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Renal Responses of the Recumbent Nonhuman Primate to Total Body Water Immersion (40532)[1]

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Introduction. Head-out water immersion in upright man results in a diuresis and natriuresis (1) which are believed to be mediated via cardiopulmonary receptor stimulation (2) brought about by the immersion-induced translocation of blood from the periphery to the thorax (3). However, studies in the nonhuman primate have shown that vagotomy does not attenuate the diuresis or natriuresis of upright water immersion (4) demonstrating that cardiopulmonary receptors with vagal afferents are not necessary for the renal responses and questioning thoracic translocation as a causal factor in this species. Gilmore and Zucker (4) have suggested that the abdominal compression evident during immersion may be a contributing factor, possibly by effects on intrarenal blood flow distribution. If the above are true, then the renal responses to immersion should occur in an animal which is immersed in a position such that there is little or no immersion-induced translocation of blood to the thorax and where the abdomen is subjected to an increase in water pressure. To test this hypothesis, experiments were performed in which the nonhuman primate was immersed while in a recumbent position to a depth at which the water pressure on the abdomen was equal to that during head-out immersion in the upright animal.

Methods. The experiments were performed on eight *Macaca fascicularis* monkeys averaging 4.8 ± 0.2 kg in weight. Four of the animals served as the immersion group (Group I) and four as time controls (Group II). The animals were sedated with ketamine HCl (5 mg/kg) administered intramuscularly followed by 30 mg/kg of pentobarbital sodium administered intravenously and supplemented as needed during the experiment. One femoral vein was cannulated for administering solutions and the other for measuring central venous pressure (CVP) via a transducer-tipped catheter (Millar Instruments; Houston, Tex.) inserted to the level of the thorax. In three of the immersed animals the infusion was administered through a brachial vein and femoral venous pressure (FVP) was measured. One femoral artery was cannulated to obtain blood samples and the other for the introduction of a second transducer-tipped catheter into the descending thoracic aorta for the measurement of arterial blood pressure (ABP). The ureters were approached *via* flank incisions and cannulated with polyethylene tubing. A tracheostomy was performed through a midline neck incision. All incisions were closed with surgical clips.

The Group I animals were secured to a wood platform and placed in a 22 × 45 × 23-in. galvanized steel tank in the recumbent position. The platform was supported on rods so that the animals were approximately 12 in. below the top of the tank. Weights were placed on the ends of the platform to prevent floating during the immersion period. The ureteral catheters were brought out through the front of the tank through water tight adapters at a level approximately 2 in. below the animal. All other catheters were made accessible by hanging them over the side of the tank. The animals were maintained on intermittent positive pressure respiration using room air supplemented with 100% oxygen. Blood gases and pH were measured periodically and were within normal limits. A schematic diagram of the experimental preparation is shown in Fig. 1.

After surgery was completed and the ani-

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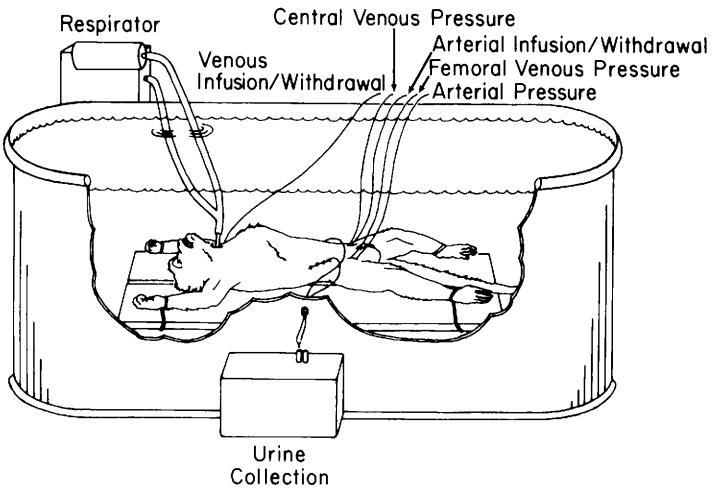

FIG. 1. Schematic diagram of the experimental preparation during the immersion phase of the experiments. The tank has been filled to a level 8–10 in. above the monkey's chest.

mal positioned in the tank an infusion of creatinine and *para*-aminohippurate (PAH) was begun. An hour later, timed urine collections were started. After 30–40 min of relatively constant urine flow the tank was filled with warm tap water (35.6 ± 0.6°) to a level 8–10 in. above the monkey's chest. This level varied depending on the measured distance from the lower abdomen to the suprasternal notch. After 40 min of immersion the platform and attached animal were lifted from the tank and postimmersion readings taken.

