Effect of Moderate Physical Exercise on Serum Lipoproteins
A Controlled Clinical Trial with Special Reference to Serum High-density Lipoproteins

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SUMMARY A controlled trial is reported on the effects of mild-to-moderate physical activity on serum lipoproteins. After two baseline examinations 100 asymptomatic middle-aged men were randomly assigned to exercise and control groups. The exercise group participated in a 4-month exercise program that consisted of 3-4 weekly sessions. The control group was advised to maintain their previous exercise habits. The success of the program was corroborated by the increase in \( \text{VO}_2 \) in the training group, but not in the control group. Serum triglycerides decreased from 1.54 ± 0.10 to 1.27 ± 0.08 mmol/l (\( p < 0.001 \)) and high-density lipoprotein (HDL) cholesterol increased from 1.27 ± 0.04 to 1.41 ± 0.04 mmol/l (\( p < 0.01 \)) in the exercise group during the trial. No change was seen in the control group. As the concentration of apolipoprotein AI stayed constant in both groups, the ratio HDL cholesterol/apolipoprotein AI increased only in the exercise group. The level of low-density lipoprotein (LDL) cholesterol and apolipoprotein AII decreased in both groups during the trial. The alterations in serum triglycerides and HDL cholesterol in the exercise group were not dependent on weight reduction; similar changes were also seen in subjects with constant body weight during the intervention.

EPIDEMIOLOGIC STUDIES have suggested that high physical activity is associated with low incidence of coronary heart disease.\(^1\)\(^,\)\(^2\) The mechanism by which physical exercise influences coronary risk factors is not known. Muscular activity may directly protect the cardiovascular system through neural and hemostatic mechanisms or by increasing the vascularity of myocardium. Alternatively, physical exercise may have beneficial effects on the risk factors of coronary heart disease, such as serum lipids and blood pressure.

Although several associations between serum lipid levels and physical activity have been reported, it is not clear whether the changes in serum lipid concentrations are directly attributable to physical exercise itself. Subjects active at work or during leisure time tend to have lower serum cholesterol and triglyceride concentrations than those with a sedentary occupation or lifestyle, but the differences are not always evident when other factors known to affect serum lipids are controlled.\(^3\)\(^,\)\(^4\) The conflicting results in experimental and clinical studies are more difficult to explain, but may be due to confounding factors such as changes in the diet or body weight and seasonal variations in serum lipid concentrations.

Considerable evidence has accumulated indicating that the serum level of high-density lipoproteins (HDL) is inversely related to the development of coronary heart disease.\(^7\)\(^,\)\(^8\) On the other hand, the concentration of HDL has been demonstrated to be high in subjects with very vigorous physical activity.\(^10\)\(^–\)\(^12\) We report here the results of a controlled study on the effects of mild-to-moderate physical exercise on HDL and other lipoproteins in asymptomatic middle-aged men.

Methods

Subjects

The subjects were recruited from a group of 110 men, ages 40-45 years, who were contacted through an advertisement published in the local newspapers and read in the local radio broadcasting. All participants had been physically rather inactive during the year preceding the study. Persons who were taking antihypertensive, antidiabetic and hypolipidemic medications and persons with cardiac or other medical disorders that would contraindicate physical training were excluded. All participants gave informed consent before the study.

Experimental Design

A schematic presentation of the experimental design is shown in figure 1. Information on previous physical activity, cigarette smoking and alcohol consumption (1-month recall) was obtained from all par-
participants with a questionnaire in the beginning of the study (time point I). A 12-hour postabsorptive blood sample was drawn for blood glucose and serum cholesterol and triglyceride determinations. A progressive submaximal exercise test was performed in the afternoon on an electrically braked Siemens-Elema bicycle ergometer to familiarize the subjects with the testing procedure and to determine the work intensity for the subsequent tests. The work load was increased stepwise in four consecutive 3-minute periods to attain 85% of the age-specific maximal pulse level. Subjective load was evaluated according to Borg.13 During the test a bipolar CM5 (V5 and manubrium) ECG was continuously monitored and recorded at 3-minute intervals. Blood pressure was measured at the end of each 3-minute period. Subjects with signs of latent coronary heart disease (significant arrhythmias or ST-segment depression or typical angina pectoris) or excessive pressor response during the exercise testing were excluded from the study and referred to their own physician for evaluation of the cardiac status. The recruitment was continued until 100 participants who fulfilled the selection criteria had been found.

