J. Physiol. (1944) 102, 415–428 612.463:612.014.461.2

THE SECRETION OF URINE DURING DEHYDRATION AND REHYDRATION

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(*Received* 29 *July* 1943)

Functional studies of the kidney have usually been made while subjects have been passing large volumes of urine. Admittedly, the general characteristics of urine passed during short periods of water restriction are well known, and a number of clinical tests have been devised based upon the capacity of a person when so restricted to produce a concentrated urine. On the whole, these tests have not contributed much to our knowledge of renal physiology and will not be discussed. A few people, however [Adolph, 1921, 1923; Coller & Maddock, 1933; Chesley, 1938; Nadal, Pedersen & Maddock, 1941], have braved the difficulties and planned experiments which allowed them to investigate the secretion of urine when the intake of water was low. The knowledge accumulated by these and other workers may be summarized as follows.

If in a temperate climate the total intake of water, including water of metabolism, is less than 1500 c.c./day, the volume of urine is small, and it is highly concentrated, but even in complete water deprivation some urine is secreted. This has a specific gravity of over 1030 if the concentrating ability of the kidney is normal, and it contains 6–8 g. of solids per 100 c.c. [Lashmet & Newburgh, 1932]. Coller & Maddock [1935] considered that the total solids to be excreted were of the order of 35–40 g./day, and that, therefore, 500 c.c. of urine per day were needed to carry off the waste products of the body. Chesley [1938] found that below a critical volume of 21–30 c.c./hr. the total solids were always concentrated by the kidney to the same extent, which was the maximum extent of which that kidney was capable, so that the amount of them excreted depended mainly upon the volume of the urine. He also showed that below this critical volume the concentrations of urea and endogenous creatinine were always the same, and he therefore held that the clearances of these substances varied exactly with the output of water at these low volumes. He considered that his findings demonstrated a direct relationship between the glomerular filtration rate and the rate of urine flow, but he did not measure the filtration rate by estimating the inulin clearances. There were no records of this having been done in dehydrated persons, but Shannon [1936] has estimated the creatinine clearances in dogs at very low rates of urine flow. In this species the creatinine and inulin clearances have the same value, and Shannon found that there was a tendency for these clearances to fall when the minute volume of the urine was reduced below 0·5 c.c. but not by more than 10–20%. If the animal had been deprived of water for 24 hr. and had become dehydrated, the creatinine clearances were sometimes lower than they had been earlier in the experiment at comparable rates of urine flow.

The present investigation was prompted by the fact that the vicissitudes of war were forcing people to live and work in places where they were extremely short of water. Little was known about the way in which the healthy kidney reacted to dehydration, and, since this was a matter of cardinal importance, it was decided to study it. To do so, normal men and women were dehydrated experimentally by depriving them of water, and the functions of their kidneys were studied in various ways and under varying degrees of bodily hydration. Some of the experiments have embraced preliminary days on a standardized diet, 3 or 4 days of dehydration, and a period of rehydration. They have been designed to study the effects of food, water and salt upon the daily output of the kidney and they therefore necessarily involved the continuous collection of the excreta. Other experiments, planned for the study of glomerular filtration rates or to follow the effects of large doses of urea, Na and K salts, have lasted only a few hours, and, except for the dehydrating diet, the subjects have not necessarily been burdened with much experimental control except at these times.

Subject and methods

In all, twelve persons have been dehydrated, ten men and two women. Their ages have ranged from 20 to 43. The usual practice has been for them to drink no water for 84, or in one case 108 hr., and to eat only dry food such as biscuits, chocolate and potato crisps, but the dietary ingredients have varied with the dictates of the particular study. Two of the metabolism experiments have been described in some detail [Black, McCance & Young, 1944]: the necessary information about the others will be given when the results are being set out.

