Hostility and Physiological Risk in the National Heart, Lung, and Blood Institute Family Heart Study

Sarah S. Knox, PhD; Gerdi Weidner, PhD; Avril Adelman, MA; Catherine M. Stoney, PhD; R. Curtis Ellison, MD; for the Investigators of the National Heart, Lung, and Blood Institute Family Heart Study

**Background:** The present analyses investigated possible pathways for earlier reported associations in the National Heart, Lung, and Blood Institute Family Heart Study between hostility and coronary and carotid end points.

**Methods:** The cross-sectional design recruited 535 women and 491 men with average familial risk for coronary heart disease and 1950 women and 1667 men with high familial coronary risk from 3 prospective ongoing studies at 4 sites. Recruitment of high-risk participants was based on family risk score. Average-risk participants came from a randomly selected group. Outcome measures were plasminogen activator inhibitor type 1 (PAI-1), homocysteine, fibrinogen, fasting glucose, blood pressure, high-density lipoprotein cholesterol, triglycerides, low-density lipoprotein cholesterol, and “lipid metabolic disorder” (LMD) (defined as systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg; fasting glucose ≥126 mg/dL (≥7.0 mmol/L) or the use of diabetes medications; body mass index (calculated as weight in kilograms divided by the square of height in meters) ≥30; triglycerides ≥250 mg/dL (≥2.8 mmol/L), high-density lipoprotein cholesterol <40 mg/dL (<1.0 mmol/L) in men and <50 mg/dL (<1.3 mmol/L) in women; and low-density lipoprotein cholesterol level ≥130 mg/dL (≥3.4 mmol/L).

**Results:** After adjustment for age and risk-related behaviors, hostility was significantly associated with glucose level and LMD in high-risk women, with LMD in average-risk women, with PAI-1 and LMD in high-risk men, and with fibrinogen level in average-risk men.

**Conclusions:** Associations between hostility and physiological risk were only partially accounted for by health behaviors, suggesting that further investigation of mechanistic pathways is warranted.

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Evidence that hostility is a risk factor for cardiovascular disease has been accumulating for longer than a decade. Population-based studies have reported significantly greater risk of morbidity, including coronary calcification, and mortality in individuals with high levels of hostility. One such study showed associations between hostility and all-cause mortality in both sexes, but significant associations with incident myocardial infarction only in women. In the National Heart Lung and Blood Institute (NHLBI) Family Heart Study, hostility was associated with higher risk of coronary heart disease (CHD) in individuals with high familial risk for CHD but not in a random sample, and with increased risk for carotid artery atherosclerosis in the group with high familial risk but not in individuals with average risk. In both instances, the associations seemed to be strongest in the high-risk women.

The goal of the present analyses of the NHLBI Family Heart Study cohort data was to investigate physiological risk factors that might mediate the associations between hostility and cardiovascular end points that we found in previous analyses. Our hypothesis was that hostility would be associated with multiple measures of cardiovascular risk, but that these associations would be only partially explained by the influence of hostility on health-related behaviors. Associations not explained by health-related behaviors were hypothesized to be associated with central nervous system changes associated with hostile affect. Earlier studies have demonstrated modified adrenergic responsiveness and changes in heart rate variability in association with hostility that indicate neuroendocrine influences unrelated to health behaviors.
METHODS

COHORT DESCRIPTION AND SELECTION

The NHLBI Family Heart Study is a multicenter, population-based study designed to identify and evaluate genetic and non-genetic determinants of CHD, preclinical atherosclerosis, and cardiovascular disease risk factors. A description of the methods and design was previously published.12 Families were chosen at random or on the basis of higher-than-expected risk of CHD (high-risk group) from previously established population-based cohort studies, including the Framingham Heart Study (in Framingham, Mass), the Atherosclerosis Risk in Communities cohort (in North Carolina and Minnesota), and the Utah Health Family Tree Study (in Salt Lake City). The high-risk group was defined on the basis of a family risk score, which reflects a comparison of the family’s age- and sex-specific incidence of CHD with that expected in the general population.13 The study protocol was approved by institutional review boards at each site.

