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SOME POSTURAL ADJUSTMENTS OF SALT AND WATER EXCRETION^{1, 2}

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Among the acute adjustments of the normal human to orthostatic posture is a diminution in the rate of excretion of water and certain electrolytes (2, 3). This is associated with variable reductions of renal plasma flow and glomerular filtration rate (2, 4) and may actually occur without any appreciable change in the latter (3). The changes in renal hemodynamics are related to a fall in blood pressure and cardiac output which usually follows the assumption of upright posture (5, 6).

The causal sequence leading to orthostatic antidiuresis and antisialuresis is unknown. In acute experiments Pitressin administration leads to water retention without antisialuresis (7). That antisialuresis may occur without antidiuresis is less clear, although there is evidence that it may occur during alcohol diuresis (8, 9) which probably works through depression of the supraoptic posterior pituitary system. It also apparently occurs in venous congestion of the limbs in patients with diabetes insipidus (10). Orthostatic antisialuresis is reported to have been blocked by neck constriction (11) and legwrapping (12). Hypotonic expansion of the extracellular fluid volume in hydrated recumbent subjects results in increased sodium excretion (13). On the other hand, the administration of hyperoncotic albumin solutions results in diminished sodium excretion (14). In this instance antisialuresis is related to antidiuresis and is at least partially independent of the posterior pituitary since it occurs in patients with diabetes insipidus (15).

It was the purpose of the experiments reported here to investigate the effect on salt and water excretion of upright posture complicated as little

as possible by vasomotor changes. An attempt was also made to determine whether the antidiuresis and the antisialuresis of standing are interdependent or controlled by separate mechanisms. To this end three sets of experiments were performed. In the first the effect of standing on salt and water excretion was measured. In the second an attempt was made to inhibit the secretion of Pitressin by administering alcohol to the subjects. In the third set of experiments legwrapping was employed to inhibit postural antisialuresis. The results obtained in the last two sets of experiments were compared with the first, using each subject as his own control.

METHODS

The subjects were normal adult laboratory personnel and medical students. No attempt was made to control the diet over the days preceding the experiments. The experiments were done in the morning with the subjects fasting. Upon arising in the morning the subjects emptied their bladders, noted the time and ingested 250 to 400 cc. of water. Upon arrival at the laboratory they again voided (U_1) and then rested supine. Voided urine was collected every 20 minutes and 150 cc. of water were ingested after each urine collection. After water diuresis had been established (one to two hours), the subjects were tilted to 60° from the horizontal position for one hour. To avoid marked shifts in fluid compartments and vasomotor effects the subjects were encouraged to shift their legs occasionally during this hour. Following the orthostatic period, urine collections were made for another hour with the subject supine. The experimental period was thus bracketed by two control periods. This was considered important because of known fluctuations in salt and water excretion during various hours of the day, and from day to day. The experiments were performed in a quiet room with only essential personnel entering and leaving the room. Smoking was interdicted because of the antidiuretic and vasomotor effects associated with it.

In the experiments in which alcohol was administered, 25 cc. of 95 per cent ethanol and 125 cc. of grapefruit juice were substituted for the 150 cc. of water ingested at the time of tilting and 20 minutes before it. This is

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TABLE I
Control experiments

Subject	Control period preceding tilt					Maximum tilt effect					Last period of second control				
	Creati- nine clear- ance	Urine ml./ min.	Na mEq./ min.	Cl mEq./ min.	K mEq./ min.	Creati- nine clear- ance	Urine ml./ min.	Na mEq./ min.	Cl mEq./ min.	K mEq./ min.	Creati- nine clear- ance	Urine ml./ min.	Na mEq./ min.	Cl mEq./ min.	K mEq./ min.
M. L. P.	121	13.0	.191	.156	.110	125	3.1	.063	.053	.029	152	13.3	.143	.101	.086
M. B.	119	13.2	.112	.092	.106	101	2.36	.040	.065	.066	111	16.0	.176	.138	.140
M. B.	107	14.1	.177	.226	.153	97	4.5	.082	.115	.052	108	14.2	.250	.195	.137
C. M.	111	11.8	.348	.339	.159	100	2.45	.105	.147	.078	109	11.0	.284	.276	.143
E. V. N.	83	13.0	.208	.180	.107	70	4.75	.045	.082	.064	81	10.2	.179	.144	.089
D. McC.	96	11.7	.102	.106	.117	87	6.6	.053	.076	.077	101	13.0	.147	.151	.139
M. Y.	96	12.3	.180	.226	.049	84	6.1	.090	.142	.020	83	6.7	.154	.181	.088

