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THE EFFECT OF EXERCISE ON CHLORIDE EXCRETION IN MAN DURING WATER DIURESIS AND DURING TEA DIURESIS

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In studies on the effect of exercise on urinary excretion in man, some diuretic is habitually used to facilitate frequent sampling of urine. Water has been most usually employed in this connexion, but tea was used in one major work on the subject [MacKeith, Pembrey, Spurrell, Warner & Westlake, 1923]. Comparison of results obtained under the action of these two different diuretics is unreliable, owing to the different conditions prevailing in the different sets of experiments, especially in regard to the severity and duration of the exercise undertaken. An attempt has now been made to differentiate the changes in urinary excretion due to the exercise and those due to the diuretic employed, by experiments under more comparable conditions.

Methods

Students of both sexes were used as subjects, details of whom are given in the appendix. The last meal was taken 5–6 hr. previously, and a glass of water 2½–3 hr. before the experiment. The exercise was short and severe—an 'all-out' sprint occupying 40–60 sec.

The first comparison was made, in co-operation with the Biochemistry Department, between two different groups of subjects, at one year's interval. On the first occasion, small amounts of water were taken repeatedly in order to promote a reasonable flow of urine, and on the second occasion, a pint of tea was taken in one draught. The beverage was made by extracting ½ oz. Indian tea with boiling water for 5 min. and contained less than 20 mg. NaCl/100 c.c. The exercise followed when diuresis was well established, two pre-exercise and four post-exercise urine samples being collected for subsequent analysis by the rest of the class. In the remaining experiments a more accurate comparison was made by using each subject for both experiments. These were done at the same time of day (afternoon); 1 pt. of fluid (either water or tea) was imbibed within 2–5 min. and the exercise taken 30–40 min. later when diuresis was well established. Urine sampling was more frequent than in the class experiments, but chloride only was analysed (electrometric titration method [Eggleton, Eggleton & Hamilton, 1937]).

Results

Class experiments

The main results of the class experiment on the effect of exercise on urinary excretion during water diuresis have been published already [Eggleton, 1942*a*]. Their interest at the moment lies in the comparison with them of the results

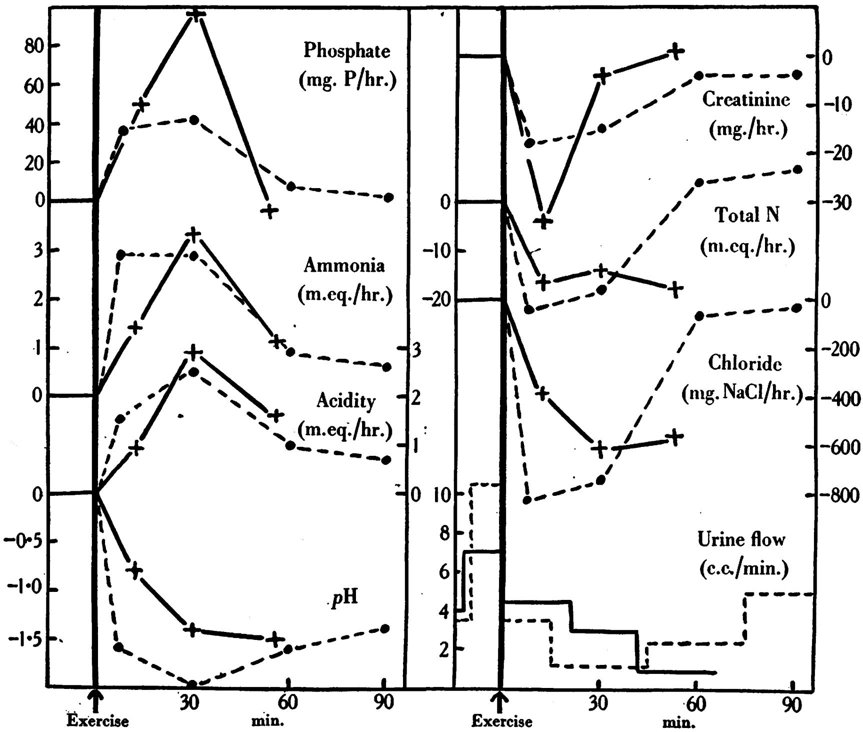

Fig. 1. Average changes in urinary excretion following exercise during tea and during water diuresis. +——+ Water diuresis (average of seven subjects). ●- - - -● Tea diuresis (average of five subjects).

obtained subsequently during a tea diuresis. Such a comparison of the average results (calculated as changes on a pre-exercise value of zero) is shown in Fig. 1.