After these initial determinations all subjects received dietary instructions that recommended reduced usage of saturated fats and simple carbohydrates and avoidance of excessive alcohol consumption. Weight loss was not encouraged. These recommendations were made to make the diet of the test persons as uniform as possible and to avoid nonspecific diet-induced changes later during the experimental period between time points II and IV.

Two months after the initial studies the participants came to the laboratory for the baseline determinations of the intervention trial. The laboratory investigations at this time point (II) included hemoglobin, serum lipids and lipoproteins measured in the morning after an overnight fast. A peroral glucose tolerance test (50 g of glucose followed by blood glucose determinations at 60 and 120 minutes) was performed on each subject. A submaximal exercise test was carried out in the afternoon according to the same protocol as in the initial studies.

After these determinations 100 participants selected for the intervention trial were randomly assigned to two groups: physical training (group A) and control (group B). There were no differences in the blood values or other characteristics between the two groups before the beginning of the intervention (table I).

The biochemical studies and the exercise testing were repeated on all subjects 2 months (time point III) and 4 months (time point IV) after the beginning of the intervention. A glucose tolerance test was carried out only at the end of the experimental period (time point IV). The subjects were advised to avoid physical exercise on the day before the tests. Body weight was recorded during all visits.

Six men in group A and four men in group B did not complete the trial. The causes for the dropouts were: moving away from the town (two men in group A and one man in group B), lack of time (three men in group A) or unspecified reasons (one man in group A and three men in group B). The measurements in the subjects who withdrew from the study before its completion are not included in the calculations unless otherwise indicated.

<table>
<thead>
<tr>
<th>Table 1. Baseline Characteristics (Time Point II) of Groups A and B</th>
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</thead>
<tbody>
<tr>
<td><strong>Group</strong></td>
</tr>
<tr>
<td>Body weight (kg)</td>
</tr>
<tr>
<td>VO₂ (ml/kg · min)</td>
</tr>
<tr>
<td>Cholesterol (mmol/l)</td>
</tr>
<tr>
<td>Triglycerides (mmol/l)</td>
</tr>
<tr>
<td>VLDL cholesterol (mmol/l)</td>
</tr>
<tr>
<td>LDL cholesterol (mmol/l)</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/l)</td>
</tr>
<tr>
<td>Smoking status</td>
</tr>
<tr>
<td>Alcohol consumption (ml/month)*</td>
</tr>
</tbody>
</table>

*Values are mean ± SEM.
*Alcohol consumption was estimated with 1-month recall technique and is expressed as ml of absolute alcohol used per month.
Intervention Program

The subjects assigned to the exercise group were given an individualized training program that consisted of walking, jogging, swimming, skiing, or cycling. During the first 8 weeks (i.e., between time points II and III) the program included three weekly training sessions at an intensity that was adjusted to get the previously nonactive participants accustomed to physical exercise. The subjects were instructed to determine their training heart rates from 10-second pulse counts estimated several times during the exercise. The prescribed intensity during the acclimatization period was calculated from the modified Balke's formula: resting heart rate + 0.40 \times (maximal heart rate – resting heart rate). The participants were advised to have a warm-up period of 15 minutes before and a 10-minute slow-down period after the 30-minute exercise period to avoid the risks of too-vigorous changes of physical activity. Since the subjects exercised without supervision they were asked to keep a daily log book in which they recorded the length of the training sessions and the heart rates during the exercise.

During the second part of the intervention program (between time points III and IV) the subjects in group A were asked to meet the minimum of one unsupervised training session every second day. The intensity of the physical activity was increased so that the target heart rate during the exercise was resting heart rate + 0.66 \times (maximal heart rate – resting heart rate). In addition, all subjects participated in one supervised session per month and met the exercise physiologist at regular intervals for adjustments in the training programs.

The subjects in the control group (group B) were asked to maintain their previous exercise habits during the experimental period. They were promised that after the completion of the trial the experience from the intervention group would be used for planning of an ideal exercise program for the whole group.

