CHARACTERIZATION OF THE NATRIURESIS CAUSED IN NORMAL MAN BY IMMERSION IN WATER

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(Received 15 February 1972)

SUMMARY

1. The effects of 4–6 h of water immersion on the renal excretion of water and electrolytes were studied in thirteen normal male subjects in balance on a constant diet containing 150 mEq of Na and 100 mEq of K per day. Each subject was studied during a control period, consisting of quiet sitting, and during water immersion to the neck.

2. Immersion resulted in a natriuresis beginning within the first hour, with the rate of sodium excretion eventually exceeding that of the control period by 3–4-fold; potassium excretion also increased. Despite a progressively negative water balance during the immersion studies, urine flow was greater during the first 4 h and free water clearance was greater during the first 2 h of immersion than during the control study.

3. The demonstration of a highly significant increase in fractional excretion of sodium during immersion suggests that the natriuresis of water immersion is not attributable to changes in filtered sodium load.

4. The prompt onset of the natriuresis, the concomitant kaliuresis and the fact that aldosterone secretion under the conditions of study was probably already suppressed make it unlikely that the natriuresis of water immersion is mediated solely by decreases in aldosterone activity.

5. The data suggest that the natriuresis caused by water immersion is the result of decreased fractional reabsorption of sodium proximal to the renal diluting site. The mechanism whereby increased proximal tubular sodium rejection occurs in relation to immersion remains unclear.

Key words: natriuresis, water immersion, volume homeostasis, potassium excretion.

Previous studies from this laboratory have demonstrated that water immersion has profound effects on the renin–aldosterone system and renal sodium excretion (Epstein & Saruta, 1971; Correspondence: Dr Murray Epstein, Veterans Administration Hospital, 1201 N.W. 16th Street, Miami, Fla. 33125, U.S.A.

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Water immersion up to the neck for 6 h produces a 50% decrease in plasma renin activity and urinary aldosterone excretion in normal subjects in balance on a low sodium (10 mEq per day) diet. Although the rate of sodium excretion ($U_{Na,V}$) during immersion is 20-fold greater than during the control period, the absolute increase in sodium excretion during water immersion is exceedingly small, possibly reflecting the limitations imposed by the sodium-depleted and volume-contracted state of the subjects.

The present study was therefore undertaken to assess the effects of water immersion on renal sodium excretion during a sodium intake (150 mEq) more nearly approximating to that of the normal diet. It was anticipated that such studies would further elucidate the mechanisms involved in the natriuresis caused by water immersion.

**MATERIALS AND METHODS**

Thirteen healthy male subjects between the ages of 18 and 24 years were studied. None had a history of hypertension, cardiovascular disease or diabetes. Significant renal disease was excluded by documenting a normal urine sediment and creatinine clearance and negative urine cultures. The subjects were housed during the study in an environmentally controlled metabolic ward at a constant temperature and were fed on a diet containing 150 mEq of sodium, 100 mEq of potassium and 2000 ml of water per day, which remained unchanged throughout the study. Daily 24 h urine collections were made for determination of sodium, potassium and creatinine.

Control and immersion studies were carried out on the 3rd and 5th days of dietary equilibration, respectively, by which time all subjects had achieved sodium balance. On study days, identical protocols were carried out as follows.

The subject was awakened at 07.00 hours and instructed to sit quietly for 1 h. At 07.30 hours he was given an oral water load (400 ml) and at 08.00 hours blood was drawn for determination of serum electrolytes, creatinine and protein concentration and plasma haematocrit (0 hour samples). After completely emptying the bladder, the study began with the subject assuming a seated position for 6 h. During control studies, the subject sat quietly outside the immersion tank for the 6 h period. During immersion, seven subjects sat in the study tank immersed in water up to the neck for the 6 h period. In six other subjects, the protocol for immersion was modified so that a 4-h period of immersion was immediately preceded and followed by 1 h of quiet sitting outside the tank.

Each subject voided urine spontaneously every hour. During immersion, the subject stood briefly on a platform in the immersion tank to void. To maintain an adequate urine flow, 200 ml of water was administered orally every hour during each study. Sodium, potassium and creatinine were measured in samples of the hourly urine collections. Blood was collected at 2-h intervals throughout the study. All subjects were weighed every morning at 07.00 hours after emptying the bladder, and before and after each study.

