# Exercise-related changes in serum catecholamines and potassium: Effect of sustained exercise above and below lactate threshold

**Plasma potassium and catecholamines exhibit rapid shifts during exercise testing, particularly when exercise intensity exceeds lactate threshold. To assess changes that may occur during sustained exercise, we studied 10 healthy men to determine the effect of 20 minutes of exercise at 25 W above lactate threshold (ALT) and 20 minutes of exercise at 25 W below lactate threshold (BLT). Both conditions showed elevation of catecholamines at end exercise compared to baseline, but catecholamine levels ALT were significantly higher than the levels BLT (2270 ± 190 versus 900 ± 230 pg/ml norepinephrine, $p < 0.001$; 509 ± 69 versus 150 ± 18 pg/ml epinephrine, $p < 0.001$). This difference persisted at 2 minutes of recovery (1620 ± 130 versus 590 ± 60 pg/ml norepinephrine, $p < 0.001$; 216 ± 31 versus 98 ± 16 pg/ml epinephrine, $p < 0.001$). Both conditions resulted in a significant elevation in potassium at end exercise compared to baseline, but the potassium levels ALT were significantly higher than the levels BLT (1.1 ± 0.1 mEq/L versus 0.5 ± 0.1 mEq/L, $p < 0.001$. The fall in potassium in the immediate post-exercise period was significantly greater following exercise ALT (−0.8 ± 0.1 mEq/L versus −0.2 ± 0.1 mEq/L, $p < 0.001$). Thus sustained exercise slightly ALT resulted in a significant potassium flux and very elevated catecholamine levels. Avoiding these metabolic stresses by exercising BLT may decrease chances for exercise-related arrhythmia or other cardiac dysfunction in susceptible patients. (Am Heart J 1989;117:1070.)**

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Regular exercise has been shown to reduce overall risk for cardiovascular mortality.[1-4] Parodoxically, the act of performing exercise itself is associated with an increased risk for cardiac events, particularly for those who exercise infrequently.[1] Metabolic changes occurring during exercise, particularly elevated catecholamines and potassium shifts, may contribute to the risk of a cardiac event. Studies have shown that significant exercise-related changes in catecholamine and potassium levels do not occur until after exercise intensity surpasses lactate threshold,[5-8] a term used to refer to the point during incremental exercise beyond which a sudden increase in lactate can be measured.[9,10] Of note, these studies all involve changes occurring during exercise testing.

Exercise training usually involves sustained exercise at a certain intensity, as opposed to the progressive incremental exercise commonly performed during treadmill exercise testing. However, the effects of prolonged exercise (in relation to lactate threshold) on shifts in potassium and catecholamines have not been examined. Therefore we assessed the effect of sustained exercise (20 minutes) slightly above and below lactate threshold on catecholamine and potassium levels.

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## METHODS

Ten healthy men volunteers were studied (age range 26 to 34 years). Subjects had no known medical problems and were not taking any medications. Each subject served as his own control. All subjects participated in three exercise sessions on a bicycle ergometer with an indwelling intravenous catheter in the forearm: an initial maximal incremental exercise test for determination of lactate threshold, and two subsequent bouts during which the subject exercised for 20 minutes at 25 W above lactate threshold (ALT) or 25 W below lactate threshold (BLT). The sustained exercise sessions were assigned randomly and were performed on separate days within the period of 7 days. Heart rate and ectopic activity were continuously monitored during and following each test.

