Familial Resemblance for Resting Blood Pressure with Particular Reference to Racial Differences: Preliminary Analyses from the HERITAGE Family Study

CHI GU,[1] INGRID BORECKI,[1] JACQUES GAGNON,[2] CLAUDE BOUCHARD,[2] ARTHUR S. LEON,[3] JAMES S. SKINNER,[4] JACK H. WILMORE,[5] AND D.C. RAO[1,6]

Abstract Resting blood pressure in both white and black families participating in the HERITAGE Family Study was analyzed using a simple familial correlation model to assess familial influences. The two samples of black and white families were analyzed separately and together, providing an opportunity to test for heterogeneity in the familial resemblance. Maximal heritability was 46% for systolic blood pressure (SBP) and 31% for diastolic blood pressure (DBP) in the pooled sample. Noticeably higher heritabilities were found in the black sample (68% for SBP and 56% for DBP) than in the white sample (43% for SBP and 24% for DBP). The patterns of familial correlations were similar in blacks and whites, with the exception that spouse resemblance was significant in white families but not in black families. These results along with the finding that the magnitude of the familial correlations was higher in the black sample than in the white sample suggest that the effects of host and familial environmental factors differ between the races.

A genetic basis for the biological mechanisms affecting blood pressure and hypertension has been evident in numerous studies. Several investigations have reported a substantial influence of environmental and social factors on the variability of blood pressure (Williams 1992; Fumo et al. 1992; Ward 1983; Dressler 1991), but recent studies using animal models and young twins strongly support the role of genotypes in mediating blood pressure and hypertension (Kreutz et al. 1995; McCaughran et al. 1984; Grim et al. 1984; Yu

[1] Division of Biostatistics, Washington University School of Medicine, Box 8067, 600 S. Euclid Avenue, St. Louis, MO 63110.

[2] Physical Activity Sciences Laboratory, Laval University, Ste-Foy, Québec, Canada.

[3] School of Kinesiology and Leisure Studies, University of Minnesota, Minneapolis, MN 55455.

[4] Department of Kinesiology, Indiana University, Bloomington, IN 47405.

[5] Department of Kinesiology and Health Education, University of Texas, Austin, TX 78712.

[6] Departments of Psychiatry and Genetics, Washington University School of Medicine, St. Louis, MO 63110.

Human Biology, February 1998, v. 70, no. 1, pp. 77–90.

KEY WORDS: BLOOD PRESSURE, FAMILIAL CORRELATIONS, POPULATION HETEROGENEITY, BLACKS, AFRICAN AMERICANS, WHITES, HERITAGE FAMILY STUDY

et al. 1990; Levine et al. 1982), implicating the angiotensionogen gene as a probable susceptibility locus controlling the physiological pathways (Jeunemaitre et al. 1992). Identifying specific mutations is difficult, undoubtedly because blood pressure is a complex quantitative trait with, possibly, a considerable amount of genetic heterogeneity. Furthermore, differences in the distribution of blood pressure and the rate of hypertension between white and black populations have long been noticed and studied (Harburg et al. 1978; Levin 1983; Seedat 1990; Langford et al. 1991; Somova et al. 1995), although specific factors affecting these differences have been difficult to identify.

The HERITAGE Family Study is a massive effort to identify and document the role of genetic and environmental factors in cardiovascular, metabolic, and hormonal responses to endurance exercise training (Bouchard et al. 1995). Blood pressure measurements and many other metabolic indicators were collected from both Caucasian (white) and African American (black) families. These measurements provide a basis for quantifying the familial aggregation for blood pressure regulation and for exploring potential ethnic differences in the familial patterns.

As a preliminary investigation, we evaluated the family data on resting blood pressure in both black and white Americans using a simple familial correlation model. Although many blood pressure studies have been done in the past, the current study is novel in that both white and black families were sampled under the same sampling and measurement protocols, and all the members of the families were sedentary at the beginning of the study (Bouchard et al. 1995). Individuals were considered sedentary if they had no regular physical activity over the previous 6 months, meaning no activities lasting 30 min or more involving an energy expenditure of at least 7 METS (based on American Heart Association criteria) for subjects 50 years of age or older and 8 METS for those younger than 50 years for more than once a week. (One MET equals 3.5 ml O_2 uptake per kilogram of body weight per minute.) Familial correlations were estimated within each group separately and in a pooled sample, and potential heterogeneity between the white and black familial patterns was assessed.