It is clear that most of the changes observed are common to both experiments and can, therefore, be attributed to the exercise as such. This results in an increase in the output of phosphate, of titratable acidity and ammonia, and a fall in *p*H; and a temporary reduction in the output of creatinine, chloride and total nitrogen. Minor differences between the two sets of results, either in time lag or in magnitude, can be readily explained by slight differences in technique on the two occasions. In the water-diuresis experiment, for example, some minutes elapsed between the collection of the last pre-exercise sample and performance of the exercise; the first post-exercise sample was, therefore, a mixed one, and changes in composition due to the exercise were thus artificially reduced. In the tea-diuresis experiment the exercise was rather less severe and of longer duration (90 sec. instead of 50–60) owing to a misunderstanding of instructions, and the increase in phosphate output was therefore less. The apparent difference in depression of creatinine excretion is, however, barely significant, this analysis being the least reliable of any in student hands.

The only differences of any significance between the two sets of experiments lie in the excretion of chloride, of total nitrogen, and of water. During the tea diuresis both total nitrogen and chloride excretion return to their pre-exercise level within an hour, but during the water diuresis they do not. This latter result confirms the observation of Havard & Reay [1937] in regard to chloride excretion. The experiment was, however, terminated sooner than that performed during tea diuresis, and the results therefore do not negative the possibility of a later return to normal values.

In order to determine whether the exercise or the diuretic employed was responsible for the observed differences in the results of these two class experiments, a more careful comparison was made on a group of individuals, attention being focused on chloride excretion and water output. For this purpose, eleven subjects were used, each performing the same amount of exercise on two succeeding afternoons; on one day a pint of water was taken first and on the other a pint of tea. In nine of these subjects, control experiments on tea and water diureses were made, without exercise.

Chloride excretion in water diuresis

In eight of the nine subjects tested, water diuresis itself led to a considerable diminution in chloride output. Curves of the average rate of urine flow and chloride excretion for these eight subjects are shown in Fig. 2. It is strange that this effect accompanying a water diuresis has not previously been emphasized, for evidence of its existence is not lacking in the literature. Marshall [1920], for example, who was attempting to demonstrate a rise in chloride excretion during water diuresis in man had to admit 'at the height of urine flow, the elimination of chloride is diminished'. What he did not admit, but can be seen clearly in his protocols, is a still greater decrease in chloride excretion as the diuresis continued; this occurred in all the subjects investigated. Priestley [1921] and Adolph & Ericsen [1926] obtained a similar result.

A study of individual curves shows no close time relationship between the decrease in chloride output and increase in water excretion. In Fig. 3 two extreme cases are plotted; in one (subject G), the greatest fall in chloride excretion precedes the main onset of diuresis, and in the other (subject L), the lowest point on the curve is reached only as the diuresis is passing off. This fact suggests the possibility that two distinct mechanisms may be involved, the relative sensitivity of the two varying in different individuals. A comparison of the total output of water and of chloride in the different subjects, however, suggests the existence of an inverse relationship between the two. In Table 1 is shown the total output of urine in the eight subjects, in descending order of

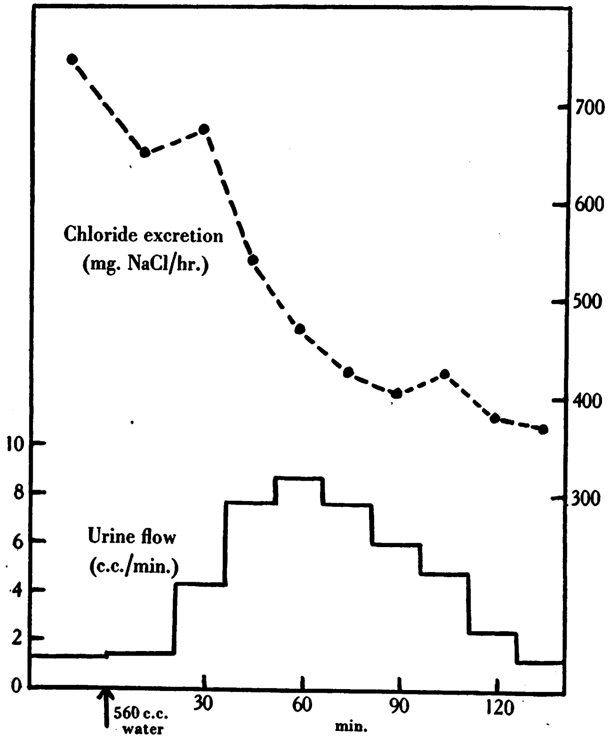

Fig. 2. The effect of a water diuresis on chloride excretion. Average of eight subjects.

magnitude, together with the decrease in total chloride excretion expressed as a percentage change on the normal resting output. Although the relationship is not a close one, there is a definite trend in the direction of greater inhibition of chloride excretion with smaller diuresis.

