# Blood Lipid Response to 20 Weeks of Supervised Exercise in a Large Biracial Population: The HERITAGE Family Study

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**We studied the effects of 20 weeks of supervised cycle-ergometer exercise on plasma lipids in 675 healthy, sedentary, normolipidemic white and black men and women aged 17 to 65 years, participating in the HERITAGE Family Study. Fasting plasma lipids were assessed twice at baseline and 24 and 72 hours after the last exercise session and adjusted for plasma volume changes. No significant differences from the mean baseline levels were observed for total, low-density lipoprotein (LDL), and very–low-density lipoprotein (VLDL) cholesterol and apolipoprotein B (Apo B). A significant reduction ($P < .01$) from baseline levels in plasma total and VLDL triglycerides was observed only in the 24-hour posttraining specimens, reflecting a response to the last bout of exercise. High-density lipoprotein (HDL) cholesterol increased 3.6% for the combined group, primarily due to an increase in $HDL_2$, with an associated increase in Apo A-1 ($P < .001$). No significant differences were noted in the HDL response by sex, race, or age. An inverse correlation ($r = -.241$) was observed between the increase in HDL cholesterol and change in body fat only in men, and the increase in HDL cholesterol was unrelated to the change in maximal oxygen uptake ($\dot{V}O_2max$).**



ALTHOUGH MULTIPLE risk factors are involved in the etiology of atherosclerosis and coronary heart disease (CHD), blood cholesterol and its associated lipoprotein carriers are at "center stage" as the primary targets for primary and secondary interventions.[1-3] Total blood cholesterol has been conclusively linked to the severity of atherosclerosis and development of CHD events, with a continuous ascending relationship beginning at a plasma total cholesterol level less than 180 mg/dL (4.65 mmol/L). Extensive epidemiologic, autopsy, laboratory, and clinical trial data indicate that most of the risk associated with total cholesterol can be attributed to the low-density lipoprotein (LDL) cholesterol fraction.[1-4] In general, a 1% change in LDL cholesterol is associated with a 2% to 3% difference in the risk for CHD.[3]

LDL is directly involved in the induction of coronary atherosclerosis following its infiltration of the intimal lining and its subsequent oxidation.[5] Apolipoprotein B (Apo B) is the sole protein on the surface of LDL and is the ligand for LDL–cell receptor binding. Apo B is also carried by very–low-density lipoprotein (VLDL) and intermediate-density lipoprotein, the precursors of LDL. The Apo B concentration is strongly associated with the risk of CHD in epidemiologic studies.[1,6] A strong inverse association also has been established between plasma high-density lipoprotein (HDL) cholesterol and CHD events in many epidemiologic studies.[7] It is estimated that for every 1-mg/dL (0.026-mmol/L) increase in HDL cholesterol, the risk for a CHD event is reduced by 2% in men and at least 3% in women.[7] According to US National Cholesterol Education Program (NCEP) treatment algorithms for the prevention of CHD, a HDL cholesterol level of 35 mg/dL (0.90 mmol/L) or less is a major risk factor for CHD, while HDL cholesterol greater than 60 mg/dL (1.60 mmol/L) is a negative risk factor for CHD.[3] The primary mechanism for the apparent antiatherogenic effect of HDL appears to be cholesterol removal from peripheral tissues, with its subsequent esterification and transfer either to triglyceride-rich lipoproteins or directly to the liver by a process known as reverse cholesterol transport.[8,9]

There are two major metabolically interrelated subclasses of HDL, designated $HDL_2$ (density 1.063 to 1.125 g/mL) and $HDL_3$ (density 1.125 to 1.21 g/mL).[9,10] Patsch et al[11] demonstrated that $HDL_3$ particles are converted to large, lipid-enriched $HDL_2$ particles by assimilation of lipids derived from lipolysis of VLDL or by transfer from cell membranes. Most of the variation in plasma HDL in a population is due to differences in the level of $HDL_2$. $HDL_2$ cholesterol in some earlier epidemiologic studies appeared to be a better marker for CHD risk than $HDL_3$; however, recent data suggest that reduced levels of either subfraction increase the risk of CHD.[10] Apo A-1 is the principal protein present on HDL and functions as an activator of lecithin: cholesterol acyltransferase, associated with reverse cholesterol transfer by catalyzing the esterification of cholesterol on the HDL particle surface.

A consensus now proposes that physical inactivity is another major risk factor for CHD.[17,18] One of the proposed mechanisms for the apparent protective effect of regular endurance exercise against CHD is an improvement in the blood lipid profile, particularly an increase in HDL cholesterol levels.[17,18] The HERITAGE Family Study provides a unique opportunity to study the effects of a supervised and standardized exercise program on plasma lipids, lipoproteins, and apolipoproteins in a large biracial population of young and middle-aged men and women.

