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Central venous pressure and plasma arginine vasopressin during water immersion in man*

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Summary: The influence of increased central venous pressure (CVP) on the plasma concentration of arginine vasopressin (pAVP) was examined in 7 healthy males subjected to water immersion (WI) up to the neck following overnight food- and fluid restriction. During WI the subject sat upright in a pool (water temperature = 35.0° C) for 6 h. In control experiments the subject assumed the same position outside the pool wearing a water perfused garment (water temperature = 34.6° C). CVP increased markedly during WI and after 20 min of immersion it attained a level which was significantly higher than the control value (10.9 ± 1.5 (mean ± SE) vs. 2.2 ± 1.3 mm Hg, $p < 0.01$). This increase was sustained throughout the 6 h WI period. Simultaneously, after 20 min pAVP during WI was significantly lower than control values (1.8 ± 0.3 vs. 2.2 ± 0.3 pg · ml^{-1}, $p < 0.05$) and sustained throughout WI. Systolic arterial pressure increased significantly by 7–10 mm Hg ($p < 0.05$) after 2 h of WI, while diastolic arterial pressure was unchanged. Heart rate was decreased by 10 bpm throughout immersion. There was no change in plasma osmolality when comparing control with immersion. A pronounced osmotic diuresis, natriuresis and kaliuresis occurred during WI, counteracting an acute significant increase in plasma volume of 6.5 ± 1.9% ($P < 0.01$ within 20 min of immersion). We conclude that an increase in CVP due to WI is accompanied by suppressed pAVP.

Key words: Arginine vasopressin — Central venous pressure — Central volume expansion — Water immersion

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Introduction

The release of arginine vasopressin (AVP) from the neurohypophysis is influenced by both osmotic and nonosmotic stimuli (Weitzman and Kleeman 1979; Robertson 1980; Schrier and Bichet 1981). Osmotic regulation is reasonably well studied while the nonosmotic control mechanisms remain incompletely understood. During lower body negative pressure (LBNP), which induces central hypovolemia, Rogge and Moore (1968) measured an increase in antidiuretic hormone activity in peripheral venous blood, and Baylis et al. (1978) and Bonde-Petersen et al. (1982) found an increase in plasma AVP (pAVP). On the other hand Goldsmith et al. (1982) found no change in pAVP during graded LBNP, though catecholamines rose and central venous pressure (CVP) decreased. Robertson and Athar (1976) showed that upright posture increased pAVP and lowered the osmotic threshold for its release. Head up tilt caused significant but moderate increments of pAVP in a biphasic pattern (Weitzman and Kleeman 1979).

Fewer investigations have analysed AVP secretion during central blood volume expansion in man. Gauer and Henry (1976) and Gauer (1979) stated that central blood volume expansion through stretch of atrial mechanoreceptors suppresses AVP secretion leading to an increased diuresis. This increase in diuresis has been demonstrated during negative pressure breathing and water immersion (WI) in man (Gauer and Henry 1976; Epstein 1978a). In dogs, left atrial distension decreases pAVP (Schultz et al. 1982; Ledsome et al. 1983). In normal man, Epstein et al. (1981) measured pAVP during 4 h of WI to the neck in a thermoneutral bath (34.5° C) and concluded that isoosmotic central blood volume in-

crease suppressed pAVP. In another WI study, Greenleaf et al. (1983) found no significant change in pAVP when comparing with prestudy levels. In neither of these two studies was CVP measured. Goldsmith et al. (1984) measured pAVP, CVP and arterial pressure in humans during lower body positive pressure with a medical antishock trouser suit, during infusion with saline and during head down tilt. They could not confirm suppression of pAVP during the manoeuvers, though CVP increased.

The purpose of the present study was therefore to test the theory of Gauer and Henry (1976) in man, measuring CVP during central blood volume expansion induced by WI for 6 hours, and to relate the time course of CVP to that of pAVP. Furthermore, since Khosla and Dubois (1979; 1981) and Greenleaf et al. (1981) found a decrease in plasma osmolality (Osm) during WI, it was of interest to investigate the possible role which changes in Osm might play in WI-induced suppression of AVP secretion.

Material and methods

Seven healthy males age 19—28 years, weight 61.8—92.8 kg, and height 168—199 cm participated in the experiment. All had a negative history for hypertension, cardiovascular- or kidney diseases. Informed consent was obtained after the subjects had read a description of the experimental protocol.

During WI to the neck (sternoclavicular notch) the subject was sitting in a swimming pool kept at 35.0 ± 0.2° C. During control experiments the subject was sitting beside the swimming pool wearing a water perfused garment (liquid conditioned coverall, size 8A W/O 334/78 series 7 type 3, Beaufort). An air pressure driven water pump perfused the garment with water taken from the pool. The temperature in the garment was 34.6 ± 0.3° C. The water perfused garment was used in the control experiment in order to ensure the same skin temperature as during water immersion. The air temperature was 28—31° C. During WI the subject had the arms on arm rests just above the water surface for blood pressure measurements and blood sampling. Therefore, during control experiments, the arms were kept outside the garment and elevated to a horizontal position above heart level. The subject was placed in a specially constructed chair which was used both in the control experiments and in the pool in order to ensure that he retained the same position. As the arm blood pressure was measured with the upper arms elevated 20 cm above heart level the measured blood pressures were corrected by adding 15 mm Hg.

