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Am J Physiol Regulatory Integrative Comp Physiol 239:476-482, 1980.

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Thirst following water deprivation in humans

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ROLLS, BARBARA J., R. J. WOOD, E. T. ROLLS, H. LIND, W. LIND, AND J. G. G. LEDINGHAM. *Thirst following water deprivation in humans.* Am. J. Physiol. 239 (Regulatory Integrative Comp. Physiol. 8): R476–R482, 1980.—The effect of 24-h water deprivation and subsequent drinking on systemic fluid balance and subjective sensations has been determined in human beings. The deprivation caused significant intracellular and extracellular depletions, thirst, and a dry unpleasant tasting mouth. During rehydration, subjects drank 65% of their total intake within 2.5 min. The marked decrease in drinking rate thereafter, and the alleviation of thirst, occurred before plasma dilution had become significant. This attenuation of drinking was subjectively attributed to stomach fullness. Presystemic factors may therefore be important for drinking termination in humans. Within 20 min systemic deficits were removed, but intermittent drinking continued at a low rate, reportedly to alleviate unpleasant oral sensations. Following rehydration, the concentrated urine of hydropenia had disappeared. However, the excretion of solute-free water varied between subjects. Plasma renin activity was significantly elevated by water deprivation, while after rehydration this activity had decreased to levels not significantly different from predeprivation values.

cellular dehydration; extracellular dehydration; drinking; subjective sensations; renin activity; excretion

DESPITE CLINICAL PROBLEMS OF THIRST and the recent advances in the understanding of the controls of drinking in experimental animals, relatively little is known about thirst in humans. Much of the work on human drinking has centered on the issue of whether thirst is due to a dry mouth or to a general depletion of body fluids. Few measures of plasma variables such as osmolality have been made in relation to drinking, and if measures were taken, the techniques available were unsophisticated compared to those currently used. The few studies of possible stimuli of thirst in human beings indicate that hypertonicity, induced for example by hypertonic NaCl, is a potent thirst stimulus (22), and that the subjective sensation accompanying this stimulus is a dry mouth (5). Thirst is also associated with depletion of the extracellular fluid compartment arising from vomiting, diarrhea, or hemorrhage. That extracellular volume reduction is a thirst stimulus in humans has been shown experimentally in studies of sodium depletion, which leads to excessive thirst (13). Thirst may be experienced by patients suffering chronic renal failure, in which plasma sodium concentration is low and renin levels are high (4). This thirst could be mediated by the renin-angiotensin system, since bilateral nephrectomy reduced both thirst and renin levels in these patients. Extracellular fluid depletion may be associated with an unpleasant, dry oral sensation (13).

To obtain a more precise understanding of how signals from the cellular and extracellular fluid compartments may contribute to the initiation and the termination of drinking in human beings, it is necessary to measure the changes in these compartments that are associated with the initiation and termination of drinking, as has been done for the rat, dog, and monkey (19). This is the aim of this study. To assess these changes, plasma samples were taken repeatedly, and measurements were made of plasma sodium concentration and osmolality (to estimate cellular hydration), and plasma protein and hematocrit (to estimate plasma volume), as well as plasma renin activity, to assess the state of the renin-angiotensin system. The samples of plasma were taken before and after 24 h of fluid deprivation. During drinking following the deprivation, fluid intake was monitored and plasma samples were taken repeatedly. Urine composition was also assessed during the experiment. An advantage of using humans was that the subjective sensations associated with dehydration and rehydration could be monitored. Thus the first systematic investigation of both the physiological factors and the subjective sensations associated with deprivation-induced drinking in humans is reported here. This type of investigation must be basic to our understanding of thirst in human beings.

METHODS

Subjects. The subjects were five males aged 24–33 yr; they weighed 63–84 kg (69.3 ± 4.0, mean ± SE). All were healthy nonsmokers.

Deprivation and rehydration. On *day 1*, subjects were instructed to take breakfast as usual but not to take any diuretics such as tea or coffee. The fluid deprivation began between 10 and 11 A.M. and the subjects were instructed not to take drinks of any kind. They were to eat normally, but were not allowed moist foods, such as salads, fruit, or soups. They were asked to engage in their usual activity during the dehydration period. On *day 2*, after 24 h of deprivation the subjects were allowed to rehydrate. Subjects were offered tap water at room temperature from a 1,000-ml jug that was replaced on a balance between drinks. Water intake was monitored for 1 h, during which time no food was available. No further fluid or food was allowed for 90 min after the termination of the rehydration period so that the renal response to rehydration could be assessed.

