Hematocrit, Blood Pressure, and Hypertension

The Gubbio Population Study

Massimo Cirillo, Martino Laurenzi, Maurizio Trevisan, and Jeremiah Stamler

for the Gubbio Study Research Group

Baseline data from the Gubbio Population Study in north central Italy were used to investigate the relation of hematocrit to blood pressure and hypertension among 2,809 men and women aged 25–74 years. Independent of gender, age, and other confounders, the hypertensive group had a higher hematocrit than the nonhypertensive group (p<0.001). In comparison with the untreated hypertensive group, the hypertensive group being treated with diuretics or with other drugs only had similar mean hematocrit levels despite significantly lower blood pressures. Hematocrit was positively correlated with systolic pressure (r=0.085, p<0.01 and r=0.264, p<0.001 for men and women, respectively) and diastolic pressure (r=0.214, p<0.01 and r=0.266, p<0.001). In both sexes, whether or not the treated hypertensive group was included, age-adjusted prevalence of hypertension and average blood pressure were higher for persons in higher quintiles of hematocrit (p<0.001). The association of hematocrit with blood pressure and hypertension was significant and independent of several confounders. The regression coefficient of blood pressure on hematocrit ranged between 0.410 and 0.620 mm Hg per unit of hematocrit for systolic pressure and between 0.371 and 0.581 for diastolic pressure, depending on gender and whether the treated hypertensive group was included in multiple regression analysis. Based on exponentiation of the multiple logistic coefficient, prevalence of hypertension was at least two times greater for persons whose hematocrit levels were higher by 10 units. (Hypertension 1992;20:319–326)

KEY WORDS • hematocrit • blood pressure • hypertension, essential • Gubbio population study

Hematocrit is the most important determinant of whole blood viscosity.1 Blood viscosity and vascular resistance affect total peripheral resistance to blood flow,2 which is abnormally high in the established phase of primary hypertension.3 It has been reported that hematocrit is increased or normal in human hypertension* 9 and increased in rat genetic hypertension.8-10 In genetically hypertensive rats, it has also been shown that reduction of hematocrit with maintenance of blood volume reduces blood pressure.11-13 Correspondingly, clinical studies have reported that increase of hematocrit is followed by increase in blood pressure and possibly onset of hypertension in anemic patients.14-20 Many clinical and experimental studies have been done on the relation between hematocrit and blood pressure, but the epidemiological literature does not identify hematocrit as an important independent correlate of blood pressure in general populations. The present study of men and women from the Gubbio Population Study in north central Italy21 shows that a significant positive association exists between hematocrit and blood pressure or hypertension, independent of other factors related to these end points.

Methods

In the Gubbio Study, the target population was defined as all persons aged 5 years and older dwelling within the borough limited by the ancient wall of this hill town in north central Italy.21 Potential participants first received a letter signed by the mayor and by the president of the Local Health Unit explaining the scope and the details of the study. A personal contact by a member of the study team followed, during which further explanation was given and any questions were answered. Contacted individuals were also informed that participation was voluntary. In the baseline survey, 5,376 individuals were examined (response rate, 92.2%). The 25–74-year-old age group consisted of 3,706 individuals (1,684 men and 2,022 women). The present report deals with findings on 2,809 individuals 25–74 years old (1,275 men and 1,534 women) with complete data for the variables under study.

Participants were asked to refrain from eating for at least 2 hours before the visit and from smoking and
strenuous exercise for 1/2 hour before. Blood pressure was measured by trained medical doctors using mercury sphygmomanometers and cuffs of appropriate size. Three consecutive determinations of arterial pressure and heart rate were performed with the participant in the sitting position, the first one after 5 minutes of quiet rest after application of the cuff. The mean of the last two measurements was used in the analyses. Hypertension was defined as an average diastolic pressure of 90 mm Hg or greater. Information was also collected on treatment status with particular regard to antihypertensive drug use. Participants on current, regular antihypertensive drug treatment were regarded as hypertensive independently of measured blood pressure. They were analyzed separately from the group of untreated hypertensive subjects in most of the statistical procedures. The effect of antihypertensive drug treatment on hematocrit was also studied in the subgroup of hypertensive subjects receiving only nondiuretic drugs (e.g., sympatholytic agents, vasodilators, calcium channel blockers, angiotensin-converting enzyme inhibitors) to avoid the confounding effect of diuretic-induced reduction of plasma volume.22

