Effects of training and a single session of exercise on lipids and apolipoproteins in hypercholesterolemic men

STEPHEN F. CROUSE, BARBARA C. O'BRIEN, PETER W. GRANDJEAN, ROBERT C. LOWE, JAMES ROHACK, AND JOHN S. GREEN. Effects of training and a single session of exercise on lipids and apolipoproteins in hypercholesterolemic men. J. Appl. Physiol. 83(6): 2019–2028, 1997.—To differentiate between transient (acute) and training (chronic) effects of exercise at two different intensities on blood lipids and apolipoproteins (apo), 26 hypercholesterolemic men (cholesterol = 258 mg/dl, age = 47 yr, weight = 81.9 kg) trained three times per week for 24 wk, 350 kcal/session at high (80% maximal O2 uptake, n = 12) or moderate (50% maximal O2 uptake, n = 14) intensity. Serum lipid and apolipoprotein (apo) concentrations (plasma volume adjusted) were measured before and immediately, 24, and 48 h after exercise on four different occasions corresponding to 0, 8, 16, and 24 wk of training. Data were analyzed using three-way repeated-measures multivariate analysis of variance followed by analysis of variance and Duncan's procedures (α = 0.05). A transient 6% rise in low-density-lipoprotein cholesterol measured before training at the 24-h time point was no longer evident after training. Triglycerides fell total and total lipoprotein concentrations, along with higher HDL-C and HDL2-C, all changes often attributed to training, have been measured in trained individuals immediately and up to 72 h after completion of exhaustive physical exercise (9, 10, 22, 31). Because the time of blood sampling was either not controlled or occurred ≤48 h after the last training session in the majority of published training-lipid studies, findings attributed to training may have been confounded by transient changes in blood lipid concentrations induced by recent exercise. On the basis of these findings, it can be logically proposed that the lipid benefit of exercise arises, at least in part, from a transient lipid response to the most recent episode(s) of exercise. This proposition has been advanced by Holloszy et al. (18) and later by Haskell (16), but we are aware of no published training studies in which it has been tested, even though it has important relevance for exercise recommendations to improve public health.

Whether the transient lipid response itself is altered by training is another dimension of this problem. Qualitatively different transient changes in lipids and apolipoproteins have been shown to occur after a single session of exercise in trained compared with untrained normo- and hypercholesterolemic individuals (4, 22, 26). This naturally leads to the conjecture that training influences lipid metabolism and that the effect is manifested, at least in part, as an altered transient response. This hypothesis has not been tested in a longitudinal training study. Thus the primary objective of our study was twofold: 1) to differentiate between transient (acute) and training (chronic) effects of exercise; and 2) to test the hypothesis that the transient lipid response to recent exercise is altered by training.
exercise on blood lipid and apolipoprotein concentrations in hypercholesterolemic men and 2) to determine the extent to which the transient response is altered by training.

We recently reported that intensity of exercise did not influence the transient changes in lipid and apolipoprotein concentrations that occurred up to 48 h after exercise in untrained, hypercholesterolemic men (4). This does not, however, rule out the possibility that after training the transient response is modified by the intensity at which exercise is performed. Support for this notion is provided by the findings that larger postexercise increases in HDL-C concentrations may occur in trained runners after high- compared with low-intensity exercise (15, 17). Thus a secondary purpose of our study was to test the hypothesis that, after training, relatively greater postexercise changes in lipids and apolipoproteins, particularly a greater rise in HDL-C, would occur after a single session of high-compared with moderate-intensity exercise.

