THE EFFECT OF A HIGH WATER INTAKE ON SALT CONSUMPTION, TASTE THRESHOLDS AND SALIVARY SECRETION IN MAN

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This paper describes the changes in salt consumption, taste thresholds and salivary secretion, which took place in two normal subjects during an 11-day period of drinking about 8-10 l. of water a day.

It has been noted in normal man that the ingestion of large amounts of water results in an increased loss of sodium in the urine which may lead to a negative sodium balance (Regnier, 1916; Strauss, 1922; Kunstmann, 1933). In such circumstances an increase in the demand for salt, and a change in the salt taste threshold might therefore be expected. The salivary secretion was investigated in order to study the accompanying changes in the sodium: potassium (Na:K) ratio in the saliva, and because patients with compulsive polydipsia often complain of a dry mouth.

METHODS

Experimental procedure

The experiments were made on two men, subject 1, aged forty, weighing 82.5 kg, and subject 2, aged thirty, weighing 65.8 kg. The observations covered an uninterrupted period of 22 days (28 May-18 June 1956), which was divided into three parts. The first (the control period), during which the water intake was normal, lasted 5 days in subject 1, and 6 days in subject 2; the second (the experimental period), in which the intake of water (in addition to tea and coffee) was $10-12 \ 1/24$ hr in subject 1, and $7.5-9 \ 1/24$ hr in subject 2, continued for 12 days; the third (the post-experimental period), began with an initial period of 26 hr fluid deprivation, and ended with a period of normal water intake, lasting 4 days in subject 1, and 3 days in subject 2. As far as was possible both subjects carried on with their normal activities throughout the 22 days.

Fluid intake

During the control period and the latter part of the post-experimental period, the intake of fluids (including tea and coffee) was only governed by the subjects' inclinations and was not measured. During the experimental period the average intake of water was approximately the same for both subjects (122 and 124 ml./kg/24 hr); the consumption of tea and coffee was about the same as in the control period. The intake of water was spread fairly evenly throughout the

24 hr; 250–500 ml. was taken every 30–60 min, except for two interruptions, one of $2\frac{1}{2}$ hr from 5 to 7.30 p.m. and the other, during the night, lasting 4 hr in subject 1, and up to 5 hr in subject 2. Alcohol was not taken during the experiment.

Fluid deprivation. This test was performed 4 weeks before the experiment was begun, and again at 5.30 p.m. on the last day of the experimental period. Fluids were withheld for 26 hr ending at 7.30 p.m.

Diet. Lunch, tea and dinner were prepared without added salt by the hospital diet kitchen. These meals were the same for both subjects, and apart from minor variations in the type of vegetable and fruit, were the same every day. Breakfasts (toast, butter and tea) were eaten at home and were of known composition; they were slightly different for the two subjects. All food was weighed and the sodium content calculated from the tables of McCance & Widdowson (1946) (see Tables 1 and 2).

Added salt intake. The subjects were allowed to add as much salt as they wished to their food, but the amount they added (see Tables 1 and 2) was concealed from them. Heavy metal saltcellars were used; they contained varying amounts of salt, and were weighed and refilled each day by a third person. The salt from the salt-cellars is referred to as the 'added salt intake'.

Sodium balance. The excretion of sodium in the urine was measured each day. The daily sodium balance was calculated by adding the dietary sodium intake to the sodium taken from the salt-cellar and subtracting the sodium excreted in the urine; losses in the faeces and sweat were not included.

Salivary secretion and taste thresholds

Saliva was collected in response first to chewing 8 g paraffin wax (m.p. 44° C) for 3 min and then to sucking an acid-drop for 1 min (A. C. Kerr, personal communication). Each subject had his own piece of wax which he used throughout the experiment. All resting saliva was swallowed before each stimulus was applied. During the collection period the saliva was allowed to run into a measuring cylinder; any saliva remaining in the mouth at the end of the collection period was added. The volume of saliva secreted was measured, and its sodium and potassium content determined with a flame photometer. The volume of saliva obtained in response to the acid-drop includes the volume of that fraction of the acid-drop which dissolved in the saliva, and is therefore slightly greater than the volume actually secreted. This error has been disregarded; it is of the order of 1 ml.

