STUDIES ON THE RENAL CONCENTRATING MECHANISM. III. EFFECT OF HEAVY EXERCISE

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Heavy exercise decreases urine flow, sodium excretion, glomerular filtration rate and effective renal blood flow in man (1–8). In addition, albumin, casts and red blood cells are often found in the urine sediment after exercise (9–12). Since the renal concentrating ability is a sensitive measure of renal impairment, the present study was undertaken to determine the effect of exercise on this function. Heavy exercise was found to impair concentrating ability in hydropenic normal men. This impairment was observed when the subjects exercised without prior solute loading and also during a small osmotic diuresis, but was not found when the subjects exercised during a large osmotic diuresis.

METHODS

The subjects were six paid volunteer medical students and two physicians. The medical students were selected for their ability to pass the "bladder emptying test" described in the preceding paper (13). Urine was collected by voluntary voiding in all experiments. The subjects took no fluid after lunch of the day prior to the experiment and ate a dry supper. The following experiments were performed:

I. Heavy exercise without solute loading

A. Stair-running exercise. After three to four preliminary half-hour urine collection periods four subjects (G.C., L.G., R.L. and J.P.) began running up and down three flights of stairs at 8:00 or 8:30 a.m. In 30 minutes they completed 15 trips and were exhausted. Since the subjects could not void immediately after exercise the first period was one hour long. Thereafter the subjects collected urine at half-hour intervals for three hours. In a repeated experiment, Subject R.L. received 100 mU of vasopressin intravenously just prior to exercise since an infusion could not be given during stair-running. In this experiment he was able to void at the end of exercise. In the preceding paper (13) the effect of small changes in solute excretion on the concentrating ability in the same subjects is described.

B. Step exercise. In Subjects W.A. and A.M. the exercise consisted of stepping up and down a 17 inch step every three seconds for 30 minutes. Step exercise appeared to be as exhausting as stair-running and had the advantage that it could be performed during a continuous intravenous infusion. Subject A.M. was given an infusion of 0.9 per cent saline at 0.6 ml. per minute to which vasopressin was added to provide 100 mU per hour during and after exercise. Exercise was not begun until 10:15 or 10:30 a.m. to permit comparison with studies during osmotic diuresis (see II below). Observation continued for two hours after exercise.

II. Heavy exercise during solute loading

A. Small osmotic diuresis. In three subjects (W.A., A.M., and T.T.) a diuresis was established by the infusion of 5 per cent mannitol in 0.36 per cent saline solution at a rate of 3.6 to 3.9 ml. per minute for two hours prior to exercise. Vasopressin was added to provide 200 mU per hour. Then at 10:15 or 10:30 a.m. the subjects began step exercise for one-half hour. Urine collections were obtained at intervals of 15 or 30 minutes before, during, and for 90 to 105 minutes after exercise.

B. Large osmotic diuresis. In three subjects (W.A., A.M., and L.R.) a large diuresis was established by the infusion of 5 per cent mannitol in 0.36 per cent saline at 18 to 20 ml. per minute for 90 minutes prior to exercise. Vasopressin was added to provide 200 mU per hour. Step exercise was begun at 10 or 10:30 a.m. Urine was collected at 15 minute intervals before, during, and for 105 to 120 minutes after exercise.

Chemical methods and calculations

Chemical methods and calculations are given in the preceding report (13). Glomerular filtration rate was estimated by the clearances of creatinine and mannitol.

In experiments performed without solute loading the osmotic urine/plasma (U/P) ratio was high and changes in this term could be used to evaluate concentrating ability. However, during mannitol diuresis there was a progressive fall in osmotic U/P ratio and it was increasingly difficult to evaluate changes in this variable. Under these circumstances the concentrating ability can be evaluated in terms of the relationship between net water reabsorption (T^cH_2O) and osmolal clearance (C_{osm}) (14). Such an evaluation is feasible if osmolal clearance is considered to represent the volume of isotonic fluid delivered to the concentrating site so that

