Longitudinal Study (32 Years) of Exercise Tolerance, Breathing Response, Blood Pressure, and Blood Lipids in Young Men

Richard F. Gillum, Henry L. Taylor, Joseph Anderson, and Henry Blackburn

Changes in exercise tolerance, blood lipids, and blood pressure from youth to middle age was studied in 106 subjects followed 32 years. In addition, the responses to cold pressor and CO₂ stress were studied as correlates of future lipids and blood pressure. Treadmill exercise test, cold pressor test, response to breathing a mixture of 6% CO₂ and 21% O₂ for 5 minutes, blood pressure, and lipid measurements were performed in 1947 when subjects were 20 ± 2 years old. Exercise, blood pressure and lipid tests were repeated in 1979. Tracking of blood pressure and pulse response to exercise over the period was demonstrated. Baseline exercise response correlated with future blood pressure, cholesterol, triglycerides, and high density lipoproteins. Change in exercise pulse rate over the period correlated with change in cholesterol. Cold pressor systolic blood pressure response correlated with future systolic blood pressure and triglycerides. Pulse and blood pressure response to CO₂ breathing correlated with cholesterol, triglyceride and high density lipoprotein 32 years later. These correlations were independent of baseline values of the variables and body mass index. Individuals who were judged "fit" (exercise pulse rate < median) at both baseline and follow-up had the best cardiovascular risk profile (blood pressure and lipids). Blood pressure and pulse response to exercise tracked between ages 20 and 50. Exercise, cold pressor, and CO₂ responses in youth correlated with blood lipid levels in middle age. (Arteriosclerosis 1:455-462, November/December 1981)

Despite the recent decline in mortality from ischemic heart disease and stroke, these sequelae of arteriosclerosis and hypertension are still leading causes of death among adults and major public health problems in all industrialized nations. Elevated levels of serum cholesterol and blood pressure, together with cigarette smoking, are well established as powerful risk factors for ischemic heart disease. Elevated blood pressure is the primary risk factor for stroke. Recently, increasing attention has been given to the study of physical inactivity both as an independent risk factor for future ischemic heart disease and as a determinant of blood lipid and blood pressure levels. The studies of Paffenbarger et al. have indicated that self-reported physical inactivity in college may be a risk factor for subsequent ischemic heart disease and hypertension. Other studies have indicated that physical inactivity is associated with greater increase in heart rate during exercise, with relative body weight, blood pressure levels, blood cholesterol levels, and lower high density lipoprotein levels. Other studies indicate that exercise training programs favorably alter levels of these risk factors. It has not been determined to what extent changes in physical activity from youth to middle age contribute to the development of the undesirable risk factor profiles that are so prevalent among middle-aged men, but relatively uncommon among children and adolescents.
The cold pressor test has received considerable attention over the years as a possible predictor of future ischemic heart disease and hypertension.13-15 The former has been confirmed in one study of middle-aged men,15 but the latter was not confirmed in a large cohort of young pilots on long-term follow-up.14 The mechanisms that determine the success of the cold pressor test in discriminating between subjects with high and low risk for ischemic heart disease have not been established. Another physiologic stress test receiving some attention, which has not been studied in a prospective manner is the response to an anoxic stimulus with or without 3% to 5% CO₂ in the inspired gas to prevent hypocapnia.16, 17 Yet another stress test uses hyperventilation induced by breathing 5% to 7% CO₂, which has been shown to produce increases in pulse rate, blood pressure, and cardiac output by a combination of direct peripheral vasodilatation and central vasoconstriction.18-22

We had the unique opportunity to prospectively examine changing exercise tolerance and the rise of serum cholesterol and blood pressure from adolescence to middle age in college students extensively studied at baseline and followed for 32 years with repeated measurements of exercise tolerance, blood lipids, and blood pressure. In addition, cold pressor and CO₂ breathing tests were performed at baseline. This paper reports the results of analyses that tested the following hypotheses:

1. Exercise tolerance, as determined by treadmill exercise testing, demonstrates tracking from adolescence to middle age.

