J. Physiol. (1947) 106, 237–244 612.792.1:547.495.9

CREATININE LOSSES IN THE SWEAT DURING WORK IN HOT HUMID ENVIRONMENTS

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(*Received* 10 *May* 1946)

Except for the work of Talbert and his collaborators (Talbert, Silvers & Johnson, 1926; Talbert & Haugen, 1928), few attempts have been made to correlate the concentration of substances in the sweat with the concentration of the same substances in the plasma. When, therefore, a number of renal creatinine clearances were being done on subjects working in a hot humid environment, it was considered desirable to estimate creatinine not only in the plasma and in the urine but also in the sweat. Talbert, Silvers & Johnson (1926) found a direct relationship between the total non-protein nitrogen of blood and sweat. Was there the same direct relationship for the creatinine contents?

METHODS

Creatinine was determined in serial samples of sweat from two subjects after a dose of creatinine, and on other occasions from the same two subjects, and from two others without the administration of creatinine. Creatinine determinations were also done on saliva collected from the subjects during their exposure to heat, in order to compare the creatinine content of sweat with that of another secretion.

The subjects were all men, between the ages of 34 and 22, and fully acclimatized to work under the environmental conditions of the test. Each exposure was for 160 min. in an air-conditioned chamber maintained at a dry-bulb temperature of 100° F. and a wet-bulb temperature of 93° F. (relative humidity 77 %); the air movement was below 50 ft./min. The men were naked except for a bag completely enclosing one arm in which the sweat was collected.

The complete experimental routine was as follows:

6.00 a.m. Subject drank 1000 c.c. water.
7.30 a.m. Breakfast—not standardized.
8.00 a.m. Subject drank 500 c.c. of 5 % creatinine solution in water if its clearance was being estimated.
8.45 a.m. Blood sample taken.
9.00 a.m. Subject entered climatic chamber.
11.40 a.m. Subject left climatic chamber.
11.45 a.m. Blood sample taken.

The subjects were weighed to the nearest 5 g. immediately on entering the chamber, and their rectal temperatures and standing pulse rates were taken; these three measurements were repeated 10 min. later, the subjects having been sitting quietly meanwhile. The following routine was then carried out for 6 cycles of 25 min. each:

0– 5 min. Rest.	16–24 min. Rest.
5–15 min. Work.	24–25 min. Weigh.
15–16 min. Weigh.	

Sweat samples were taken after each weighing; standing pulse rates and rectal temperatures were taken before and after each bout of work. The work consisted of stepping on and off a stool 1 ft. high; for the first two cycles the rate of stepping was 24 times per min. (metabolic cost 250 kg.cal./hr.) and for the remaining cycles 12 times per min. (metabolic cost 150 kg.cal./hr.); in the fifth cycle, however, only 5 min. work was done, giving the subject an extra 5 min. rest without which he would often have been unable to continue for the sixth cycle; in some cases, when they were not allowed to drink, the subjects were unable to complete six cycles and left the chamber after 110 min. The mean metabolic rate for the full test was 120 kg.cal./hr. In all cases the subjects worked to exhaustion. The water and salt intake of the subjects while in the chamber varied in different tests, according to the other needs of the experiment, but within each experiment it was strictly controlled; in addition the chloride content of each sample of sweat was estimated and as the sweat rate was measured for each cycle it was therefore possible to calculate the exact salt and water balance of the subjects at any time during the exposure. Various conditions were imposed in different exposures, between the gross over-replacement of both salt and water losses and no intake of either.

Sweat was collected in impermeable bags which enclosed the whole of the arm from just below the axilla. The arms were washed first with soap and water, then with distilled water, until the washings were chloride free. The arms were then dried before the dry and chemically clean bags were put on. Once sweating was established samples could be obtained every 10 or 15 min. as required. The sweat collected in this way was only faintly cloudy after it had stood for some time; it was not possible to remove this residual cloudiness.

Blood was obtained by venepuncture, with a minimum of stasis. The samples were collected under medicinal liquid paraffin, with potassium oxalate as the anti-coagulant. Plasma was obtained by centrifuging the blood under paraffin wax.

In certain of the experiments saliva was collected by spitting into bottles; no saliva samples were taken immediately after drinking. All the saliva collected from one subject during one exposure was pooled to make a single sample, which was cleared by filtering through a hard paper. Thus, whereas for each exposure there were a number of samples of sweat, two for each cycle, there was only one sample of saliva.

