Time course of loss of adaptations after stopping prolonged intense endurance training

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COYLE, EDWARD F., WADE H. MARTIN III, DAVID R. SINACORE, MICHAEL J. JOYNER, JAMES M. HAGBERG, AND JOHN O. HOLLOSZY. *Time course of loss of adaptations after stopping prolonged intense endurance training.* J. Appl. Physiol.: Respirat. Environ. Exercise Physiol. 57(6): 1857–1864, 1984.—Seven endurance exercise-trained subjects were studied 12, 21, 56, and 84 days after cessation of training. Maximal O_2 uptake ($\dot{V}O_{2\,max}$) declined 7% ($P < 0.05$) during the first 21 days of inactivity and stabilized after 56 days at a level 16% ($P < 0.05$) below the initial trained value. After 84 days of detraining the experimental subjects still had a higher $\dot{V}O_{2\,max}$ than did eight sedentary control subjects who had never trained (50.8 vs. 43.3 $ml \cdot kg^{-1} \cdot min^{-1}$), due primarily to a larger arterial-mixed venous O_2 ($a\text{-}\bar{v}O_2$) difference. Stroke volume (SV) during exercise was high initially and declined during the early detraining period to a level not different from control. Skeletal muscle capillarization did not decline with inactivity and remained 50% above ($P < 0.05$) sedentary control. Citrate synthase and succinate dehydrogenase activities in muscle declined with a half-time of 12 days and stabilized at levels 50% above sedentary control ($P < 0.05$). The initial decline in $\dot{V}O_{2\,max}$ was related to a reduced SV and the later decline to a reduced $a\text{-}\bar{v}O_2$ difference. Muscle capillarization and oxidative enzyme activity remained above sedentary levels and this may help explain why $a\text{-}\bar{v}O_2$ difference and $\dot{V}O_{2\,max}$ after 84 days of detraining were still higher than in untrained subjects.

maximal oxygen uptake; detraining; cardiac output; oxidative capacity; myoglobin; capillarization

ENDURANCE EXERCISE TRAINING induces increases in maximal stroke volume and cardiac output as well as in the capillarization and respiratory capacity of skeletal muscle (1, 7, 10). Little information is available regarding how rapidly these adaptations are lost when highly trained individuals who have exercised regularly for prolonged periods stop training. Previous studies either employed short periods of detraining (11) or involved previously sedentary individuals who participated in mild-to-moderate training programs for a few weeks and then stopped training (8, 9, 14).

In the present study we determined the effects of detraining for 12 wk on maximal O_2 uptake ($\dot{V}O_{2\,max}$), stroke volume (SV) during exercise, skeletal muscle mitochondrial marker enzyme levels and myoglobin concentration, and capillary density in skeletal muscle. The subjects, who had been training for prolonged periods, were all quite highly trained. However, they differed considerably in their $\dot{V}O_{2\,max}$. Our goals were *1*) to obtain information regarding how rapidly and completely the adaptations to long-term endurance training are lost when highly trained individuals adopt a sedentary life style and 2) to try to obtain insights regarding the factors that determine $\dot{V}O_{2\,max}$.

METHODS

Subjects and training. The physical characteristics and training history of the subjects are presented in Table 1. This study was approved by the Human Studies Committee of Washington University School of Medicine. The subjects gave their written informed consent after the study design and the risks involved were explained to them. Prior to becoming inactive these subjects had been performing endurance training for an average of 10 ± 3 yr (range 1–20 yr). Four of the subjects were runners, three of whom (*subjects A, B,* and *C*) competed in track (1,500–10,000 m) and cross-country, while the fourth runner (*subject D*) trained moderately (30 km/wk) for 2 yr before training more intensely in preparing for this study as described below. Three subjects trained using a cycle ergometer. *Subject E* (Table 1) was a woman who had competed in swimming and running and had been doing long-distance bicycling during the 2 yr prior to this study. *Subject F* had trained regularly for 20 yr with only brief interruptions (<3 mo), and he had been cycling intensely during the 2 yr before this study. *Subject G* was a recreational athlete who first performed regular endurance training for the year prior to this study.

The training regimen of the subjects was standardized during the 10- to 12-mo period prior to detraining. Generally, for the first 6 mo they trained at least 5 days/wk for ~60 min/day at an exercise intensity corresponding to 70–80% $\dot{V}O_{2\,max}$. During the 6-mo period immediately prior to detraining they did two to three sessions of interval training and three to four 60-min sessions of steady-state exercise at 70–80% of $\dot{V}O_{2\,max}$ per week. The interval training involved performing six bouts of exercise of 5-min duration at an intensity eliciting $\dot{V}O_{2\,max}$.