MATERIALS AND METHODS

Subjects

Physically untrained adult men with known or suspected elevated total cholesterol concentrations were recruited from the Texas A & M University and the greater College Station, TX, communities to participate in the study. Potential volunteers were solicited for participation through advertisements placed in university faculty and staff publications and through phone contacts to men with elevated cholesterol previously measured during cholesterol screenings on the university campus, at a local medical clinic, and at a local manufacturing plant. Exclusionary criteria included total cholesterol <200 mg/dl, regular aerobic exercise in the past 3 mo, medical contraindications to exercise, and use of tobacco products or drugs known to alter lipid metabolism. Thirty-seven volunteers met the study criteria and gave written informed consent to participate. Twenty-six of the 37 subjects completed all phases of the data collection and $90\%$ of all supervised training sessions; only data from these 26 subjects are included in the analyses. Eighteen of the 26 men could be classified as having high blood cholesterol ($>240$ mg/dl) and 8 as having borderline-high blood cholesterol ($200-239$ mg/dl) on the basis of the pretraining assessment of lipids (24). The molecular basis for cholesterol elevation was not determined for any of the subjects. However, the suggestion of a heritable trait for hypercholesterolemia was evident for 2 of the 26 subjects, who self-reported blood relatives with known high blood cholesterol on the medical history screening instrument used in the study. Of the 11 subjects who were lost to follow-up, 3 men relocated, 6 gave time conflicts as reason for dropping out, and 2 developed physical problems that prohibited cycle ergometer exercise. Lipid and physiological characteristics of the 11 dropouts were not different before training from the 26 men who completed the study (t-test, $P > 0.05$).

Procedures

General study protocol. All research procedures were approved by the Texas A & M University Institutional Review Board for Human Subjects in Research. On the first visit to the laboratory, the cholesterol status of all volunteers was verified by Reflotron analysis, and subjects were asked to complete a detailed medical and activity questionnaire. Subjects meeting the study criteria were asked to return to the laboratory, where they were informed of the study procedures, read and signed an institutionally approved informed consent instrument, were familiarized with the exercise testing equipment, and received instructions for completing the diet records. The 37 subjects meeting the study criteria were phased into the study in 4 cohorts consisting of 10, 9, 9, and 9 subjects each session spaced 2 wk apart to accommodate subject scheduling preferences as well as our own laboratory testing limitations. Physiological and demographic assessments were completed on the second visit to the laboratory. Three to 7 days later, subjects returned a third time, were assigned randomly to a moderate (50% of maximal O$_2$ uptake (V$_{O2max}$)) or high (80% V$_{O2max}$) exercise-intensity group, and completed the pretraining experimental exercise protocol. The men began their individualized training program within 1 wk of completing the experimental exercise protocol. All testing procedures were repeated after 8, 16, and 24 wk of training. In general, pretraining and posttraining blood sampling procedures were matched for time of day ($\pm 1\ h$). Exercise was withheld for 60–72 h before the preexercise blood sample was drawn at the beginning of each experimental exercise protocol (Fig. 1).

Diet procedures. Subjects were instructed to maintain their normal dietary habits throughout the study. No attempt was made to modify the nutrient composition of the men’s diets or total caloric intake. Dietary habits, however, were assessed on four separate occasions coinciding with each testing period. For each assessment, subjects were instructed to record their dietary intake for 3 days, including 1 weekend day. The 3-day dietary records were analyzed for total caloric intake and for carbohydrate, fat, protein, and cholesterol composition using a commercially available computer software program (NutriProctor; San Diego, CA).

Physiological assessments. Percent fat and lean body mass were calculated from body density measured hydrostatically at residual volume (2). Waist girths and waist-to-hip ratios were measured as indexes of regional adiposity. An incremental maximal exercise test was conducted on a friction-braked cycle ergometer (model 868, Monark) using the following protocol: 2 min at 15 W then 2 min at 60 W for warm-up, followed by a 30-W increase every 2 min until exhaustion. Blood pressure, heart rate, ratings of perceived exertion, and a 12-lead electrocardiogram (model Q4000, Quinton Instrument, Seattle, WA) were recorded at the end of each stage, at maximal exertion, and every 2 min throughout a 6-min recovery. Respiratory gas exchange (O$_2$ uptake and CO$_2$ output) was measured continuously and averaged over 15-s intervals using a commercially available automated system (model 2001 Exercise Stress Testing System, Medical Graphics); V$_{O2max}$ was defined as the highest observed O$_2$ uptake (ml/min). At least two of the following criteria were required for the exercise test to be considered valid: 1) achievement of maximum heart rate within 10 beats/min of the age-predicted maximum, 2) rating of perceived exertion >18, 3) respiratory exchange ratio >1.1 at maximal exertion, or 4) O$_2$ uptake plateau, despite further increases in workload.

