Ambulatory Blood Pressure and Family History of Hypertension in Healthy Men and Women

Iris B. Goldstein, David Shapiro, and Donald Guthrie

Background: Family history of hypertension is a primary predictor of high blood pressure (BP). This study attempted to determine whether there is a gradual increase in BP between individuals with two hypertensive parents, one hypertensive parent, and normotensive parents and whether this increase is apparent with both ambulatory and casual BP assessments in men as well as in women.

Methods: A total of 220 healthy men and women, aged 22 to 50 years, completed two 24-h ambulatory BP sessions (one work day and one off work day). Based on family history information obtained from parents, three groups were formed: subjects with two hypertensive parents, one hypertensive parent, and normotensive parents. Work and off work days did not differ; analyses were based on mean values of the 2 days.

Results: Men with two hypertensive parents had higher daytime and night-time ambulatory BP than men with normotensive parents. Those with one hypertensive parent had intermediate BP levels. Ambulatory BP was not associated with family history in women. Also, men with one or two hypertensive parents had higher ambulatory BP than women with hypertensive parents, whereas offspring of normotensive parents exhibited no sex differences in BP.

Conclusions: Elevated systolic and diastolic BP throughout the day and night seems to characterize men with two hypertensive parents. In evaluating the relationship between family history of hypertension and BP, it is important to use ambulatory BP measures, differentiate between individuals with one and with two hypertensive parents, and focus on gender differences in BP.

Key Words: Ambulatory blood pressure, family history, hypertension.
The current study focuses on 24-h ambulatory BP in healthy individuals between the ages of 22 and 50 years, with two hypertensive parents, one hypertensive parent, and normotensive parents. Ambulatory BP was recorded on both work and off work days. A large sample of men and women allowed us to explore the relevance of subjects’ sex to the issue of hypertensive risk. We predicted that the greatest casual and ambulatory BP differences would occur between subjects with two hypertensive parents and those with normotensive parents, with offspring of one hypertensive parent at intermediate BP levels.

**Methods**

**Subjects**

Subjects were adults, 22 to 50 years of age, employed in full-time day shifts in a variety of jobs, the majority (82%) of whom were employed at the University of California. The remainder worked in the surrounding Los Angeles area. They were screened for significant health problems and use of drugs or medications that might affect cardiovascular functions or complicate interpretation of the ambulatory BP data (ie, coronary heart disease, diabetes, use of antihypertensive drugs). Subjects with severe obesity (body mass index [BMI] \( \geq 32 \text{ kg/m}^2 \)) or a prior diagnosis of hypertension were excluded. Also excluded were postmenopausal women and women who were pregnant or lactating within the previous 12 months.

During telephone screening 526 people were excluded because they did not meet the study criteria. Once the study began 12 subjects were rejected because of equipment problems. The final sample consisted of 220 subjects, with equal numbers of men and women. They were divided into three groups in terms of parental hypertensive status: 1) FH+, those with two hypertensive parents \( (n = 47) \); 2) FH+, those with one hypertensive parent \( (n = 66) \); 3) FH-, those with two normotensive parents \( (n = 107) \). The three groups were matched for age and education. Ethnic groupings were similar in subjects with and without a family history of hypertension. Ethnic distribution of the entire sample of subjects was as follows: 41% white, 31% Asian, 16% African-American, and 12% Latin-American. All subjects gave informed consent, approved by the UCLA Institutional Review Board.

For a subject to qualify as a hypertensive offspring, the parent must have been diagnosed with hypertension before the age of 60 years, with hypertension being present at least 1 year. In a study of more than 3000 individuals, Lascaux-Lefebre et al concluded that hypertension diagnosed after 60 years of age in a parent was not a significant risk factor for hypertension in the offspring. To determine family history group, we interviewed parents by telephone. Parents had to have had a physical examination within the past year, knowledge of BP level, and, if pertinent, information on current antihypertensive status and medications. Subjects were excluded if parents’ BP status was unclear. Also, both parents had to be true birth parents, with at least one parent currently living. Where one parent was deceased, that parent had to have reached the age of 45 years, and there had to be a surviving spouse to confirm the deceased parent’s BP status before death. Although parents’ hypertension status is best verified by medical examination and records, individuals’ reports of their own medical status have been found to agree 100% with information from medical diagnoses. Whenever necessary, parent’s hypertension status was verified by medical records.