Taste thresholds were measured by a method based on the 'choice method no. 2' of Richter & MacLean (1939). The subject, who is blindfolded, is presented with two beakers, one containing about 25 ml. distilled water, the other a similar amount of the test solution. The beakers are placed in the two hands, and are interchanged at irregular intervals between trials. The subject takes sips from each beaker until he recognizes the presence of a salt or sweet taste, or decides that neither can be identified with certainty. After each trial the fluid is discarded, none being swallowed. The whole procedure occupies 20-25 min for each subject.

The following solutions were used in random order: sodium chloride (%): 0.10, 0.08, 0.06, 0.04, 0.03, 0.02, 0.015, 0.01, 0.0075, 0.005, 0.003; sucrose (%): 1.0, 0.8, 0.6, 0.5, 0.4, 0.3, 0.2, 0.14, 0.09, 0.06, 0.04. The solutions were used at room temperature. They were freshly prepared every 4 days with the same distilled water as that used in the control beaker. The taste thresholds were always measured before saliva was collected; both tests were performed before dinner, between 6 and 7.30 p.m.

Statistical procedures

For any two variates, correlation coefficients r_1 for subject 1 and r_2 for subject 2 have been transformed to z_1 and z_2 . The ratio of the weighted mean \bar{z} to its standard deviation has been used to calculate the probability P of the correlation being due to chance (Fisher, 1936).

RESULTS

The results are given in Tables 1 and 2, and illustrated in Figs. 2 and 3.

Sodium balance

The changes in sodium balance were quite different in the two subjects, and are described first because of their potential relevance to the changes which occurred in the salivary sodium: potassium ratio, the added salt intake, and the salt taste threshold. Subject 1 was in sodium equilibrium during the control period, but during the experimental period he developed a substantial negative cumulative sodium balance which persisted to the end of the postexperimental period. Subject 2 was in mild negative sodium balance during the control period, and during the experimental period the cumulative sodium balance gradually reached equilibrium. In the post-experimental period this balance was slightly negative.

Salivary flow, and sodium and potassium concentrations

The volume of saliva secreted in response to the stimuli used was not affected by the high water intake. In subject 1 the salivary flow in response to wax chewing ranged from 4.7 to 6.3 ml./min, and with the acid-drop from 9.5 to 11.7 ml./min. In subject 2 the corresponding figures were 3.0-4.6, and 7.1-9.2 ml./min respectively, excluding the diminished flows obtained at the end of both periods of fluid deprivation.

The sodium concentration in subject 1 ranged from 30 to 50 m-equiv/l. and in subject 2 from 11 to 29 m-equiv/l. In the two specimens obtained daily from each subject this concentration nearly always varied in the same direction as the salivary flow. The potassium concentration in subject 1 ranged from 15.9to 19.2, and in subject 2 from 19.8 to 28.4 m-equiv/l. In subject 1 the potassium concentration was not related to the salivary flow; in subject 2 it was slightly lower at the higher rates of flow.

Salivary sodium: potassium ratio

Since sodium: potassium ratios tend to increase with the rate of salivary flow (Prader, Gautier, Gautier & Naef, 1955), it is necessary to allow for this variable when they are compared. In each subject, therefore, the two daily Na: K ratios have been plotted against their corresponding salivary flows (Fig. 1). The line through these two points gives an estimate of the Na: K ratio for any other rate of flow on that day, and enables all Na: K ratios obtained throughout the experiment in one subject to be compared at a standard rate of flow. The rate chosen was the mean flow rate of all observations in each subject (subject 1, 7.92 ml./min; subject 2, 5.72 ml./min). The Na: K ratios at these mean rates of flow are those compared below.

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The Na: K ratio in subject 1 was always above 1.95; during water drinking, before he developed a negative sodium balance, the Na: K ratio rose and reached a peak of 2.65 on the day that the rate of sodium loss was greatest. The Na: K ratio in subject 2 was always below 1.05; during the control period when he developed a slight negative sodium balance, the Na: K ratio fell from 1.04 to 0.66; during water drinking, when sodium equilibrium was restored, the Na: K ratio gradually rose to 0.81-0.85.



Fig. 1. The relation of the salivary Na:K ratio to the rate of salivary flow. Each line joins the two observations obtained from one subject on one day; the lower rate of flow on each day was obtained in response to chewing wax, and the higher in response to sucking an acid-drop. The dotted lines represent the standard rate of flow at which all the Na:K ratios in one subject have been compared (see text).