2. Change in exercise tolerance is significantly related to change in blood cholesterol and blood pressure between adolescence and middle age.

3. Baseline levels of exercise tolerance, cold pressor response, and CO₂ breathing response are correlates of blood lipid and blood pressure levels at baseline and middle age.

Methods

With the cooperation of the University of Minnesota Student Health Service, we recruited volunteers in 1947 at the time of college entrance physical examination. The students were invited to participate in a study of cardiovascular physiology and aging. The informed consent of all participants was obtained after the procedures were explained. In 1947 all volunteers came to the laboratory in the morning following a fast. A half day of testing included the following:

After undressing and resting quietly at least 10 minutes, the subjects had their blood pressure measured twice in the right arm in a supine position and the two readings averaged. We took a venous blood sample for serum cholesterol (CHL) analysis by the method of Bloor15 and then took a detailed medical history and gave a physical examination. Height, weight, triceps, and subscapular skinfold thickness were measured. A single-stage treadmill exercise test was performed; each subject walked for 15 minutes at 3 miles per hour at a 5% grade. Pulse rate and systolic blood pressure (SBP) were measured in the standing position preceding exercise, at 5-minute intervals during exercise, and for 10 minutes after exercise. A cold pressor test was performed using the following procedure: A resting pulse and blood pressure were determined before the test. Then the subject’s hand was immersed to the wrist in a bucket of ice water for 60 seconds. Pulse and blood pressure were measured at 30 and 60 seconds after immersion and then at 1, 3, and 5 minutes after the hand was withdrawn from the ice water. A CO₂ breathing test was performed as follows: Before the test, pulse rate and SBP were determined with the subject seated. At the 32-year follow-up examination in 1979, the treadmill exercise was repeated using the same procedures as at baseline, except that heart rate was determined from continuous electrocardiographic monitoring rather than pulse rate measurement. One author (HL Taylor) participated in both baseline and follow-up testing. Height, weight, triceps, subscapular skinfold thickness, and blood pressure were measured as at baseline. Plasma CHL, triglyceride (TGL), high density lipoprotein (HDL), and low density lipoprotein (LDL) cholesterol were determined in the laboratory of the Minnesota Lipid Research Clinic using previously described methods.23

Means, standard deviations, and correlation coefficients were calculated using standard methods. Two-tailed p values are presented for all correlations. Differences in means between the two groups were assessed using Student’s t test. Comparisons of means among more than two groups were performed by one-way analysis of variance. Confounding of the relationships by one or more factors was controlled by using partial correlation analysis.

Results

Baseline characteristics of the population in 1947 are shown in table 1. Baseline characteristics of those lost to follow-up were compared to those subjects followed to 1979. There were no significant differences in age, weight, body mass index (BMI), blood pressure; however, baseline serum cholesterol was approximately 10 mg/dl higher in those lost to follow-up. Six of the subjects undergoing follow-up examinations did not have treadmill testing because of previous myo-
Table 1. Baseline and Follow-Up Characteristics of the Study Cohort

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>1947 Mean ± SD</th>
<th>1979 Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>20.5 ± 2</td>
<td>20.5 ± 2.0</td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Height (cm)</th>
<th>1947 Mean ± SD</th>
<th>1979 Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>177.5 ± 6.6</td>
<td>177.7 ± 6.9</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>1947 Mean ± SD</th>
<th>1979 Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>74.1 ± 11.9</td>
<td>87.4 ± 15.2</td>
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</table>