In one of the nine subjects investigated, a completely different result was obtained. The chloride excretion increased steadily with increase in rate of urine flow during the onset of the diuresis, as can be seen in Fig. 4. The same phenomenon was observed in the exercise experiment, during the onset of diuresis before the exercise, and would appear, therefore, to be of regular occurrence in this individual. On the two occasions on which the resting rate of flow was measured, it was considerably lower than that encountered in any other subject: 0·28 and 0·36 c.c./min. in contrast with a minimum value of 0·65 c.c./min. in any other. The subject is apparently quite normal and healthy, and unfortunately opportunity has been lacking for any further investigation which might throw light on this abnormality.

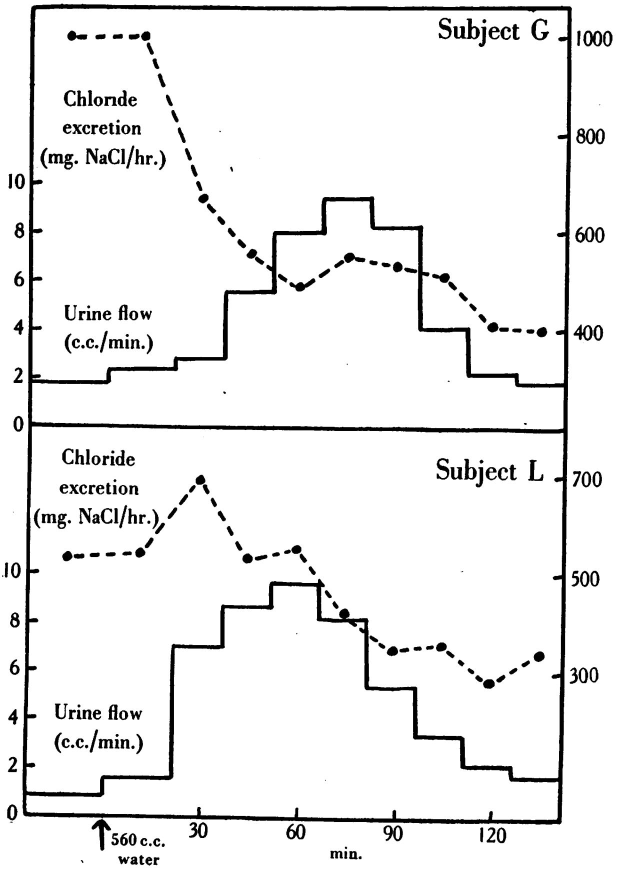

Fig. 3. Showing the lack of close relationship between the course of the decrease in chloride excretion (right ordinate) and increase in rate of urine flow (left ordinate) during water diuresis in two different subjects.

TABLE 1. Comparison of the response of different subjects to 560 c.c. water

Subject	Total urine output in 2½ hr. c.c.	Reduction in total chloride output %	Subject	Total urine output in 2½ hr. c.c.	Reduction in total chloride output %
D	885	10	G	675	42
C	795	21	M	660	39
L	730	16	F	530	50
H	705	20	B	370	41

Chloride excretion in tea diuresis

Comparison of water and tea diureses in the same individuals did not yield as much information as had been anticipated. The tea was not tolerated well (the same brand as that used earlier could no longer be obtained), and in many cases the stomach emptied irregularly, or in part by way of the oesophagus. Thus a comparison of total output of water in the two forms of diuresis was possible in only five subjects. In these, the tea diuresis was consistently greater than the water diuresis, on the average 35% greater.

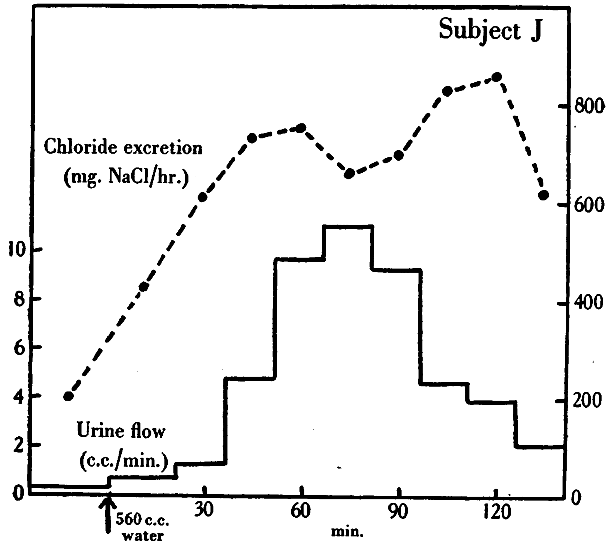

Fig. 4. Abnormal behaviour of chloride excretion during water diuresis in one individual.

