THE EFFECT OF HIGH AND LOW SALT INTAKE AND REPEATED EPISODES OF SWEATING ON THE HUMAN ECCRINE SWEAT GLAND*

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Although the cytologic changes occurring in the eccrine sweat gland as a result of profuse sweating have been extensively studied in recent years (1, 2, 3), no attempts have been made to correlate these changes with the physiologic function of the gland under varying conditions. It seems reasonable to assume that such correlations can be made based on the observations that after repeated episodes of profuse sweating not only is the cytologic structure of the sweat gland altered but its function as well. It has been shown, for example, that acclimatization to heat manifested by a diminished sodium excretion by the sweat gland is accompanied by a decrease in the number of large pale cells within the eccrine secretory coil (4). It was, therefore, concluded that the large pale cell is in some way concerned with sodium excretion by the sweat gland.

The present study is concerned with the morphologic changes occurring in the cells of the human eccrine sweat gland as a result of repeated daily episodes of profuse sweating in salt-depleted and salt-loaded human subjects.

METHOD

Three normal young adult males were used as experimental subjects. Subjects were salt loaded by the oral administration of 12 gms. sodium chloride in addition to their regular daily diet containing an estimated 8 gm. of sodium chloride for five days prior to the episodes of sweating. During sweating salt loaded subjects were given 1.8 gms. of sodium chloride and 250 ml. of water at half-hourly intervals during sweating. A regular diet containing approximately 8 gms. of NaCl and an oral salt supplement of an additional 8–10 gms. was also given during each day of sweating making a total salt intake of approximately 40 gms. daily. After a rest period of at least one month after sweating subjects were salt depleted by means of a rice and fruit diet for one week prior to and during the five days of sweating. 250 ml. of water were given orally at half-hourly intervals during sweating but no salt. In both groups sweating was induced in a heat cabinet maintained at a temperature of approximately 105° F. Subjects were kept in the cabinet for six hours daily on five consecutive days. Biopsy specimens were obtained from the skin of the interscapular area of the back before and after each episode of sweating. All specimens were fixed in Helley's solution, serially sectioned and stained with either Giemsa stain buffered to pH 6.5 or the McManus-PAS procedure controlled with diastase (5).

RESULTS

A. First Day

Before sweating, the eccrine sweat glands in subjects on a high salt intake had a normal appearance (Fig. 1). In salt-depleted subjects, on the other hand, even before sweating the cells of the secretory coil were moderately reduced in size resulting in a widened lumen of the secretory coil (Fig. 2). The glycogen content of these secretory cells, however, was normal. The coil portion of the duct in salt-depleted subjects was glycogen-free in marked contrast to the rich glycogen content of the duct in salt-loaded subjects.

After six hours of sweating in salt-loaded subjects there was an incomplete loss of glycogen from the secretory coil and no loss of glycogen from the duct (Fig. 3). Variable amounts of vacuolization and atrophy of the large pale cells of the secretory coil were present but in no case was this very marked. Approximately 50–60% of the Schiff-positive, diastase-resistant (SPDR) granules of the small dark cells were depleted.

In the salt-depleted subjects six hours of sweating produced almost complete loss of glycogen from the cells of the secretory coil although an occasional cell retained its pre-sweating concentration of glycogen (Fig. 4). The cells of the secretory coil were much reduced in size, especially the large pale cell with considerably more distortion and vacuolization than that seen in