<table>
<thead>
<tr>
<th>Relative weight (%)</th>
<th>1947 Mean ± SD</th>
<th>1979 Mean ± SD</th>
</tr>
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<tbody>
<tr>
<td>107.3 ± 15.6</td>
<td>112.1 ± 17.5</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Body mass index (kg · m⁻²)</th>
<th>1947 Mean ± SD</th>
<th>1979 Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>23.5 ± 3.6</td>
<td>27.6 ± 4.2</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Sum skinfolds (mm) *</th>
<th>1947 Mean ± SD</th>
<th>1979 Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>27.1 ± 11.4</td>
<td>33.5 ± 11.3</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Body density (kg · m⁻³)</th>
<th>1947 Mean ± SD</th>
<th>1979 Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.069 ± 0.016</td>
<td>1.075 ± 0.009</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Total cholesterol (mg · dl⁻¹)</th>
<th>1947 Mean ± SD</th>
<th>1979 Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>172.5 ± 32.2</td>
<td>206.0 ± 38.5</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>LDL cholesterol (mg · dl⁻¹)</th>
<th>1947 Mean ± SD</th>
<th>1979 Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>45.4 ± 10.9</td>
<td>50.0 ± 13.8</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HDL cholesterol (mg · dl⁻¹)</th>
<th>1947 Mean ± SD</th>
<th>1979 Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.01 ± 0.99</td>
<td>3.8 ± 0.75</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>LDL/HDL</th>
<th>1947 Mean ± SD</th>
<th>1979 Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Triglycerides</th>
<th>1947 Mean ± SD</th>
<th>1979 Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>136.6 ± 74.2</td>
<td>138.7 ± 76.5</td>
<td></td>
</tr>
</tbody>
</table>

Table 2 presents correlations of exercise response variables with follow-up exercise variables. With the exception of resting pulse, each baseline variable was correlated significantly with its counterpart at 32-year follow-up. The magnitude of this correlation was approximately 0.40. This demonstrates a remarkable degree of tracking (the tendency of an individual to maintain his relative rank in a population over time) over a long follow-up period.

Table 4 presents cross-sectional correlations of exercise pulse rate with blood pressure and blood lipids at baseline and follow-up. The rise in pulse rate with exercise was significantly correlated with body mass index \[ \text{BMI} = \frac{\text{weight (kg)}}{\text{height}^2 (\text{m}^2)} \] and skinfold thickness at both baseline and follow-up.
follow-up. Change in pulse rate was also significantly correlated with blood cholesterol (CHL) at both times and also with blood triglyceride (TGL) levels at follow-up. No significant correlation of any of the exercise variables with high density lipoprotein (HDL) was noted. Partial correlation analyses revealed these correlations to be independent of age, height, and BMI.

Table 5 presents correlations of baseline exercise pulse variables with 32-year follow-up levels of blood pressure and blood lipids. Exercise pulse was a significant correlate of follow-up SBP, while change in pulse was a significant correlate of follow-up blood CHL, HDL, TGL, and LDL/HDL ratio. These correlations were independent of weight, BMI and blood CHL at baseline and of change in weight or BMI between baseline and follow-up.

Exercise SBP was significantly correlated with resting blood pressure, weight, body mass index,
skinfold thickness and blood cholesterol at baseline and follow-up (table 6). The correlations with cholesterol were independent of body mass index. Baseline 10- and 15-minute exercise SBP was significantly correlated with follow-up triglyceride levels \( r = 0.31 \) and \( 0.34, p < 0.01 \). A 10- and 15-minute SBP rise was also significantly correlated with follow-up TGL levels. Correlations of exercise SBP with follow-up rest SBP were similar to those of resting baseline SBP with follow-up SBP \( r = 0.32, p < 0.01 \). Change in SBP at baseline was not significantly correlated with follow-up blood pressure.

Change in exercise pulse rate between baseline and follow-up was significantly correlated with change in the following variables over the same period: SBP \( r = 0.24, p < 0.05 \), blood CHL \( r = 0.28, p < 0.01 \). Only the correlation of change in exercise pulse rate to blood pressure and lipids at follow-up was significantly correlated with follow-up TGL levels. Correlations with follow-up SBP were, as expected, well correlated with change in resting blood pressure, however, there was no significant correlation with change in blood CHL.

Table 7 shows the relationship of three measures of response to exercise at both baseline and follow-up to blood pressure and lipids at follow-up. Subjects judged to be “fit” at both examinations tended to have lower SBP, CHL, LDL, TGL, and higher HDL at follow-up. Results for HDL were essentially unchanged when current smokers and daily users of alcohol were excluded.