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## SUBJECTS AND METHODS

### *Protocol*

The HERITAGE design and methods have been previously described in detail.[20] In brief, sedentary members of two generations of white and black families were exercise-trained under supervision for 20 weeks at the 4 participating clinical centers. In the investigation reported here, blood lipid levels were compared before and after training.

The study protocol was approved by the Institutional Review Board protecting human subjects in research projects at each of the 4 participating clinical centers. Participants received incremental $1,000 honoraria for successful completion of the study.

### *Subjects*

The white participants were members of two-generation families consisting of both natural parents under 65 years of age and at least 2 offspring aged 17 to 40 years. The black participants were of similar age but were from family units often as small as 2 first-degree relatives, ie, a natural parent and 1 offspring or 2 full siblings. Race was derived by the self-classification of the participants. To be eligible for the study, participants were required to be in good health, but sedentary for at least the previous 3 months, to meet other eligibility criteria, to pass a physician-administered physical examination, and to have no significant electrocardiographic abnormalities on a cycle ergometer maximal exercise test. Exclusion criteria included treated or untreated hyperlipidemia and hypertension, diabetes mellitus requiring medication, or a body mass index (BMI) exceeding 40 kg/m$^2$. In a few instances, the latter criterion was omitted by the examining physician because of an absence of other exclusionary criteria and a demonstrated ability to perform prescribed exercise during baseline evaluation.

### *Clinical Procedures*

Following health screening, participants completed a battery of health-habit questionnaires assessing smoking and alcohol consumption habits, medication use, and menstrual history: the ARIC-Baecke Physical Activity Questionnaire,[21,22] the Willett Food Frequency Questionnaire,[23] and the Minnesota Eating Pattern Assessment Tool (EPAT),[24] which measures high and low dietary fat sources.

Participants were counseled at baseline and at the midpoint of the training program (10 weeks) not to alter their health habits and to continue their usual eating pattern (as repeatedly assessed by the EPAT), physical activity outside of the study (as assessed by the ARIC-Baecke Questionnaire), alcohol and tobacco use, and oral contraceptive or hormonal replacement therapy. Good adherence was generally observed.

In addition to anthropometric measurements and the BMI (weight/height$^2$), underwater weighing was used to determine body density, fat-free mass, and percent body fat.[20,25] Corrections were made for residual lung volume by the oxygen-dilution method[26] at 3 of the clinical centers and by the helium-dilution method at the fourth center (Laval University).[27]

Maximal cycle ergometer exercise tests were performed twice on 2 separate days (at least 48 hours apart) before training and twice after completion of training for the determination of maximal oxygen uptake ($\dot{V}O_2$max) as previously described.[20,28] In brief, exercise was performed on SensorMedics 800S cycle ergometers (Yorba Linda, CA) connected to a SensorMedics 2900 metabolic measurement cart. The criteria for $\dot{V}O_2$max were a respiratory exchange ratio greater than 1.1, a plateau in $\dot{V}O_2$ (change of $<100$ mL $\cdot$ min$^{-1}$ during the last 20-second interval of the test), and a heart rate within 10 bpm of the predicted maximal heart rate for the participant's age. All HERITAGE subjects achieved $\dot{V}O_2$max by one or more of these criteria in at least one of the two exercise tests both pretraining and posttraining. The average $\dot{V}O_2$max for the two tests was used as the $\dot{V}O_2$max for each subject if the values were within 5% of each other. If they differed by more than 5%, the higher of the two values was used. The reproducibility of $\dot{V}O_2$max had an intraclass correlation of .97 with a coefficient of variation of 5% and no significant differences among clinical centers.[28]

### *Blood Lipid Determinations*

Blood samples were obtained from an antecubital vein into vacutainer tubes containing EDTA in the morning after a 12-hour fast with participants in a semirecumbent position, twice at baseline and 24 and 72 hours after the last exercise training session. For eumenorrheic women, all samples were obtained in the early follicular phase of the menstrual cycle at baseline and 24 hours posttraining, at which time blood serum cholesterol alterations are reportedly minimal.[29] Plasma samples from the 3 US HERITAGE clinical centers were shipped refrigerated with ice packs to the HERITAGE Lipid Core Laboratory at the Lipid Research Center of Laval University Medical Center for determination of plasma lipids, lipoproteins, and specific apolipoproteins. This laboratory is a participant in several lipid laboratory certification programs.