**Determination of lactate threshold.** Lactate threshold

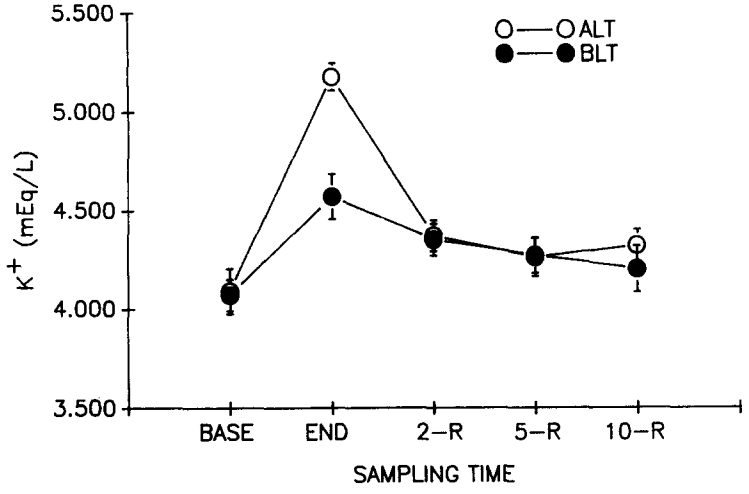


**Fig. 1.** Potassium levels as a function of time and exercise intensity. Error bars represent SEM. $K^+$, Potassium; *ALT*, above lactate threshold; *BLT*, below lactate threshold; *BASE*, baseline; *END*, end exercise; *2-R*, 2-minute recovery; *5-R*, 5-minute recovery; *10-R*, 10-minute recovery.

was determined from a progressive incremental exercise test (4-minute stages, 25 W increments) to volitional fatigue, during which blood was drawn through an indwelling venous catheter for lactate analysis. The exercise intensity corresponding to lactate threshold was determined by regression of exercise intensity work rate on venous lactate. When the correlation coefficient decreased with increasing work rate, the intersection of the two lines of best fit was used as the lactate threshold.

**Sustained exercise.** Each sustained exercise period was preceded by a 5-minute progressive warm-up on the bicycle. Subjects then maintained constant exercise intensity at either 25 W above or below the intensity corresponding to their lactate threshold. Venous blood samples were drawn through the indwelling catheter at baseline, end exercise, 2 minutes of recovery, 5 minutes of recovery, and 10 minutes of recovery. At each of these sampling points, blood was analyzed for (1) potassium, (2) norepinephrine, (3) epinephrine, (4) venous pH, (5) hematocrit, and (6) glucose. Lactate was analyzed at baseline and end exercise. Catecholamines were analyzed with high performance liquid chromatography with electrochemical detection.

All values are reported as means ± S.E.M. Groups were compared by use of paired *t* test and two-way analysis of variance for repeated measures (time). Statistical significance was accepted at $p < 0.01$.

## RESULTS

The mean peak work rate during the initial maximal exercise test was 220 ± 20 W, with a range of 150 to 375 W. The mean peak oxygen consumption (determined via ventilatory measurements during exercise) was 44 ± 2 ml/kg/min.

The mean work rate at lactate threshold was 135 ± 15 W (range 90 to 260 W). The mean heart rate at lactate threshold was 122 ± 5 beats/min, which corresponded to 67 ± 6% of peak heart rate during the exercise test and 64 ± 8% of age-predicted maximum heart rate (determined as 220 − age).

The lactate level at end-exercise ALT was 7.5 ± 0.7 (range 4.5 to 13); at end-exercise BLT, the mean lactate level was 2.1 ± .3 (range 1 to 4.4). The mean heart rate during the final 15 minutes of exercise ALT was 155 ± 4, which corresponded to 85% maximal heart rate on the initial exercise test. Compared to this, the mean heart rate during the final 15 minutes of exercise BLT was 114 ± 4, which corresponded to 63% of maximal heart rate on the initial exercise test. No significant arrhythmia or changes in the electrocardiogram (ECG) were noted during any exercise period.

**Effect of exercise ALT and BLT on serum potassium** (Fig. 1). Exercise ALT resulted in a significantly greater rise in potassium between base and end exercise than was seen for exercise BLT (1.1 ± 0.1 versus 0.5 ± 0.1 mEq/L, $p < 0.001$). In addition, the fall in potassium during the first 2 minutes of recovery following exercise ALT was significantly greater than that seen following exercise BLT (−0.8 ± 0.1 versus −0.2 ± 0.1 mEq/L, $p < 0.001$). There was no significant difference between exercise conditions with respect to venous pH, serum glucose, or hematocrit at any sampling point.