Immersion was done in a waterproof tank described in detail by Epstein & Saruta (1971). A constant water temperature of $34 \pm 0.5^\circ C$ was maintained by two heat exchangers with a combined output of 3.95 kWh controlled by an adjustable temperature-calibrated control meter, with input derived from two thermistors immersed at different water levels.

Sodium and potassium were analysed with a IL flame photometer. Creatinine was measured by an automated adaptation of Jaffé's picric acid reaction (Bonsnes & Taussky, 1945). Urine
### Table 1. Effects of immersion on urinary excretory patterns; results are the mean ± SE of seven subjects

<table>
<thead>
<tr>
<th>Group</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>V (ml/min)</td>
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<tr>
<td>Control</td>
<td>2.0 ± 0.7</td>
<td>2.7 ± 0.6</td>
<td>2.1 ± 0.5</td>
<td>3.8 ± 0.4</td>
<td>3.1 ± 0.7</td>
<td>3.9 ± 0.5</td>
</tr>
<tr>
<td>Immersion</td>
<td>5.2 ± 0.9†</td>
<td>7.6 ± 0.3†</td>
<td>4.8 ± 0.5*</td>
<td>6.2 ± 0.5*</td>
<td>3.7 ± 0.4</td>
<td>5.5 ± 0.6</td>
</tr>
<tr>
<td>U_{Na}V (μEq/min)</td>
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</tr>
<tr>
<td>Control</td>
<td>59 ± 5.5</td>
<td>57.5 ± 8.5</td>
<td>63.9 ± 12.8</td>
<td>71.1 ± 9.5</td>
<td>64.7 ± 6.4</td>
<td>64.4 ± 4.6</td>
</tr>
<tr>
<td>Immersion</td>
<td>112.9 ± 6.8†</td>
<td>168.9 ± 9.6†</td>
<td>220.9 ± 17.2†</td>
<td>236.3 ± 13.6†</td>
<td>234.4 ± 6.3†</td>
<td>219.9 ± 26.3†</td>
</tr>
<tr>
<td>U_{K}V (μEq/min)</td>
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<tr>
<td>Control</td>
<td>51.0 ± 7.5</td>
<td>54.8 ± 5.2</td>
<td>55.9 ± 7.4</td>
<td>67.7 ± 9.9</td>
<td>61.3 ± 8.4</td>
<td>56.4 ± 8.8</td>
</tr>
<tr>
<td>Immersion</td>
<td>92.1 ± 7.7†</td>
<td>115.8 ± 9.4†</td>
<td>105.6 ± 7.2†</td>
<td>92.1 ± 5.7*</td>
<td>70.5 ± 4.4</td>
<td>56.9 ± 7.0</td>
</tr>
<tr>
<td>C_{cr} (ml/min)</td>
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<tr>
<td>Control</td>
<td>117.0 ± 12.7</td>
<td>112.8 ± 8.6</td>
<td>115.8 ± 8.4</td>
<td>117.5 ± 8.9</td>
<td>125.1 ± 7.9</td>
<td>126.0 ± 8.7</td>
</tr>
<tr>
<td>Immersion</td>
<td>142.3 ± 4.6*</td>
<td>126.4 ± 5.7</td>
<td>132.4 ± 7.0</td>
<td>129.4 ± 7.1</td>
<td>130.8 ± 7.0</td>
<td>138.3 ± 11.1</td>
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<tr>
<td>C_{Na}/C_{cr} × 100</td>
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<tr>
<td>Control</td>
<td>0.37 ± 0.03</td>
<td>0.36 ± 0.04</td>
<td>0.39 ± 0.06</td>
<td>0.44 ± 0.06</td>
<td>0.37 ± 0.04</td>
<td>0.37 ± 0.02</td>
</tr>
<tr>
<td>Immersion</td>
<td>0.55 ± 0.03*</td>
<td>0.91 ± 0.08†</td>
<td>1.17 ± 0.11†</td>
<td>1.25 ± 0.07†</td>
<td>1.24 ± 0.07†</td>
<td>1.21 ± 0.05†</td>
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<tr>
<td>C_{H2O} (ml/min)</td>
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<tr>
<td>Control</td>
<td>-0.2 ± 0.6</td>
<td>0.5 ± 0.6</td>
<td>-0.2 ± 0.4</td>
<td>1.5 ± 0.4</td>
<td>0.9 ± 0.7</td>
<td>1.7 ± 0.5</td>
</tr>
<tr>
<td>Immersion</td>
<td>2.2 ± 0.9*</td>
<td>4.3 ± 0.3†</td>
<td>1.4 ± 0.6</td>
<td>2.8 ± 0.6</td>
<td>0.6 ± 0.4</td>
<td>2.6 ± 0.3</td>
</tr>
<tr>
<td>C_{osm} (ml/min)</td>
<td></td>
<td></td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>Control</td>
<td>2.2 ± 0.2</td>
<td>2.2 ± 0.1</td>
<td>2.2 ± 0.2</td>
<td>2.3 ± 0.1</td>
<td>2.2 ± 0.1</td>
<td>2.2 ± 0.1</td>
</tr>
<tr>
<td>Immersion</td>
<td>3.0 ± 0.1†</td>
<td>3.3 ± 0.2†</td>
<td>3.5 ± 0.2†</td>
<td>3.4 ± 0.2†</td>
<td>3.1 ± 0.1†</td>
<td>2.9 ± 0.3</td>
</tr>
</tbody>
</table>