TABLE II
Experiments in which alcohol was given before tilt

Subject	Control period preceding tilt					Maximum tilt effect					Last period of second control				
	Creati- nine clear- ance	Urine ml./ min.	Na mEq./ min.	Cl mEq./ min.	K mEq./ min.	Creati- nine clear- ance	Urine ml./ min.	Na mEq./ min.	Cl mEq./ min.	K mEq./ min.	Creati- nine clear- ance	Urine ml./ min.	Na mEq./ min.	Cl mEq./ min.	K mEq./ min.
M. L. P.	144	11.8	.200	.212	.254	111	10.7	.068	.058	.081	126	11.4	.125	.089	.091
M. B.	113	10.8	.121	.111	.070	101	10.5	.040	.052	.034	104	13.6	.101	.079	.134
C. M.	125	13.2	.371	.360	.138	119	7.2	.057	.073	.036	100	8.7	.124	.110	.044
D. McC.	87	11.6	.123	.131	.055	87	13.0	.065	.078	.019	84	2.75	.137	.143	.032
M. Y.	115	15.7	.210	.227	.047	111	11.8	.080	.107	.014	116	12.4	.152	.149	.088

TABLE III
Experiment in which alcohol was given but subject remained supine through usual tilt period

Subject	Control period preceding tilt					Maximum tilt effect					Last period of second control				
	Creati- nine clear- ance	Urine ml./ min.	Na mEq./ min.	Cl mEq./ min.	K mEq./ min.	Creati- nine clear- ance	Urine ml./ min.	Na mEq./ min.	Cl mEq./ min.	K mEq./ min.	Creati- nine clear- ance	Urine ml./ min.	Na mEq./ min.	Cl mEq./ min.	K mEq./ min.
M. L. P.	148	13.5	.179	.166	.128	140	15.8	.126	.128	.052	130	5.8	.130	.105	.042

TABLE IV
Experiments in which legs were wrapped before tilt

Subject	Control period preceding tilt					Maximum tilt effect					Last period of second control				
	Creati- nine clear- ance	Urine ml./ min.	Na mEq./ min.	Cl mEq./ min.	K mEq./ min.	Creati- nine clear- ance	Urine ml./ min.	Na mEq./ min.	Cl mEq./ min.	K mEq./ min.	Creati- nine clear- ance	Urine ml./ min.	Na mEq./ min.	Cl mEq./ min.	K mEq./ min.
M. L. P.	137	13.6	.181	.177	.090	117	8.3	.142	.128	.073	127	13.6	.255	.172	.075
M. L. P.	137	11.5	.136	.141	.122	134	3.9	.086	.082	.057	131	11.6	.135	.104	.087
M. B.	134	19.1	.168	.164	.088	134	3.4	.144	.156	.067	142	14.8	.229	.160	.092
C. M.	120	13.9	.264	.340	.111	108	6.5	.216	.262	.076	115	10.1	.273	.332	.097
C. M.	109	11.5	.338	.274	.161	104	4.8	.216	.235	.141	98	10.6	.268	.244	.151
E. V. N.	106	13.7	.206	.219	.141	99	3.65	.080	.106	.077	101	10.2	.159	.184	.095
E. V. N.	107	12.7	.178	.203	.124	95	3.8	.098	.155	.095	104	9.8	.181	.179	.110
D. McC.	98	12.4	.040	.046	.027	87	9.4	.024	.059	.037	98	7.7	.063	.101	.052
M. Y.	98	15.0	.208	.266	.101	83	9.5	.082	.142	.101	92	12.2	.254	.235	.104

equivalent to about three whiskey highballs and produced a mild degree of inebriation in the subjects.

In the experiments in which legwrapping was employed the legs were wrapped tightly with three inch "Ace" bandages from the toes to the groin just before tilting.

The bandages were removed as soon as the supine position was again assumed.