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TABLE I

Effects of one-half hour of heavy exercise in four normal men *

	Before exercise	First hour	Second hour	Third hour	Fourth hour
Urine flow (V), *ml./min.*	.48 (.38–.71)	.18 (.14–.25)	.43 (.37–.50)	.60 (.55–.66)	.54 (.48–.64)
Osmolal clearance (C_{osm}), *ml./min.*	1.90 (1.51–2.76)	.53 (.42–.70)	1.30 (1.06–1.72)	1.89 (1.62–2.03)	1.91 (1.85–1.94)
Osmotic urine/plasma (U/P) ratio	3.95 (3.78–4.20)	2.90 (2.81–3.03)	3.03 (2.68–3.42)	3.18 (2.89–3.71)	3.62 (3.16–3.92)
Creatinine (C_{cr}) clearance, *ml./min.*	135 (127–143)	91 (82–102)	148 (137–159)	146 (137–161)	142 (121–155)
Na excretion ($U_{Na}V$), *μEq./min.*	85 (48–151)	23 (18–39)	48 (32–64)	63 (41–87)	88 (72–118)
K excretion (U_KV), *μEq./min.*	32 (25–43)	19 (13–25)	39 (31–56)	36 (29–44)	54 (42–71)
Plasma osmolality (P_{osm}), *mOsm./Kg.*	295 (292–297)	300 (297–302)		298 (296–300)	299 (297–300)

* Mean data and range of values are given for one and one-half to two hours before exercise and for each hour from the beginning of exercise.

T^cH_2O (calculated as C_{osm} minus urine flow) would represent the net rate of water reabsorption at that site.

RESULTS

I. Heavy exercise without solute loading

Four stair-running experiments are summarized in Table I. There was an abrupt decrease in urine flow, osmolal clearance and sodium excretion to less than half of pre-exercise values with a gradual return to pre-exercise values by the third or fourth hour. Creatinine clearance and potassium excretion decreased by about one-third with exercise and then returned to pre-exercise values within two hours. Figure 1 shows the results of a repeat stair-running experiment (Subject R.L.) and two step-exercise experiments (Subjects W.A. and A.M.) in which urine collections were obtained at the end of exercise. In these experiments the decrease in creatinine clearance as well as other functions appeared to be greater in the exercise period than in the next half-hour period. However, the likelihood of errors due to incomplete urine collection at such low urine flows is large. The osmotic U/P ratio decreased in all seven experiments. The values were 3.78 to 4.20 before exercise and decreased to 2.66 to 3.03 after exercise, except in Subject W.A. whose pre-exercise maximum osmotic U/P ratio was only 3.10 and in whom the value fell to 1.88 in the first post-exercise period. About half of the decrease in urine osmolality could be accounted for by a decrease in total electrolyte concentration (calculated as twice the sum of the change in sodium and potassium concentration), while the remainder presumably represented a decrease in urea concentration although this was not measured directly. The lowest values of U/P ratio often occurred after exercise and persisted in some instances through the fourth hour. Plasma osmolality usually increased after exercise and remained increased thereafter, the largest increment being 8 mOsm. per Kg.

II. Heavy exercise during solute loading

Exercise during osmotic diuresis also caused an abrupt decrease in urine flow, osmolal clearance and electrolyte excretion (Table II). After exercise all values rapidly returned to pre-exercise levels. With small solute loads there was a 20 to 35 per cent decrease in mannitol and creatinine clearance during exercise. With large solute loads mannitol and creatinine clearances showed no consistent change. Plasma osmolality was increased by 5 to 15 mOsm. per Kg. by solute loading but was little further altered by exercise.

TABLE II

*Effect of heavy exercise during osmotic diuresis**

	Subject W. A.				Subject A. M.				Subject T. T.			
	Pre-exercise	Exercise	Post-exercise 1	Post-exercise 2	Pre-exercise	Exercise	Post-exercise 1	Post-exercise 2	Pre-exercise	Exercise	Post-exercise 1	Post-exercise 2
Small mannitol load												
V, *ml./min.*	1.73	1.11	1.73	2.18	1.48	.69	1.55	1.80	2.02†	1.22	1.86	2.47†
C_{osm}, *ml./min.*	4.00	2.60	3.64	4.75	4.41	2.01	3.88	4.96	5.73	3.38	4.81	6.27
T^cH_2O, *ml./min.*	2.27	1.49	1.91	2.57	2.93	1.32	2.33	3.16	3.71	2.16	2.95	3.80
U/P	2.31	2.34	2.11	2.18	2.98	2.93	2.52	2.76	2.84	2.76	2.59	2.54
C_{man}, *ml./min.*	69	55	66		93	50‡	76‡	86‡	122	94	115	110
C_{cr}, *ml./min.*	119	87	128	107	127	78	135	137	183	138	168	159
$U_{Na}V$, *μEq./min.*	103	58	17	99	174	26	52‡	133	271	68	157	351
U_KV, *μEq./min.*	57	35	42	50	51	29	44‡	33	107	62	61	111
	Subject W. A.				Subject A. M.				Subject L. R.			
Large mannitol load												
V, *ml./min.*	11.58	6.80	11.37	13.97	9.02	8.20	13.13	19.43	8.73†	7.86	7.50	12.93
C_{osm}, *ml./min.*	15.38	10.38	15.36	17.98	14.93	14.05	19.91	26.63	15.11	14.25	12.69	19.93
T^cH_2O, *ml./min.*	3.90	3.58	3.99	4.01	5.91	5 85	6.78	7.20	6.38	6.39	5.19	7.00
U/P	1.34	1.53	1.36	1.29	1.66	1.72	1.54	1.37	1.73	1.83	1.69	1.55
C_{man}, *ml./min.*	74	60	60	57	79	77	93	87	105	114	101	114
C_{cr}, *ml./min.*	90	90	103	120	113	108	112	92	141	156	134	160
$U_{Na}V$, *μEq./min.*	625	159	520	665	386	288	675	1,205	576	398	351	828
U_KV, *μEq./min.*	82	91	70	89	45	66	65	95	87	108	56	52