Materials and Methods

For the current analysis 86 white families and 74 black families with data on baseline blood pressure were used. A detailed study protocol was reported by Bouchard et al. (1995). The essential participation criteria include ages 16–65 years, healthy but sedentary families, body mass index (BMI) usually under 40 kg/m^2, and systolic/diastolic blood pressure less than 159/99 mm Hg. Individuals with definite or possible coronary heart disease, chronic or recurrent respiratory problems, and uncontrolled endocrine and metabolic disorders (including diabetes or the use of lipid-lowering drugs) were also excluded from the study. The rationale for admitting people with

mild hypertension (systolic blood pressure 140–159 mm Hg and/or diastolic blood pressure 90–99 mm Hg) without complication is that exercise training is reported to reduce elevated levels of both systolic and diastolic blood pressure by about 10 mm Hg on average (Fagard and Tipton 1994).

Variables and Adjustments. Resting blood pressure measurements were made on two separate days before the start of exercise training (baseline). Only the baseline measures were used here. On each of the two days subjects were tested before 11:00 A.M. in the postabsorptive state with no caffeine-containing beverages and tobacco products for at least 2 hr before measurement. Measurements were performed in a quiet room at neutral ambient temperature (24–25°C) with the lights dimmed; before measurement, subjects rested for at least 5 min in a reclining chair with their legs elevated and the chair's back support reclined at about 45° from the ground. Blood pressure was determined using a properly fitted cuff connected to a Colin STBP-780 automated unit. Earphones were worn by the technicians during measurements to confirm blood pressure values. On each of the two days the first blood pressure reading was discarded, and up to three valid measurements were made. A measurement was considered valid if the automated reading was consistent with the manual reading. For the purposes of this analysis the average of all subsequent valid readings taken on both days for a subject (up to a maximum of six) was defined as the blood pressure value for that subject.

Table 1 shows the sample sizes, means, and standard deviations for the baseline measures and for age separately in each of the sex and generation groups (fathers, mothers, sons, and daughters). The mean blood pressure level is higher overall in blacks and in the parent generation and is higher in males than in females in whites but not in blacks. However, based on a comparison of standard errors, the differences are not statistically significant.

The measurements of systolic blood pressure (SBP) and diastolic blood pressure (DBP) were then adjusted for the effects of baseline age using a stepwise multiple regression procedure; the adjustments were done separately in each of the four sex-by-generation groups and separately by race. In summary, a given variable was regressed on a polynomial in age in a stepwise manner, retaining only those terms that were significant at the 5% level. The phenotype used in the genetic analysis was defined as the age-adjusted and standardized residual score from the regression analysis. Significant age terms and percentages of variance accounted for in each of the sex-by-generation-by-race groups for each phenotype are given in Table 2. Age terms were significant for a few subgroups.

Statistical Method. The familial resemblance for blood pressure is modeled as interindividual correlations among four groups of family members, namely, fathers (f), mothers (m), sons (s), and daughters (d). There are eight correlations in three familial classes: one spouse (fm), four parent-offspring

Table 1. Sample Sizes, Means, and Standardized Deviations for Baseline Measures Presented Separately for Each Sex and Generation Group by Race in the HERITAGE Family Study

	Father			*Mother*			*Son*			*Daughter*		
Variable	*N*	*Mean*	*SD*	*N*	*Mean*	*SD*	*N*	*Mean*	*SD*	*N*	*Mean*	*SD*
White												
Age	85	52.886	5.236	85	51.483	5.039	127	24.696	5.917	137	24.229	5.818
DBP	85	72.647	8.513	85	67.912	6.738	127	65.232	7.665	137	61.354	6.610
SBP	85	121.789	12.930	85	116.911	11.331	127	119.146	8.370	137	110.100	7.679
Black												
Age	22	50.409	7.481	37	47.568	7.108	50	26.780	6.753	84	26.464	7.375
DBP	22	75.500	8.898	37	77.257	8.800	50	71.170	6.891	84	70.399	8.218
SBP	22	125.485	12.843	37	128.018	14.367	50	123.973	9.048	84	119.343	11.355

Table 2. Significant Age Terms[a] (% Variance Accounted for) Used for Data Adjustment of Baseline Blood Pressure Measures in the HERITAGE Family Study

Variable	*Fathers*	*Mothers*	*Sons*	*Daughters*
SBP, white	none	age^3 (15.9%)	none	none
SBP, black	none	none	none	none
DBP, white	none	none	age (12.1%)	age (4.0%)
DBP, black	none	none	none	age (7.5%)

a. $p < 0.05$

(fs, fd, ms, md), and three sib correlations (ss, dd, sd). Assuming that the phenotypes within a family jointly follow a multivariate normal distribution, we used the computer program SEGPATH (Province and Rao 1995) to derive maximum-likelihood estimates of the correlations and likelihood ratio tests of hypotheses.

