Sympathoadrenal Response to Water Immersion

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MAN IN NORMAL gravity is primarily upright and an efficient system of reflex cardiovascular mechanisms have envolved which compensate for the hydrostatic pressure effects of body fluids due to gravity. When one stands erect most of the large arteries and veins are oriented parallel to the gravitational field and significant hydrostatic pressures are produced in these long columns of blood. 400 to 600 cc. of plasma may be pooled in the extracellular space of the legs within 20 minutes of quiet standing.[1] The circulatory mechanisms that compensate for the dependent pooling of blood and maintain venous return and cardiac output include: the tissue pressure of the extremities, the muscle pump of the legs, the abdominothoracic pump mechanism, the return on unabsorbed capillary filtrate by the lymphatics, and reflex vasoconstriction and cardio-acceleration.[1] If for some reason these compensatory mechanisms are insufficient or are delayed, orthostatic hypotension and syncope may result.

The normal human subject when passively tilted erect (70-90°) responds with a moderate increase in heart rate, a slight rise in diastolic blood pressure, a slight fall in systolic blood pressure, a decrease in pulse pressure and occasionally, syncope.[1] Orthostatic intolerance with an increased heart rate and decreased pulse pressure on the tilt table, relative to control tilt, is a consequence of prolonged bed rest,[2] and more recently has been demonstrated after exposure of human subjects to complete water immersion for 6 to 12 hours.[3] The physiologic mechanisms responsible for the loss of orthostatic tolerance following bed rest and water immersion are unknown, but may be related to diminished blood volume, decreased muscle or tissue pressure in the extremities, or to functional alterations in the sympathetic nervous system.

Noradrenaline is the neurohormone of sympathetic (adrenergic) nerves and is released from adrenergic nerve endings.[4] Although noradrenaline is also found in the adrenal medulla, adrenaline is in the human the chief medullary hormone.[4] The release of adrenaline and noradrenaline is reflected in the urinary output of both free and conjugated forms of the two hormones.[4]

The increased vasomotor activity during standing, evidenced by the increase in heart rate and the rise in diastolic blood pressure, is accompanied by an in-

Fig. 1. Subject in suit before experiment.

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creased endogenous production of noradrenaline. Serum levels[5, 6] and urinary output of noradrenaline[7] are increased during quiet standing or vertical tilt. This increased production and output of noradrenaline is assumed to be due to activation of the vasomotor system as it occurs in bilaterally adrenalectomized subjects.[8]

In order to ascertain the role of the sympathetic nervous system in the impairment of orthostatic tolerance following water immersion, the urinary catecholamine response of sixteen subjects to six hours of complete water immersion was studied and related to subsequent orthostatic tolerance on the tilt table.

METHODS

The water immersion facility was a steel tank (7x7x 9 feet) lined with fiberglass internally for rust protection. Large windows in two sides permitted observation of the subject. The water temperature was thermostatically controlled at 33° C. A filter system connected to a pump cleaned the water on demand. The subjects wore a modified rubber skin-diving suit and had no skin contact with the water (Fig. 1). A urine relief receptacle drained through a polyethylene tube through the tank wall, enabling the subjects to void at will. Filtered air was delivered to a modified partial pressure helmet and exhausted from the helmet through a regulator which compensated breathing pressure for ambient water pressure. The immersion runs began at 0800 and continued for 6 hours. The subjects had unrestricted activity in this water-filled "room". The only instructions were to "do anything you want but remain primarily upright." The resulting buoyancy of each subject was such that he was able to regulate his depth entirely by controlling his chest size.

The sixteen subjects used in this study were healthy young men between the ages of 22 and 32. All had prior experience in the immersion tank. Subjects were told to avoid strenuous activity and to get a normal night's sleep and to report to the tank room after their usual breakfast without coffee. At 0800 the subjects voided and entered the tank. A six hour urine sample was then obtained, its volume and specific gravity noted and a 100 cc. aliquot acidified to pH 2.0 to 3.0 with 2N H_2SO_4 and frozen for subsequent catecholamine determination. On the subject's control day the same schedule was followed except that six hours of normal office activity was substituted for immersion. Two control and one immersion urine were collected from each subject.