Detraining and testing sequence. On the last day of training, and 12, 21, 56, and 84 days after cessation of

TABLE 1. *Physical characteristics and training history of subjects prior to detraining*

Subj	Training Mode	Sex	Training, yr	Uninterrupted Training, mo	Age, yr	Weight, kg	$\dot{V}O_{2\,max}$, ml·kg^{-1}·min^{-1}	$\dot{Q}_{max,\,est}$, ml·kg^{-1}·min^{-1}	Capillary Density, cap·mm^{2}	Citrate Synthase, mol·kg protein^{-1}·h^{-1}
A	Running	M	16	10	28	63.1	75.5	483	443	9.6
B	Running	M	7	36	21	77.2	69.5	427	488	10.0
C	Running	M	12	10	30	65.5	66.9	462	507	11.3
D	Running	M	3	12	24	65.8	61.7	394	469	10.8
E	Cycling	F	12	10	29	49.6	54.0	426	456	8.7
F	Cycling	M	20	24	47	76.2	53.9	337	486	12.2
G	Cycling	M	1	12	25	78.6	53.1	354	428	7.8
Mean ± SE			10.1 ±2.6	14.9 ±4.4	29.1 ±3.2	68.0 ±3.0	62.1 ±3.3	412 ±20.3	468 ±10.5	10.0 ±0.6

$\dot{V}O_{2\,max}$, maximal O_2 uptake; maximal cardiac output is estimated to be product of maximum stroke volume and maximal heart rate ($\dot{Q}_{max,\,est}$).

training a series of exercise tests and a muscle biopsy were performed, always in the same sequence. First, the subjects' response to 15 min of exercise at 75% of their trained $\dot{V}O_{2\,max}$ was measured, and after a rest $\dot{V}O_{2\,max}$ was determined. Seventeen hours later cardiac output was measured during three separate 10-min bouts of exercise at 55, 65, and 75% of $\dot{V}O_{2\,max}$. Two hours later a muscle biopsy was performed. There is approximately a 48-h delay before an increase in muscle mitochondrial enzymes occurs following a bout of exercise in rats (3). Therefore, the acute exercise testing should not have affected the enzyme activities for that time point; however, it could have had a small effect on the enzyme levels at subsequent time points.

Except for the exercise required by the testing the subjects limited their physical activity to the minimal level required by their sedentary jobs. Typically, these subjects walked <500 m/day at a slow pace. Six of the seven subjects detrained for 84 days. One subject (*C*, Table 1) detrained for 42 days. His final test results were included in the mean of the 56-day results, and the missing data point for *day 84* was estimated as described by Winer (23).

Measurement of maximal O_2 uptake. The subjects' $\dot{V}O_{2\,max}$ was measured using a continuous exercise test lasting between 8 and 10 min. The runners were evaluated while running up a grade on a treadmill, and the cyclists pedaled a cycle ergometer. The cyclists were also evaluated during treadmill running when trained and after 12 wk of detraining to verify that they could attain $\dot{V}O_{2\,max}$ during cycling. Work rate was increased every 2 min until the subjects were unable to continue exercising. A clear leveling off of O_2 uptake ($\dot{V}O_2$) occurred in all the tests. Expired gases were collected in neoprene meteorological balloons at 30-s intervals beginning at 3 min and analyzed for O_2 and CO_2 with a mass spectrometer (Perkin-Elmer MGA 1100) which was calibrated with gases analyzed by the Scholander technique. Expired air volumes were measured in a dry gas meter (Parkinson-Cowan CD4) calibrated against a Tissot spirometer.

Cardiac output. The noninvasive CO_2 rebreathing method of Defares (6), modified for computer application, was used to determine cardiac output ($\dot{Q}$). $\dot{V}O_2$, CO_2 production ($\dot{V}CO_2$), and end-tidal P_{CO_2} were determined on a breath-by-breath basis using a heated Fleish no. 3 pneumotachograph, a Validyne DP45 pressure transducer, and a Perkin-Elmer mass spectrometer model MGA 1100 interfaced with a PDP 8 computer. Arterial P_{CO_2} was estimated from corrected end-tidal P_{CO_2} (19), and arterial and venous CO_2 content were calculated from the dissociation curve presented by McHardy (16). After 4 min of treadmill exercise that resulted in steady-state $\dot{V}O_2$, $\dot{V}CO_2$, and end-tidal P_{CO_2}, the subjects rebreathed 5% CO_2-95% O_2 from an anesthesia bag. Mixed venous CO_2 was estimated from *breaths 3, 4,* and *5* by extrapolating the exponential rise in end-tidal P_{CO_2} to equilibrium (13) using computer analysis. Three separate determinations of $\dot{Q}$ were made during each exercise bout at a given intensity; the measurements were made after 4, 7, and 10 min of exercise. This approach was made possible by the finding that $\dot{V}CO_2$ and end-tidal P_{CO_2} return to steady state within 60 s after a period of rebreathing. The reproducibility of the $\dot{Q}$ measurements was good. In 100 exercise tests the average coefficient of variation (SD/mean × 100%) for the three measurements during a bout of exercise was 6.5 ± 0.4%. The test-retest correlation $\dot{Q}$ measurements on the same individuals on two separate days was 0.98 for 40 trials on 10 subjects.

$\dot{Q}$ measurements with the CO_2 rebreathing method require a stable $\dot{V}CO_2$ and end-tidal P_{CO_2} prior to the determination of mixed venous P_{CO_2}. It has been our experience that it is difficult to obtain a stable $\dot{V}CO_2$ and end-tidal P_{CO_2} at exercise intensities that elicit hyperventilation. However, studies using invasive methods (2) for measuring $\dot{Q}$ have shown that maximum SV is attained at submaximal exercise intensities during exercise in the upright position with a leveling off of SV at exercise intensities requiring between 40 to 50% of $\dot{V}O_{2\,max}$. Therefore, in the present study $\dot{Q}$ at $\dot{V}O_{2\,max}$ was estimated by multiplying exercise SV by maximal heart rate ($\dot{Q}_{max,\,est}$). Maximal heart rate (HR_{max}) was measured electrocardiographically and defined as the highest HR obtained during the $\dot{V}O_{2\,max}$ test. Exercise SV was taken as the average of measurements made at 55, 65, and 75% $\dot{V}O_{2\,max}$.