Inulin was determined both in urine and plasma by an unpublished method devised by S. W. Cole. This depends upon the colour which develops when fructose, HCl and resorcinol are heated together under standard conditions. Resorcinol is a more satisfactory and sensitive reagent than diphenylamine. The intensity of the colour was measured in a photoelectric colorimeter. Diodone was determined by Alpert's [1941] method. For the measurement of the glomerular filtration rates and renal plasma flows in the hydrated subjects, 3·0 g. of inulin and 2·0 c.c. of diodone were injected intravenously as a priming solution [Smith, Goldring & Chasis, 1938] in 2·5 c.c. of 'normal' saline. This was followed by a maintenance infusion which contained 4·0 g. of inulin and 6·0 c.c. of diodone in 50 c.c. of 'normal' saline. In all these experiments the subjects emptied their bladders after the maintenance infusion had been running for about 20 min. The exact time was noted, and then at intervals of about 30 min. the subjects emptied their bladders voluntarily till two or three samples had been collected. They found no difficulty in doing this. To assist them the maintenance infusion was stopped for 1 or 2 min. and the subjects voided their urine standing in the natural position. Men only were used for these experiments. The blood for analysis was taken by vein puncture midway between one urine collection and the next.

Urine samples were preserved with toluene, 'weighed solids' were determined by weighing the residue after 5 c.c. of urine had been dried overnight at 93° C. The same pipette was always used for these measurements. The chlorides in the plasma were determined by Sendroy's [1937] iodine titration method. Chlorides in the urine, urea, Na, K, phosphates and other radicles were determined by the methods given by McCance [1937] and McCance & Widdowson [1937].

Presentation and discussion of the results

The inulin and diodone clearances

These results have already been reported in a brief note [Black, McCance & Young, 1942]. It is only necessary here to state that dehydration, uncomplicated by starvation but sufficiently severe to make the subjects lose 4–7 % of their body weight, slightly reduced the inulin clearances of three subjects and made no difference to a fourth. At the same time dehydration appeared to increase the diodone clearances of three of the men and to bring about a small fall in one. It is evident therefore that the glomerular filtration rates of these men, and also their renal plasma flows, were little changed by their dehydration. These are important points, not only in themselves but because they mean that the changes which characterize the urine during dehydration of this severity must be essentially the result of alterations in tubular activity.

The effects of large doses of NaCl, KCl *and urea*

In general, all these experiments were carried out in the same way. On the morning after a normal evening meal and night, a strong solution of the salt was administered, and the effect upon the volume of the urine and upon the composition of the plasma was followed during the next few hours. The subject was then dehydrated for 3 days in the way already described, the salt solution was given and, as before, the plasma and urine were collected periodically for some hours. Somewhat similar experiments were carried out by Adolph [1921], but at that time no samples of blood appear to have been taken for analysis, and very little data about the urine were given.

(*a*) NaCl. Two persons were used for these tests and both responded in the same way, so the results for only one of them will be described. Miss H. drank 500 c.c. of a solution containing 18 g. NaCl on each occasion and a summary of the findings is given in Table 1. It will be noted that the effect

TABLE 1. The effect of taking 500 c.c. of 3·6 % NaCl on the secretion of urine during dehydration

	Urine volume c.c./min.		Urine urea m.mol./l.		Urine Na m.eq./l.		Urine K m.eq./l.		U/P osmotic ratio*	
Time	Normal	Dehydrated	Normal	Dehydrated	Normal	Dehydrated	Normal	Dehydrated	Normal	Dehydrated
Before salt	0·46	0·36	490	588	148	205	136	59	3·10	4·24
After salt 1	1·93	1·56	178	280	249	305	69	51	2·61	3·23
After salt 2	1·57	1·65	213	235	269	322	97	36	2·77	3·36

$$* \text{ U/P ratio} = \frac{\text{m.mol. of urea} + 2 \text{ (m.eq. of Na} + \text{K) in the urine}}{\text{m.mol. of urea} + 2 \text{ (m.eq. of Na} + \text{K) in the plasma}}.$$

of the salt solution was essentially the same when she was normal and dehydrated and consisted in: (1) A diuresis. (2) A fall in the concentration of urea in the urine. This was partly a dilution effect due to the forced diuresis. From the data given, however, it will be clear that there was a rise in the output of urea per minute, the result presumably of the increased output of water, for it is well known that the magnitude of the urea clearance depends upon the rate of excretion of water. (3) A rise in the concentration of Na in the urine. This corresponded to a rise in the serum Na which went up from 320 to 328 mg./100 c.c. when Miss H. was 'normal', and from 328 to 348 when she was dehydrated. (4) A fall in the concentration of K in the urine, but a small one relative to the increase in the minute volume. It was not observed when the other subject was fully hydrated. Since the rise in the output of water never led to the expected fall in the concentration of K in the urine, and once to no fall at all, it is evident that the excretion of K was being regulated by several factors (see later). (5) A fall in the osmotic U/P ratio. This was not expected, but it seems to be a general finding in this type of diuresis if the output of water is initially low.