The urine sample was extracted by the method of von Euler and Hellner[9] and adrenaline and noradrenaline were measured by bioassay. The various flourometric methods now available for the determination of adrenaline and noradrenaline are not completely satisfactory as urine contains many known and unknown materials which are flourometrically active and, are therefore a source of error in the method. For these reasons and because bioassay measures the biological activity of the naturally occurring isomers of adrenaline and noradrenaline, the bioassay was used in preference to the flourometric method. The cats blood pressure,

TABLE I. URINARY OUTPUT OF ADRENALINE AND NORADRENALINE DURING SIX HOURS OF OFFICE ROUTINE (CONTROL) AND DURING SIX HOURS OF WATER IMMERSION

Subject	Urine Volume cc./hours		Adrenaline μg./hour		Noradrenaline μg./hour	
	Control	Immersion	Control	Immersion	Control	Immersion
1. D.G.	218	2312	0.65	2.00	2.72	0.77
	225		0.53		2.48	
2. G.B.	690	1657	0.46	1.02	1.86	0.69
	467		0.58		1.58	
3. D.B.	312	985	1.18	0.97	1.22	0.89
	323		0.78		2.46	
4. R.G.	192	1610	0.39	1.42	1.36	0.70
	215		0.32		3.55	
5. E.S.	264	766	0.94	1.26	2.79	0.88
6. T.H.	270	1120	0.51	0.63	1.09	0.54
7. R.O.	225	810	0.95	0.31	2.87	0.30
	172		0.37		3.84	
8. T.K.	144	244	0.61	0.31	1.90	1.37
	98		0.94		1.79	
9. C.S.	382	1115	1.01	0.95	2.90	1.47
	205		0.29		2.05	
10. R.M.	191	1650	0.31	1.02	4.20	2.48
11. G.M.	142	775	0.29	0.36	2.11	0.94
	315		0.56		2.47	
12. M.M.	329	1234	1.43	1.05	2.44	0.74
	380		0.45		2.06	
13. D.B.G.	760	905	0.29	0.56	0.98	2.40
14. G.P.	426	1412	0.36	0.71	2.83	2.85
	500		1.03		4.77	
15. S.M.	234	1258	0.32	.50	0.98	2.63
	366		0.59		2.96	
16. R.F.	267	1403	1.00	2.10	4.36	4.52
	192		1.13		3.42	
MEAN	304	1203	0.65	0.96	2.50	1.51
SE±			0.06	0.13	0.18	0.29
T			1.27		2.95	
P			<0.15>0.10		<0.01	

sensitive to noradrenaline, and the fowls rectal cecum, sensitive to adrenaline, were used. The bioassay techniques used have been described in detail.[9, 10]

The heart rate and blood pressure response to passive vertical tilt (70°) was determined for six of the sixteen subjects following immersion and following a six hour control period. The subjects left the tank unassisted, sat in a chair while the immersion gear was removed (approximately 5 minutes) and then mounted the tilt table where they lay recumbent until a stable heart rate and blood pressure were obtained (approximately 8 minutes). Heart rate was measured in beats per minute from Lead I of a conventional four-limb lead electrocardiogram continuously during the tilt. Blood pressure was taken by auscultation with a standard clinical sphygmomanometer, the last audible sound being considered as diastole. Blood pressure was measured every minute during the ten minute tilt.

RESULTS

All sixteen subjects excreted increased amounts of dilute urine during immersion. The rate of urine flow during immersion was approximately four times the control rate (Table I). The characteristics and probable mechanisms of this immersion diuresis have been described in detail.[11] The urinary adrenaline and noradrenaline were calculated on the basis of an estimated 24-hour urine output and are expressed in micrograms per hour. The catecholamine levels are therefore not related to the rate of urine flow.