A venous blood sample was obtained from each participant for routine laboratory investigations (automated chemistry by Astra 8, Beckman, Brea, Calif.), including measurement of hematological indexes (Coulter Counter, Electronics Ltd., Luton Bebs, UK); the latter was performed on blood samples treated with tripotassium ethylenediaminetetraacetate as anticoagulant and diluted in Isoton 2. Calibration was done daily with a standard suspension of erythrocytes (Kontron 4C Plus). Twenty percent of daily samples were submitted as blind duplicates to measure technical error, which was less than 1% of the mean value of hematocrit measurements. As reported,21 a fraction of the venous blood sample was used to determine maximal rate of sodium–lithium countertransport in red blood cells. A first-voided morning urine sample was also obtained for determination of urinary concentration of sodium and potassium. Habitual daily alcohol intake was obtained by use of a standardized questionnaire.

Smoking habits, which are known to affect hematocrit,23,24 were investigated by means of a questionnaire administered by the physician. To validate this information, the level of carbon monoxide in the breath, taken as an index of smoking habit,25 was measured with an Ecolyzer instrument (Pittsburgh, Pa.) in 76.9% of men and 72.7% of women.

Simple correlation analysis, analysis of variance (ANOVA), and multiple linear and logistic regression analyses were used for statistical evaluation of the results.

Results

Table 1 shows the mean±SD for selected variables by gender and blood pressure status. In each of the blood pressure groups, the expected difference between the sexes was observed for hematocrit. The percentage of smokers, the number of cigarettes smoked per day, and the level of carbon monoxide in the breath were higher in men. Carbon monoxide in the breath and reported number of cigarettes smoked per day were strongly correlated both in men (r=0.75, n=981, p<0.001) and women (r=0.68, n=1,115, p<0.001). Descriptive data for the other variables under study have been reported previously.20

Compared with nonhypertensive participants, untreated hypertensive participants had higher mean values of age, body mass index, hematocrit, and obviously of blood pressure in both sexes (Table 1). Among women, the percentage of smokers was lower in untreated hypertensive than in nonhypertensive participants. Among men, this difference was not significant, but untreated hypertensive men reported a significantly greater number of cigarettes smoked per day than nonhypertensive men.

Untreated hypertensive participants and those receiving drug treatment had similar mean values of body mass index, hematocrit, and carbon monoxide in the breath. The percentage of smokers and mean number of cigarettes smoked per day were lower among drug-treated than untreated hypertensive participants, but the difference was not significant. Hypertensive participants receiving drug treatment had significantly higher mean age than untreated hypertensive participants. They also had significantly lower blood pressure than untreated hypertensive participants, on average by

<table>
<thead>
<tr>
<th>Variable</th>
<th>NH</th>
<th>UH</th>
<th>TH</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>47.5±14.4</td>
<td>51.1±12.0*</td>
<td>57.3±9.5†</td>
</tr>
<tr>
<td><strong>Body mass index (kg/m²)</strong></td>
<td>26.2±3.4</td>
<td>28.2±3.7‡</td>
<td>29.1±4.0</td>
</tr>
<tr>
<td><strong>Systolic pressure (mm Hg)</strong></td>
<td>126.5±16.4</td>
<td>148.7±23.4‡</td>
<td>149.9±23.4</td>
</tr>
<tr>
<td><strong>Diastolic pressure (mm Hg)</strong></td>
<td>75.4±7.9</td>
<td>95.5±5.8†</td>
<td>85.6±11.0†</td>
</tr>
<tr>
<td><strong>Hematocrit (×10⁻²)</strong></td>
<td>45.2±3.0</td>
<td>46.6±3.6‡</td>
<td>46.0±3.2</td>
</tr>
<tr>
<td><strong>Smokers (%)</strong></td>
<td>52.1</td>
<td>43.7</td>
<td>38.9</td>
</tr>
<tr>
<td><strong>Cigarettes/day per smoker</strong></td>
<td>16.0±10.1</td>
<td>20.1±10.1*</td>
<td>14.5±11.3</td>
</tr>
<tr>
<td><strong>Carbon monoxide in breath</strong></td>
<td>6.48±5.07</td>
<td>5.70±4.81</td>
<td>5.14±4.10</td>
</tr>
</tbody>
</table>