**Procedures**

After the initial telephone screening of subjects and of their parents, subjects were seen on three separate sessions. During the initial session subjects were seated at least 5 min, followed by three casual BP readings taken with a mercury column sphygmomanometer according to standard assessments. Subjects provided information on demographics and health and filled out questionnaires. Height and weight were assessed to obtain a measure of BMI (in kilogram per meter squared). Three casual readings were taken again before each of the two ambulatory BP sessions (see next section), providing a total of nine casual assessments.

**Ambulatory BP Monitoring**

Ambulatory monitoring occurred on two separate sessions, one work day and one off work day, with days being counterbalanced. Approximately 0.5 h before subject’s work shift three casual BP readings were recorded, followed by the application of the ambulatory BP monitor and an activity monitor. Subjects were instructed to keep arms still and at their sides each time the instrument operates, whatever their posture or activity at the time. During the off work day, recordings commenced as close as possible to the beginning time of their work day. Subjects returned the following day to have the monitor removed. Casual and ambulatory BP measurements were repeated during the second ambulatory session 1 week later.

Ambulatory BP was recorded by the Accutracker II (Suntech Medical Instruments, Raleigh, NC), which has been used widely in clinical and research studies and has established reliability and validity. On each measurement occasion single readings of systolic BP and diastolic BP were obtained. The ambulatory recorder was programmed to operate on a variable schedule three times per hour during waking hours and once per hour during sleep (based on subject’s estimates of time of going to sleep and awakening). An activity monitor (Mini-Motionlogger, Ambulatory Monitoring Inc., Ardsley, NY) confirmed the differentiation of sleep from awake readings and accounted for the effects of activity on BP.

Ambulatory data were first edited for artifacts based on Accutrack reading codes (insufficient electrocardiogram or Korotkoff sounds) and extreme values (>220/130 or
<80/40 mm Hg). Editing was done by set rules.16 Far outside values were excluded by the box plot program of Systat (Evanston, IL). Classification of each reading as wake or sleep was based on diary entries and postsession reports. Only night-time sleep values were included in the sleep category and daytime wake values in the wake category. Systolic and diastolic means were obtained for sleep category and daytime wake values in the wake and sleep ambulatory BP. Because of similar findings for work and off work days, analyses were based on the mean of these values during the 2 days.

**Data Analysis**

To determine the relationship between subject characteristics (Table 1) and family history of hypertension, we performed a two-way analysis of variance (ANOVA) with Family History Group (FH+ +, FH+, FH−) and Sex (men, women) as independent variables. We also analyzed systolic and diastolic BP (casual, wake, and sleep) in Family History Group × Sex analyses by means of analysis of covariance (ANCOVA), using Age as a covariate. No other variables, including BMI and activity level as measured by the actigraph, were significant covariates. Bonferroni corrections were used in postanalysis of significant ($P < .05$) interactions. To understand how sex of the parent with hypertension relates to BP in the offspring, we did an ANCOVA of only the FH+ group with BP as the dependent variable and two independent variables: Sex of Parent and Sex of Offspring. Finally, separate analysis of activity confirmed earlier findings that awakening and rising during the night did not affect ambulatory BP.15

### Results

The ANOVA results showed significant Sex effects, with men having larger values for BMI and alcohol intake than women (Table 1). With regard to BP (Table 2), ANCOVA results of the FH × Sex analyses revealed that casual, wake, and sleep BP were higher in men than in women (all $P$ values $< .0001$). Family History effects were significant for all of the BP values: systolic BP casual, $P = .0001$; diastolic BP casual, $P = .002$; systolic BP wake, $P = .002$; diastolic BP wake, $P = .0001$; systolic BP sleep, $P = .037$; diastolic BP sleep, $P = .0001$. The BP was highest in FH+ +, intermediate in FH+, and lowest in FH− subjects. During all measurement conditions there was an approximate difference of 7/4 mm Hg between the FH+ + and the FH− groups. For casual systolic BP and casual, wake, and sleep diastolic BP, BP for FH+ + was significantly higher than FH+ and FH−. For systolic BP wake and sleep, the differences were significant only between