Muscle biopsy and tissue preparation. Muscle samples were obtained using a needle biopsy from the left gastrocnemius of the runners and the left vastus lateralis of the cyclists. After removing gross blood and connective tissue the specimen was divided longitudinally. One portion for enzymatic analysis, weighing ~40 mg, was frozen in liquid N_2 and stored at −70°C. Another portion for

histochemical analysis was oriented, mounted in an embedding matrix (OCT), and frozen in isopentane cooled to its freezing point with liquid N_2.

Muscle biopsy assays. The muscle samples were weighed at −20°C on a Roller-Smith torsion balance and homogenized in 50 vol of 50% glycerol containing 20 mM sodium phosphate buffer, pH 7.4, 5 mM β-mercaptoethanol, 0.5 mM ethylenediaminetetraacetate, and 0.02% bovine serum albumin. The enzymatic assays were conducted at 25°C, and all the homogenates were assayed for a given enzyme on the same day. The activities of citrate synthase, succinate dehydrogenase (SDH), and creatine kinase (CK) were determined fluorometrically as described by Chi et al. (4). Protein in the homogenates was measured colorimetrically (15) with bovine serum albumin as standard. Although an attempt was made to remove blood, fat, and connective tissue from each biopsy before freezing it, it was clear that the samples were variably contaminated with nonmuscle elements. Therefore the original data based on fresh weight were recalculated on the basis of constituents more directly related to muscle fiber mass. Two of these were protein and CK activity. Protein did not seem totally satisfactory because it does not correct for blood and only partially for connective tissue. CK was used because it does not appear to vary with detraining or among human muscle fiber types (4) and is unchanged in muscle of highly trained rats (cf. Ref. 10). To make it easier to compare our results with those in the literature, the data are reported on a protein basis, but the protein has been normalized for CK (4). The data were first calculated on the basis of actual protein content. In the case of CK, call this CKp. The highest CKp among the samples from a given individual was identified (CKp_{max}). The citrate synthase and SDH activities and the myoglobin concentration for a particular sample were then multiplied by the ratio of CKp_{max}-to-CKp for that sample. For the samples on the control subjects the original data expressed on a protein basis were multiplied by the ratio of the average CKp_{max} of the seven detraining subjects to the CKp of the control sample.

Myoglobin. The myoglobin concentration of the muscle biopsy samples was determined by radioimmunoassay as described by Moller and Sylven (17). Aliquots of the homogenates prepared for the enzyme determinations were diluted (final dilution: 1:60,000) using a 10 mM sodium phosphate buffer at pH 7.8. Reagents were obtained from Nuclear Medical Systems (Newport Beach, CA). Samples were analyzed in duplicate.

Capillarization and muscle fiber area. The muscle samples prepared for histochemical analysis were sectioned transversely (10 μ) at −20°C using a Cryostat microtome. Sections were fixed, treated with a 1% amylase solution, and stained with periodic acid-Schiff reagent to visualize capillaries (1). The stained sections were analyzed by magnifying (×296) and projecting numerous artifact free 0.25-mm^2 areas onto a screen. The number of whole and fractionated fibers and the number of capillaries within the known area were determined, and the capillary-to-fiber ratio was calculated. The mean number of capillaries around the whole fibers within the area was determined. The mean muscle fiber area was measured from serial sections stained for $NADH_2$-tetrazolium reductase (18) by tracing the perimeter of individual fibers using a computerized planimeter. This method was less influenced by tissue artifact and irregularities than was the determination of fiber area by counting the number of fibers within a known area. The capillary density (cap/mm^2) was calculated: cap/mm^2 = (cap/fiber)·(fibers/mm^2). In 10 biopsy samples the mean coefficient of variation for four determinations was cap around fiber, ±6.8% cap/fiber, ±8.1%; cap/mm^2, ±7.2%; and fiber area, ±3.6%.

Methodological control subjects. Seven men served as controls for the measurements of $\dot{V}O_{2\,max}$, SV, and HR_{max}. Each control subject was paired with an experimental subject and tested at the beginning and end of the experimental subject's detraining period. These men did not alter their physical activity during this period.

Sedentary control subjects. The values after 84 days of inactivity were compared with those of sedentary control subjects. These control subjects were normally active individuals who either have never engaged in regular physical training or who have not done so during the previous 8 yr. Eight subjects were evaluated for each comparison. Muscle biopsies were obtained from their vastus lateralis or gastrocnemius muscles.

Statistical analysis. A repeated measures analysis of variance and Tukey's post hoc test identified means which differed at the various testing periods during detraining. Significant differences between sedentary controls and the detrained subjects (84 days) were identified using Student's *t* test for unpaired observations.