Analytical Methods

Maximal oxygen uptake (VO\textsubscript{2}) (l/min) was calculated using the indirect method. Work load/heart rate pairs recorded during the graded exercise were extrapolated to the predicted age-specific maximal heart rate and the corresponding work load and oxygen uptake were estimated according to Lange-Andersen et al.\textsuperscript{13}

Cholesterol and triglyceride concentration in serum and in various lipoprotein fractions was measured by an Autoanalyzer II apparatus (Technicon Instruments, Tarrytown, New York) using enzymatic assay (Boehringer Mannheim GmbH, Germany). The Autoanalyzer results were calculated by taking into account the carryover and baseline corrections in all determinations. Serum lipoprotein fractionation was carried out using the procedure recommended in Lipid Research Clinic Manual of Laboratory Operations\textsuperscript{16} with minor modifications. Heparin-manganese was replaced with dextran-sulphate-magnesium chloride (1.0 ml serum + 50 \mu l of 2% dextran-sulphate (m.w. 500,000) + 50 \mu l of 2.0 mol/1 MgCl\textsubscript{2})\textsuperscript{17} in the precipitation of very low density lipoproteins (VLDL) and low-density lipoproteins (LDL), as this method gave more reproducible results combined with the enzymatic cholesterol determination.

The concentration of apolipoproteins A1 and AII was measured with a radial immunodiffusion procedure similar to the method described by Cheung and Albers.\textsuperscript{18} Fifty microliters of plasma were mixed with an equal volume of tetramethylurea. After adding 650 \mu l of a solution containing 0.01 M Tris chloride, pH 8.0, and 6 M urea, the mixture was incubated overnight at room temperature. Four-microliter samples were pipetted in duplicate on agarose plates containing antiserum (4% anti-A1 and 8% anti-AII) and 0.02 M Tris chloride, pH 8.0, 0.15 M NaCl, 1 mM EDTA and 1% bovine serum albumin. After 48-hour diffusion the immunoprecipitates were measured with a calibrating viewer. Standard preparations of A1 and AII were included in all plates.

Statistical Methods

Differences in the mean values were tested with the \textit{t} test and a paired \textit{t} test, if necessary, before and after logarithmic transformation. Analyses of correlation was performed using a computer program (HYLPS program, University of Helsinki).

Results

Baseline Measurements

Weak but statistically significant associations were observed between maximal oxygen uptake calculated per kg body weight (ml/kg · min) and total serum triglyceride (\(r = -0.29, \ n = 100\)) and VLDL cholesterol (\(r = -0.25, \ n = 100\)) concentrations in the baseline studies before the beginning of the intervention (time point II). Other lipid fractions did not correlate significantly to maximal oxygen uptake (data not shown).

Serum triglyceride levels were slightly lower in non-smokers than smokers (1.30 ± 0.06 vs 1.89 ± 0.21 mmol/l, \(p < 0.05\)), while the levels of the other serum lipids were not related to the smoking status. A weak positive correlation (\(r = 0.26, \ n = 100\)) was present between HDL cholesterol level and alcohol consumption measured by 1-month recall technique. No significant associations were observed between alcohol consumption and total serum cholesterol, triglyceride or LDL cholesterol concentrations in the study group.

Effect of Exercise Program on Body Weight and VO\textsubscript{2}

A small but statistically significant reduction in the mean body weight was evident both in the exercise group (−0.91 ± 0.23 kg; \(p < 0.01\), paired comparison) and in the control group (−0.64 ± 0.24 kg; \(p < 0.01\), paired comparison) between time points II and IV (table 2). The difference in the body weight between the two groups was not statistically significant at any time during the study. Sixteen subjects
(37%) lost more than 1 kg of the body weight in group A and 17 (37%) in group B.

Physical training resulted in a highly significant increase in maximal oxygen uptake in the exercise group. This was evident already after the acclimatization period (p < 0.001, paired comparison) and became more pronounced during the second training period (table 3). In contrast, VO₂ decreased in the control group (p < 0.01). Comparison of the mean values indicated that the mean VO₂ was significantly higher (p < 0.001) in group A than in group B at the end of the 4-month experiment (time point IV), but not in the middle of the training period (time point III). The results were essentially similar when the maximal oxygen uptake was calculated per kg body weight (ml/kg · min).

