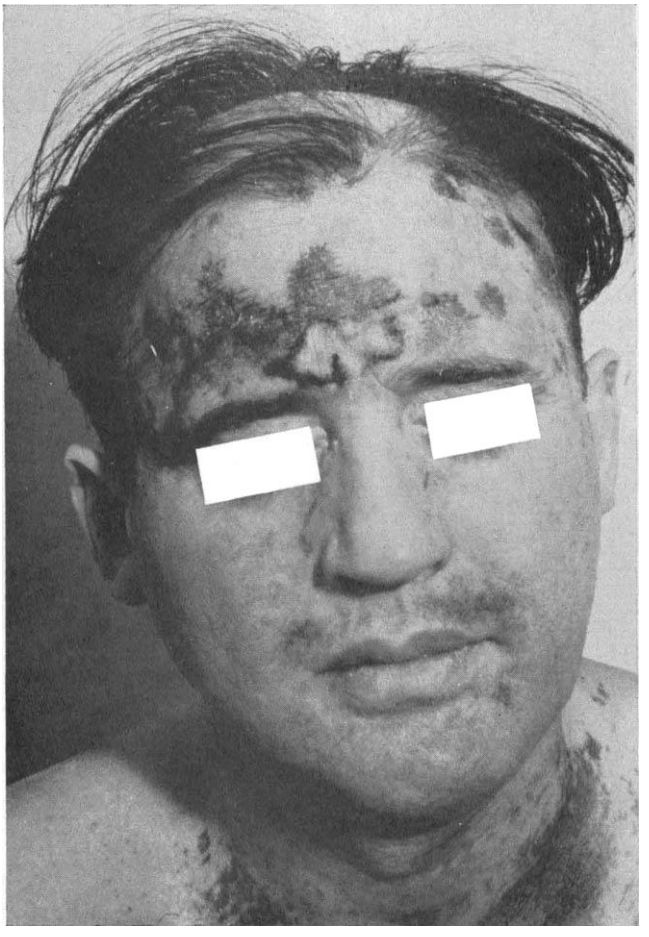

FIG. 7. GROUP II, CASE B (M.R.)
(Post-Atabrine Atrophy.)
Patchy sweat excretion in post atabrine atrophy. Starch-iodine test after exposure to heat.

There was a moderate gaseous alkalosis after heating (pH before heating 7.60—after heating 7.67; CO_2 before heating 57.9 vol. %—after heating 56.9 vol. %). This compares with the findings in the case reported from Guam (3) and may be evidence of hyperventilation.

[4] These investigations and the blood analyses were carried out through the courtesy of Dr. Maurice Bruger, Chief of the Division of Pathological Chemistry, N. Y. Post Graduate Hospital and Medical school. We wish to express our gratitude for his constructive cooperation.

The second abnormal finding was most pronounced and of great interest: The blood pressure before the heating was 154/92; but immediately after heating the *diastolic pressure dropped to zero* and the readings were *146/0!*