RESULTS

Maximal O_2 uptake. $\dot{V}O_{2\,max}$ in the trained state averaged 62 $ml \cdot kg^{-1} \cdot min^{-1}$ with values ranging from 53.1 to 75.5 $ml \cdot kg^{-1} \cdot min^{-1}$ (Table 1). This rather large range was not due to differences in training effort, since all the subjects trained as close to their physiological limits as tolerable. In the trained state, $\dot{V}O_{2\,max}$ was highly related to SV and $\dot{Q}_{max,\,est}$. The correlations between trained $\dot{V}O_{2\,max}$ ($l \cdot min^{-1}$) and maximal SV (ml) or $\dot{Q}_{max,\,est}$ ($l \cdot min^{-1}$) were 0.95 and 0.96, respectively, ($P < 0.001$). When the measurements were expressed in terms of body weight, the correlations between $\dot{V}O_{2\,max}$ ($ml \cdot kg^{-1} \cdot min^{-1}$) and SV ($ml \cdot kg^{-1}$) and $\dot{Q}_{max,\,est}$ ($ml \cdot kg^{-1} \cdot min^{-1}$) were 0.85 and 0.82, respectively ($P < 0.01$ for both).

When training was stopped, $\dot{V}O_{2\,max}$ declined in all subjects (Fig. 1) and was 7% ($P < 0.05$) below trained levels after 12 days of inactivity (Table 2). A further decline did not occur during the 12- to 21-day period possibly due to a training effect of the testing on the 12th day. During the 21- to 56-day period of inactivity, $\dot{V}O_{2\,max}$ declined significantly ($P < 0.05$) to a level 14% below the trained level. During the 56- to 84-day period, $\dot{V}O_{2\,max}$ declined only 0.11 $l \cdot min^{-1}$, which was not significant (Table 2). A small gain in body weight during this period contributed to the 4% decline in $\dot{V}O_{2\,max}$ expressed as milliliters per kilogram per minute, which also was not significant (Table 2; Fig. 1). As might be

expected the subjects with the highest initial $\dot{V}O_{2\,max}$ had the greatest decline. There was a correlation of 0.93 ($P < 0.001$) between trained $\dot{V}O_{2\,max}$ and percent decline of $\dot{V}O_{2\,max}$ with inactivity. The subjects' $\dot{V}O_{2\,max}$ ranged from 46 to 56 $ml \cdot kg^{-1} \cdot min^{-1}$ at 84 days, which is substantially less than the 22 $ml \cdot kg^{-1} \cdot min^{-1}$ range observed when trained (Fig. 1). Body weight remained stable for 56 days and increased by only 3% above trained levels between 56 and 84 days of inactivity. Therefore, similar trends are seen when $\dot{V}O_{2\,max}$ is expressed as liters per minute or milliliters per kilogram per minute.

Exercise stroke volume and maximal heart rate. A plateau value of SV was observed during exercise at 55, 65, and 75% of $\dot{V}O_{2\,max}$ with mean values at these intensities agreeing within ±3% during each testing period. The mean coefficient of variation for SV measured at the three exercise intensities was 6.5 ± 0.4%. SV during upright exercise had declined 10% ($P < 0.05$) below trained levels when measured after 12 days of inactivity (Table 2). During the 12- to 84-day period, SV averaged 10–14% below trained levels. Most of the change in HR_{max} occurred within the first 12 days. HR_{max} was significantly ($P < 0.05$) increased by 4, 5, 6, and 5% after 12, 21, 56, and 84 days of inactivity, respectively (Table 2).

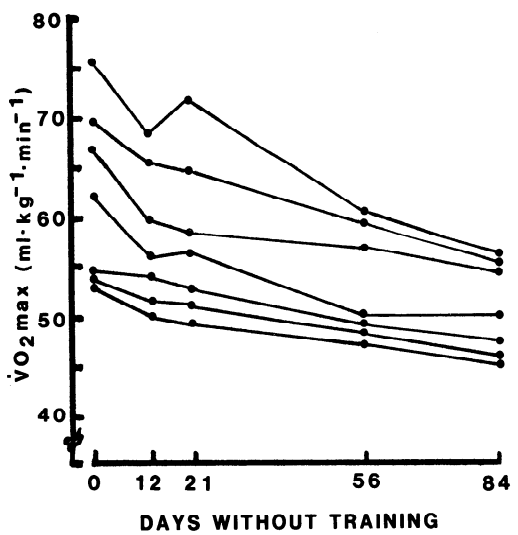

FIG. 1. Maximal O_2 uptake ($\dot{V}O_{2\,max}$) in subjects when trained (*day 0*) and after 12, 21, 56, and 84 days without training.

Maximal cardiac output and arterial-mixed venous O_2 ($a\text{-}\bar{v}O_2$) difference. Since SV was not directly measured during maximal exercise, we carefully monitored the $\dot{V}O_2$ vs. HR relationship during incremental exercise because it can reflect a change in SV during intense exercise. In a previous study of trained ischemic heart disease patients, we noted that a decline in SV during intense exercise was reflected in a reduction in O_2 pulse or a flattening of the $\dot{V}O_2$ vs. HR relationship (5). In the present study during each of the testing periods the $\dot{V}O_2$ vs. HR relationship was linear from the submaximal intensities at which SV was measured up to $\dot{V}O_{2\,max}$ (Fig. 2). This provides indirect evidence that the SV measured during submaximal exercise at each testing period in the present study is similar to the SV at $\dot{V}O_{2\,max}$. It therefore appears possible to obtain a reasonable estimate of $\dot{Q}_{max}$ by multiplying maximum SV determined during submaximal exercise by HR_{max}.

$\dot{Q}_{max,\,est}$ was reduced 8% below the trained level after 21 days of detraining (Table 2). During the 21- to 84-day period $\dot{Q}_{max,\,est}$ averaged 8–9% below trained levels. As shown in Fig. 3 this indicates that the 9% decline ($P < 0.05$) in $\dot{V}O_{2\,max}$ that occurred during the 21- to 84-day period was associated with a significant ($P < 0.05$) decrease in maximum $a\text{-}\bar{v}O_2$ difference, since $\dot{Q}_{max,\,est}$ remained stable during this period.