* P < 0.05 differences from control.
† P < 0.005 differences from control.
and serum were analysed for total solutes with a Fiske osmometer. Creatinine (C_e), osmolar (C_om) and free water (C_H2O) clearances were calculated by the conventional formulae. In the presentation of the data, mean values are followed by the standard error of the mean, as an index of dispersion. Tests of statistical significance were calculated by means of a paired t test.

Permission for the study was obtained from each subject after a detailed description of the procedures and their potential complications. No complications occurred. The protocol was approved by the Human Experimentation Committees of the University of Miami School of Medicine and the Miami Veterans Administration Hospital.

**RESULTS**

**Urinary sodium and potassium**

The effects of 6 h of water immersion on sodium and potassium excretion are shown in Tables 1 and 2 and Fig. 1. During quiet sitting (control), the rate of sodium excretion was constant, ranging from 58 to 71 μEq/min, despite a doubling of urine flow. By contrast, water immersion up to the neck (immersion) resulted in a highly significant increase in UNaV as compared with the control period, beginning at hour 1 (P<0.005). During the final 5 h of study, UNaV during immersion was 3-4-fold greater than during the comparable control periods (P<0.005). As shown in Table 2, the absolute quantity of sodium excreted during 6 h of immersion was 3-fold greater than the control value (P<0.001).

**Table 2.** Changes in body weight and electrolyte balance during 6 h of water immersion; results are the mean±SE of seven subjects

<table>
<thead>
<tr>
<th></th>
<th>Change in body wt. (kg)</th>
<th>Na balance (mEq/6 h)</th>
<th>K balance (mEq/6 h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>-0.2±0.2</td>
<td>-23.0±2.5</td>
<td>-20.9±2.6</td>
</tr>
<tr>
<td>Immersion</td>
<td>-1.3±0.1</td>
<td>-71.6±4.0</td>
<td>-35.4±2.8</td>
</tr>
<tr>
<td>P&lt;0.005</td>
<td>P&lt;0.001</td>
<td>P&lt;0.005</td>
<td></td>
</tr>
</tbody>
</table>

Although all studies were done with the subjects in balance on a constant sodium intake, data for sodium excretion in the period immediately preceding immersion had not been determined. Additional studies were therefore carried out in six subjects to determine basal sodium excretion during the 1 h immediately preceding immersion. As shown in Fig. 2, UNaV during the hour of quiet sitting immediately preceding immersion did not differ from the first hour of the control study. A significant increase in UNaV again occurred during the initial hour of immersion, as was observed in the seven subjects in whom basal sodium excretion during the preceeding 1-h period of quiet sitting had not been determined. Return to quiet sitting after 4 h of immersion was accompanied by a prompt decrease in UNaV as compared with the final hour of immersion (P<0.005), although sodium excretion was still increased as compared with the control period (P<0.005).