Cholesterol and triglyceride levels were determined in plasma and lipoproteins by enzymatic methods using a Technicon RA-500 analyzer (Bayer, Tarrytown, NY). Plasma VLDLs were isolated by ultracentrifugation.[30] The HDL fraction was obtained after precipitation of LDL in the infranatant by the heparin–manganese chloride method.[31] Selective precipitation was used to isolate $HDL_2$ and $HDL_3$ subfractions using dextran sulfate.[32]

The Apo A-1 level was measured in the infranatant and Apo B in the plasma and infranatant fraction by the rocket-immunoelectrophoretic method of Laurel.[33] The apolipolipoprotein measurements were calibrated with reference standards from the Centers for Disease Control and Prevention (Atlanta, GA).

Extensive quality control procedures were implemented to ensure high quality lipid and other study data.[34,35] These include repeat lipid assays in 5% of all samples and analyses of split specimens prepared at each clinical center. Results from plasma specimens containing chylomicrons were discarded for the analyses in this study as being suggestive of the nonfasting status.

To adjust for possible acute or chronic plasma volume changes associated with exercise, plasma total proteins were analyzed using the biuret method (Roche Molecular Biochemicals, Dallas, TX) on the initial pretraining specimen and both posttraining specimens. Posttraining plasma lipid parameters were corrected based on the correlation of pretraining to posttraining plasma total protein levels. In this report, the two baseline lipid values were averaged and compared with the average of the two corrected post-training lipid values.

### *Exercise Training Program*

Participants trained on cycle ergometers (Universal Aerocycle, Cedar Rapids, IA) under supervision at the 4 clinical centers, all using the same standardized exercise protocol.[20] In brief, participants exercised 3 times per week for 20 weeks, progressing from a duration of 30 to 50 minutes per session for the last 6 weeks of training. Similarly, exercise intensity was progressively increased from the heart rate associated with 55% $\dot{V}O_2$max at baseline testing to that associated with 75% $\dot{V}O_2$max for the last 8 weeks of training. The power output of the cycle ergometer was automatically adjusted to the heart rate response during exercise via built-in computerized controls.

### *Data Analysis*

All data were analyzed at the Washington University (St Louis) Data Coordinating Center using the SAS statistical package (version 6.12; SAS Institute, Cary, NC). Data are expressed as the mean $\pm$ SD. Paired $t$ tests were used to determine significant differences between pretraining and posttraining data. ANOVA and Tukey's HSD test[36] were

implemented to determine the influence of gender, generation (parents *v* offspring), and race (black *v* white) on the magnitude of change in any given variable. The strength of linear associations between two variables was evaluated by Pearson product-moment correlation coefficients. Statistical significance was established at a $P$ level less than .05.

## RESULTS

### *Baseline Characteristics*

Of 745 participants who completed the 20-week HERITAGE exercise program, 675 (217 black and 458 white participants) had both suitable pretraining and posttraining plasma lipid and lipoprotein data. Table 1 shows the baseline characteristics of this study population by sex. The mean age of the men and women was 35.6 and 34.4 years, respectively. The mean age for the older generation (parents) was 51.5 years, and for the younger generation (offspring) 26.5 years. Based on the current National Health and Nutrition Examination Survey II and National Heart, Lung, and Blood Institute standards, their mean baseline BMI places them in the overweight category.[37] The $\dot{V}O_2$max levels indicate that both the men and women at baseline had average functional capacity for their age based on American College of Sports Medicine (ACSM) $\dot{V}O_2$max standards.[38] The prevalence of cigarette smokers (at least 10 cigarettes per day) was well below the average rate of over 20% for American adults, with similar rates found in fathers and sons; however, almost twice as many daughters smoked as compared with the mothers (data not shown). About 40% of the women in the study were on oral contraceptives or hormone replacement therapy (data not shown), and this remained constant throughout the study.

Baseline dietary analyses from the Willett Food Frequency Questionnaire for the men showed a mean daily energy intake of 2,376.3 ± 1,031.6 kcal with 31.9% ± 5.9% of energy from fat and 11.5% ± 2.7% from saturated fat, a mean daily cholesterol intake of 311.2 ± 180.2 mg, and a mean daily alcohol intake of 7.2 ± 12.1 g (or 2.1% of daily energy intake). For the women, the mean total daily energy intake was 2,099.1 ± 975.6 kcal with 30.7% ± 6.0% of energy from dietary fat and 11.0% ± 2.7% from saturated fat, a mean daily cholesterol intake of 267.5 ± 139.0 mg/d, and a mean daily alcohol intake of 3.2 ± 5.9 g (or 1.1% of daily energy intake). Additional details on the dietary habits of HERITAGE participants will be the subject of a separate publication. No significant change in dietary lipid intake was noted on repeated EPAT assessments.