(*b*) KCl. M.T. took 12 g. of KCl by mouth in 100 c.c. of water, once when he was normally hydrated and once when he had lost about 4 % of his body weight by dehydration. His results are given in Table 2. It will be seen that M.T. reacted to the KCl in very much the same way on both occasions, and the changes in his serum K were also identical, the fasting values being 15·2 and 15·4 mg./100 c.c. and the figures 1½ hr. later 20·2 and 20·4 mg./100 c.c. The only finding which needs individual comment is the excretion of Na, which was evidently accelerated on both days by taking the K. It is this

TABLE 2. The effect of KCl on the secretion of urine during dehydration

Time	Urine volume c.c./min.		Urine K m.eq./l.		Urine Na m.eq./l.		Urine urea m.mol./l.		U/P osmotic ratio (see Table 1)	
	Normal	Dehydrated	Normal	Dehydrated	Normal	Dehydrated	Normal	Dehydrated	Normal	Dehydrated
Before KCl	0·80	0·54	69	97	115	149	372	357	2·45	2·80
After KCl 1	4·20	3·30	110	121	167	145	90	97	2·05	2·05
After KCl 2	2·82	1·80	131	205	148	124	150	155	2·25	2·60

interrelationship between the excretions of Na and K which prevented a greater fall in the concentration of K in Miss H.'s urine during her salt diuresis and made M. T. when normally hydrated secrete a higher instead of a lower concentration of Na in his urine (Table 2). As in Table 1 the fall in the osmotic U/P ratio will be noted.

(*c*) *Urea.* 35 g. of urea dissolved in 350 c.c. of water were slowly injected intravenously into Miss T. The time taken over this operation was about 40 min. Table 3 shows the effect. It will be seen that: (1) There was a rise

TABLE 3. The effect of giving 35 g. of urea in 350 c.c. of water intravenously

Time	Serum urea m.mol./l.		Urine volume c.c./min.		Urine urea m.mol./l.		Urine Na m.eq./l.		U/P osmotic ratio (see Table 1)	
	Normal	Dehydrated	Normal	Dehydrated	Normal	Dehydrated	Normal	Dehydrated	Normal	Dehydrated
Before injection	4·4	5·0	0·48	0·29	357	487	120	125	2·55	3·05
After injection 1	18·7	21·3	2·05	0·97	533	742	54	15	2·25	2·55
After injection 2	17·3	19·3	2·41	0·88	450	792	99	17	2·28	2·71

in the output of water on both occasions, but a smaller one during dehydration. (2) There was a similar rise in the serum urea on the two occasions. This was accompanied by an increase in the concentration of urea in the urine. (3) There was a fall in the concentration of Na in the urine. The increase in the urine volume was enough to explain this when Miss T. was normally hydrated but not when she was dehydrated, and this fall in the output of Na was accompanied by an equally great fall in the output of Cl. The serum Na did not change, but the serum Cl fell from 391 to 359 mg./100 c.c. when Miss T. was dehydrated, and these changes are probably examples of the ability of urea to produce an alkalosis, a phenomenon which was at one time briefly reported by Adolph [1925]. The fall in the serum Cl was probably the cause of the diminished excretion of Cl but the Na results are not so easily explained. (4) The U/P osmotic ratio fell on both occasions.