### Table 6. Correlation of Follow-up Blood Pressure and Blood Lipids with Baseline Exercise and Blood Pressure

<table>
<thead>
<tr>
<th>Baseline (1947) exercise systolic blood pressure</th>
<th>10-min rise</th>
<th>15-min rise</th>
<th>10-min rise</th>
<th>15-min rise</th>
</tr>
</thead>
<tbody>
<tr>
<td>1979 measurements:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP</td>
<td>0.62*</td>
<td>0.59*</td>
<td>0.08</td>
<td>-0.04</td>
</tr>
<tr>
<td>DBP</td>
<td>0.30*</td>
<td>0.30*</td>
<td>-0.04</td>
<td>-0.09</td>
</tr>
<tr>
<td>Chol</td>
<td>0.29*</td>
<td>0.32*</td>
<td>0.20†</td>
<td>0.20†</td>
</tr>
<tr>
<td>LDL</td>
<td>0.14</td>
<td>0.15</td>
<td>0.12</td>
<td>0.12</td>
</tr>
<tr>
<td>HDL</td>
<td>-0.05</td>
<td>-0.10</td>
<td>-0.22†</td>
<td>-0.29*</td>
</tr>
<tr>
<td>TGL</td>
<td>0.26*</td>
<td>0.35*</td>
<td>0.24†</td>
<td>0.34*</td>
</tr>
<tr>
<td>Wt</td>
<td>0.38*</td>
<td>0.36*</td>
<td>0.28*</td>
<td>0.21†</td>
</tr>
<tr>
<td>SF</td>
<td>0.37*</td>
<td>0.37*</td>
<td>0.33*</td>
<td>0.28*</td>
</tr>
</tbody>
</table>

SBP = systolic blood pressure; DBP = diastolic blood pressure; Wt = weight; BMI = body mass index; SF = skinfold thickness; Chol = cholesterol; LDL = low density lipoproteins; HDL = high density lipoproteins; TGL = triglycerides.

*Student’s \( t \) test, both vs neither, \( p < 0.05 \).
†Student’s \( t \) test, both vs neither, \( p < 0.05 \) when subjects with a TGL level greater than 500 were excluded.

\( F \) = one-way analysis statistical test; \( p \) = probability factor; for other abbreviations see table 4.

### Table 7. Heart Rate Response to Exercise at Baseline and Follow-up and Blood Pressure and Blood Lipids at Follow-up

<table>
<thead>
<tr>
<th>Response measure 1 (15-min exercise pulse ≤ median):</th>
<th>Mean:</th>
<th>SBP</th>
<th>DBP</th>
<th>Chol</th>
<th>LDL</th>
<th>HDL</th>
<th>TGL</th>
<th>LDL/HDL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Below median at</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Both</td>
<td>32</td>
<td>129.7</td>
<td>83.3</td>
<td>192.6</td>
<td>123.5</td>
<td>47.4</td>
<td>108.9</td>
<td>2.7</td>
</tr>
<tr>
<td>1979 only</td>
<td>19</td>
<td>130.7</td>
<td>83.4</td>
<td>202.7</td>
<td>132.9</td>
<td>46.2</td>
<td>117.6</td>
<td>3.1</td>
</tr>
<tr>
<td>1947 only</td>
<td>18</td>
<td>129.9</td>
<td>80.5</td>
<td>210.4</td>
<td>138.2</td>
<td>45.5</td>
<td>133.3</td>
<td>3.2</td>
</tr>
<tr>
<td>Neither</td>
<td>27</td>
<td>139.2</td>
<td>82.6</td>
<td>217.4</td>
<td>132.8</td>
<td>44.1</td>
<td>187.3</td>
<td>3.0</td>
</tr>
<tr>
<td>F</td>
<td>1.9</td>
<td>0.25</td>
<td>0.20</td>
<td>0.06</td>
<td>0.46</td>
<td>3.2</td>
<td>1.4</td>
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<tr>
<td>( p )</td>
<td>0.13</td>
<td>0.87</td>
<td>0.12</td>
<td>0.41</td>
<td>0.71</td>
<td>0.03</td>
<td>0.24</td>
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</table>