Among families selected at random were a number of families exhibiting high risk for CHD. For the purpose of the prent analyses, all probands with high family risk scores, including those from the random group, were combined into a high-risk group. This resulted in the following 2 comparisons: subjects with a high familial risk for CHD and those with a low-to-medium familial risk (hereafter referred to as the average-risk group). There were 1026 average-risk subjects from 291 families and 3617 high-risk subjects from 915 families. Because 95.6% of the sample was of European descent, there was not enough power for reliable analyses in African American subjects; therefore, only data from the European American subjects are reported in this study. The final groups consisted of 491 average-risk men, 1667 high-risk men, 535 average-risk women, and 1950 high-risk women. At the time of the study’s clinic visit, the ages of the participants ranged from 25 to 93 years.

HOSTILITY

Hostility was measured as the total of the following 3 subscales from the Cook and Medley Hostility Scale14: cynicism, hostile affect, and aggressive responding. These particular subscales were chosen for the study because of their demonstrated ability to predict early mortality in a prospective study of lawyers.15 That study indicated that the sum of these 3 subscales was a better predictor of mortality than the full Cook-Medley scale, so the measure used in the present study is a combined measure of these 3 subscales. Because the number of items on the different subscales varied from 5 to 13, meaning that a total hostility score would give more weight to the scale with the most items, the average score of each scale was used so that all subscores would have equal weight. Because the items were scored as true or false (0 or 1), the scaling was standardized so that the score on each subscale ranged from 0 to 1; thus, the total hostility subscale score could range from 0 to 3.

HEALTH-RELATED BEHAVIORS

Information on lifestyle factors was obtained by interview during the clinic visit. These factors included current smoking status, alcohol consumption (type of alcohol and number of glasses, converted to total grams of alcohol per week), and the energy expended in physical activity coded as metabolic (MET) minutes per week. This was calculated by adding the metabolic index in MET minutes per week attributed to strenuous, moderate, and light physical activity, where strenuous is defined as requiring 8 METs; medium, 4 METs; and light, 1.5 METs.16 Body mass index (BMI; calculated as weight in kilograms divided by the square of height in meters) was used as the best proxy for the balance between energy intake and expenditure.

PHYSIOLOGICAL RISK FACTORS

Because earlier studies have reported associations between hostility and physiological risk factors such as lipids,17,18 homocysteine,19 fasting glucose,20 and clotting factors,21 these variables were included in the analyses as possible mediating pathways, along with seated blood pressure (average of the second and third measurements) after a 5-minute rest, measured with a random-zero sphygmomanometer. Also included were concentrations of plasminogen activator inhibitor type 1 (PAI-1), fibrinogen, fasting glucose, and lipids.

The fact that a cluster of factors including elevated blood pressure, high abdominal obesity, elevated fasting glucose level, low concentrations of high-density lipoprotein cholesterol (HDL-C), and high concentrations of triglycerides, often referred to as the metabolic syndrome, has been associated with increased cardiovascular risk,12,22 prompted us to investigate possible pleotropic influences of hostility on metabolic functioning. We wanted to know whether hostility was associated with serious metabolic dysfunction. The metabolic syndrome involves a cluster of risk factors that increases cardiovascular risk at any given level of low-density lipoprotein (LDL-C).23 The lipid metabolic index created for the present study instead included LDL-C concentration as one of the components. To further ensure robustness, we decided to define the lipid metabolic index as being present when at least 4 factors (rather than the 3 factors called for in Adult Treatment Panel III guidelines) had significantly elevated levels. These included blood pressure equivalent to stage 1 hypertension24 (ie, systolic blood pressure $\geq$140 mm Hg or diastolic blood pressure $\geq$90 mm Hg or the use of blood pressure medication), fasting glucose levels high enough to indicate diabetes25 (ie, $\geq$126 mg/dL [\$\geq$7.0 mmol/L]) or the use of diabetes medication, BMI greater than or equal to 30, triglyceride level of greater than 250 mg/dL (\$>\text{2.8 mmol}/\text{L})$, HDL-C less than 40 mg/dL ($<\text{1.0 mmol}/\text{L}$) for men and less than 50 mg/dL ($<\text{1.3 mmol}/\text{L}$) for women, and LDL-C greater than or equal to 130 mg/dL ($\geq$3.4 mmol/L). Because men and women with high familial risk for CHD in this cohort had shown increased risk for clinical events, we wanted to use a robust indicator of metabolic dysfunction in our search for mediators.