**Effect of exercise ALT and BLT on catecholamine levels.** Exercise ALT and BLT resulted in significant elevations in catecholamine levels over baseline. Two-way (time × treatment) analysis of variance showed an overall effect of time on catecholamine levels, an overall effect of exercise ALT that differed

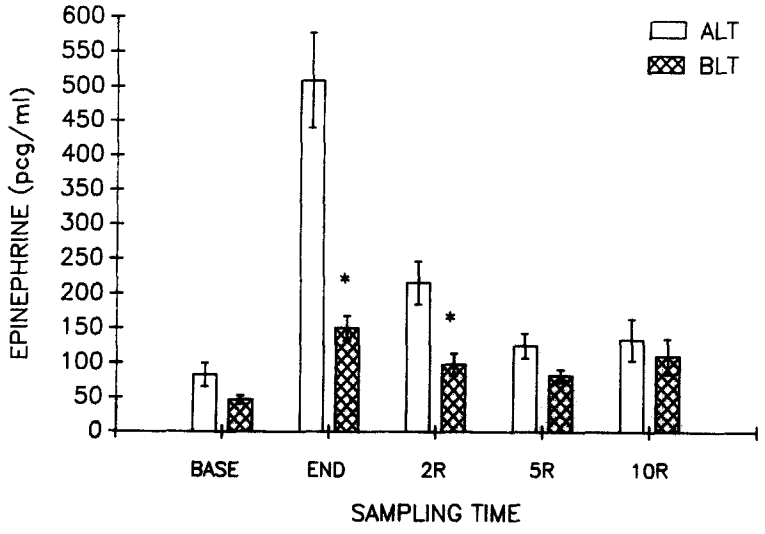


**Fig. 2.** Exercise-related epinephrine levels above and below lactate threshold. Error bars represent SEM. *$p < 0.01$. Abbreviations same as in Fig. 1.

from that seen BLT, and a significant interaction of exercise intensity with the time effect (all $p < 0.0005$). This effect can be seen in Figs. 2 and 3 by the shapes of the curves for exercise ALT and BLT.

Norepinephrine at end exercise ALT was significantly higher than that seen at end exercise BLT (2270 ± 190 versus 900 ± 23 pg/ml, $p < 0.001$). ALT 2-minute recovery norepinephrine levels remained significantly higher than those seen following exercise BLT (1620 ± 130 versus 590 ± 60 pg/ml, $p < 0.001$). A similar situation was present for epinephrine levels, where both end exercise and 2-minute recovery ALT levels were significantly higher ($p < 0.001$) than corresponding sampling points in the BLT condition.

## DISCUSSION

Prior studies have shown that catecholamines and plasma potassium both begin to rise after incremental exercise surpasses lactate threshold. This is the first study that evaluates how these parameters are affected by sustained exercise, a model that more closely mimics exercise training.

A regular exercise program is associated with an overall reduced risk for sudden cardiac death,[1-4] and exercise prescription is designed to enable patients to safely achieve this goal. Given the fact that acute cardiac events may be precipitated by exercise,[1,11] this study was performed to determine how exercise-related metabolic stresses (i.e., elevated catecholamines and rapid potassium flux) that may precipitate or contribute to cardiac dysfunction are affected by sustained exercise ALT and BLT. The results indicate that 20 minutes of exercise slightly ALT results in significantly higher levels of catecholamines at peak exercise and recovery when compared to exercise slightly BLT. In addition, exercise ALT results in significantly higher potassium levels at the end of exercise, followed by a significantly greater fall in potassium during the immediate recovery period than is seen with exercise BLT.

**Lactate threshold.** Lactate threshold refers to the exercise intensity above which a significant rise in plasma lactate occurs.[10] Lactate threshold was used as the criterion for defining exercise conditions in this study because both catecholamine levels[5,6] and potassium levels[7,8] have been shown to have a nonlinear increase during progressive incremental exercise, paralleling the curve of the exercise-related elevation of plasma lactate.

The lactate threshold reflects a physiologic response to exercise, and is influenced both by level of conditioning[10] and by the type of exercise performed.[12] The lactate threshold does not occur at the same percentage of maximal heart rate in all patients, nor can it be related to the same percentage of maximal oxygen uptake. Katch et al.[13] found that 17 of 31 subjects were ALT when exercising at 80% maximum heart rate, while 14 of 31 were BLT.[13] The authors note that these two groups undergo different stress during exercise, even though they are working at the same relative percent of maximal heart rate.