<table>
<thead>
<tr>
<th>Response measure 2 (15-min exercise pulse change ≤ median):</th>
<th>Mean:</th>
<th>SBP</th>
<th>DBP</th>
<th>Chol</th>
<th>LDL</th>
<th>HDL</th>
<th>TGL</th>
<th>LDL/HDL</th>
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<tbody>
<tr>
<td>Below median at</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Both</td>
<td>33</td>
<td>132.7</td>
<td>84.4</td>
<td>196.1</td>
<td>128.1</td>
<td>46.5</td>
<td>107.4</td>
<td>2.9</td>
</tr>
<tr>
<td>1979 only</td>
<td>16</td>
<td>135.6</td>
<td>81.6</td>
<td>195.0</td>
<td>123.2</td>
<td>44.1</td>
<td>138.5</td>
<td>3.0</td>
</tr>
<tr>
<td>1947 only</td>
<td>22</td>
<td>124.7</td>
<td>78.0</td>
<td>205.0</td>
<td>130.0</td>
<td>47.3</td>
<td>138.3</td>
<td>2.8</td>
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<tr>
<td>Neither</td>
<td>25</td>
<td>137.5</td>
<td>83.7</td>
<td>222.8</td>
<td>140.0</td>
<td>44.8</td>
<td>174.5</td>
<td>3.1</td>
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<tr>
<td>F</td>
<td>2.5</td>
<td>1.9</td>
<td>2.5</td>
<td>1.1</td>
<td>0.40</td>
<td>1.9</td>
<td>0.878</td>
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<tr>
<td>( p )</td>
<td>0.07</td>
<td>0.13</td>
<td>0.06</td>
<td>0.35</td>
<td>0.75</td>
<td>0.13</td>
<td>0.57</td>
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<table>
<thead>
<tr>
<th>Response measure 3 (15-min exercise pulse ≤ 30th percentile):</th>
<th>Mean:</th>
<th>SBP</th>
<th>DBP</th>
<th>Chol</th>
<th>LDL</th>
<th>HDL</th>
<th>TGL</th>
<th>LDL/HDL</th>
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<tbody>
<tr>
<td>Below median at</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Both</td>
<td>14</td>
<td>123.6</td>
<td>80.1</td>
<td>189.3</td>
<td>119.8</td>
<td>47.9</td>
<td>107.7</td>
<td>2.6</td>
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<tr>
<td>1979 only</td>
<td>14</td>
<td>131.0</td>
<td>83.9</td>
<td>200.6</td>
<td>130.8</td>
<td>46.1</td>
<td>118.4</td>
<td>3.0</td>
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<tr>
<td>1947 only</td>
<td>21</td>
<td>129.5</td>
<td>81.6</td>
<td>197.5</td>
<td>130.4</td>
<td>44.9</td>
<td>111.0</td>
<td>3.1</td>
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<td>47</td>
<td>137.1</td>
<td>82.7</td>
<td>214.1</td>
<td>134.0</td>
<td>45.7</td>
<td>163.4</td>
<td>3.0</td>
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<td>F</td>
<td>2.8</td>
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<td>1.8</td>
<td>0.7</td>
<td>0.2</td>
<td>2.0</td>
<td>0.9</td>
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<tr>
<td>( p )</td>
<td>0.05</td>
<td>0.8</td>
<td>0.16</td>
<td>0.6</td>
<td>0.9</td>
<td>0.1</td>
<td>0.5</td>
<td></td>
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</tbody>
</table>

*Student’s \( t \) test, both vs neither, \( p < 0.05 \).
†Student’s \( t \) test, both vs neither, \( p < 0.05 \) when subjects with a TGL level greater than 500 were excluded.