Experimental exercise protocol. Subjects reported to the laboratory in the morning after a 12-h fast (water allowed ad libitum), and preexercise blood samples were drawn after 5 min of seated rest (blood collection procedures described below). Within 10 min of collection of the preexercise blood sample, subjects began exercise on a stationary cycle ergometer. The exercise protocol consisted of three successive 1-min rides at 15, 30, and 60 W for warm-up followed by exercise at their assigned intensity (moderate or high) for a duration required to expend 350 kcal of energy. Duration (min) was
determined by dividing 350 kcal by the rate of energy expenditure (kcal/min) at the required exercise intensity. The rate of energy expenditure was calculated from the energy-O2 equivalent (23) at the respiratory exchange ratio corresponding to 50 and 80% \( \dot{V}O_{2max} \). Respiratory gas exchange, exchange ratio, heart rate, and blood pressure were measured at 10-min intervals throughout the exercise session, and the workload was adjusted as necessary to maintain the prescribed intensity. Blood samples were obtained immediately postexercise (IPE, i.e., 5 min postexercise), then again 24 (+24 h) and 48 h (+48 h) later (time of day controlled within ±1 h). All exercise was discontinued for 48 h after the completion of the experimental exercise session until all postexercise blood sampling procedures were completed.

Blood sampling and biochemical analysis. After 5 min of seated rest, blood was drawn without stasis from an antecubital vein into 15-ml Vacutainer tubes containing a separation gel with a clot activator (no. 6432, Becton Dickinson). Hematocrit and hemoglobin concentrations were determined in fresh whole blood and were used to estimate changes in plasma volume after the experimental exercise session (8). Serum was isolated within 3 h of collection at 4°C by centrifugation (1,500 g for 30 min). HDL and LDL were separated from aliquots of serum by precipitation (14, 35). Serum and the HDL and LDL fractions were frozen at -60°C.

Aliquots of frozen serum samples collected during the experimental exercise protocol (4 samples/subject) were thawed within 2 wk of the completion of each training period (pretraining and 8, 16, and 24 wk) and analyzed for concentrations of TC, TG, HDL-C, and LDL-C (1, 3). Serum HDL-C concentration was calculated as the difference between HDL-C and LDL-C; LDL-C was estimated (13). All samples for apo A-I and apo B testing were thawed and analyzed after completion of the study (27). Samples from each subject were analyzed in the same analytic run, and assays were performed in duplicate, then averaged for statistical analysis. Internal quality control was maintained during each analytic run using serum of known lipid and apolipoprotein content. No differences in the average lipid values of the control serum among the four study training periods (pretraining and 8, 16, and 24 wk) were significant [analysis of variance (ANOVA), \( P > 0.05 \)], indicating that laboratory drift over the 24-wk study was negligible. Interassay coefficients of variation were 6% for HDL-C and LDL-C, 4.8% for TC, 7.9% for TG, 3.2% for apo A-I, and 3.6% for apo B.

Exercise training. Exercise training consisted of riding a cycle ergometer at 50% \( \dot{V}O_{2max} \) for the moderate-intensity group or 80% \( \dot{V}O_{2max} \) for the high-intensity group 3 days/wk for 24 wk (72 supervised training sessions). The rate of energy expenditure, workload, and duration of the exercise sessions were calculated from energy-O2 equivalents as described for the experimental exercise protocol. An individualized, progressive training protocol was utilized so that each subject could meet the caloric requirement of each exercise session without rest intervals. The energy expenditure for both intensity groups was increased 50 kcal every 2 wk from 200 kcal initially to a peak of 350 kcal by the 7th wk of training. Each individual’s exercise prescription was adjusted for increases in \( \dot{V}O_{2max} \) measured at weeks 8 and 16 to ensure that the prescribed exercise intensity and caloric consumption were maintained throughout the study.