Intake of added salt

In both subjects the added salt intake rose soon after the start of the experimental period, and then returned toward the control values, though the high intake of water continued (Figs. 2, 3). From the second to the fourth day of the experimental period the food was tasteless unless large amounts of salt were added; on these days the thought of adding salt caused profuse salivation.



Fig. 2. Subject 1. The changes in the salt taste threshold and in the amount of salt taken from the salt-cellar throughout the experiment.



Fig. 3. Subject 2. The changes in the salt taste threshold and in the amount of salt taken from the salt-cellar throughout the experiment.

During the control period the added salt intake in subject 1 varied between 26 and 47 m-equiv/day and rose to a peak of 85 m-equiv/day in the experimental period; in subject 2 the control values were 24-36 m-equiv/day, and the peak intake during the experimental period was 64 m-equiv/day. It should be noted that the dietary salt intake (excluding the added salt) was always less in subject 1 than in subject 2, and that this difference was most pronounced during the experimental period; in both subjects the dietary salt intake rose during the experimental period.

Taste thresholds

Salt. In both subjects the salt taste threshold fell soon after the start of the experimental period and then returned to the control values, though the high intake of water continued. In subject 1 the salt taste threshold varied between 0.01 and 0.08% when the water intake was normal (Fig. 2). From the beginning of the experimental period the threshold gradually fell to 0.005-0.003% on the fourth, sixth and seventh day. It was 0.02% on the fifth day, when this subject had a severe headache. After the seventh day the threshold rose again towards its previous value, while water drinking continued.

In subject 2 the salt taste threshold varied between 0.0075% (on one day only) and 0.03% when the fluid intake was normal. From the second day of the experimental period to the seventh day it was always 0.0075 or 0.005%. During the latter part of the experimental period the threshold returned toward its previous level.

Sucrose. The changes in the sucrose taste threshold were similar to, but less pronounced than, those that occurred in the salt taste threshold.

Correlations between added salt intake, taste thresholds and sodium: potassium ratio

The added salt intake was negatively correlated with the salt taste threshold $(r_1 = -0.26, r_2 = -0.40; P < 0.05)$; the correlation with the sucrose taste threshold was of doubtful significance $(r_1 = -0.36, r_2 = -0.23; 0.07 > P < 0.08)$. The salt and sucrose taste thresholds were significantly correlated $(r_1 = 0.20, r_2 = 0.55; P < 0.04)$. There was no correlation between the salivary sodium: potassium ratio and the added salt intake $(r_1 = 0.19, r_2 = 0.13; P = 0.3)$.

DISCUSSION

The results show that the secretion of saliva in response to wax chewing and to an acid-drop is not increased by drinking large amounts of water. In both subjects the rates of flow were always higher than those reported by most previous workers (Schneyer & Levin, 1954; Prader *et al.* 1955; White, Entmacher, Rubin & Leiter, 1955), presumably because more potent stimuli were used (Kerr, 1956).