The Group II animals underwent the same surgical preparation and protocol as Group I except they were not placed in the tank but remained recumbent on the operating table. Also, these animals were not ventilated and femoral venous pressure was not measured.

Creatinine and PAH clearances were determined using the standard clearance technique. They were dissolved in isotonic sodium chloride and infused at a rate of 0.75 ml/min to maintain plasma levels constant. Four milliliter arterial blood samples were obtained at the midpoint of alternate urine collection periods using heparinized syringes. After separating the plasma, the red cells were reconstituted with 6% dextran in isotonic saline and returned to the animal intravenously. All pressures were monitored with a Hewlett–Packard 8-channel recorder. Creatinine and PAH concentrations were determined with a Technicon autoanalyzer, sodium and potassium by flame photometry (FLM-1, Radiometer, Copenhagen), and osmolality by freezing point depression (Advanced Instruments, Inc.). These data were used to compute basic renal functions with the aid of an IBM 1800 computer. Statistical analysis was done using an analysis of variance with repeated measures design and Newman–Keuls test for within-group comparisons and unpaired *t* test for between-group comparisons (5). Probability values less than 0.05 were considered as statistically significant.

Results. Table I shows the systemic and renal hemodynamic effects of recumbent immersion. Immersion (Group I) was associated with significant increases in CVP and FVP but no change in mean arterial blood pressure (MABP), heart rate (HR), creatinine clearance (C_{cr}), PAH clearance (C_{PAH}), or hematocrit (HCT). The time control animals (Group II) had no change in any of these parameters during the course of the experiment. MABP was significantly higher in Group I than in Group II for all time periods but there were no group differences with respect to other hemodynamic parameters.

As shown in Table II, immersion had no effect on the renal excretion of salt and water. Urine flow ($\dot{V}$), sodium excretion ($U_{NA}\dot{V}$), fractional sodium excretion (F_{Na}), potassium excretion ($U_K\dot{V}$), osmolar clearance (C_{osm}), and free-water clearance (C_{H_2O}) remained unchanged. Likewise, the Group II animals showed no changes in renal excretion and

TABLE I. EFFECTS OF RECUMBENT IMMERSION ON SYSTEMIC AND RENAL HEMODYNAMICS[a]

		Time (min)						
		Preimmersion		Immersion				Postimmersion
	Group	10	20	30	40	50	60	70
MABP	I (4)	121.8 ± 5.3[b]	114.8 ± 7.2[b]	127.2 ± 11.7[b]	125.3 ± 11.5[b]	125.1 ± 11.1[b]	124.3 ± 6.4[b]	122.8 ± 5.6[b]
(mm Hg)	II (4)	80.5 ± 5.7	79.5 ± 7.3	78 ± 4.8	80 ± 4.2	81.5 ± 3.9	83.3 ± 8.3	86.3 ± 6.2
HR	I (4)	198 ± 15	198 ± 16	185 ± 18	191 ± 15	191 ± 15	194 ± 14	195 ± 17
(beats/min)	II (4)	183 ± 24	185 ± 25	191 ± 23	185 ± 26	186 ± 24	184 ± 25	182 ± 26
CVP	I (3)	2.7 ± 2.2	3.4 ± 2.5	15.4 ± 0.5[b,c]	15.1 ± 1.7[b,c]	15.1 ± 1.4[b,c]	14.9 ± 1.3[b,c]	2.4 ± 1.6
(cm H_2O)	II (4)	−1.3 ± 3.9	−1.5 ± 3.8	−1.6 ± 3.9	−1.6 ± 3.8	−1.8 ± 3.8	−1.8 ± 3.8	−2.0 ± 3.8
FVP	I (3)	4.5 ± 2.9	3.8 ± 2.6	21.8 ± 2.4[c]	21.3 ± 2.0[c]	21.8 ± 1.7[c]	21.0 ± 1.4[c]	1.3 ± 0.9
(cm H_2O)	II	..						
C_{cr}	I (4)	0.58 ± 0.06	0.61 ± 0.07	0.84 ± 0.25	0.60 ± 0.12	0.56 ± 0.12	0.67 ± 0.17	0.59 ± 0.09
(ml/min/g)	II (4)	0.72 ± 0.10	0.60 ± 0.07	0.74 ± 0.16	0.68 ± 0.02	0.68 ± 0.11	0.67 ± 0.12	0.59 ± 0.11
C_{PAH}	I (4)	1.82 ± 0.41	1.83 ± 0.40	2.61 ± 0.78	1.86 ± 0.44	1.66 ± 0.48	1.78 ±0.43	1.33 ± 0.20
(ml/min/g)	II (3)	2.35 ± 0.78	2.24 ± 0.55	3.00 ± 0.76	2.18 ± 0.69	2.45 ± 0.93	2.21 ± 0.34	2.03 ± 0.90
HCT	I (4)	39.5 ± 1.9	40.3 ± 1.8	40.5 ± 1.8	40.3 ± 2.0	40.5 ± 1.4	40.3 ± 1.2	39.3 ± 1.7
(%)	II (4)	36.8 ± 4.0	36.8 ± 4.0	36.3 ± 4.3	36.3 ± 4.3	35.8 ± 4.5	35.5 ± 4.5	35.3 ± 4.5