In order to avoid the effects of pain only one venipuncture was performed in most of the experiments. This is thought to be justified because changes in serum

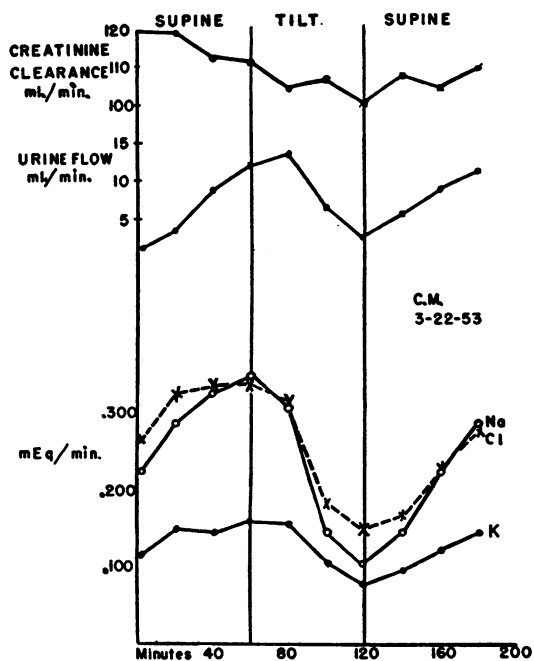


FIG. 1. THE EFFECT OF ASSUMING THE ORTHOSTATIC POSITION ON SALT AND WATER EXCRETION

concentrations were slight while the changes in urinary constituents were marked.

Creatinine determinations were performed on serum and urine immediately after the experiment by the method of Peters (16). Sodium and potassium were measured

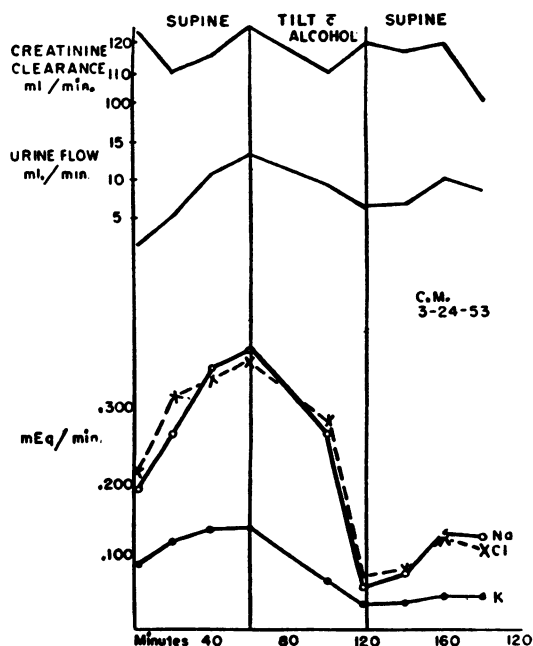


FIG. 2. THE EFFECT OF ALCOHOL ON THE POSTURAL ADJUSTMENTS OF SALT AND WATER EXCRETION

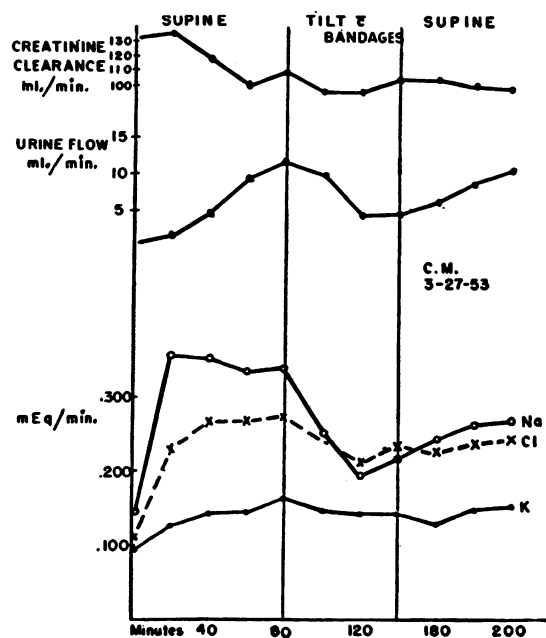


FIG. 3. THE EFFECT OF LEGWRAPPING ON THE POSTURAL ADJUSTMENTS OF SALT AND WATER EXCRETION

with a Beckman Model B. flame photometer. Chloride was measured by the potentiometric method of Sanderson (17).