Statistical analysis. The independent factors were exercise intensity (moderate- and high-intensity groups), training period (pretraining and 8, 16, and 24 wk), and time of blood sampling after a single session of exercise (preexercise, IPE, +24 h, and +48 h). The dependent variables of interest were TC, TG, LDL-C, HDL-C, HDL2-C, HDL3-C, apo A-I, and apo B.
concentrations. Statistical analysis was completed using log10-
transformed TC data, since the TC data measured before
training were not normally distributed. Data in Tables 1 and
2 are presented in original units (mg/dl). An intensity-by-
training period-by-time multivariate ANOVA (MANOVA) with
repeated measures on the second and third factors was
employed for the global analysis, since the lipid and lipopro-
tein variables were interrelated. Follow-up procedures for
significant MANOVA effects included repeated-measures in-
tensity-by-training period-by-time ANOVA procedures; Dun-
can’s new multiple range test was employed for post hoc
analysis where appropriate. The physiological and diet data
were analyzed using 2 (intensity)-by-4 (period) ANOVA with
repeated measures on the second factor (Table 1); Duncan’s
new multiple range test was employed for post hoc
analyses. Correlational analyses were used to explore relationships
between 24-wk changes (calculated as the difference between
pretraining and 24-wk preexercise values) in VO2max, weight,
waist girth, waist-to-hip ratios, and all lipids and apolipopro-
teins. Because of the exploratory nature of the study, the
comparisonwise α level was set at 0.05 for all statistical tests of
significance. Thus the experimentwise α level may exceed
0.05 in some instances. All lipid concentrations measured
after the experimental exercise sessions (IPE, +24 h, and
+48 h) were adjusted for changes in plasma volume.

RESULTS

Physical Characteristics and Diet

The average values for each physiological and di-
etary variable of interest were collapsed across inten-
tivity groups for analysis. As shown in Table 1, the
endurance training program effectively raised VO2max
(−36%) and resulted in a small but significant reduc-
tion in total body weight (−1.4 kg) and waist girth (−3.2 cm).
Neither estimated total caloric intake nor diet composition changed significantly over the 24-wk study.

Lipids and Apolipoproteins

The average values for plasma volume-adjusted lip-
ids and apolipoproteins at each time point within each
group and period are presented in Table 2. Significant
factors by MANOVA included 1) training period-by-
time interaction, 2) intensity-by-time interaction, 3) main
effect for time, and 4) main effect for training period. Univariate ANOVA follow-up procedures re-
vealed a significant training period-by-time interaction
only for LDL-C, which supports the conclusion that the
transient change in LDL-C after a single session of
exercise was altered after training (Fig. 2). Further-
more, the intensity-by-time interaction was significant
for LDL-C and HDL2-C, suggesting that the transient
response for these two lipoprotein lipids depended on the
intensity at which the exercise was performed (Fig. 3).
Transient changes in plasma volume-adjusted TC, TG,
HDL-C, HDL3-C, apo A-I, and apo B concentrations
were significant at IPE to +48 h (main effect for time
was significant for these variables), demonstrating that
changes in these lipids and apolipoproteins occurred in
response to a single session of exercise regardless of
exercise intensity or training status (Fig. 4). Finally, in
these hypercholesterolemic subjects, training was ac-
companied by a significant change in TC, HDL2-C,
HDL3-C, apo A-I, and apo B concentrations (Fig. 5).
No correlations between 24-wk changes in any lipid or
apolipoprotein variable and the physiological variables
oxygen uptake, body weight, waist girth, and waist-to-
hip ratio approached significance.

DISCUSSION

To our knowledge, we are the first to show that the
profile characteristics of the transient LDL-C response
after a single session of exercise depend on the training
status of hypercholesterolemic men. Before training,
LDL-C concentration was elevated over preexercise
values at +24 and +48 h, but after training this rise
was not evident and, in fact, LDL-C fell slightly (4%) by
+24 h (Fig. 2). When pretraining values were compared
with those measured at corresponding time points after
training, LDL-C was 6% (11 mg/dl) lower at +48 h after
8 wk of training and 9% (17 mg/dl) lower at +24 h after
24 wk of training. Exercise intensity had no detectable
influence on this training response. Thus training may
suppress the LDL-C rise noted in hypercholesterolemic
men after a single session of exercise. Despite this effect
on the transient LDL-C response, the average LDL-C
concentration (mean LDL-C value collapsed across the
intensity and time factors) did not change with training
(main effect for training period was not significant for
LDL-C), a finding consistent with most published train-

Table 1. Physiological characteristics and diet data
over 24 wk of training in hypercholesterolemic men