BLOOD COLLECTION AND ASSAYS

Blood was drawn from the antecubital vein after 12 hours of fasting. Vacuum tubes (Becton Dickinson and Co, Franklin Lakes, NJ) without additives were used for measurement of lipids and glucose, and vacuum tubes with citrate (citrate-blood ratio of 1:9) were used for measurement of PAI-1 antigen and fibrinogen. We added EDTA to vacuum tubes for homocysteine analyses. Samples were stored in a $-70^\circ\text{C}$ freezer, then shipped on dry ice to the Family Health Study Central Laboratory at the Department of Laboratory Medicine and Pathology, University of Minnesota, Minneapolis. Level of PAI-1 antigen was measured by means of enzyme-linked immunosorbent assay26 using reagents from Diagnostica Stago, Inc, Parsippany, NJ (Asserachrom PAI-1 kit 00577). Plasma fibrinogen was measured by using the Clauss method.27 Concentrations of plasma cholesterol, triglycerides, and HDL-C were analyzed using enzymatic methods; LDL-C was calculated according to the Friedewald equation except...
when triglyceride values exceeded 400 mg/dL (>4.5 mmol/L) when it was measured by means of ultracentrifugation. Twenty serum glucose was measured on a clinical chemistry slide (EKTACHEM; Eastman Kodak Co, Rochester, NY), and total plasma homocysteine was determined by means of high-performance liquid chromatography with fluorescence detection, using a modification of a method originally described by Araki and Sako.

### STATISTICAL ANALYSIS

Generalized estimating equations were used to calculate multiple regression coefficients. Family was specified as the clustering variable, and robust standard errors of estimate were obtained under an independence working correlation matrix to account for the dependence of the data within families. All analyses were conducted using the SAS software package version 6.12 (SAS Institute Inc, Cary, NC). Analyses of hostility were stratified by age and because the subjects older than 65 years had slightly higher hostility scores than those younger, each individual physiological risk variable was first regressed on hostility and age. The risk variables were then regressed on hostility and age plus the covariates representing other health-related behaviors. The goal was to ascertain whether the individual associations with hostility were mediated by health-related behaviors. Because the aim was to understand the relative importance of individual health behaviors in explaining the association of hostility to physiological risk factors, the raw scores of all variables were first standardized to a mean of zero and an SD of 1. This meant that the regression coefficients resulting from the SAS GENMOD analyses were also standardized so that the reduction in \( \beta \) values resulting from each covariate could be compared with the reduction associated with other covariates to ascertain their relative importance. We also indicated the covariate that was most important in explaining variance of variables that go from significant to nonsignificant.

### RESULTS

Descriptive characteristics of the cohort can be seen in Table 1. The high-risk group had significantly worse lipid profiles than the average-risk group, was more likely to include smokers, and had higher diastolic blood pressure.

Table 2, 3, 4, and 5 show the associations in the different groups between hostility and the physiological variables with adjustments for age only and also for additional relevant health-related behaviors. In the case where a value went from significant to nonsignificant after adjustment, the covariate that was most responsible for reducing the \( \beta \) value is listed, with the \( \beta \) value for the covariate in the model in parentheses.

#### FIBRINOGEN

Hostility was significantly associated with fibrinogen in all groups. After adjusting for health-related behaviors, it was reduced to nonsignificance in all groups except average-risk men. Average-risk women were still at borderline significance (\( P = .06 \)). The covariates that were responsible for most of the reduction in the \( \beta \) coefficients were BMI in women and smoking in men.