**Table 1. Baseline Characteristics of the HERITAGE Family Study Population With Adequate Lipid Data (mean ± SD)**

| Variable | Men (n = 299) | Women (n = 376) |
|---|---|---|
| Age (yr) | 35.6 ± 14.1 | 34.4 ± 13.2 |
| Body mass (kg) | 84.6 ± 16.7 | 69.3 ± 15.1 |
| BMI (kg/m²) | 26.9 ± 4.9 | 26.2 ± 5.6 |
| Body fat UWW (%) | 23.0 ± 23.0 | 31.6 ± 9.8 |
| $\dot{V}O_2$ max | | |
| mL/min | 2,968.8 ± 35.1 | 1,857.6 ± 367.7 |
| mL · kg$^{-1}$ · min$^{-1}$ | 35.1 ± 6.9 | 26.5 ± 5.3 |
| Cigarette smokers (%) | 12.5 ± 3.3 | 14.8 ± 3.6 |

Abbreviation: UWW, underwater weighing.

**Table 2. Mean Changes in Physical Fitness and Body Composition With 20 Weeks of Exercise Training**

| Variable | Men | Women | Significant Difference |
|---|---|---|---|
| ΔBody mass (kg) | −0.42 ± 2.2 | −0.18 ± 2.4 | a |
| ΔFat mass (kg) | −0.93 ± 1.7 | −0.63 ± 2.0 | a,b |
| %Δ$\dot{V}O_2$ max (mL/min) | +15.1 ± 7.6 | +18.6 ± 9.5 | a |

[a]Significant difference pretraining *v* posttraining for both sexes ($P < .05$).

[b]Significant difference pretraining *v* posttraining between the sexes ($P < .05$).

### *Physical Fitness and Body Composition Changes*

A detailed description of the changes in body composition with exercise training in the HERITAGE study was recently published.[39] Table 2 shows some of the pretraining to posttraining changes in body composition and $\dot{V}O_2$max among participants with adequate lipid data. Moderate increases in $\dot{V}O_2$max were noted in both men and women, with a trend for a greater mean increase in women (NS). Small, but statistically significant ($P < .05$), decreases in body mass resulted from training, with the fat loss significantly greater in men compared with women ($P < .05$).[39]

### *Baseline Plasma Lipids and Changes with Training*

Tables 3 and 4 present the mean values for baseline and plasma volume–adjusted posttraining plasma lipids, lipoproteins, and apolipoproteins. $S_1$ and $S_2$ are the baseline values, and $S_3$ and $S_4$ refer to the posttraining values. On average, both men and women had normolipidemic baseline plasma lipid patterns. Based on Lipid Research Clinic Prevalence Study reference data, the baseline total cholesterol, LDL cholesterol, and HDL cholesterol levels found in our study population were in the 25th percentile for American and Canadian women and men of similar ages, while triglyceride levels were average or slightly higher than average (75th percentile) for the various study subgroups.[40] The lipid profile for the men was less favorable, in terms of the risk of CHD, than for the women, with significantly higher plasma concentrations of total ($P < .02$), LDL ($P < .01$), and VLDL cholesterol ($P < .0001$), total and VLDL triglycerides ($P < .0001$), and Apo B and LDL-Apo B ($P < .0002$). Further, the men had significantly lower baseline HDL, $HDL_2$ and $HDL_3$ cholesterol and Apo A-1 levels than the women ($P < .0001$).

Preliminary analysis showed small but significantly lower ($P < .0001$) concentrations in the 24-hour posttraining plasma specimens ($S_3$) compared with 72-hour posttraining specimens ($S_4$) for plasma total proteins (grams per liter) and each unadjusted lipid variable studied. The mean plasma total protein value for $S_3$ also was significantly lower than the baseline value ($P < .0001$). The plasma volume adjustments resulted in significantly closer agreement and correlation between $S_3$ and $S_4$ for all lipid variables.

Plasma volume–adjusted lipid levels are shown in Tables 3 and 4 for the individual mean 24-hour and 72-hour posttraining levels and the combined posttraining mean concentrations. No significant changes were observed following training in the adjusted mean plasma total, LDL, and VLDL cholesterol or Apo B in either sex. However, adjusted total triglyceride and VLDL

**Table 3. Baseline and Posttraining Adjusted Plasma Lipid Levels (mean ± SD, mg/dL) for HERITAGE Study Women Participants (n = 376)**