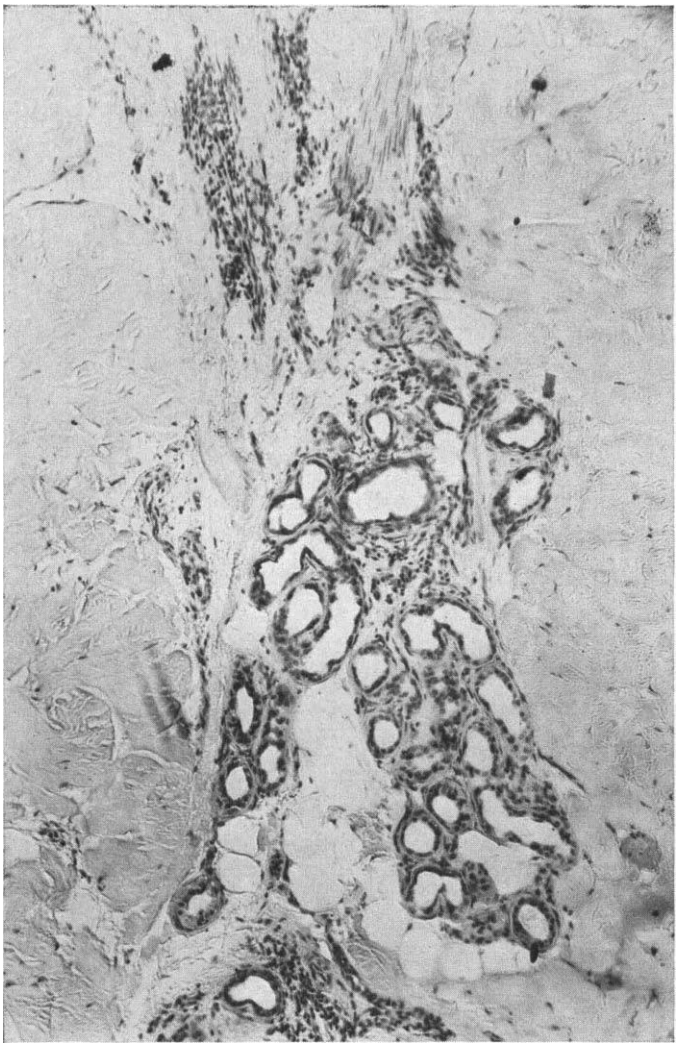

FIG. 8. GROUP II, CASE B (M.R.)
(Post-Atabrine Atrophy)

Dilated and atrophic sweat gland with focal chronic inflammation. The longitudinally arranged spindle cells and inflammatory cells at the apex of the gland may be remnants of a periductal inflammation; the duct proper having disappeared. 164×

Histologic Examinations

Biopsy specimens were taken from left upper back (before heating) and from symmetrical site of right upper back (after heating); serial sections revealed:

The epidermis is markedly thinned. The horny layer is lamellated and somewhat widened. There is patchy pigmentation of the basal cell layer. There is a perivascular infiltrate in the papillae and in the upper corium. Occasional chromatophores are seen in the upper cutis. The sweat glands show various features of atrophy and dilatation (Fig. 8), in some

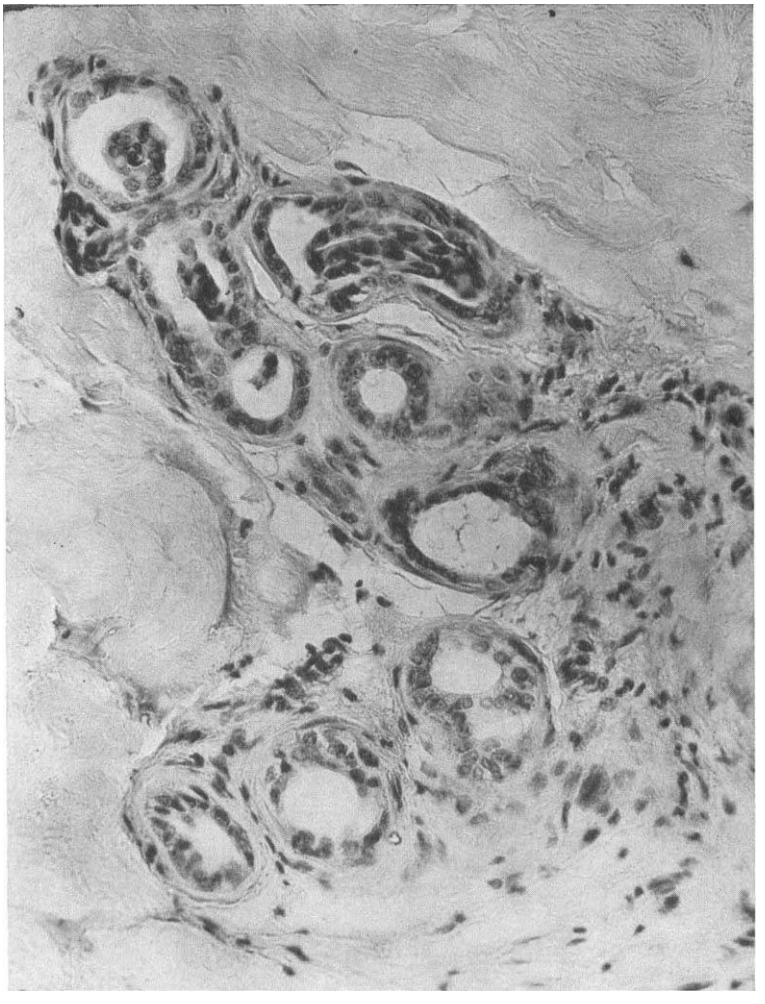

FIG. 9. GROUP II, CASE B (M.R.)
(Post-Atrabrine Atrophy)
Intraluminal proliferation of sweat gland. 500×

areas epithelial proliferation (Fig. 9). Fibroblasts, lymphocytes and fine fibrosis around the tubules of sweat glands resemble the picture seen in lichenoid atabrine dermatitis. Short sections of sweat ducts may be seen in the cutis; they are not connected to their glands, nor do they reach the surface. One gains the impression that the sweat ducts have become atrophic, leaving behind a strand of longitudinally arranged sheath cells (Fig. 10). Plugged follicles with surrounding inflammation are seen.

