Dissociation of Aldosterone and 17-Hydroxycorticosteroid (17-OHCS) Release During Water Immersion in Normal Man[1,2] (36023)

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(Introduced by W. H. Hulet)

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Water immersion to the neck results in a redistribution of extracellular fluid volume, with an increase in intrathoracic blood volume (1). Previous studies from this laboratory have demonstrated that water immersion has profound effects on the renin–aldosterone system and renal sodium handling. Six hours of water immersion to the neck produced a 50% decrease in plasma renin activity and urinary aldosterone excretion in normal subjects (2). Since several lines of evidence have suggested that ACTH plays a role in the physiological control of aldosterone release (3), it is not clear whether this suppression of the renin–aldosterone system (RAS) is selective or represents a generalized suppression of adrenocortical secretion mediated via the pituitary–adrenal axis. Furthermore, recent studies by Lipman *et al.* (4) have demonstrated a generalized decrease in pituitary–adrenal reserve following 2 weeks of absolute bed rest. Since similar changes in the redistribution of extracellular fluid occur during both bed rest and water immersion (1), it is possible that adrenocortical secretion may be similarly affected during water immersion.

The current study was undertaken to assess the effects of water immersion on both aldosterone and 17-hydroxycorticosteroid (17-OHCS) release in normal man under conditions of carefully controlled sodium and potassium balance, posture, and time of day.

Materials and Methods. Six healthy male airmen between the ages of 19 and 25 years were studied. All were volunteers from whom informed consent was obtained. None had demonstrable 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 room at a constant temperature and were fed a constant freeze-dehydrated diet, reconstituted at the time of serving with measured volumes of distilled water. The sodium and potassium content of the diet was determined from analyses of both an ashed aliquot of 1 day's food and individual analysis of the various food items. The composition of each subject's diet remained unchanged throughout the study and contained 10 mEq of sodium, 88–120 mEq of potassium, and 2500 ml of water. Daily 24-hr urine collections were made for determination of sodium, potassium, and creatinine.

When each subject had achieved sodium balance, a control study was carried out on day 5 and an immersion study on day 7 of dietary sodium deprivation. On study days, identical protocols were carried out as follows:

The subject was awakened at 0600 and instructed to sit quietly for 1.5 hr. At 0645, he was given a 400 ml oral water load and at 0730, blood was drawn for determination of plasma renin activity, plasma cortisol, serum electrolytes, and serum creatinine. After voiding and completely emptying his bladder, the subject then assumed a seated position for 8 hr. During control studies, the subject sat quietly outside the immersion tank for the 8-hr period. During immersion, the subject sat in the study tank immersed in water to the neck for 4 hr (immersion), followed by

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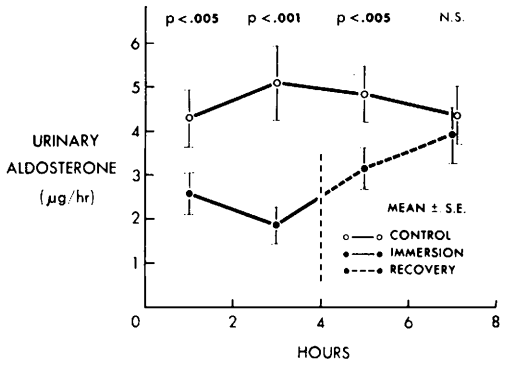

FIG. 1. Comparison of changes in urinary aldosterone excretion during control and during water immersion to the neck. Aldosterone excretion was markedly decreased during immerson and the initial 2 hr of recovery.

4 hours of quiet sitting outside the tank (recovery). At hourly intervals, the subject stood briefly on a platform in the immersion tank to void spontaneously. To maintain an adequate urine flow, 200 ml water was administered orally every hour during each study. Sodium, potassium, and creatinine were measured on aliquots of the hourly urine collections. Aldosterone and 17-OHCS excretion were determined on aliquots of pooled 2-hr urine collections. Blood was collected at 2-hr intervals throughout the study.