| Variable | Baseline (mean S1 + S2) | Posttraining | | | Mean Baseline *v* Mean Posttraining *P* |
|---|---|---|---|---|---|
| | | 24 h (S3) | 72 h (S4) | Mean (S3 + S4) | |
| Total cholesterol | 168.0 ± 33.6 | 168.4 ± 33.7 | 169.6 ± 34.6 | 169.0 ± 33.4 | NS |
| Triglyceride | 95.9 ± 48.7 | 94.5 ± 55.1 | 95.5 ± 54.0 | 95.3 ± 52.3 | NS |
| LDL cholesterol | 115.5 ± 29.4 | 111.3 ± 29.1 | 110.9 ± 29.8 | 111.1 ± 28.7 | NS |
| VLDL cholesterol | 12.2 ± 8.2 | 11.9 ± 9.8 | 12.3 ± 9.8 | 12.1 ± 9.3 | NS |
| VLDL triglycerides | 86.5 ± 66.5 | 73.2 ± 60.7 | 85.7 ± 71.9 | 79.6 ± 63.0 | .001 |
| HDL cholesterol | 44.3 ± 10.2 | 45.0 ± 10.5 | 46.2 ± 11.1 | 45.7 ± 10.7 | .001 |
| $HDL_2$ cholesterol | 16.4 ± 7.6 | 17.4 ± 8.2 | 18.4 ± 8.3 | 17.9 ± 8.0 | .0001 |
| $HDL_3$ cholesterol | 28.1 ± 5.5 | 27.6 ± 5.4 | 27.9 ± 5.4 | 27.8 ± 4.9 | NS |
| Ratio total/HDL cholesterol | 4.0 ± 1.1 | 3.9 ± 1.1 | 3.8 ± 1.1 | 3.9 ± 1.1 | NS |
| Apo A-1 | 119.7 ± 17.1 | 120.6 ± 17.3 | 122.9 ± 18.0 | 121.8 ± 16.8 | .001 |
| Apo B | 80.4 ± 21.8 | 81.4 ± 21.9 | 81.0 ± 21.9 | 81.2 ± 21.8 | NS |
| LDL-Apo B | 73.8 ± 20.1 | 74.6 ± 19.9 | 74.0 ± 20.1 | 74.3 ± 19.7 | NS |

NOTE. To convert mg/dL to mmol/L, divide cholesterol values by 38.7 and triglyceride by 88.54.
Abbreviation: S, plasma specimen.

triglyceride concentrations were significantly lower at 24 hours posttraining ($S_3$) in both sexes compared with the mean baseline and 72-hour posttraining ($S_4$) levels ($P < .0001$). At 72 hours posttraining, adjusted total and VLDL triglycerides were no longer significantly different from the mean baseline levels, although for the men, the mean posttraining triglycerides and VLDL triglycerides were significantly lower than the mean baseline levels (Table 4). Thus, the reduction in triglyceride levels in this study at 24 hours posttraining appears to reflect a persistent or delayed effect of the last bout of exercise rather than a training effect. Also, following plasma volume adjustments, HDL cholesterol no longer showed significant differences in the mean values between $S_3$ and $S_4$ for the men; however, for the women, the $S_3$ value remained slightly lower than the $S_4$ value ($P < .0001$) for all of these HDL-related variables, perhaps also reflecting residual effects of the last exercise bout. Both the men and women showed significant increases in the mean adjusted posttraining values compared with mean baseline values for total plasma HDL and $HDL_2$ cholesterol and Apo A-1 ($P < .01$); however, a significant increase in $HDL_3$ cholesterol ($P < .001$) was noted only in the male group.

Figure 1 shows a comparison of the percent changes in HDL cholesterol by gender and generation. The mean increase for the entire cohort was 3.62%. It should be noted that in the absence of adjustments for plasma volume changes, the posttraining change in HDL cholesterol would be less than 3% for the combined group. There was a trend for the offspring to have a greater increase in HDL cholesterol after exercise training as compared with the parents ($P < .07$). Otherwise, no statistically significant differences were noted in training-induced HDL cholesterol changes by sex, generational, and race subgroup analyses, ie, men versus women, dads versus sons, moms versus daughters, and blacks versus whites (data not shown). However, there was a significantly greater increase in mean $HDL_2$ cholesterol levels in black as compared with white participants ($P < .0001$). Further, black participants experienced a significant reduction in $HDL_3$ cholesterol (mean, −0.7 mg/dL), in contrast to an increase (mean, +0.49 mg/dL) for the white participants ($P < .001$, data not shown). In addition, subgroup analyses (data not shown) showed greater increases in Apo A-1 in the women compared with men ($P < .01$), black compared with white participants ($P < .01$), and offspring compared with parents ($P < .05$).

