HYPERTENSION is an important risk factor for coronary heart disease, stroke and congestive heart failure.1-4 The degree of risk is directly proportionate to the level and duration of the blood pressure elevation. Control of even mildly elevated blood pressure significantly reduces the clinical consequences of hypertension.5 Measures to prevent the development of high blood pressure would presumably be even more effective.

It is generally accepted that weight, heart rate, blood glucose, salt and alcohol consumption, hematocrit and smoking status correlate with blood pressure levels.6-8 However, with few exceptions, these studies have been cross-sectional, so it is not clear whether these correlated conditions predate, accompany, or occur after elevation in blood pressure. Data collected by the Normative Aging Study allow prospective examination of the effects of these and other factors on the subsequent rate of change in blood pressure and on the development of elevated levels of blood pressure. A sample of men recruited from the Boston area has been under surveillance since 1963. The subjects who were initially normotensive...
were followed for 10 years to evaluate the effects of a large number of factors of possible pathogenic significance to blood pressure.

Methods

Subjects

This study is based on a population of 2000 male volunteers participating in the Normative Aging Study, a longitudinal study of aging initiated by the Veterans Administration in 1963. Only subjects who were free of significant disease were accepted into the study. Study participants return for repeat evaluation on the average of once every 5 years. For inclusion in the present analysis, participants had to satisfy the following criteria: blood pressure less than 140 mm Hg systolic and 90 mm Hg diastolic in both arms at the first examination, complete information at intake on all the independent variables of interest, and availability of blood pressure determinations from two subsequent examinations. Loss to follow-up excluded 18% of the original study population. The 1166 subjects who satisfied these criteria were 23-80 years old at the first examination (mean 42 years). The subjects who were excluded because of loss to follow-up were similar to those who were included in the study in all respects, including age, skinfold thickness, body mass index, hematocrit and systolic and diastolic blood pressures. A detailed description of the study population is given elsewhere.24

Procedures

At each of the three serial physical examinations, blood pressure was measured by an examining physician using a standard mercury sphygmomanometer and a 14-cm cuff. With the subject seated, systolic blood pressure and fifth-phase diastolic blood pressure were measured to the nearest 2 mm Hg in each arm. The measurements were taken during one visit for each of the three physical examinations. The recommendations of the American and British Heart Associations were followed for reading the pressure.18 The palpatory method was used to check auscultatory systolic readings. There was no systematic difference in the way blood pressures were taken from one examination to another.

At the first examination, subjects reported to the study center at 8:00 a.m. after an overnight fast and abstinence from smoking. Serum and anticoagulated blood were obtained by venipuncture and were analyzed for hematocrit,16 uric acid,17 phosphorus,18 cholesterol19 and total protein.20 Two-hour glucose21 levels were measured after a 100-g glucose load.

Each subject completed a Cornell Medical Index,22 a self-report health questionnaire of 195 yes-no questions, at entry into the Normative Aging Study. An answer of “yes” to a question suggests a departure from a “normal” physiologic or emotional health state. Five measures of life stress (exhaustion, emotional reactivity, anger, anxiety and inability to rest) were formed by combining conceptually similar items from the Cornell Medical Index into scales using techniques of item analysis and factor analysis. A measure of internal consistency reliability (coefficient α) was computed for each scale that contained three or more items.23 Table 1 presents the five scales formed along with reliability estimates. The scale reliabilities were high for scales formed retrospectively, and were only slightly lower than the scales formed in a similar manner by Haynes et al.24 in their study of stress and coronary heart disease in the Framingham Heart Study population. Scores for each subject on a given scale were formed by summing his responses (yes = 1, no = 0) to items on the scale.

Alcohol consumption was indicated by one of the questions in the Cornell Medical Index. High consumers were defined as subjects who answered “yes” to the question, “Do you usually take two or more alcoholic drinks a day?” Smoking history was obtained by a trained interviewer. Smoking habits included the current number of cigarettes smoked per day and the number of years of cigarette smoking at the time of the initial examination. Weight and height were measured with the subjects wearing only stockings and undershorts. Subscapular and triceps skinfolds were measured in the standard manner using a Lange skinfold caliper.