NH, nonhypertensive group; UH, untreated hypertensive group; TH, drug-treated hypertensive group. Values are mean±SD.

*p<0.01, †p<0.001 vs. nonhypertensive group.

†p<0.001 vs. untreated hypertensive group.

§Available in 76.9% of men and 72.7% of women.
about 10 mm Hg, with the exception of systolic pressure of drug-treated hypertensive men, which was not different from that of untreated hypertensive men (Table 1).

Analysis by age and sex (Table 2) indicated that the mean hematocrit of hypertensives was higher than that of nonhypertensives in both sexes and all ages except for hypertensive women 25–34 years old (four hypertensive women only). Age-adjusted analyses indicated that in both sexes, hypertensive participants had significantly higher mean hematocrit than nonhypertensive participants. A significantly higher mean hematocrit in hypertensive participants was confirmed when the analyses were repeated with control for body mass index as well as for age (men, hematocrit \( \times 10^{-2} = 46.2 \) versus 45.3, \( F = 27.1, p < 0.001 \); women, hematocrit \( \times 10^{-2} = 41.4 \) versus 40.4, \( F = 88.3, p < 0.001 \)). A difference in hematocrit was also obtained when the age-adjusted analysis was done in hypertensive and nonhypertensive groups with exclusion of smokers (men, hematocrit \( \times 10^{-2} = 45.6 \) versus 44.7, \( n = 170 \) versus 473, \( F = 10.0, p = 0.002 \); women, hematocrit \( \times 10^{-2} = 41.3 \) versus 40.1, \( n = 330 \) versus 762, \( F = 85.4, p < 0.001 \)). Age-controlled comparison between nonhypertensive and untreated hypertensive participants with diastolic pressure 90–99 mm Hg indicated a significantly higher hematocrit in this mildly hypertensive subgroup (men, hematocrit \( \times 10^{-2} = 46.8 \) versus 45.3, \( n = 102 \) versus 987, \( F = 21.9, p < 0.001 \); women, hematocrit \( \times 10^{-2} = 41.1 \) versus 40.3, \( n = 111 \) versus 1,137, \( F = 20.1, p < 0.001 \)).

As stated above, the hypertensive group receiving drug treatment had mean hematocrit similar to that of the untreated hypertensive group (Tables 1 and 2). After exclusion from the analysis of the hypertensive group treated with diuretics (i.e., thiazides and related agents, loop diuretics, and potassium-sparring diuretics), those receiving drug treatment exclusively with sympathetic agents (i.e., centrally acting agents, \( \alpha \)- and/or \( \beta \)-blockers), arteriolar vasodilators, angiotensin converting enzyme inhibitors, and/or calcium channel blockers had similar mean hematocrit but lower blood pressure (Table 3) than the sex-matched untreated hypertensive group (Table 1).

In simple correlation analysis (Table 4), hematocrit was significantly correlated with systolic and diastolic pressure. When hypertensive participants receiving drug treatment were excluded from the analysis, hematocrit was still correlated with diastolic pressure in both men and women and with systolic pressure in women (systolic pressure, \( r = 0.058, p = 0.053 \) and \( r = 0.211, p < 0.001 \); diastolic pressure, \( r = 0.196, p < 0.001 \) and \( r = 0.223, p < 0.001 \), \( n = 1,113 \) and 1,271 for men and women, respectively). Hematocrit also correlated positively and significantly with body mass index, number of cigarettes smoked per day, and carbon monoxide in the breath. Among women, hematocrit was also positively correlated with age, whereas among men, it was negatively correlated with age. Simple correlation data between blood pressure and age, body mass index, pulse rate, serum cholesterol, serum glucose, serum uric acid, habitual alcohol intake, urinary sodium-to-potassium ratio, and erythrocyte sodium—lithium countertransport in this population sample have already been reported.