The air temperature and the temperature of the water during WI and of the in- and outgoing water in the thermosuit was measured by an electric thermometer (Ellab, Copenhagen, Denmark, type d179, 12 channels) and printed out every 20 min.

The concentration of AVP in plasma (pAVP) was measured by radio immuno assay (Bie and Warberg 1983). Blood samples of mixed venous blood taken through a central venous catheter were collected in prechilled, disposable polypropylene syringes (10 ml, Brunswick) and immediately transferred to polyethylene test tubes (10 ml, Minisorp) containing 12.5 IE of heparin per ml blood. The blood samples were immediately separated by centrifugation at 4° C for 10 min, and 2 ml of plasma was stored at −20° C for later analysis of control- and WI samples in the same assay. Synthetic AVP (Ferring) served as reference preparation. The least detectable quantity of AVP was 0.3—0.6 pg/tube.

Central venous pressure (CVP) was measured through an indwelling 60 cm long catheter (Intracath) introduced through a cubital vein until the tip reached an inthrathoracic vein. The catheter was connected to the dome of a pressure transducer (Siemens Elema AB, E033E) by a 180 cm plastic tube. The pressure transducer was placed at a level with the subjects right nipple (arms and body in the same relative positions during both control and WI) and connected to a pressure amplifier (Siemens 863). From a strip chart recording (Clevite Brush, mark 220) the mean CVP value was measured with an accuracy of 0.2 mm Hg. Position of the catheter was confirmed by typical waveforms and by characteristic responses to respiratory manoeuvers.

Plasma osmolality (Osm) was measured with an osmometer (Advanced osmometer, model 3L) by freezing point depression. Two ml of plasma were taken from the same plasma sample as for AVP determination and stored at −20° C. It was previously established that storing at this temperature does not change Osm by taking 12 samples from one subject within 5 min, measuring osmolality immediately in 6 samples while the 6 remaining were examined after storage at −20° C. Osm was 295.0 ± 0.1 mosm·kg^{-1} (mean ± SE) in the immediately examined samples and 295.3 ± 0.2 mosm·kg^{-1} in the frozen ones. There was no significant difference.

Hematocrit (Hct) was measured in Na-heparinized tubes (Micro-Haematocrit) on an autocrit centrifuge (Clay-Adams). Raw Hct values were corrected for trapped plasma and for whole-body Hct by multiplication with the factors 0.96 and 0.93 (0.893), respectively.

Hemoglobin (Hb) was measured by a spectrophotometer (Zeiss, M4 QIII) by a cyanid method.

Percent changes in plasma volume (PV) were calculated from concomitant Hct and Hb concentrations, using the formula of Dill and Costill (1974).

Systolic (SAP) and diastolic (DAP) arterial pressures were measured with a mercury sphygmomanometer (Erkameter 300) and a stethoscope. The beginning of the fourth Korotkoff sound indicated DAP. Heart rate was measured by palpating the radial artery.

Urine was sampled at hourly intervals and diuresis ($\dot{V}_U$) measured in a 100 ml measuring glass with an accuracy of ±2 ml. Urine osmolality (U_{osm}) was measured as described above, and concentrations of sodium and potassium in urine (U_{Na} and U_K) were measured in a flame photometer (Radiometer FLM 3). Sodium excretion ($U_{Na}\dot{V}_U$), potassium excretion ($U_K\dot{V}_U$), osmotic excretion ($U_{osm}\dot{V}_U$), osmotic clearence (C_{osm}), and solute free water absorption (T^cH_2O) were calculated using conventional formulae.

Experimental procedure

The subjects were studied one at a time. The control and WI studies were separated by 3—7 days (30 days for one subject) and the sequence randomised among the subjects. The experimental protocols during control and WI were similar and carried out as follows.