Accurate detection of lactate threshold requires direct assessment by venous sampling of lactate, or indirect assessment through measurement of ventilation and gas exchange during exercise.[9,10,14,15] The

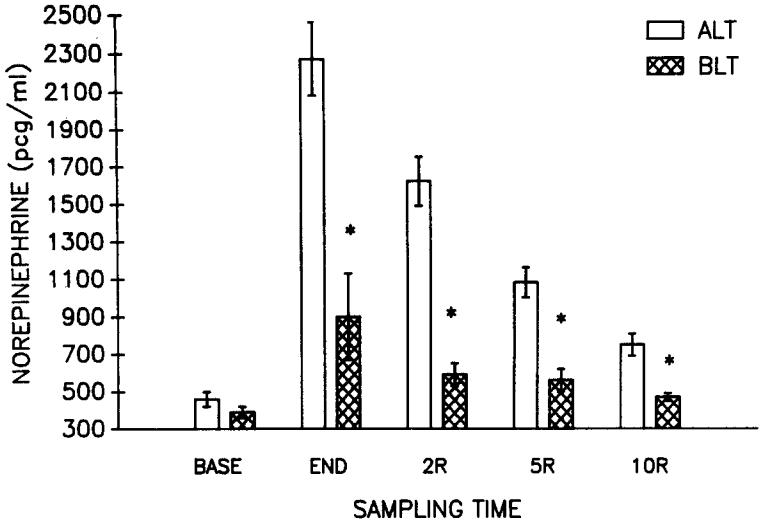


**Fig. 3.** Exercise-related norepinephrine levels above and below lactate threshold. Error bars represent SEM. $*p < 0.01$. Abbreviations same as in Fig. 1.

use of lactate threshold to assign exercise intensity in this study equalized the group with respect to physiologic performance, and ensured that well-conditioned and poorly-conditioned subjects exercised at an equivalent workload ALT.

**Catecholamines.** Prior studies[5,6] have shown that catecholamines do not have a linear response to progressive exercise, showing a more rapid elevation after exercise intensity surpasses lactate threshold. Our data show that sustained exercise BLT results in a statistically significant rise in norepinephrine and epinephrine at end exercise, but the magnitude is dramatically less than that seen at end exercise ALT.

Dimsdale et al.[16] noted that catecholamine levels increased during incremental exercise, and continued to increase during the recovery period after exercise. We did not observe this pattern during the recovery period for either condition following sustained exercise. It is difficult to compare the studies, however, as Dimsdale et al. did not stratify subjects based upon lactate threshold, and were not studying subjects after prolonged exercise.

**Potassium.** Rapid potassium changes are a well-documented effect of intense progressive exercise.[7,8,17] Similar to catecholamines, however, potassium levels do not show a linear response to incremental exercise.[7,8] In a prior study we showed that patients who exercise ALT during an exercise test have significantly greater elevations in potassium at peak exercise and a significantly greater fall in early recovery than those who exercise BLT.[8] The present study extends the observations of progressive incremental exercise to steady-state exercise.

Factors regulating rapid shifts in potassium include pH, insulin, and catecholamines.[18-21] Williams et al.,[21] employing adrenergic blockade to study exercise-related potassium changes, found that catecholamines are the most important modulators of rapid potassium shifts during incremental exercise; catecholamines were shown to affect potassium levels independently of venous pH, serum glucose levels, or insulin effect.[21] The results of our study also suggest that catecholamines are responsible for the different degree of potassium flux observed with sustained exercise ALT and BLT. While catecholamine levels significantly differed between the two conditions, there was no significant difference in venous pH or glucose at any sampling point. Furthermore, the absence of a significant difference in hematocrit between the two groups at each sampling point rules out hemoconcentration as a factor explaining the differences in potassium and catecholamine levels in the two exercise conditions.

**Clinical implications.** The clinical implications of these data are limited by the fact that we studied normal subjects with very low likelihood of having cardiac disease. The catecholamine and potassium response may be different in normal individuals and in those with heart disease. Of note, however, many victims of exercise-related sudden death have no prior history of cardiac disease. The findings are useful to patients without demonstrable heart disease in whom a method for reducing potential metablic fluxes during exercise is desired. In addition, this study provides the framework for studying other groups of patients (i.e., patients with docu-

mented coronary disease or arrhythmia, subjects in older age groups, patients on beta blockers, etc.).

