

HYPERTENSION, TYPE 2 DIABETES, AND BLOOD GROUPS IN A POPULATION OF AFRICAN ANCESTRY

Objective: To evaluate the possible relationship of hypertension and diabetes with the ABO, Rhesus, and Duffy blood groups, which are known markers of African ancestry.

Design: Population-based study.

Setting and Participants: A random sample of 1253 Barbados residents, ≥ 40 years of age.

Main Outcome Measures: Hypertension was defined as a systolic blood pressure >140 mm Hg or a diastolic blood pressure >90 mm Hg or use of antihypertensive treatment; type 2 diabetes was defined as a glycosylated hemoglobin level $>10\%$ and/or a history of treatment in those >30 years of age.

Results: In logistic regression analyses, elevated diastolic blood pressure was positively associated with years of age (odds ratio [OR] 1.03, 95% confidence interval CI 1.02–1.05), the Rhesus D+ antigen (OR 2.68, 95% CI 1.21–5.97) and body mass index (OR 1.53, 95% CI 1.19–1.96), but negatively associated with the ABO blood group A allele (OR 0.68, 95% CI .48–.97). A separate logistic regression model indicated that the likelihood of diabetes increased with years of age (OR 1.03, 95% CI 1.01–1.04), hypertension (OR 1.56, 95% CI 1.10–2.20), body mass index (OR 1.68, 95% CI 1.29–2.20), and waist-hip ratio (OR 1.36, 95% CI 1.05–1.75), but decreased with presence of the Rhesus C+ antigen (OR .66, 95% CI .44–.97).

Conclusions: The associations of diabetes and hypertension to these blood groups support possible genetic influences on both conditions in this and similar African-origin populations; however, further investigations in other settings are necessary to more fully elucidate these findings. (*Ethn Dis.* 2006;16:822–829)

Key Words: Duffy and Rhesus Blood Groups, ABO, Blood Pressure, Diabetes

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INTRODUCTION

Westernized populations of African origin have significantly higher rates of hypertension and type 2 diabetes than do European-origin populations.^{1,2} These conditions are highly prevalent in Barbados, West Indies,^{3,4} and in other populations of African descent, including African Americans, who have similar ancestral origins.^{5,6} The reasons for these disparities, however, are not well quantified, and considerable controversy exists on the specific mechanisms and extent to which genetic factors may contribute.

Certain blood groups are known to have phenotypic frequency differences in African and European-origin populations,⁷ and these blood systems have been used as markers of African ancestry.^{8–10} Studying the distribution of these markers may help in understanding the disproportionate incidence of hypertension and type 2 diabetes in persons of African heritage. We hypothesize that both conditions are likely influenced by multiple genes that, either directly or indirectly, regulate key underlying mechanisms (eg, glucose metabolism, renin levels); as such, the varying frequency of these genes across populations may lead to varying levels of risk. Several studies have investigated the possible relationship of type 2 diabetes to the ABO, Rhesus (Rh), and

Duffy blood groups^{11–15}; most were conducted in predominantly European-origin populations, and the findings have been inconsistent. Although some studies exploring the relationship between blood pressure and these same blood groups have included populations of African descent,^{16–20} their findings have been similarly inconclusive. The purpose of this investigation is to evaluate whether the ABO, Rh, and Duffy blood groups are associated with type 2 diabetes and/or hypertension in Barbados, a population of relatively low admixture.^{21,22} To our knowledge, no study of this type has been carried out among a random sample of a predominantly African-origin population.

METHODS

Study Population

This investigation is based on a subset ($n=1253$) of the Barbados Eye Study (BES) cohort. The BES was a population-based prevalence study aimed at evaluating the prevalence and risk factors for major eye diseases in a population of predominantly African descent. The BES included 4709 randomly selected participants (84% of those eligible) between 40 and 84 years of age; 4631 were examined at the study site. Of these, 1253 (93% of those examined between July 1, 1989, and June 30, 1990) completed typing for the ABO, Rh, and Duffy blood groups, thus representing the basis for the present investigation.