The relationship between the increments in V and UNaV during each period was examined. The mean percentage increase in V and UNaV during each hour of immersion as compared with its appropriate control hour was calculated as follows. The percentage increment was
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computed for each subject by using the expression \( [(X)_i - (X)_c \times 100]/(X)_c \). The resultant percentage increments for all subjects were then averaged to obtain the mean percentage increase for that hour of study. As shown in Fig. 3, the mean percentage increment in \( U_{Na}V \)

\[ \text{increased during the first 3 h of immersion, when the mean percentage increment in } V \text{ was decreasing.} \]

The rate of potassium excretion \( (U_KV) \) did not vary significantly during the control period,

\( X \)
ranging from 51 to 68 μEq/min. Immersion produced a significant increase in U_KV beginning at hour 1 and persisting up to hour 4. During the final 2 h, U_KV was not significantly different from the control value when U_NaV remained elevated. Net potassium excretion during immersion was almost double that found during the control period (P < 0.005) (Table 2).

**Urine volume, C_H2O, C_osm and C_cr (Table 1)**

Urine flow during the control period ranged from 2.0 to 3.9 ml/min. Despite identical water loads during control and immersion studies, urine flow rates during the initial 4 h of immersion exceeded those observed during the control period (P < 0.05). The increase in urine flow was

![Graph](image)

**Fig. 2. Effect of water immersion after 1 h of quiet sitting, on the rate of sodium excretion (U_NaV) in six additional sodium-replete subjects (150 mEq of Na diet) in whom U_NaV was determined in the hour immediately preceding immersion. During this hour, U_NaV was not significantly different from the control value (P > 0.2). Sodium excretion increased promptly with immersion. During 1 h of quiet sitting after immersion, U_NaV decreased as compared with the final hour of immersion (P < 0.005), but continued to exceed the control value (P < 0.005). Results are the mean ± SE. Control and experimental are indicated as in Fig. 1.**

attributable to increases in both C_H2O and C_osm. The C_H2O was greater during the initial 2 h of immersion (P < 0.02) than during the corresponding control period, but there were no significant differences during the final 4 h. The C_osm during immersion exceeded the comparable control values during the first 5 h of study, reflecting the increase in U_NaV.

Creatinine clearance (C_cr) was constant throughout the control period, being in the range 113–126 ml/min. Immersion did not alter C_cr, except for an increase during the initial hour of
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Fig. 3. Relationship of percentage increments during immersion, as compared with control values, in rates of urine flow (\(\bar{V}\), V) and sodium excretion (■, \(U_{Na}V\)). Values are the mean ± SE for seven subjects. During the first 3 h of immersion, the mean increment in \(U_{Na}V\) increased progressively, while the mean increment in V was decreasing.

Fig. 4. Changes in creatinine clearance during water immersion for the six subjects used to obtain the results shown in Fig. 2. During the 4 h of immersion, \(C_{cr}\) did not differ from the control value when \(U_{Na}V\) had significantly increased. Results are the mean ± SE. Control and experimental are indicated as in Fig. 1.
study \((P < 0.05)\). This increase in \(C_e\) appeared to be a function of the initial hour of study rather than of immersion per se, as shown in Fig. 4, where the study was begun and measurements were made during an initial hour of quiet sitting.

**Changes in body weight**

As shown in Table 2, 6 h of immersion was associated with a decrease in mean body weight of 1.3 kg, a change significantly greater than the 0.2 kg loss seen during the control period \((P < 0.005)\).

**Serum protein and electrolytes and plasma haematocrit**

As shown in Table 3, serum sodium, potassium and protein concentrations and plasma haematocrit did not change significantly during the control or immersion studies when compared with values obtained immediately before each study (0 hour). The sole exception was a small increase in serum protein concentration after 2 h of the control period. Comparisons at each time of control with immersion values for each of these determinations showed significant differences only for serum sodium concentrations at 2, 4 and 6 h. These differences were not considered to be meaningful because the 0 hour serum sodium concentration during immersion was greater by 3.9 mEq/l than the comparable control value.

**DISCUSSION**

Water immersion up to the neck has been shown to suppress plasma renin activity and urinary aldosterone excretion significantly in normal subjects in balance on a 10 mEq sodium diet (Epstein & Saruta, 1971; Epstein et al., 1971). Although the rate of sodium excretion increased 20-fold during immersion, the total quantity of sodium excreted during 6 h of immersion up
to the neck was less than 7 mEq, raising the question of the relevance of this observation to circumstances where sodium intake is within the physiological range. The present studies demonstrate that immersion up to the neck for normal subjects in balance on a 150 mEq sodium diet produces an earlier (hour 1 rather than hour 4) and greater increase in the rate of sodium excretion than in comparable subjects studied on a 10 mEq sodium intake (Fig. 1). The total quantity of sodium excreted during the 6 h of immersion was nearly 10-fold greater than that found in subjects on a 10 mEq sodium diet (Epstein & Saruta, 1971). In the present study, immersion also resulted in an earlier increase in the rate of potassium excretion (hour 1 rather than hour 2) than in the previous study of subjects on a 10 mEq sodium diet.