The effect of the tea on chloride excretion was even greater. In spite of the fact that the chloride excretion should have been depressed by the volume of water in which the tea was taken, it was in fact increased in all cases, even when the water output was depressed owing to nausea. The average change in rate of chloride excretion for all subjects except J (in whom no normal resting chloride value could reasonably be assessed), expressed as a percentage of the normal resting value, was 150% in tea diuresis and 70% in water diuresis. The results plotted in Fig. 5 give some idea of the magnitude of the opposing actions of water and of tea on chloride excretion when the diuresis is uninterrupted. The resting value of 1·0–1·2 g. NaCl/hr. (the experiments were performed at 1 week's interval) rose to 1·8 g./hr. under the action of tea and fell to 0·4 g./hr. under the action of water.

The actual course of the chloride excretion varied widely in different subjects, as in the water-diuresis experiments, even when the stomach appeared to empty normally. The variation in urine output among the few successful experiments was, however, too small to permit any deductions to be made from a comparison of total water and total chloride output, as was done in the case of water diuresis (Table 1).

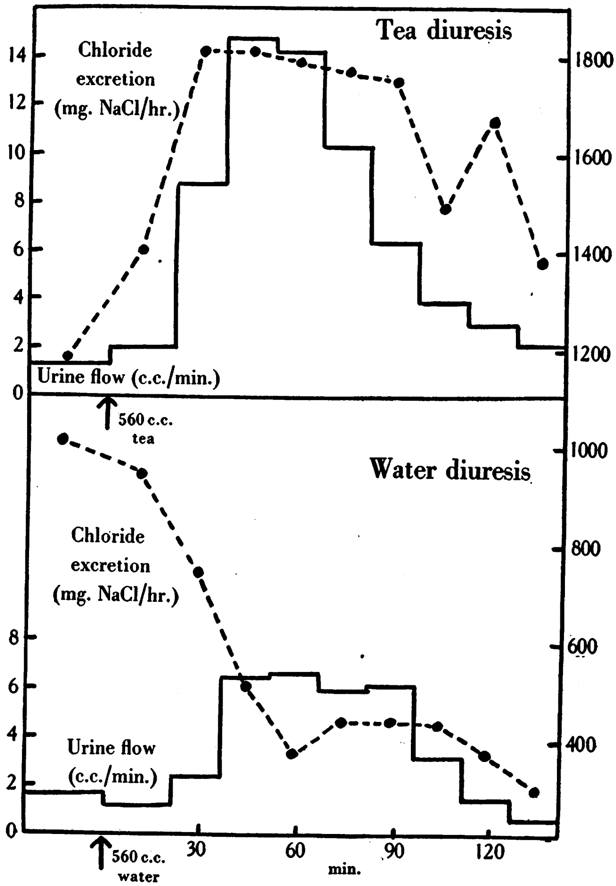

Fig. 5. Showing the opposing actions of water and of tea on the chloride excretion in one subject (F).

Individual variation in the course of water diuresis following exercise

In Fig. 6 is illustrated the wide range of individual response to exercise encountered during the water diuresis. If this occurred in the class experiment of 1941, it passed unnoticed, possibly owing to the fact that sampling was continued for only 60 min. after the exercise and that the water was taken in divided small doses; one of the eight subjects used then was considered abnormal in showing practically no inhibition of urine flow. He returned in 1942 for the purpose of this experiment and his curve (E) in Fig. 6 closely resembles that obtained in 1941; in 1941, however, less inhibition was observed in the first ¼ hr. after the exercise. The curves in Fig. 6 are arranged in order of increasing duration of inhibition. In the penultimate one (average of subjects G and K), the inhibition immediately following the exercise is separated from the later stage by a temporary return of diuresis. In the last curve (D),