The BES protocol was standardized and comprehensive, including blood pressure measurements with a random zero sphygmomanometer; measure-

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ments of height, weight, and abdominal and hip circumferences; and a detailed interview, including medical, family, and ocular history, medication use, demographic information, alcohol use, smoking history, education, and occupation. Additionally, ocular measurements included visual acuity, perimetry, tonometry, and fundus photography, along with a comprehensive ophthalmologic evaluation. Blood was drawn to measure glycosylated hemoglobin (GHb) (3754 participants; GHb was not measured during the first months of the study) and for typing of the ABO, Rh, and Duffy blood groups.

Laboratory Blood Tests

Glycosylated hemoglobin (GHb) assays were performed by affinity chromatography of venous whole blood by using Glyc-Affin GHb kits (Isolab, Akron, Ohio). Typing was complete for the blood groups as follows: ABO (blood grouping reagent Anti-A, Anti-B, Anti-A,B [Human Polyclonal, Immucor Inc, Norcross, Ga]); Rh (blood grouping reagent Anti-C, Anti-E, Anti-c, Anti-3, Anti-CDE [high protein reagents] and blood grouping reagent Anti-D [high protein reagent] for slide, rapid tube, and microplate tests [Immucor Inc]); and Duffy (blood grouping reagent Anti-Fy^a for indirect antiglobulin tests [Immucor Inc]).

Quality Control Assessments

Blood pressure measurements were assessed by digit preference monitoring and ongoing serial replicate evaluations, with re-training provided on an as-needed basis. Quality control (QC) assessments indicated good reproducibility for all laboratory measures. Duplicate testing for GHb was performed on a random sample ($n=264$) and yielded an intraclass correlation coefficient of .89. Additionally, duplicate samples ($n=66$) were drawn for QC evaluation of blood group typing. The results, based on unweighted kappa (κ) statistics and percentage agreement, are as follows: ABO blood group, $\kappa=.97$, exact agreement 98.5%; Rhesus C, D, and E antigens, $\kappa=.96$, 1.00, and .87 (respectively), exact agreement =98.5%, 100.0%, and 95.4%, respectively; Duffy Fy^a antigen, $\kappa=.82$, exact agreement=96.9%.

Statistical Analyses

Factors evaluated in the analyses included: 1) age, sex; 2) self-reported ancestry (African-derived, African and European [mixed], European-derived, other); 3) height, weight, body mass index (BMI) (kg/m^2) (classified as values above the upper quintile [high], values below the lower quintile [low], and values in between [medium]), and waist-hip ratio (WHR) (similarly categorized as high, medium, low); 4) systolic blood pressure (SBP) (average of two measurements), diastolic blood pressure (DBP) (similarly measured), history of antihypertensive treatment, and hypertension (defined as SBP>140 mm Hg or DBP>90 mm Hg or use of antihypertensive treatment); 5) GHb level, history of physician-diagnosed diabetes and treatment, type 2 diabetes (defined as GHb>10% [two standard deviations above the mean of persons without a diabetes history], and/or history of treatment in persons with late diabetes onset [>30 years]); 6) socioeconomic status (SES, defined as education duration ≤ 9 years and

service occupations [low], education >9 years and professional occupations [high], and other [medium]); and 7) smoking history and alcohol use.

Mantel-Haenszel (MH) age- and sex-adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were used to compare blood pressure and diabetes variables for each of the blood group types. Significant blood group variables were subsequently included in logistic regression models to evaluate associations with variables relating to hypertension and diabetes, while controlling for possible confounders. The Statistical Analysis System (SAS)²³ was used to analyze the data for this report.