<table>
<thead>
<tr>
<th></th>
<th>Pretraining</th>
<th>8 wk</th>
<th>16 wk</th>
<th>24 wk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>47 ± 10</td>
<td>47</td>
<td>47</td>
<td>47</td>
</tr>
<tr>
<td>Height, cm</td>
<td>176 ± 6</td>
<td>176</td>
<td>176</td>
<td>176</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>81.9 ± 13.1*</td>
<td>81.6</td>
<td>80.5 ± 13.0†</td>
<td>80.5 ± 13.0†</td>
</tr>
<tr>
<td>%Fat</td>
<td>28 ± 4</td>
<td>27</td>
<td>27</td>
<td>27</td>
</tr>
<tr>
<td>Waist-to-hip ratio</td>
<td>1.02 ± 0.02</td>
<td>1.01</td>
<td>1.01 ± 0.04</td>
<td>1.01 ± 0.03</td>
</tr>
<tr>
<td>Waist girth, cm</td>
<td>95.5 ± 10.7*</td>
<td>95.1</td>
<td>93.0 ± 10.4†</td>
<td>92.3 ± 10.7†</td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>125 ± 15</td>
<td>124</td>
<td>121 ± 15</td>
<td>126 ± 12</td>
</tr>
<tr>
<td>DBP, mmHg</td>
<td>82 ± 11</td>
<td>81</td>
<td>80</td>
<td>82</td>
</tr>
<tr>
<td>VO2max, l/min</td>
<td>2.53 ± 0.43*</td>
<td>3.00</td>
<td>3.40 ± 0.53‡</td>
<td>3.45 ± 0.49‡</td>
</tr>
<tr>
<td>Kcals/I, kcal/day</td>
<td>1,910 ± 567</td>
<td>2,114</td>
<td>2,048 ± 632</td>
<td>2,000 ± 650</td>
</tr>
<tr>
<td>CHO, g/day</td>
<td>204 ± 59</td>
<td>229</td>
<td>232 ± 68</td>
<td>221 ± 79</td>
</tr>
<tr>
<td>Fat, g/day</td>
<td>79 ± 31</td>
<td>89</td>
<td>78 ± 36</td>
<td>81 ± 35</td>
</tr>
<tr>
<td>Pro, g/day</td>
<td>82 ± 24</td>
<td>88</td>
<td>90 ± 31</td>
<td>83 ± 28</td>
</tr>
<tr>
<td>Chol, mg/day</td>
<td>260 ± 165</td>
<td>261</td>
<td>308 ± 201</td>
<td>284 ± 166</td>
</tr>
</tbody>
</table>

Values are means ± SE collapsed across intensity groups; n = 26. SBP, resting systolic blood pressure; DBP, resting diastolic blood pressure; VO2max, maximal O2 uptake; Kcals/I, estimated total di-
etary caloric intake; CHO, estimated dietary carbohydrate intake; Pro, estimated dietary protein intake; Chol, estimated dietary chole-
terol intake. Dissimilar symbols (*, †, ‡) within a row indicate significant difference (P < 0.05).
ing studies in normcholesterolemic subjects (7, 10). These results taken together suggest that the primary effect of training on LDL-C is to alter the transient, postexercise metabolism of this circulating lipoprotein, rather than to cause a long-term change in blood LDL-C concentration.

We are aware of no comparable longitudinal studies that have been published. In a cross-sectional investigation, Kantor and associates (22) reported that plasma volume-adjusted LDL-C concentrations were significantly lower than preexercise values in trained and untrained men 10 min after cycle ergometer exercise; LDL-C concentration subsequently returned to baseline (preexercise) within 24 h and remained stable over the next 2 days. Similarly, in our study the nadir of the transient LDL-C response was IPE regardless of training status, but this was followed by a 4–12% rise above preexercise and IPE values 24–48 h later, at least through 16 wk of training. As pointed out above, this postexercise rise was attenuated after 24 wk of training.

This delayed rise contrasts with results of other studies in normcholesterolemic men in which LDL-C concentrations were unchanged from preexercise values 24 and 48 h after exercise (5, 15, 21, 22). We can only speculate as to why our findings differ from those of others. Our subjects were older and carried a greater proportion of body weight as fat than subjects in related studies, both factors that could conceivably influence postexercise lipid metabolism and alter the LDL-C response. It is also reasonable to propose that the abnormal resting lipid metabolism known to accompany some types of hypercholesterolemia (20, 30) may contribute to the unique response to exercise noted in our subjects. Whatever the cause, our data suggest that en-