### Table 1. Subject characteristics based on sex and family history of hypertension (FH)

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th>Women</th>
<th>FH+ +</th>
<th>FH+</th>
<th>FH−</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$(n = 110)$</td>
<td>$(n = 110)$</td>
<td>$(n = 47)$</td>
<td>$(n = 66)$</td>
<td>$(n = 107)$</td>
</tr>
<tr>
<td>Age (y)</td>
<td>32.8 (7.0)</td>
<td>32.1 (7.3)</td>
<td>32.6 (6.9)</td>
<td>32.3 (7.2)</td>
<td>32.4 (7.3)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.5 (3.2)*</td>
<td>23.8 (3.4)</td>
<td>24.8 (3.0)</td>
<td>25.0 (3.3)</td>
<td>24.2 (3.5)</td>
</tr>
<tr>
<td>Education (y)</td>
<td>17.2 (2.5)</td>
<td>16.6 (2.3)</td>
<td>17.0 (2.5)</td>
<td>16.7 (2.3)</td>
<td>17.0 (2.5)</td>
</tr>
<tr>
<td>Coffee (cups/d)</td>
<td>1.3 (1.3)</td>
<td>1.3 (1.2)</td>
<td>1.1 (1.0)</td>
<td>1.4 (1.2)</td>
<td>1.5 (1.3)</td>
</tr>
<tr>
<td>Alcohol (drinks/wk)</td>
<td>2.7 (3.8)*</td>
<td>1.4 (1.7)</td>
<td>1.6 (2.7)</td>
<td>2.2 (2.7)</td>
<td>2.4 (3.3)</td>
</tr>
<tr>
<td>Smokers (% total)</td>
<td>13.6</td>
<td>10.0</td>
<td>8.5</td>
<td>19.7</td>
<td>8.4</td>
</tr>
<tr>
<td>Exercise (h/wk)</td>
<td>8.0 (8.5)</td>
<td>7.1 (6.5)</td>
<td>7.9 (6.3)</td>
<td>6.5 (6.9)</td>
<td>8.3 (8.4)</td>
</tr>
</tbody>
</table>

Values represent mean ± SD. Values are derived from ANOVAs with sex and FH as factors. There were no significant interactions. Findings for the smokers category are based on χ².

* $P < .05$ for men versus women.

### Table 2. Subjects’ casual and ambulatory blood pressure (mean ± SD) based on sex and family history of hypertension (FH)

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th>Women</th>
<th>FH+ +</th>
<th>FH+</th>
<th>FH−</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$(n = 110)$</td>
<td>$(n = 110)$</td>
<td>$(n = 47)$</td>
<td>$(n = 66)$</td>
<td>$(n = 107)$</td>
</tr>
<tr>
<td>SBP casual</td>
<td>120.2 (8.7)*</td>
<td>108.5 (8.2)</td>
<td>118.3 (12.0)†</td>
<td>113.1 (10.0)</td>
<td>111.6 (8.4)</td>
</tr>
<tr>
<td>DBP casual</td>
<td>76.4 (7.6)*</td>
<td>70.1 (7.3)</td>
<td>75.8 (9.0)‡</td>
<td>72.6 (7.7)</td>
<td>71.3 (7.3)</td>
</tr>
<tr>
<td>SBP wake</td>
<td>134.3 (12.8)*</td>
<td>122.9 (10.5)</td>
<td>132.2 (14.9)†</td>
<td>128.5 (13.2)</td>
<td>125.2 (10.7)</td>
</tr>
<tr>
<td>DBP wake</td>
<td>75.3 (6.2)*</td>
<td>70.2 (6.2)</td>
<td>75.4 (8.1)‡</td>
<td>71.7 (6.2)</td>
<td>71.2 (5.7)</td>
</tr>
<tr>
<td>SBP sleep</td>
<td>122.7 (16.7)*</td>
<td>111.1 (14.0)</td>
<td>120.7 (17.6)†</td>
<td>116.3 (15.9)</td>
<td>113.7 (15.3)</td>
</tr>
<tr>
<td>DBP sleep</td>
<td>65.3 (6.5)*</td>
<td>59.8 (5.7)</td>
<td>65.1 (7.8)‡</td>
<td>61.8 (5.8)</td>
<td>60.8 (6.1)</td>
</tr>
</tbody>
</table>

Values are in mm Hg. Values are derived from ANOVAs with sex and FH as factors. Ambulatory values are based on the mean of the combined work day and the off work day. Interactions for wake and sleep blood pressure are shown in Figs. 1 and 2. DBP = diastolic blood pressure; SBP = systolic blood pressure.

* $P < .05$ for men versus women; † $P < .05$ for FH+ + versus FH−; ‡ $P < .05$ for FH+ + versus FH+, FH−.
the two extreme groups (FH+ + and FH−). None of the BP analyses of Sex of Parent × Sex of Offspring were significant.