All subjects had been told not to smoke, drink coffe, tea or alcohol from the day before experimentation and were fast-

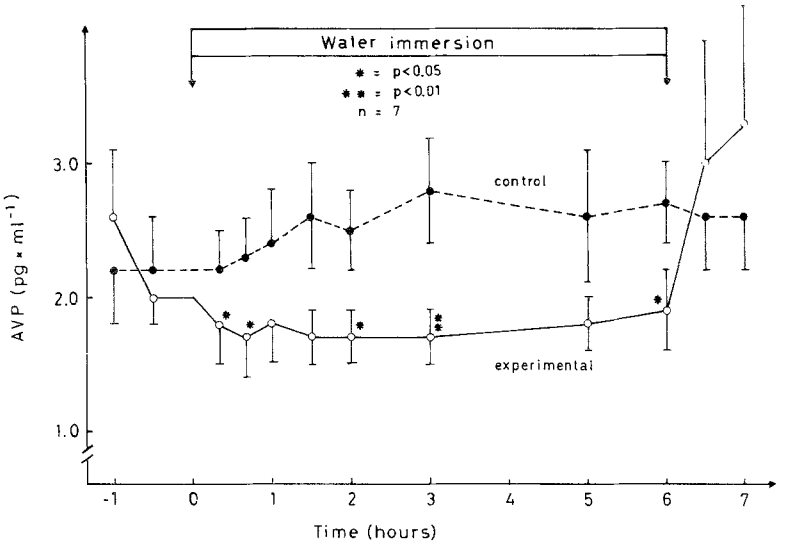

Fig. 1. Plasma concentration of arginine vasopressin (AVP) in $pg \cdot ml^{-1}$ (mean $\pm$SE of 7 subjects) versus time in hours during control (●) and water immersion to the neck (○). Stars indicate significant change compared to control at the same hour

ing (no food nor drink) from 19.00 h until the end of the experiment the following afternoon. Thus the subject was mildly dehydrated during the experiment. This was necessary to obtain an adequately high level of pAVP during standard conditions. Prior to WI the subject slept at the laboratory from 22.00 h and was awakened at 06.30 h, and allowed to wash and urinate. Thereafter the venous catheter was placed during ECG surveillance with the subject in the supine position. The catheter was flushed with 10 ml of isotonic saline every half hour and 1 ml of heparin solution in saline (50 IE per ml) was used to just fill the catheter after flushing or blood sampling. The catheter dead spaces were emptied before each sampling. The amount of saline given during the experiment was equal to the amount of blood taken. At 07.15 h the subject, wearing shorts, was placed beside the swimming pool resting in the chair for 45 min. From 08.00 to 09.00 h (-1—0 h prestudy period) and from 15.00 to 16.00 h (6—7 h, poststudy period) the subject sat in the chair beside the pool both during the control study and WI. During control, the subject was sitting in the chair wearing the water perfused garment from 09.00 to 15.00 h. while during WI the subject sat in the swimming pool from 09.00 to 15.00 h (0—6 h). During both studies the measurements were performed in the following sequence: blood sample collection (10 ml for determination of pAVP, Osm, Hct and Hb), CVP, SAP, DAP and HR at the following experimental hours: -1, -0.5, 0.33, 0.67, 1, 1.5, 2, 3, 4 (no blood sample), 5, 6, 6.5 and 7. At hourly intervals starting at -1 h, the subject was requested to void directly after the measurements completely emptying the bladder and briefly standing on the seat of the chair.

Before and after experimentation the subject was weighed. To exclude serious kidney diseases a Labstix was used in the first urine sample.

Data were evaluated statistically by paired t-tests. A significance level of 0.05 was accepted.

The protocol was registered by the ethical commission of Copenhagen and was in compliance with the principles set forth in the declaration of Helsinki. No complications occurred.

Results

After 20 min of WI, pAVP was significantly lower than control values (1.8 ± 0.3 vs. 2.2 ± 0.3 $pg \cdot ml^{-1}$, mean $\pm$SE, $p < 0.05$, Fig. 1). This sup-

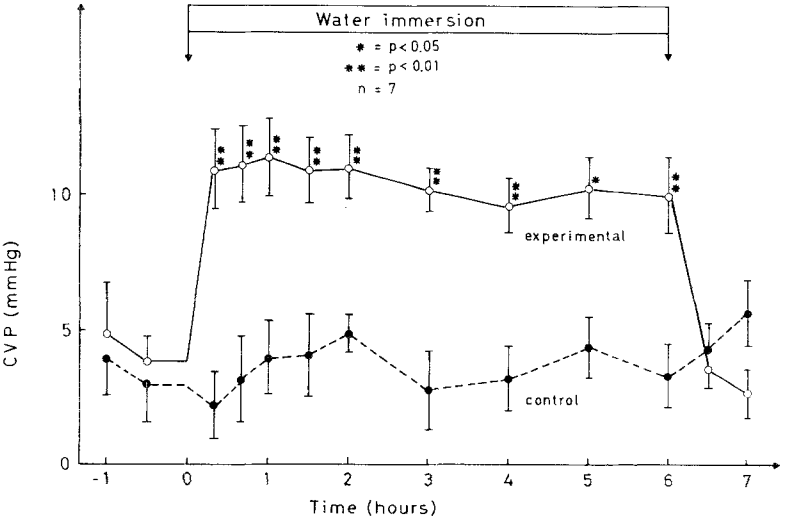

Fig. 2. Central venous pressure (CVP) in mm Hg (mean $\pm$SE of 7 subjects) versus time in hours during control (●) and water immersion to the neck (○). Stars indicate significant change compared to control at the same hour