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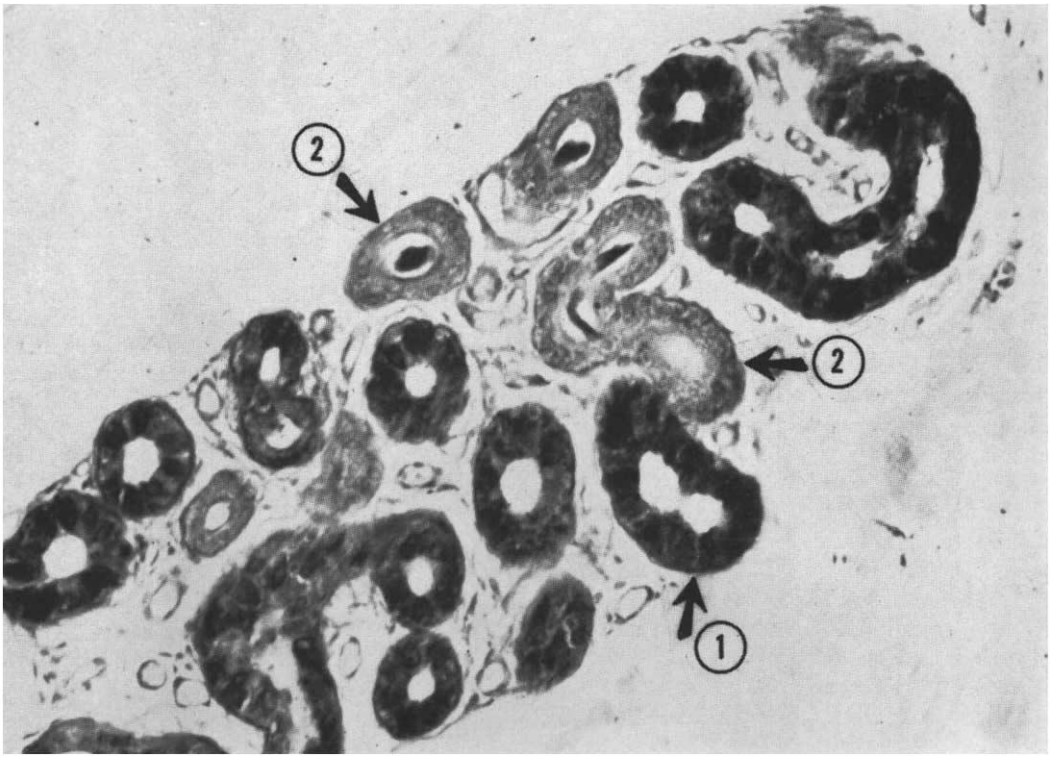

FIG. 1. First day. Salt-loaded subject before sweating. The secretory coil is rich in glycogen and has a normal appearance (arrow 1). Glycogen is present in both the luminal and basal cells of the duct (arrow 2). (PAS-McManus procedure. × 136).

the salt-loaded subjects. Complete depletion of the granular content of the small dark cells was seen in the majority of cells. The cells of the duct remained glycogen-free.

B. Second Day

In salt-loaded subjects before sweating the sweat glands appeared almost entirely normal. The slight changes produced by the first episode of sweating were no longer present. Glycogen was present in normal amounts in the secretory coil and duct and much of the SPDR granules within the small dark cells had been replaced. In the sweat glands of salt-depleted subjects, however, moderate distortion of the secretory coil was still present due mainly to atrophy of the large pale cells. Glycogen was present in the secretory coil as well as the basal and luminal cells of the duct. There was little to no replacement of the SPDR granular content of the small dark cells which had been depleted by the first episode of sweating.

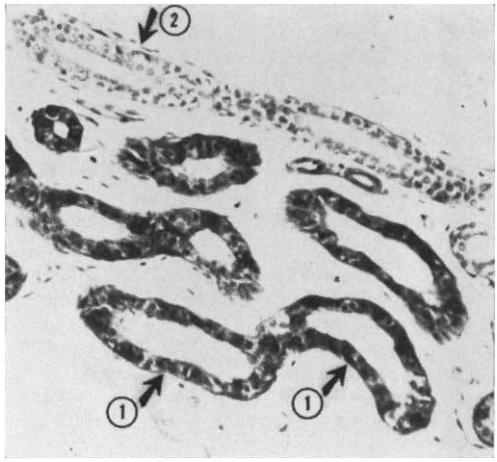

FIG. 2. First day. Salt-depleted subject before sweating. The secretory coil is rich in glycogen but the cells are atrophic (arrow 1). Both the luminal and basal cells of the duct are glycogen-free (arrow 2). (PAS-McManus procedure. × 80).