[a] Values are means ± SE; figures in parentheses represent number of animals.
[b] Significantly different from group II values at $P < 0.05$.
[c] Significantly different from pre- and postimmersion values at $P < 0.05$.

TABLE II. EFFECTS OF RECUMBENT IMMERSION ON RENAL EXCRETION[a]

		Time (min)						
		Preimmersion		Immersion				Postimmersion
	Group	10	20	30	40	50	60	70
$\dot{V}$, (ml/min)	I (4)	0.17 ± 0.07	0.16 ± 0.06	0.22 ± 0.08	0.18 ± 0.05	0.14 ± 0.04	0.16 ± 0.02	0.18 ± 0.04
	II (4)	0.24 ± 0.14	0.21 ± 0.11	0.28 ± 0.17	0.25 ± 0.12	0.24 ± 0.10	0.29 ± 0.12	0.29 ± 0.14
$U_{Na}\dot{V}$, (μeq/min)	I (4)	12.9 ± 9.4	11.8 ± 8.9	18.1 ± 11.3	13.2 ± 5.6	8.6 ± 5.0	8.2 ± 4.4	11.3 ± 6.4
	II (4)	18.5 ± 17.3	15.2 ± 12.2	21.2 ± 17.7	16.1 ± 11.9	13.8 ± 9.7	20.7 ± 12.5	20.6 ± 14.9
F_{Na}, (%)	I (4)	0.73 ± 0.50	0.65 ± 0.48	0.86 ± 0.58	0.77 ± 0.30	0.44 ± 0.21	0.41 ± 0.18	0.64 ± 0.32
	II (4)	0.79 ± 0.62	0.79 ± 0.51	0.94 ± 0.63	0.78 ± 0.51	0.72 ± 0.42	1.14 ± 0.58	1.10 ± 0.59
$U_K\dot{V}$, (μeq/min)	I (4)	9.2 ± 0.6	10.2 ± 1.2	15.3 ± 3.3	11.5 ± 1.9	10.1 ± 2.2	10.1 ± 2.5	6.0 ± 0.8
	II (4)	16.8 ± 7.4	13.4 ± 4.6	16.7 ± 6.0	15.3 ± 4.0	15.3 ± 4.8	15.1 ± 3.3	13.9 ± 4.1
C_{osm}, (ml/min)	I (4)	0.26 ± 0.08	0.26 ± 0.07	0.38 ± 0.10	0.29 ± 0.08	0.24 ± 0.09	0.26 ± 0.06	0.27 ± 0.06
	II (4)	0.39 ± 0.19	0.34 ± 0.14	0.49 ± 0.25	0.38 ± 0.13	0.36 ± 0.10	0.44 ± 0.11	0.39 ± 0.17
C_{H_2O}, (ml/min)	I (4)	−0.10 ± 0.03	−0.11 ± 0.03	−0.16 ± 0.05	−0.10 ± 0.06	−0.10 ± 0.06	−0.11 ± 0.04	−0.09 ± 0.03
	II (4)	−0.15 ± 0.05	−0.13 ± 0.03	−0.21 ± 0.09	−0.13 ± 0.01	−0.12 ± 0.04	−0.12 ± 0.05	−0.10 ± 0.05

[a] Values are means ± SE; figures in parentheses represent number of animals.

there were no differences between the groups.