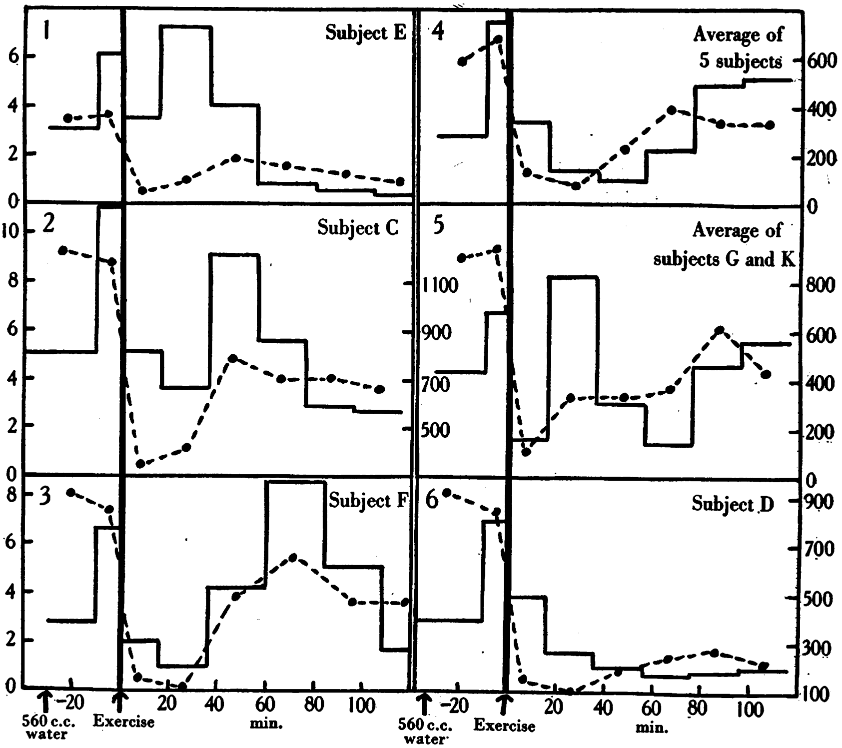

Fig. 6. The effect of strenuous exercise on the course of a water diuresis in different individuals. —— Rate of urine flow (c.c./min.). •------• Chloride excretion (mg. NaCl/hr.).

diuresis had shown no sign of returning by the end of the experiment. The possible and probable causes of this inhibition, and of the changes in output of chloride, will be considered in the discussion.

In spite of the inhibition of urine flow following the exercise, no consistent relationship was observed between the total output of water with and without exercise over the period studied. Subject D, for example, who gave one of the smallest responses after exercise (330 c.c. in 2½ hr.), showed the largest water diuresis (885 c.c./2½ hr.) without exercise. In contrast with this result, three subjects (C, F and G) actually showed a larger total output of water in the exercise experiment than in the uninterrupted water diuresis. Comparison of chloride excretion under the same two sets of conditions yields a similar negative result. The total chloride output was reduced on the average to 70% of its normal value by the water diuresis, and to 62% of the normal value as the result of combined water diuresis and exercise, but owing to the wide individual variation this small difference has no significance.

Comparison of tea and water diureses (with exercise)

Only eight successful experiments were made with tea diuresis, nausea or vomiting having occurred in the remaining three. In all eight cases, the total output of urine in the 2½ hr. following the drink was greater than in the water-diuresis experiments. These figures are shown in Table 2. The relative constancy

TABLE 2. The relative magnitude of tea and of water diuresis with exercise in different individuals

Subject	Urine output in 2·5 hr. c.c. Tea diuresis	Water diuresis	Ratio of tea/water diuresis
A	825	525	1·57
B	477	325	1·47
C	876	838	1·05
D	552	330	1·67
E	924	472	1·96
F	953	672	1·41
H	965	585	1·65
J	660	406	1·62
		Average	1·55

of the ratio of the two suggests that the large variations observed in the total output of different individuals is not a haphazard effect, but due to some specific difference in their reaction to exercise and the diuretic combined. This impression is enhanced when individual curves of tea diuresis and of water diuresis are compared. Three different types of response are shown in Fig. 7, and the same parallelism in response to the two diuretics was shown in the remaining five subjects. As in the water-diuresis experiments, there is little apparent relation to be seen in the tea diuresis between the output of chloride and the course of diuresis. The total chloride output is consistently higher than that following a water diuresis, as can be seen from the figures in Table 3. In the pre-exercise period it increases markedly with the onset of diuresis (contrary to its behaviour in water diuresis), and is already raised above normal in the first sample (Fig. 7).

The few comparisons available between experiments under tea diuresis, with and without exercise, yield results similar to those obtained under water diuresis. No regular relationship was found in any individual, either in regard to total output of water or of chloride. In two subjects, the urine output was appreciably decreased as a result of the exercise, in one it was unchanged and in the fourth increased; and the chloride excretion was increased in two, and decreased in two.