The general model (with no constraints on parameters) and two categories of null hypotheses were evaluated. One category of null hypotheses tested for sex and/or generation differences, including no sex differences in the offspring, no sex differences in parents or offspring, and no sex or generation differences (models 2–4 in Table 3). The other category tested the significance of the familial correlations, including no sibling resemblance, no parent-offspring resemblance, no spouse resemblance, and no familial resemblance at all (models 5–8 in Table 3).

Null hypotheses were tested using the likelihood ratio test, which is -2 times the difference in the log-likelihoods ($-2 \ln L$) obtained under the constrained and the general models. The log-likelihood ratio asymptotically follows a chi-square distribution with the degrees of freedom equal to the difference in the number of parameters estimated under the two nested models (Rao 1973). Constraints and degrees of freedom are presented in Table 3. Parsimonious models were developed and tested by grouping nonrejected null hypotheses. For nonnested parsimonious models that cannot be rejected the comparison of their fit is assisted by the Akaike (1974) information criterion (AIC), which is -2 times the log-likelihood plus twice the number of estimated parameters. The model with the lowest AIC is considered the most parsimonious one statistically. Maximal heritability h^2 was estimated under the most parsimonious model using

$$h^2 = (r_{po} + r_{sib})(1 + r_{fm})/(1 + r_{fm} + 2r_{fm}r_{po}), \quad (1)$$

where r_{po}, r_{sib}, and r_{fm} denote parent-offspring, sib-sib, and father-mother (spouse) correlations, respectively.

Table 3. Summary of Hypothesis Tests for Familial Resemblances of Blood Pressure in the HERITAGE Family Study

Model	*d.f*	*SBP, White*			*SBP, Black*			*DBP, White*			*DBP, Black*		
		χ^2	*p*	*AIC*	χ^2	*p*	*AIC*	χ^2	*p*	*AIC*	χ^2	*p*	*AIC*
1. General model				16.00			16.00			16.00			16.00
2. fs = fd, ms = md, sd = ss = dd	4	2.326	0.676	10.3	2.130	0.712	10.1	5.749	0.219	13.7	4.494	0.343	12.5
3. fs = fd = ms = md, sd = ss = dd	5	2.533	0.772	8.5	4.531	0.476	10.5	7.553	0.183	13.6	5.167	0.396	11.2
4. fs = fd = ms = md = sd = ss = dd	6	3.889	0.692	7.9	4.542	0.604	8.5	7.566	0.272	11.6	5.410	0.492	9.4
5. sd = ss = dd = 0	3	23.021	0.000	33.0	8.849	0.031	18.8	9.839	0.020	19.8	12.014	0.007	22.0
6. fs = fd = ms = md = 0	4	12.384	0.015	20.4	9.226	0.056	17.2	7.844	0.097	15.8	8.655	0.070	16.7
7. fm = 0	1	8.179	0.004	22.2	0.148	0.701	14.1	13.123	0.000	27.1	2.429	0.119	16.4
8. fm = fs = fd = ms = md = sd = ss = dd = 0	8	44.334	0.000	44.3	20.896	0.007	20.9	30.719	0.000	30.7	23.425	0.003	23.4
Parsimonious models													
4	6	3.889	0.692	7.9	4.542	0.604	8.5	7.566	0.272	11.6	5.410	0.492	9.4
4 and 7	7	13.543	0.060	15.5	5.064	0.652	7.1	20.816	0.004	22.8	6.851	0.445	8.9

We subtracted ($-2 \ln L$) under the general model from the AIC of all the submodels for easy comparison.

fs, father-son; fd, father-daughter; ms, mother-son; md, mother-daughter; sd, son-daughter; ss, son-son; dd, daughter-daughter.

Results

Model-fitting results for both white and black samples are presented in Table 3. For baseline SBP none of the hypotheses pertaining to sex and/or generation differences were rejected in either sample. In both samples there was no evidence of sex differences in offspring (model 2, $p = 0.676$ and $p = 0.712$ for white and black samples, respectively), no sex differences in parents or offspring (model 3, $p = 0.772$ vs. $p = 0.476$), and no sex or generation differences (model 4, $p = 0.692$ vs. $p = 0.604$). Sibling resemblance was significant in both white and black samples (model 5, $p < 0.001$ vs. $p = 0.031$). The parent-offspring correlation estimates were substantial in both the black and white samples, although they were of borderline significance in blacks perhaps because of the small sample size ($p = 0.056$). Spouse resemblance was significantly different from 0 in the white sample (model 7, $p < 0.001$) but not in the black sample ($p = 0.701$). The most parsimonious model turned out to be different for the two ethnic samples: model 4 (no sex or generation differences) for the white sample and models 4 and 7 (no sex or generation differences with zero spouse correlation) for the black sample.