Respiratory enzyme activities. The activities of citrate synthase and SDH declined roughly in parallel with a half-time of ~12 days. Reductions in activity were observed up to *day 56* (−39%; $P < 0.05$). Citrate synthase and SDH activities did not decrease during the period between *days 56* to *84*, indicating that stabilization had occurred (Table 3).

Myoglobin. Myoglobin concentration was not affected by detraining. Additionally, myoglobin concentration in the seven trained subjects was not significantly different from that in eight sedentary control subjects (Table 4).

TABLE 2. *Changes during detraining*

	Trained	12 Days	21 Days	56 Days	84 Days
$\dot{V}O_{2\,max}$, $l \cdot min^{-1}$	4.22 ± 0.31	3.93 ± 0.27*	3.94 ± 0.30*	3.67 ± 0.25*†	3.56 ± 0.23*†
%Δ		−7%	−7%	−14%	−16%
$\dot{V}O_{2\,max}$, $ml \cdot kg^{-1} \cdot min^{-1}$	62.1 ± 3.3	57.7 ± 2.6*	57.9 ± 3.1*	53.2 ± 2.1*†	50.8 ± 1.9*†
%Δ		−7%	−7%	−14%	−18%
Weight, kg	68.0 ± 3.9	68.4 ± 4.1	68.2 ± 4.3	69.1 ± 4.3	70.1 ± 4.4*†
%Δ		+0.6%	+0.3%	+1.6%	+3.1%
HR_{max}, $beats \cdot min^{-1}$	187 ± 3	195 ± 2*	195 ± 2*	199 ± 3*	197 ± 2*
%Δ		+4%	+4%	+6%	+5%
SV, ml	148 ± 8	134 ± 9*	131 ± 9*	127 ± 6*	129 ± 6*
%Δ		−10%	−11%	−14%	−13%
$\dot{Q}_{max,\,est}$, $l \cdot min^{-1}$	27.8 ± 1.5	26.0 ± 1.7	25.5 ± 1.7*	25.2 ± 1.1*	25.2 ± 1.2*
%Δ		−7%	−8%	−9%	−10%
Maximum $a\text{-}\bar{v}O_2$ difference, $ml \cdot 100\ ml^{-1}$	15.1 ± 0.5	15.1 ± 0.4	15.4 ± 0.4	14.5 ± 0.5	14.1 ± 0.5*†
%Δ		+0.4%	+2%	−4%	−7%
O_2 pulse at max, $ml \cdot beat^{-1}$	22.6 ± 1.7	20.2 ± 1.4*	20.2 ± 1.5*	18.4 ± 1.3*†	18.2 ± 1.3*†
%Δ		−11%	−11%	−19%	−20%

Values are means ± SE and % change (Δ) from trained for 7 subjects. $\dot{V}O_{2\,max}$, maximal O_2 uptake; HR_{max}, maximal heart rate; SV, stroke volume; $\dot{Q}_{max,\,est}$, cardiac output estimated as product of maximum SV and HR_{max}; $a\text{-}\bar{v}O_2$ difference, arterial-mixed venous O_2 difference. * Significantly different from trained; $P < 0.05$. † Significantly different from 21 days; $P < 0.05$.

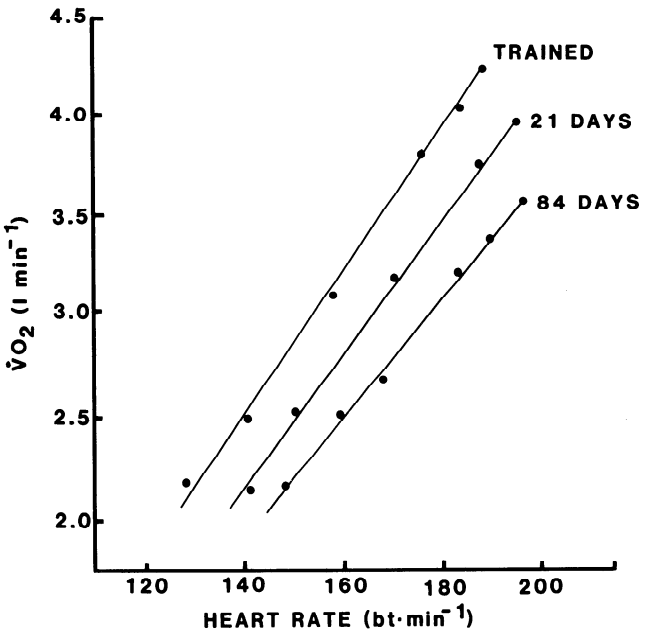

FIG. 2. O_2 uptake ($\dot{V}O_2$) and heart rate relationship during submaximal and maximal exercise when subjects were trained and following 21 and 84 days of inactivity.