Creatinine in the sweat and in the saliva was estimated directly; for plasma, the estimation was done on the filtrate after precipitating the protein with the Folin-Wu mixed reagents. The method of Peters & Van Slyke (1932) was used, but, instead of the standard recommended, a stronger one was used consisting of 3 c.c. of creatinine solution, 0·06 mg./c.c., with 17 c.c. of water. The comparisons were made in a photoelectric colorimeter, using monochromatic light, wavelength 500 Å. In all cases therefore only apparent creatinine was being measured. When the sample was not clear a correction for cloudiness was obtained by measuring the absorption of the sample with added reagents immediately on mixing and before the colour had time to develop. The accuracy of this estimation is considerably greater than that of visual colorimetry, being about ± 1 %.

RESULTS

The over-all physiological response was substantially the same whatever the salt and water intake; there were some slight quantitative differences which could be correlated with differences in the salt and water balances.

These differences will be discussed in a separate paper; but in all cases the general pattern was as shown in Fig. 1. The rectal temperature rose to about 102° F. in the first 70 min., there was then often a slight fall before a steady value was reached. The standing pulse rate immediately after work rose to about 160 beats/min., and there was only partial recovery during rest. The sweat rate rose rapidly and reached a maximum, in some cases of more than

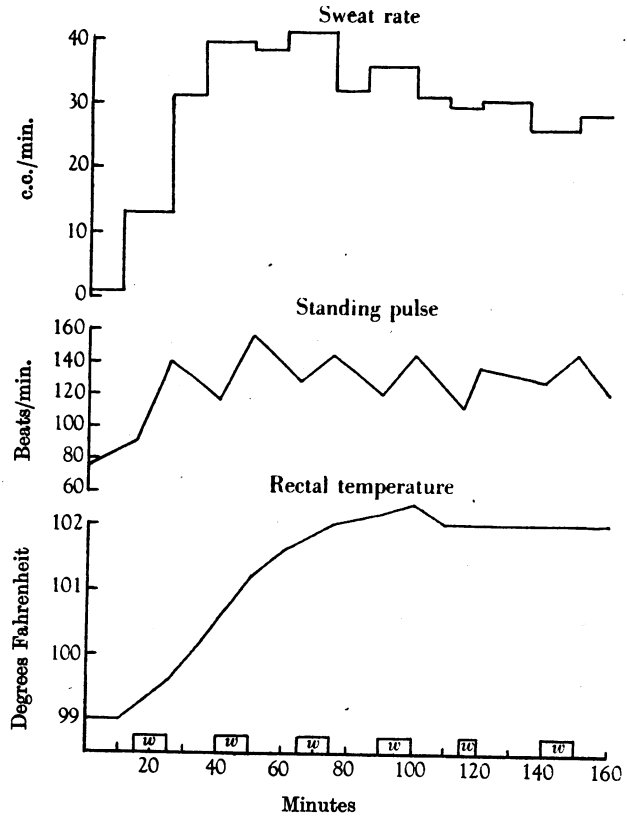

Fig. 1. Sweat rate, pulse rate (standing) and rectal temperature during exposure to heat. Actual results from experiments on subject B. (8 October 1945). Full water and salt replacement. Work periods represented by blocks marked *w*.

60 c.c./min., before the maximum rectal temperature was reached; it then usually showed a steady diminution for the rest of the exposure; this falling off of sweat rate during a long and severe exposure to heat has been described by others, including Robinson, Turrell & Gerking (1945).

In all cases the chloride concentration was relatively low at the beginning of each exposure and rose as the exposure continued; this has been described elsewhere (Ladell, 1945*a*). In all exposures the creatinine content of the initial sample of sweat was, on the other hand, high, irrespective of whether