Subjective ratings. Immediately before rehydration, subjects were asked how many cups of water they thought they could drink. Before the dehydration and again before the rehydration they were asked to give answers to the following questions using a visual analogue scale (10-cm line), How thirsty do you feel now? (not at all thirsty——very thirsty); How pleasant would it be to drink some water now? (very unpleasant——very pleasant); How dry does your mouth feel now? (not at all dry——very dry); How would you describe the taste in your mouth? (normal——very unpleasant); How full does your stomach feel now? (not at all full——very full). The visual analogue scale was an ungraduated 10-cm line marked at opposite ends with the end values shown in parentheses above. Each visual analogue scale was on a separate slip of paper. Thus, for example, the scale for thirst was on a slip of paper marked "How thirsty do you feel now," and was a plain 10-cm line marked at one end "not at all thirsty" and at the other end "very thirsty." The subject was asked to mark a point on the line to indicate his response to the question. Changes in rating were later calculated for each subject as a difference (in cm) from the position on the line of their initial rating. The separate slips of paper with these questions were given to the subjects to be filled in at regular intervals (2.5, 5, 7.5, 10, 12.5, 15, 20, 30, 40, 50, and 60 min after the initiation of drinking) while the blood was being drawn and when the subjects were not drinking. On each occasion a new slip of paper inscribed with the question and the visual analogue was used.

Subjects were also asked to describe how they felt during the deprivation and rehydration periods. For example, they attempted to explain why they were drinking at any particular time.

Body fluid sampling procedure. On the 1st day, immediately preceding the start of the dehydration period, subjects were asked to empty the bladder and collect a small sample of urine. Urine was again collected 1 h later and the total volume produced was measured and a sample was taken. After filling in the preliminary questionnaire on height, weight, and subjective sensation, a blood sample was drawn by puncture of an arm vein. Of this sample, 20 ml were taken off into vials prepared with EDTA, centrifuged at 2,700 rpm for 10 min at 4°C, and frozen for later renin activity assay. The remaining small volume of blood was taken into a heparinized tube for centrifugation and chemical analysis.

On the 2nd day, 24 h after the start of the deprivation period, a questionnaire to assess subjective sensations was administered before the subjects were asked to empty the bladder and provide a urine sample. An intravenous line was then inserted into an arm vein for the repeated withdrawal of blood samples throughout the experiment. When blood was not being drawn, the catheter was filled with sodium heparin (250 U/ml) in isotonic saline. At the time when the subject was offered drinking water a blood sample was drawn, comprising 20 ml for renin assay and a small volume for chemical analysis. Blood samples of 2.5 ml were drawn at 2.5, 5, 7.5, 10, 12.5, 15, 20, 30, 40, and 50 min thereafter. At 60 min an additional 20 ml was taken for renin assay. At the end of the drinking period, the intravenous line was withdrawn and the subject was again asked to collect urine. The total volume of urine produced since emptying the bladder before the start of the experiment was recorded and a sample taken for chemical analysis. This procedure of measuring urine volume and taking a urine sample was repeated at 90 and 120 min after the start of the experiment.

Chemical analyses. Plasma and urine osmolality were determined with a semiautomatic osmometer (Precision Instruments model "Osmette S") and plasma and urine sodium concentrations were measured with an internal standard flame photometer (Instrumentation Laboratory, model 343). Plasma protein was calculated from refractive index determined with a constant temperature refractometer (Bellingham and Stanley Immersion model, Abbe form). Blood samples for hematocrit determination were spun in heparinized capillary tubes for 5 min at 4,000 rpm. In reading the red cell layer, no correction was made for trapped plasma and the buffy coat was excluded from this measurement.

Renin assay. The frozen plasma samples obtained during the experiment were assayed for renin activity by a radioimmunoassay method (20).

Statistical analyses. Analyses of variance were performed on all the subjective and physiological data by a within subjects design. The significance of individual effects was determined from a Newman-Keuls multiple comparisons test.