For DBP again none of the sex and/or generation differences were significant in either sample. Namely, in both samples, there was no evidence for sex differences in offspring (model 2, $p = 0.219$ and $p = 0.343$ for white and black samples, respectively), no sex differences in parents or offspring (model 3, $p = 0.183$ vs. $p = 0.396$), and no sex or generation differences (model 4, $p = 0.272$ vs. $p = 0.492$). As with SBP, sibling resemblance for DBP was significant in both white and black samples (model 5, $p = 0.020$ vs. $p = 0.007$), whereas evidence for significant parent-offspring correlations was borderline in both samples (model 6, $p = 0.097$ vs. p 0.070). Spouse resemblance was significantly different from 0 in the white sample (model 7, $p < 0.001$) but, again, not in the black sample ($p = 0.119$). Therefore the most parsimonious hypothesis was again given by model 4 (no sex or generation differences) for the white sample and by models 4 and 7 (no sex or generation differences with zero spouse correlation) for the black sample.

We also performed the analysis for the pooled sample of black and white families (results not shown). There were no detectable differences by sex and/or generation, and familial correlations were significant. The most parsimonious model for both SBP and DBP in the pooled sample was model 4.

Estimates of the correlations ($\pm$ SE) are presented in Table 4 under both the general and the most parsimonious models. Familial resemblance is apparent in both white and black samples for both SBP and DBP, and the patterns of sibling and parent-offspring correlations are simple. Because there is significant spouse resemblance for the white sample, some portion of the familial resemblance is likely due to common environmental factors. Al-

Table 4. Estimates of Familial Correlations (± SE) under the General Model and the Most Parsimonious Model in Each Race and in the Pooled Sample

	SBP, White		*SBP, Black*		*SBP, Pooled*		*DBP, White*		*DBP, Black*		*DBP, Pooled*	
Parameter	*General*	*Most Parsimonious*	*General*	*Most Parsimonious*	*General*	*Most Parsimonious*	*General*	*Most Parsimonious*	*General*	*Most Parsimonious*	*General*	*Most Parsimonious*
fm	0.31 ± 0.10	0.32 ± 0.09	0.18 ± 0.30	(0)	0.31 ± 0.09	0.33 ± 0.08	0.38 ± 0.09	0.38 ± 0.09	0.25 ± 0.20	(0)	0.36 ± 0.08	0.37 ± 0.08
fs	0.26 ± 0.09	0.24 ± 0.05	0.56 ± 0.30	0.34 ± 0.07	0.29 ± 0.08	0.26 ± 0.04	0.16 ± 0.09	0.13 ± 0.05	−0.10 ± 0.13	0.28 ± 0.07	0.19 ± 0.08	0.17 ± 0.04
fd	0.19 ± 0.10	(0.24)	0.42 ± 0.28	(0.34)	0.23 ± 0.09	(0.26)	0.20 ± 0.08	(0.13)	0.50 ± 0.11	(0.28)	0.25 ± 0.07	(0.17)
ms	0.13 ± 0.10	(0.24)	0.30 ± 0.22	(0.34)	0.15 ± 0.09	(0.26)	0.05 ± 0.09	(0.13)	0.19 ± 0.16	(0.28)	0.10 ± 0.08	(0.17)
md	0.22 ± 0.09	(0.24)	0.22 ± 0.23	(0.34)	0.24 ± 0.08	(0.26)	0.09 ± 0.08	(0.13)	0.21 ± 0.16	(0.28)	0.12 ± 0.07	(0.17)
ss	0.30 ± 0.14	(0.24)	0.33 ± 0.28	(0.34)	0.33 ± 0.12	(0.26)	0.20 ± 0.12	(0.13)	−0.07 ± 0.20	(0.28)	0.21 ± 0.11	(0.17)
dd	0.38 ± 0.12	(0.24)	0.54 ± 0.15	(0.34)	0.43 ± 0.10	(0.26)	−0.08 ± 0.10	(0.13)	0.41 ± 0.14	(0.28)	0.04 ± 0.09	(0.17)
sd	0.25 ± 0.09	(0.24)	0.22 ± 0.19	(0.34)	0.25 ± 0.08	(0.26)	0.21 ± 0.08	(0.13)	0.51 ± 0.09	(0.28)	0.26 ± 0.07	(0.17)
Heritability (%)		43		68		46		24		56		31

fm, father-mother; fs, father-son; fd, father-daughter; ms, mother-son; md, mother-daughter; ss, son-son; dd, daughter-daughter; sd, son-daughter.
Numbers in parentheses were set to be equal to the coefficients estimated in the model.