Discussion of Cases of Group II

In summarizing then, these 2 cases also present the 5 characteristics previously described as parts of a syndrome of *sweat retention*, with the qualification that the sweat retention is explained by the lack of sweat ducts, and not by

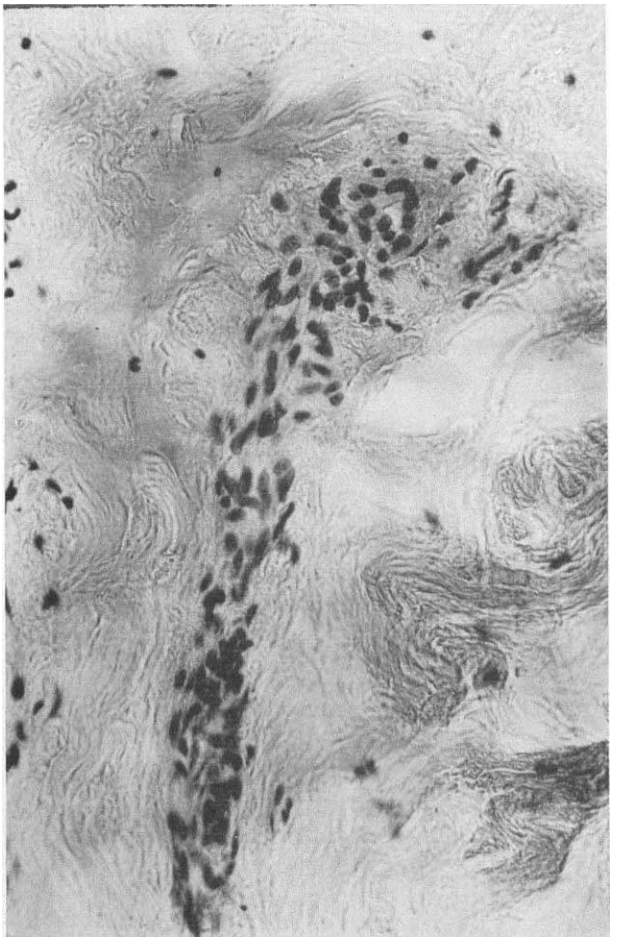

FIG. 10. GROUP II, CASE B (M.R.)
(Post-Atabrine Atrophy)
Atrophic segment of sweat duct in cutis. The ring of round nuclei near the upper end represents remnants of the original epithelial lining. 500×

plugging of pores. Particularly striking was the alternation of skin areas with demonstrable pouring-out of sweat on the surface, and of other areas which remained completely dry.

The appearance of vesiculo-papules during the heat-experiment in Case B on areas which did not show surface excretion of sweat, was very similar to the development of lesions under the same conditions in Case 4) of Group I. How-

ever, the lesions in Case 4), Group I were distinctly more superficial. The deeper location of lesions in cases of Group II may be explained by the absence of any excretory sweat ducts in the post-atabrine atrophy.

The peculiar spotty erythema seen in patient M.R. (Case B) which appeared together with other severe signs of faulty adjustment to elevations of environmental temperature, evidently represents a *compensatory mechanism for dissipating* heat which is called forth by the reduced surface for sweat evaporation. Extreme *peripheral vasodilation* during this reaction is obviously the cause of the *drop of the diastolic blood pressure from 92 to zero*, whereas the systolic pressure remained (146 mm.), close to its level before the heating experiment. Many of the other disturbances (palpitations, dizziness) of this patient on exposure to heat may be explained by the increase of pulse pressure.

This mechanism of counteracting heat accumulation in the body differs from that in the case of tropical anidrotic asthenia described by Sulzberger, Zimmerman, and Emerson (3). There, hyperventilation was considered as the probable predominant compensatory process to dissipate heat; while in the present case hyperventilation was apparently of lesser significance.

Similarly to the findings in Sulzberger, Zimmerman and Emerson's patient with tropical anidrotic asthenia (3), R. Brenning (11) found hyperventilation as a sole compensatory mechanism for dissipating warmth on exposure to heat in a patient with congenital anidrosis, whereas peripheral vasodilatation was missing. The author regards this failure of peripheral vascular response as the cause of grave systemic disturbances observed in his patient at raised environmental temperature as well as under physical strain.

The significance of the histologic findings and their relations to the functional and clinical manifestations is more obvious in the two cases of post atabrine atrophy (Group II) than in the patients of the preceding group. It is evident that no sweat can be delivered to the surface in all these areas where the straight parts of the ducts and sweat pores are absent, or not connected with the acini.