A diuresis due to a hypertonic solution might have been expected to take place in a dehydrated person without a fall in the osmotic pressure of the urine or in the U/P osmotic ratio, but the present experiments have all shown that under such conditions the U/P osmotic ratios do fall. It is difficult to explain this observation because it is not known what controls the output of water when the kidney is secreting a urine with the highest specific gravity of which it is capable. It may be the total osmotic pressure of the urine; it may be the concentration of some specific ingredient. Chaussin [1920], Adolph [1923] and others [Baird & Haldane, 1922; Davies, Haldane & Peskett, 1922] have all considered this problem, and it will be mentioned again later. Be that as it may, the present results are in complete agreement with those of Adolph [1923] and show that dehydrated and normal persons react in essentially the same way to these osmotic violations of their internal environment. The kidney commences at once to excrete the NaCl, KCl or urea, but because of its well-known osmotic limitations it is obvious that it would be forced to draw upon water already present in the body in order to do so completely. Thus the administration of much of a solution more concentrated than the kidney can excrete will inevitably make a person more dehydrated. The salt may be excreted, in which case water already in the body will be excreted with it. If, however, the salt is retained, the osmotic pressure of the body, already higher than normal, will be raised still more. The difference between the osmotic pressure of the administered solution, however, and that of concentrated human urine is no direct indication of the harm which its ingestion is likely to produce.

In one respect the experiments with NaCl and KCl make an interesting contrast with the one in which urea was used. No new principles are involved, but it will be noted that in the two former there was a considerable rise in the concentration of Na and K in the urine, but the changes in the plasma were relatively small. Consequently, the U/P ratios of the ingested ion rose. In the urea experiment there was a large rise in the concentration in the plasma, and consequently, although the urinary concentrations also rose, the U/P ratio fell—and fell, moreover, to less than half its original value.

24 *hr. volumes and total solids*

The volumes of urine passed daily by these subjects during dehydration varied from 335 to 864 c.c., i.e. from 0·23 to 0·59 c.c./min., but only on one occasion did the minute volume exceed 0·48 c.c. Chesley [1938] found volumes as low as 0·156 c.c./min. following complete abstinence from water for 30–60 hr. The lowest volume passed by Nadal, Pedersen & Maddock's [1941] fasting subject in 24 hr. was 409 c.c., but one of Coller & Maddock's [1935] volunteers secreted only 273 c.c. in 24 hr. when he was taking a dry maintenance diet. Table 4 shows the daily urine output of two subjects who were carrying out balance experiments [Black *et al.* 1944]. It will be noted that the output of water fell on the first day of the dehydration period and then remained very constant. On this first day the sum of the urea and mineral substances excreted was less than the quantity passed when each person was hydrated. This was largely due to a fall in the output of urea.

TABLE 4. The effect of dehydration upon the specific gravity of the urine and upon the excretion of urea, minerals and total solids

Day	Urine volume c.c./day	Specific gravity	Weighed solids g./100 c.c.	Weighed solids g./day	Urea and minerals* g./day	Urea g./day
		Subject D.B.				
Prelim. average	1931	1012	2·0	39	34	20
Dehydr. 1	666	1030	5·3	35	29	15
2	652	1033	7·2	47	36	21
3	615	1037	8·7	55	38	24
Rehydr. 1	597	1033	7·6	45	39	27
2	1195	1015	3·7	44	31	26
3	1886	1012	2·2	42	36	22
		Subject J.H.				
Prelim. average	1935	1012	1·6	31	26	15
Dehydr. 1	570	1035	5·3	30	22	13
2	590	1034	5·4	32	30	19
3	595	1034	5·5	33	30	20
4	605	1035	6·3	38	32	21
Rehydr. 1	506	1036	7·1	36	26	20
2	1746	1010	—	—	31	23
3	1990	1010	1·8	36	30	18

* $Na+K+Ca+Mg+Cl+PO_4+SO_4$.

On the second and subsequent days of dehydration, however, both men excreted more urea, and these findings confirm those of Coller & Maddock [1935]. There was little change in the daily excretion of mineral substances during these dehydration periods [Black *et al.* 1944]. In D.B. the output of 'weighed solids' increased considerably more than that of urea and minerals as dehydration progressed, and it remained high on the rehydration days. The increase in the undetermined fraction of the weighed solids accounted for the rise in the specific gravity of the urine on the second and third days of D.B.'s dehydration. Price, Miller & Hayman [1940] have shown that the proportion of the specific gravity accounted for by measuring the urea, creatinine and all the inorganic salts varies from 70 to 90% according to the amount of protein in the food. Although the same diet was given to the present subjects throughout the experiments, there was evidence that their endogenous metabolism altered during the period of dehydration [Black *et al.* 1944], and this may have been the cause of the increased excretion of undetermined solids.