\( F \) = one-way analysis statistical test; \( p \) = probability factor; for other abbreviations see table 4.
At baseline, pulse rate response to cold pressor stimulus was significantly correlated only with SBP (r = 0.42, p < 0.001). It was not predictive of blood pressure or blood lipids at follow-up. SBP at 60 seconds was significantly correlated with serum CHL at baseline only and with SBP (r = 0.31, p < 0.001) at follow-up. Change in SBP with cold stimulus was correlated with blood CHL at baseline (r = 0.33, p < 0.001) with follow-up SBP (r = 0.23, p < 0.05) and with follow-up blood TGL (r = 0.26, p < 0.01). The 60-second diastolic blood pressure (DBP) and change in DBP were not correlated with CHL at baseline nor with blood pressure or blood lipids at follow-up.

Pulse response to CO₂ stimulus at 5 minutes was significantly correlated with SBP at baseline (r = 0.41, p = 0.001), but not with CHL or hemoglobin at baseline. CO₂ blood pressure response was not correlated with CHL or hemoglobin at baseline. Change in pulse rate in response to 5 minutes of CO₂ breathing was significantly correlated with follow-up blood TGL (r = 0.34, p = 0.01) and HDL (r = 0.36, p = 0.008). Change in SBP from rest to five minutes of CO₂ breathing was significantly correlated with follow-up CHL (r = 0.27, p = 0.05), triglyceride (r = 0.42, p = 0.002) and HDL (r = 0.29, p = 0.04). Partial correlation analysis revealed these correlations to remain significant after controlling for baseline cholesterol, baseline body mass index, change in BMI from baseline to follow-up, singly and together (table 8). Pulse and SBP response to CO₂ were not related to 1979 smoking or alcohol use. This eliminated the possibility of confounding by these correlates of HDL.

### Table 8. Partial Corrections of Baseline CO₂-Induced Rise in Pulse and SBP with Follow-Up Cholesterol and Triglyceride

<table>
<thead>
<tr>
<th>Controlling: Baseline cholesterol</th>
<th>Pulse rise</th>
<th>SBP rise</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chol</td>
<td>0.26</td>
<td>0.23</td>
</tr>
<tr>
<td>TGL</td>
<td>0.36†</td>
<td>0.40†</td>
</tr>
<tr>
<td>HDL</td>
<td>-0.36†</td>
<td>-0.29*</td>
</tr>
<tr>
<td>Baseline BMI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chol</td>
<td>0.18</td>
<td>0.27</td>
</tr>
<tr>
<td>TGL</td>
<td>0.35†</td>
<td>0.42†</td>
</tr>
<tr>
<td>HDL</td>
<td>-0.34†</td>
<td>-0.29*</td>
</tr>
<tr>
<td>Change in BMI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chol</td>
<td>0.18</td>
<td>0.28</td>
</tr>
<tr>
<td>TGL</td>
<td>0.32*</td>
<td>0.41†</td>
</tr>
<tr>
<td>HDL</td>
<td>-0.36†</td>
<td>-0.28*</td>
</tr>
<tr>
<td>All</td>
<td>0.19</td>
<td>0.20</td>
</tr>
<tr>
<td>TGL</td>
<td>0.32*</td>
<td>0.38†</td>
</tr>
<tr>
<td>HDL</td>
<td>-0.33*</td>
<td>-0.29*</td>
</tr>
</tbody>
</table>

*p ≤ 0.05.
†p ≤ 0.01.

Discussion

The present study reveals tracking of heart rate and pulse and blood pressure response to exercise over a 32-year period. In addition, several exercise pulse and blood pressure response variables are related to blood pressure and lipid levels both cross-sectionally and prospectively over a 32-year follow-up period. These relationships appear to be independent of BMI. None of these variables explained more than 10% of the variation in follow-up blood pressure or lipid levels. Cold pressor test pulse rate and blood pressure response at baseline were not correlates of follow-up blood pressure or blood lipids. However, pulse and SBP response to CO₂ breathing were significantly correlated with follow-up levels of CHL, TGL, and HDL.