With regard to smoking habit, blood pressure was negatively correlated with number of cigarettes smoked per day (systolic pressure, \( r = -0.121, p < 0.001 \) and \( r = -0.185, p < 0.001 \); diastolic pressure, \( r = -0.092, p < 0.001 \) and \( r = -0.121, p < 0.001 \), \( n = 1,269 \) and 1,525 for men and women, respectively). Similar correlations were found between blood pressure and carbon monoxide in the breath (systolic pressure, \( r = -0.060, p = NS \) and \( r = -0.113, p < 0.001 \); diastolic pressure, \( r = -0.072, p < 0.001 \) and \( r = -0.123, p < 0.001 \), \( n = 981 \) and 1,114 for men and women, respectively). These findings were confirmed when drug-treated hypertensive participants were excluded from the analysis (data not shown).

To investigate further the relation of hematocrit with blood pressure, participants were divided into quintiles

| Table 2. Hematocrit by Gender and Age in the Nonhypertensive Group, All Hypertensive Group, Untreated Hypertensive Group, and Drug-Treated Hypertensive Group |
|-----------------|-----------------|-----------------|-----------------|-----------------|
| Age group (years) | Men (n=1,275) | Women (n=1,354) |                  |                  |
|                  | NH | H | UH | TH |                  | NH | H | UH | TH |
| 25–34            | 45.6 (228) | 47.6 (12) | 47.6 (12) | ... | 39.7 (231) | 39.6 (4) | 39.6 (4) | ... |
| 35–44            | 45.4 (225) | 47.5 (44) | 46.9 (27) | 48.4 (17) | 39.5 (262) | 40.8 (22) | 42.2 (12) | 39.2 (10) |
| 45–54            | 45.3 (177) | 46.1 (74) | 46.0 (34) | 46.2 (40) | 40.2 (238) | 41.2 (79) | 40.6 (34) | 41.6 (45) |
| 55–64            | 45.4 (207) | 46.1 (102) | 46.8 (37) | 45.7 (65) | 40.5 (241) | 41.8 (169) | 41.8 (52) | 41.8 (117) |
| 65–74            | 44.3 (150) | 45.6 (56) | 46.4 (16) | 45.3 (40) | 41.2 (165) | 42.8 (123) | 42.1 (32) | 43.0 (91) |

**NH,** nonhypertensive group; **H,** all hypertensive group; **UH,** untreated hypertensive group; **TH,** drug-treated hypertensive group. Hematocrit values are presented as mean \( \times 10^{-2} (n) \).

\( *p<0.001 \) hypertensive vs. nonhypertensive group.

| Table 3. Age, Blood Pressure, and Hematocrit in Hypertensive Individuals Receiving Antihypertensive Treatment With Drug Other Than Diuretics* |
|-----------------|-----------------|-----------------|
| Variable        | Men (n=89)      | Women (n=135)   |
| Age (years)     | 57.4±5.5t       | 60.8±7.9t       |
| Systolic pressure (mm Hg) | 142.8±25.5t | 153.2±22.7t |
| Diastolic pressure (mm Hg) | 86.2±10.3t | 85.1±10.8t |
| Hematocrit \( \times 10^{-2} \) | 46.4±2.9 | 41.9±3.3 |

Values are mean±SD.

*Sympatholytic agents, vasodilators, calcium channel blockers, and/or angiotensin converting enzyme inhibitors.