RESULTS

Plasma changes produced by deprivation. Predeprivation levels of the plasma variables and their elevated values after 24-h water deprivation (*time 0*, i.e., just before access was given to drinking water) are shown in Fig. 1. Plasma osmolality was increased from a mean predeprivation value of 282.4 ± 2.2 mosmol/kg to a mean postdeprivation value of 289.9 ± 1.8 mosmol/kg H_2O ($P < 0.001$). Plasma sodium concentration increased from a mean value of 140.4 ± 0.7 to 143.3 ± 0.6 meq/l ($P < 0.001$) over the same period. Plasma protein increased in concentration from a mean predeprivation value of 7.28 ± 0.20 to 7.72 ± 0.24 g/100 ml after deprivation ($P < 0.001$). Blood hematocrit also increased with deprivation from a mean value of 47.2 ± 1.8 to 48.2 ± 2.3% but this change was not significant. Plasma potassium concentration did not change significantly with deprivation. Plasma renin activity did significantly increase over the deprivation period, from 1.73 ± 0.59 to 3.15 ± 0.79 ng·ml^{-1}·h^{-1} ($P < 0.05$). (Significance levels were calculated from the Newman-Keuls test.) The analysis of variance for the whole time period—predeprivation through rehydration—(within subjects, two way) showed a significant overall variation in each of the following plasma variables over the deprivation/rehydration period; osmolality $F(12,48) = 13.88$, $P < 0.001$; sodium $F(12,48) = 12.64$, $P < 0.001$; protein $F(12,48) = 12.45$, $P < 0.001$; hematocrit $F(12,48) = 4.4$, $P < 0.001$; renin activity $F(2,8) = 8.35$, $P < 0.05$.

These changes indicate that the deprivation procedure produces a significant fluid deficit, with a loss of extracellular fluid and decrease in plasma volume, an increase

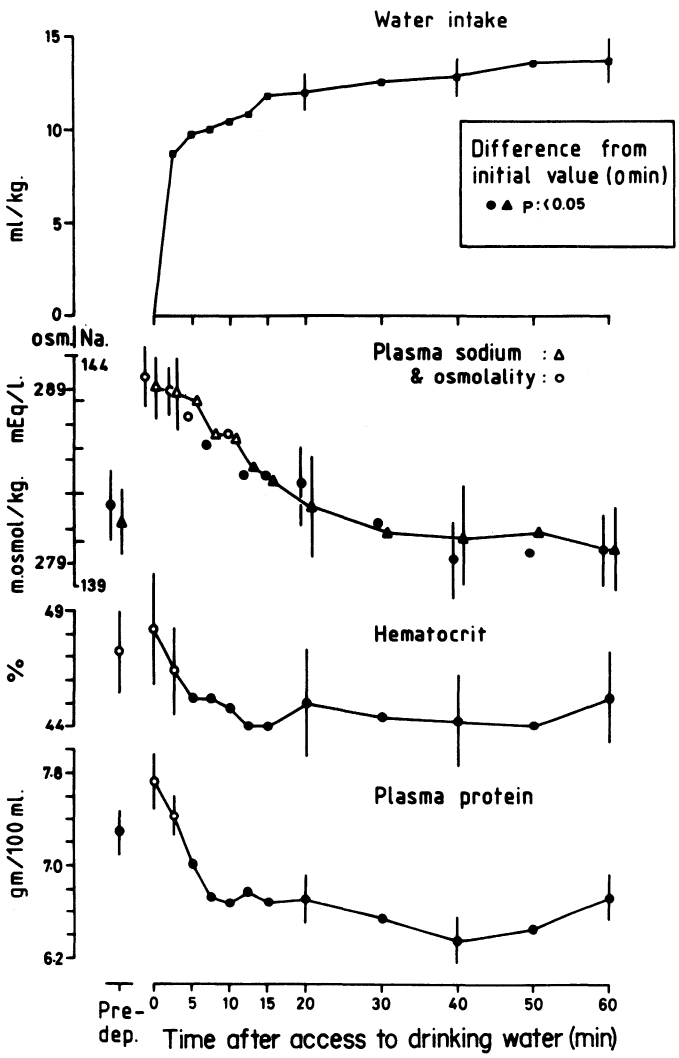

FIG. 1. Effect of 24-h water deprivation and drinking over 1 h of access to water on plasma composition in 5 male subjects. Means ± SE for water intake, plasma sodium concentration and osmolality, hematocrit, and plasma protein concentration are shown. Significant differences from initial, postdeprivation values are indicated by filled symbols ($P < 0.05$).

in renin activity, and increases in plasma electrolyte and solute concentrations.