RESULTS

Table 1 presents the characteristics of the entire BES cohort ($n=4631$) and the subsample ($n=1253$) who had additional blood drawn for typing of the ABO, Rh, and Duffy blood groups. The two groups were similar in the distribution of age, sex, anthropometric, blood pressure, and GHb measurements, as well as other demographic factors. The subsample differed slightly (but significantly) from the cohort regarding the following characteristics: more participants of African descent, a smaller average waist-hip ratio, a higher percentage of antihypertensive treatment usage, and fewer reports of ever drinking. Of note, 53% of both groups had hypertension, and 17% met the criteria for type 2 diabetes (only two persons were classified as having type 1 diabetes [age of onset <30 years] – one was receiving insulin and the other was not). The median BMI and WHR values for the sample were high ($26.4 \text{ kg}/\text{m}^2$ and .92, respectively), indicating a tendency for obesity in the population.

The distribution of phenotype frequencies for the ABO, Rh, and Duffy blood groups by self-reported race has been published previously.²¹ These data indicated significant differences in spe-

Table 1. Characteristics of the subsample vs BES cohort

Variables	Subsample (n=1253)	BES Cohort (n=4631)
Age (years), mean ± SD (median)	59.1 ± 12.2 (59)	59.0 ± 12.1 (58)
Male, %	44	43
Self-reported race, % African-origin*	96	93
Height (cm), mean ± SD (median)	164.5 ± 9.9 (164)	164.6 ± 10.0 (164)
Weight (lbs), mean ± SD (median)	159.9 ± 31.0 (159)	160.0 ± 32.1 (158)
BMI (kg/m ²), mean ± SD (median)	26.9 ± 5.4 (26.4)	26.9 ± 5.4 (26.2)
WHR, mean ± SD (median)*	.90 ± .09 (.92)	.92 ± .08 (.92)
Hypertension, %	53	53
SBP (mm Hg), mean ± SD (median)	136.8 ± 23.7 (133)	136.7 ± 23.0 (134)
DBP (mm Hg), mean ± SD (median)	80.9 ± 12.0 (80)	81.2 ± 12.1 (80)
Treatment, %*	32	29
Diabetes, %	17	17
GHb (among those with no history of diabetes), mean ± SD (median)	7.1 ± 1.4 (6.9)	7.1 ± 1.5 (6.9)
GHb (overall), mean ± SD (median)	7.7 ± 2.3 (7.1)	7.7 ± 2.3 (7.1)
Treatment, %	14	15
SES, % low	34	33
Ever smoke, %	9	11
Ever drink, %*	14	18

* *P* < .05, differences between subsample and BES cohort.

Hypertension defined as systolic blood pressure (SBP) > 140 or diastolic blood pressure (DBP) > 90 or history of anti-hypertensive treatment.

Diabetes defined as glycosylated hemoglobin (GHb) > 10% or treatment.

BES=Barbados Eye Study; SD=standard deviation; BMI=body mass index; WHR=waist-hip ratio; SES=socioeconomic status.

cific antigens between African- and European- origin participants in each of the blood groups. Participants of African descent had a higher frequency of the ABO B antigen (B, AB types) (*P* = .04) and were more likely to be Rh C- (*P* = .001) and D+ (*P* = .01) than European participants. The most common Rh phenotype among African-origin participants in the subsample was C-D+E- (56% vs 8% in Europeans, *P* = .001). Participants of African ancestry also had a lower frequency of Duffy Fy^{a+} (*P* = .001) than those participants of European ancestry. Because of the small number of mixed and European-origin participants, however, the remaining analyses are based on participants of African descent only.

Age- and sex-adjusted MH analyses for associations between blood pressure and the given blood groups are presented in Table 2. No significant associations were found between elevated SBP (>140 mm Hg) or hypertension and any of the blood types. Elevated DBP (>90 mm Hg) was negatively associated with the ABO A antigen (A,

AB types) with a significant protective effect; high DBP was also positively associated with Rh D+. Separate MH evaluations of the ABO A antigen (vs all others), the Rh C-D+ (vs all others) and C-D+E- (vs all others) resulted in no significant findings for SBP, DBP, or hypertension (data not shown).