| Table 2. Lipid and apolipoprotein data in hypercholesterolemic men over 24 wk of training |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
|                                | Pre-exercise | +24 h | Pre-exercise | +24 h | Pre-exercise | +24 h | Pre-exercise | +24 h | Pre-exercise | +24 h |
| TC‡§                           |               |       |               |       |               |       |               |       |               |       |
| HI                             | 252 ± 17      | 237   | 263 ± 21      | 265   | 257 ± 24      | 251   | 260 ± 20      | 253   | 244 ± 14      | 234   |
| MOD                            | 264 ± 44      | 253   | 265 ± 44      | 275   | 256 ± 34      | 252   | 260 ± 46      | 256   | 239 ± 30      | 241   |
| TG‡                            | 123 ± 52      | 138   | 132 ± 52      | 130   | 127 ± 45      | 157   | 126 ± 41      | 131   | 145 ± 62      | 160   |
| HDL-C‡                         | 180 ± 44      | 164   | 189 ± 44      | 189   | 185 ± 37      | 174   | 187 ± 30      | 183   | 172 ± 26      | 161   |
| HDL-C*                         | 43 ± 69       | 45    | 49 ± 70       | 51    | 49 ± 47       | 47    | 48 ± 44       | 50    | 48 ± 46       | 49    |
| HDL₃-C‡                        | 63 ± 43       | 5.2   | 7.6 ± 6.7     | 9.6   | 12.6 ± 6.7    | 9.6   | 11.0 ± 6.7    | 12.5  | 11.7 ± 6.0    | 10.3  |
| HDL₃-C*                        | 8.2 ± 43      | 9.5   | 8.1 ± 5.4     | 9.1   | 36.3 ± 5.4    | 36.7  | 37.2 ± 5.4    | 37.5  | 35.4 ± 5.4    | 35.8  |
| Apo-A-I‡                       | 146 ± 19      | 134   | 145 ± 9.5     | 146   | 142 ± 5.4     | 139   | 147 ± 4.6     | 148   | 132 ± 7.1     | 128   |
| Apo-B†                         | 94 ± 25       | 95    | 110 ± 15      | 102   | 97 ± 9.4      | 93    | 101 ± 8.9     | 96    | 91 ± 8.5      | 85    |

Values are means ± SE in mg/dl. HI, high intensity (n = 12); MOD, moderate intensity (n = 14); TC, total cholesterol; TG, triglyceride; LDL-C, low-density-lipoprotein cholesterol; HDL-C, high-density-lipoprotein cholesterol; HDL₃-C, high-density-lipoprotein fraction 2 cholesterol; HDL₃-C, high-density-lipoprotein fraction 3 cholesterol; apo A-I, apolipoprotein A-I; apo B, apolipoprotein B. All statistical tests were performed at the 0.05 level of significance: *significant main effects for time (Fig. 5); ‡significant main effects for training period (Fig. 5); §significant main effects for time × interaction (Fig. 3); †significant main effects for time × interaction (Fig. 2); ‡significant main effects for time × interaction (Fig. 4); §significant main effects for time × interaction (Fig. 5).
Durance training for 6 mo normalizes the transient postexercise LDL-C response in hypercholesterolemic men.

In addition to this apparent training effect on the transient LDL-C response, postexercise LDL-C changes, as well as those for HDL$_2$-C, varied with intensity (significant intensity-by-time interaction; Fig. 3). At 24 and 48 h after moderate-intensity exercise, LDL-C rose significantly, but HDL$_2$-C concentration remained unchanged. In contrast, immediately after high-intensity exercise, LDL-C concentration was significantly reduced from preexercise values but subsequently returned to baseline by 24 h; HDL$_2$-C concentration concurrently fell slightly, then rose significantly 16% by 48 h. This HDL$_2$-C rise led to a significant difference between intensity groups (43% higher in the high-intensity exercise group) by 48 h. At no time point were group differences in LDL-C significant. These changes produced by high-intensity exercise would generally be interpreted as favorable with respect to atherosclerotic risk. Few comparative data have been published, and results are inconsistent. Others have shown in related studies in normocholesterolemic men that transient postexercise changes in LDL-C and HDL$_2$-C concentrations were not influenced by exercise intensity (6, 15). Furthermore, in contrast to our null findings for other lipid and apolipoprotein variables, intensity has been shown to be an important mediator of a postexercise rise in TC, HDL-C, and apo A-I concentrations in normocholesterolemic, trained men (15, 17). We are unable to explain these divergent findings.