Indirect evidence suggests that exercise ALT may increase the risk for exertion-related mortality in patients with cardiac disease. A recent review of 15 cases of sudden death during cardiac rehabilitation[22] showed that nine of the patients were exercising in excess of 85% maximum heart rate, and thus were likely to have been at an exercise intensity in excess of the lactate threshold. The magnitude of catecholamine elevation and rapid potassium flux observed with exercise ALT may contribute to the mechanism underlying these events.

The data may also explain why exercise-related cardiac events often occur during the recovery period from exercise, referred to by Adams[23] as the "post-exercise vulnerable period." Northcote et al.[24] found that 8 of 30 cases of sudden death associated with playing squash occurred within 30 minutes of stopping play. Fletcher and Cantwell[25] found that sudden death occurred during the immediate recovery period in four of five patients they reported with ventricular fibrillation associated with a supervised cardiac exercise program. Other studies[26-29] have shown that ventricular arrhythmias occur as commonly or more commonly in the recovery period than during exercise itself. Of note, the single case of exercise-related sudden death in the study by Goldschlager et al.[26] of exercise-induced ventricular arrhythmia resulted from ventricular fibrillation that occurred 4 minutes after termination of exercise. The mechanism underlying post-exercise arrhythmia is frequently not clear, but our data support Opie's assertion[30] that a biochemical mechanism must be considered. The combination of elevated catecholamine levels and rapidly falling potassium during immediate recovery from exercise ALT may be particularly likely to contribute to exercise-related cardiac dysfunction, and can be avoided by exercise at a lower intensity.

If these metabolic stressors contribute to exercise-related mortality, the data in this study may indicate a practical and nonpharmacologic method for reducing the risk of exercise. An individualized assessment of exercise intensity is clearly important, given the significant difference in the two conditions in this study resulting from exercise only 25 W (which corresponds to 1 to 1.5 metabolic equivalents of oxygen consumption [METs]) on either side of the lactate threshold. While it may be impractical to determine lactate threshold, the exercise intensity corresponding to lactate threshold can be closely approximated by use of respiratory measurements during exercise.[9, 10, 14, 15] Other indices are much more likely to result in significant variance from the desired exercise intensity rate[31-33]; an exercise prescription based on a percentage of predicted maximal heart rate is particularly of poor value.[31] Thus our data support more widespread assessment of factors that reflect metabolic changes occurring during exertion (i.e., lactate or ventilatory determinations) as an adjunct to determining optimal exercise intensity.[34]

Siscovick et al.[1] found that men with low levels of habitual activity had a relative risk of cardiac arrest during exercise that was 56 times that at other times of the day, while the risk during exercise among men with a high level of habitual activity was only increased by a factor of 5. Thus habitual exercise results in significantly reduced risk for sudden death.[1, 24] Our data may contribute to understanding this phenomenon. Training results in lactate threshold occurring at a greater percentage of peak exercise intensity.[10] At the same submaximal exercise intensity then, a trained individual is less likely to be in excess of lactate threshold than one who is sedentary, and is less likely to be exposed to the potentially harmful metabolic stress attendant upon exercise ALT.

The level of exercise required to gain an epidemiologically proven long-term benefit is often less than is commonly prescribed. Blumenthal et al.[35] found that post-myocardial infarction "low intensity" exercise (characterized as training at a level <45% maximal oxygen consumption) resulted in comparable changes in heart rate and double product at submaximal and maximal workloads as "high intensity" exercise (training at 67% to 75% maximum oxygen consumption). They concluded that the additional risk of high-intensity training may not be justified by additional benefits. Determination of training exercise intensity based on lactate threshold for determining exercise intensity, rather than on a fixed percentage of maximum heart rate or on oxygen consumption that does not necessarily reflect metabolic changes, would seem to be a useful adjunct to this approach.

In conclusion, assessment of lactate threshold enabled us to identify two exercise conditions associated with significantly different metabolic responses, despite the fact that the difference between the conditions was only 50 W. Sustained exercise ALT resulted in significantly higher catecholamine levels and greater potassium flux than exercise BLT. This may contribute to exercise-related cardiac mortality, particularly that seen during the recovery phase of exercise. It would seem prudent to avoid these metabolic changes if possible,

particularly in patients with underlying heart disease or in those at increased risk for heart disease. The data suggest that assessment of lactate threshold is helpful for determining an exercise intensity below which potentially harmful metabolic stress will be significantly reduced.

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