\( t p<0.001 \) vs. sex-matched untreated hypertensive group shown in Table 1.
TABLE 4. Correlation Coefficients of Selected Variables With Hematocrit

<table>
<thead>
<tr>
<th>Variable</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>r</td>
</tr>
<tr>
<td>Age</td>
<td>1,275</td>
<td>-0.078*</td>
</tr>
<tr>
<td>Body mass index</td>
<td>1,267</td>
<td>0.167t</td>
</tr>
<tr>
<td>Systolic pressure</td>
<td>1,275</td>
<td>0.085*</td>
</tr>
<tr>
<td>Diastolic pressure</td>
<td>1,275</td>
<td>0.214t</td>
</tr>
<tr>
<td>Cigarettes/day</td>
<td>1,269</td>
<td>0.219†</td>
</tr>
<tr>
<td>Carbon monoxide in breath</td>
<td>981</td>
<td>0.174†</td>
</tr>
</tbody>
</table>

*p ≤ 0.01, †p ≤ 0.001.

of the hematocrit distribution for each of the sexes. In these analyses, age-adjusted values for prevalence of hypertension and for average systolic and diastolic pressure were significantly different among hematocrit quintiles (Figure 1, upper panel). In both sexes, a linear trend was observed between hematocrit and age-adjusted prevalence of hypertension and average diastolic pressure. The same findings were obtained after exclusion of the treated hypertensive group from the analysis (Figure 1, lower panel). The ratio of prevalence of hypertension in hematocrit quintile 5 compared with quintile 1 was 2.22 for men and 2.14 for women; it was 3.07 and 2.41, respectively, when the treated hypertensive group was excluded from the analysis. This difference was also observed among nonsmokers, with a ratio of 2.01 for men and 2.37 for women (data not shown).

Stepwise multiple regression analyses were performed to assess the independence of the relation between hematocrit and arterial pressure. Analyses were done including and not including the drug-treated hypertensive group, with systolic and diastolic pressures as dependent variables. In addition to hematocrit, other

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**Figure 1.** Scatterplots show age-adjusted values of prevalence of hypertension and of average systolic (SBP) and diastolic (DBP) blood pressures plotted vs. average hematocrit (×10^-2) for each hematocrit quintile with (panel A) and without (panel B) inclusion of hypertensive individuals receiving drug treatment (men, closed circles, solid line; women, open circles, dotted line). F ratios and p values given by age-adjusted analysis of variance.
variables included in the model were age, body mass
index, pulse rate, serum glucose, serum cholesterol,
serum uric acid, habitual alcohol intake, cigarettes per
day, erythrocyte sodium–lithium countertransport, and
urinary sodium-to-potassium ratio. Hematocrit was pos-
itively and significantly related to systolic and diastolic
pressures in all these analyses, with regression coeffi-
cient values about 0.400–0.300 mm Hg per unit of
hematocrit in men and women (Table 5). Findings were
similar when the hypertensive group receiving drug
treatment was included in the analyses (regression
coefficients, 0.509 and 0.620, /7<0.001 for systolic pres-
sure and 0.581 and 0.532, /7<0.001 for diastolic pressure,
men and women, respectively). The results were also
similar when the analyses were done only for nonsmok-
ers (regression coefficients, 0.642 and 0.774, /7<0.01
for systolic pressure and 0.522 and 0.584, /7<0.001 for
diastolic pressure, men and women, respectively). Simi-
lar results were observed when other variables, such as
white blood cell count, were included in the model (data
not shown).

Multiple logistic regression showed a significant and
independent association between hematocrit and preva-
lence of hypertension in men and women (Table 6). The
regression coefficients were similar for men and
women, with values of about 0.100 with or without
inclusion of the drug-treated hypertensive group. On
the basis of these coefficients, for persons with hemat-
ocrit higher by 10 units (e.g., 45% versus 35%), preva-
lence of hypertension was about 2.72 times greater.
Similar findings were obtained when such analyses were
done for nonsmokers (regression coefficients, 0.0656–
0.1018, /7<0.05).