#### HOMOCYSTEINE

The only significant association between hostility and homocysteine was in high-risk women. These results can be seen in Table 2. After controlling for health-related behaviors, the association was no longer significant. Follic acid intake accounted for the greatest reduction in the standardized regression coefficient.
An association between hostility and PAI-1 was found only in women, but after adjusting for all covariates, including exogenous hormones, the association was no longer significant. The variables that accounted for most of the reduction in the β value were BMI in high-risk women and physical activity in average-risk women.

**LIPIDS**

The only lipid showing an association with hostility was HDL-C in high-risk women. After adjustment, the association was no longer significant, and BMI was again the variable that most reduced the β coefficient.

**BLOOD PRESSURE**

Blood pressure was not associated with hostility in any group.

**FASTING GLUCOSE**

Subjects with diabetes were excluded from the analyses of fasting glucose. Hostility was associated with glucose only in high-risk women. This association remained significant after adjusting for all covariates.

**LIPID METABOLIC DISORDER**

After adjusting for all covariates, hostility was significantly associated with the presence of the lipid metabolic disorder in high- and average-risk women and in high-risk men. To test the robustness of these results, they were recalculated using only 1 member of each family, and the results were still significant.

Earlier analyses in this cohort revealed associations between hostility and CHD and between hostility and carotid artery atherosclerosis only in groups with high familial risk for CHD. In the present analyses, which were designed to examine mediating mechanisms in the same cohort, hostility was associated with 6 of the 10 physiological risk factors in age-adjusted regressions in the high-risk men. To test the robustness of these results, they were recalculated using only 1 member of each family, and the results were still significant.

### Table 2. Associations of Hostility With Physiological Risk Factors in High-Risk Women*

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Age Adjusted β</th>
<th>Fully Adjusted β</th>
<th>Covariate That Most Reduces β Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fully Adjusted</strong></td>
<td><strong>P</strong></td>
<td><strong>P</strong></td>
<td></td>
</tr>
<tr>
<td>Fibrinogen level</td>
<td>.070</td>
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<td>.039</td>
</tr>
<tr>
<td>Homocysteine level</td>
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<td>.01</td>
<td>.058</td>
</tr>
<tr>
<td>PAI-1 level</td>
<td>.062</td>
<td>.02</td>
<td>.018</td>
</tr>
<tr>
<td>Glucose level‡</td>
<td>.076</td>
<td>.001</td>
<td>.057</td>
</tr>
<tr>
<td>HDL-C concentration</td>
<td>−.052</td>
<td>.03</td>
<td>−.025</td>
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<tr>
<td>LDL-C concentration</td>
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<td>.024</td>
</tr>
<tr>
<td>Triglyceride level</td>
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<td>.47</td>
<td>−.005</td>
</tr>
<tr>
<td>Diastolic BP‡</td>
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<td>.50</td>
<td>−.024</td>
</tr>
<tr>
<td>Systolic BP‡</td>
<td>.023</td>
<td>.39</td>
<td>.010</td>
</tr>
<tr>
<td>LMD</td>
<td>.242</td>
<td>.01</td>
<td>.250</td>
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</tbody>
</table>

**Abbreviations:** BMI, body mass index; BP, blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LMD, lipid metabolic disorder; PAI-1, plasminogen activator inhibitor type 1.
*Fully adjusted analyses controlled for smoking status, alcohol consumption, and physical activity. All except for metabolic index also were adjusted for BMI. Homocysteine level was also adjusted for folic acid and vitamin B<sub>12</sub> intake. In women, PAI-1 was also adjusted for exogenous hormone use.
‡Excludes subjects receiving hypertensive medication.