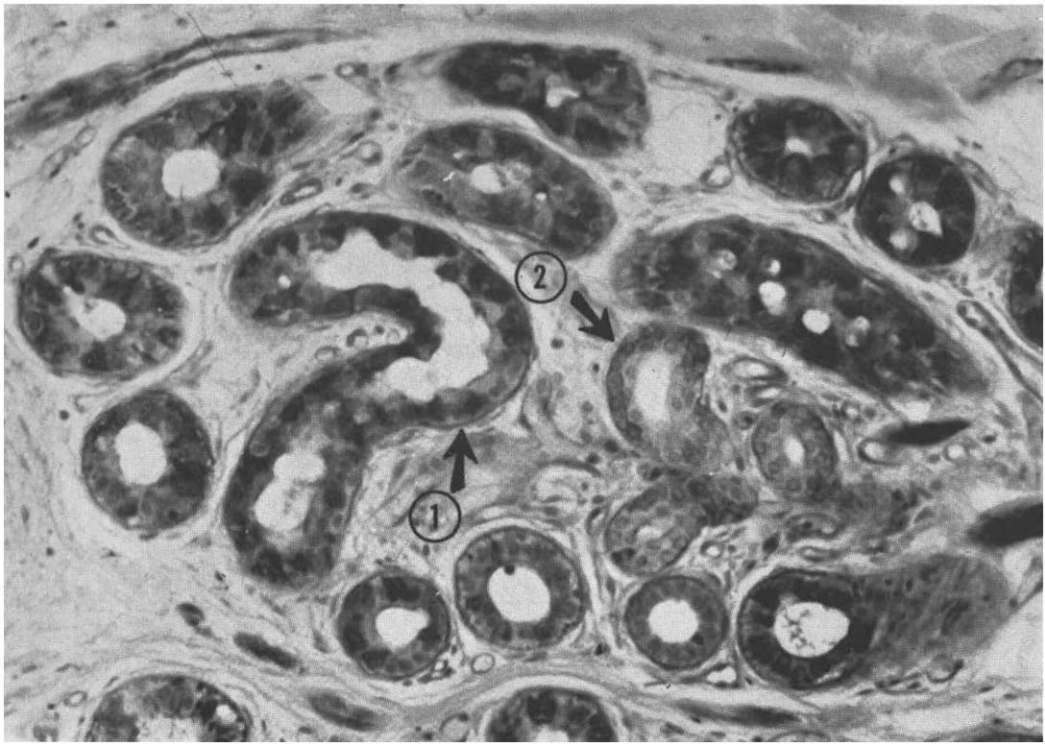

FIG. 3. First day. Salt-loaded subject after sweating. The secretory coil shows some atrophy of the large pale cells and depletion of glycogen (arrow 1). The duct retains its pre-sweating content of glycogen (arrow 2). (PAS-McManus procedure. × 136).

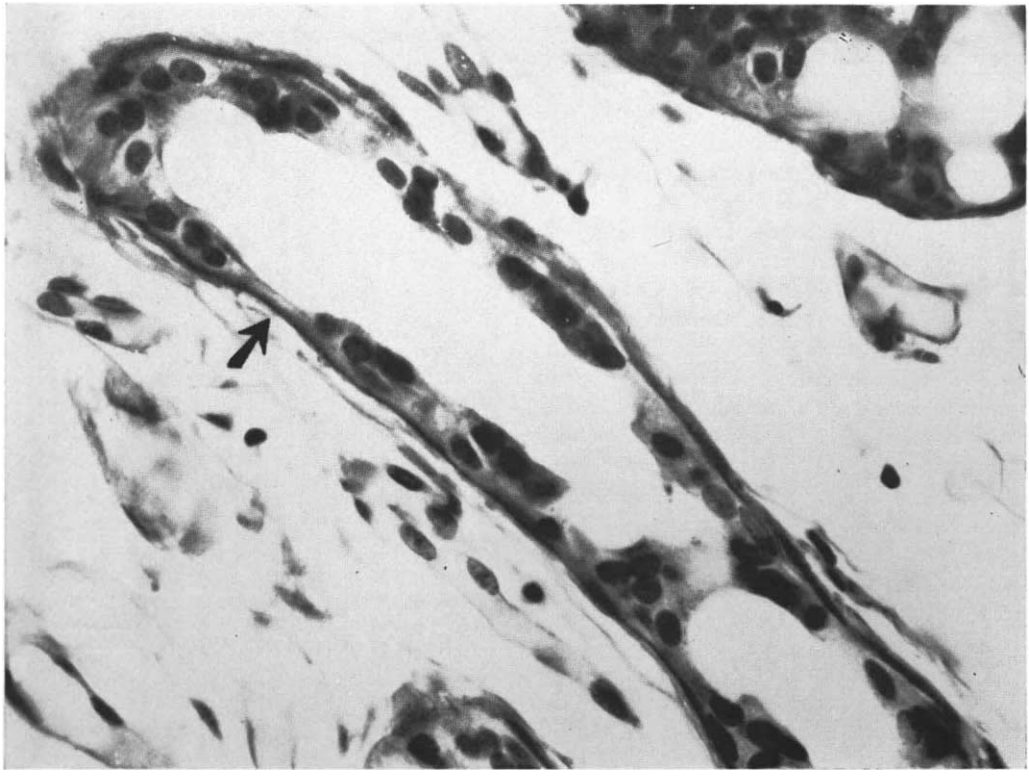

FIG. 4. First day. Salt-depleted subject after sweating. Marked atrophy of the secretory coil is present (arrow). (PAS-McManus procedure controlled with diastase. × 340).