Table 3 shows the logistic regression model used to evaluate the association of DBP (dichotomized as a categorical variable, as in the MH analyses: DBP ≤ 90 mm Hg vs DBP > 90 mm Hg) with the ABO and Rh blood groups, while controlling for age, sex, BMI, WHR, diabetes, smoking, alcohol use, and SES. The results confirmed the decreased likelihood of elevated DBP in the presence of the ABO A antigen (A, AB types) and the significant increase with presence of Rh D+. As expected, age and body size also significantly contributed to the increased risk of elevated DBP, whereas sex was not a statistically significant factor. Results of a subsequent multiple regression analysis, using DBP as a continuous variable, indicated that

the ABO blood group (A, AB vs B, O types) (*P* = .047), age (*P* < .001), and BMI (*P* = .004) were significant factors in the model, with no main or interaction effects noted for Rh D.

Mantel-Haenszel (MH) analyses for associations with factors relating to diabetes are presented in Table 4. The first column of the table presents the frequency (%) of participants with elevated GHb levels, regardless of treatment; the second column indicates the percentage of those receiving treatment, regardless of GHb level. Diabetes is defined as having a GHb level > 10% or a history of treatment. The results indicate a significant negative association between diabetes and Rh C+. Additional analyses for Rh C-D+ (vs all others) and C-D+E- (vs all others) yielded no significant associations with GHb, treatment or diabetes (data not shown).

The logistic regression model used to evaluate associations with diabetes is presented in Table 5. After controlling for age, sex, smoking, and SES, the results confirmed the decreased likeli-

Table 2. Age- and sex-adjusted Mantel-Haenszel odds ratios and 95% confidence intervals for associations of blood pressure with blood groups

Blood Type	Systolic BP		Diastolic BP		Hypertension†	
	≤140 (n=760) (%)	>140 (n=446) (%)	≤90 (n=976) (%)	>90 (n=230) (%)	No (n=567) (%)	Yes (n=639) (%)
ABO						
A vs no A‡	27	28	29	22	28	27
	1.09 (.81–1.45)		.70 (.50–.99)*		.99 (.75–1.30)	
B vs no B‡	27	24	26	26	27	26
	.80 (.60–1.08)		1.01 (.73–1.41)		.93 (.71–1.22)	
Rhesus						
C+ vs C–	24	25	25	25	25	25
	1.05 (.78–1.42)		1.02 (.73–1.43)		.99 (.75–1.32)	
D+ vs. D–	94	93	93	97	93	94
	1.12 (.66–1.88)		2.67 (1.21–5.90)*		1.37 (.83–2.26)	
E+ vs. E–	18	16	18	15	19	16
	.83 (.59–1.18)		.84 (.57–1.25)		.80 (.58–1.10)	
Duffy						
A+ vs A–	8	10	9	9	8	10
	1.10 (.71–1.70)		.97 (.59–1.62)		1.02 (.66–1.57)	

* $P < .05$.

† Systolic blood pressure >140 mm Hg or diastolic blood pressure >90 mm Hg or history of antihypertensive treatment.

‡ A vs no A (A, AB vs B, O); B vs no B (B, AB vs A, O).

BP=blood pressure.

hood of diabetes in the presence of Rh C+. Other significant risk factors included age, hypertension, BMI, and WHR. Alcohol use was also protective for diabetes in the model, a result likely due to the instability of the data and the questionable reliability of self-reported information relating to alcohol consumption, rather than a true finding. In a subsequent multiple regression analysis with GHb as a quantitative variable, the Rh C antigen ($P = .029$),

age ($P = .002$), and BMI ($P < .001$) were significant, whereas alcohol use was not ($P = .532$).

DISCUSSION

Findings from the present study lend support to the hypothesis that genetic factors related to the distribution of some blood groups may play a role in the development of both type 2

diabetes and elevated blood pressure. A significant association was found between the ABO blood group and DBP; those carrying the A allele (blood types A or AB) were less likely to have high DBP than those of type B or O. This finding, in conjunction with the lower frequency of the A allele in African-derived vs European-derived populations, suggests a potential link between the ABO system and hypertension. Additionally, in this population, Rh D+ was associated with elevated DBP in the logistic regression analysis, a finding that should be interpreted with caution, as the multiple regression model did not substantiate this result. The study did find, however, a conclusive significant negative association between diabetes and Rh C+, an antigen that is 2.5 times less frequent in Barbados African individuals than those of European origin. The relatively low frequencies of the A and Rh C+ alleles in populations of African origin may contribute to their high incidence of diabetes and hypertension.