Effects produced by controlled rehydration

Table 5 shows the effects of controlled rehydration upon the volume of the urine and upon two of its constituents. All these subjects were on standardized diets before, during and after the days under discussion. The nature and object of the experiments on G.L., O.S. and P.B. will be described later. It will be noted that a huge increase in the consumption of water invariably led to a fall in the output of water. This observation, which seems very remarkable

TABLE 5. The effect of controlled rehydration upon the volume of the urine and the percentage of urea and of chlorides in it

Subject		Intake of water + water of metabolism c.c./24 hr.	Urine volume c.c./24 hr.	Urea mg./100 c.c.	Cl mg./100 c.c.
D.B.	D*	680	615	3980	777
	A*	5230	597	4600	434
J.H.	D	474	605	3450	930
	A	3804	506	3900	605
G.L.	D	400	635	2580	1230
(High salt intake)	A	3100	510	3140	1000
G.L.	D	400	425	4170	670
(Low salt intake)	A	3120	420	4370	318
O.S.	D	400	690	1840	1320
	A	2950	610	2590	945
P.B.	D	400	720	2530	1315
	A	4390	607	3730	580

* D = during the last 24 hr. of dehydration; A = during the first 24 hr. after rehydration began.

at first sight, was made by Coller & Maddock [1935], but they do not appear to have realized its significance. The effect, which is always coupled with a fall in the concentration of urinary Cl and a rise in the concentration of urea, can be produced most easily when the diet contains ·9 g. or more of salt a day, but G.L. showed it even when there was a much smaller quantity in his food. In all these subjects the concentration of urea in the urine was higher on the first day of rehydration than on any preceding one. The output of urea sometimes rose and sometimes fell according to the magnitude of the fall in the volume of the urine and the rise in the percentage of urea in it. As soon as rehydration was completed the urine volumes became as great as they had been during the preliminary period.

Salt intakes and urine volumes

It will be seen in Table 4 that when D.B. and J.H. were dehydrated they were both passing comparatively large volumes of urine, and it was felt that the main reason for their size might be the amount of salt and nitrogenous matter which the subjects had consumed. To test this the following experiment was arranged. Three subjects were placed upon a standardized dry diet which contained little salt. For the first 3 days G.L. and P.B. took 10 g. of NaCl additional to their food and all drank as much water as they wished. On days 4, 5 and 6 all the subjects abstained from water but maintained their intakes of food and salt. On day 7 all the subjects rehydrated themselves. On day 8 G.L. and P.B. gave up taking the added NaCl and O.S. began to do so, and on this and the following day a free intake of water was encouraged. On day 10 the second dehydration period began and lasted till the end of day 12. The last day was again devoted to studying rehydration effects. The results of this experiment are shown in Table 6, and the influence of the salt intake on the urine volume is clearly demonstrated by the first two columns. The same effect is shown by G.L.'s results in Table 5.

TABLE 6. The effect of the intake of salt upon the volume, specific gravity, osmotic pressure and the urea-mineral relationships of the urine

	Average urine volume c.c./day		Average specific gravity		Average conc. of Cl m.eq./l.		Average conc. of urea m.mol./l.		Average conc. of urea + 2 (Na + K) m.osmol./l.	
Subject	Low salt	High salt	Low salt	High salt	Low salt	High salt	Low salt	High salt	Low salt	High salt
G.L.	413	700	1035	1031	163	332	620	356	1049	1036
O.S.	371	815	1033	1033	118	344	507	227	890	993
P.B.	365	633	1035	1034	164	339	564	386	1080	1160

The urea clearances

Table 7 shows some data about the excretion of urea by D.B. and J.H. Similar figures could have been given for the other subjects. It will be noted that with the onset of dehydration the clearances (UV/B) fell, and that as

TABLE 7. The effect of dehydration and partial rehydration upon the treatment of urea by the kidney