* Values represent the mean of two 15 minute urine collections except as noted. Abbreviations are the same as those used in Table I.
† One 30 minute collection.
‡ One 15 minute collection.

The effect of exercise on the concentrating ability was more difficult to evaluate during an osmotic diuresis. From previous studies (13, 15), an increase in osmotic U/P ratio would be expected when osmolal clearance decreases. Such an increase in osmotic U/P ratio was observed during exercise only in the experiments with large mannitol loads. During a small mannitol diuresis exercise was followed by a slight decrease in U/P ratio, although osmolal clearance fell markedly. This indication of impairment of concentrating ability with exercise during a small osmotic diuresis but not during a large osmotic diuresis is confirmed by examination of the relationship between osmolal clearance and water reabsorption (T^cH_2O). The data are presented graphically in Figure 2 in terms of the reciprocal values, $1/T^cH_2O$ and $1/C_{osm}$. This plot has been selected empirically because

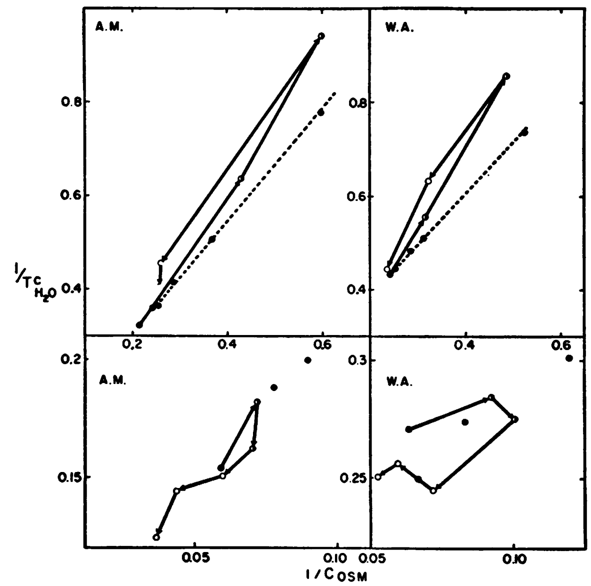

FIG. 2. THE RELATIONSHIP BETWEEN NET WATER REABSORPTION (T^cH_2O) AND OSMOLAL CLEARANCE (C_{osm}) EXPRESSED AS THE RECIPROCALS $1/T^cH_2O$ AND $1/C_{osm}$

Upper figures represent two studies during a small mannitol diuresis and lower figures two studies during a large mannitol diuresis. Each point represents a 15 minute period. Closed circles represent pre-exercise values, half closed circles values during heavy exercise, and open circles values after exercise.

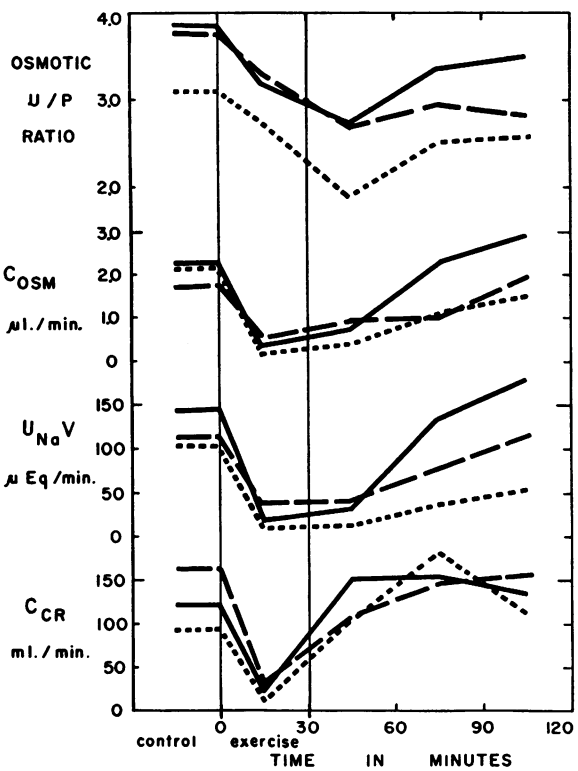

FIG. 1. THE EFFECT OF EXERCISE WITHOUT PRIOR SOLUTE LOADING ON OSMOTIC U/P RATIO, OSMOLAL CLEARANCE (C_{osm}), SODIUM EXCRETION ($U_{Na}V$) AND CREATININE CLEARANCE (C_{cr})