Immersion was carried out in a waterproof tank described in detail in a previous communication (2). The water temperature was maintained constant at 34 ± 0.5° by two heat exchangers with a combined output of 13,500 BTU/hr controlled by an adjustable temperature-calibrated control meter, with input derived from two thermisters immersed at different water levels.

Plasma renin activity (PRA) (ng/ml/hr) was measured by bioassay using the method of Skinner (5). Plasma 17-hydroxycorticosteroids (17-OHCS) was measured by the fluorescence method of Mattingly (6), urinary aldosterone by the method of Kliman and Peterson (7), and urinary 17-OHCS by the method of Reddy *et al.* (8).

In the presentation of the data, mean values are followed by the standard error of the mean as an index of dispersion. Tests of significance were calculated by means of a paired *t* test.

Results. The effect of water immersion on urinary aldosterone excretion is shown in Fig. 1. During quiet sitting (control), the rate of aldosterone excretion was relatively stable over the 8-hr period of study, with values ranging from 4.3 to 5.0 μg/hr. During the immersion study, aldosterone excretion was significantly lower throughout the 4-hr period of neck immersion and during the initial 2 hr of recovery.

Changes in PRA during immersion (Fig. 2) paralleled those occurring in urinary aldosterone, with a 30% decrease after 2 and 4 hr of immersion compared to the preimmersion values ($p<.05$). By the second and fourth hours of recovery, the mean values increased to and slightly above control levels.

In contrast, water immersion did not significantly alter urinary 17-OHCS excretion. As shown in Table I, hourly excretion of 17-OHCS did not change significantly during the control study, with mean values ranging from 309 to 353 μg/hr. Although there appeared to be a tendency for urinary 17-OHCS to decrease during the recovery, at no time did urinary 17-OHCS excretion during immersion differ significantly from that during the control study.

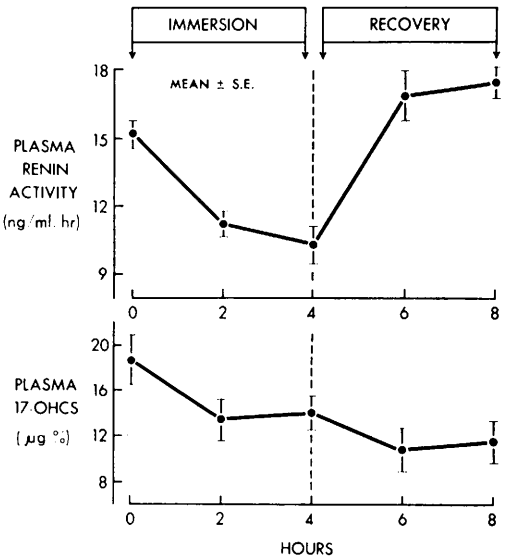

FIG. 2. Relationship between plasma renin activity and plasma 17-OHCS in six normal subjects undergoing water immersion to the neck. The significant suppression of PRA at hours 2 and 4 occurred independently of changes in plasma 17-OHCS.

TABLE I. Urinary 17-OHCS (μg/hr) During Water Immersion to the Neck.
(Results are mean ± SE of 6 subjects).

(Hr):	1–2	3–4	5–6	7–8
Control	337 ± 33	353 ± 34	347 ± 31	309 ± 36
Immersion	310 ± 35	307 ± 25		
Recovery			262 ± 38	237 ± 23
	NS	NS	NS	NS

The effect of water immersion on plasma 17-OHCS is shown in Table II and Fig. 2. During the control study, the mean levels ranged from an initial value of 21.7 to 14 μg/100 ml after 8 hr, reflecting the anticipated decrease in plasma 17-OHCS occurring during the day as a result of the diurnal rhythm in adrenal steroid secretion (9). At hours 2 and 4 of immersion, when PRA was clearly suppressed, plasma 17-OHCS was not significantly different from control ($p > .3$), and again reflected the expected diurnal fall.