The demonstration of an increase in $U_{NaV}$ from hour 2 to hour 6 without a concomitant increase in creatinine clearance (Table 1) suggests that the natriuresis is independent of the filtered sodium load. Although small unmeasured changes in creatinine clearance might have contributed to an increase in $U_{NaV}$, the demonstration of a highly significant increase in fractional excretion of sodium during every hour of the study (Table 1) indicates that the increase in $U_{NaV}$ was attributable to an increased tubular rejection of sodium, rather than to alterations in filtered sodium load.

Although other studies using the model of head-out-of-water immersion have been done under conditions of sodium intake comparable with those of the present study, significant differences in experimental design render comparisons difficult. Behn, Gauer, Kirsch & Eckert (1969) reported a 53% increase in $U_{NaV}$ in hydrated subjects (water intake=3·14% body wt./day) and a 127% increase in non-hydrated subjects (water intake=1·66% body wt./day) undergoing water immersion in the supine position. Although water intake of our subjects (2000 ml/day=2·86% body wt./day) was closer to Behn’s ‘hydrated group’, the increase in both $U_{NaV}$ and total sodium excreted over 6 h in the present study exceeded by several-fold that reported by Behn for 8 h periods of immersion. In addition, $U_{KV}$ was increased throughout the first 4 h of immersion in the present study and there was an overall increase in potassium excretion, in contrast with the 59% decrease in $U_{KV}$ demonstrated by Behn et al. (1969). Although the differences in magnitude of increase in $U_{NaV}$ with immersion may be attributable to differences in posture, time of day or other factors in experimental design in the two studies, the explanation for the divergent changes in $U_{KV}$ is not readily apparent.

The results of the present studies also differ from those previously reported in that changes in haematocrit and serum protein concentration were not seen after immersion. Kaiser, Linkenbach & Gauer (1969) and Behn et al. (1969) demonstrated small but significant increases in haematocrit (3·1 and 2·6 vol. %, respectively) after 8 h of immersion in water of supine subjects. In contrast, no significant changes were observed in the present study during 6 h of immersion in water of seated subjects. It is likely that differences in experimental design, including posture, may account for this discrepancy. In view of the significant losses of sodium and water observed and the absence of concomitant increases in haematocrit and serum protein concentration, it is likely that immersion was accompanied by shifts of intracellular and interstitial fluid into the vascular space. This interpretation is supported by the demonstration of Davis & DuBois (1971) that in the dog a rapid decrease in haematocrit occurs in the early phase of immersion.

The present data aid understanding of the mechanism whereby immersion up to the neck results in a profound natriuresis. Although urine flow rates ($V$) during immersion exceeded the control values, it is clear that the increase in $U_{NaV}$ cannot be attributed solely to the increase in
V, as indicated by the divergent rates of change of \( U_{Na}V \) and \( V \) during the first 3 h of immersion (Fig. 3). Further, the increase in \( U_{Na}V \) observed was independent of changes in creatinine clearance. Indeed, fractional excretion of sodium exceeded that of the control studies throughout the period of immersion, strongly suggesting that the natriuresis of immersion is mediated independently of changes in glomerular filtration rate.

The demonstration of a temporal dissociation between renal sodium and water excretion during immersion is consistent with evidence suggesting the presence of independent afferent mechanisms mediating antidiuretic hormone (ADH) and renin release. Brennan, Malvin, Jochim & Roberts (1971) have demonstrated that increases in left-atrial pressure cause decreases in ADH, without accompanying changes in plasma renin activity; on the other hand, increases in right-atrial pressure cause significant decreases in plasma renin activity but no appreciable changes in plasma ADH. Davis & DuBois (1971), however, have shown that there is no significant correlation in the dog between the degree of left-atrial pressure changes and changes in urine flow during water immersion. The present demonstration of divergent rates of change of \( U_{Na}V \) and \( V \) during immersion is consistent with the concept that separate receptors may govern renin and ADH release.