Data is plotted for three subjects, R.L. (solid line), A.M. (dashed line), and W.A. (dotted line).

it gives a linear representation of the data and has been found to be reproducible with various types of solute loading (14). With a small osmotic load (upper part of Figure 2) this linear relationship was evident as C_{osm} was increased from 2 to 5 ml. per minute before exercise. With exercise both C_{osm} and T^cH_2O fell abruptly but T^cH_2O was lower for a given value of C_{osm}, indicating impairment of concentrating ability; this change is shown as upward displacement in the reciprocal plot. With higher solute loads there was more scatter in the plot relating $1/T^cH_2O$ and $1/C_{osm}$ but exercise did not appear to alter this relationship (lower part of Figure 2).

DISCUSSION

The present data demonstrate that heavy exercise leads to impairment of the concentrating ability in hydropenic normal men. This impairment was observed in experiments without solute loading and also during a small osmotic diuresis, but not during a large osmotic diuresis. The effect could not be prevented by the administration of vasopressin and is therefore considered not to be the consequence of a decrease in endogenous antidiuretic hormone production. It is difficult to ascribe the decrease in osmotic U/P ratio to the decrease in total solute excretion which occurs with heavy exercise, since in most other circumstances an inverse relationship between U/P ratio and solute excretion is observed (13). On the other hand a marked decrease in sodium excretion might be an important factor, since there is evidence that active sodium transport may be the initial process leading to the formation of a concentrated urine (16, 17). When heavy exercise was performed during a large mannitol diuresis there was an abrupt decrease in sodium excretion but no impairment of concentrating ability. However, the absolute rate of sodium excretion during exercise remained high.

Another regularly observed concomitant of the exercise effect on concentrating ability was a decrease in creatinine or mannitol clearance. This effect was not observed when exercise was conducted during a large mannitol infusion. The data, however, are subject to errors due to incomplete bladder emptying and dead space effects. Presumably, decrease in renal blood flow also occurred, since para-aminohippurate clearance has been shown to decrease progressively with increasingly severe exercise (5). Acute impairment of concentrating ability has also been observed in dogs given hexamethonium (18). In these experiments impairment persisted beyond the time when solute excretion and renal hemodynamic changes had returned to control values. Such prolonged depression of osmotic U/P ratio was also observed after exercise without solute loading although this could have been due to renal dead space effects. Recently Berliner, Levinsky, Davidson and Eden (19) have noted a reduction in concentrating ability following constriction of the renal artery in dogs.

Several mechanisms for impairment of concentrating ability are suggested by these experimental results. Perhaps the simplest mechanism would be impairment due to reduction of the supply of oxygen to the active transport system at the concentrating site. In a few experiments we have not found impairment of concentrating ability in subjects breathing 10 per cent oxygen. However, there was renal vasodilatation which may have compensated for the lower O_2 tension. If the concentrating mechanism operates by establishing a high sodium and urea concentration in the renal medulla leading to the passive reabsorption of water from the collecting tubules then the supply of these solutes will be a limiting factor in concentrating ability. This supply can be reduced both by decreased filtration and by increased proximal reabsorption. A reduced flow rate in Henle's loops might also impair the hairpin countercurrent mechanism postulated by Wirz, Hargitay and Kuhn (20–22) for concentrating the fluid in these loops. Finally the slowing of blood flow through the renal medullary capillaries could impair concentrating ability if these vessels provide the only means for returning water reabsorbed from the collecting ducts to the circulation. There is at present no evidence which would lead to the selection of one of these alternatives as the cause of impaired renal concentrating ability after exercise.

SUMMARY

Heavy exercise causes impairment of concentrating ability and a decrease in creatinine and mannitol clearance in hydropenic men who are studied without prior solute loading or during a small mannitol diuresis. During a large mannitol diuresis there is no distinct change in concentrating ability or in creatinine and mannitol clearance with exercise. In all three groups exercise causes an abrupt decrease in total solute excretion and particularly in sodium excretion.

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