A unique aspect of our study was the fact that we could separate the effects of exercise training from the transient (acute) effects of exercise. This is especially relevant in light of the fact that blood for lipid analysis was collected within 48 h of the most recent training session and without regard for potential shifts in plasma volume in a majority of published studies in which a beneficial influence of training on lipids was reported (10, 32, 38). We measured lipids in blood collected 60 h after the last training session and failed to show significant training changes in established lipid risk markers TG and HDL-C, despite substantial improvements in cardiorespiratory fitness. It could be argued that our inability to detect significant changes in lipids after training in contrast to the findings of others was due to a lack of statistical power stemming from our relatively small sample size. However, the...
modest changes in TG (−2 mg/dl) and HDL-C (−1 mg/dl) we measured from pretraining to 24 wk would be of doubtful physiological consequence even if found to be statistically significant. Previous research suggests that beneficial lipid changes with training may not be independent of weight loss. Because weight loss was modest in our study (−1.4 kg), one-third to one-fifth the magnitude reported in other lipid studies designed to examine the effects of exercise and weight loss (7, 36, 38), we cannot rule out the fact that a more substantial decrease in body mass or in waist girth (as a measure of abdominal fat stores) with training may have led to favorable TG and HDL-C changes in our hypercholesterolemic subjects. To explore this notion further in our data set, we correlated 24-wk changes in body weight and waist girth, which ranged from −5.8 to +1.6 kg and from −13.9 to +1.5 cm, respectively, with changes in lipids and apolipoproteins. No significant correlations were found to support the weight loss-lipid change hypothesis. Although weight loss may be an important determinant of the magnitude of lipid changes, it has been shown that exercise training without weight loss can produce favorable alterations in lipid metabolism,
at least in overweight, normocholesterolemic men (33). It is conceivable that the effectiveness of exercise training and weight loss to promote favorable changes in these lipid risk markers is blunted with hypercholesterolemia.

In contrast to the lack of a training effect, transient and generally favorable changes in the plasma volume-adjusted concentrations of these two lipid risk markers were produced by a single session of exercise (Fig. 4). It is noteworthy that had our study been a simple training study in which a single blood sample for lipid analysis was collected within 48 h after exercise, increased HDL-C and reduced TG concentrations may have been falsely attributed to training. These results demonstrate the importance of controlling the time of blood sampling after an exercise training session when attempting to measure lipid training benefits and suggest that failure to do so may to lead to confusion with regard to the transient vs. chronic effects of exercise. Furthermore, on the basis of our findings, we propose that at least a portion of the lipid benefit of exercise with respect to these traditional lipid risk markers is realized within 48 h of completion of a single training session, a hypothesis previously advanced by Holloszy et al. (18) and Haskell (16).

In addition to these transient changes in TG and HDL-C, a rise in plasma volume-adjusted TC, HDL3-C, apo B, and apo A-I concentrations occurred 24–48 h after a single session of exercise (Fig. 4), effects that were not influenced by training status or exercise intensity. We are aware of no similarly designed longitudinal studies with which to compare our results. The magnitude and timing of the transient response reported in existing cross-sectional literature vary widely. In the majority of studies in normocholesterolemic men, plasma volume-adjusted TC, TG, apo A-I, and apo B concentrations were not significantly altered (5, 6, 15, 17, 21, 22), whereas HDL-C, HDL3-C, and HDL2-C were elevated (15, 17, 21, 22) up to 72 h after exercise. Thus the transient rise in TC, apo A-I, and apo B coincident with the fall in TG concentrations noted in our present study may be characteristic of men with elevated cholesterol and, unlike the LDL-C response, these particular transient changes are not modified by exercise training.