### Table 3. Associations of Hostility With Physiological Risk Factors in Average-Risk Women*

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Age Adjusted β</th>
<th>Fully Adjusted β</th>
<th>Covariate That Most Reduces β Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fully Adjusted</strong></td>
<td><strong>P</strong></td>
<td><strong>P</strong></td>
<td></td>
</tr>
<tr>
<td>Fibrinogen level</td>
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<td>.008</td>
<td>.076</td>
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<tr>
<td>Homocysteine level</td>
<td>.016</td>
<td>.73</td>
<td>−.050</td>
</tr>
<tr>
<td>PAI-1 level</td>
<td>.101</td>
<td>.05</td>
<td>.042</td>
</tr>
<tr>
<td>Glucose level‡</td>
<td>.100</td>
<td>.07</td>
<td>.073</td>
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<tr>
<td>HDL-C concentration</td>
<td>−.097</td>
<td>.06</td>
<td>−.062</td>
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<tr>
<td>LDL-C concentration</td>
<td>.066</td>
<td>.10</td>
<td>.054</td>
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<td>Triglyceride level</td>
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<td>.010</td>
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<tr>
<td>Diastolic BP‡</td>
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<td>.94</td>
<td>−.023</td>
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<td>Systolic BP‡</td>
<td>.053</td>
<td>.21</td>
<td>.030</td>
</tr>
<tr>
<td>LMD</td>
<td>.568</td>
<td>.003</td>
<td>.561</td>
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</table>

**Abbreviations:** BMI, body mass index; BP, blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LMD, lipid metabolic disorder; PAI-1, plasminogen activator inhibitor type 1.
*Fully adjusted analyses controlled for smoking status, alcohol consumption, and physical activity. All except for metabolic index also were adjusted for BMI. Homocysteine was also adjusted for folic acid and vitamin B<sub>12</sub> intake. In women, PAI-1 was also adjusted for exogenous hormone use.
‡Excludes diabetic subjects.
†Excludes subjects receiving hypertensive medication.

The present analyses, which were designed to examine mediating mechanisms in the same cohort, hostility was associated with 6 of the 10 physiological risk factors in age-adjusted regressions in the high-risk women, 3 factors in average-risk women, and 1 factor each in high- and average-risk men. However, high-risk men showed significant associations with 2 additional factors after adjustment. Based on our earlier analyses of clinical events, our expectation in the present study was that the greatest association between hostility and CHD and between hostility and carotid artery atherosclerosis only in groups with high familial risk for CHD. In the present analyses, which were designed to examine mediating mechanisms in the same cohort, hostility was associated with 6 of the 10 physiological risk factors in age-adjusted regressions in the high-risk men. To test the robustness of these results, they were recalculated using only 1 member of each family, and the results were still significant.

**COMMENT**

Earlier analyses in this cohort revealed associations between hostility and CHD and between hostility and carotid artery atherosclerosis only in groups with high familial risk for CHD. In the present analyses, which were designed to examine mediating mechanisms in the same cohort, hostility was associated with 6 of the 10 physiological risk factors in age-adjusted regressions in the high-risk women, 3 factors in average-risk women, and 1 factor each in high- and average-risk men. However, high-risk men showed significant associations with 2 additional factors after adjustment. Based on our earlier analyses of clinical events, our expectation in the present study was that the greatest association between hostility and CHD and between hostility and carotid artery atherosclerosis only in groups with high familial risk for CHD. In the present analyses, which were designed to examine mediating mechanisms in the same cohort, hostility was associated with 6 of the 10 physiological risk factors in age-adjusted regressions in the high-risk men. To test the robustness of these results, they were recalculated using only 1 member of each family, and the results were still significant.
that hostility increases cardiovascular risk in cohorts not differentiated by familial risk, but research in the area of mediating mechanisms is limited. One study in middle-aged male volunteers reported a significant association between hostility and PAI-1, but did not include women. With respect to fibrinogen, another earlier study reported an association with hostility in patients with CHD but not control subjects, and still another investigating only high-risk patients found that hostility along with several other psychosocial factors explained 29% of the variance in D dimer, a marker of fibrin turnover. Clearly, further research is needed to tease out the mechanisms mediating cardiovascular risk in different populations.