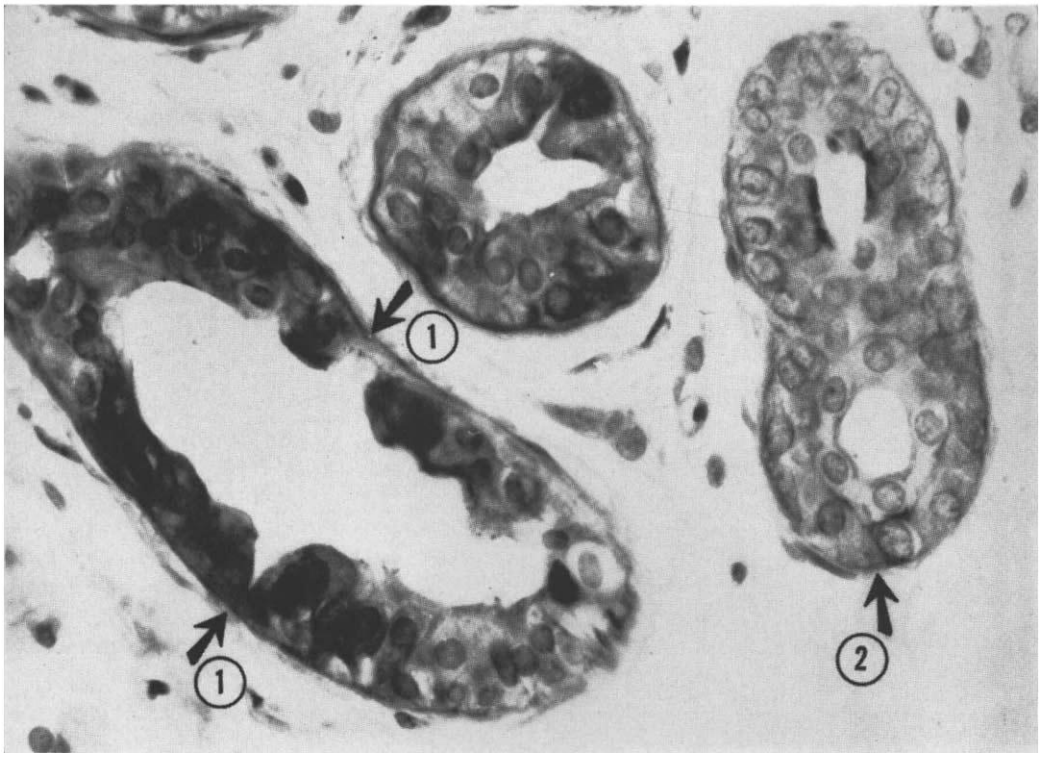

FIG. 5. Second day. Salt-loaded subject after sweating. The secretory coil shows no depletion of glycogen. A few large pale cells are atrophic (arrow 1). The duct retains its pre-sweating concentration of glycogen (arrow 2). (PAS-McManus procedure. × 340).

After sweating the secretory coil of the salt-loaded subjects showed minimal atrophy of the large pale cells. Glycogen was still present in pre-sweating amounts in both the coil and duct (Fig. 5). The SPDR granules of the small dark cells were slightly reduced in amount when compared to the pre-sweating specimens. The secretory coils of the salt-depleted subjects showed more marked distortion and vacuolization than after the first episode of sweating. Most of this change was due to decrease in size of the large pale cells although these cells still retained about two-thirds of their pre-sweating concentration of glycogen. Several of the large pale cells contained multiple nuclei apparently from fusion of adjacent cells (Fig. 6). Most of the small dark cells contained no SPDR granules. Both the luminal and basal cells of the duct were entirely depleted of their glycogen.

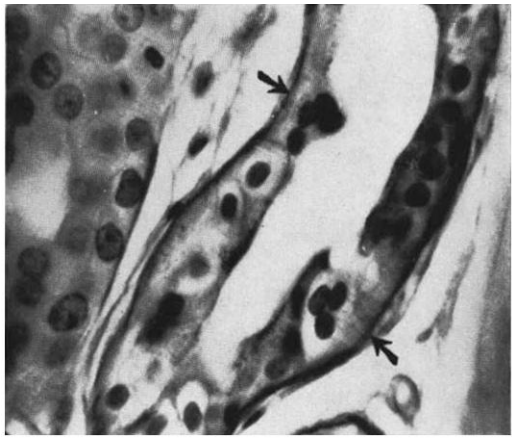

FIG. 6. Second day. Salt-depleted subject after sweating. Several multi-nucleated large pale cells are present (arrows). (PAS-McManus procedure controlled with diastase. × 320).