Discussion
This cross-sectional study shows that hematocrit is
positively and independently associated with blood
pressure and with prevalence of hypertension in men
and women from a general population. Positive signifi-
cant correlations between hematocrit and blood pres-
sure have been reported by others in univariate analy-

### TABLE 5. Multiple Linear Regression Coefficients for Systolic and Diastolic Blood Pressures by Gen-
der Without Inclusion of Hypertensive Individuals Receiving Drug Treatment

<table>
<thead>
<tr>
<th>Variable</th>
<th>Men (n=1,079)</th>
<th>Women (n=1,190)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>0.580*</td>
<td>0.853*</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>0.557*</td>
<td>0.404*</td>
</tr>
<tr>
<td>Pulse rate (bpm)</td>
<td>0.202*</td>
<td>0.193*</td>
</tr>
<tr>
<td>Hematocrit (×10⁻²)</td>
<td>0.410†</td>
<td>0.432†</td>
</tr>
<tr>
<td>Serum glucose (mg/dl)</td>
<td>0.070†</td>
<td>0.103*</td>
</tr>
<tr>
<td>Serum cholesterol (mg/dl)</td>
<td>0.023‡</td>
<td>0.048*</td>
</tr>
<tr>
<td>Serum uric acid (mg/dl)</td>
<td>0.824‡</td>
<td>NS</td>
</tr>
<tr>
<td>Alcohol intake (g/day)</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Cigarettes/day (n)</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>RBC Na-Li CT</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>UNa/K</td>
<td>NS</td>
<td>0.731*</td>
</tr>
</tbody>
</table>

SBP, systolic blood pressure (mm Hg); DBP, diastolic blood pressure (mm Hg); bpm, beats per minute;
RBC Na-Li CT, red blood cell sodium–lithium countertransport (mmol Li  • 1 of RBC⁻¹ • hr⁻¹); UNa/K,
urinary sodium/potassium ratio (mmol · l⁻¹/mmol · l⁻¹).

### TABLE 6. Multiple Logistic Regression Coefficients for Hypertension by Gender With and Without Inclusion
of Hypertensive Individuals Receiving Drug Treatment

<table>
<thead>
<tr>
<th>Variable</th>
<th>Including treated hypertensive group</th>
<th>Excluding treated hypertensive group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>0.0337*</td>
<td>0.0359*</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>0.1208*</td>
<td>0.0967*</td>
</tr>
<tr>
<td>Pulse rate (bpm)</td>
<td>0.0207†</td>
<td>0.0943*</td>
</tr>
<tr>
<td>Hematocrit (×10⁻²)</td>
<td>0.1026*</td>
<td>0.1229*</td>
</tr>
<tr>
<td>Serum glucose (mg/dl)</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Serum cholesterol (mg/dl)</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Serum uric acid (mg/dl)</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Alcohol intake (mg/dl)</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Cigarettes/day (n)</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>RBC Na-Li CT</td>
<td>1.1447†</td>
<td>1.2511†</td>
</tr>
<tr>
<td>U Na/K</td>
<td>NS</td>
<td>0.0915†</td>
</tr>
</tbody>
</table>

bp, Beats per minute; RBC Na-Li CT, red blood cell sodium–lithium countertransport (mmol Li · 1.0
RBC⁻¹ • hr⁻¹); U Na/K, urinary sodium/potassium ratio (mmol · l⁻¹/mmol · l⁻¹).

*p<0.001, †p<0.01, ‡p<0.05.
correlation between blood hemoglobin and blood pressure in adults 25–64 years old from the MONICA-Project\(^5\) and in children 5–14 years old from the Bogalusa Study\(^6\) and from the Gubbio Study.\(^3\)

High blood pressure could theoretically cause high hematocrit by, for instance, inducing hemoconcentration through increased transcapillary filtration of plasma. No research data are available in support of the hypothesis that an increase in blood pressure is followed by an increase in hematocrit. The data from the present study indicate that the mean hematocrit of the drug-treated hypertensive group—those treated both with nondoniuretics and with diuretics, i.e., independent of diuretic-induced changes of plasma volume—\(^2\) is as high as that of the untreated hypertensive group despite mean blood pressure about 10 mm Hg lower than that of the untreated hypertensive group. If high blood pressure were the only cause of high hematocrit in the hypertensive group, a reasonable expectation is that hematocrit would have lowered at least to some degree by effective antihypertensive treatment. The lack of such an effect in the present large series of genetically hypertensive individuals indicates the unlikelihood that high hematocrit is merely secondary to high blood pressure. Alternative possibilities are that hematocrit contributes to the regulation of blood pressure or that some other factors are responsible for parallel changes of hematocrit and blood pressure. Age, overweight, and tobacco smoking were significant positive correlates of both hematocrit and blood pressure in the studied population. However, the association between hematocrit and blood pressure was independent of these variables. The role of other (possibly dietary) factors not considered in the present study cannot be excluded.