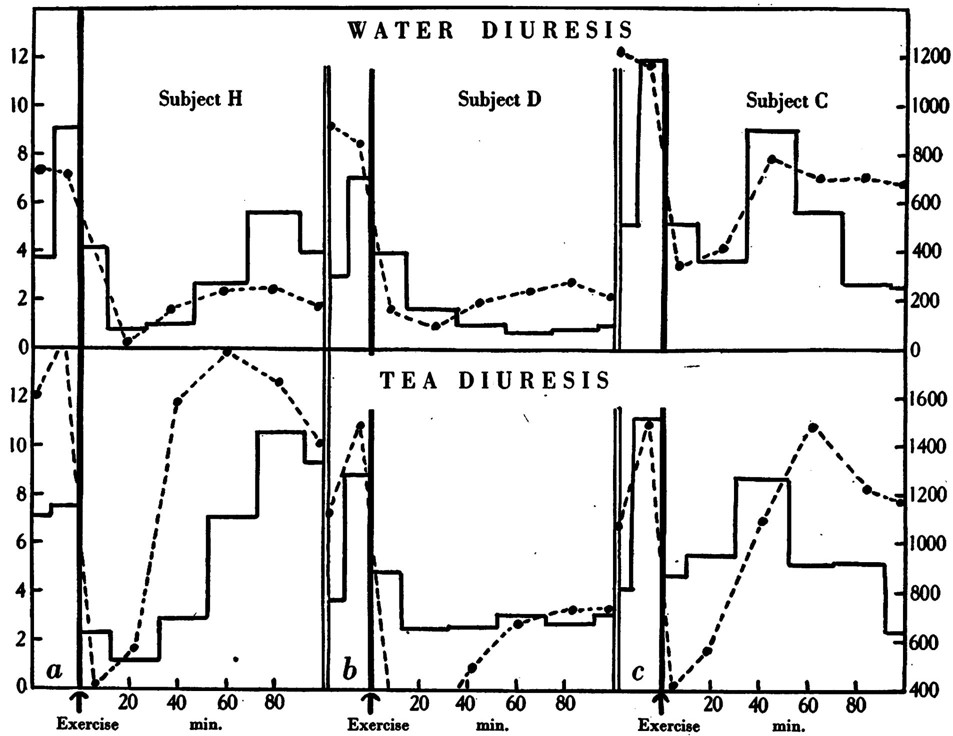

Fig. 7. Comparison of the effect of strenuous exercise on the course of a water and a tea diuresis in three different subjects. ——— Rate of urine flow (c.c./min.). •----• Chloride excretion (mg. NaCl/hr.).

TABLE 3. The total output of chloride during tea diuresis and during water diuresis with exercise

Subject	Total chloride output in 2·5 hr. g. NaCl	
	Tea diuresis	Water diuresis
A	2·27	1·75
B	2·09	0·5
C	2·88	2·02
D	1·87	1·0
E	1·87	0·46
F	3·2	1·33
H	3·7	0·8
J	2·99	0·7
Average	2·61	1·07

Discussion

It must be admitted that the original point of the research—the effect of exercise on chloride excretion—has not been fully cleared, owing to the opposing actions of the diuretics used. A comparison of the course of chloride excretion with and without exercise, however, indicates the probability that changes occurring in the 40–50 min. after exercise are the only ones which have any significance in relation to the exercise in the majority of subjects. The immediate decrease may be attributed, as also the decrease in water output, to a temporary vasoconstriction. This is indicated by the sharp decrease in creatinine excretion observed during the first 15 min. after the exercise in both class experiments, and is seen only after very strenuous exercise. In the experiments of Wilson, Long, Thompson & Thurlow [1925] on man, for example, rather less severe exercise (1–2 min. stair-running) during a water diuresis resulted in a prolonged inhibition of chloride excretion (40–60 min.) and of urine flow (60–90 min.), but had no effect on creatinine excretion.

The continued decrease of chloride excretion in the next period, observed under both tea and water diureses, coincides with, and may possibly be related to, the peak excretion of acid products of muscular activity. The factors controlling electrolyte excretion are still obscure, but there seems little doubt that if any one is greatly increased, others are diminished. Both increased sulphate and increased bicarbonate depress chloride excretion [Homer Smith, 1937] and the lactate ion may well have the same effect.

During the following hour, chloride excretion gradually rises again, there being no close correlation with increase in water output, and subsequently falls in the majority of subjects. These changes are much greater under tea diuresis than under water diuresis. The major part of the rise can be attributed to the reassertion of the caffeine effect and removal of the previous inhibiting effects (vasoconstriction and excretion of acid ions). The later fall is open to at least two interpretations: (*a*) a wearing off of the caffeine action, and/or (*b*) onset of the normal reduction accompanying the re-established diuresis. The latter explanation is favoured by the fact that it is most marked when a large diuresis has again set in, and by the similarity in the trend of the curve following water diuresis (see Fig. 6). When diuresis fails to reappear (Fig. 7*b*) this kink in the chloride-excretion curve is scarcely apparent irrespective of whether water or tea has been used as the diuretic agent.