Figure 2 shows the time course of some of the hemodynamic and renal responses to recumbent immersion during an experiment where the immersion lasted 50 min.

Discussion. Water immersion to the neck in the upright anesthetized monkey has been shown to result in a marked diuresis and natriuresis (4) similar to that observed in the conscious human (1). These responses are believed to be mediated via intrathoracic volume receptors which are stimulated by the immersion-induced increase in central blood volume (2). This effect of immersion on central blood volume is a consequence of the hydrostatic forces which are exerted differentially on the body surfaces. During upright immersion the lower extremities are subjected to a higher external pressure than the thorax. This hydrostatic pressure gradient is large

enough to cause a translocation of blood from the lower body to the thorax thus leading to an increase in central blood volume and cardiac distension (3). As a result it is believed that intrathoracic receptors are stimulated which, in turn, evoke a variety of responses thereby producing the well-documented renal responses.

A possible role of cardiopulmonary volume receptors in contributing to the renal responses to immersion has, however, not been demonstrated experimentally. The atrial stretch reflex which has been shown to utilize the vagus as the afferent limb (2) appears to be of little importance since it has been found that the vagotomized monkey shows no attenuation of the diuresis or natriuresis of immersion (4). Similar results have been reported for the dog (6, 7). These findings question the involvement of cardiopulmonary volume receptors in immersion and importance of thoracic translocation as a causal factor. Abdominal compression has also been suggested as a contributing factor possibly via a direct effect on the kidney to alter intrarenal blood flow distribution. Since a circulating natriuretic factor has also been hypothesized to be present during immersion (8, 9), it may be that this substance is of renal origin and is also released as a result of the abdominal compression having a direct effect on the kidney.

If thoracic translocation is not necessary for, and if abdominal compression does play a role in this response, the recumbent animal, immersed to a depth where the hydrostatic pressure on the abdomen is approximately equal to that in the upright immersed animal, should show a difference in salt and/or water excretion when compared with nonimmersed recumbent controls. However, in the present study, immersion caused no significant change in renal function. With regard to hemodynamic parameters, CVP and FVP did increase but probably only as a result of the water pressure being exerted on the body surfaces.

Although other studies have been performed in which subjects were immersed in a recumbent position (10–12), in none of these experiments were the subjects immersed to the same relative depth as in our study. These previous studies, although not specifying the actual depth of immersion, utilized head-out immersion. It seems reasonable to assume that in these human studies the abdomen would not be at as great a depth during head-out immersion in the recumbent position as during head-out upright immersion, and, therefore, not subject to the same degree of hydrostatic pressure.

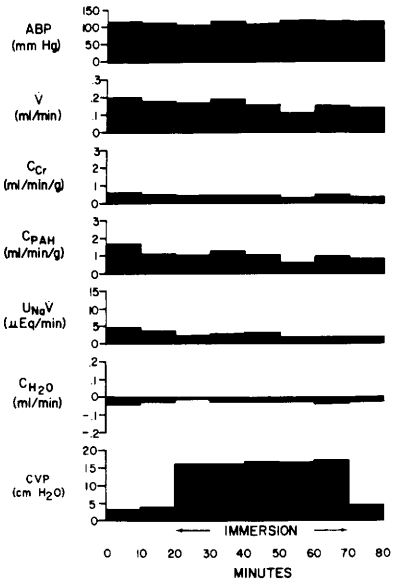

FIG. 2. Time course of the renal responses of a recumbent monkey to total body water immersion. ABP = Mean arterial pressure, $\dot{V}$ = urine flow, C_{Cr} = creatinine clearance, C_{PAH} = *para*-aminohippurate clearance, $U_{NA}\dot{V}$ = sodium excretion, C_{H_2O} = free water clearance, and CVP = central venous pressure.