### *Correlational Analyses*

Table 5 shows Pearson univariate correlation coefficients ($r$) between the percent change in HDL cholesterol following

**Table 4. Baseline and Posttraining Adjusted Plasma Lipid Levels (mean ± SD, mg/dL) for HERITAGE Study Men Participants (n = 299)**

| Variable | Baseline (mean S1 + S2) | Posttraining | | | Mean Baseline *v* Mean Posttraining *P* |
|---|---|---|---|---|---|
| | | 24 h (S3) | 72 h (S4) | Mean (S3 + S4) | |
| Total cholesterol | 174.7 ± 39.9 | 172.6 ± 39.9 | 174.9 ± 40.3 | 173.9 ± 39.4 | NS |
| Triglyceride | 127.4 ± 74.1 | 114.3 ± 68.6 | 128.0 ± 80.8 | 121.5 ± 70.9 | .01 |
| LDL cholesterol | 118.0 ± 33.7 | 117.3 ± 35.0 | 116.8 ± 34.3 | 117.1 ± 34.0 | NS |
| VLDL cholesterol | 19.5 ± 15.6 | 17.0 ± 14.0 | 19.6 ± 15.9 | 18.4 ± 14.4 | NS |
| VLDL triglycerides | 86.5 ± 66.5 | 73.3 ± 60.7 | 88.7 ± 71.9 | 79.6 ± 63.0 | .01 |
| HDL cholesterol | 37.1 ± 9.7 | 38.1 ± 10.0 | 38.3 ± 10.8 | 38.2 ± 10.2 | .001 |
| $HDL_2$ cholesterol | 10.8 ± 6.3 | 11.3 ± 6.6 | 11.6 ± 7.4 | 11.5 ± 6.7 | .001 |
| $HDL_3$ cholesterol | 26.3 ± 5.0 | 26.8 ± 5.4 | 26.6 ± 5.6 | 26.7 ± 5.6 | .001 |
| Ratio total/HDL cholesterol | 5.0 ± 1.6 | 4.8 ± 1.5 | 4.8 ± 1.5 | 4.8 ± 1.5 | NS |
| Apo A-1 | 114.3 ± 15.8 | 116.3 ± 15.9 | 117.7 ± 16.2 | 117.0 ± 15.2 | .002 |
| Apo B | 88.5 ± 25.2 | 87.8 ± 26.3 | 88.2 ± 26.3 | 88.1 ± 25.8 | NS |
| LDL-Apo B | 79.8 ± 22.8 | 79.6 ± 24.1 | 79.7 ± 24.0 | 79.7 ± 23.5 | NS |

NOTE. To convert mg/dL to mmol/L, divide cholesterol values by 38.7 and triglyceride by 88.54.
Abbreviation: S, plasma specimen.

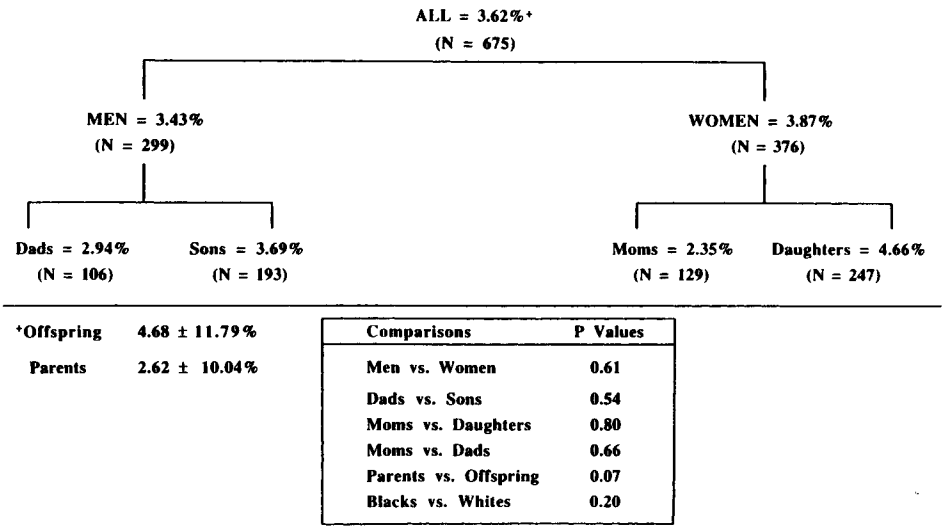


**Fig 1. Percent changes in adjusted plasma HDL cholesterol levels with training by gender and generation subgroups.**

exercise training (dependent variable) and changes in body composition, $\dot{V}O_2$max and other lipid variables. In men, but not in women, low-order, but statistically significant ($P < .05$), inverse correlations were found between the change in HDL cholesterol and changes in both body mass and percent body fat. No significant association was evident between the change in $\dot{V}O_2$max and the change in HDL cholesterol. Both sexes showed a low-order correlation between the increase in HDL cholesterol and the reduction in triglycerides and a moderate correlation between the increase in HDL cholesterol and the increase in Apo A-1.

