THE SALT EXCRETION OF MILIARIA SUBJECTS*

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As far as possible, subjects of comparable age and physique were selected. Those of groups A and B had worked for a similar number of years in the same or similar mines, doing identical work. The areas in which miliaria had occurred usually recorded temperatures of 90 - 105°F. (dry bulb) and 80 - 95°F. (wet bulb), and rock-face temperatures of 120°F or more were common. Other factors in their normal working conditions, such as ventilation and physical exertion, might vary considerably from day to day or hour to hour. Table I shows the principal data applicable to the subjects.

TABLE I. PHYSICAL DATA OF THE EXPERIMENTAL GROUPS

<table>
<thead>
<tr>
<th>Group</th>
<th>Particulars</th>
<th>No.</th>
<th>Mean age</th>
<th>Mean weight in lb.</th>
<th>Years of service underground</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Miliaria subjects</td>
<td>10</td>
<td>39</td>
<td>176</td>
<td>12.2</td>
</tr>
<tr>
<td>B</td>
<td>Control miners</td>
<td>6</td>
<td>34</td>
<td>175.5</td>
<td>14.7</td>
</tr>
<tr>
<td>C</td>
<td>Control non-miners</td>
<td>6</td>
<td>33</td>
<td>168.3</td>
<td>—</td>
</tr>
</tbody>
</table>

The dietary salt intake of these groups was unknown. All the miners (groups A and B) were married men and ate the food prepared by their wives; the majority in both groups denied adding extra salt at table and one may assume that their intake would depend on their wives' taste and would therefore be comparable in the two groups. Although salt tablets are provided in the mines, none of the subjects in either group were in the habit of taking these while at work.

Conditions of the Experiment

The men were exposed in groups of two in the climatic chamber to a moderate degree of heat and work stress. These comprised 5 hours of intermittent work and rest in an air temperature of 93°F. and a wet-bulb temperature of 90°F. Air movement was 100 ft./min. The surrounding surfaces were at air temperature. The men worked for half of every hour and rested for the remaining part of the hour. Work comprised stepping on and off a stool 1 foot in height at a rate of 6 times per minute. The average rate of oxygen consumption (i.e. rest plus work) for men of this weight is 0.5 litres/min.

At the end of each hour the interscapular area was washed with distilled water, and fresh sweat was then collected in a chemically clean test tube closed with a rubber stopper. Five such hourly collections were made. The total urine passed during and immediately after the experiment was likewise collected in a stoppered container.

The following data were recorded hourly during the experiment: heart rate, oral temperature, skin temperature, weight, water intake in ml., urine passed (if any) in ml., calculated sweat rate, and calculated state of dehydration from initial weight.

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TABLE II. MEANS AND STANDARD DEVIATIONS OF DATA OBTAINED

<table>
<thead>
<tr>
<th>Group</th>
<th>Na in sweat (mEq./l.)</th>
<th>Cl in sweat (mEq./l.)</th>
<th>Na in urine (mEq./l.)</th>
<th>Cl loss in urine (G)</th>
<th>Estimated Na loss in sweat (G)</th>
<th>Na loss in sweat (G)</th>
<th>Mean total Na (G)</th>
<th>State of dehydration at 5 hours (G)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>71·2</td>
<td>81·9</td>
<td>98·1</td>
<td>94·6</td>
<td>93·3</td>
<td>130</td>
<td>176·0 1·16</td>
<td>3·93 0·58 4·51 1904</td>
</tr>
<tr>
<td>SD</td>
<td>27·5</td>
<td>27·4</td>
<td>24·5</td>
<td>23·2</td>
<td>21·3</td>
<td>23·07</td>
<td>19·16</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>40·2</td>
<td>51·5</td>
<td>71·5</td>
<td>76·5</td>
<td>72·2</td>
<td>93·7</td>
<td>145·2 0·71</td>
<td>2·33 0·28 2·61 1754</td>
</tr>
<tr>
<td>SD</td>
<td>10·8</td>
<td>16·7</td>
<td>21·3</td>
<td>25·8</td>
<td>29·3</td>
<td>34·27</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>41·8</td>
<td>56·9</td>
<td>72·8</td>
<td>70·1</td>
<td>82·2</td>
<td>113·5</td>
<td>175·0 0·98</td>
<td>1·49 0·39 1·88 1009</td>
</tr>
<tr>
<td>SD</td>
<td>18·8</td>
<td>26·0</td>
<td>33·2</td>
<td>28·6</td>
<td>27·2</td>
<td>31·97</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

A = Miliaria (miners). B = Controls (miners). C = Controls (non-miners).