Two six hour controls and one six hour immersion urine were collected from each of sixteen subjects. One of the controls was inadvertently destroyed during the catecholamine determination of each of four subjects (E.S., T.H., R.M and D.B.G.). The mean rates of catecholamine excretion are presented for 28 control and 16 immersion urines (Table I and Fig. 2). The

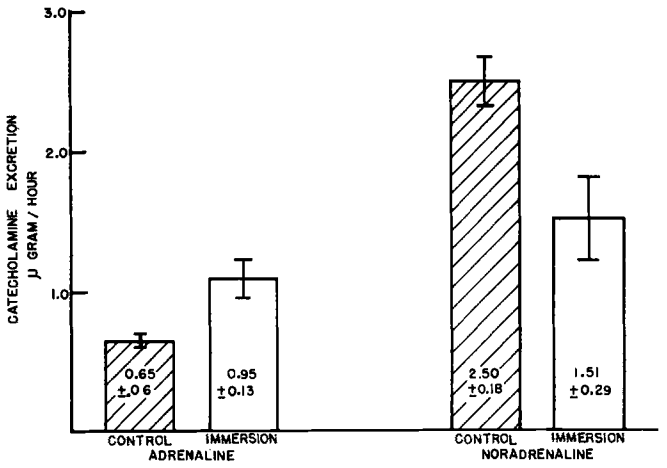

Fig. 2. Rate of catecholamine excretion.

mean urinary excretion of adrenaline during the control period was 0.65 ± 0.06 (Standard Error) μg./hour. During immersion the mean excretion rate was 0.96 ± 0.13 μg./hour, but the observed increase is not significantly different. ($p < 0.15 > 0.10$). The mean excretion rate of noradrenaline during the control period was 2.50 ± 0.18 μg./hour, while the immersion rate was 1.51 ± 0.29 μg./hour. The urinary excretion of noradrenaline during immersion is significantly less than that during the control period ($p < 0.01$).

In a single subject (R.F.) urine specimens were collected serially every two hours during the immersion period. The noradrenaline values were 2.25, 1.26 and 1.01 μg./hour for the first, second and third two hour period, respectively (Fig. 3). demonstrating a pro-

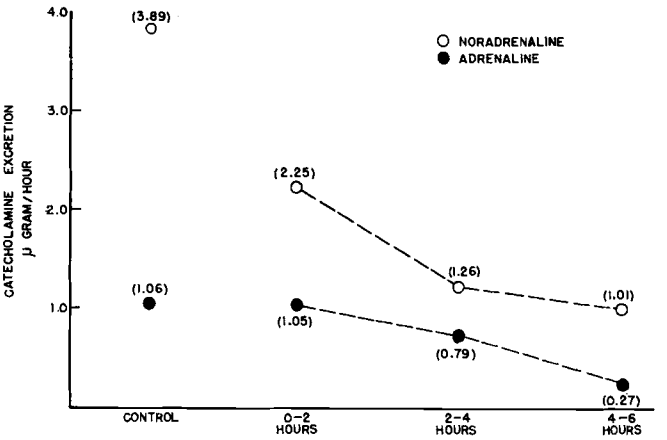

Fig. 3. Catecholamine excretion in subject (R.F.).

gressive decline in noradrenaline excretion during the immersion period. The subject climbed partially out of the tank to void every two hours requiring moderate muscular exertion.

The heart rate and systolic and diastolic blood pressure response during recumbency and at 2, 5 and 10 minutes after vertical tilt are seen in Tables II and III. Heart rate increases moderately during the control tilt from a recumbent mean of 73 beats/minute to 90, 93 and 96 at 2, 5 and 10 minutes of tilt respectively. After immersion the heart rate increased from a recumbent mean of 66 to 97, 95 and 102 during tilt. The mean pulse rate during tilt after immersion is not significantly higher than during control tilt, at 2, 5 and 10 minutes. The systolic blood pressure fell somewhat more during tilt after immersion than during control tilt and the diastolic pressure rose somewhat more but the observed differences in the means of control and immersion tilts are not significant (Table II and III). The maximum increase in heart rate was calculated by subtracting the fastest rate recorded during the tilt, regardless of its time of occurrence, from the resting or recumbent heart rate (Table IV). The mean maximum increase in heart rate after immersion is 41.5 beats/minute as compared to a 27.8 beats/minute increase during control tilt. The difference is highly significant ($p < 0.005$ paired samples). The maximum decrease in pulse pressure was calculated similarly (Table IV). The mean maximum decrease in pulse pressure is 20.1 mm. Hg for the control tilt and 31.3 for the post-immersion tilt. This difference is also significant ($< 0.05 > 0.025$ paired samples).