Table 5. Tests for Heterogeneity of Familial Patterns of Blood Pressure

Model	*d.f.*	*SBP*		*DBP*	
		χ^2	*p*	χ^2	*p*
1. General model	8	4.707	0.79	11.011	0.20
2. fs = fd, md = md, sd = ss = dd	4	3.805	0.43	5.273	0.26
3. fs = fd = ms = md, sd = ss = dd	3	1.909	0.59	4.674	0.20
4. fs = fd = ms = md = sd = ss = dd	2	1.763	0.41	4.550	0.10
5. sd = ss = dd = 0	5	5.796	0.33	4.446	0.49
6. fs = fd = ms = md = 0	4	1.408	0.84	7.072	0.13
7. fm = 0	7	5.828	0.56	10.131	0.18
Parsimonious (4 and 7)	1	3.057	0.08	5.251	0.02

fs, father-son; fd, father-daughter; ms, mother-son; md, mother-daughter; sd, son-daughter; ss, son-son; dd, daughter-daughter; fm, father-mother.

though nonsignificance of the spouse correlation in blacks is consistent with a primarily genetic cause, it is unclear to what degree the small sample size contributed to the nonsignificance of the spouse resemblance. Therefore a primarily genetic pathway cannot be inferred in the blacks.

The maximum heritabilities (familial resemblances) are also presented in Table 4 under the most parsimonious models. These estimates range from 24% for DBP in the white sample to 68% for SBP in the black sample. We reiterate that these heritability estimates represent the effects of both genetic and familial environmental factors.

To assess the degree of heterogeneity in the familial resemblance of blood pressure between the white and black samples, we performed a simple likelihood ratio test under the general and the restricted null hypotheses and under the parsimonious model. Results of the hypothesis tests are given in Table 5. Familial patterns appear to be largely consistent between the two groups. Only under the parsimonious model is the test for heterogeneity significant for DBP ($p = 0.02$) and borderline for SBP ($p = 0.08$), suggesting weak heterogeneity between the two samples; this is attributable to the difference in the spouse correlations.

Discussion

Studies of young children, monozygotic twins, and animal models support a genetic influence on blood pressure [e.g., see Grim et. al. (1984), Rice et al. (1989), Hunt et al. (1989), Williams et al. (1991), Morishita et al. (1996), Kreutz et al. (1995), McCaughran et al. (1984), Jablonskis and Howe (1994), and Calhoun and Oparil (1995)]. Familial resemblance of blood pressure levels has been studied by many investigators in various ethnic groups and pop-

ulations [e.g., see Yu et al. (1990), Majumder et al. (1990), Rice et al. (1991, 1992), Darlu et al. (1990), and Wilson et al. (1991)]. Most of these studies reported a significant heritability, and estimates for white populations ranged from low to high. Using path analysis models, Pérusse et al. (1989) found heritabilities of 0.49 and 0.56 for children and 0.18 and 0.08 for adults for SBP and DBP, respectively. Friedlander et al. (1988) reported a heritabilities of 0.20 and 0.28 for SBP and DBP, respectively, whereas Hanis et al. (1983) estimated the heritability for SBP to be 0.15. A recent study on cardiovascular risk factors by Knuiman et al. (1996) reported a heritability of 27% for blood pressure. Although most of these studies agree on a genetic basis for human blood pressure levels, differences in the estimates of the strength of the familial component reflect varying constellations of environmental factors and gene-environment interaction effects.

Relatively few studies consider black families. In one large study involving blacks in the Detroit Project, Moll et al. (1983) reported a heritability of 0.35 in blacks versus 0.43 in whites for SBP and 0.53 in blacks versus 0.38 in whites for DBP. However, according to the standard errors reported there, the differences in the heritabilities between blacks and whites were not statistically significant. In the present study we estimated the maximum heritability under the most parsimonious model as 68% for SBP in blacks, which is twice as large as that found by Moll et al. (1983). The maximum heritability for DBP in the present study is 56%, which is in close agreement with Moll et al.'s (1983) results. For white samples our estimate is 43% for SBP, which is the same as in Moll et al.'s (1983) study. For DBP our estimate is 24%, which is within one standard error of Moll's estimate. Therefore it appears that the estimates obtained in the present study are comparable to those obtained from the Detroit Project, with the possible exception of SBP in blacks.