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TABLE

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			Wax			Acid-drop			Taste th	reshold		From	Cumulative
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Dav	(l./24 hr)	(ml./min) (meauiv/l.)	Na:K	(mim/.lm)	menuiv/L)	Na.: K	Na.:K	(%)	()()	dlet (m_equiv)	cellar (m aquin)	balance
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								;	1	1	9.0.4	20.3	R-0 -
1	02-0	8.0	41.2	2:34	10.8	46.7	2.54	2-41	0-08	0.8	53-4	46.6	- 13.3
n	0.20	5.5	35-2	2.19	6 .6	43.6	2.54	2.38	0.01	0.2	53.4	38-8	+ 6.3
4	0.20	5.8	36-8	2.04	10.2	44·0	2.20	2.11	0.01	9-0	53-4	31.2	+ 22.7
ð	0.20	5.3	33-2	1.91	11-0	48-0	2.53	2.19	0.06	9-0	53-4	39-2	+ 57.7
9	10-00	5.0	31.5	1.85	10.7	40-8	2-09	1-97	0.06	9-0	54-7	34.8	+ 38.9
7	09-6	5.0	32.8	2.04	10-4	42-4	2-47	2.27	0.02	0.5	54.7	37.9	- 19.8
œ	10-00	5.1	30-4	1.84	11-0	43.6	2.45	2.13	0.01	0.3	54.7	73.6	- 20.3
6	9-73	0-9	43.5	2.53	9.8	44-4	2.58	2.55	0.005	0.2	62.7	56.7	1 48.5
10	10-00	5.7	36.8	2.31	10-6	46.7	2.84	2-55	0.02	0.5	62.7	85.3	- 19-7
11	9-75	6 ·3	44-0	2.62	6-6	44·0	2.70	2.65	0.003	0.14	62.7	50.3	- 121-3
12	9-75	5.0	31.6	1.92	11-0	48-4	2.81	2.35	0.005	0.2	62-7	43.7	- 161-2
13	10-00	5 ·3	37-5	2.33	9-5	42-4	2.62	2.51	0.02	0.5	62-7	41.7	- 206-9
14	10-00	5.5	36-8	2.29	10-8	43.6	2.54	2.40	0-01	I	62-7	66.3	- 248-1
15	11-00	5.3	34.0	2.24	11-3	44·0	2.75	2.46	0.015	0.3	62.7	57.7	- 259-8
16	11-00	4-7	30.0	1.89	11.1	46-0	2.61	2.25	0.04	9-0	62-7	59-0	-250.2
17	4.75	5.1	41.5	2.16	8.6	44-0	2.37	2.28	I	I	62-7	54.3	- 292-2
18	0	4.9	39-6	2.37	10-2	50-0	2.89	2.66	I	0-4	62.1	46.1	- 242.8
19	0.20	4 ·8	37-5	2.25	10-0	44.0	2.65	2.49	0.04	9.0	62.1	29-7	- 274-0
20	0.20	4.9	36-0	2.12	11-7	49-2	2.86	2.45	0-03	0.2	62.1	40.1	- 302.4
21	0.20	50	34.8	2.05	10-5	46-4	2.52	2.30	I	0-4	62.1	56-7	-313-1
22	0-20	1	I	1	l	1	I	I	0.02	0.3	62-1	29-8	-317.0
Control fluid	0	4.7	42.5	2.39	10-4	49-0	2.64	2.53	I	Í		l	
Tomation						* See text.							

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† Four weeks before day 1.

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0-015 0-2 66-2 46-2 0-77 0-76
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† Four weeks before day 1.

TABLE 2. Observations on subject 2 throughout the experiment

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The concentration of sodium in the saliva was very different in the two subjects, but both were within the normal range. The potassium concentrations differed less and were also normal. The Na:K ratio was much higher in subject 1 than in subject 2, even when allowance is made for the different rates of flow. It has been established that for flows up to 3 ml./min (Prader *et al.* 1955) the Na:K ratio increases with the rate of flow. The results presented in this paper provide evidence that the Na:K ratio continues to increase at higher rates of flow.

The Na:K ratio has been found to be relatively constant in any one individual (Prader *et al.* 1955; A. C. Kerr, personal communication). This is confirmed by the observations reported here, which show that, four weeks before the experiment, the ratio fell within the same range as during the experiment. This was still true seven months later, when the Na:K ratios were determined in the same way on two successive days (subject 1, 2.40, 2.45; subject 2, 1.00, 1.07).

The difference in the Na:K ratios of the two subjects may have been due to differences in aldosterone secretion (Simpson & Tait, 1955). This explanation is reasonable if aldosterone secretion is related to the sodium balance, for this was quite different in the two subjects. On the other hand, both subjects showed evidence of an increase in extracellular fluid volume (de Wardener and Herxheimer, 1957), and it has been suggested that it is changes in this volume which control aldosterone secretion (Bartter, Liddle, Duncan, Barber & Delea, 1956).

In each subject both the salt content of the diet and the added salt intake increased during the experimental period. The rise in added salt intake from the salt-cellar therefore cannot be attributed to a diminished dietary intake; neither does it seem to be related to the sodium balance. The simultaneous fall in the salt taste threshold also fails to explain the increased demand for added salt, for one would expect that with an increased sensitivity to salt, a smaller addition would suffice to make food palatable. It is suggested, therefore, that the increased intake of added salt was caused by an increased desire, which was of central origin.