The current findings are consistent with the observation of Paffenbarger et al. that levels of self-reported physical activity in youth may be predictive of subsequent ischemic heart disease and hypertension. The present study suggests that the effects on blood lipids and blood pressure may be important in explaining this observation. Self-reported activity levels were not measured in the present cohort at baseline. It is generally assumed that heart rate response to exercise is determined by fitness and hence by habitual physical activity, together with genetically determined constitutional factors. Also consistent with Paffenbarger's findings is the present observation that individuals judged "fit" at both baseline and follow-up have the best risk profile; those judged "fit" at either time, the worst; and those judged to be "fit" at only one time, intermediate values (Table 7). The lack of cross-sectional correlation of exercise pulse rate with HDL values is consistent with other observations that the degree of habitual physical activity is a better predictor than measured cardiopulmonary fitness among sedentary middle-aged subjects, but not among active college students. In light of this, the finding that baseline exercise variables are significantly related to HDL at 32-year follow-up is all the more intriguing. We suggest that some determinant, (e.g., sympathetic nervous system reactivity) of the cardiovascular response to the stress of physical activity, as well as to the perhaps analogous stimulus of CO₂ breathing in youth may also be a determinant or a correlate of a determinant of HDL levels. It is puzzling that such a relationship should no longer hold in middle age.

Exercise, cold exposure, and hypercapnia all activate the central nervous system to evoke sympathetic nervous and, to a lesser extent, adrenal responses. Sympathetic nervous activity not only has pressor effects but also affects lipid metabolism by stim-
ulating lipolysis. The resulting release of free fatty acids from adipose tissue may provide more substrate for hepatic synthesis of triglyceride-rich, very low density lipoprotein (VLDL) which may then form cholesterol-rich LDL. The role of the sympathetic system in HDL metabolism is not understood. Beta adrenergic blockade with propranolol has been found to decrease HDL level and increase triglycerides in hypertensives. The evidence regarding the chronic effects of exercise and emotional stress on blood pressure and total cholesterol is conflicting.

The present study confirms other observations about the lack of predictive power of the cold pressor test for future hypertension. The predictive power of the cold pressor test in middle age for subsequent ischemic heart disease is probably related to the existence of preclinical arteriosclerotic vascular disease.

The subjects studied in the current investigation obviously represent a very select and homogeneous group. This fact has the advantage of reducing or eliminating the possibility of confounding the results by variables related to blood pressure and blood lipids, such as age, sex, race, and socioeconomic status. While strengthening the study's internal validity, this same fact limits its external generalizability. In addition, the relatively small sample size of the cohort affects the precision of estimation of statistical parameters and hence the power to detect weak relationships. The rather substantial loss to follow-up over the 32-year interval could impair the generalizability of the analyses presented here. Another potential source of bias might be a change in measurement techniques for exercise over the time span between examinations, especially if such changes were nonrandom and somehow related to baseline levels of exercise, cold pressor or CO2 variables, and to blood pressure and blood cholesterol. The use of different blood cholesterol techniques at baseline and follow-up precludes precise estimation of absolute change. We used great care to duplicate the original exercise procedures at the follow-up examination, and it seems unlikely that inadvertent departure from it would be differentially related to any one particular subgroup. A cold pressor test preceded exercise by 5 to 15 minutes at baseline but not at follow-up. Any such systematic bias would not severely affect the validity of correlation coefficients; however, it would make an error of unknown quantity in the estimates of absolute change in pulse and blood pressure response to exercise over the follow-up period.

Results of the present study have important implications for the primary prevention of ischemic heart disease and hypertension. They suggest that cardiovascular fitness as measured by pulse response to exercise is a correlate of cardiovascular risk factors, blood pressure, and blood lipids, independent of body weight. Further research is needed to determine whether the determinants of cardiopulmonary fitness and response to CO2 breathing are related to blood pressure and blood lipids independent of habitual physical activity.

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