**Effect of Exercise Program on Serum Lipids and Glucose Tolerance**

The effect of the training program on serum lipids and lipoproteins is shown in figures 2–5. A progressive decrease in fasting serum triglyceride concentration, statistically significant after only 2 months, occurred in the exercise group but not in the control group (fig. 2). The triglyceride level was significantly lower in group A than in group B at the end of the experiment (time point IV) (1.27 ± 0.08 mmol/l vs 1.58 ± 0.13 mmol/l, p < 0.05) but not at time point III. The change in group A was evident both in subjects with normal (<1.7 mmol/l) and elevated (>1.7 mmol/l) serum triglycerides in the baseline measurements (data not shown). Total serum cholesterol and LDL cholesterol levels decreased slightly but significantly in both groups during the trial (figs. 3 and 4). No difference was observed in the mean values between the two groups at any time during the intervention.

The concentration of HDL cholesterol increased progressively in group A during the exercise program.
(fig. 5 and table 4). As no significant change occurred in the concentration of apolipoprotein Al in either group, the HDL cholesterol/apolipoprotein Al ratio increased in the exercise group but not in the control group (table 4). The level of apolipoprotein AlII decreased and the ratio of HDL cholesterol/apolipoprotein AlII increased slightly in both groups between time points II and IV.

Fasting blood glucose concentration and the results of peroral glucose tolerance test did not change in either group during the intervention period.

Correlations Between Serum Lipid Fractions, VO₂ and Body Weight During the Trial

The relationships between plasma lipids and lipoproteins and physical performance at the end of the intervention period are shown in table 5. A weak but statistically significant positive correlation ($r = 0.31$, $n = 43$) was observed in group A between VO₂ (calculated per kg body weight) and HDL cholesterol concentration. VO₂ was related also to the concentrations of LDL and VLDL cholesterol in group A, but these correlations were negative. No consistent association was present between various lipid fractions and VO₂ in the control group.

The correlations between the changes in serum triglycerides, HDL cholesterol, body weight and VO₂ (ml/kg·min) in group A during the training period (between time points II and IV) are shown in table 6. A significant negative association was observed between the changes in HDL cholesterol and fasting serum triglycerides ($r = -0.37$) (fig. 6). Despite the parallel increase in HDL cholesterol and VO₂ during

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**Table 4. Mean Serum HDL Cholesterol, Apolipoprotein AI and Apolipoprotein AlII Concentration and HDL Cholesterol/apolipoprotein AI Ratio in Group A (Training) and Group B (Control) Before (II) and After (IV) the Intervention Period**

<table>
<thead>
<tr>
<th>Group</th>
<th>Time point</th>
<th>HDL cholesterol (mmol/l)</th>
<th>Apolipoprotein AI (mg/dl)</th>
<th>Apolipoprotein AlII (mg/dl)</th>
<th>HDL cholesterol/apolipoprotein AlII (mmol/mg × 10⁴)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>II</td>
<td>1.27 ± 0.04</td>
<td>159 ± 3</td>
<td>40.0 ± 1.0</td>
<td>7.9 ± 1.0</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>1.41 ± 0.04†</td>
<td>161 ± 2</td>
<td>35.8 ± 0.8§</td>
<td>8.4 ± 0.4</td>
</tr>
<tr>
<td>B</td>
<td>II</td>
<td>1.24 ± 0.04</td>
<td>155 ± 3</td>
<td>37.8 ± 1.0</td>
<td>8.1 ± 1.1</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>1.26 ± 0.03§</td>
<td>158 ± 4</td>
<td>35.9 ± 1.0*</td>
<td>8.0 ± 1.0</td>
</tr>
</tbody>
</table>

Values are mean ± SEM.
Significance in difference between time points II and IV, paired comparison:
* $p < 0.05$.
† $p < 0.01$.
§ $p < 0.001$.
Significance in difference between groups A and B:
§§ $p < 0.01$. 

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**FIGURE 4.** Fasting serum low-density lipoprotein (LDL) cholesterol concentration in the exercise and in the control group during the trial. The shaded area represents the time period before the beginning of the exercise intervention. Values are mean ± SEM.

**FIGURE 5.** Fasting serum high-density lipoprotein (HDL) cholesterol concentration in the exercise and in the control group during the trial. The shaded area represents the time period before the beginning of the exercise intervention. Values are mean ± SEM.