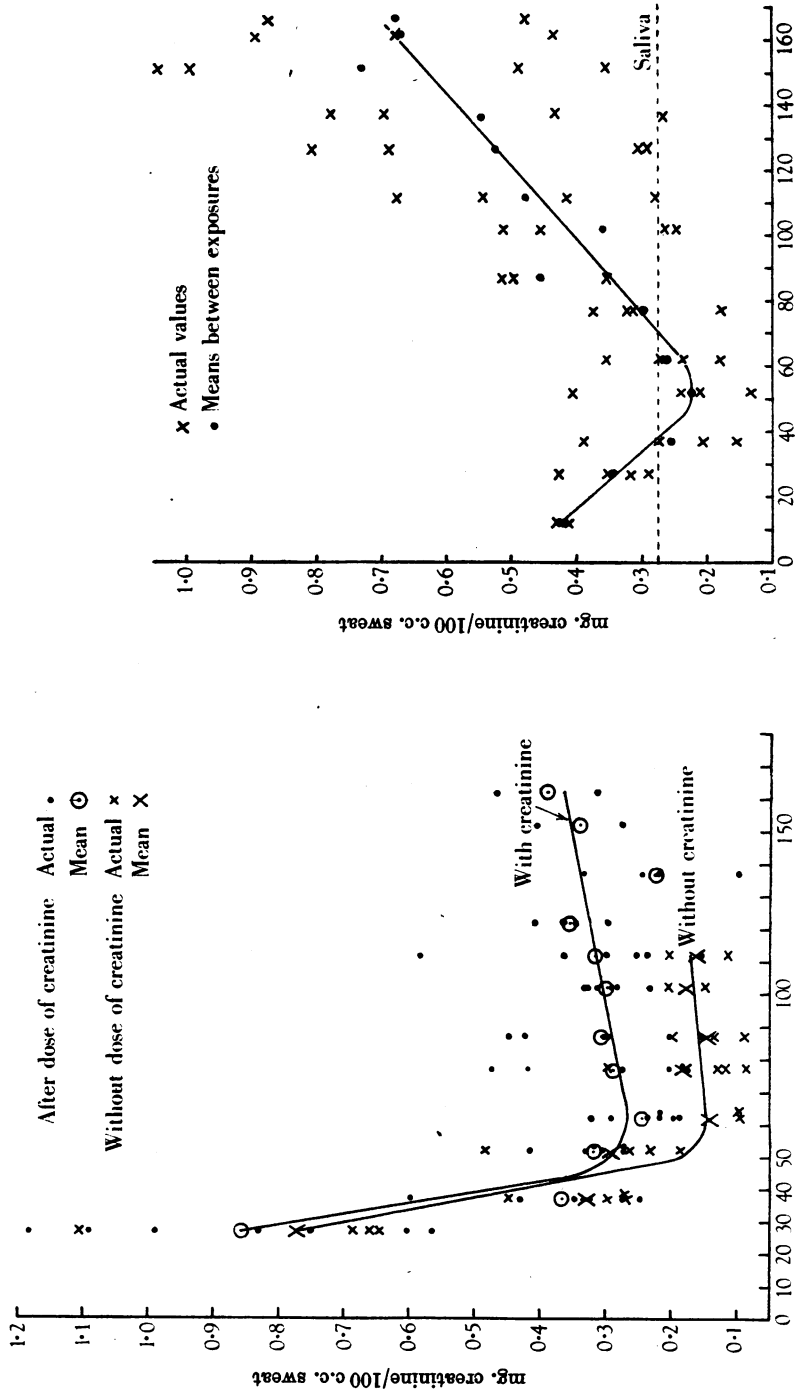

Fig. 2*a*.

Fig. 2*b*.

Fig. 2. Changes in creatinine concentration in the sweat during exposure to heat. (*a*) Subject G.: with and without a dose of creatinine before the test. (*b*) Subject L.: without creatinine. The dotted line indicates the concentration of creatinine in the saliva (mean of three observations).

the subject had had creatinine or not. High concentrations were sometimes found at the end as well as at the beginning; in the mid-period low values were usually found (see Fig. 2, *a*, *b*). In subjects G. and B. the concentration of creatinine in the early samples of sweat was more than 1·0 mg./100 c.c. In all subjects the concentration fell to 0·3 mg./100 c.c. or less when the sweat rate was greatest. Subject L., who reached a high maximum sweat rate soon after entering the chamber, had the lowest initial concentrations, but the lowest of all the series was found with B., whose sweat on one occasion contained no detectable creatinine.

The effect of a single dose of creatinine before the exposure was followed in subjects G. and B. Ignoring the first samples from each exposure, which were taken before sweating was fully established and in which, as already pointed out, the creatinine contents were uniformly high, the creatinine content of the sweat was 50 % higher after taking creatinine. The results are summarized, with some statistical details, in Table 1; this table also shows, for comparison, the mean values for the two subjects who did not have creatinine.

TABLE 1. Creatinine content of sweat with and without a dose of creatinine before exposure to heat. Values in mg./100 c.c.