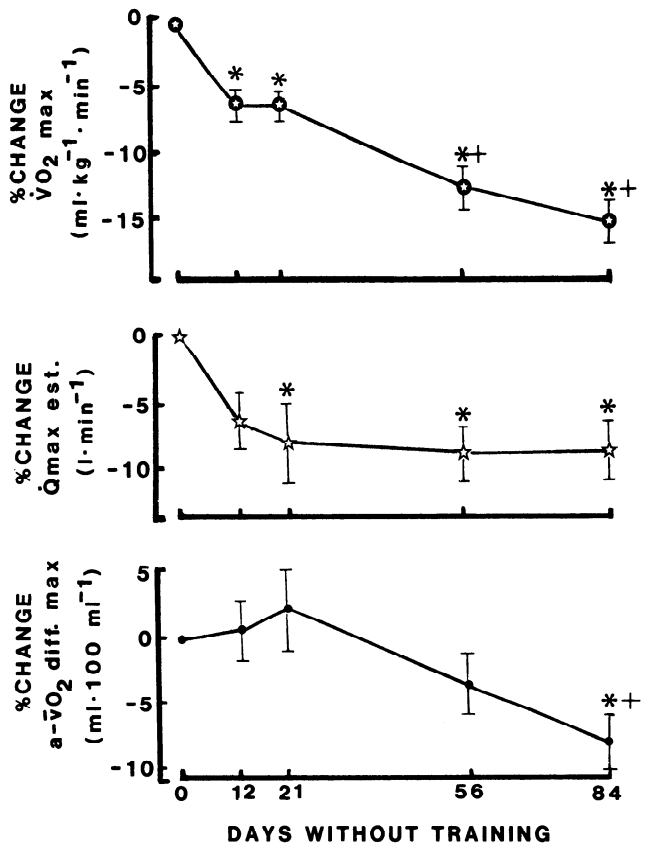

FIG. 3. Effects of detraining upon percent change of maximal O_2 uptake ($\dot{V}O_{2\,max}$), estimated maximal cardiac output ($\dot{Q}_{max\ est}$), and calculated arterial-mixed venous O_2 difference at $\dot{V}O_{2\,max}$ (a-$\bar{v}O_2$ diff max). * Significantly lower than trained (*day 0*); $P < 0.05$. † Significantly lower than 21 days; $P < 0.05$.

Myoglobin concentration is expressed both per gram of protein and per gram of protein normalized for CK activity.

Capillarization. Capillarization of muscle did not change significantly during the 84-day period of detraining (Table 5). The mean number of capillaries around a fiber and capillaries per fiber did not vary by more than 7% during the detraining period. The mean area occupied by a fiber also did not change, and therefore the number of capillaries per square millimeter was not significantly affected.

Methodological control subjects. The initial and final mean $\dot{V}O_{2\,max}$ and SV values in the seven methodological control subjects differed by <3%.

Comparison with sedentary controls. Table 6 indicates that after 84 days of inactivity the $\dot{V}O_{2\,max}$ of the experimental subjects was 17.3% higher ($P < 0.05$) than that of the sedentary controls. Since there were no significant differences in SV or $\dot{Q}_{max,\ est}$, the higher $\dot{V}O_{2\,max}$ in the detraining subjects compared with the sedentary controls appears to be due to a significantly ($P < 0.05$) higher maximum a-$\bar{v}O_2$ difference. The detrained subjects (at 84 days) also had substantially higher muscle mitochondrial enzyme activities and muscle capillarization than the sedendary controls. As shown in Table 3, citrate synthase and SDH were 49–52% higher ($P < 0.02$), and capillarization (Table 5, i.e., cap around fiber, cap/fiber, cap/mm^2) was 42–50% higher ($P < 0.05$), in the detrained than in the control subjects' muscles.

DISCUSSION

One purpose of this study was to determine how rapidly the cardiovascular and skeletal muscle adaptations to endurance exercise-training are lost when highly trained people stop training. Previous studies of prolonged detraining in people (8, 9, 14) and laboratory animals (3) have shown that the enzymatic adaptations to a few months of endurance exercise are rapidly lost. There is controversy regarding the rate of decline in $\dot{V}O_{2\,max}$ following cessation of brief training. Henriksson and Reitman (9) reported that no decline in $\dot{V}O_{2\,max}$ occurred during 6 wk of detraining, while Klausen et al. (14) found a rapid decline of $\dot{V}O_{2\,max}$ during the first 4 wk and a slower decline to base line during the second 4 wk of detraining. In a study on trained athletes Houston et al. (11) found an average decrease of 4% in $\dot{V}O_{2\,max}$ with 2 wk of detraining. In the present study the total decrease in $\dot{V}O_{2\,max}$ during 12 wk of detraining averaged 16% with a rapid decline of 7% in the first 2–3 wk and a further decline of 9% during the period from 3 to 8 wk. These results are similar to those of Klausen et al. (14), Houston et al. (11), and Fox et al. (8) and disagree with Henriksson and Reitman's (9) finding that $\dot{V}O_{2\,max}$ does not decrease during 6 wk of detraining. Bed-rest deconditioning has been shown to dramatically reduce exercise SV and $\dot{V}O_{2\,max}$ (21); however, this treatment creates orthostatic intolerance during exercise and is unlike normal inactivity (cf. Ref. 20).