SD = Standard deviation + -.

No appreciable differences between groups were noted as regards temperature or weight change.

Sodium and Chloride Concentrations in Sweat

The ratio of sodium to chloride approached unity in all sweat samples, the former invariably giving a slightly greater value; this incidentally provided a check on the accuracy of the laboratory techniques. Fig. 1 represents graphically the mean hourly concentrations of sodium for the 3 groups; Table II gives the mean values and standard deviations for the same; and comparisons between groups are shown in Table III, using Student's 't' test of significance for small samples.

It will be observed that differences between group A on the one hand, and groups B and C on the other, are significant after 1 hour and that, when groups B and C are combined as a single control group, there is a highly significant difference after 1 hour and a difference of lower significance after 2, 3 and 4 hours. A striking fact was that only one subject of group A showed values below the means of those in the control groups. This was the subject previously mentioned, who had recently suffered from a single episode of 2 months' miliaria. Conversely, no member of the control groups showed a 1-hour salt concentration as high as the mean of group A.

An estimate of the total amount of sodium lost in the sweat was made by calculating the volume of sweat produced from the weight loss, water intake and urine output; the mean sodium concentration in the sweat over 5 hours, converted from mEq./l. into G. per litre, then allowed an estimate to be made. The results so obtained show that the miliaria subjects not only produced a higher concentration of sodium in their sweat, but also lost a significantly larger quantity.

<table>
<thead>
<tr>
<th>Groups compared</th>
<th>A : B</th>
<th>A : C</th>
<th>B : C</th>
<th>A : B + C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na (sweat)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 hour</td>
<td>-05</td>
<td>-05</td>
<td>NS</td>
<td>-01</td>
</tr>
<tr>
<td>2 hours</td>
<td>-05</td>
<td>0·1</td>
<td>NS</td>
<td>-05</td>
</tr>
<tr>
<td>3 hours</td>
<td>0·05</td>
<td>0·05</td>
<td>NS</td>
<td>-05</td>
</tr>
<tr>
<td>4 hours</td>
<td>NS</td>
<td>0·1</td>
<td>NS</td>
<td>-05</td>
</tr>
<tr>
<td>5 hours</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Cl (sweat)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 hour</td>
<td>-05</td>
<td>-05</td>
<td>NS</td>
<td>-01</td>
</tr>
<tr>
<td>2 hours</td>
<td>-05</td>
<td>0·1</td>
<td>NS</td>
<td>-05</td>
</tr>
<tr>
<td>3 hours</td>
<td>0·05</td>
<td>0·05</td>
<td>NS</td>
<td>-05</td>
</tr>
<tr>
<td>4 hours</td>
<td>NS</td>
<td>NS</td>
<td>0·1</td>
<td>NS</td>
</tr>
<tr>
<td>5 hours</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Estimated Na loss in sweat</td>
<td>NS</td>
<td>-01</td>
<td>NS</td>
<td>-02</td>
</tr>
<tr>
<td>Na concentration in urine</td>
<td>-05</td>
<td>NS</td>
<td>NS</td>
<td>-05</td>
</tr>
<tr>
<td>Na loss in urine</td>
<td>-05</td>
<td>NS</td>
<td>NS</td>
<td>0·1</td>
</tr>
<tr>
<td>5-hour state of dehydration</td>
<td>NS</td>
<td>-01</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Heart rate</td>
<td>-01</td>
<td>NS</td>
<td>NS</td>
<td>-01</td>
</tr>
</tbody>
</table>

Note: The above results are obtained by the 't' test. Levels of -05 to -01 are regarded as 'significant' to 'highly significant'. NS and 0·1 are 'not significant'.

Urine

The miliaria group showed a significantly higher figure for sodium concentration than group B, or groups B and
C combined (Fig. 1). The average total loss of sodium in the urine of group A is also significantly greater than that in group B; this finding, to be discussed later, is of great importance. The urinary chlorides show far less difference between groups.

State of Dehydration

The hourly sweat rates (Table IV) of the miliaria subjects were greater than those of the controls, although not significantly so (at the 95% level). All groups drank water ad libitum and at the end of the 5th hour the miliaria men were dehydrated to the extent of 1,904 G., compared to 1,754 and 1,009 G. of the control groups (Table II); the differences were not significant at the 95% level.

Heat Regulation

The initial weights of the groups were similar. The mean rate of heat production of the groups would therefore be similar also. Sweat rates, replacement of fluid losses, and temperatures (Table IV) showed no significant differences. The two significant differences were in the higher heart rates of the miliaria group (A) and their higher NaCl concentration in sweat (Table II).