The possibility must be considered that the observed increase in \( U_{Na}V \) during immersion is related to changes in renin–angiotensin activity per se. Previous studies have demonstrated that immersion is associated with significant decreases in plasma renin activity (Epstein & Saruta, 1971; Epstein et al., 1971) and presumably in circulating concentrations of angiotensin II. Although infusion of angiotensin II may result in significant anti-natriuresis, opposite effects have also been demonstrated, depending on differences in species, dose, duration of infusion and clinical setting (Page & McCubbin, 1968). In view of these uncertainties, it would be difficult to invoke a direct causal relationship between the natriuresis caused by immersion and the concomitant changes in plasma renin activity.

Similarly, although the observed increase in \( U_{Na}V \) during immersion is associated with a decrease in aldosterone excretion (Epstein & Saruta, 1971; Epstein et al., 1971), it would also appear unlikely that a decrease in aldosterone effect plays a significant role in mediating the natriuresis during the initial 2 h of study. Previous studies have suggested that circulating aldosterone concentrations remain elevated for 15–20 min after abrupt discontinuation of angiotensin infusion (Fraser, James, Brown, Isaac, Lever & Robertson, 1965). Further, several lines of evidence have suggested that even after changes in aldosterone have occurred there is a 1–2 h lag period before changes in renal sodium excretion result (Ross, Reddy, Rivera & Thorn, 1959; Crabbé, 1961). In the present studies, the already probably low values for aldosterone secretion resulting from high sodium intake, together with the rapidity of onset of the increase in sodium excretion observed, make it unlikely that these changes were mediated by decreasing aldosterone concentrations. Finally, the increase in \( U_{Na}V \) during the initial 4 h of immersion was accompanied by an increase in \( U_{K}V \), rather than the decrease that might have been anticipated as a result of lessened aldosterone effect. Taken together, these data suggest that suppression of aldosterone could not be the sole factor responsible for the prompt and brisk natriuresis observed. A lessened aldosterone effect might, of course, contribute to the later sustained natriuresis.

The demonstration of an increase in \( C_{\text{H}_2\text{O}} \) during the initial 2 h of immersion, when \( U_{Na}V \) increased significantly, suggests an increase in sodium rejection proximal to the diluting site. Such an interpretation is consistent with the simultaneous increases in both \( U_{Na}V \) and \( U_{K}V \),
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making it likely that an increase in solute delivery to distal reabsorptive sites had occurred. Alternatively, the early increase in $C_{H_2O}$ may result from an initial inhibition of ADH by water immersion \textit{per se} (Gauer, Henry & Behn, 1970; McCally & Wunder, 1971), which is subsequently overcome by the stimulus to ADH-release induced by the progressive volume contraction caused by immersion (Behn \textit{et al}., 1969).

Several lines of evidence have suggested that receptors in the low-pressure vascular bed may constitute the afferent limb of a reflex regulating renal sodium handling. On the basis of recent studies, it has been proposed that these afferent receptors probably reside either in the atria, the intrapericardial segments of the great veins of the thorax or both (Goetz, Hermreck, Slick & Starke, 1970). Carswell, Hainsworth & Ledsome (1970) have demonstrated that blood from dogs whose left atria are distended with balloons produces a significant but small natriuresis in isolated perfused kidneys. Goetz \textit{et al}.

(1970) have demonstrated that the natriuretic response to dextran infusion is diminished when the mean atrial transmural pressure is prevented from rising. Inasmuch as water immersion results in an increase in blood volume in the low-pressure system (Gauer \textit{et al}., 1970), stimulation of the atrial receptors, with a consequent natriuresis, might be anticipated.

The mechanism whereby stimulation of these afferent receptors alters renal sodium handling is not yet clear. Several possibilities have been suggested, including changes in intrarenal haemodynamics (Hollenberg, Epstein, Guttman, Basch & Merrill, 1970; Kilcoyne & Cannon, 1971; Rashid, Hollenberg, Adams, Solomon, Abrams & Merrill, 1972), alterations in the hydrostatic or colloid osmotic pressure governing the rate of removal of reabsorbate from the peritubular spaces (Brenner & Galla, 1971), or mediation by a hormonal inhibitor of renal tubular sodium reabsorption (Bourgoignie, Klahr & Bricker, 1971; Bricker, Klahr, Purkerson, Schultze, Avioli & Birge, 1968; Buckalew, Martinez & Green, 1970).