SUMMARY AND CONCLUSIONS

1. Several authors have recently reported a syndrome of skin alterations and symptoms related to prickly heat, as observed and studied under tropical conditions. Patients presenting features of this syndrome are seen also in temperate zones. The present authors propose the designation "*Sweat Retention Syndrome*" for this complex of disturbances.

2. The "Sweat Retention Syndrome" is characterized by severe attacks of pruritus, often associated with the rapid development of small, shiny papules, papulo-vesicular or vesicular lesions, together with systemic symptoms on elevation of environmental temperature and relative humidity. Relief and objective improvement are often obtained by environmental conditions which reduce the sensible perspiration, such as constantly cool, dry surroundings, or hot, dry atmosphere.

3. Stimuli normally followed by a generalized pouring out of sweat on the

skin surface, produce in these patients sensible perspiration only in limited skin areas, which may be small and few in number.

4. Various special laboratory examinations of sweat output and of pH on the skin surface performed both before and after heating support the assumption that this syndrome is caused to a great extent by sweat retention.

5. The Sweat Retention Syndrome is not always due to the same mechanism but may result from, or be associated with processes which are essentially different, and has been encountered in certain dermatoses which otherwise have little or nothing in common. The present report describes this syndrome in two groups of patients.

In Group I there are cases with atopic dermatitis, ichthyosis, and seborrheic dermatitis.

In Group II this syndrome is described as a common sequela of lichenoid atabrine dermatitis, when this condition is followed by superficial degenerative skin alterations and widespread atrophy of the sweat ducts.

6. In some patients *peripheral vasodilatation* apparently is an important mechanism to compensate for the impaired ability to dissipate heat through the evaporation of sweat. In other patients hyperventilation may be the major compensatory mechanism, and combinations may exist.

7. The histopathologic alteration which may best explain the sweat retention in Group I is horny plugging of the orifices of the sweat pores[5] in the cases of atopic dermatitis, ichthyosis and seborrheic dermatitis; while in the patients of Group II with atrophy after atabrine dermatitis, the important change is evidently the disappearance of the sweat ducts and pores, leaving the coil glands deprived of their outlets.

8. This preliminary report of our findings is intended to call attention to the following questions, among the many now requiring further elucidation:

A. What are the causes of the horny plugging of sweat glands? and how common and significant is the "Sweat Retention Syndrome"? and in what patients and in how many different dermatoses does it play a substantial role, even in temperate zones?

B. How many patients whose itching and eruptions are aggravated by heat, high humidity, exercise, etc. are suffering from manifestations of the Sweat Retention Syndrome?

C. When diseases of the skin (as well as other diseases such as asthma, arthritis, etc.) are greatly benefited by moving to another environment, in

[5] After completion of this manuscript, J. P. O'Brien's paper on miliaria rubra, tropical anhidrosis, and anhidrotic asthenia has appeared (Brit. J. Derm. & Syph. **59**: 125, 1947). As a result of these investigations all of which were carried out in tropical cases, O'Brien, like Sulzberger et al (3) furnishes histologic and clinical evidence that these three conditions present different phases of the effect of plugging of the orifices of sweat ducts. His findings are in many points very similar to the results of our present studies in "temperate" climes. Moreover, in conformity with the assumption of Pollitzer (4), O'Brien arrives at the conclusion that a depletion of lipids in the stratum corneum is responsible for the obstruction of the sweat ducts.

particular to one with constant low humidity, in how far is this due to easier loss of fluid by direct evaporation and thus reduction of the necessity for calling upon sensible perspiration?

D. What are all the compensatory mechanisms for dissipating heat which may be called into play by patients who cannot pour out sensible perspiration over areas of normal extent? and what transient or permanent effects can the repeated use of these compensatory mechanisms have upon the skin itself, upon the circulatory and respiratory systems, upon other viscera and upon the systemic functions and economy?

DISCUSSIONS

Dr. Clarence S. Livingood: I am very much interested in this paper and wish to congratulate Dr. Sulzberger and his associates, because I feel that this is a most important subject and one which has been neglected. Their studies constitute an important contribution to our knowledge on this particular syndrome, and the general physiology of sweating.