The causes of the varying degrees of inhibition of water output after exercise in different individuals is again largely a matter of surmise. The decreased output during the first 15 min. may be attributed either entirely to vasoconstriction or in part also to a nervous interference with the pituitary mechanism. Rydin & Verney [1937] have shown clearly in dogs that mild exercise, or the anticipation thereof, during a water diuresis, produces a temporary inhibition of urine flow which can be attributed to release of anti-diuretic hormone. It is likely, therefore, that this factor operates in any type of exercise, and was probably the only one concerned in the experiments of MacKeith *et al.* [1923] on man; they observed a temporary reduction in rate of urine flow during a tea diuresis whenever a walk gave place to a trot. In subject E no further explanation is required. In the remaining subjects, a further period of inhibition lasting from 20 to 60 min. precedes the return of diuresis, and in two (G and K) this prolonged period is separated from the initial period of inhibition by a short-lived return of diuresis.

It is unlikely that delayed absorption can account for this large individual variation. True, there is little accurate evidence as to the rate of absorption of water in man. In dogs weighing 10 kg., Klisiecki, Pickford, Rothschild & Verney [1932] found 250 c.c. absorbed in 35 min. on the average. From less direct measurements in man, Smirk [1933] concluded that absorption was complete (1000 c.c. in 27–55 min., and 500 c.c. in 22 min.) before maximum diuresis was attained. In our experiments, not less than 30 min. elapsed between the drink and the exercise, and in one or two cases where full diuresis had not set in by this time, the exercise was delayed a further 10–15 min.

The only factor peculiar to the particular type of exercise employed in these experiments (short and strenuous), apart from the temporary vasoconstriction, is the undoubted concentration of the blood which follows. Gregersen, Dill & Meade [unpublished experiment quoted by Gregersen, 1938] demonstrated a 12–16% concentration of the blood (haemoglobin, plasma dye, and plasma proteins) as a result of 90 sec. intensive running, and computed that 500 c.c. water had left the blood stream in the next 90 sec. The *status quo* was restored fully only 1 hr. later. Chloride does not pass readily into muscle fibres, and it is likely that plasma chloride is concentrated to the same degree as other constituents in these circumstances. This concentration of electrolytes will lead to an active secretion of anti-diuretic substance. It seems not improbable that the degree of plasma concentration and its duration might well vary in different subjects, with consequent variation in the secretion of anti-diuretic hormone, both in amount and duration, sufficient to account for the variable prolonged inhibition of diuresis observed in our experiments. In addition, the possibility remains that the 'pituitary mechanism' is more readily stimulated in some individuals than in others, a possibility suggested by previous work on a comparison of water and alcohol diureses [Eggleton, 1942*b*]. The relative constancy of the duration of this inhibition in any one subject under tea and water diureses (Fig. 7) would support equally either hypothesis. Viewing the evidence as a whole, it seems justifiable to conclude that the most likely cause of the prolonged inhibition of urine flow following the exercise is secretion of the anti-diuretic hormone.

To what extent the changes in chloride excretion may also be explained on this basis is a more open question. If lack of anti-diuretic hormone is responsible for the decrease in chloride excretion observed in a water diuresis, the temporary increase in excretion of this ion during the prolonged inhibition of urine flow following the exercise might be attributed to reappearance of the hormone in circulation. The lack of any close correlation between the increased water output and decreased chloride excretion, however, either in an uninterrupted water diuresis (Fig. 3) or following exercise (Fig. 6), does not lend much support to this view. Nor have other workers succeeded in demonstrating any increase in chloride excretion as a result of injected pituitrin unless massive doses of the hormone are used [Stehle, 1926; Corey & Britton, 1941]. Without further evidence, no certain conclusion as to the mechanism responsible for the suppression of chloride excretion during a water diuresis can be drawn.

The inverse relationship between magnitude of water diuresis and of decrease in chloride excretion suggested by the results presented in Table 1 does not necessarily lend support to either view. There is a considerable body of evidence in favour of the generally accepted belief that chloride excretion is increased with increased rate of urine flow owing to the faster passage of fluid through the tubules with consequent reduced opportunity for chloride reabsorption. In the results presented here, there are several hints that this factor is in operation in water diuresis, in opposition to the specific chloride-inhibiting action also present. In the curve of the average results (Fig. 2), for example, the decrease in chloride excretion in the earlier stages of the diuresis is temporarily checked with the first sharp rise in rate of urine flow, and in subject L (Fig. 3) this effect is very marked: similar results were obtained by Priestley [1921]. The inverse relationship suggested in Table 1 could be explained on this basis, the lack of any closer relationship being attributable to the varying strength of the opposing chloride-inhibiting factor in different individuals. In subject J (Fig. 4) one must assume a complete absence of this latter factor.