## DISCUSSION

This is the largest reported study on the contribution of endurance exercise training to blood lipid parameters, and the only study that includes both black and white men and women in a broad age range. A concerted effort was made to reduce potential confounding biological, physiological, behavioral, and study design–related variables that can affect the responsiveness of blood lipids to exercise training. Such variables undoubtedly contributed to the variability of results among previous exercise-lipid studies. These measures included requiring the participants at baseline not to perform strenuous exercise regularly for at least 3 months before baseline screening; excluding people receiving lipid-lowering medications and those who were potential candidates for such agents based on NCEP guidelines; monitoring in an attempt to maintain constant levels during exercise training for recreational physical activity, dietary lipid intake, cigarette smoking, alcohol consumption, and use of oral contraceptives and hormone replacement therapies, as well as other medications affecting blood lipids; providing a prescribed level of supervised exercise with a monetary remuneration for successful completion of the study to help ensure compliance; blood sampling at the same phase in the menstrual cycle at baseline and posttraining for eumenorrheic women; discarding blood specimens containing chylomicrons, suggesting a nonfasting status; adjusting for possible exercise-induced plasma volume changes; and using rigorous laboratory quality-control procedures.

**Table 5. Correlation (*r*) Between Posttraining Changes in Plasma HDL Cholesterol and Changes in Body Composition, Fitness, and Other Lipid Parameters by Gender**

| Independent Variable | Men | Women |
|---|---|---|
| Change in % body fat | −.244§ | .025 |
| Change in $\dot{V}O_2$ max (mL/min) | .054 | .026 |
| Change in triglycerides (mg/dL) | −.192‡ | −.160† |
| Change in Apo A-1 (mg/dL) | .459§ | .422§ |

*$P < .05$.
†$P < .01$.
‡$P < .001$.
§$P < .0001$.

As a group, the HERITAGE population at baseline was slightly overweight, despite a mean daily energy intake, obtained from the Willett Questionnaire,[23] in the average range for American and Canadian men and women,[41] and within guidelines recommended by the Food and Nutrition Board of the National Academy of Sciences.[42] This finding is consistent with their self-reported sedentary life-style. However, it should be noted that a great deal of variability was evident in the reported daily energy intake. Both women and men had an average baseline functional capacity based on ACSM $\dot{V}O_2$max standards.[38] As a group, aside from their sedentary life-style, the participants reported relatively good health habits, with a subaverage number of cigarette smokers and a relatively low alcohol and dietary lipid consumption for North Americans. Thus, based on their life habits and our exclusion criteria, it is not surprising that the participants as a group were normolipidemic with subaverage plasma total, LDL, and HDL cholesterol and normal triglyceride levels based on the Lipid Research Clinics Prevalence Study reference data.[40] Twenty weeks of supervised moderate-intensity cycle-ergometer training resulted in a significant mean improvement in $\dot{V}O_2$max for both the men and women. This was associated with a small reduction in fat mass, more marked in men than in women.

The HERITAGE training program failed to significantly alter mean total, LDL, and VLDL cholesterol or Apo B levels. The absence of a change in total and LDL cholesterol and Apo B with training is in agreement with most (but not all) previous exercise studies.[19,43,44] However, a meta-analysis of 27 exercise

training studies limited to female subjects observed a small but significant ($P < .02$) reduction in total cholesterol (from 194 to 190 mg/dL).[45] The absence in the present study of a significant change in VLDL cholesterol with training is in contrast to the reduction in this lipid parameter commonly reported by other exercise training studies.[19,43]

The most consistently reported plasma lipid change with exercise training is a reduction in plasma triglycerides, particularly when the baseline levels were elevated.[19,43-46] In the present study with normolipidemic men and women, significant reductions in plasma total and VLDL triglycerides were limited to the blood specimen obtained 24 hours following the last training session, which persisted after plasma volume adjustments. The acute beneficial effect of a single session of endurance exercise on plasma triglycerides has long been recognized.[19,43,44,46-48] Dufaux et al[48] observed that the reduction in plasma triglycerides following an acute bout of aerobic exercise persists for 24 to 48 hours, consistent with the findings in this study. Increased lipoprotein lipase activity induced by exercise is believed to be involved in catabolizing VLDL triglycerides to provide fatty acids for fuel for skeletal muscle.[43,44,46-48] Durstine and Haskell[43] concluded, based on a review of the literature, that reductions in triglycerides with exercise training can result from both the effects of "a single exercise session and habitual exercise."