Different magnitudes of spouse resemblance in blood pressure have been reported in previous studies. Krieger et al. (1980) reported significant positive blood pressure spouse correlations in a Brazilian population, and Morton et al. (1980) found no significant spouse correlation for Japanese Americans. Rice et al. (1991) reported a significant spouse resemblance of SBP for the Quebec Family Study but not for the Tecumseh Study, and showed that spouse resemblance was the source of SBP heterogeneity between the two studies. We found significant differences in the spouse resemblance for both SBP and DBP between whites and blacks, suggesting that, although the genetic architecture regulating blood pressure may be similar for both whites and blacks, familial environmental factors also play an important role in the white families. Factors potentially affecting the spouse resemblance vary widely, from marriage instability and assortative mating to dietary sodium and potassium intake to overweight or obesity and undoubtedly other factors. Another possibility is that there actually may be spouse resemblance in blacks but that the number of black spouse pairs ($n = 17$) was too small

to attain significance. Nonetheless, the somewhat divergent parsimonious models appear to be distinguished by the presence of a spouse correlation (0.38 for white vs. 0 for black) and suggest the presence of heterogeneity, although the significance was only borderline.

Under the most parsimonious models there were no significant differences in the correlations by generation or sex in both white and black samples. By comparing the magnitude of the estimates together with their standard errors (Table 4), we found that the familial correlations for SBP are slightly higher in blacks than in whites, whereas those for DBP are significantly higher in blacks. Although this does not necessarily indicate that the genetic mechanism of blood pressure regulation differs between whites and blacks, the observation that hypertension and clinical complications resulting from elevated blood pressure are more frequent among blacks than among whites suggests the possibility of different host factors (Brazy 1994). Furthermore, the degree of African admixture, measured by both genealogical information and genetic markers, has been found to be correlated with blood pressure both in adults (Darlu et al. 1990) and in infants (Levin et al. 1987) and may indicate that differences in blood pressure distribution are of genetic origin. In fact, specific genetic factors have been proposed as being responsible for some of the observed differences in familial resemblance between blacks and whites.

One study has provided evidence for stronger familial aggregation for aldosterone excretion in black children compared with white children (Manatunga et al. 1992). Because aldosterone levels are inversely correlated with blood pressure, these findings suggest a possible genetic mechanism that could generate interracial differences in heritability. In another study a DNA polymorphism in the α_2-adrenergic receptor gene identified an allele for which homozygotes were significantly more frequent among hypertensive patients compared with normal control subjects and among blacks compared with whites (Lockette et al. 1995). Again, these results suggest that a genetic polymorphism in or near the α_2-adrenergic receptor gene can contribute to the development of hypertension in blacks. Alternatively, such environmental factors as dietary potassium intake (Langford et al. 1991), socioeconomic status (Seedat 1990), and educational level (Hames and Greenland 1996) and such psychosocial variables as anxiety, anger, expression, active coping, and family instability (Somova et al. 1995) could also contribute to the familial resemblance of blood pressure.

Both white and black families in the HERITAGE Family Study were sampled using the same recruitment criteria. One of the most important criteria was that the families be sedentary; this criterion offers a powerful control over a possibly important source of familial environmental variation (Sparling et al. 1994). Other common environmental influences resulting from such sources as physical fitness, cohort effects, extreme obesity, and various metabolic complications are expected to be minimal in this study. Our analysis of the resting blood pressure data in the white and black samples of the

HERITAGE Family Study is consistent with a genetic basis for human blood pressure levels and suggests heterogeneity in the familial components for blood pressure between the two populations. Identification of specific genetic and familial environmental factors with further exploration of the possible ethnic differences in the mode of inheritance has the potential to reveal important new information about the mechanisms regulating blood pressure.

Acknowledgments The HERITAGE study is supported by the National Heart, Lung, and Blood Institute through grants HL45670 (awarded to C. Bouchard), HL47323 (awarded to A.S. Leon), HL47317 (awarded to D.C. Rao), HL47327 (awarded to J.S. Skinner), and HL47321 (awarded to J.H. Wilmore). Thanks are expressed to all the co-principal investigators, investigators, co-investigators, local project coordinators, research assistants, laboratory technicians, and secretaries who contributed to the study. Finally, the entire HERITAGE consortium is very thankful to those hard-working participating families whose involvement alone made this study feasible.