The possibility that hematocrit has a direct role in the regulation of the blood pressure is supported by experimental and clinical observations. In patients with different forms of anemia, a significant increase of total peripheral resistance and arterial pressure and at times development of hypertension may occur when low hematocrit is increased by transfusion of packed red blood cells\(^15\) or by erythropoietin administration.\(^17\)\(^–\)\(^20\) Correspondingly, myeloproliferative polychromatia rubra vera is often associated with high blood pressure, which can be controlled by hematocrit reduction.\(^3\) Controlled clinical studies of the effect of normovolemic hemodilution on blood pressure have not been done in humans, but it has been shown that this procedure improves blood flow and relieves symptoms in patients with peripheral vascular disease.\(^22\)\(^–\)\(^24\) In genetically hypertensive rats, normovolemic reduction of hematocrit by about 10 units causes a 20–30 mm Hg reduction in blood pressure,\(^11\)\(^–\)\(^13\) which is negated by transfusion of packed red blood cells.\(^13\) In dogs, acute normovolemic reduction of hematocrit induces a large reduction of peripheral resistance without significant changes of cardiac output.\(^25\) Finally, available data indicate that whole blood viscosity is also a correlate of left ventricular hypertrophy.\(^36\)

Although extrapolation of cross-sectional observations must be made with caution, results of the present study indicate that a 10-unit increase in hematocrit (e.g., from 35% to 45%) would be associated with an increase of 4–6 mm Hg in arterial pressure and with a twofold increased risk of hypertension. These estimates are close to the blood pressure changes observed in anemic patients after hematocrit is increased by blood transfusion or by erythropoietin treatment.\(^14\)\(^–\)\(^20\)

Reasonable mechanisms underlying the association between hematocrit and blood pressure are the relations of hematocrit with whole blood viscosity,\(^1\) of whole blood viscosity with peripheral resistance, and of peripheral resistance with blood pressure.\(^2\) It has been proposed that with treatment of anemia, cessation of vasodilation (previously present because of tissue hypoxia) and increased blood viscosity, both resulting from the therapeutic increase in hematocrit, account for the increased peripheral resistance with rise of blood pressure observed.\(^17\)\(^–\)\(^18\) It seems unlikely that a hypoxia-related mechanism can explain the association between hematocrit and blood pressure in general populations. Therefore, the greater blood viscosity caused by higher hematocrit and the consequent increased resistance to blood flow appear the most reasonable causes underlying the association between hematocrit and blood pressure in the present report. In this regard, it is noteworthy that large changes in hematocrit do not lead to large changes in blood viscosity, and therefore intrinsic resistance to blood flow, but also vascular resistance of small vessels in isolated organs.\(^27\)\(^–\)\(^28\)

High hematocrit in hypertension could reflect a true increase in red blood cell mass as well as hemoconcentration caused by a reduction in plasma volume. Plasma volume in established essential hypertension is reported to be normal, low, or also high in some individuals.\(^29\) This might lead to the conclusion that hypertensive individuals have a continuum of plasma volume values not different from that of nonhypertensive individuals or that low, normal, or high plasma volumes reflect different forms of essential hypertension or different stages of the disease. Data from the present report cannot rule out the possibility that high hematocrit is characteristic of hypertensive people with reduced plasma volume. However, high hematocrit in hypertension was shown to be independent of confounders such as gender, age, body mass index, smoking habit, antihypertensive treatment, and severity of hypertension, suggesting that high hematocrit was not specific to a particular hypertensive group. Moreover, most of the hypertensive participants treated with nondiuretics (Table 3) were receiving sympatholytic agents or vasodilators, or both, drugs that induce an expansion of plasma volume.\(^2\) Nevertheless, this subgroup of treated hypertensive individuals had high average hematocrit. Finally, in genetically hypertensive rats, hematocrit is high\(^8\)\(^–\)\(^10\) despite normal plasma volume.\(^10\) These observations are not concordant with the hypothesis that high hematocrit depends on reduced plasma volume in hypertension.