	No creatinine			After creatinine			Comparison between means with and without creatinine		
	No. of			No. of					
Subject	Samples	Ex-posures	Mean	Samples	Ex-posures	Mean	Difference between means	Stand. error of diff. between means	Prob. of difference occurring by chance
G.	19	4	0·211	52	7	0·302	0·091	0·029	<0·003
B.	20	3	0·167	14	2	0·253	0·086	0·044	0·05
Results from G. and B. as a single series	39	7	0·189	66	9	0·291	0·102	0·024	0·003
P.	11	1	0·275	—	—	—	—	—	—
L.	49	4	0·439	—	—	—	—	—	—

Note. The first sample in each exposure is not included in the above figures.

Preliminary statistical analysis shows that not much weight can be given to this 50 % difference, since, although the difference is highly significant for subject G., and slightly less so for the results from G. and B. pooled and treated together, it is of doubtful significance for B.

By contrast, the effect of a dose of creatinine on the creatinine content of the saliva was clear. During each of a number of exposures a single sample of saliva was taken. The mean creatinine concentration in seven such samples of saliva from G. and B., when they had no creatinine, was 0·455 mg./100 c.c.; in another seven samples, after they had had creatinine, it was 1·379 mg./100 c.c., a three-fold increase. The standard error of the difference between the means was 0·236; thus the difference of 0·924 mg. is highly significant and may be accepted as due to the higher creatinine content of the blood. Neither P. nor L.

had creatinine; the creatinine content of P.'s saliva, one observation only, was 0·318 mg./100 c.c.; and the mean of three observations on saliva from L. was 0·276 mg./100 c.c. A comparison of these figures with the tables and with Fig. 2 (*b*), shows that, after taking creatinine, the creatinine content of the saliva is higher than that of the sweat, but that without creatinine it tends to be lower. In no case was a low salivary creatinine found when the blood creatinine was raised.

With one exception, the creatinine content of the blood was only measured on the subjects who had had creatinine. The mean of nine estimations on plasma from subjects 45 min. after taking 5 g. creatinine by mouth was 5·20 mg./100 c.c., and of eight estimations on samples obtained when they came out of the heat was 5·92 mg./100 c.c. Table 2, which gives the results in detail,

TABLE 2. The creatinine of plasma in subjects G. and B. after 5 g. creatinine by mouth, and in L. without creatinine

Subject	Plasma creatinine (mg./100 c.c.) Before entering chamber	After leaving chamber
G.	2·44	—
	5·88	8·32
	5·553	5·422
	6·550	4·908
	4·807	4·871
	4·315	4·633
	6·830	7·450
B.	8·29	5·01
	2·196	6·805
L.	—	0·809

shows that the effect of the exposure to the heat on the creatinine content of the plasma was variable. The normal blood creatinine is stated by Harrison (1944) to lie between 0·7 and 2·0 mg./100 c.c.; hence the 5 g. dose of creatinine had raised the concentration by at least three-fold, as it did that in the saliva.

It was thought that the high creatinine content of the sweat samples obtained at the beginning of each exposure might have been due to substances giving the Jaffe reaction being washed off the skin by the first sweat. Three tests were therefore done on subject G. to investigate this possibility; G. was chosen because he showed the highest initial concentrations. In these tests the subject put a bag on his arm but remained in the cold; several small quantities of warm distilled water were then successively introduced into the bag. This water was rubbed all over the arm through the bag, and after 25 min., when about 30 c.c. of water had been introduced (an amount comparable to the volume of sweat produced from an arm in the first 25 min. exposure to the heat) a sample was taken and its creatinine content estimated. In two of these tests the subject washed his arm thoroughly with tap water and then with distilled water before putting on the bag; in these the apparent creatinine

content was 0·242 mg. and 0·158 mg./100 c.c. respectively; in the third test the arm was not washed, but the creatinine content of the sample was 0·101 mg./100 c.c. As the creatinine content of the initial sweat was much greater than this on all occasions, the presence of substances on the skin surface giving the Jaffe reaction cannot be the cause of the high concentrations; on the other hand, it is not possible to exclude the accumulation of such substances in the lumen of the sweat glands when they are at rest.

