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Changes in Plasma Concentration of Epinephrine and Norepinephrine With Muscular Work. (23561)

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Although it has long been known that adrenal medullary hormones are released during physical work, their interrelationship and the sequence of events leading to their release are not well understood. After discovery of norepinephrine as the postganglionic adrenergic nerve transmitter(1) and its role as an adrenal medullary hormone(2), it became obvious that many of the earlier experiments on the adrenal medulla failed to differentiate between epinephrine and norepinephrine. Consequently, the separate roles of epinephrine and norepinephrine during muscular work need to be established more clearly. A rise in catechol amine activity during muscular work was first demonstrated by Hartman(3) and, soon afterwards, verified by Cannon(4). Raab(5), using a non-specific chemical method, reported an increase in epinephrine-like compounds in human blood during exercise. More recently, von Euler and Hellner(6) showed an increased urinary excretion of both epinephrine and norepinephrine after prolonged work. Catechol amine concentrations in plasma probably give a more dynamic picture of transitory changes in sympathetic activity associated with work, than does excretion of these substances in urine. New technics for direct determination of the catechol amines in plasma are now available. Using these technics, we undertook to discover what changes occur in plasma concentration of epinephrine and norepinephrine in normal young men after moderate work (walking) and acute and chronic, severe work (running).

Methods. Six young, male volunteers (mean weight 73 kg) were used as subjects. They wore T-shirts, Army fatigue trousers, socks and sneakers. Breakfast was withheld. At 10 A.M. they began to walk on a treadmill at 3.5 mph on a 5% grade. After 30 minutes, they were immediately transferred to another treadmill, where they ran for 5 minutes at 7 mph on a 5% grade (2 men were able to run only 2.5 minutes). The run was an acute, exhausting stress for all. Blood was drawn just prior to the walk, within 2 minutes after the run, and at 15, 30, and 75 minute intervals following the run. These samples have been designated as "Control, 2, 15, 30, and 75 minutes." In a separate series on 5 of the same subjects, samples were taken within 2 minutes after the walk was completed. Plasma catechol amines were also determined on 3 well-trained athletes 5 to 8 minutes after running 18 miles in times varying from 1.8 to 2 hours. All blood samples* were taken from antecubital vein, with subject in reclining position, treated and analyzed for epinephrine and norepinephrine by the method of Weil-Malherbe and Bone(7,8) as reported by Gray and Young(9).

Results. It is apparent from Table I that there is a marked elevation (about 3-fold) in norepinephrine within 2 minutes after acute, severe work, with a drop to control levels within 15-30 minutes.

Epinephrine levels, however, are much less consistent than norepinephrine levels and show wide variation between individuals. The 2 minute, post exercise epinephrine levels vary from marked increase in one individual to no detectable change in 2 other subjects. The epinephrine levels, when elevated, return to normal in 15-30 minutes.

No change from control was found in epinephrine concentrations in the separate series after the walk, and in 4 of the 5 sub-

* The plasma removed for analysis was placed in lucite tubes, frozen in dry ice, isopropyl alcohol mixture, and shipped frozen to Biochemistry Dept., Walter Reed Army Inst. of Research, Washington, D.C., where the determinations were carried out.

TABLE I. Plasma Catechol Amine Levels* after Acute, Severe Work.

Subject	Control		2 min.		15 min.		30 min.		75 min.	
	E	NE	E	NE	E	NE	E	NE	E	NE
Ca	<.1	2.8	<.1	12.4					<.1	2.6
Mc	.1	2.2	1.4	7.9			.2	2.8	.1	2.1
De	<.1	3.2	.4	8.2	<.1	4.2	<.1	2.6		
Co	"	2.2	<.1	7.8	"	2.9	"	5.3		
Pi	.3	1.8	.6	6.1	.1	4.3	"	2.4		
Wi	.2	2.6	.7	6.0	.4	3.9	.3	3.6		

* All values are in μg/l.

Epinephrine values less than .1 μg are not detectable by this technic.

jects no change was found in norepinephrine values. In the fifth subject (De), the norepinephrine concentration changes from 2.1 to 4.5 μg/l.

Subjective evaluation of subjects by the authors with respect to motivation, muscular fatigue, difficulty in completing the test, and severity of emotional response suggests an association between increase in concentration of epinephrine in plasma and emotional stress; whereas muscular fatigue and difficulty in completing the work appeared associated with high norepinephrine levels in the plasma.

After prolonged, severe exercise, the plasma concentration of both catechol amines was elevated in 3 marathon runners following an 18 mile run (Table II). It seems likely that the values immediately after the run, *i.e.*, at times comparable to the acute experiments, were even higher than those reported in Table II.

Consistent elevation of plasma norepinephrine post exercise is in agreement with the work of Elmadjian(10) who found a marked increase in urinary excretion of norepinephrine and only a moderate rise in urinary excretion of epinephrine in active professional hockey players after a game. It is not surprising to find epinephrine and norepinephrine varying independently in their responses to exercise, since a selective release of epinephrine and norepinephrine has been shown to occur(11). Von Euler has suggested that the high plasma norepinephrine concentration following muscular work may result from a reflex release caused by vasodilatation of the blood vessels, in the muscle, with exercise(12). This would tend to cause a compensatory vasoconstriction. This hypothesis has gained support from the work of Goodall and Meehan(13) on the human centrifuge and is in accord with our results.

TABLE II. Plasma Catechol Amine Levels* after an 18 Mile Run.

Subject	D.T.		J.D.		W.G.	
	E	NE	E	NE	E	NE
Pre	<.1	3.0	<.1	2.5	<.1	2.5
Post	.2	8.7	.2	5.5	.3	4.7

* All values are in μg/l.

Epinephrine values <.1 μg are not detectable by this technic.

Summary. 1. Concentration of epinephrine and norepinephrine has been measured in human plasma after acute and chronic work. 2. Norepinephrine increases markedly with acute muscular work (about 3-fold) and returns to normal within 15-30 minutes after work. 3. Epinephrine response to acute muscular work shows wide variation between individuals, varying from marked rise to no detectable change. Epinephrine values, when elevated, also return to control levels within 15-30 minutes.

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