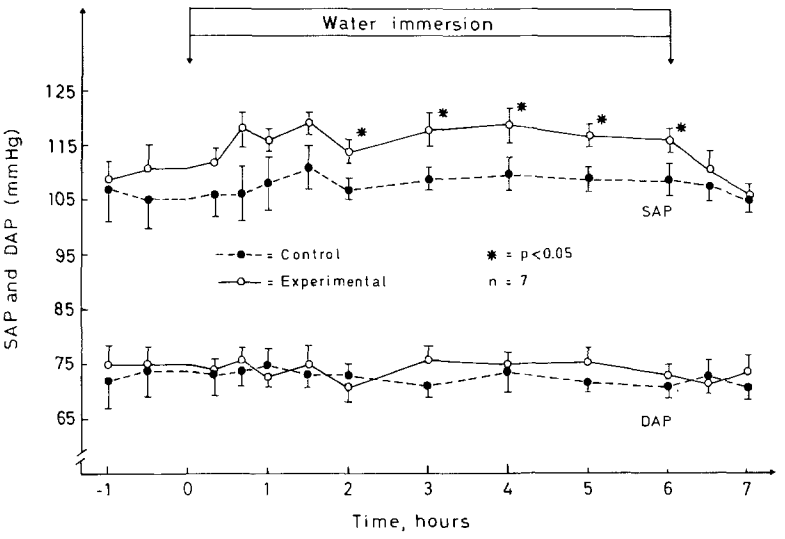

Fig. 3. Systolic (SAP) and diastolic (DAP) arterial pressure in mm Hg (mean ±SE of 7 subjects) versus time in hours during control (●) and water immersion to the neck (○). The pressures are corrected for elevation of the arms of 20 cm = 15 mm Hg. Stars indicate significant change compared to control at the same hour

pression of AVP was sustained throughout WI and after 6 h of immersion pAVP was still significantly lower than that observed during control (1.9 ± 0.3 vs. 2.7 ± 0.3 pg·ml^{-1}, $p < 0.02$, Fig. 1). During recovery after WI, pAVP increased from 1.9 ± 0.3 pg·ml^{-1} to 3.0 ± 0.9 pg·ml^{-1} (0.5 h of recovery) and to 3.3 ± 1.0 pg·ml^{-1} (1 h of recovery) whereas the control values were unaltered. Two subjects showed no suppression of pAVP during WI though their diuresis increased. Of the five subjects having an AVP suppression two showed very large increases during recovery (one subject from 3.0 pg·ml^{-1} to 9.1 pg·ml^{-1} and the other from 1.2 pg·ml^{-1} to 4.3 pg·ml^{-1} after 1 h of recovery). A third subject only showed an increase from 1.5 pg·ml^{-1} to 1.9 pg·ml^{-1}. Two of the subjects, who showed suppressed pAVP during WI, did not show any increase during recovery though diuresis decreased.

CVP increased markedly during WI and after 20 min of immersion it attained a level which was significantly higher than the control value (10.9 ± 1.5 vs. 2.2 ± 1.3 mm Hg, $p < 0.01$, Fig. 2). The increase was sustained throughout WI although a slight but insignificant decrease was observed from 11.4 ± 1.4 mm Hg after 1 h of WI to 10.0 ± 1.4 mm Hg after 6 h. CVP decreased below control level after 1 h recovery. During control CVP fluctuated from 2.2 ± 1.3 mm Hg after 20 min in the thermosuit to 5.7 ± 1.2 mm Hg at the end of the study.

SAP increased significantly after 2 h WI by 7—10 mm Hg ($p < 0.05$), while DAP was unchanged (Fig. 3). After WI, SAP recovered after 1 hour.

HR during WI decreased significantly ($p < 0.05$) after 20 min compared with control from 78 ± 3 bmp to 68 ± 4 bpm. This decrease was

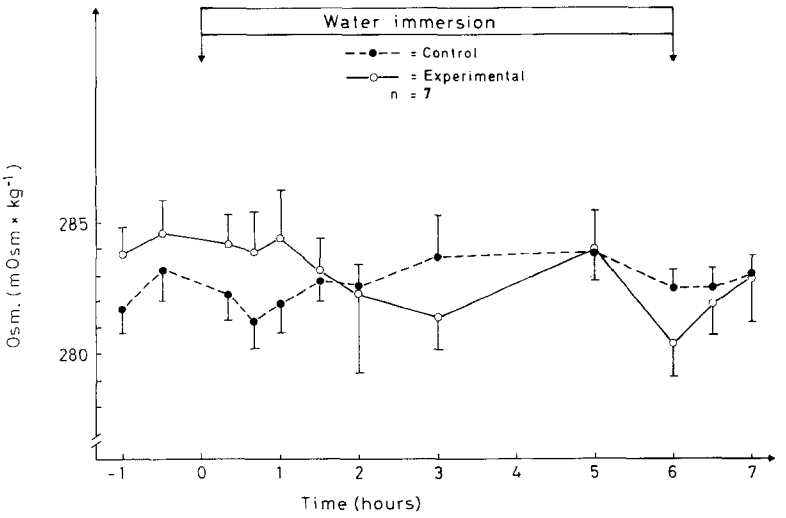

Fig. 4. Plasma osmolality (Osm) in mosm·kg^{-1} (mean ±SE of 7 subjects) versus time in hours during control (●) and water immersion to the neck (○)