One subject (G.P.) fainted after 6 minutes of this post-immersion tilt (Fig. 4). Pallor, bradycardia, restlessness, hyperpnea, nausea and dimming of vision

TABLE II. PULSE RATE IN BEATS/MINUTE, AND SYSTOLIC AND DIASTOLIC BLOOD PRESSURES IN MM. HG OF SIX SUBJECTS ON THE TILT TABLE AFTER SIX HOURS OF COMPLETE WATER IMMERSION

Subject Number	Recumbent Pulse Rate	Recumbent Blood Pressure Syst.	Recumbent Blood Pressure Diast.	Tilted After 2 Minutes Pulse Rate	Tilted After 2 Minutes Blood Pressure Syst.	Tilted After 2 Minutes Blood Pressure Diast.	Tilted After 5 Minutes Pulse Rate	Tilted After 5 Minutes Blood Pressure Syst.	Tilted After 5 Minutes Blood Pressure Diast.	Tilted After 10 Minutes Pulse Rate	Tilted After 10 Minutes Blood Pressure Syst.	Tilted After 10 Minutes Blood Pressure Diast.
1	60	155	92	78	136	102	82	155	102	86	148	106
2	72	120	70	92	118	87	103	108	94	97	119	88
3	57	124	64	110	116	98	114	118	100	109	120	98
4	72	112	74	108	110	82	96	110	80	107	110	90
5	68	126	80	99	116	90	68	90	60	*—	—	—
6	58	128	58	96	116	64	104	116	68	114	101	70
MEAN	66	128	73	97	119	87	95	116	84	102	119	90
SE±	2.8	6.0	4.9	4.8	3.6	5.5	6.8	8.7	7.1	5.5	6.4	4.9

* Subject fainted at sixth minute.

TABLE III. PULSE RATE IN BEATS/MINUTE, AND SYSTOLIC AND DIASTOLIC BLOOD PRESSURE IN MM. HG OF SIX SUBJECTS ON THE TILT TABLE AFTER SIX HOURS OF OFFICE ACTIVITY CONTROL

Subject Number	Recumbent Pulse Rate	Recumbent Blood Pressure Syst.	Recumbent Blood Pressure Diast.	Tilted After 2 Minutes Pulse Rate	Tilted After 2 Minutes Blood Pressure Syst.	Tilted After 2 Minutes Blood Pressure Diast.	Tilted After 5 Minutes Pulse Rate	Tilted After 5 Minutes Blood Pressure Syst.	Tilted After 5 Minutes Blood Pressure Diast.	Tilted After 10 Minutes Pulse Rate	Tilted After 10 Minutes Blood Pressure Syst.	Tilted After 10 Minutes Blood Pressure Diast.
1	61	154	86	67	146	90	63	151	98	65	152	96
2	80	112	70	98	110	78	96	108	75	106	110	74
3	56	112	76	84	114	90	93	120	88	100	128	86
4	68	109	78	86	114	86	91	181	90	88	110	82
5	91	136	78	103	134	84	101	131	80	108	134	78
6	79	140	58	101	135	62	113	125	64	112	120	80
MEAN	73	127	74	90	126	82	93	125	83	96	126	83
SE±	5.4	7.6	3.9	5.6	7.9	4.3	6.7	6.0	4.9	7.2	6.4	3.1

TABLE IV. THE MAXIMUM INCREASE IN PULSE RATE IN BEATS/MINUTE AND THE MAXIMUM DECREASE IN PULSE PRESSURE IN MM. HG DURING TILT OF SIX SUBJECTS FOLLOWING SIX-HOUR CONTROL AND SIX-HOUR IMMERSION PERIODS

Subject Number	Maximum Change in Pulse Pressure Control	Maximum Change in Pulse Pressure Immersion	Maximum Change in Pulse Rate Control	Maximum Change in Pulse Rate Immersion
1	16	29	10	29
2	10	36	26	31
3	18	44	52	61
4	15	20	24	40
5	10	20	22	32
6	42	39	33	56
MEAN	20.1	31.3	27.8	41.5
SE±	4.5	4.1	5.7	5.6
n	6	6	6	6
T (paired samples)	2.16		4.91	
P	<0.05>0.025		<0.005	

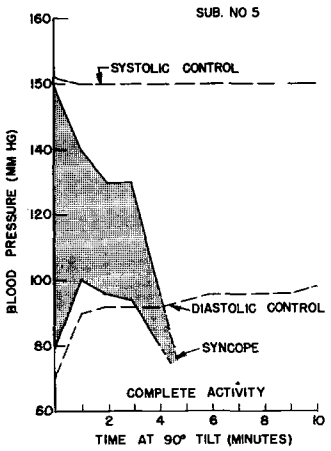

Fig. 4. Blood pressure, post-immersion tilt. Subject (G.P.).