C. Third Day

Before sweating, the glands of the salt-loaded subjects appeared normal. Normal amounts of glycogen were present in both the secretory coil and duct and the majority of small dark cells contained their pre-sweating concentration of SPDR granules. In the salt-depleted subjects consider-

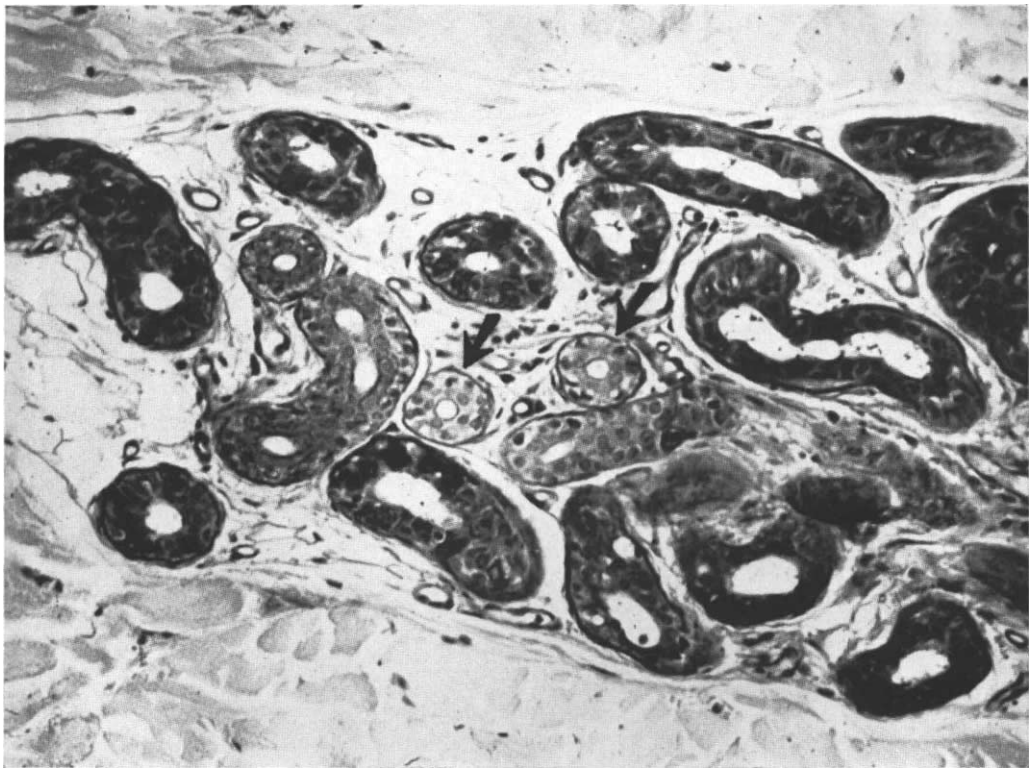

FIG. 7. Third day. Salt-depleted subject before sweating. No glycogen is present in either the basal or luminal cells of the duct (arrows). (PAS-McManus procedure. × 136).

able distortion of the secretory coil was again noted due to changes in the large pale cells. These cells, however, contained normal amounts of glycogen. The content of SPDR granules within the small dark cells had increased slightly. Glycogen was completely absent from both the luminal and basal cells of the duct (Fig. 7).

After sweating in the salt-loaded subjects, the secretory coil and duct showed virtually no change when compared to the pre-sweating specimens. A few large pale cells, however, showed a slight reduction in size. Glycogen was not depleted from either the secretory coil or duct. In the sweat glands of salt-depleted subjects, on the other hand, atrophy and vacuolization were again marked after sweating. There was slight depletion of the glycogen content of the secretory coil. The duct of one subject contained small amounts of glycogen within the luminal cells of the duct although none was seen in this subject before sweating. The duct of the other two subjects contained no glycogen. In all salt-depleted subjects, however, marked vacuolization of many of the basal cells of the duct was observed (Fig. 8). These vacuoles were adjacent to the nucleus giving this structure a creseent-shaped configuration.

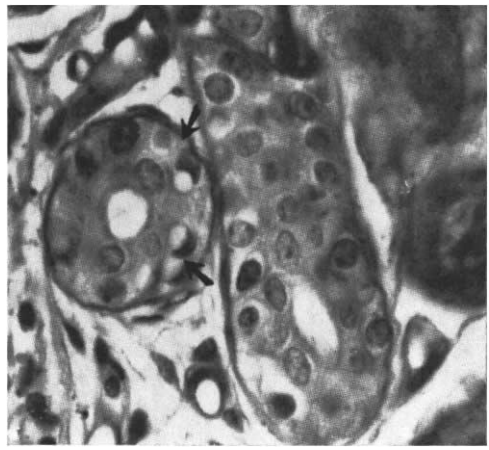

FIG. 8. Third day. Salt-depleted subject after sweating. Vacuoles are present adjacent to the nucleus in several basal cells of the duct (arrows). (PAS-McManus procedure. × 320).