Table 3. Logistic regression results for associations with elevated diastolic blood pressure*

Risk Factor	Odds Ratio	95% Confidence Interval
Age	1.03	(1.02–1.05)
Female sex	1.16	(.82–1.63)
ABO (presence of A allele)	.68	(.48–.97)
Rhesus (D+)	2.68	(1.21–5.97)
BMI	1.53	(1.19–1.96)

* Elevated diastolic blood pressure (DBP) categorized >90 mm Hg.

BMI=body mass index.

In addition to the variables presented in the table, the model included diabetes (glycosylated hemoglobin >10% and/or treatment), smoking, drinking, socioeconomic status, and waist-hip ratio. Age was entered as a continuous variable.

Table 4. Age and sex-adjusted Mantel-Haenszel odds ratios and 95% confidence intervals for associations of diabetes with blood groups

Blood Type	GHb		Treatment		Diabetes§	
	≤10 (n=1080) (%)	>10 (n=124) (%)	No (n=1027) (%)	Yes (n=177) (%)	No (n=1001) (%)	Yes (n=203) (%)
ABO						
A vs no A†	27	26	27	29	27	29
	.97 (.63–1.49)		1.17 (.82–1.68)		1.12 (.80–1.58)	
B vs no B†	26	29	25	31	26	30
	1.16 (.76–1.75)		1.32 (.93–1.88)		1.21 (.87–1.70)	
Rhesus						
C+ vs C–	25	18	25	20	26	19
	.69 (.43–1.11)		.73 (.49–1.09)		.67 (.45–.98)*	
D+ vs D–	93	93	94	91	94	93
	1.08 (.51–2.33)		.75 (.41–1.36)		.90 (.49–1.62)	
E+ vs E–	17	16	17	17	17	16
	.90 (.54–1.49)		.99 (.64–1.51)		.92 (.61–1.39)	
Duffy						
A+ vs A–	9	6	9	7	9	7
	.62 (.29–1.32)		.64 (.34–1.20)		.64 (.35–1.16)	

* P<.05.

† Two participants with type 1 diabetes were excluded from this analysis.

‡ A vs no A (A, AB vs B, O); B vs no B (B, AB vs A, O).

§ Glycosylated hemoglobin (GHb) >10% or history of treatment.

African ancestry is an established risk factor for both type 2 diabetes and hypertension.^{1–6,24,25} However, the reason(s) for the disparity in rates of these conditions in African vs European populations is still not well understood. We theorize that specific blood systems shown to be markers of African descent^{7–10} may provide evidence for certain genetic influences on diabetes and hypertension. As such, the ABO, Rh, and Duffy blood groups were selected for this investigation. Perhaps

these markers, significantly more (or less) common among African-derived populations, contribute to the increased rates of disease.

The distribution of blood types in African- and European-origin participants in this study has been previously described²¹ and follows similar patterns to those reported elsewhere for each of the three blood group systems.^{7,26,27} That is, African-derived individuals tend to have a higher frequency of the ABO B antigen and are predominantly

Rh C–D+E–, whereas European-derived individuals are more likely to carry the ABO A antigen and exhibit the Rh C+D+E– phenotype. The frequency of the Duffy A antigen is markedly different among the two groups; persons of African ancestry have a much lower frequency of the A+ antigen compared to those of European descent. Our data,²¹ which are consistent with others,²² therefore suggest that Barbados has a low degree of genetic admixture involving individuals of European origin.