Table 1. Effect of water immersion on diuresis ($\dot{V}_U$), sodium excretion ($U_{Na}\dot{V}_U$), potassium excretion ($U_K\dot{V}_U$), urine osmolality (U_{osm}), osmotic excretion ($U_{osm}\dot{V}_U$), osmotic clearence (C_{osm}), and free water absorption (T^cH_2O). Values are means ± SE. Number of subjects is indicated in parentheses

	Prestudy	Immersion						Poststudy
	0 h	1 h	2 h	3 h	4 h	5 h	6 h	7 h
$\dot{V}_U$(ml·min^{-1})								
Control	0.7±0.2(7)	0.5±0.0(7)	0.4±0.0(7)	0.5±0.0(7)	0.4±0.0(6)	0.4±0.0(6)	0.4±0.0(6)	0.4±0.0(6)
Immersion	0.6±0.1(6)	0.7±0.1(6)*	0.9±0.1(6)*	1.5±0.3(7)**	1.9±0.4(7)*	1.7±0.4(7)**	1.6±0.4(7)*	0.6±0.1(6)
$U_{Na}\dot{V}_U$(μeq·min^{-1})								
Control	58±30(5)	46±11(6)	42±9(6)	46±11(6)	38±8(5)	34±4(5)	26±3(5)	28±3(5)
Immersion	87±10(6)	96±17(6)*	142±30(6)*	235±39(7)**	271±34(7)**	245±31(7)**	235±30(7)**	115±14(6)*
$U_K\dot{V}_U$(μeq·min^{-1})								
Control	58±14(6)	58±8(6)	55±8(6)	58±8(6)	61±6(5)	61±6(5)	54±7(5)	59±5(5)
Immersion	64±11(6)	65±11(6)	91±7(6)*	132±22(7)*	115±18(7)	81±12(7)	63±12(7)	43±5(6)
U_{osm}(mosm·kg^{-1})								
Control	1021±80(6)	1041±79(6)	1053±80(6)	1062±83(6)	1065±102(5)	1092±111(5)	1058±102(5)	1105±118(5)
Immersion	1068±56(6)	957±49(6)	962±49(6)	825±78(7)	724±97(7)	670±113(7)	674±105(7)	839±47(6)
$U_{osm}\dot{V}_U$(mosm·min^{-1})								
Control	0.7±0.3(6)	0.5±0.1(6)	0.5±0.1(6)	0.5±0.1(6)	0.4±0.1(5)	0.5±0.1(5)	0.4±0.1(5)	0.5±0.1(5)
Immersion	0.6±0.1(6)	0.7±0.1(6)	0.8±0.1(6)*	1.1±0.1(7)*	1.1±0.1(7)**	0.9±0.1(7)*	0.9±0.1(7)*	0.5±0.0(6)
C_{osm}(ml·min^{-1})								
Control	2.6±0.9(6)	1.8±0.2(6)	1.7±0.2(6)	1.8±0.3(6)	1.5±0.2(5)	1.5±0.3(5)	1.4±0.3(4)	1.6±0.3(4)
Immersion	2.2±0.2(6)	2.4±0.2(6)	2.9±0.3(6)*	3.7±0.4(7)*	4.0±0.4(7)**	3.1±0.4(7)*	3.0±0.4(7)	1.7±0.2(6)
T^cH_2O(ml·min^{-1})								
Control	1.9±0.7(6)	1.3±0.2(6)	1.3±0.2(6)	1.4±0.2(6)	1.2±0.2(5)	1.0±0.3(5)	1.1±0.3(4)	1.3±0.3(4)
Immersion	1.6±0.1(6)	1.7±0.2(6)	2.1±0.2(6)	2.3±0.4(7)	2.1±0.3(7)*	1.4±0.3(7)	1.5±0.2(7)	1.1±0.1(6)

* = $P<0.05$ and ** = $P<0.01$ as compared with controls

Table 2. Effect of water immersion on blood hematocrit (Hct), hemoglobin (Hb), and plasma volume change (ΔPV) calculated from changes of Hct and Hb. Hct values are corrected for trapped plasma and for whole-body Hct by multiplication with 0.893. Values are means ± SE of seven subjects