Urinary changes during deprivation. The analysis of variance showed a significant overall variation in urine composition. Urine osmolality [$F(4,16) = 5.56$, $P < 0.01$]; urine sodium [$F(4,16) = 6.0$, $P < 0.01$]; urine potassium [$F(4,16) = 3.91$, $P < 0.05$], all changed significantly over the dehydration/rehydration period. The rate of urine flow also varied significantly [$F(3,12) = 5.22$, $P < 0.05$], as did the rate of osmolal clearance (C_{osmol}) [$F(3,12) = 4.51$, $P < 0.05$]. Changes within the dehydration period accounted for some of this significant variation (see Table 1, significant differences derived from the Newman-Keuls test). Thus urine osmolality increased from a predeprivation value of 694.6 ± 140.2 mosmol/kg to a postdeprivation value of 1,067.2 ± 49.3 mosmol/kg H_2O ($P < 0.05$), and urine sodium concentration increased from a mean value of 103.5 ± 42.6 to 198.2 ± 13.5 meq/l ($P < 0.05$). Urine potassium concentrations and the rate of osmolal clearance (C_{osmol}) and free water clearance (C_{H_2O}) did not change significantly. Data for the rate of urine flow after deprivation, but before rehydration began, was not obtained, so that a comparison between flow rates before and after deprivation cannot be made. However, it is likely that an antidiuresis occurred during the dehydration in response to the hemoconcentration. The changes in the concentration of the urine are consistent with the reabsorption of water by the kidneys under the influence of antidiuretic hormone.

Drinking during rehydration. Drinking proceeded at a high rate early in the rehydration, with 65% of the total 1-h intake being consumed in the first 2.5 min of access to water (Fig. 1). After 2.5 min, drinking proceeded relatively slowly and the size of individual drinks decreased rapidly. The mean volume of the first draft was 371.7 ± 58.3 ml, whereas the volume of all drafts taken after 2.5 min averaged only 52.4 ± 16.8 ml.

The amount consumed over the rehydration period was significantly correlated with the amount subjects estimated they would drink before the experiment ($r = 0.945$, $n = 10$, $P < 0.001$).

Plasma changes during rehydration. During the 60-min rehydration period, the effect of absorption of the ingested water on plasma variables was marked (see Fig. 1). Plasma dilution became apparent during the first 5 min of drinking, and at 7.5 min plasma osmolality had decreased below the starting level just significantly ($P < 0.05$) (see Fig. 1). However, plasma osmolality did not remain consistently below initial values to a significant degree until 12.5 min ($P < 0.01$). At that time plasma sodium also became significantly less than its initial value ($P < 0.05$). By 15 min, both of these variables were not significantly different from predeprivation levels. No sig-

TABLE 1. *Effect of 24-h water deprivation and drinking on urine composition and excretion*

	Predeprivation, min		Postdeprivation, min			
	0	60	−10	70	90	120
			(0- to 60-min water access)			
Composition						
Urine osmol	632 ±176	695 ±141	1,067* ±49	829 ±50	379 ±164	399 ±139
Urine Na	102 ±33	104 ±43	198* ±14	171 ±16	47 ±29	43 ±18
Urine K	53 ±10	70 ±12	72 ±17	61 ±9	33 ±14	33 ±10
Excretion						
Urine flow, ml/min	1.04 ±0.27		0.93 ±0.14	6.63* ±2.4	2.57 ±0.89	
μeq Na/min excreted	113 ±56		158 ±27	66 ±29	55 ±15	
μeq K/min excreted	74 ±23		54 ±6	100 ±14	56 ±19	
C_{osmol}, ml/min	2.46 ±0.69		2.84 ±0.39	3.79* ±0.36	2.18 ±0.24	
C_{H_2O}, ml/min	−1.42 ±0.59		−1.91 ±0.59	+2.84 ±2.16	+0.39 ±0.86	

Values are means ± SE for 5 male subjects. Urine osmol is osmolality in mosmol/kg H_2O; urine Na is sodium concentration in meq/l; urine K is potassium concentration in meq/l; C_{osmol} is osmolal clearance; C_{H_2O} is free water clearance. Significant differences from predeprivation values: * $P < 0.05$.

nificant changes in plasma potassium concentration occurred during the rehydration period. The effect of absorption on the measures of plasma volume was rapid, with plasma protein concentration falling to a value not significantly different from predeprivation values within the first 2.5 min. By 5 min, this parameter had further decreased and by 7.5 min was significantly less than predeprivation values ($P < 0.05$). This relationship was maintained for the remainder of the rehydration period with some further decrease in plasma protein between 30 and 40 min. The changes in hematocrit were similar in pattern to the plasma protein changes so that by 5 min the hematocrit was significantly below its initial value ($P < 0.01$). Between 12.5 and 15 min, and again at 50 min, hematocrit was significantly below the predeprivation value ($P < 0.05$).