Received 24 January 1997; revision received 3 June 1997.

Literature Cited

Akaike, H. 1974. A new look at the statistical model identification. *IEEE Trans. Automat. Control* 19:716–723.

Bouchard, C., A.S. Leon, D.C. Rao et al. 1995. The HERITAGE family study: Aims, design, and measurement protocol. *Med. Sci. Sports Exercise* 27(5):721–729.

Brazy, P.C. 1994. Kidney disease and hypertension in blacks. *Curr. Opin. Nephrol. Hypertens.* 3(5):554–557.

Calhoun, D.A., and S. Oparil. 1995. Racial differences in the pathogenesis of hypertension. *Am. J. Med. Sci.* 310(suppl. 1):S86–S90.

Darlu, P., P. Sagnier, and E. Bois. 1990. Genealogical and genetical African admixture estimations, blood pressure, and hypertension in a Caribbean community. *Ann. Hum. Biol.* 17(5):387–397.

Dressler, W.W. 1991. Social class, skin color, and arterial blood pressure in two societies. *Ethnicity Dis.* 1(1):60–77.

Fagard, R.H., and C.M. Tipton. 1994. Physical activity, fitness, and hypertension. In *Physical Activity, Fitness, and Health: International Proceedings and Consensus Statement*, C. Bouchard, R.J. Shepard, and T. Stephens, eds. Champaign, IL: Human Kinetics Publishers, 633–654.

Friedlander, Y., J. Kark, and Y. Stein. 1988. Biological and environmental sources of familial aggregation of blood pressure: The Jerusalem Lipid Research Clinic. *Int. J. Epidemiol.* 17(1):70–76.

Fumo, M.T., S. Teeger, R.M. Lang et al. 1992. Diurnal blood pressure variation and cardiac mass in American blacks and whites and South African blacks. *Am. J. Hypertens.* 5(3):111–116.

Grim, C., F. Luft, M. Weinberger et al. 1984. Genetic, familial, and racial influences on blood pressure control systems in man. *Aust. NZ J. Med.* 14(4):453–457.

Hames, C.G., and K.J. Greenland. 1996. Ethnicity and cardiovascular disease: The Evans County heart study. *Am. J. Med. Sci.* 311(3):130–134.

Hanis, C.L., C.F. Sing, W.R. Clarke et al. 1983. Multivariate models for human genetic analysis: Aggregation, coaggregation, and tracking of systolic blood pressure and weight. *Am. J. Hum. Genet.* 35(6):1196–1210.

Harburg, E., L. Gleibermann, F. Ozgoren et al. 1978. Skin color, ethnicity, and blood pressure. I and II. *Am. J. Public Health* 68(12):1177–1188.

Hunt, S.C., S.J. Hasstedt, H. Kuida et al. 1989. Genetic heritability and common environmental components of resting and stressed blood pressures, lipids, and body mass index in Utah pedigrees and twins. *Am. J. Epidemiol.* 129(3):625–638.

Jablonskis, L.T., and P.R. Howe. 1994. Elevated plasma adrenaline in spontaneously hypertensive rats. *Blood Pressure* 3(1–2):106–111.

Jeunemaitre, X., B. Rigat, A. Charru et al. 1992. Sib pair linkage analysis of renin gene haplotypes in human essential hypertension. *Hum. Genet.* 88(3):301–306.

Knuiman, M.W., M.L. Divitini, T.A. Welborn et al. 1996. Familial correlations, cohabitation effects, and heritability for cardiovascular risk factors. *Ann. Epidemiol.* 6(3):188–194.

Kreutz, R., N. Hubner, M.R. James et al. 1995. Dissection of a quantitative trait locus for genetic hypertension on rat chromosome 10. *Proc. Natl. Acad. Sci. USA* 92(19):8778–8782.

Krieger, H., N.E. Morton, D.C. Rao et al. 1980. Familial determinants of blood pressure in northern Brazil. *Hum. Genet.* 53:415–418.

Langford, H.G., W.C. Cushman, and H. Hsu. 1991. Chronic effect of KCl on black-white differences in plasma renin activity, aldosterone, and urinary electrolytes. *Am. J. Hypertens.* 4(5, pt. 1):399–403.

Levin, S. 1983. Significance of hypertension in children. *Clin. Cardiol.* 6(8):373–377.

Levin, S., A. Herman, and L. Irwig. 1987. Systolic blood pressure differences in black, colored, and white infants. *Am. J. Epidemiol.* 125(2):221–230.