### Table 5. Correlations Between Maximal Oxygen Uptake Capacity (Calculated per Kilogram Body Weight) and the Concentration of Various Serum Lipid Fractions in the Training Group (A; n = 44) and in the Control Group (B; n = 46) at the End of the Trial (Time Point IV)

<table>
<thead>
<tr>
<th>Serum lipid fraction</th>
<th>Group A Correlation coefficient (r)</th>
<th>Group B Correlation coefficient (r)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triglyceride</td>
<td>-0.22</td>
<td>-0.23</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>-0.17</td>
<td>-0.06</td>
</tr>
<tr>
<td>VLDL cholesterol</td>
<td>-0.34*</td>
<td>-0.01</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>-0.31*</td>
<td>+0.04</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>+0.31*</td>
<td>+0.10</td>
</tr>
</tbody>
</table>

*p < 0.05.

### Table 6. Correlations Between the Changes in Serum Triglycerides, HDL Cholesterol, Body Weight and VO₂ (ml/kg * min) in the Exercise Group During the Intervention Program (Time Point IV-Time Point II) (n = 44)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Correlation coefficient (r)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDL cholesterol vs body weight</td>
<td>+0.33*</td>
</tr>
<tr>
<td>HDL cholesterol vs VO₂</td>
<td>-0.37*</td>
</tr>
<tr>
<td>HDL cholesterol vs triglycerides</td>
<td>-0.37*</td>
</tr>
<tr>
<td>Triglycerides vs VO₂</td>
<td>+0.23</td>
</tr>
<tr>
<td>Triglycerides vs body weight</td>
<td>-0.08</td>
</tr>
</tbody>
</table>

*p < 0.05.

The training period, a weak negative correlation (r = -0.37) was present between the respective changes in the two parameters (fig. 7). Furthermore, a weak positive correlation (r = 0.33) was present between the changes in HDL cholesterol and body weight despite the opposite changes in the absolute mean values (fig. 8). No correlation (r = 0.13, NS) was observed between the initial VO₂ and the change in HDL cholesterol level.

To further investigate the relationship between the changes in body weight and in serum lipids we calculated separately the lipid levels in those subjects of group A who maintained their body weight within 1 kg during the intervention program. The results (table 7) demonstrate a significant decrease in fasting serum triglycerides and LDL cholesterol concentration and a highly significant increase in HDL cholesterol despite the constant body weight. In fact, the absolute increase in HDL cholesterol was slightly higher in this group than in the whole group A both after mild (time point III) and moderate (time point IV) training. On

### Table 7. Plasma Lipids and Lipoproteins in Subjects of Group A (training group) Who Maintained a Constant Body Weight (within ± 1 kg) During the Exercise Program (n = 25)

<table>
<thead>
<tr>
<th>Serum lipid fraction (nmol/l)</th>
<th>Time point</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>II</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>6.8 ± 0.3</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>1.48 ± 0.11</td>
</tr>
<tr>
<td>VLDL cholesterol</td>
<td>0.79 ± 0.08</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>4.8 ± 0.3</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>1.25 ± 0.05</td>
</tr>
</tbody>
</table>

Significance on difference to the initial value, paired comparison:

* p < 0.05.
† p < 0.001.
the other hand, the concentration of HDL did not change significantly in those subjects of group B who lost more than 1 kg of body weight during the trial (data not shown).

Discussion

A significant but weak association was seen in the baseline studies between VO₂ and VLDL (fasting serum triglyceride and VLDL cholesterol) but not between VO₂ and LDL concentration. This observation is consistent with the few studies published so far on the relationship between serum lipids and work performance. Thus, in a population study comprising 650 middle-aged men, the subjects with maximal oxygen uptake capacity in the lowest quintile had lower serum triglyceride concentrations but normal serum
cholesterol levels compared with the men in the four upper quintiles. Furthermore, asymptomatic men with different types of hyperlipoproteinemia have been reported to have lower working capacity than normolipemic controls. This difference was particularly striking in subjects with hypertriglyceridemia, but was also significant in patients with pure hypercholesterolemia and mixed lipemia.