In summary, the present study reports, in a general population sample, an independent significant association between hematocrit and prevalence of hypertension and a positive relation between hematocrit and blood pressure. Hematocrit is, on average, high in hypertensive individuals despite reduction of blood pressure even in the hypertensive group treated with drugs other than diuretics, suggesting that high hematocrit in hypertension is not secondary to high blood pressure. These data are consistent with the hypothesis that variations of hematocrit even within its "normal"
range might contribute to regulation of blood pressure and facilitate onset or maintenance of hypertension. The results of the study suggest the need for a controlled intervention study to test the effect of hematocrit reduction on blood pressure in high-hematocrit hypertensive people. Proceeding from the hypothesis that hematocrit positively affects blood pressure, further research should examine the definition of "normal" hematocrit from a cardiovascular point of view and the factors (diet, tobacco smoking, overweight, and possibly others) responsible for the regulation of hematocrit level.

Acknowledgments

The Gubbio Population Study was supported, planned, and carried out by the Center for Epidemiological Research, Merck Sharp & Dohme, Italy (MSD, Italy) in cooperation with the Center for Preventive Medicine (CPM) in Gubbio. Determination of erythrocyte sodium-lithium countertransport was performed in the laboratory of the Institute of Internal Medicine and Metabolic Diseases (IIMMD), Second Medical School, University of Naples, Italy; determination of serum lipids was performed in the laboratory of the Istituto Superiore di Sanità (ISS), Rome, Italy. The study was made possible thanks to the people of Gubbio, its community leaders, particularly Dr. Sanio Panfile and Oliviero Faramelli, and its physicians.

The research has been supervised and guided by a Scientific Policy Board, whose members are Prof. Pietro Angeletti (Chairman, MSD, Rome), Prof. Mario Mancini (IIMMD), Prof. Rose Stamler and Prof. Jeremiah Stamler of the Department of Community Health and Preventive Medicine (DCHPM), Northwestern University Medical School, Chicago, Prof. Alessandro Menotti (ISS), and Prof. Alberto Zanchetti, Institute of Internal Medicine, University of Milan, Italy.

Thanks are expressed for the fine cooperation of the staff of the Gubbio Civil Hospital, particularly Dr. Walter Panarelli, Dr. Mario Angeletti, Dr. Ondina Cardoni, Dr. Giuseppe Montanari, Dr. Andrea Trenti, and the staff of the Gubbio Civil Hospital laboratory, particularly Beatrice Fiorucci, Dr. Nicoletta Bettelli, Dr. Cristina Manuali, Giuseppe Monarchi, and Dr. Paolo Menichetti. It is a pleasure also to acknowledge the fine work of the field survey team (CPM): Katia Bartoletti, Dr. Federica Biancarelli, Dr. Luciano Matarazzì, Anita Scavizzi, Dr. Oscar Terradura, Dr. Guido Monacelli, Dr. Nando Scarpelli, Dr. Luigi Codovini, Dr. Claudio Cancellotti, Panfilia Mastrogiuseppe, Paola Stocchi, Cristina Rogari, Dr. Ida Blasi, Renata Bartolini, Annamaria Bartoletti, Valeria Ciufoli, Laura Braca, and of its supervisor Dr. Massimo Panfili.

Thanks are also gratefully expressed to Dr. Luigi Carcatelli (MSD, Italy) for his support and Dr. Ed Roccella of the National Heart, Lung, and Blood Institute, Bethesda, MD., for his valuable assistance; to Dr. Alan Dyer, Dr. Kiang Liu, and Dan Garside of the DCHP in Chicago; and to Dr. Vittorio Krogh of the Department of Social and Preventive Medicine, State University of New York at Buffalo, for their aid in the joint statistical analyses in Italy and the USA.

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*Hypertension*. 1992;20:319-326
doi: 10.1161/01.HYP.20.3.319

*Hypertension* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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