As hypothesized, after adjustment for health-related behaviors, many of the significant associations of risk factors with hostility were reduced, indicating that, especially in high-risk women, health-related behaviors are an important factor mediating the influence of hostility on cardiovascular risk. However, health behaviors did not account for all of the variance in the association between hostility and CVD risk. Among other things, after adjusting for covariates, associations with lipid metabolic risk in all women and in high-risk men still remained.

Associations between hostility and components of the metabolic syndrome have also been found in other studies. A study of 134 children defined metabolic syndrome on the basis of having at least 2 of the following risk factors above the 75th percentile of scores for their age, race, and sex groups: BMI, insulin resistance index, ratio of triglyceride to HDL-C, and mean arterial blood pressure. Those investigators found that children who exhibited high hostility scores at baseline were likely to exhibit the metabolic syndrome at follow-up. Another study found that hostility was related to individual components of the metabolic syndrome. That study used waist-hip ratio and BMI as covariates rather than as components of the metabolic syndrome and found that BMI mediated the associations between hostility and fasting insulin, triglyceride, and HDL-C. Waist-hip ratio mediated the relationship between hostility and fasting insulin. A third study found that hostility was correlated with fasting glucose in women but not in men, but that this correlation was reduced when controlling for BMI. When the correlations were calculated by race, an association with fasting glucose was found in African American subjects, even after adjustment for BMI. In the present study we performed the analyses in 2 ways. First, we examined the association of hostility to individual factors controlling for age, BMI, physical activity, smoking, and alcohol consumption, then we examined the association of hostility with a cluster of factors we have called a lipid metabolic disorder. That study used waist-hip ratio and BMI as covariates rather than as components of the metabolic syndrome. That study used waist-hip ratio and BMI as covariates rather than as components of the metabolic syndrome. That study used waist-hip ratio and BMI as covariates rather than as components of the metabolic syndrome.

### Table 4. Associations of Hostility With Physiological Risk Factors in High-Risk Men

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Age Adjusted β</th>
<th>P Value</th>
<th>Fully Adjusted β</th>
<th>P Value</th>
<th>Covariate That Most Reduces β Value</th>
</tr>
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<tbody>
<tr>
<td>Fibrinogen level</td>
<td>.060</td>
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<td>.032</td>
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<td>Smoking (β = .17)</td>
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<td>Homocysteine level</td>
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<tr>
<td>PAI-1 level</td>
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<tr>
<td>Diastolic BP‡</td>
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<td>.155</td>
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Abbreviations: BMI, body mass index; BP, blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LMD, lipid metabolic disorder; PAI-1, plasminogen activator inhibitor type 1.

*Fully adjusted analyses controlled for smoking status, alcohol consumption, and physical activity. All except for metabolic index also were adjusted for body mass index. Homocysteine was also adjusted for folic acid and vitamin B₆ intake.
†Excludes diabetic subjects.
‡Excludes subjects receiving hypertensive medication.

### Table 5. Association of Hostility With Physiological Risk Factors in Average-Risk Men

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Age Adjusted β</th>
<th>P Value</th>
<th>Fully Adjusted β</th>
<th>P Value</th>
<th>Covariate That Most Reduces β Value</th>
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<tr>
<td>Fibrinogen level</td>
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<td>Smoking (β = .14)</td>
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<td>Homocysteine level</td>
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<td>.62</td>
<td>−.002</td>
<td>.99</td>
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<td>PAI-1 level</td>
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<td>Glucose level†</td>
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<tr>
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<tr>
<td>LMD</td>
<td>−.043</td>
<td>.79</td>
<td>−.020</td>
<td>.90</td>
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</table>

Abbreviations: BP, blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LMD, lipid metabolic disorder; PAI-1, plasminogen activator inhibitor type 1.