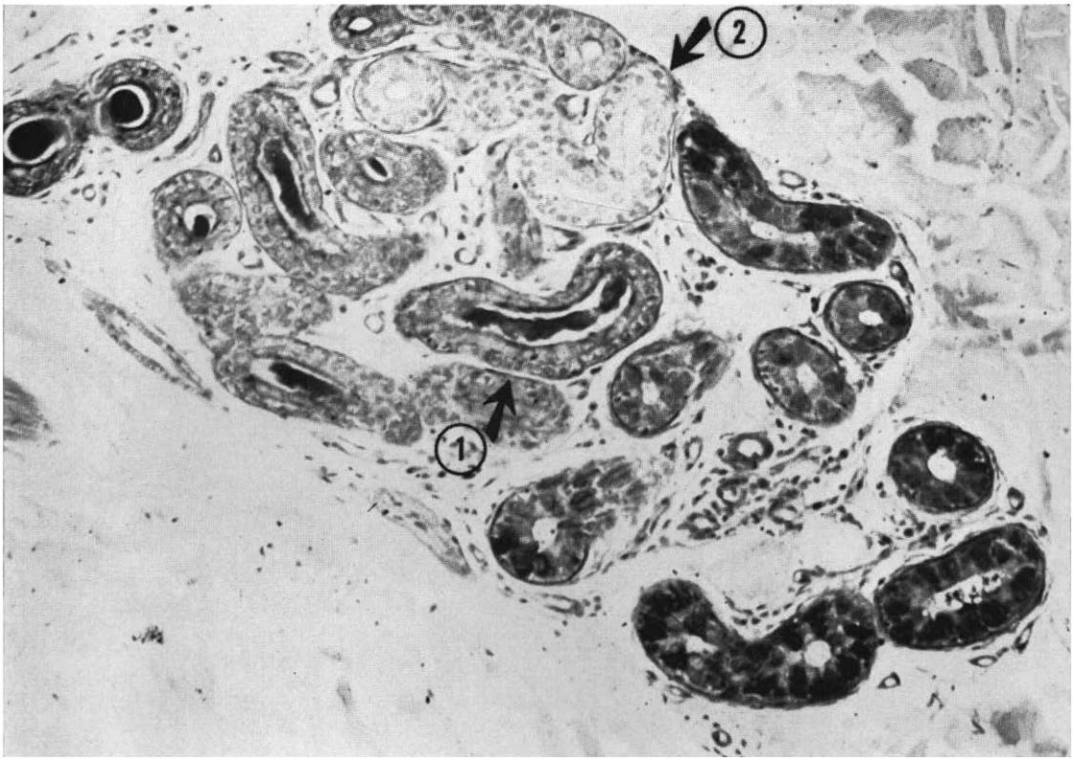

FIG. 9. Fourth day. Salt-depleted subject before sweating. Glycogen is present in some segments of the duct (arrow 1) but not in others (arrow 2). (PAS-McManus procedure. × 109).

D. Fourth Day

Before sweating both the secretory coil and duct of the salt-loaded subjects were entirely normal. In the salt-depleted subjects atrophy of the large pale cells was still present. Normal amounts of glycogen were present in the secretory coil but only in segments of the duct (Fig. 9). The amount of granular material in the small dark cells was small and had not increased. Many of the basal cells of the duct were still vacuolated. The most striking finding, however, was the many mitotic figures present in the basal cells of the duct (Fig. 10).

After sweating the secretory coil and duct of the salt-loaded subjects were essentially unchanged when compared with their pre-sweating appearance. In the salt-depleted subjects the changes in the secretory coil were more severe than had been previously seen and consisted of further atrophy and vacuolization of the secretory coil. There was a slight reduction in the glycogen content of the secretory coil but the duct was again completely depleted of its glycogen (Fig. 11). The SPDR content of the small dark cells was unchanged when compared with the pre-

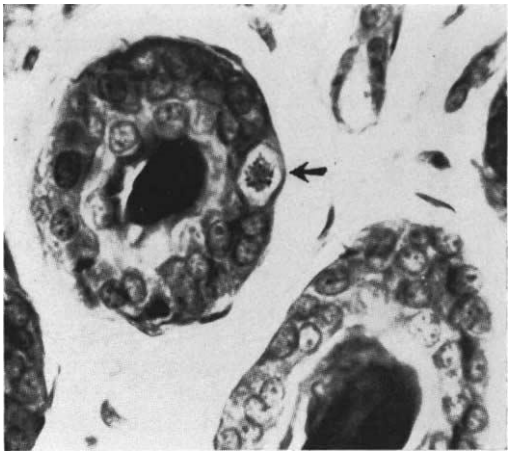

FIG. 10. Fourth day. Salt-depleted subject after sweating. Mitosis is occurring in a basal cell of the duct (arrow). (PAS-McManus procedure. × 256).