The effect of rehydration on plasma renin activity was to decrease this parameter from an initial 3.15 ± 0.79 to 2.53 ± 0.63 $ng \cdot ml^{-1} \cdot h^{-1}$. This latter value is not significantly above the predeprivation value (1.73 ± 0.59 $ng \cdot ml^{-1} \cdot h^{-1}$).

Urinary changes during and following rehydration. During the period from just before the start of drinking (10 min preceding) and the collection of urine after the end of rehydration (70 min from the start of drinking), the urine became relatively dilute (see Table 1). Urine osmolality and sodium concentration both decreased to values that were still higher than, but not significantly different from, predeprivation values. Urine potassium concentration remained relatively unchanged. During the rehydration period then, urine composition had changed from a high initial concentration typical of hydropenia, to a more normal state. By 90 min after the start of drinking and after the rehydration period had ended, urine concentration decreased further. Urine osmolality, sodium, and potassium concentrations all fell significantly below initial, postdeprivation values—osmolality ($P < 0.01$), sodium ($P < 0.05$), and potassium ($P < 0.05$). At the same time as these changes in concentration occurred, urine flow rate increased significantly above both pre- and postdeprivation ($P < 0.05$ compared to initial value) values. Because electrolyte excretion did not vary significantly from predeprivation values, the significant increase in osmolal clearance ($P < 0.05$) compared to initial values must be due to the medullary washout of urea under conditions of a rising urine flow. The change of C_{H_2O} to a positive value was not characteristic of all subjects, so that overall this change was not statistically significant. Between 90 and 120 min, the urine osmolality and sodium and potassium concentrations did not change further to any significant degree while the rate of urine flow and C_{osmol} decreased to a rate not significantly greater than the predeprivation level. The diuresis had effectively terminated by this time.

Subjective ratings. The changes in subjective ratings produced by the water deprivation, and during the subsequent rehydration, are shown in Fig. 2. The changes are expressed as differences on the 10-cm visual analogue scale from the value for each subject immediately before the start of drinking following the 24-h water deprivation (*time 0*). First, it is clear that the subjective ratings altered significantly during the water deprivation and subsequent rehydration (3-way analysis of variance, within subjects design; effect of time $F(12,48) = 9.14$, $P < 0.01$; effect of question asked $F(4,16) = 6.18$, $P < 0.01$ (interaction between time and question asked $F(48,192) = 2.78$, $P < 0.001$). Second, the subjective ratings data for each question asked was subjected to a two-way Anova within subjects design followed by appropriate Newman-Keuls tests. The results of the Newman-Keuls analysis in which the ratings after 24-h water deprivation ("initial state") were compared with the ratings at other times are indicated on Fig. 2. Ratings of thirst ("How thirsty do you feel now?") increased following 24-h water deprivation (see Fig. 2) ($P < 0.01$) and showed an initial very rapid decrease after drinking started, apparent and significant within 2.5 min, followed by a more gradual return to the predeprivation level over the remainder of the 1-h test period (overall, $F(12,48) = 7.31$, $P < 0.01$). The palatability of water (assessed by "How pleasant would it be to drink some water now?") was increased by water deprivation ($P < 0.01$) and decreased rapidly within 2.5 min, approaching the predeprivation palatability over *min 5–30* (overall, $F(12,48) = 12.82$, $P < 0.01$). Ratings of dryness of the mouth were also increased by water deprivation ($P < 0.05$) and decreased very rapidly (in the first 2.5 min) after the onset of drinking (overall, $F(12,48) = 3.41$, $P < 0.01$). The rating designed to assess the unpleasant almost putrid taste in the mouth that lingered after access to water in a pilot study and was given by subjects as the reason for small bouts of drinking occurring in that study from *min 15–60* ("How would you describe the taste in your mouth?") moved towards unpleasantness after the water deprivation ($P < 0.05$) and returned to the predeprivation level only slowly over the 1-h drinking test, (Fig. 2) (overall, $F(12,48) = 2.50$, $P < 0.05$). After access to water for 1 h all these subjective ratings were not significantly different from their predeprivation values. The ratings of stomach fullness increased within 2.5 min of the start of drinking ($P < 0.01$), reached a maximum at 5–7.5 min after the start of drinking, and returned only relatively gradually towards the predeprivation value (overall, $F(12,48) = 6.54$, $P < 0.01$).