Maximum SV during upright exercise also declined rapidly during the first 3 wk of detraining; this decrease averaged 11%. By 8 wk maximum SV had stabilized at 86% of the trained value and did not decrease further during the next 4 wk. The decrease in SV was partly compensated for by an increase in HR_{max}; as a conse-

TABLE 3. *Changes during detraining in activities of citrate synthase and succinate dehydrogenase and comparison with sedentary controls*

	Trained	6 Days	12 Days	21 Days	56 Days	84 Days	Sedentary Controls
Citrate synthase	10.0 ± 0.6	9.5 ± 0.7	8.3 ± 0.6*	7.7 ± 0.4*	6.0 ± 0.4*†	6.1 ± 0.5*†	4.1 ± 0.2‡
%Δ		−6.3%	−17.1%	−23.7%	−40.6%	−39.6%	
SDH	4.43 ± 0.27	4.04 ± 0.22	3.61 ± 0.13*	3.37 ± 0.23	2.73 ± 0.08*†	2.99 ± 0.22*†	1.97 ± 0.13‡
%Δ		−8.8%	−18.5%	−23.9%	−38.4%	−32.5%	

Values are means ± SE for 7 detraining subjects and 8 sedentary controls. Enzyme activities are expressed as (mol·kg protein^{-1}·h^{-1})·(CK_{max}·CK^{-1}), see METHODS for details. SDH, succinate dehydrogenase; CK, creatine kinase. * Significantly lower than trained; $P < 0.05$. † Significantly lower than 21 days; $P < 0.05$. ‡ Sedentary controls significantly lower than 84 days; $P < 0.02$.

TABLE 4. *Myoglobin concentration in detraining subjects and in sedentary controls*

Myoglobin	Trained	6 Days	12 Days	21 Days	56 Days	84 Days	Sedentary Controls
mg·g protein^{-1}	43.3 ±4.4	43.6 ±5.3	43.6 ±5.1	41.0 ±3.4	40.1 ±2.1	40.7 ±4.0	38.5 ±3.3
(mg·g protein^{-1})·(CKp_{max}·CKp^{-1})	46.4 ±4.2	47.3 ±4.8	48.3 ±3.8	51.5 ±3.1	49.5 ±3.7	45.8 ±3.4	43.5 ±1.6

Values are means ± SE for 7 detraining subjects and 8 sedentary controls. Concentration is expressed both per gram of protein and per gram of protein normalized for creatine kinase activity (CKp_{max}·CKp^{-1}); see METHODS.

quence, maximum cardiac output underwent a decrease of only 8% during the first 3 wk and a total decrease of 10% over 84 days. After 12 wk of detraining maximum SV during upright exercise was not significantly different from that of the sedentary control subjects.

As in previous studies (9, 11, 14) there was a large and rapid decrease in mitochondrial enzyme levels in muscle after cessation of training. This decrease averaged ~40% after 8 wk of detraining. However, in contrast with the previous studies in humans (9, 14) and rats (3) in which the preceding training was for only a few months, skeletal muscle mitochondrial enzyme levels in the highly trained subjects in the present study did not decrease to untrained values but stabilized after 8 wk of detraining at levels ~50% above the sedentary control value. The only exception to this pattern was *subject G* who had trained for only 1 yr and whose muscle mitochondrial enzymes were back to control levels after 84 days of detraining. In a detailed analysis of single muscle fibers on *subjects A, C,* and *F* we found that their mitochondrial enzyme levels in whole muscle homogenates after 84 days of detraining were 50% higher than those of sedentary controls almost entirely as the result of a persistent 80% elevation above control of mitochondrial enzymes in type II fibers (4) In contrast, mitochondrial enzyme activities in type I fibers had returned essentially to control values after 84 days of detraining. This finding is of considerable interest, since it implies that in contrast with short-term endurance training many years of regularly performed intense endurance exercise results in long-lasting adaptations. These could perhaps involve changes in the recruitment pattern of the type II fibers or in the firing frequency of the nerves innervating them.

In addition to the persistent elevation of mitochondrial enzyme levels, capillary density in skeletal muscle remained significantly elevated above sedentary control values after 84 days of detraining. Of all the adaptations to endurance training evaluated in this study, muscle capillary density was the only one to show no decline during 12 wk of detraining. This persistent increase in muscle capillary density is apparently also a consequence of long-term adaptations induced by prolonged training, since Klausen et al. (14) found a significant decline in capillary density during 8 wk of detraining in previously sedentary subjects who had trained for only 8 wk.

Studies on rats have shown an increase in muscle myoglobin concentration in response to exercise training (cf. Ref. 10). No such effect has been observed in humans (12, 22). In the present study there was also no difference in muscle myoglobin concentration between the trained and sedentary subjects. Furthermore, there was no change in myoglobin concentration with detraining. These findings provide evidence for a species difference in the adaptive response of muscle myoglobin to endurance exercise.

A second purpose of this study was to use detraining as a tool to try to obtain insights regarding the factors responsible for the higher $\dot{V}O_{2\,max}$ seen in the trained compared with the untrained state. For this approach to provide useful information there must be major differences in the rates at which the various adaptations to training are lost. In the present study the entire decrease in $\dot{V}O_{2\,max}$ during the first 3 wk of detraining, which averaged 7%, appears to have been due to the decrease in $\dot{Q}_{max,\,est}$ of 8% over the same period. However, since maximum SV, HR_{max}, and $\dot{Q}_{max,\,est}$ did not change significantly between the 21st and 84th days of detraining, loss of some other adaptation must account for the further 9% decrease in $\dot{V}O_{2\,max}$ during this period. The latter decrease in $\dot{V}O_{2\,max}$ could be almost entirely accounted for by a decline in maximum a-$\bar{v}O_2$ difference of 9%. These findings are in keeping with the results of earlier studies on the responses to training which showed that both increased delivery of O_2 to and increased extraction of O_2 by the working muscles contribute to the increase in $\dot{V}O_{2\,max}$ (cf. Ref. 20).