In the past four years I have seen approximately 50 patients with this syndrome. About 15 of them had no preceeding cutaneous disease, 6 had had generalized eczematous or exfoliative dermatitis, and the remainder had had atabrine dermatitis. All of these patients had intense pruritus on thermal stimulation or following injection of a therapeutic dose of pilocarpine. These patients had the same distribution of loss of sweating as that described by Dr. Sulzberger. Preservation of sweating on the brow, as well as the upper lip, and in some cases in the axilla with complete absence of sweating on other parts of the cutaneous surface was a constant finding. It must be agreed that Dr. Sulzberger's explanation of this sweating loss is an adequate one, but in addition it is my feeling that there must be some central mechanism involved. I think that we will find a significant number of these patients in clinical practice if we are aware of the sequence of events. I am sure that this loss of sweating explains the residual pruritus which frequently occurs in individuals who have had widespread dermatitis. It is difficult to explain the occurrence of this syndrome in those individuals who had atabrine dermatitis. I do not agree that this can be explained entirely on the fact that these same individuals were living in a tropical climate, because the incidence was many times greater in those patients who had atabrine dermatitis than in the patients who did not have the disease. In closing I would like to state that Dr. Sulzberger and his associates have opened up a new field of investigation, and it is hoped that other workers will continue it.

Dr. Walter C. Lobitz, Jr.: I enjoyed the report of Doctors Sulzberger, Herrmann, and Zak very much. Perhaps the hyperkeratotic plugging of the openings of the sweat glands, as is seen histologically in miliaria, or prickly heat, should be re-emphasized. Such abnormalities of the kerato-hyalin cycle of the epidermis may be primary in this disease and bring to mind the problem of abnormal vitamin A metabolism. In our studies of a patient with generalized miliaria we were able to reproduce the histologic, physiologic, and pharmacologic findings reported today and previously by Doctor Sulzberger and his co-workers. In addition, we were able to demonstrate an abnormal absorption and utilization of vitamin A (a flat curve) by means of the vitamin A tolerance test described by Ruch, Brunsting, and Osterberg (Proc. Staff. Meet. Mayo Clinic **21**: 209–217, May 29, 1946). Tests for visual dark adaptation also disclosed clinical night blindness in that patient.

Dr. Marion B. Sulzberger: I am grateful to Doctors Livingood and Lobitz for their pertinent and interesting discussions. In reply to Dr. Livingood, while the exact mechanism of the manifestations is not yet entirely clear, the simplest hypothesis—and that which is best supported—is that varying numbers of sweat glands become so plugged at their orifices that no sweat can come out. If a central or nervous mechanism were at play it would be very difficult indeed to explain why the face remained unaffected as well as other isolated patches. I believe that the face continues to sweat because the sweat glands in that area

have larger and better openings which are not so easily plugged and also because the sebaceous glands of the face put out a greater quantity of sebum and thereby keep the skin inuncted with natural grease and thus may contribute to the prevention of the formation of the horny plugs.

In regard to Dr. Lobitz' remarks, I am glad that he brought up the question of vitamin A. We have been treating some of our cases with large doses of Vitamin A. While we think that some of them may have benefited to some degree, that is all we can say to date and it is still too early to be certain even of this.

I believe that the mechanism of the plugging of the sweat glands and of sweat retention may well play a role in many cases of what appear to be common skin diseases and in the production of itching crisis in many different kinds of eruptions. In particular, it is my conviction that the possibility of this mechanism should be studied anew in relation to dyshidrosis and other recurrent eruptions of the hands and in relation to nummular eczema and certain other dermatoses of unknown etiology. Moreover, I would like to call attention to the fact that when openings of the sweat glands are plugged, the sweat, instead of pouring out and being removed from the skin surface, often pours into the cutaneous tissues. Of course, when this occurs all substances which are secreted with the sweat are actually injected into the skin at each attempt at sweating. A person with tropical anidrotic asthenia thus gives himself what one might call intercutaneous injections at about two million sites every time he starts to sweat; and these two million injections contain everything which happens to be in the sweat. This mechanism could well produce sensitization in susceptible individuals, sensitization to whatever drugs, food or other products that happen to be secreted with the sweat. I have often wondered if such a mechanism may not have been concerned, for example, in the production of the lichenoid atabrine eruptions seen in the South Pacific. Atabrine is a drug which is likely to be excreted with the sweat; and in the tropical zones, with their prevalence of prickly heat and tropical anidrotic asthenia, many persons taking atabrine would in all probability be reinjecting the atabrine into their cutaneous tissues where the sweat glands are plugged. It may therefor be more than a mere coincidence that lichenoid atabrine eruptions have occurred in greatest number in those geographic areas and in those groups of individuals where prickly heat and tropical anidrotic asthenia are also most common. Perhaps even in the common eruptions due to allergens such as food and drugs, we should consider the possibility that plugging of the sweat pores and autochthonous injections of materials contained in sweat may play a significant role in both sensitization and elicitation of local lesions.

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