Table 5. Logistic regression results for associations with diabetes*

Risk Factor	Odds Ratio	95% Confidence Interval
Age (years)	1.03	(1.01–1.04)
Female sex	1.04	(.73–1.49)
Rhesus (C+)	.66	(.44–.97)
Hypertension†	1.56	(1.10–2.20)
BMI	1.68	(1.29–2.20)
WHR	1.36	(1.05–1.75)
Ever drink	.47	(.24–.91)

* Glycosylated hemoglobin (GHb) >10% or treatment. In addition to the variables presented in the table, the model included smoking and socioeconomic status (indicator of school and occupation). Age was entered as a continuous variable.

† Hypertension is defined as systolic blood pressure >140 mm Hg or diastolic blood pressure >90 mm Hg or history of antihypertensive treatment.

BMI=body mass index; WHR=waist-hip ratio.

Blood Pressure

Three decades ago, MacLean et al¹⁸ were among the first to report a correlation of DBP with genetic markers known to be more common in sub-Saharan African than European populations, thus supporting the theory that African ancestry may influence variation in blood pressure. Subsequently, evaluations between certain blood types and elevated blood pressure have been carried out in various populations and have resulted in somewhat inconclusive findings. Kesteloot and Van Houte²⁸

A significant association was found between the ABO blood group and DBP; those carrying the A allele (blood types A or AB) were less likely to have high DBP than those of type B or O.

reported an association between the ABO blood group and blood pressure among >42,000 Belgian men. They found that those with blood type AB had the highest values of SBP and DBP, whereas no significant differences in blood pressure were noted according to Rh D+ and D- phenotypes. A multiple regression analysis indicated that blood types B and AB made significant but very small contributions to DBP. Another study of 621 male and 577 female youths (17 years of age) in Israel²⁹ reported a positive association between the ABO blood group A antigen and elevated SBP and DBP among only the males, with no significant findings for the Rh system. A third investigation suggested significant associations between SBP, in particular, and the ABO B antigen among a subsample of youths of European descent ($n=573$) from Bogalusa and a concordant, yet not significant, effect in their African-origin subsample ($n=325$).¹⁹ The authors suggest, however, that height may account for the detected differences, as individuals with the B antigen were significantly taller than non-B individuals, and the strongest association in the discriminant analysis was exhibited between ABO blood type and height.

More recently, two studies by Robinson et al support the role of genetics on blood pressure in African Caribbean populations.^{16,17} The first reported a genetic influence on the increase of BP with age among normotensive

individuals in Barbados,¹⁶ and the second found a significant association of SBP with the Rh blood group among a population-based sample of 141 Afro-Caribbeans in Dominica.¹⁷ Although we did not find significant associations with SBP and any blood type in the present study, the logistic analyses indicated an association with the Rh and ABO blood groups and DBP (>90 mm Hg vs ≤ 90 mm Hg). While the association with Rh D+ was not maintained in the subsequent multiple regression analysis, age, BMI, and absence of the ABO A antigen were related to DBP, after controlling for factors known to be associated with hypertension. Since African-origin populations tend to have a higher frequency of the ABO B antigen, this association with DBP supports the hypothesis that they may be at greater risk of developing elevated DBP because of their lower frequency of the A antigen (a possible protective factor).

Earlier studies observed that individuals of African descent with elevated BP had a significantly higher frequency of low-renin hypertension when compared with European hypertensives.³⁰ Although the reason for the possible protective effect of the A antigen is not well understood, we speculate that since blood pressure is multifactorial, perhaps the ABO antigens play a role by influencing renin levels and affecting plasma angiotensin and aldosterone secretion, thus indirectly influencing arterial pressure. Additional investigations of possible relationships between the angiotensinogen (AGT) gene and the ABO blood group would be helpful to determine if such a hypothesis is substantiated.

In light of the recent finding by Robinson et al,¹⁷ who reported a significant association between AGT and the Rh blood group D haplotype in Afro-Caribbeans, the possibility of a "hypertension gene" on chromosome 1, where both the AGT gene and the Rhesus blood group reside, should be further

examined. One cannot discount the possibility that these and/or other genes in close proximity are co-segregating or are in linkage disequilibrium and contributing to the development of hypertension.