RESULTS

Pulse and blood pressure were determined and remained fairly constant in all experiments. The means of the three groups were: Tilt alone; supine P 65, B.P. 117/75, standing P 70, B.P. 120/83. Alcohol experiments; supine P 61, B.P. 115/73,

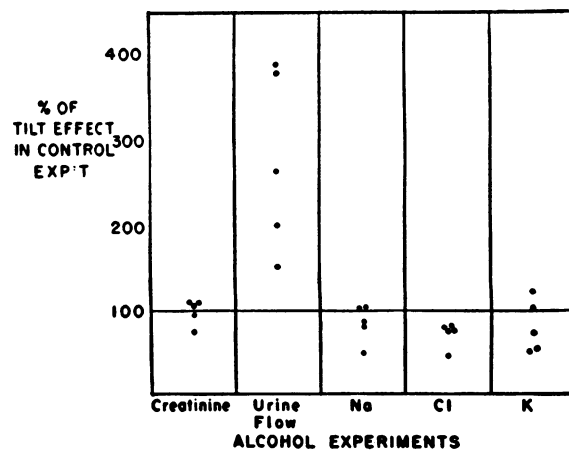


FIG. 4. THE EFFECT OF ALCOHOL EXPRESSED AS PERCENTAGE OF THE UNCOMPLICATED TILT EXPERIMENTS USING EACH SUBJECT AS HIS OWN CONTROL

standing P 78, B.P. 113/77. Legwrapping experiments; supine P 66, B.P. 121/78, standing P 70, B.P. 121/84.

In order to conserve space only one collection period from each control and the experimental hour is shown in Tables I to IV. The last collection of the two control periods and the experimental period in which maximum effect was noted are used. The three types of experiments on one of the subjects are shown in Figures 1-3. Table V is derived from the preceding tables by dividing each experimental result by the comparable figure in the first control so that each experimental result is expressed as a percentage of the control. Figures 4 and 5 are derived from Table V. In these figures each subject's tilt experiment served as a control for the legwrapping and alcohol experiments. The latter are expressed as percentages of the control study, *i.e.*, (Tilt/Supine) (alcohol) ÷ (Tilt/Supine) (Control study) × 100 per cent.

In most of the experiments there was a fall in creatinine clearance to about 90 per cent of the control values. In the uncomplicated tilt experiments there was usually a greater percentage fall in water excretion than there was in electrolyte excretion so that the urine was concentrated as compared with the control period. In most of the experiments the greatest electrolyte change was in sodium and the least in potassium; chloride effect was intermediate. When alcohol was administered salt excretion fell more than in the uncomplicated tilt experiments while water excretion remained at 90 per cent of the control value on the

TABLE V

Comparison of maximum tilt effect to control period preceding tilt

Each number represents the ratio:

$$\frac{\text{Value in tilt period}}{\text{Value in control period}} \times 100$$

Subject	Creatinine	Urine flow	Na	Cl	K
<i>A. Experiments with tilt alone</i>					
M. L. P.	103	24	33	34	26
M. B.	85	18	36	71	62
M. B.	91	32	46	51	34
C. M.	90	21	30	43	51
E. V. N.	84	36	22	45	60
D. McC.	91	56	52	72	66
M. Y.	88	49	50	63	41
<i>B. Experiments in which alcohol was given</i>					
M. L. P.	77	91	34	27	32
M. B.	90	97	33	47	49
C. M.	95	55	15	20	26
C. McC.	100	112	53	59	35
M. Y.	97	75	42	47	30
<i>C. Experiments in which legs were wrapped</i>					
M. L. P.	86	61	79	72	81
M. L. P.	98	34	63	58	47
M. B.	100	18	86	93	76
C. M.	90	47	82	77	68
C. M.	96	42	64	86	88
E. V. N.	93	27	39	48	55
E. V. N.	89	30	55	76	77
D. McC.	89	76	60	128	137
M. Y.	85	63	40	53	100