*Fully adjusted analyses controlled for smoking status, alcohol consumption, and physical activity. All except for metabolic index also were adjusted for body mass index. Homocysteine was also adjusted for folic acid and vitamin B₆ intake.
†Excludes diabetic subjects.
‡Excludes subjects receiving hypertensive medication.
pathway involves an influence on behaviors that affect risk. For example, high-hostility individuals have been reported to smoke more and to consume more caffeine, alcohol, and animal fat than low-hostility people. The second pathway involves neuroendocrine changes associated with hostile emotions, an example of which can be seen in the positive association between hostility and resting triglyceride concentrations that remained in young white women in the Coronary Artery Risk Development in Young Adults Study after adjustment for relevant health-related behaviors (dietary fat intake, smoking status, BMI, alcohol consumption, and physical activity). A third possible pathway involves genetic factors or gene-environment interactions. The present results suggest that multiple pathways may be involved. Some of the associations between hostility and physiological risk factors were reduced when the analyses were adjusted for health-related behaviors, indicating that the associations were primarily mediated through these behaviors. However, several associations remained strong even after adjustment, indicating the involvement of other, probably neuroendocrine, mediators.

Gene expression associated with cardiovascular risk might also be triggered by the neuroendocrine concomitants of hostile emotion, or there might be a direct genetic link to hostility that involves cardiovascular risk. A genome scan of the present data set found no significant linkage for the total hostility score or any of its subscales, but several likelihood of odds (LOD) scores were in the range of 1.77 to 1.97. Such findings could indicate no linkage or small contributions from multiple genes. Because hostile characteristics show stability over time, the body of a hostile individual continually reacts to stimuli perceived as threatening or conflictual. Although the short-term effects of sympathetic activation involving increased secretion of catecholamines and glucocorticoids can be beneficial in helping the body mobilize energy needed to respond to an acute situation, the long-term neuroendocrine consequences can be damaging, especially to the cardiovascular system. Because most of the research on the physiological correlates of hostility that might explain its association with cardiovascular risk endpoints has been performed on acute cardiovascular reactivity, the mechanisms mediating long-term consequences are still unclear. One such study reported β-adrenergic down-regulation in hostile compared with nonhostile men and hypothesized that this was a result of excessive and prolonged neuroendocrine activation. It has been shown that reactivity occurring in the context of chronic stress seems to down-regulate sympathetic and hypothalamic-pituitary axis reactivity. When catecholamine concentrations are chronically elevated, the body down-regulates the number of receptors in an attempt to restore autonomic balance.

There are several limitations to this study. The first is the cross-sectional nature of the design, which does not address antecedent-consequent relations as well as a prospective study does. Health behaviors might not explain all of the variance, because we were measuring current health behaviors that may not adequately reflect the influence of past behaviors. As is usual with psychosocial measurements, the hostility data are self-reported, and there is always the risk of bias associated with self-report measures. In addition, the physiological factors measured in this study vary over time, and our measurements were taken at only 1 time point. An average of multiple measures would have been preferable. Finally, the association between hostility and physiological risk measures may be explained by a still unexplained common causal factor. Further research will be required to examine this possibility more fully.

CONCLUSIONS

Of the 3 possible mediating pathways discussed, the health behavior pathway seems to be the strongest, because controlling for these behaviors in the present study reduced the impact of physiological risk, especially in the most vulnerable group, the high-risk women. This finding is consistent with those of earlier studies demonstrating associations between hostility and health-related behaviors. However, health behaviors did not explain all of the variance. Added to the accumulating data on the associations between hostility and cardiovascular morbidity and mortality, these results indicate that further investigation of mechanistic pathways is warranted.

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Author Affiliations: Division of Epidemiology, Statistics, and Prevention Research, National Institute of Child Health & Human Development, National Institutes of Health, Bethesda, Md (Dr Knox); Preventive Medicine Research Institute, Sausalito, Calif (Dr Weidner); Division of Biostatistics, Washington University School of Medicine, St Louis, Mo (Ms Adelman); Department of
Psychology, The Ohio State University, Columbus (Dr. Stoney); and Section of Preventive Medicine and Epidemiology, Boston University School of Medicine, Boston, Mass (Dr. Ellison).

Correspondence: Sarah S. Knox, PhD, Division of Epidemiology, Statistics and Prevention Research, National Institute of Child Health & Human Development, 6100 Executive Blvd/5C01, Bethesda, MD 20892 (knoxs@mail.nih.gov).

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