The decrease in O_2 extraction by the muscle coincided with a large decrease in muscle mitochondria as reflected in citrate synthase and SDH levels. Since capillary density did not decline, it is likely that the reduction in maximum a-$\bar{v}O_2$ difference and the associated decline in $\dot{V}O_{2\,max}$ during the period between 21 and 56 days was attributable to the decrease in muscle mitochondria. We

TABLE 5. *Muscle capillarization and fiber area during detraining and comparison with sedentary controls*

	Trained	6 Days	12 Days	21 Days	56 Days	84 Days	Sedentary Controls
Cap around fiber	5.78 ± 0.44	5.77 ± 0.44	5.79 ± 0.46	6.01 ± 0.37	5.65 ± 0.44	5.60 ± 0.36	3.91 ± 0.50*
Cap/fiber	2.36 ± 0.19	2.46 ± 0.22	2.34 ± 0.16	2.34 ± 0.16	2.29 ± 0.18	2.34 ± 0.18	1.65 ± 0.20*
Cap/mm^2	464 ± 12	497 ± 11	467 ± 11	450 ± 12	438 ± 20	476 ± 30	318 ± 20*
Fiber area, μm^2	5,082 ± 417	4,931 ± 440	4,999 ± 191	5,263 ± 450	5,244 ± 417	5,023 ± 547	5,195 ± 590
No. of fibers counted	492 ± 87	485 ± 121	548 ± 115	611 ± 35	487 ± 87	680 ± 136	548 ± 172

Values are means ± SE for 7 detraining subjects and 8 sedentary controls. * Significantly lower than 84 days; $P < 0.05$.

TABLE 6. *Comparison of sedentary control subjects and detrained subjects after 84 days of inactivity*

	Age, yr	Weight, kg	$\dot{V}O_{2\,max}$, $ml \cdot kg^{-1} \cdot min^{-1}$	SV_{max}, ml	HR_{max}, beats·min^{-1}	$\dot{Q}_{max,est}$, $ml \cdot kg^{-1} \cdot min^{-1}$	a-$\bar{v}O_2$ Difference, $ml \cdot 100\ ml^{-1}$	O_2 Pulse at max, $ml \cdot kg^{-1} \cdot beat^{-1}$
Sedentary controls	27.5 ± 1.5	71.3 ± 1.9	43.3 ± 1.5	128 ± 6	192 ± 2	344 ± 12	12.6 ± 0.3	0.226 ± 0.009
84 days of detraining	29.3 ± 3.2	70.1 ± 3.1	50.8 ± 1.9*	129 ± 6	197 ± 2	364 ± 17	14.1 ± 0.5*	0.260 ± 0.011*
% Diff from sedentary controls		−1.7%	+17.3%	+0.8%	+2.6%	+5.8%	+11.9%*	+15.0%*

Values are means ± SE for 7 detrained subjects and 8 sedentary controls. $\dot{V}O_{2\,max}$, maximal O_2 uptake; SV_{max}, maximum stroke volume; HR_{max}, maximal heart rate; $\dot{Q}_{max,est}$, cardiac output estimated as product of SV_{max} and HR_{max}; a-$\bar{v}$, arterial-mixed venous. * Significantly higher than sedentary control; $P < 0.05$.

cannot, however, exclude the possibility that maximum a-$\bar{v}O_2$ difference was declining as a result of other factors such as reduced muscle blood flow or capillary transit time.

The $\dot{V}O_{2\,max}$ capacities of the highly trained individuals in this study varied over a wide range. Since the frequency, duration, and relative intensity of their training sessions were similar, it seems likely that the differences in $\dot{V}O_{2\,max}$ reflected their inherent, possibly genetic, potential to adapt to endurance training. *Subjects A, B,* and *C,* with $\dot{V}O_{2\,max}$ values of 76, 70, and 67 $ml \cdot kg^{-1} \cdot min^{-1}$, respectively, were successful competitive athletes. The other three male subjects had $\dot{V}O_{2\,max}$ values in the range that can be attained with intense training by highly motivated men who do not have the genetic potential to be endurance athletes. It seems clear from a comparison of these men that the physiological characteristic that distinguishes highly trained athletes with a high $\dot{V}O_{2\,max}$ from highly trained nonendurance athletes is the athletes' much larger maximum SV and $\dot{Q}_{max}$. No such relationship is seen for muscle mitochondrial enzymes, which were actually highest in *subject F* with the next to lowest $\dot{V}O_{2\,max}$. An interesting exception is the one female subject whose $\dot{Q}_{max}$ was in the same range as that of the athletes but whose $\dot{V}O_{2\,max}$ was similar to that of the trained male nonendurance athletes. Clearly further studies are needed to determine whether this is a normal response for females or whether it is an idiosyncrasy of the woman who we studied.

We conclude from our results that both a decrease in maximum SV and a decrease in maximum a-$\bar{v}O_2$ difference contribute to the decrease in $\dot{V}O_{2\,max}$ when highly trained individuals detrain. The decrease in maximum a-$\bar{v}O_2$ difference appears to be associated with a decrease in muscle mitochondria, since capillary density did not change. Highly trained people who have been exercising intensely on a regular basis for a long time appear to differ from individuals who have just trained for a few months in that there is no loss of the increased muscle capillary density and only a partial loss of the increase in muscle mitochondria during 3 mo of detraining.

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