Levine, R.S., C.H. Hennekens, A. Perry et al. 1982. Genetic variance of blood pressure levels in infant twins. *Am. J. Epidemiol.* 116(5):759–764.

Lockette, W., S. Ghosh, S. Farrow et al. 1995. Alpha 2-adrenergic receptor gene polymorphism and hypertension in blacks. *Am. J. Hypertens.* 8(4, pt. 1):390–394.

Majumder, P.P., S.K. Bhattacharya, B.N. Mukherjee et al. 1990. Genetic epidemiological study of blood pressure in a sedentary rural agricultural population of West Bengal, India. *Am. J. Phys. Anthropol.* 81(4):563–572.

Manatunga, A.K., T.K. Reister, J.Z. Miller et al. 1992. Genetic influences on the urinary excretion of aldosterone in children. *Hypertension* 19(2):192–197.

McCaughran, J.A., E. Edwards, N. Schechter et al. 1984. Alpha 1- and alpha-2-adrenoceptor binding in the Dahl rat model of hypertension. *Brain Res. Bull.* 12(6):697–702.

Moll, P.P., T.L. Harburg, M.A. Burns et al. 1983. Heredity, stress, and blood pressure, a family set approach: The Detroit Project revisited. *J. Chron. Dis.* 36(4):317–328.

Morishita, R., J. Higaki, N. Tomita et al. 1996. Role of transcriptional cis-elements, angiotensinogen gene-activating elements of angiotensinogen gene in blood pressure regulation. *Hypertension* 27(3, pt. 2):502–507.

Morton, N.E., C.L. Gulbrandsen, D.C. Rao et al. 1980. Determinants of blood pressure in Japanese-American families. *Hum. Genet.* 53:261–266.

Pérusse, L., T. Rice, C. Bouchard et al. 1989. Cardiovascular risk factors in a French-Canadian population: Resolution of genetic and familial environmental effects on blood pressure by using extensive information on environmental correlates. *Am. J. Hum. Genet.* 45(2):240–251.

Province, M., and D.C. Rao. 1995. General purpose model and a computer program for combined segregation and path analysis (SEGPATH): Automatically creating computer programs from symbolic language model specifications. *Genet. Epidemiol.* 12:203–219.

Rao, C.R. 1973. *Linear Statistical Inference and Its Applications.* New York: Wiley.

Rice, T., A. Nirmala, P.C. Reddy et al. 1992. Familial resemblance of blood pressure with residual household environmental effects in consanguineous and nonconsanguineous families from Andhra Pradesh, India. *Hum. Biol.* 64(6):869–889.

Rice, T., M.A. Province, J.B. Keller et al. 1991. Heterogeneity among populations for familial aggregation of blood pressure. *Am. J. Hum. Biol.* 3:515–523.

Rice, T., G.P. Vogler, L. Perusse et al. 1989. Cardiovascular risk factors in a French Canadian population: Resolution of genetic and familial environmental effects on blood pressure using twins, adoptees, and extensive information on environmental correlates. *Genet. Epidemiol.* 6(5):571–588.

Seedat, Y. 1990. Perspectives of hypertension in black patients: Black vs. white differences. *J. Cardiovasc. Pharmacol.* 16(suppl. 7):S67–S70.

Somova, L.I., C. Connolly, and K. Diara. 1995. Psychosocial predictors of hypertension in black and white Africans. *J. Hypertens.* 13(2):193–199.

Sparling, P.B., T.D. Noakes, K. Steyn et al. 1994. Level of physical activity and CHD risk factors in black South African men. *Med. Sci. Sports Exercise* 26(7):896–902.

Ward, R.H. 1983. Genetic and sociocultural components of high blood pressure. *Am. J. Phys. Anthropol.* 62(1):91–105.

Williams, D.R. 1992. Black-white differences in blood pressure: The role of social factors. *Ethnicity Dis.* 2(2):126–141.

Williams, R.R., S.C. Hunt, S.J. Hasstedt et al. 1991. Are there interactions and relations between genetic and environmental factors predisposing to high blood pressure? *Hypertension* 18(suppl. 3):I29–I37.

Wilson, T.W., L.R. Hollifield, and C.E. Grim. 1991. Systolic blood pressure levels in black populations in sub-Sahara Africa, the West Indies, and the United States: A meta-analysis. *Hypertension* 18(suppl. 3):I87–I91.

Yu, M., C.J. Chen, C.J. Wang et al. 1990. Chronological changes in genetic variance and heritability of systolic and diastolic blood pressure among Chinese twin neonates. *Acta Genet. Med. Gemellol.* 39(1):99–108.