In addition to filling in the visual analogue scales, subjects were asked to give a verbal description of their subjective sensations during rehydration. The subjects independently gave similar subjective reports that are summarized by the following quotations. "During rehydration, I found I was drinking mainly to eliminate a 'tacky' mouth." "My first drinks were stopped by a full feeling in the stomach; subsequently cycles of a slightly dry mouth induced drinking. The relief of the dry mouth after the initial drinks required only a small amount of fluid to be consumed, but the effect of this fluid on the dry mouth was transitory."

DISCUSSION

Following overnight fluid deprivation with food available, human subjects showed significant depletions of both the cellular and extracellular fluid compartments. These changes were within the range we have previously reported in the rat (16) and the dog (15) and that we

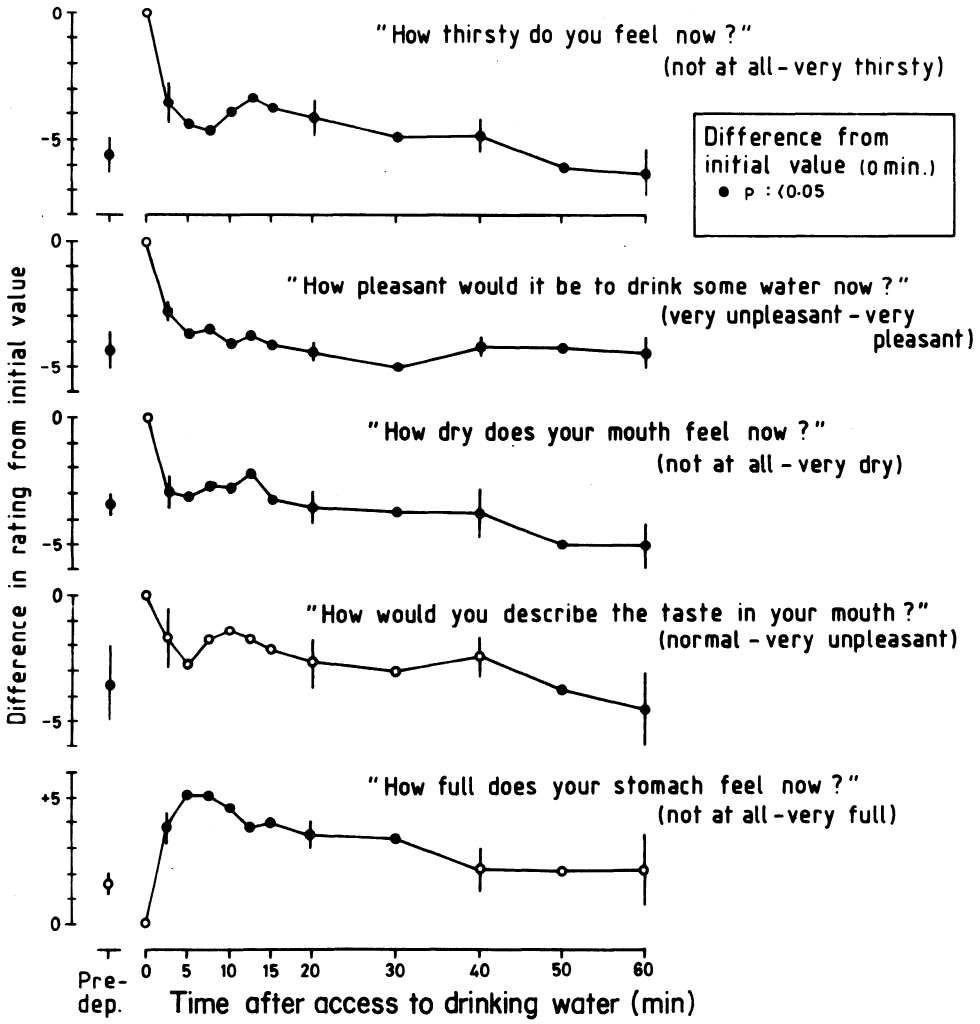

FIG. 2. Effect of 24-h water deprivation and drinking over 1 h of access to water on subjective ratings in 5 male subjects. Data shown are differences (in cm) from initial values and significant differences are indicated by filled symbols ($P < 0.05$).