The most important change in the blood lipid profile with exercise training, from the cardiovascular health perspective, observed in this and most (but not all) other studies is a modest increase in mean plasma HDL cholesterol. We observed a modest mean 1.2-mg/dL (0.031-mmol/L, or 3.4%) increase in HDL cholesterol in male subjects and a 1.4-mg/dL (0.038-mmol/L, or 3.9%) increase in female subjects with training. No racial difference was noted in responsiveness; however, a trend was noted for a greater increase in HDL cholesterol in younger men and women ($P < .07$). A review of the literature reveals that only about half of the published studies in men, and fewer than half of those involving women demonstrated significant increases in plasma HDL cholesterol with training.[19,43-46,49] A meta-analysis of 95 of these exercise training studies, involving over 2,000 participants, by Tran et al[49] found an average increase in HDL of about 5%, with a range of increase from 2.8 to 8.0 mg/dL (0.072 to 0.207 mmol/L), which is greater than the change noted in this study. In terms of a reduction in the potential risk of CHD, epidemiologic data suggest that each 1-mg/dL (0.02-mmol/L) increase in HDL cholesterol is associated with at least a 2% reduction in risk.[7]

The increase in HDL cholesterol in the HERITAGE Study primarily involved the $HDL_2$ fraction and was associated with an increase in Apo A-1, again in agreement with previous reports.[9,43,50,51] A small but significant ($P < .001$) increase in $HDL_3$ cholesterol was noted only in the men. Subgroup analysis showed that this change was limited to white men, with the black male subgroup experiencing about a 2% decline in the $HDL_3$ cholesterol fraction (data not shown). A decline in $HDL_3$ with training has been previously reported.[9,43,50,51] Increases in HDL cholesterol and Apo A-1 with exercise training have been reported to be generally associated with an increase in lipoprotein lipase activity, which also was observed in this study (data not presented), and these observations are consistent with both decreased HDL protein catabolism and increased HDL Apo A-1 synthesis.[50,52]

As noted in this and other reported studies, a great deal of variability exists in the response of HDL cholesterol to exercise training.[9,43,50,51] This variability is probably strongly related to genetic factors currently under investigation in the HERITAGE Study, as well as the numerous potential confounding life-style variables elaborated earlier. In addition, this variability may reflect differences among study populations in the exercise intervention approach and prescription (including mode, intensity, and volume of exercise), and in study methods, including the timing of blood sampling following completion of the exercise training and whether plasma volume changes were accounted for.[19,43,46,53] We are currently further exploring nongenetic reasons for the variability in the responsiveness of blood lipids, particularly HDL cholesterol, to exercise training noted in the HERITAGE Study.

Controversy exists as to whether endurance exercise training has an independent effect on HDL cholesterol or whether the effect is dependent on an associated loss of body weight. In a previous study in one of our laboratories (A.S.L.), 12 weeks of supervised exercise training was provided in a small group of young overweight men along with standard lipid-controlled meals supplied by a metabolic kitchen.[54] The effect on blood lipids of exercise training with the body weight held constant was compared with the effect on blood lipids of weight reduction by a restricted energy intake and a similar weight reduction by exercise alone. Independent and additive effects of weight reduction and exercise on increasing HDL cholesterol were demonstrated. A study by Schwartz[55] essentially confirmed these findings. More recently, Thompson et al[50] demonstrated a 10% increase in HDL cholesterol with 1 year of supervised endurance exercise in overweight men whose body weight was kept constant. In that study, defined diets were provided by a metabolic kitchen for 18 days prior to each assessment of blood lipids. In contrast, in an often-quoted randomized controlled 1-year study involving moderately overweight men, Wood et al[56] demonstrated similar increases in HDL (and $HDL_2$) cholesterol associated with weight loss due to caloric restriction or exercise, with no change in HDL cholesterol following exercise training when body weight remained constant. In the current study, the relatively modest increase in HDL cholesterol with 20 weeks of exercise training was associated with a small weight loss; however, only low-level correlations, limited to the male participants, were observed between the increase in HDL cholesterol and the loss of body weight and fat. It is possible that supervised programs provide more exercise than unsupervised programs and thereby are more likely to obtain an HDL cholesterol response even in the absence of weight loss, as suggested by Thompson et al.[50] More research is clearly needed to better define the independent effects of weight loss and change in body composition on plasma HDL cholesterol, as well as other lipids. Another observation which requires confirmation is the absence of a significant association in this study between the increase in HDL cholesterol and increase in $\dot{V}O_2max$ with exercise training, a relationship suggested by most, but not all, cross-sectional studies.[57,58]

In summary, in the HERITAGE Family Study, 20 weeks of supervised moderate-intensity exercise resulted in similar modest mean increases in plasma HDL cholesterol in young and middle-aged, initially sedentary, normolipidemic black and white men and women. This change primarily involved the $HDL_2$ fraction and was accompanied by a significant increase in Apo A-1. There was a significant inverse association of the increase in HDL cholesterol with the change in body fat in men only, and no association of the change in HDL cholesterol with the change in $\dot{V}O_2max$ with training. The only other significant change observed in blood lipids was a reduction in plasma triglycerides, which appeared to be primarily due to metabolic changes related to the last bout of exercise.

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