	Prestudy	Immersion						Poststudy
	−1 h	⅓ h	1 h	2 h	3 h	5 h	6 h	7 h
Hct (%)								
Control	40.5±1.4	40.5±1.4	40.1±1.4	40.1±1.4	40.2±1.4	40.2±1.5	39.9±1.4	39.7±1.3
Immersion	39.5±1.1	37.7±1.0*	37.3±0.9*	37.1±0.9*	37.1±0.8*	38.0±0.9	37.9±0.9	40.1±1.0
Hb (g·dl^{-1})								
Control	16.1±0.6	15.7±0.5	15.3±0.5	15.3±0.5	15.4±0.5	15.3±0.4	15.5±0.5	15.5±0.6
Immersion	14.9±0.6	14.2±0.5*	14.3±0.6*	14.2±0.5*	14.5±0.4*	14.9±0.6	14.8±0.5	15.6±0.6
ΔPV (%)								
Control	0	−0.8±1.1	+2.5±2.1	+2.2±1.1	+1.4±1.6	+2.4±1.6	+1.1±1.0	+1.6±2.3
Immersion	0	+6.5±1.9**	+6.9±1.9	+7.9±2.3	+5.4±2.9	+1.9±2.6	+2.6±2.8	−6.1±2.7

* = $P<0.05$ and ** = $P<0.01$ as compared with controls

maintained throughout immersion and HR returned to control level during 30 min of recovery.

Osm did not change when comparing control and WI, indicating that the changes in pAVP was not caused by an osmotic stimulus (Fig. 4).

The total 8 h diuresis increased significantly during WI compared to control from 239±28 ml to 632±79 ml ($p<0.001$). $\dot{V}_U$ increased during WI with a peak value after 4 h (Table 1). There was a pronounced natriuresis and kaliuresis. T^cH_2O increased during immersion when compared to control values indicating an osmotic diuresis. The reason for the partly reduced number of subjects in Table 1, is due to not all subjects being able to void every hour and to a technical failure in one experiment.

Hct and Hb decreased significantly during WI ($p<0.05$) after 20 min indicating an acute hemodilution (Table 2). PV increased significantly by

6.5 ±1.9% after 20 min of WI ($p<0.01$, compared to control) but almost came back to control level after 5 h WI.

There was a loss in bodyweight of 0.85±0.13 kg and 1.07±0.18 kg during control and WI respectively during the 8 h period.

Discussion

Our data demonstrated that increases in CVP and decreases in pAVP were concomitant during WI to the neck and took place within 20 min. The changes were sustained throughout the 6 h immersion period. CVP returned below the corresponding control level during recovery while the mean pAVP value increased above. Both CVP and pAVP were stabilized during WI and the scatters were less when compared with control (Fig. 1 and 2). The suppression of pAVP was not caused by variation in Osm (Fig. 4). Epstein et al. (1981) demonstrated a suppression of pAVP during 4 h WI in hydropenics. Greenleaf et al. (1983) could not find a significant fall in pAVP during WI, but they did not use a timed control study. Therefore their values obtained during immersion were compared with pre-immersion values. Our data support the findings of Epstein et al. (1981).

Goldsmith et al. (1984) were not able to suppress pAVP during central colume expansion with lower body positive pressure (LBPP), infusion and head down tilt. A reason for this could be the rather small increases in CVP during these manoeuvers. During LBPP, CVP increased from 4.8±1.9 (mean ±SD) to 7.3±2.5 mm Hg, during infusion of saline from 4.7±1.9 to 7.3±2.2 mm Hg and during head down tilt from 5.1±1.3 to 9.0±1.4 mm Hg. In our study the increase in CVP was substantially higher.

In our experiment there was a decrease in pAVP from 2.6±0.5 $pg \cdot ml^{-1}$ to 2.0±0.2 $pg \cdot ml^{-1}$ before WI (Fig. 1). This variation was probably due to episodic secretions as described by Weitzman et al. (1977) and Hammer and Engell (1982). A combination of episodic secretions, stress and differences in experimental designs could account for the conflicting results in litterature.

In the experiment of Epstein et al. (1981) 4 out of 12 subjects did not show any suppression of pAVP during immersion. In our experiment 2 out of 7 had unchanged pAVP levels when comparing control with immersion though CVP increased during WI and decreased during recovery. Epstein et al. (1981) were not able to demonstrate a return to control level of pAVP during recovery after WI. In our experiment only 3 subjects had an increase during recovery and with a large scatter. This could indicate that the suppressive mechanisms of AVP secretion vary to a large degree between individuals.