have recently observed in the rhesus monkey (19, 24) under the same dehydration conditions following a similar deprivation period. In these other species the contribution of the fluid deficits to deprivation-induced thirst has been assessed by selectively rehydrating the two fluid compartments and measuring residual fluid intake. In the rat, removal of the cellular thirst stimulus with preloads of water reduced drinking by 64–69% depending on the route of the preload, whereas removal of the extracellular deficit reduced drinking by 20–26% (16). In the dog, removal of the central osmotic stimulus with intracarotid water infusions reduced drinking by 72%, and reexpansion of the extracellular fluid compartment with intravenous isotonic saline reduced drinking by 27% (15). In the monkey, the extracellular depletion appears to contribute less to deprivation-induced drinking than in the other animals, in that removal of the cellular thirst stimulus with intravenous water reduced drinking by 85%, and removal of the extracellular stimulus with intravenous saline reduced drinking by only 5%. Selective stimulus removal experiments have not yet been performed in man, but since the results show that the plasma changes produced by water deprivation in man are similar to those in the other species, it is likely that either or both the cellular and extracellular deficits stimulate some drinking, but the relative contribution in humans of each deficit is unknown.

Consistent with the extracellular depletion, it was found, as in a previous study (12) that plasma renin activity was elevated in human beings following water deprivation. This very interesting increase in plasma renin activity may be physiologically significant because the basal values are within the normal range for humans (7), and the higher values are similar to those found when increased renin activity is associated with changes in fluid balance and sodium excretion following salt restriction (9). It is possible that angiotensin could mediate the drinking following extracellular depletions in human beings and in other species, but there is still no conclusive evidence on this important issue, since removal of the source of angiotensin by bilateral nephrectomy (17) or blockade of angiotensin receptors with a competitive angiotensin inhibitor (1, 8, 14) do not affect deprivation-induced drinking. At least, the results described here show that in human subjects, when 24-h water deprivation causes thirst, plasma renin levels are significantly elevated.

The rate of drinking by humans during rehydration is similar to that of the monkey and is more rapid than that of the rat and slower than that of the dog (19). Our subjects drank very rapidly immediately after being given access to water, taking 65% of the total hourly intake in the first 2.5 min. Drinking proceeded at a much slower rate during the rest of the hour. The procedure of giving

the subjective questionnaire and rating scales, and sampling blood, is not likely to have greatly influenced drinking behavior, since in a pilot study where no subjective reports or blood samples were required of the subjects similar patterns of intake were observed.

The analysis of plasma composition following drinking in this experiment allows some assessment to be made of the role of systemic rehydration in the termination of drinking. Plasma sodium and osmolality began to decrease between 5 and 7.5 min after the start of drinking but were not consistently and significantly below initial values until 12.5 min. Thus rehydration of the cellular fluid compartment did not appear to be rapid enough to account for the early decrease in the rate of drinking (see Fig. 1). From 12.5 min onward, plasma dilution could be an important factor in limiting further drinking. By comparison the change in plasma volume was rapid. Within 5 min of the start of drinking plasma volume had returned to predeprivation levels, and by 7.5 min a significant hypervolemia was present. This rapid repletion of plasma volume may result from food being present in the gut, so that the ingestion of water produced an isotonic fluid that was rapidly absorbed, or from a shift of extracellular fluid into the vasculature, as well as from absorption of some water. Whether this rapid hypervolemia contributes to the termination of drinking in humans is uncertain, but it is unlikely to make a major contribution in view of the finding that extracellular depletion accounts for only 5% of the drinking following deprivation in the monkey and no more than 27% in the rat or dog (19). Thus in humans, cellular rehydration does not appear to be sufficiently rapid to account for the early decrease in the rate of drinking, and expansion of plasma volume, although rapid, may not be a powerful factor in terminating drinking.