Training was not without some effect, however. Average TC, HDL2-C, HDL3-C, apo A-I, and apo B concentrations were significantly different from pretraining values in our hypercholesterolemic subjects after 8–16 wk of training (Fig. 5), effects that likely reflect more long-lasting (as opposed to transient) metabolic adaptations to exercise and occur regardless of intensity and time of measurement after exercise. Caloric intake and the nutrient composition of the subject’s diet remained stable by our assessment throughout the 24-wk training period. Thus it is unlikely that the lipid and apolipoprotein responses were confounded by diet. These apparent training results should be interpreted with caution, however, since a nonexercising control group was not included in our study design, and therefore we cannot rule out the influence of seasonal variation on our data. Few comparative training studies in hypercholesterolemic men have been published, although reductions in TC and TG along with increases in HDL-C after training have been variously reported (19, 28, 29). The rise in HDL2-C concentration coincident with a fall in HDL3-C in our study is indicative of subtle changes in HDL metabolism after training that would not be apparent if only HDL-C concentrations had been measured and may reflect enhanced reverse cholesterol transport in these individuals. Increased HDL2-C concentrations have been measured after training in normocholesterolemic men, especially after exercise-induced weight loss (38, 39). An increase in synthesis and a decrease in catabolism are thought to be responsible for the rise in apo A-I with training in normocholesterolemic subjects (32, 36, 37). Without kinetic data, we can only speculate that an opposite effect occurred after training in our hypercholesterolemic subjects, i.e., catabolism was enhanced or synthesis decreased (perhaps a combination of both), to cause the measured fall in apo A-I concentration. Others have shown that apo A-I synthetic rates are lower in hypertriglyceridemic than in normal subjects (11), suggesting a link between apo A-I synthesis and lipid status. Whether apo A-I metabolism is similarly affected by hypercholesterolemia remains to be determined, but a decrease in synthesis would be consistent with our data.

Although apo B has seldom been measured in exercise studies, present evidence in normocholesterolemic subjects suggests that weight loss in addition to exercise is required to induce a decrease in this putative atherogenic apolipoprotein (37, 39). Our results do not support the need for substantial weight loss, since significant reductions in apo B occurred in our hypercholesterolemic subjects with minimal changes in body weight. Furthermore, in our data, 24-wk changes in body weight and waist girth did not correlate with changes in apo B concentrations.

In conclusion, we have shown that a single session of exercise produces transient changes in lipid and apolipoprotein concentrations in hypercholesterolemic men that are uniquely different from those produced by exercise training. Of immediate therapeutic importance in exercise prescription to lower heart disease risk in this population, favorable changes in the traditional lipid risk markers HDL-C and TG may represent a transient response to the most recent episode of exercise as opposed to an adaptive response to chronic exercise training. Furthermore, these transient changes are produced by moderate- or high-intensity caloric-equivalent exercise. Chronic exercise training appears to produce different effects. A transient rise in LDL-C concentration produced by a single session of exercise was no longer evident after training, suggesting that some aspects of postexercise lipid metabolism are altered by training. Modest reductions in TC, HDL3-C, and apo A-I and B concentrations, along with a rise in HDL2-C, also accompany training by hypercholesterolemic men, and these changes are not affected by training intensity. Although TG and HDL-C were not responsive to training in our study, we cannot rule out the fact that a strategy of exercise training combined...
with substantial weight loss and a low-fat, low-cholesterol diet may have produced more favorable changes in these lipids, as has been demonstrated by others in normocholesterolemic subjects. Because our data show that changes in lipids and apolipoproteins are prolonged for up to 48 h after a single session of exercise, we recommend that exercise be performed at least every other day by hypercholesterolemic men to maintain the transient lipid benefit and carried out repeatedly over the course of several months to produce long-term metabolic and cardiovascular adaptations conducive to good health. Furthermore, in future studies designed to test the effect of training on lipids, exercise should be discontinued \( \leq 60 \) h before blood sampling to control for the transient effects of the last episode of exercise.

We are grateful to Jana Crouse and Susan Lee for assistance in the preparation of the manuscript and to Drs. Nicolaas Pronk and Dennis Jacobsen for technical assistance in data collection.

This study was supported by American Heart Association, Texas Affiliate Grant 99G-033.

The Applied Exercise Science Laboratory, Department of Health and Kinesiology, the Department of Biochemistry/Biophysics, and the College of Medicine, Health Science Center, Texas A & M University are collaborating sites where the work was completed.

Address for reprint requests: S. F. Crouse, Applied Exercise Science Laboratory, Dept. of Health and Kinesiology, Texas A & M University, College Station, TX 77843.

Received 21 January 1997; accepted in final form 22 July 1997.

REFERENCES