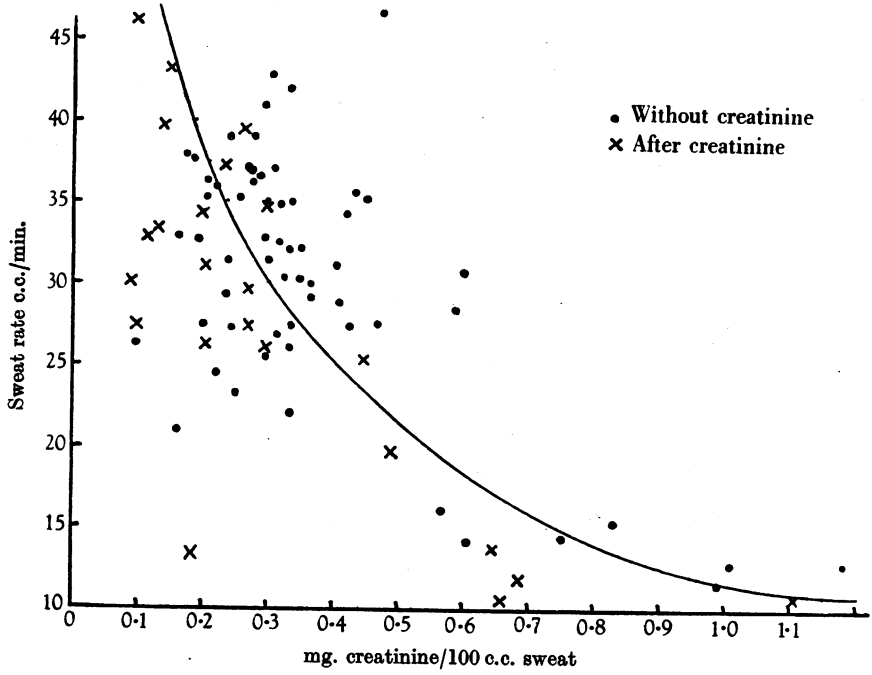

Fig. 3. Subject G. Relation between the creatinine concentration in the sweat and the sweat rate. The curve is the regression line for concentration and the reciprocal of the sweat rate; it has a correlation coefficient of 0·93.

In general, the higher the sweat rates the less creatinine was found in the sweat, and conversely. The subjects who had low initial sweat rates, G. and B., had more creatinine in their early samples than had L. who began to sweat fast almost immediately on entering the chamber. Statistical tests confirmed this impression. For 186 observations there was a correlation coefficient of 0·58 between creatinine concentration in the sweat and the reciprocal of the sweat rate. Taking each of the three subjects G., B. and L. separately, the correlation coefficients were 0·93, 0·72 and 0·39 respectively for 83, 39 and 51 observations; the results for P. were not analysed separately. All these coefficients are significant. In Fig. 3 the sweat rate is plotted against the creatinine concentration for subject G.; the regression line is also shown.

DISCUSSION

Whereas the creatinine contents of both the saliva and the blood increase three-fold after a dose of 5 g. of creatinine, there is only a slight increase in the creatinine content of the sweat. The sweat creatinine appears to be more closely linked with the rate of sweating than with the level of creatinine in the blood; thus the slower the rate of sweating the greater the creatinine content. Statistically there is good correlation between the reciprocal of the sweat rate and the sweat creatinine. This reciprocal relationship between creatinine content and sweat rate is the opposite of what has been observed for chloride concentration (Ladell, 1945*b*); a number of other authors have also reported that the greater the sweat rate the more nearly does the chloride content of the sweat approach that of the plasma (Dill, Hall & Edwards, 1938; Johnson, Pitts & Consolazio, 1944). There would therefore appear to be two mechanisms at least involved in the production of sweat from body fluids. Mosher's (1933) suggestion that there is an essential similarity between sweat and urine may be correct; but the fact that the creatinine content of the sweat is little affected by that of the blood, whereas the urinary creatinine is greatly affected, indicates that the mode of production of the two fluids must be very different.

SUMMARY

1. The creatinine contents of serial samples of sweat from men working in a hot humid environment were measured and compared with the creatinine contents of saliva and of plasma obtained at the same time.

2. Increasing the creatinine content of the blood raised that of the saliva correspondingly, but had little effect on that of the sweat.

3. There is a reciprocal relationship between sweat rate and the creatinine content of sweat.

I am indebted to Dr E. Arnold Carmichael and to Dr B. McArdle for their advice and encouragement; and to Dr B. S. Platt for the use of certain apparatus. I also wish to thank my subjects for their loyal co-operation in carrying out these tests.

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