An examination of plasma changes during rehydration in conjunction with changes in excretion gives an indication of the precision with which the behavioral response is regulated according to physiological requirements. In the dog, water intake is frequently very similar to overall fluid losses (2), and plasma dilution below normal is not generally significant (15). Individual dogs do exhibit some plasma dilution and excrete a hypotonic urine following drinking, but the volume of excess urine excreted is still relatively small compared to initial intake in this species (18) (Wood and Rolls, unpublished study). The monkey also appears to be capable of repairing fluid deficits without undue plasma dilution (24), but the renal response has not yet been determined. The rat, by comparison, typically shows plasma overdilution but a persistent hypovolemia (21). The subjects in this study showed a variable renal response following rehydrational drinking. Plasma overdilution did not appear to be significant, but there was significant hypervolemia. Two of the five subjects excreted little or no excess urine following drinking, whereas the other three subjects excreted hypotonic urine at rates well above predeprivation levels. As in the dog, electrolyte excretion following drinking did not increase significantly above normal so that the removal of the cellular fluid deficit was not a result of excretion of excess salts. The diuresis (increased urine flow, positive C_{H_2O}) in these subjects represented primarily the excretion of excess water. It is apparent that some humans ingest almost exactly the volume of water required to restore normal fluid balance, whereas in others, intake is in excess of that necessary.

The subjective ratings associated with the dehydration and rehydration showed regular and significant changes. The subjective sensations of thirst, the pleasantness of the taste of water, the dryness of the mouth, and the unpleasantness of the taste in the mouth, were all significantly elevated following the 24-h water deprivation. During rehydration, all these measures (except the unpleasantness of the taste in the mouth) returned to the predeprivation levels within 2.5–5 min after the onset of drinking. In the same early time period, a great part of the drinking occurred, and the rate of drinking after this slowed. Thus drinking started when values of these subjective states were elevated, and the rate of drinking declined as the subjective states declined. This is consistent with a close connection between these subjective states and drinking.

The most salient sensation associated with the deprivation was that of a dry "tacky" mouth. Local osmotic dehydration in the oropharynx is clearly an important component of the overall thirst [see Wolf (23) for discussion of the evidence for a "dry mouth theory" of thirst]. In the present study mild fluid deprivation produces thirst that is primarily ascribed subjectively to dryness of the mouth and throat. Thus, at the time of initial water access, subjective ratings for dry mouth and unpleasant taste were high. With the vigorous drinking that ensued, these ratings declined significantly over a few minutes. The drinking that occurred later was reported by the subjects to be primarily to alleviate the unpleasant oral sensations. The drinking occurred promptly when the sensations became unpleasant and rapidly alleviated the symptoms. This relationship between intake and oral sensations during the later part of the rehydration period is not clear from the subjective rating data (see Fig. 2), since the subjective ratings were obtained at fixed times and not necessarily when drinking occurred. Also the relationship of peripheral stimuli such as a dry mouth, to systemic fluid balance is not a simple one inasmuch as the oral sensations were reported to persist well into the rehydration period, after the initiating deficits had been effectively abolished.

The changes in the subjective states during the first 2.5–5 min after access to water preceded the major changes in plasma osmolality. This suggests that preabsorptive factors play a role in the decline of these subjective states (as well as in the termination of drinking). One such factor could be stomach distension, although the subjective feelings were frequently reported to comprise more than just stomach distension (they could also possibly reflect intestinal stimulation). It is an interesting parallel that if in the monkey the stomach is drained via a gastric cannula after drinking has terminated following 24-h deprivation, drinking begins again almost immediately (10, 11). Both the subjective sensations of stomach fullness in humans, and the gastric drainage experiment in the monkey, suggest the importance of gastric and possibly intestinal factors in the termination of drinking in primate species. If thirst is very intense, however,

fullness of the stomach and gut may be relatively ineffective in terminating drinking. In his graphic account of desert thirst, King (6) described an irresistable urge to drink that was not influenced by fullness of the stomach. The men repeatedly filled their stomachs to capacity, vomited the fluid up, and promptly drank again.

In conclusion, we find that although systemic depletions are produced by water deprivation in humans and are probably involved in initiating drinking, systemic rehydration does not seem to be sufficient to account for the early termination of drinking in man. Thus it is likely that a combination of oropharyngeal stimulation, gut distension, perhaps osmotic effects of water in the gut and hepatic portal system, and systemic dilution and expansion produced by absorbed water, normally terminate drinking, and it may be that temporal contiguity between these factors is important for their full effectiveness (3). Factors such as oropharyngeal stimulation by water and gut distension may be relatively important early in satiety, and the effects of absorbed water may be more important later in maintaining satiety.

This research was supported by the Medical Research Council of Great Britain.

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Received 17 December 1979; accepted in final form 27 May 1980.

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