DISCUSSION

1. Factors affecting Sodium and Chloride Concentration in Sweat

The observed differences between miliaria subjects and controls appear to support the hypothesis which this experiment was designed to test. Nevertheless, certain possible sources of error must be considered; they comprise the following:

Salt Intake

As stated above, it is unlikely that group A had a higher intake of salt than the control groups. It should be remembered, too, that several of these chronic miliaria subjects had not been exposed to conditions of heat and humidity for many months before the experiment and would consequently have little cause to consume more than the average intake of salt. It does not seem, therefore, that the high concentration of salt in the sweat in group A could be attributed to an excessive salt intake, as reported by several writers.7-12 It is also to be mentioned that under certain conditions the chloride concentration of human sweat does not rise with addition of salt to the drinking water,18 or may actually fall.14 A full list of references to work on the various factors that may influence the salt concentration in the sweat may be found in Robinson and Robinson;11 the present-day view is expressed by Leithead,15 who states: 'It is fairly clear from the work of several observers that changes in sweat chloride are related far more to the intake of salt than to acclimatization to heat'. We feel that this factor is not operative in our experiment.

Normal Values

There seems to be no unanimity on what constitutes the normal range of values for sodium and chloride concentrations in sweat. Robinson and Robinson11 review the literature and mention values of 5 - 148 mEq./l. in supposedly normal subjects in hot environments; they add that average values of sweat chlorides ranging from 18 to 97 have been reported in at least 86 studies. Similar wide variations are summarized by Altman.16 Some of the discrepancies are no doubt due to the fact that scarcely any two sets of experiments have been conducted under identical conditions; environmental temperature and humidity, sweat rate, state of work or rest, degree of acclimatization, and methods of sweat production, show wide variations. Thus the collection of sweat may have been performed as in our cases, or by encasing the whole or a part of the body in an impermeable bag, or by micropipette from the palmar sweat pores,17 or from different areas of the body surface.18

In other investigations19, 20 sweat produced by pilocarpine iontophoresis or mecholyl injection has been used to draw up a range of normal and abnormal values. As an example of the possible fallacies inherent in this diversity of experimental method, we refer to Weiner and Van Heyningen's statement21 that sweat collected in an arm bag does not give the same results as total body sweat. Robinson and Robinson11 have stated that values of 80 mEq./l. or more reported in the literature are most frequently found in samples collected from local skin areas enclosed in impermeable barriers. Where the skin is aerated and sweat residues efficiently washed off, sweat-chloride values rarely exceeded 60 mEq./l., even in unacclimatized men. The figures reported by Conn and co-workers22, 23 (mean of 42 and range of 15 - 60 mEq./l.) were produced under his standard conditions of sweating and agree closely with our one-hour results for controls.

Although it is impossible to set precise limits to the normal range of concentration of sodium and chloride in sweat, we may nevertheless regard significant differences between our miliaria and control groups as important, so long as we make our comparisons between these groups and do not try to equate them with all supposedly normal values determined elsewhere. Our figures show that the greatest relative differences between groups are found at one hour and suggest that this measurement would in future suffice for similar investigations.
Effect of Age

Siegenthaler et al. found that the concentration of sodium in sweat increased with age, averaging 32.6 mEq./L between 20 and 25 years and 54.3 mEq./L in subjects over 50. The scatter in each series (10-80 and 15-116), as well as the fact that use was made of pilocarpine iontophoresis, do not permit us to take these figures as standard values; they do however suggest that age might be a factor in salt concentration of sweat, however produced. In our own small series the age distribution between groups is reasonably close, and in none of the groups was there an observable relation between age and concentration of electrolytes.

State of Acclimatization

Judged on the usual criteria of acclimatization to heat—heart rate, temperature, sweat rate, and NaCl concentration in sweat—our subjects present an equivocal picture. Sweat rates and temperatures were not significantly different in the three groups. In the miliaria subjects the heart rates and NaCl concentration in the sweat and urine were raised. On these two criteria of acclimatization the miliaria group (A) could be regarded as relatively less well acclimatized (some of them had, of course, also been away from underground work for some months because of their medical condition). It must be stated that the lack of difference between the two control groups, one that had worked underground, the other that had not, was surprising. The degree of stress employed was not very severe, and this fact might have failed to differentiate between the groups in their state of acclimatization. A difference between acclimatized and unacclimatized men in heart rates, temperatures, and NaCl in sweat, is now well documented.