Subject	Day of exp.	Urine volume c.c./min.	Blood urea mg./100 c.c.	Urine urea mg./100 c.c.	U/P urea ratio	Urea clearance c.c./min.	Urine chloride m.eq./l.
D.B.	Prelim. av.	1·34	33	1040	32	42·0	86
	Dehydr. 1	0·46	40	2210	55	26·0	217
	2	0·45	54	3230	60	27·0	202
	3	0·43	58	3980	69	29·5	219
	Rehydr. 1	0·41	50	4600	92	38·0	122
J.H.	Prelim.	1·34	20	780	38	52·0	77
	Dehydr. 1	0·40	28	2250	81	31·8	268
	2	0·41	42	3200	77	31·4	246
	3	0·41	44	3400	77	31·8	244
	4	0·42	47	3450	74	30·2	263
	Rehydr. 1	0·35	45	3900	87	30·5	170

dehydration progressed the blood ureas rose but the clearances did not change again. Urea clearances are well known to vary with the urine volumes when these are less than 2·0 c.c./min. Incidentally, this is equally true for dehydrated as for normal persons, for when Miss H., M.T. and other dehydrated subjects took large doses of hypertonic salt (Tables 1 and 2), the resulting diuresis always raised the urea clearances in the characteristic fashion. It was, therefore, the fall in the output of water with the onset of dehydration which reduced the urea clearances of D.B. and J.H. and hence (see Table 4) the total amount of urea excreted. The urea which was retained accumulated in the body fluids, and raised the concentration in the blood. This in turn allowed the output to rise without any change taking place in the clearances. Some part of the rise in the blood urea during dehydration was due to the increased production of urea which was taking place at that time [Black *et al.* 1944], and it was presumably this extra production which forced the outputs to rise above their pre-dehydration levels. It will be appreciated from Table 7 that throughout the 3 or 4 days of dehydration the percentage of urea in the urine rose *pari passu* with that in the blood. Had it not done so the U/P urea ratio and the clearances would have fallen. There is no evidence that either D.B. or J.H. ever produced the highest concentration of urinary urea of which they were capable, and it must remain uncertain how much further they could have raised the percentage of urea in their urines under the conditions to which they were subjected at that time. The administration of urea to Miss T. when she was dehydrated, however, probably raised the concentration of urea in her urine to its maximum, for in spite of a rise in urine volume her urea clearances remained low until the blood urea began to fall.

The most interesting figures in Table 7 are those for the first day of rehydration. In spite of a fall in urine volume D.B.'s clearance rose and J.H.'s did not fall. The percentage of urea in the plasma fell and that in the urine rose, and both these changes increased the U/P ratio. These increases, coupled with a fall in the minute volume of the urine, are a direct refutation of Chesley's [1938] contention that when the urine flows are reduced below a certain 'critical' limit, the urea clearances and the urine volumes necessarily vary together.

A general explanation of these findings will now be given, but there are many difficult points still to be cleared up. (*a*) The volume of the urine varied with the intake of salt (Table 6), or, more precisely, with the amount entering the distal part of the nephron [Shannon, 1942 *a*, *b*], where there seems to be a limiting concentration for chloride [Adolph, 1921; Baird & Haldane, 1922] and for other osmotically active substances [Davies, Haldane & Peskett, 1922]. Table 7 shows that in D.B. and J.H. the urinary Cl reached its ceiling on the first day of dehydration. These concentrations were not so high as the 'maximum' set up by Miss H. or by Davies *et al.* [1922] subject after large doses of NaCl by mouth; neither were they so high as the concentration produced by O.S., G.L. and P.B. on their high salt diets. J.H., moreover, one morning some time after this experiment took 20 g. of NaCl in 400 c.c. of water and subsequently excreted 1·14% of Cl in his urine (322 m.eq./l.). It may be assumed therefore that both men could have produced higher concentrations of Cl in the urine given the appropriate conditions. Nevertheless, the effects of rehydration show that the amount of salt to be excreted must have been one of the agents fixing and maintaining the output of water during the days of dehydration. With the onset of rehydration the concentration of chloride in the plasma fell and presumably less reached the distal part of the nephron. Possibly also there was some change in the hormone balance. At all events, so much less Cl presented itself for excretion that the output of water fell as did the percentage of Cl in that water (Table 7). This last enabled the kidney to raise the concentration of urea [Chaussin, 1920]. (*b*) Shannon [1936] showed that the glomerular filtration rates (measured by the creatinine clearances) and the urea clearances of dogs tended to increase with rehydration even before the urine volumes began to rise. He found too that the urea/creatinine clearance ratios were higher during rehydration than in dehydration. If the kidneys of our subjects were responding to rehydration in the same way, one or both of these changes may have accounted for the rise in D. B.'s urea clearance on the first day of rehydration. In keeping with this is the fact that D. B.'s glomerular filtration rate did fall slightly during dehydration and presumably therefore may have returned to normal when rehydration began.