In both subjects the taste thresholds obtained during the control period were at the lower end of the normal ranges reported by Richter & MacLean (1939), and Richter & Campbell (1939). After two or three days of water drinking there was a striking fall in the salt taste threshold associated with an intense desire for salt. Several days before water drinking ceased the taste threshold returned to its control values, and the craving for salt disappeared. There was a similar, but smaller, change in the sucrose taste threshold, but this was not accompanied by a craving for sugar.

These changes are difficult to explain. The lowering of the salt taste threshold was not related to the concentration of sodium in the saliva, nor to any of the changes in the blood which are reported elsewhere (de Wardener and Herxheimer, 1957). The plasma osmolarity did not change significantly, and the plasma sodium concentration rose. There was, however, evidence suggesting that sodium was transferred from the cells to the extracellular fluid. This change may possibly have affected the salt taste threshold either at receptor level or centrally.

SUMMARY

1. The effect of an 11-day period of drinking about 10 l. of water a day has been studied in two normal subjects.

2. The flow of saliva, when chewing wax or sucking an acid-drop, was unaffected by the high water intake.

3. Subject 1 lost a considerable amount of sodium and developed a negative sodium balance during the period of water drinking. His salivary Na: K ratio was always above 1.9, and reached its peak when the loss of sodium was greatest. Subject 2 showed a slight negative sodium balance during the control period, but during the period of water drinking sodium equilibrium was restored and maintained. The Na: K ratio in this subject was always below 1.1, and fell to its lowest level when sodium equilibrium was being restored.

4. Soon after water drinking began both subjects felt an intense desire for salt, and added much more salt to their food.

5. In both subjects the salt taste threshold fell sharply 2 or 3 days after the start of water drinking, and rose again to its initial level before the end of the period of high water intake. The sucrose taste threshold showed similar, but less marked changes.

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REFERENCES

BARTTER, F. C., LIDDLE, G. W., DUNCAN, L. E., BARBER, J. K. & DELEA, C. (1956). The regulation of aldosterone secretion in man: the role of fluid volume. J. clin. Invest. 35, 1306-1315.

DE WARDENER, H. E. & HERXHEIMER, A. (1957). The effect of a high water intake on the kidney's ability to concentrate the urine in man. J. Physiol. 139, 42-52.

FISHER, R. A. (1936). Statistical Methods for Research Workers, 6th ed. Sect. 35, p. 199. Edinburgh: Oliver and Boyd.

KERR, A. C. (1956). Talking about saliva. Dent. Practit. 7, 30-35.

KUNSTMANN, H. (1933). Über die Wirkung der Zufuhr grosser Wassermengen auf den Organismus. Arch. exp. Path. Pharmak. 170, 701-718.

MCCANCE, R. A. & WIDDOWSON, E. M. (1946). Chemical composition of foods. Spec. Rep. Ser. med. Res. Coun., Lond., no. 235 (2nd ed.).

PRADER, A., GAUTIER, E., GAUTIER, R. & NAEF, D. (1955). Die Na- und K- Konzentration im gemischten Speichel. Helv. paediat. acta, 10, 29-55.

REGNIER, A. (1916). Über den Einfluss diätetischer Massnahmen auf das osmotische Gleichgewicht des Blutes beim normalen Menschen. Z. exp. Path. Ther. 18, 139-164.

RICHTER, C. P. & CAMPBELL, K. H. (1939). Sucrose taste thresholds of rats and humans. Amer. J. Physiol. 128, 291-297.

RICHTEB, C. P. & MACLEAN, A. (1939). Salt taste threshold of humans. Amer. J. Physiol. 126, 1-6.

- SCHNEYER, L. H. & LEVIN, L. K. (1954). Rate of secretion by exogenously stimulated salivary gland pairs of man. J. appl. Physiol. 7, 609-613.
- SIMPSON, S. A. & TAIT, J. F. (1955). The possible role of electrocortin in human metabolism. Ciba Foundation Colloquia on Endocrinology, 8, 204–224.
- STRAUSS, H. (1922). Über die Wirkung der Aufnahme grosser Wassermengen auf den Organismus. Klin. Wechr. 1, 1302–1305.
- WHITE, A. G., ENTMACHER, P. S., RUBIN, G. & LEITER, L. (1955). Physiological and pharmacological regulation of human salivary electrolyte concentrations. J. clin. Invest. 34, 246-255.