The results of these previous recumbent immersion studies are conflicting, probably because of methodological differences. Behn *et al.* (10) reported increases in both urine flow and sodium excretion during head-out immersion in human subjects lying recumbent on a cot. However, the control values which these investigators used for comparison were obtained during the 36-hr period preceding immersion with the subjects undergoing "routine activity." The renal responses of their subjects could have been due to the assumption of a recumbent posture (13) rather than the immersion per se. Boening *et al.* (11) also noted an increased salt and water excretion in immersed recumbent subjects. However, their subjects were reclining in a deck chair during the immersion period suggesting that the upper portion of the body

may have been higher than the lower trunk thus possibly generating a hydrostatic pressure gradient with some translocation of blood to the thorax. In contrast, Epstein *et al.* (12), utilizing recumbent controls in their studies, could detect no consistent significant effects of head-out immersion with their subjects lying on a cot. However, as noted above, none of these previous studies took immersion depth into account by considering external pressure on the abdomen as a contributing factor.

It should be noted that the immersed animals used in the present study were ventilated throughout the course of each experiment. Continuous positive pressure breathing using positive end-expiratory pressure (PEEP) has been shown to cause an antidiuresis in the dog (14) and an inhibition of the immersion diuresis in man (15). Both of these effects are presumably due to a transthoracic counterpressure which decreases central blood volume. However, Baratz *et al.* (16) found that intermittent positive pressure breathing (IPPB) with an end-expiratory pressure of zero had no effect on urine flow or circulatory dynamics. Moreover, Gilmore and Zucker (4) were unable to detect any differences between the renal responses of upright immersed monkeys which were subjected to IPPB and monkeys which were not mechanically ventilated. Therefore, the use of IPPB with an end-expiratory pressure of zero should have no bearing on the results of our study. In addition, our immersed animals were ventilated throughout the control periods also so that this variable was adequately controlled.

The results of the present experiments and previous experiments from this laboratory have shown the following. First, the renal responses to immersion do not occur during recumbency, regardless of the depth of the water. Therefore, the hydrostatic pressure gradient generated by the water pressure on the body surfaces, an effect present in the upright posture but absent during recumbency, must be the causal factor leading to the renal responses. This would suggest that translocation of blood to the thorax is necessary although we cannot completely rule out the possibility that some translocation may have occurred in the present experiments. The increases in CVP and FVP would suggest that these changes were an effect of external pressure but more objective evidence is needed to determine if part of the rise in CVP reflected an increase in central blood volume. The afferent neural pathway involved is not vagal (4) but may be via cardiopulmonary volume receptors with nonvagal afferents. Perhaps the cardiac sympathetic afferent nerves are involved since they have been implicated as a volume receptor pathway during volume expansion (17). Second, the abdominal compression observed during upright immersion does not contribute to the diuresis or natriuresis. This does not allow us to rule out changes in intrarenal blood flow distribution or release of a humoral substance of renal origin as possible factors involved in the renal responses but suggests that these effects may occur only in the upright immersed animal. Third, our results question the mechanism suggested by Davis and DuBois (6) that the initiator of the diuresis of immersion is hemodilution occurring as a result of the external pressure outside the body shifting hyposmotic interstitial fluid into the blood. If this mechanism is operating then our animals, particularly at the immersion depth used, should have shown a decreased hematocrit and diuresis. Since neither of the above occurred, we do not believe that hemodilution is a significant factor in the monkey.

With regard to the efferent mechanism, hemodynamic changes do not seem to be the major determinants since GFR and ERPF remain relatively constant during immersion in both man (9) and the monkey (4) while urine flow and sodium excretion continue to increase. In addition, treatment of subjects with deoxycorticosterone (4, 18) or ADH (4) fail to abolish the renal responses. An immersion-induced release of a humoral factor of natriuretic character has been suggested (8, 9) but the quick off response of the diuresis and natriuresis in the monkey (4) may not be compatible with a humoral mechanism.

In summary, although a translocation of blood volume appears to be necessary for the renal responses induced by head-out immersion, both the afferent and efferent mechanisms remain to be fully elucidated.

Summary. Experiments were performed to determine the extent to which thoracic trans-

location of blood and abdominal compression contribute to the diuresis and natriuresis during head-out water immersion in the anesthetized nonhuman primate. Neither a diuresis nor natriuresis occurred in animals immersed in the recumbent posture to a depth such that the abdomen was subjected to the same water pressure as during head-out upright immersion. It is concluded that the abdominal compression observed during upright immersion does not contribute per se to the renal responses and that the immersion-induced translocation of blood to the thorax may be the causal factor during this volume stimulus.

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