We observed a highly significant decrease in serum triglyceride and VLDL cholesterol concentration in the training group, but not in the control subjects. The change was evident already after the first 2-month period that consisted of light exercise and was further accentuated during training with higher frequency and intensity. The earlier literature on the effects of physical conditioning on serum triglycerides is partially conflicting: A decrease has been described in several but not in all investigations. It has also been suggested that physical training will lower serum triglycerides only in subjects with true hypertriglyceridemia. This contention is not supported by the present results: A significant decrease occurred both in subjects with normal and elevated triglyceride levels. The contradiction between the present study and some of the earlier results can probably be explained by differences in the experimental design. First, the training period of this investigation lasted for 4 months, in contrast to the shorter programs used in some of the earlier experiments. Second, the decrease in serum triglycerides has been reported to reach the maximum 12-36 hours after a single exercise (sampling time used in this study) with gradual return to the preexercise level in 3-5 days. Thus, subtle changes will probably be overlooked if the measurements are carried out late after the last training session.

The mechanism of the exercise-induced reduction in serum triglyceride concentration is not clear. The decrease cannot be attributed solely to weight reduction, although this factor probably contributes to the change in some subjects. Thus, a highly significant change took place in our subjects who maintained a constant body weight during the entire training program. It was earlier shown that serum triglyceride concentration decreases during an exercise program, even though the participants increase their caloric intake to compensate for additional caloric expenditure. Another possible mechanism, increased uptake of serum triglycerides by the contracting muscle, is probably operative during prolonged heavy exercise, but does not explain the changes during the training programs consisting of less vigorous exercise. Thus, the most likely explanation for the observed decrease in serum triglycerides is a direct but more chronic effect of increased physical activity on VLDL synthesis or catabolism.

Serum cholesterol and LDL cholesterol decreased both in the exercise and in the control subjects. The cause of the parallel changes in LDL concentration in the two groups is not clear, but could be due to the seasonal trends typical for the Finnish population during the spring months (the time of the intervention program of the present study). The earlier literature on the effects of physical training on serum cholesterol level is conflicting. No consistent change has generally been observed, but in some studies the fall in serum cholesterol has been obvious. In any case, our results strongly emphasize the importance of the experimental design of the study. Without randomization to experimental and control groups, the change in LDL cholesterol would probably have been attributed to the exercise program.

The exercise group had a progressive increase in HDL cholesterol that was detectable after mild training. In contrast, the control group showed no alteration in HDL cholesterol, indicating that the change in the exercise group was not due to seasonal variation or other nonspecific factors. Several previous investigations have reported high serum HDL cholesterol levels in subjects who practice strenuous physical exercise. The elevation has, however, been obvious only when exceptionally well-trained persons have been compared with their more sedentary counterparts. In fact, it has been suggested that the threshold for increasing HDL cholesterol is about 70 km of jogging per week. The present results clearly indicate that aerobic training with much lower intensity and frequency will influence the level of HDL cholesterol. The increase observed in all but three of the 44 participants further demonstrate that HDL cholesterol can be modified on most of the previously inactive middle-aged men regardless of the initial HDL cholesterol level.

Although HDL cholesterol increased 11% in the exercise group, no change occurred in the serum concentration of apolipoprotein AI, the major protein component of HDL. Thus, the ratio HDL cholesterol/apolipoprotein AI increased in the training group but remained constant in the control subjects. The concentration of apolipoprotein AII, another peptide of HDL, decreased slightly but significantly in both groups. The cause of the divergent changes in the various components of HDL is unknown. It has earlier been reported that the ratio of HDL cholesterol/apolipoprotein AI varies in different disease states, and in fact, there is some evidence that the level of HDL cholesterol is a better predictor of coronary heart disease than the concentration of apolipoprotein AI. Little is known of the factors that influence the plasma concentration of apolipoprotein AII. The most likely explanation for the parallel decrease of this apolipoprotein in the two experimental groups is seasonal variation. Preliminary calculations based on a larger material (Ehnholm C: unpublished results) suggest that the serum level of apolipoprotein AII is indeed lower in the Finnish population during the spring months than in the fall.

It is not clear whether the exercise-induced elevation of HDL cholesterol is a direct result of the increase in physical training or is due to some other factor associated with physical activity during leisure time. The serum level of HDL is known to be influenced by several factors that might be modified by physical activity or by accompanying changes in
lifestyle. Thus, consumption of alcohol raises HDL cholesterol level, but cigarette smoking may have an opposite action. A carbohydrate-rich diet has been reported to lower the concentration of both HDL cholesterol and apolipoprotein A1. Weight reduction has consistently been shown to raise plasma HDL cholesterol level.