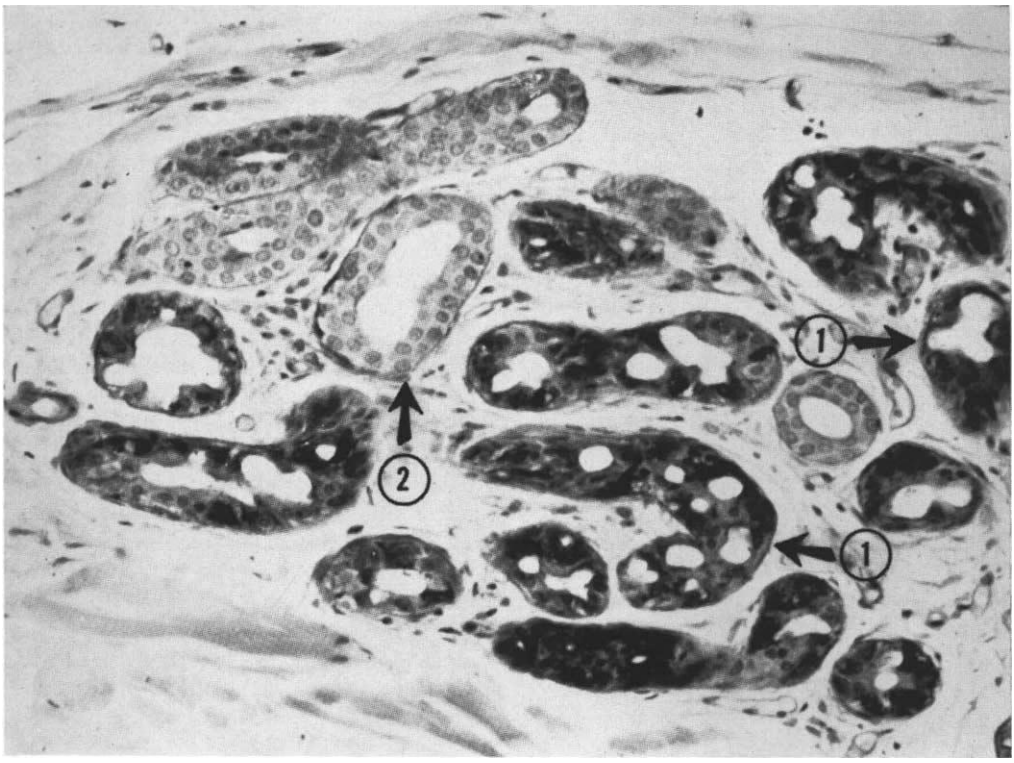

FIG. 11. Fourth day. Salt-depleted subject after sweating. The secretory coil has retained its pre-sweating concentration of glycogen and shows many areas of vacuolization and atrophy (arrow 1). The duct contains no glycogen (arrow 2). (PAS-McManus procedure. × 136).

sweating specimens. Many of the basal cells of the duct were again vacuolated.

E. Fifth Day

Before sweating the eccrine sweat gland of the salt-loaded subjects appeared entirely normal. In the salt-depleted subjects glycogen in the secretory coil had returned to its pre-sweating concentration. The large pale cells were still atrophic and many contained multiple nuclei. The small dark cells had regained their original concentration of SPDR granules. Glycogen was also present in moderate amounts in both the luminal and basal cells of the duct. A few vacuolated ductal basal cells were observed as well as several mitotic figures in these cells.

After sweating the secretory coil and duct of the salt-loaded subjects showed no change. In the salt-depleted subjects there was again slight reduction in the glycogen content of the secretory coil. Moderate atrophy and vacuolization of the large pale cells was present but not to such a severe degree as that which occurred after the fourth day of sweating. There was no depletion of SPDR granules from the small dark cells of the secretory coil. Both the basal and luminal cells of the duct were completely depleted of their glycogen content. A few vacuolated ductal basal cells were seen as well as a few mitotic figures in these cells.