It will, however, be observed that in our experiment there was no significant difference in the excretion of salt in the sweat of acclimatized and non-acclimatized controls (groups B and C); this agrees with Leithead's observation.

Individual Variations

While there is no known inherent racial difference, several observers have stressed an individual factor in determining the concentration of electrolytes in sweat; according to Johnson et al. such individual idiosyncrasy is the central factor.

Sodium and Chloride Concentrations in the Sweat of Miliaria Subjects

The crucial question posed by our results is that of cause or effect. Are the high sodium and chloride concentrations in group A an aetiologic factor in, or are they the result of, miliaria? The latter hypothesis has been assumed by a few previous workers who have measured chloride concentrations in miliaria subjects. Thus Ladell and co-workers, in their classical work on disorders caused by heat postulated that exhaustion of the sweat glands, one that had worked underground, the other that had not, was surprising. The degree of stress employed was not very severe, and this fact might have failed to differentiate between the groups in their state of acclimatization. A difference between acclimatized and unacclimatized men in heart rates, temperatures, and NaCl in sweat, is now well documented. It will, however, be observed that in our experiment there was no significant difference in the excretion of salt in the sweat of acclimatized and non-acclimatized controls (groups B and C); this agrees with Leithead's observation.

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to their predisposition to miliaria. A fact we feel to be important is that sufferers from fibrocystic pancreatic disease show low sodium values in the urine.

Acquired

The only other known cause of high salt excretion in both sweat and urine is adrenal insufficiency. Chronic heat stress has been mentioned as producing the general adaptation syndrome of Selye, and particularly adrenal cortical hypofunction in the stage of exhaustion. If Selye's version is correct—that the so-called collagen diseases may be evoked by stress—it is interesting to recall that generalized systemic sclerosis has an extremely high incidence, and that discoid lupus erythematosus frequently shows a florid pattern, in gold miners.

The significantly higher heart rates of the miliaria cases could also be construed as a sign of an excessive cardiovascular reaction to stress. However, it is impossible to rule out completely the possibility that the higher heart rates and higher NaCl concentration in sweat of the miliaria subjects are due to a loss of acclimatization.

Horne and Mole were apparently the first to suggest that miliaria might be a manifestation of some general metabolic disturbance; Sargent and Slutsky, in a brilliant appraisal of all the facts available to them, then suggested that the seat of this metabolic disturbance was primarily in the pituitary-adrenal system.

Though the present paper is concerned with experimental rather than clinical findings, a single case history is so suggestive as to merit quotation:

A White miner, aged 40, and with 21 years' underground service, was brought to this hospital severely gassed with Derm., was unable to work underground without recurring episodes of miliaria. He had never previously suffered from miliaria.

Though Sargent and Slutsky concluded that neuroendocrine factors were the cause of miliaria, they stated that sweat-gland fatigue was the keystone of this hypothesis. Our results suggest that, unless this is accompanied by renal tubular fatigue, the presence of simultaneous excess of salt in sweat and urine invalidates this hypothesis. We believe that adrenal cortical hypofunction—the word 'fatigue' might be applicable here—provides an adequate explanation of the observed phenomena. In agreement with Conn et al. we regard the electrolyte content of thermal sweat as an index of adrenal cortical function; no intrinsic disorder of the sweat glands needs to be postulated. Shuster has recently produced indirect evidence to confirm this conclusion, and has shown that aldosterone is responsible for the fall in sweat sodium on a low-sodium diet, and finally Conn has shown that symptoms of loss of aclimatization are associated with diminished production of aldosterone or the administration of an aldosterone antagonist.

We feel, therefore, that chronic miliaria may be the end-result of a train of circumstances initiated by a loss of aclimatization.

SUMMARY

Physiological responses to 5 hours of moderate work in a heat chamber were studied in 10 sufferers from chronic miliaria and 12 control subjects. Six of the latter were acclimatized men, working under the conditions in which miliaria had been contracted by the 10 former.

The miliaria group showed a significantly higher concentration, and produced a significantly greater quantity, of salt in both sweat and urine. There is no evidence of a higher salt intake in this group.

The results obtained after 1 hour showed the greatest differences, and this time is regarded as the optimum for testing.

The findings support the hypothesis that increased concentrations of salt in the sweat are an aetiological factor in miliaria.

The possible causes of increased salt excretion, persisting for years after leaving the miliaria-producing environment, are discussed.

The state of acclimatization may be a factor in accounting for the observed differences. A significantly higher heart rate in the miliaria cases may be construed as a stress reaction.

Similarly, chronic miliaria may be regarded as a manifestation of stress.

REFERENCES