The excretion of the minerals

It was shown in the balance experiments [Black *et al.* 1944], and in Table 4, that the output of Na, K and Cl and of total minerals changed little during dehydration. Table 8 now shows that D. B.'s output of Na per litre of urine

TABLE 8. The relationship of urine volume, and plasma levels to the excretion of Na, K and Cl

	Plasma			Urine			
Day of exp.	Na mg./100 c.c.	K mg./100 c.c.	Cl mg./100 c.c.	Volume c.c./day	Na mg./100 c.c.	K mg./100 c.c.	Cl mg./100 c.c.
Prelim. average	340	19·3	377	1931	184	107	301
Dehydr. 1	346	19·0	388	666	370	470	769
3	369	15·1	406	615	483	520	777
Rehydr. 1	354	16·0	360	597	332	336	434
2	340	16·6	374	1886	137	129	255

was higher on the third day of dehydration than it had been on the first. This may reflect the rise in the serum Na, but the concentration of K was also higher in spite of a fall in the serum K. Furthermore, on the first day of rehydration the percentage of K in the urine fell greatly although the serum K was rising, and the urinary concentration of Na was lower than it had been on the first day of dehydration, although the serum Na was still above its normal level at that time. It is obvious, therefore, that the excretion of these minerals was not regulated, as was that of urea, simply by their concentrations in the plasma. Recent work, reviewed by Shannon [1942*b*], has indicated that so far as NaCl is concerned the suprarenal and gonadal hormones, and the anti-diuretic hormone of the pituitary, may all be involved.

The relationship between the excretion of osmotically active substances and the urine volume

It has generally been assumed [Smith, 1937] that the extent to which the urine can be concentrated is limited by the total osmotic pressure which it exerts. A more complicated but possibly more correct view may be that the limiting factor is the sum of the U/P ratios of all the urinary constituents. The reciprocity between Cl and urea, which was so assiduously studied by Chaussin [1920], can most easily be explained along such lines. The effect of controlled rehydration, moreover (Tables 4, 5 and 7), and the effects of salt (Table 6), can be accounted for best in that way. There is some evidence, however, which suggests that it is more often the specific effect of one of the urinary constituents which fixes the volume [Adolph, 1923]. The concentration of urea in human urine, for instance, seldom exceeds 4%, and it is well known [Davies *et al.* 1922] that there is a ceiling for Cl, or for Cl and HCO_3, and that a diuresis results if the kidney is called upon to excrete more of these substances than it can accommodate in the volume of urine suggested by the water requirements of the body at that time. These two mechanisms are not incompatible and, given the appropriate conditions, either could probably be reproduced in the same person. In other words, both operate. According to some authors, however [Baird & Haldane, 1922; Davies *et al.* 1922; Gilman & Kidd, 1938], the maximum concentrations of Cl and of urea may coexist. The present experiments suggest that they can only do so under very special conditions. The experiment, which is illustrated in Table 6, showed that the addition of 10 g. of NaCl to the diet increased the urine volumes by about 300 c.c. (Incidentally this volume was insufficient to accommodate 10 g. of NaCl even at the maximum concentration of about 2% (342 m.eq./l.). Yet fully 10 g. of NaCl were excreted when the intake of salt was raised, and considerably more than had been excreted when the intake of salt was low. The two facts which integrate these observations are: (1) when the subjects were on a low salt intake the concentration of Na in the urine was far below the maximum; (2) when the intake of salt was high the total volume of the urine was always more than enough to accommodate 10 g. of NaCl at the accepted maximum concentrations.) It is evident, therefore, that the NaCl to be excreted was one of the factors fixing the urine volumes when the intake of salt was high, and, since at that time the urinary concentrations were round about the highest which the body can produce, the Cl to be excreted may have been the only factor controlling the output of water. The present experiments do not point to any one substance as being solely responsible for fixing the urine volumes when the intake of salt was lower, but the effects of rehydration on G.L. at that time, and upon D.B. and J.H., suggest that NaCl must have been playing some part. These subjects all showed the urinary changes characteristic of rehydration in controlled stages, although none of them had had maximum concentrations of Cl in their urines during dehydration (see Table 7). Furthermore, the specific gravity of the urines, and the average osmotic pressure exerted by the urea together with the Na and K salts, were about the same whether the intakes of salt were high or low (see Table 6). The contributions of urea and of the minerals, however, varied very much, and hence it seems probable that the total osmotic pressure for these substances had the final say in the volume of water to be excreted during dehydration. It is possible that, by raising the blood ureas, 'maximum' concentrations of urea could be produced in the urine, and that this could be done without reducing the concentration of minerals, but the present experiments give no indication that during dehydration 'maximum' concentrations of urea and of minerals should be expected simultaneously. Further work on these matters is in progress.