It has been demonstrated that plasma renin activity and plasma aldosterone were suppressed during WI (Epstein et al. 1975b; Epstein 1978a). As it has been suggested that angiotensin II stimulates AVP release (Weitzman and Kleeman 1979) the suppression of AVP secretion during central volume expansion could be due to a decreased plasma renin-angiotensin level and thus secondary in character. Epstein et al. (1981) suggested a dissociation of the two systems. This is supported by the findings of Bonde-Petersen et al. (1982), who used a converting enzyme blocking agent (Captopril) during LBNP to block the formation of angiotensin II. Plasma AVP increased ten to twentyfold during LBNP in humans when combined with Captopril administration. In cardiac-denervated dogs, hemorrhage increased plasma renin activity while the AVP release was markedly attenuated when compared with non-denervated dogs (Wang et al. 1983). Bie and Warberg (1983) documented no change in pAVP during infusion of Angiotensin II in dogs. Therefore the suppressive mechanisms of the renin-angiotensin system and AVP are probably dissociated during WI.

The significant increase in CVP in our experiment is less than measured by others (Arborelius et al. 1972; Echt et al. 1974; Gauer and Henry 1976). This is probably due to the relative dehydrated state of the subjects. SAP increased significantly in the present experiment during WI by 7–10 mm Hg after 2 h. This is in accordance with the intra-arterial measurements of Arborelius et al. (1972), who found an increase in SAP of 14 mm Hg. The increase in SAP could also be a reason for the decrease in pAVP by affecting arterial baroreceptors. Possibly both low pressure- and arterial baroreceptors play a role in the nonosmotic regulation of AVP. However, the changes in CVP are more pronounced and acute than the changes in SAP.

Osm did not change due to WI suggesting an isoosmotic central volume expansion. Our results are within the range of Epstein et al. (1981), who used a similar prestudy protocol. Therefore we conclude that osmoreceptors do not play a role in AVP suppression during WI in hydropenics.

In our study a pronounced diuresis, natriuresis and kaliuresis occurred. Both diuresis and natriuresis had peak values at the 4th hour of immer-

sion (Table 1). This is in accordance with results of other investigators (Epstein 1978a) regarding hydropenic subjects. In well hydrated subjects undergoing WI the peak value of diuresis occurs earlier and is dissociated from natriuresis (Epstein 1978a).

As pAVP decreased during WI in our study it was somewhat surprising, that T^cH_2O increased significantly at the 4th hour compared to control (Table 1). Epstein et al. (1975a; 1981) found no significant change following the same protocol regarding food and fluid restriction as we did. Behn et al. (1969) examined subjects during WI for 8 h in two different states of hydration: A hydrated state (Water intake equal to $3.14\% \pm 1.08$ (mean $\pm$SD) of body weight/day) and a hydropenic state (water intake equal to $1.66\% \pm 0.20$ (mean $\pm$SD) of body weight/day). In the hydrated state, the immersion induced diuresis was mainly due to an increase in free water clearence ($-T^cH_2O$) while in the hydropenic state the diuresis was in large part accomplished by an increase in C_{osm}. An increase in solute excretion can *per se* increase T^cH_2O. Therefore, an explanation for an increase in our study of this parameter could be due to the increase in natriuresis, probably caused by proximal tubular rejection of sodium. The suppression of pAVP was not enough to counteract the increase in T^cH_2O. Therefore, the diuresis during WI in hydropenics was not caused by pAVP suppression but by increased solute excretion, which among several could be caused by a natriuretic factor. Epstein et al. (1978b) documented an increase in such a factor in urine of normal men undergoing WI.

Our results indicated that an early hemodilution during WI occurred (Table 2). Therefore, the increase in CVP during immersion was a result of both blood volume shifts and transfer of interstitial fluid to the circulation. This is supported by the findings of Greenleaf et al. (1981; 1983); Greenleaf (1984) and Khosla and Dubois (1979; 1981).

In conclusion, this study indicated that an acute isoosmotic central volume expansion during WI was accompanied by suppressed pAVP in hydropenic subjects. The increase in CVP and the suppression of AVP were sustained throughout a 6 h immersion period. During recovery from WI the mean pAVP value increased above the control level while CVP decreased below. The increase in CVP was followed by an increase in osmotic diuresis, natriuresis and kaliuresis which counteracted the acute increase in plasma volume.

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References

Arborelius M, Balldin UI, Lilja B, Lundgren CEG (1972) Hemodynamic changes in man during immersion with the head above water. Aerospace Med 43:592—59

Baylis PH, Stockley RA, Heath DA (1978) Influence of lower body negative pressure upon arginine vasopressin release. Clin Endocrin 9:89—95

Behn C, Gauer OH, Kirsch K, Eckert P (1969) Effects of sustained intrathoracic vascular distension on body fluid distribution and renal excretion in man. Pflügers Arch 313:123—135

Bie P, Warberg J (1983) Effects on intravascular pressures of vasopressin and angiotensin II in dogs. Am J Physiol 245:R906—14

Bonde-Petersen F, Hesse B, Rasmussen S, Christensen NJ, Giese J, Nielsen MD, Warberg J (1982) Cardiovascular and endocrine effects of gravitational stresses (LBNP). The influence of angiotensin-converting enzyme inhibition with captopril. The Physiol [Suppl] 25:S73—S74