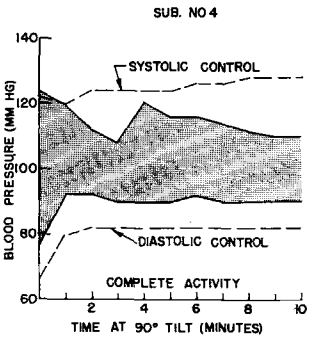

Fig. 5. Blood pressure, post-immersion tilt. Subject (M.M.).

were noted over a minute's time. No subjects fainted during the control tilts. The heart rate and blood pressure response to control and post-immersion tilt of another subject (M.M.) are presented to show the characteristic alterations in orthostatic tolerance following water immersion (Fig. 5).

DISCUSSION

The data presented confirm the apparent decrease in orthostatic tolerance following water immersion that has been previously described.[3] The blood pressure and heart rate responses to tilt after immersion are significantly different from controls when tested as paired samples. One subject fainted on the tilt table following immersion while none fainted during control

tilt. The incidence of fainting in normal subjects tilted for twenty minutes is described as between 10 (12) and 20 (13) per cent. A large number of subjects would be needed to demonstrate significantly an increased incidence of fainting of normal subjects during tilt after immersion.

The urinary excretion of adrenaline is increased during immersion, although not significantly. This increase is most likely related to the emotion or anxiety associated with the immersion procedure. In one subject (R.F.) the adrenaline content of the urine for the last two hours of immersion was only 25 per cent of that present in the first two-hour specimen (Fig. 3). Goodall and Berman have shown that during the stress of acceleration an increased urinary excretion of adrenaline was related to the attendant anticipation and anxiety and not to the stress itself.[14] The increase in urinary adrenaline observed at the same time noradrenaline excretion is decreased demonstrates the independant release of these hormones, previously demonstrated in anxiety[14] and hypothalamic stimulation.[4]

Noradrenaline excretion is significantly decreased during six hours of water immersion. It has been observed that the noradrenaline output of human subjects is slightly less during bed rest than during daily activity[4] and increases in an exponential fashion with increasing muscular work.[5] Sundin has shown that normal subjects excrete considerably larger amounts of noradrenaline when tilted to 75 degrees in comparison with the excretion in the recumbent position.[7] It is assumed that the increased noradrenaline excretion during standing and during exercise is related to the associated increase in vasomotor activity. Conversely the diminished noradrenaline excretion of water immersion may be related to diminished vasomotor activity, as in the water immersion situation both the level of muscular activity and the cardiovascular compensations necessary for changes in posture are minimized.[3]

The relation of the decreased output of noradrenaline during water immersion to the subsequent impairment of tilt table tolerance remains to be determined by further study of the sympathoadrenal response to tilt following immersion.

In a weightless environment, there will be no hydrostatic pressure effects due to gravity, and therefore no demand on reflex sympathetic compensation. Analogous situations occur in bed rest where hydrostatic pressure effects are minimized by the horizontal position and in water immersion where hydrostatic pressures are neutralized by ambient water pressure. It has been suggested that because of prolonged disuse reflex vasomotor responses may become less efficient in the weightless state and that intolerance to acceleration and orthostasis may result. The observation that noradrenaline excretion is reduced during prolonged bed rest and during prolonged water immersion support this suggestion.

SUMMARY

The urinary excretion of adrenaline and noradrenaline was measured by bioassay for sixteen (16) normal human subjects during six (6) hours of complete water immersion. The excretion of adrenaline was moderately increased, possibly related to the anxiety associated with the immersion. The excretion of noradrenaline was significantly ($p < 0.01$) reduced during immersion. Six (6) subjects were studied during passive vertical tilt following immersion. Orthostatic intolerance was demonstrated and the increase in pulse rate and decrease in pulse pressure were significantly different from the control tilt. The probable mechanisms of the reduced noradrenaline excretion during immersion and its relation to the post-immersion impairment of orthostatic tolerance are discussed.

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