Why the strong association of the Rh D antigen with DBP from the present logistic analyses was not maintained in our multiple regression model is not clear. SBP and DBP measurements were not normally distributed in this cohort, and in an effort to explain the nonsignificant Rh results, additional regression analyses were performed, applying log and square root transformations to the BP measurements. The results, however, remained virtually unchanged (data not shown). Therefore, we conclude that the reasons for the nonsignificant finding with Rh D may be due to sample size considerations, only 6% of the sample carried the D- antigen, or perhaps that the MH result was simply a chance finding. Nevertheless, findings from the literature as well as the present study support, to varying degrees, associations between the ABO and Rh blood groups and SBP/DBP, thus suggesting a genetic influence on blood pressure.

Diabetes

Several reports have evaluated the possible relationship between diabetes and the Rh blood group, though the populations have been varied and the findings inconsistent. Results from the population-based San Antonio Heart Study ($n=1237$) found a high prevalence of type 2 diabetes mellitus among Mexican Americans with CDEe, CcDE, cDE, and cDe phenotypes, with a low prevalence among individuals with CcDEe and CcDe phenotypes.¹⁴ Similarly, a study of 180 patients with diabetes mellitus and 1000 controls in Oslo, Norway, reported a deficiency of phenotypes with the CDe haplotype and an excess of those with cDE among diabetics.¹² Conversely, the opposite

pattern was noted among 1033 patients with diabetes and 1351 controls in Germany.¹³ Gloria-Bottini et al¹¹ reported an increase in glucose and HbA1C levels among DCcEe individuals and decreased levels among those with ddcee, compared to the mean values for other genotypes in a study of 278 individuals with type 2 diabetes in Italy. Findings from the present study support the San Antonio and Norway reports, noting a significantly ($P < .05$) lower frequency of the CDe phenotype among those with diabetes than those without. In particular, our investigation suggests that the C- antigen is a potential risk factor for type 2 diabetes. The inconsistent findings from the various studies may be the result of distribution differences of the Rh C, D, and E antigens in the different populations; however, the significant results in each point to the likelihood of a real association between diabetes and the Rh blood group. We theorize that the Rh blood system may play some role in the process of glucose metabolism and may influence the clinical expression of diabetes. This hypothesis is supported by Gloria-Bottini et al,¹¹ who reported that the contribution of Rh to GHb level is $\approx 5\%$.

In addition to the findings discussed above, describing significant associations between diabetes and hypertension with various blood groups, several studies have reported nonsignificant results. Berg et al¹² reported no association between the ABO blood group and diabetes in Oslo, and Miller concluded that both hypertension and glucose metabolism were unrelated to the Duffy antigens among 722 African-origin patients admitted to a hospital in Baltimore, Maryland.^{15,20} Our findings support these conclusions; with the Duffy A antigen exhibiting no relationship to either diabetes or hypertension, and the ABO blood group resulting in no association with diabetes. We cannot yet comment on the mechanisms through which particular genes control blood glucose levels (or blood pressure

for that matter); thus, future investigations are necessary to fully elucidate these genetic contributions to both diabetes and hypertension.

The present study has several limitations, including the relatively small sample size, the lack of a sufficient control group of European-derived individuals, and the small number of blood markers of African ancestry. However, the study's major strengths include the population-based design (as opposed to most others that are case-control) and the standardized protocol with quality control measurements.

In summary, the association between the ABO blood group and DBP in the Barbados African-origin population seems to support the role of this blood system in BP variation. Individuals of African ancestry tend to have a lower frequency of the A antigen compared to those of European ancestry, and this antigen may have some protective effect on the development of elevated DBP by influencing renin levels and aldosterone secretion, while possibly interacting with other genes such as AGT. Likewise, Rh C+ was negatively associated with diabetes in this study, which may be due to a direct (or indirect) influence of the Rh antigens on the process of glucose metabolism. Further confirmatory studies are needed to adequately evaluate these hypotheses.

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APPENDIX 1

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