Bricker NS (1979) Extracellular fluid volume regulation: On the evidence for a biologic control system. In: Epstein M (ed) The kidney in liver disease. Elsevier, New York, pp 19—30

Dill DB, Costill DL (1974) Calculation of percentage changes in volumes of blood, plasma, and red cells in dehydration. J Appl Physiol 37:247—248

Echt M, Lange L, Gauer OH (1974) Changes in peripheral venous tone and central transmural venous pressure during immersion in a thermo-neutral bath. Pflügers Arch 352:211—217

Epstein M, Pins DS, Miller M (1975a) Suppression of ADH during water immersion in normal man. J Appl Physiol 38:1038—1044

Epstein M, Pins DS, Sancho J, Haber E (1975b) Suppression of plasma renin and plasma aldosterone during water immersion in normal man. J Clin Endocrinol Metab 41:618—625

Epstein M (1978a) Renal effects of head-out water immersion in man: Implications for an understanding of volume homeostasis. Physiol Rev 58:529—581

Epstein M, Bricker NS, Bourgoignie JJ (1978b) Presence of a natriuretic factor in urine of normal men undergoing water immersion. Kidney Int 13:152—158

Epstein M, Preston S, Weitzman RE (1981) Isoosomotic central blood volume expansion suppresses plasma arginine vasopressin in normal man. J Clin Endocrinol Metab 52:256—262

Gauer OH (1979) Mechanoreceptors in the intrathoracic circulation and plasma volume control. In: Epstein M (ed) The kidney in liver disease, Elsevier, New York, pp 3—17

Gauer OH, Henry JP (1976) Neurohormonal control of plasma volume. In: Guyton AC, Cowley AW (eds) International review of physiology. Cardiovascular physiology II. University Park Press, Baltimore MD, 9:145—190

Goldsmith SR, Francis GS, Cowley AW, Cohn JN (1982) Response of vasopressin and norepinephrine to lower body negative pressure in humans. Am J Physiol 243:H970—H973

Goldsmith SR, Cowley AW, Francis GS, Cohn JN (1984) Effect of increased intracardiac and arterial pressure on plasma vasopressin in humans. Am J Physiol 246:H647—H651

Greenleaf JE (1984) Physiology of fluid and electrolyte responses during inactivity: Water immersion and bed rest. Med Sci Sports Exerc 16:20—25

Greenleaf JE, Shvartz E, Keil LC (1981) Hemodilution, vasopressin suppression and diuresis during water immersion in man. Aviat Space Environ Med 52:329—336

Greenleaf JE, Morse JT, Barnes PR, Silver J, Keil LC (1983) Hypervolemia and plasma vasopressin response during water immersion in men. J Appl Physiol: Respirat Environ Exercise Physiol 55:1688—1693

Hammer M, Engell HC (1982) Episodic secretion of vasopressin in man. Acta Endocrinol 101:517—523

Khosla SS, Dubois AB (1979) Fluid shifts during initial phase of immersion diuresis in man. J Appl Physiol: Respirat Environ Exercise Physiol 46:703—708

Khosla SS, Dubois AB (1981) Osmoregulation and interstitial fluid pressure changes in humans during water immersion. J Appl Physiol: Respirat Environ Exercise Physiol 51:686—692

Ledsome JR, Ngsee J, Wilson N (1983) Plasma vasopressin concentration in the anaesthetized dog before, during and after atrial distension. J Physiol 338:413—421

Robertson GL (1980) Control of the posterior pituitary and antidiuretic hormone secretion. Contr Nephrol 21:33—40

Robertson GL, Athar S (1976) The interaction of blood osmolality and blood volume in regulating plasma vasopressin in man. J Clin Endocrinol Metab 42:613—620

Rogge JD, Moore WW (1968) Influence of lower body negative pressure on peripheral venous ADH levels in man. J Appl Physiol 25:134—138

Schrier RW, Bichet DG (1981) Osmotic and nonosmotic control of vasopressin release and the pathogenesis of impaired water excretion in adrenal, thyroid and edematous disorders. J Lab Clin Med 98:1—15

Schultz HD, Fater DC, Sundet WD, Geer PG, Goetz KL (1982) Reflexes elicited by acute stretch of atrial vs. pulmonary receptors in conscious dogs. Am J Physiol 242:H1065—H1076

Wang BC, Sundet WD, Hakumaki MOK, Goetz KL (1983) Vasopressin and renin responses to hemorrhage in conscious, cardiac-denervated dogs. Am J Physiol 245:H399—H405

Weitzman RE, Kleeman CR (1979) The clinical physiology of water metabolism. Part I: The physiologic regulation of arginine vasopressin secretion and thirst [Medical Progress] West J Med 131:373—400

Weitzman RE, Fischer DA, Distefano JJ, Bennett CM (1977) Episodic secretion of arginine vasopressin. Am J Physiol 233:E32—E36

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