Practical considerations

Leaving aside the difficult points of detail which often tend to obscure the general principles, the present experiments clearly show that raising the salt intake of a person who is kept short of water makes his dehydration worse by increasing the volume of his urine. Diet during dehydration, therefore, should be as free of salt as possible and, logically, everything should be done to diminish the urinary solids calling for excretion. Whether sea water should be taken by a shipwrecked mariner demands a little more thought, for this involves the consumption of water as well as salt. If the subjects G.L., O.S. and P.B. had taken their 10 g. of salt in the form of sea water (or 3·3 % NaCl), and if we were to consider only the increased output of water and salt and the volume of sea water drunk, we might reach the interesting if somewhat dangerous conclusion that the men would have been none the worse for their potations. Further reflexion, however, suggests that they would have been worse, for their plasma sodiums, and, consequently, in all probability the osmotic pressure of their body fluids, would have been higher, and, had they taken more than 10 g. of NaCl, or had their basal diets not had very little salt in them, they would certainly have been worse, for the concentration of Cl in their urines had already reached its limits, and consequently the next 300 c.c. of sea water would have had a much more disastrous effect.

The results of the present experiments, and a general consideration of the known facts about the specific gravity and other characteristics of the urine passed during a period of water deprivation, suggest that a dehydrated man can do himself no good by drinking his own urine. By so doing he is merely asking his kidneys to repeat work which they have already done, and cannot be expected to do better.

Summary

1. In human dehydration produced by 3 or 4 days without water, the glomerular filtration rates and the diodone clearances fell little if at all in men who had lost up to 7% of their body weights.

2. Large doses of NaCl, KCl and urea led to diuresis even during dehydration. The increased flow of urine was accompanied by a fall in the urine/plasma osmotic ratio, and each diuretic produced specific changes in the composition of the plasma and the urine.

3. When the diet was standardized the daily output of water depended upon the intake of salt. When this was moderately high (5–15 g./day), the output of water could always be demonstrated to fall with the onset of rehydration, and the urine at this time contained more urea and less NaCl per litre than it had done during the days of dehydration.

4. Dehydration reduced the urea clearances, mainly if not solely by reducing the urine volumes. In the early stages of rehydration the clearances did not fall further—and in at least one case they rose—in spite of the decreased output of water characteristic of that period.

5. The output of minerals during dehydration and rehydration was regulated by factors other than their concentrations in the plasma.

6. When the intake of NaCl was sufficiently high the output of water may have been regulated solely by the salt presenting itself for excretion, but this was certainly not so when the intake of salt was low. It is suggested that the total osmotic pressure of the urine was responsible at all times.

The authors are much indebted to the subjects for putting up with a good deal of discomfort on their behalf. W. F. Y. received a personal grant from the Medical Research Council.

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