The hypothesis tested was whether any of 20 baseline variables had an effect on blood pressure change. Multiple linear regression was used to evaluate the relationship of the baseline variables to blood pressure slope. For each subject the slope was obtained for the regression line that best fit three serial measurements of systolic pressure. (The mean of left and right arm was used as the estimate of systolic pressure at each examination.) The same procedure was followed to obtain the slope for diastolic pressure. Multiple logistic regression was used to evaluate the relationship of the baseline variables to subsequent elevation of blood pressure (> 159 mm Hg systolic or > 94 mm Hg diastolic). Maximal likelihood estimates of the coefficients were used.25 Variables representing age, alcohol consumption status and several psychosocial scales were created using standard dummy coding of categorical variables.26 Subjects 50 years of age or older were the reference group for age, and those drinking fewer than two drinks a day were the reference group for alcohol consumption status. For each psychosocial scale of daily life stress, a “no stress” group was defined as subjects who answered “no” to all items defining the specified scale. This group was used as the reference group for daily life stress. All others were considered to be in the “stress” group.

Results

For the entire study sample, the average yearly change (slope) in systolic blood pressure was 0.17 ± 1.44 mm Hg (±SD) and in diastolic blood pressure was 0.02 ± 0.96 mm Hg. The relationship of 20 independent variables to both systolic and diastolic pressure slope is shown in table 2. Separate regression analyses of systolic pressure slope on each of these in-
dependent variables with initial (T1) systolic pressure controlled indicated that body mass index (weight/height²), subscapular skinfold, 2-hour glucose, and hematocrit were positively related and membership in the 20–39-year age group was negatively related to slope. The relationship of age to systolic pressure slope indicated that systolic pressure in subjects 20–39 years old at the first examination did not increase as rapidly as in subjects 50 years or older. Regressions of diastolic pressure slope on each of the independent variables with T1 diastolic pressure controlled indicated body mass index and hematocrit were significant predictors of diastolic pressure slope.

Results of stepwise multiple linear regression are shown in table 3 with independent variables that had significant (p < 0.05) correlations with blood pressure slope. When the 20 independent variables plus T1 blood pressure were considered, five (T1 systolic pressure, age 20–39 years, age 40–49 years, hematocrit and subscapular skinfold thickness) were significant predictors of systolic pressure slope and three (T1 diastolic pressure, hematocrit and body mass index) were significant predictors of diastolic pressure slope. The variables are listed in the order in which they entered the regression analysis. The strong relationships between initial level and slope are consistent with regression to the mean.²⁷ Although age appears to play an important role for systolic slope, it was notably absent from the set of predictors for diastolic slope.

The impact of the independent variables on blood pressure may also be appreciated from an analysis that considers elevated blood pressure as the dependent variable. In the present report, we arbitrarily defined “elevated” as both right and left arm readings greater than 159 mm Hg systolic or 94 mm Hg diastolic. Participants with elevated blood pressure at the second or third examinations were identified. The average length of time between the first and the third examinations was 10 years.

Twenty-nine participants (2.5%) had elevated blood pressure at the second or the third examinations. The diastolic component tended to be elevated more often than the systolic component. Results of a stepwise multiple logistic regression, with all 20 independent variables in the predictor variable set, are presented in table 4. After systolic and diastolic blood pressure were forced into the equation first, only hematocrit was identified as a significant predictor of elevated blood pressure.

The above analyses were repeated after excluding the 35 participants receiving antihypertensive therapy. No material differences in the results of the linear or logistic regressions were observed. None of these 35
subjects was included in the group of 29 subjects with elevated blood pressure at follow-up examinations.