As the diet history of the participants was not recorded, we could not exclude a change in the daily food composition as the cause of the changes in serum HDL cholesterol. However, we consider this explanation less likely for several reasons. Diet instruction was given to the whole experimental group in the beginning of the study to make the diet in the two groups as uniform as possible. Second, experience from a study conducted in American volunteers of similar age suggests that physical training will not induce changes in the ratio of dietary fats, carbohydrates and proteins. It is also unlikely that the exercise group would have increased the consumption of alcohol enough to explain the elevation of HDL cholesterol. Finally, our results clearly demonstrate that weight reduction is not the cause of the increase in HDL cholesterol induced by physical activity. Thus, a weak positive association was observed between the changes in the body weight and HDL cholesterol concentration. Furthermore, a highly significant elevation of HDL cholesterol was seen also in the subjects who maintained their body weight constant during the intervention.

An unexpected finding was the weak but significant negative correlation between the changes in VO2 and HDL cholesterol in the exercise group. This observation might be taken to indicate that physical exercise itself does not cause the increase in HDL cholesterol during the training program. Several reservations should be considered, however. First, other factors, such as the changes in alcohol consumption or in the body weight, may have confounded the positive correlation. Second, the threshold for the exercise-induced increase in HDL cholesterol is low, and the relationship is not linear when the intensity of the training is augmented. Also, a positive, although weak, association was present between HDL cholesterol concentration and VO2 in the exercise group at the end of the experiment.

The variable most strongly associated with the increase in HDL cholesterol in the exercise group was the increase in serum triglycerides. A negative association has earlier been demonstrated in cross-sectional studies between serum triglyceride and HDL cholesterol levels. Also, the concentration of the two lipoprotein classes change into opposite directions under a variety of physiological and pathological conditions. The common denominator in the metabolism of HDL and VLDL has been suggested to be lipoprotein lipase, the enzyme responsible for the catabolism of triglyceride-rich lipoproteins in the peripheral tissues. Thus, a negative correlation has been reported between serum triglyceride concentration and the activity of adipose tissue lipoprotein lipase in normal subjects and in several disease states, whereas a positive relationship is present between HDL cholesterol and the activity of adipose tissue lipoprotein lipase in normal subjects. Furthermore, there is evidence that a part of HDL is derived from the catabolism of VLDL by lipoprotein lipase, although the details of the reaction are not known.

In view of these associations it is interesting that physical exercise has been shown to influence the activity of the lipoprotein lipase system both in man and in experimental animals. Thus, chronic training stimulates the activity of lipoprotein lipase in three skeletal muscle fiber types of rat. In man even the activity of adipose tissue lipoprotein lipase may be augmented by physical exercise. Therefore, one explanation for the reciprocal changes in serum triglycerides and HDL cholesterol during chronic exercise is a transfer in the equilibrium between VLDL and HDL induced by the activation of lipoprotein lipase of skeletal muscle and possibly of adipose tissue. Further evidence to support such a hypothesis can, however, be obtained only by simultaneous measurement of the serum concentrations of VLDL and HDL and the activity of lipoprotein lipase in several peripheral tissues.

In summary, our results suggest that mild-to-moderate physical activity lowers serum triglyceride and raises HDL cholesterol level in healthy, middle-aged men. Our results might also indicate that mild-to-moderate physical exercise is a useful adjunct to therapeutic measures used in the primary and possibly secondary prevention of coronary heart disease. However, caution is necessary in this context. Although the high serum level of HDL cholesterol is associated with low risk of coronary heart disease both in cross-sectional and prospective studies, the causal relationship has not yet been established. Furthermore, HDL fraction measured with the precipitation technique is a heterogeneous mixture of macromolecules, and some evidence suggests that the cholesterol-rich HDL2 subfraction is a better predictor of the development of coronary heart disease than total HDL level. Finally, despite the controlled design of our study we could not exclude the possibility that other changes in the lifestyle than physical activity itself contribute to the favorable development in the lipoprotein spectrum during the exercise programs.

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