The natriuresis induced by several vasoactive agents as well as by salt loading is associated with a redistribution of intrarenal blood flow, with an increase in cortical blood flow (Hollenberg \textit{et al}., 1970; Kilcoyne & Cannon, 1971; Rashid \textit{et al}., 1972). Kilcoyne & Cannon (1971) have demonstrated that the sodium retention induced by thoracic inferior vena caval constriction in dogs is associated with a decline in superficial cortical blood flow. Water immersion is thought to produce a redistribution of plasma volume opposite to that found in the ‘caval’ dog, with a relative increase in intrathoracic volume (Gauer \textit{et al}., 1970). One might, therefore, anticipate opposite effects, with an increase in superficial cortical blood flow and a consequent natriuresis.

Alternatively, the natriuresis of immersion may be mediated by an increase in hydrostatic pressure or a decrease in colloid osmotic pressure in the peritubular capillaries (transcapillary Starling forces), thus favouring a decrease in the net reabsorption of tubular fluid. Although neither peripheral plasma haematocrit nor serum protein concentration changed during immersion, the possible role of such physical factors cannot be assessed in the absence of direct measurements of peritubular capillary fluid.

Recent evidence suggests that a hormonal inhibitor of tubular sodium reabsorption may constitute the efferent limb of the natriuretic response. The demonstration by Carswell \textit{et al}.

(1970) of a significant natriuresis in isolated dog kidneys perfused with blood obtained from donor dogs whose left atria were distended suggests that such changes may be attributable to humoral influences. The possible relationships of this substance to the factor in the plasma of saline-loaded dogs that reduces short-circuit current in the toad bladder (Buckalew \textit{et al}.,
1970) or the factor in uraemic plasma that inhibits p-aminohippuric acid transport in renal cortical slices (Bricker et al., 1968) remains to be elucidated.

The data presented here demonstrate that the previously described increase in sodium excretion induced by water immersion in subjects ingesting sodium-restricted diets (Epstein & Saruta, 1971; Epstein et al., 1971) is greatly amplified in subjects studied during a 150 mEq sodium balance close to that of the normal diet. Neither increase in glomerular filtration rate nor suppression of aldosterone accounts completely for this natriuresis. The concomitant increase in both $C_{H_2O}$ and $U_{Na V}$ during hours 1–2 indicates that the marked increase in $U_{Na V}$ probably reflects decreased fractional reabsorption of sodium proximal to the diluting site. The mechanism whereby increased proximal tubular rejection occurs, however, remains to be elucidated.

Despite such questions, the magnitude and reproducibility of the changes seen with immersion suggest that this model may have implications beyond an understanding of the physiology of immersion alone. Water immersion and the weightlessness of space flight appear to have many physiologically similar consequences (Gauer et al., 1970; McCally & Wunder, 1971), including the induction of a significant diuresis, natriuresis (Adey, Cockett, Mack, Meehan & Pace, 1969; Lutwak, Whedon, Lachance, Reid & Lipscomb, 1969) and potassium loss (Leach, Alexander & Johnson, 1972). Thus, studies of the effects of water immersion may be relevant to an understanding of the fluid and electrolyte changes accompanying manned space flight. Carefully controlled water immersion also constitutes a meaningful tool for assessing renin–aldosterone responsiveness and renal sodium excretion in various disease states characterized by disordered sodium homeostasis (M. Epstein, D. C. Duncan & L. M. Fishman, unpublished work).

ACKNOWLEDGMENTS

This work was supported by grants from the General Clinical Research Centers Program of the Division of Research Resources, National Institutes of Health (RR-261), the Florida Heart Association and by VA Training Grants in Nephrology (TR-139) and Endocrinology and Metabolism (TR-177). M.E. is an investigator of the Howard Hughes Medical Institute.

We gratefully acknowledge the assistance in several aspects of this study by Kenneth Bailey, Norman Arthur, Ronald J. Conroy and Mrs Cecelia Traband, and the constructive criticism provided by Dr Carlos A. Vaamonde.

REFERENCES


Sodium homeostasis during water immersion