**Discussion**

We used data from a large-scale prospective study to provide information on factors related to changes in blood pressure. Multiple linear regression analysis and multiple logistic regression analysis showed that initial blood pressure and hematocrit were independently related both to blood pressure slope and to elevated blood pressure. A relationship between initial and follow-up blood pressures has also been reported. The independent effect of hematocrit on blood pressure is consistent with findings from previous cross-sectional studies. Even within the normal range of hemoglobin values, a significant variation in the prevalence of hypertension was found proportionate to the hemoglobin level in the Framingham Heart Study. This relationship was stronger for diastolic than for systolic pressures. A positive relationship between hematocrit and blood pressure may be secondary to an underlying alteration in blood volume. Another possibility is that enhanced production of erythropoietin related in some way to the higher blood pressure by stimulating red cell production.

Weight has repeatedly been shown to correlate with blood pressure level in cross-sectional studies. In our prospective analysis, anthropometric measurements of body build were found to be significant predictors of blood pressure slope, with baseline blood pressure controlled. Body mass index was positively and independently associated with diastolic pressure slope. Although no measurement of body build significantly predicted elevated blood pressure, body mass index approached statistical significance ($p = 0.11$). Similar to our findings, a prospective study from Chicago showed that baseline relative weight was positively related to follow-up diastolic pressure but not to follow-up systolic pressure. Some investigators believe that skinfold thickness provides a more accurate assessment of adiposity than does relative weight. It is unclear whether adiposity per se or some other associated factor has greater significance to blood pressure. In our study, the subscapular skinfold thickness was positively and independently associated with systolic pressure slope. Kahn et al. reported that both subscapular skinfold thickness and relative

<table>
<thead>
<tr>
<th>Independent variable</th>
<th>Systolic blood pressure slope</th>
<th>Diastolic blood pressure slope</th>
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<tbody>
<tr>
<td></td>
<td>Coefficient</td>
<td>SEM</td>
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<tr>
<td>Age group</td>
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<tr>
<td>20–39 years†</td>
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<tr>
<td>40–49 years‡</td>
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<td>Body mass index</td>
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<tr>
<td>Subscapular skinfold</td>
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<tr>
<td>Weight</td>
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<td>2-hour glucose</td>
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</table>

*Each independent variable is examined individually in separate regression analyses for relation to systolic pressure slope with initial ($T_1$) systolic level adjusted and for relation to diastolic pressure slope with $T_1$ diastolic level adjusted.

†Effects are relative to age group 50+ years (1 = 20–39 years, 0 = other years).
‡Effects are relative to age group 50+ years (1 = 40–49 years, 0 = other years).
§$p < 0.05$.
$\bullet p < 0.001$. 

TABLE 2. Partial Linear Regression Coefficients for Systolic and Diastolic Blood Pressure Slopes*
weight were associated with subsequent elevation of blood pressure; however, no multivariate analysis was performed.

Stamler et al.8 reported a positive relationship of age and follow-up systolic pressure. Systolic pressure tended to increase more rapidly in older subjects than in younger subjects. In a Canadian study with a 27-year follow-up, age had increasing importance in determining future levels of systolic pressure as the prediction time lengthened.34

The role of psychologic status in initiating, predisposing or precipitating elevated blood pressure has received increased attention.85 Anxiety, fear and anger are often accompanied by increased blood pressure on a short-term basis. These findings suggest that repeated episodes involving heightened emotional reactions could result in sustained high blood pressure. Such findings have been reported with anxiety, tension and neuroticism.86, 87 However, other studies have not found such relationships.88-92 We detected no association between psychologic status and blood pressure. However, the psychologic measures available to us may not have been sensitive enough to detect subtle relationships.

In conclusion, our results indicate that there are independent predictive factors for change and elevation in blood pressure, in addition to baseline blood pressure itself. The mechanisms by which such factors influence blood pressure are unclear. However, identifying hypertension-prone subjects and delaying or preventing elevated blood pressure may be possible.

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