In the tea-diuresis experiments, these changes accompanying a water diuresis are masked by the opposing action of the tea extract in increasing chloride excretion. In total effect this action more than counteracts the inhibitory effect of the water on chloride output, so that the pint of tea causes a total output of chloride well above the normal for any individual. We have obtained no clear-cut evidence as to whether this increased chloride excretion is due to an increased glomerular filtration rate or to a specific action on chloride output, though the lack of correlation between height of diuresis and magnitude of increase in chloride excretion (Figs. 5, 7) might be accepted in support of the latter hypothesis. This conclusion would be unaffected by acceptance of the more recent views of the action of caffeine [Goodman & Gilman, 1940]—that its main diuretic action is due to inhibition of water reabsorption rather than to increased glomerular filtration. Admittedly, interpretation of the results obtained is complicated by the fact that the tea extract was administered in a large bulk of water. It might well be suggested that the variation in response of different individuals was due merely to differences in their response to the water, the course of chloride excretion following ingestion of the tea being the resultant of increase due to tea extract and decrease due to the water. This simple explanation is, however, not substantiated by a detailed comparison of the course of chloride excretion in tea and water diureses in different individuals.

The experiments as a whole throw some further light on the problem of individual variation in response. It has been demonstrated previously [Eggleton, 1942*b*] that a large individual variation exists in the diuretic response to water, and it was expected that these individual variations would persist when the effect of exercise was superimposed. This, however, was not observed. Subject D, for example, who showed the largest diuretic response to water alone, gave one of the smallest responses to water with exercise. Variations in response to exercise are presumably masking variations in response to the diuretic. Experiments on tea diuresis fully confirm this conclusion. Individual variations have been shown to occur in response to tea, which are correlated with those in response to water, the average diuretic response to the former being 1·35 times that to the latter. As in the case of water diuresis, however, individual variation in response to exercise overrides that in response to tea. When exercise is superimposed on both diureses, the correlation between the response to water and the response to tea is once more apparent, and, in any one subject, the effect of the exercise is the same whether diuresis is produced by tea or by water (Table 2).

Summary

1. A short period of severe exercise superimposed on a tea diuresis results, as in a water diuresis, in an increased excretion of phosphate, titratable acidity and ammonia, and a fall in *p*H. A temporary decrease in output of creatinine, total nitrogen and chloride also occurs under both sets of conditions (Fig. 1).

2. The more permanent decrease in total nitrogen, chloride and water output following exercise during water diuresis is not observed during tea diuresis.

3. A more accurate comparison of the effects of exercise on the output of water and chloride during the two types of diuresis, made on the same individuals, gave the following results:

(*a*) A large individual variation occurred in the duration of inhibition of water diuresis as the result of such exercise (Fig. 6).

(*b*) This variation was not haphazard; the same duration of inhibition was observed also under tea diuresis in the same individual (Fig. 7).

(*c*) The total output of water also varied widely in different individuals. That following tea diuresis was always greater and bore a fairly regular relation to that following water diuresis (1·55 times as great) (Table 2).

(*d*) Chloride excretion was greatly diminished for 35 min. after the exercise in both types of diuresis. The subsequent rise was much greater in the tea diuresis but fell again as water output increased. The total chloride output in water-diuresis experiments was only 40% of that in the tea-diuresis experiments (Table 3).

4. Control-diuresis experiments without exercise showed:

(*a*) A decrease in chloride output during water diuresis (Fig. 2), averaging 30%. The course of this change was not closely related to the increase in output of water (Fig. 3), and in absolute magnitude varied roughly inversely with the degree of diuresis (Table 1).

(*b*) An increase in chloride output during tea diuresis (Fig. 5), averaging 50%.

5. It is suggested that the inhibition of diuresis immediately following the exercise is due to vasoconstriction and nervous interference with the pituitary mechanism, and that the more variable and prolonged inhibition may be due to secretion of anti-diuretic hormone resulting from the concentration of blood resultant on the exercise.

Appendix

Subject	Sex	Body wt. kg.	Subject	Sex	Body wt. kg.
A	♂	68	G	♂	66
B	♂	71·5	H	♀	58·5
C	♂	61	J	♀	63
D	♂	69	K	♀	65·5
E	♂	57·5	L	♀	51
F	♂	73·5	M	♂	75

All subjects were between 19 and 21 years of age.

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