DISCUSSION

It is apparent that the cytologic effects of profuse sweating on the human eccrine sweat gland are in part dependent on salt intake. In subjects who are salt-loaded for several days prior to sweating and who are kept salt-loaded despite sodium losses in both urine and sweat only minimal cytologic changes occur in the sweat gland and only during the first few episodes of sweating. These changes for the most part are confined to the large pale cells of the secretory coil and consist of slight to moderate reduction in the size of these cells. In subjects who are salt-

depleted before sweating and are kept salt-depleted during the daily episodes of sweating more marked cytologic changes in the sweat glands were produced. Even before sweating had occurred atrophy of the large pale cells of the secretory coil was apparent, the SPDR granular content of the small dark cells was reduced and no glycogen was present in the cells of the duct. With each day of sweating more severe changes occurred in the secretory coil consisting mainly of atrophy of the large pale cells and the formation of multinucleated large pale cells which were not seen in the salt-loaded subjects. Furthermore, sweating produced depletion of glycogen from the secretory coil on each day of sweating in the salt-depleted subjects although this was most prominent on the first day. It is of interest to note that in the salt-loaded subjects some glycogen loss occurred also on the first day but could not be observed after the subsequent episodes of sweating. Glycogen reappeared in the duct of salt-depleted subjects prior to sweating from the second day on but was always depleted by sweating in contrast to the salt-loaded subjects in which on no day was there complete depletion of ductal glycogen. The most striking change in the duct, however, was the appearance of vacuolization and mitotic figures in the basal cells after the third episode of sweating in the salt-depleted subjects. These changes were not observed in the salt-loaded subjects.

In a previous study (3) in which the effects of repeated episodes of profuse sweating were reported it was attempted to keep the experimental subjects neither salt-depleted nor salt-loaded. In this study 1.8 gms. of NaCl during each hour of sweating in addition to a regular diet containing approximately 8 gms. of salt were given daily providing a salt intake of approximately 19 gms. daily. It was thought that this level of salt intake would be adequate to maintain sodium balance. On the basis of subsequent studies (4) on the excretion of sodium by the sweat gland this assumption proved to be incorrect in that a salt intake of less than 20 gms. daily will result in a negative sodium balance in a profusely sweating subject. The morphologic effects on the sweat gland of profuse sweating in subjects in the process of salt-depletion can thus be compared with the results of the present study. In the former case the changes seen in the sweat glands were in many respects intermediate between the two extremes of the current study although the changes seen in the secretory coil of the salt-depleting studies were frequently more severe than those seen in the salt-depleted subjects. Severe changes in the duct, however, did not occur. With regard to glycogen depletion of both coil and duct as a result of sweating the subjects in the process of salt depletion closely resembled the salt-loaded subjects of the present study in that after the first day of sweating glycogen was not lost from either the coil of duct despite six hours of profuse sweating. It is thus apparent that the major effect of sodium depletion on the sweat gland involves the secretory coil but with more severe restriction of sodium intake ductal changes are produced as well.

The functional significance of these anatomic changes will not be entirely clear until correlative studies can be performed. These are in progress. It seems apparent, however, that the process of acclimatization to heat involves cytologic changes within the sweat gland. In a recent study (3) it was suggested that acclimatization may occur independent of adrenal cortical hyperactivity. Conn *et al* (6), however, have shown that the administration of desoxycorticosterone acetate (DOCA) to subjects for several days prior to sweating will result in a lowered excretion of sodium by the sweat gland, a process similar to, if not identical with, that occurring in natural acclimatization. In the present study the finding of atrophy of the large, pale cells of the secretory coil as well as lack of glycogen in the duct prior to sweating suggests adrenal factors in acclimatization since a salt-free diet for a week which results in increased adrenal cortical activity leads to cytologic changes within the sweat gland even before sweating has occurred.

SUMMARY

The effects of repeated episodes of profuse sweating on the human eccrine sweat gland differ markedly in salt-depleted and salt-loaded subjects. Salt-depletion *per se* results in changes in both the secretory coil and duct even before the first episode of sweating. The possible relationships of these findings to the process of acclimatization has been discussed.

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DISCUSSION

DR. FARRINGTON DANIELS, JR. (Portland, Oregon): This is another contribution of great importance in the field of the physiology of sweating. As you will remember, perhaps 15 years ago, we were under the influence of what might be called a con game in which the adrenal gland was all and the sweat gland was merely its slave in the periphery. It is a lesson I think for physiologists that they should study the organ of response as well as the magic gland on the inside to which they usually attribute all these changes.

I did have one question. Did you state that the salt-depleted subjects had changes in their sweat glands before the heat stress? I suppose the amount of pre-stress sweating would be a function of the climate in which they live. If you can change a sweat gland without sweating just on the basis of salt limitation, this is an extremely interesting change.

DR. DONALD C. ABELE (in closing): Dr. Daniels, yes, it is correct, that after a week of salt depletion there are present the early changes seen prior to any sweating stress and this may be some evidence that adrenal stimulation may play some role in these changes, if a week of salt depletion is enough to cause adrenal stimulation.