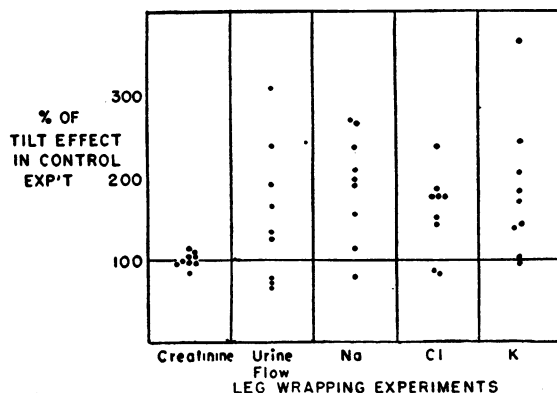


FIG. 5. THE EFFECT OF LEGWRAPPING EXPRESSED AS IN FIGURE 4.

average with production of a dilute urine. In a single experiment in which alcohol was given without the 60° tilt, water excretion rose while salt excretion fell slightly during the second hour (Table III).

In some of the legwrapping experiments the expected postural antidiuresis was diminished, but this was not always the case. On the other hand, there was a consistent reduction of the expected postural antisaluresis. This effect is most noticeable when each subject's uncomplicated tilt experiment was used as control for the legwrapping experiment.

DISCUSSION

From the data it can be suggested that the mechanisms controlling salt and water excretion under the stimulus of standing can function to a large extent independently. That alcohol produced inhibition of an expected orthostatic antidiuresis suggests that this postural adaptation may

be under supraoptic posterior pituitary control, although it may have been due in part to a suppression of antidiuretic activity existing before the tilt. The result is the converse of water retention without salt retention produced acutely by the administration of Pitressin (7).

There are several possible explanations for the reduction in postural antisaluresis produced by legwrapping. Postural antisaluresis may be produced by a stretch of veins in the lower part of the body. The increase over the control orthostatic antisaluresis in the alcohol experiments is not in agreement with this, since the blood volume is, if anything, diminished by the subsequent dehydration. The collapse of veins in the upper part of the body is a possible explanation, but the antisaluresis produced by hyperoncotic albumin (13) is not in agreement. The latter expands the intravascular space at the expense of the interstitial fluid space. The antisaluresis may be mediated in part by the fairly consistent 10 per cent fall in creatinine clearance which occurred upon standing. However, it should be noted that the fall in creatinine clearance was approximately the same whether or not the legs were wrapped. Since the postural antisaluresis was diminished following legwrapping, the fall in glomerular filtration rate is not an adequate explanation for the entire postural effect on salt excretion.

A loss of interstitial fluid from some volume sensitive area is a reasonable explanation for postural antisaluresis. Both the legwrapping and alcohol experiments support this suggestion, as do the experiments of Strauss, Davis, Rosenbaum, and Rossmeisl (13) who administered hypotonic solutions which would in part expand the interstitial space. The antisaluresis produced by hyperoncotic albumin (14, 15), venous compression of the legs (18) and the superior vena cava syndrome (19) are probably caused by the mechanism responsible for postural salt retention. It is difficult to reconcile the observations of Lewis, Buie, Sevier, and Harrison (11) in which it was suggested that the volume sensitive locus is in the cranium because postural antisaluresis was inhibited by neck constriction. This observation does not fit with the observations on the superior vena cava syndrome (19) in which intracranial venous pressure is also high. Netravisesesh (20) was un-

able to confirm the neck constriction experiments, and in a single experiment employing the control-tilt-control protocol, neck compression failed to block the expected postural antisaluresis, although the compression was enough to produce facial edema.

Partially independent posture-sensitive mechanisms for the control of salt and water excretion seem to be present. Normally they function together and altering one of them may change the response of the other. In the light of present knowledge the best explanation is that there is some locus sensitive to the volume of the interstitial space which initiates postural antidiuresis and antisaluresis. Postural antidiuresis may be mediated through the posterior pituitary. The pathway mediating postural antisaluresis is not clear at this time.

SUMMARY

In the normal human subject undergoing moderate water diuresis quiet standing results in a slight depression of creatinine clearance and a marked depression of sodium, chloride, potassium, and water excretion as compared with control measurements in the supine position. If the legs are wrapped with elastic bandages before the orthostatic position is assumed the depression of salt excretion is inhibited with varying effect on the antidiuresis. On the other hand, administration of alcohol inhibits the orthostatic antidiuresis and enhances the orthostatic inhibition of salt excretion.

It is suggested that there are separate postural adjustments of water and salt excretion, the former under diencephalic posterior pituitary control and the latter under the control of some mechanism sensitive to the distribution of interstitial fluid.

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