Discussion. This and previous studies (2) demonstrate that during neck immersion, urinary aldosterone and plasma renin activity are markedly suppressed. Although present evidence favors the concept that the regulation of adrenal aldosterone secretion is largely independent of adrenal cortisol secretion (10), the possibility must be considered that the decreases in urinary aldosterone and plasma renin activity observed during immersion represent a generalized suppression of adrenalcortical activity. Such changes might be the result of decreases in circulating ACTH levels, since aldosterone secretion may be affected by ACTH (3).

The current study demonstrates that, in contrast to the observed decreases in urinary aldosterone and plasma renin activity, urinary 17-OHCS excretion was not significantly altered by neck immersion. It is possible that urinary 17-OHCS excretion may not acutely reflect changes in adrenal steroid secretion (9). Furthermore, transient changes in plasma 17-OHCS levels may be masked by the measurement of urinary 17-OHCS excretion in a pooled 2-hr urine specimen, which integrates adrenocortical secretion over a relatively long period. Therefore, determinations of plasma 17-OHCS were also made at regular intervals, to assess possible changes in adrenal glucocorticoid secretion in relation to immersion. In these studies, no differences were found in plasma 17-OHCS levels measured at 2 hr intervals during both control and immersion periods. The slow decrease in plasma 17-OHCS seen during both periods is regularly observed in unstressed normal subjects and is a reflection of an undisturbed circadian rhythm of pituitary–adrenal function under the conditions of this study.

These data demonstrate that the suppression of the renin–aldosterone system occurring during neck immersion appears to be selective and not a manifestation of a generalized decrease in adrenocortical activity. Furthermore, since plasma 17-OHCS levels closely parallel changes in plasma ACTH (11), the constancy of plasma and urinary 17-OHCS observed during control and immersion periods strongly suggests that immersion under the conditions studied here is not attended by significant alterations in circulating ACTH. This study thus further supports the concept of independent control of adrenal mineralocorticoid and glucocorticoid secretion and suggests that the changes seen during water immersion are

TABLE II. Plasma 17-OHCS (μg/100 ml) During Water Immersion to the Neck.
(Results are mean ± SE of 6 subjects).

	Preimmersion	(hr): 2	4	6	8
Control	21.7 ± 3.5	16.3 ± 2.1	13.9 ± 2.2	15.5 ± 2.9	14.1 ± 2.5
Immersion	18.6 ± 1.7	13.5 ± 1.8	14.1 ± 1.6		
Recovery				10.9 ± 2.0	11.6 ± 2.0
	NS	NS	NS	NS	NS

specifically related to alterations in the renin–aldosterone system.

Finally, these data may be relevant to current investigations of the physiological consequences of weightlessness. Both prolonged bed rest and water immersion have been widely utilized as models for studying the metabolic effects of weightlessness (1). The lack of change in glucocorticoid activity encountered in the present study contrasts with the impairment of pituitary–adrenal reserve demonstrated by Lipman *et al.* (4) utilizing the model of prolonged bed rest, suggesting that caution should be exercised in extrapolating metabolic data from either of the analogs of weightlessness to the actual zero-gravity state.

Summary. Since previous studies have demonstrated a profound suppression of the renin–aldosterone system during water immersion in man, the specificity of this suppression of adrenal function was assessed. Urinary aldosterone and 17-OHCS release were simultaneously measured in six normal subjects studied during a control period and during water immersion under identical conditions of diet, posture, and time of day. There was a marked decrease in aldosterone excretion during immersion and during the initial 2 hr of recovery ($p<.005$). In contrast, neither urinary nor plasma 17-OHCS was significantly altered by immersion. The dissociation observed between the effects of immersion on aldosterone and 17-OHCS activity suggests that the suppression of the renin–aldosterone system is selective and further supports the concept of independent control of adrenal mineralocorticoid and glucocorticoid secretion.

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