The Family History × Sex interaction showed that a strong positive family history (FH+ +) was associated with higher ambulatory BP in men but not in women (see Figs. 1 and 2). Significant interaction effects were as follows: systolic BP wake (P = .005), diastolic BP wake (P = .027), systolic BP sleep (P = .014), diastolic BP sleep (P = .045). Compared to FH− men, FH+ + men had higher systolic and diastolic BP (13 to 14/6 to 7 mm Hg) during wake and sleep. Also, for men during sleep diastolic BP for FH+ + was 5 mm Hg higher than FH+, and during wake systolic BP was 8 mm Hg higher in FH+ than FH−. Finally, although men had consistently higher BP than women, the Sex difference was significant only within the FH+ + and FH+ groups, not within FH−. There were no significant interactions for casual BP.

**Discussion**

**BP Findings**

Our findings of elevated BP in men compared with women are consistent with other investigations of office BP. Also in agreement with other studies is the higher casual BP exhibited in individuals with two hypertensive parents relative to those with a negative hypertension family history, with offspring of only one hypertensive parent at intermediate levels. However, unlike these studies, our results with a somewhat older population demonstrated additional casual BP differences between subjects with one and with two hypertensive parents. Ambulatory data during waking and sleep also revealed highest BP levels in
offspring of two hypertensive parents. This was confirmed previously in other ambulatory studies of premenopausal female nurses and in high school and university students. However, van Hoof et al found that in young adults only daytime readings were significant. In other investigations of ambulatory BP, where individuals with either one or two hypertensive parents were studied as a group and compared to offspring of normotensive parents, a positive family history was associated with higher BP during daytime and night-time hours or only during the day. However, in these studies casual BP differences were not significant. In contrast to studies focusing on individuals with two hypertensive parents, when offspring with one and two hypertensive parents are combined, family history seems less likely to be associated with standard office BP.

Although BMI of men was larger than that of women, neither BMI, alcohol intake, nor any other variables were significant covariates in the ANOVA. Moreover, putting BMI into the model as an additional factor (FH group × Gender × BMI), with age as a covariate, did not alter the findings. Even within men there were no BMI differences between family history groups. Gender × BMI was not significant.

**Relationship of Findings to Sex**

The family history literature indicates that sex of parent and sex of offspring may be meaningful factors in the risk associated with parental hypertension. However, studies that explored the parent’s sex have reported contradictory findings on whether paternal or maternal hypertension is of greater importance as a risk factor for elevated BP in offspring and whether the risk exists for the son or the daughter. Our findings indicate that although the parent’s sex is not a factor in elevations in either casual or ambulatory BP among offspring, sex of offspring is relevant, but only for ambulatory BP. Compared to men with normotensive parents, those with two hypertensive parents had elevated BP during both daytime and night-time hours. For women, however, BP was not associated with family history. In addition, among those with at least one hypertensive parent men had consistently higher waking and sleeping systolic and diastolic BP than women. In contrast, there were no sex differences among the offspring of normotensive parents.

The lack of a relationship between family history of hypertension and BP in women may be because women in this age group have relatively low BP compared to men. Although BP increases with age in all individuals, before menopause many women appear to be protected against hypertension. Only after menopause BP elevations in women become as prevalent as they are in men. Increases in BP after menopause may be due to a number of possible causes: reduced estrogen levels, exaggerated response to androgens, increased oxidative stress and plasma endothelin, and changes in the renin-angiotensin system.

The interaction of family history and sex has been reported infrequently. Lawler et al found that undergraduate college men with a parental history of hypertension had higher systolic BP levels during rest and tasks than men with normotensive parents, with no such difference among women. In contrast, Hahn et al reported that in a similarly aged sample, parental history was related to higher screening systolic and diastolic BP in women, but not in men. Both groups of investigators looked at younger populations than the subjects in our study, and 24-h ambulatory BP was not recorded.

In addition to elevated BP in offspring of two hypertensive parents, these offspring may exhibit greater septal and posterior wall thickness and left ventricular mass. Some investigators suspect that changes in cardiac and vascular morphology may precede and eventually lead to elevations in BP, although a causal link between these events has not been established.

Hypertension may be also related to disturbed autonomic control of the cardiovascular system, such as increased sympathetic activity. However, catecholamines are not consistently elevated in offspring of hypertensive parents. Compared to those with normotensive parents, in individuals with a positive family history the ambulatory BP responses to the environment could be augmented by reduced baroreflex buffering, providing another possible mechanism for the development of hypertension.

High BP aggregating in families is associated with shared family environment and genetics. Not only does the occurrence of two hypertensive parents increase the genetic component of elevated BP in offspring, but a shared environment (health habits inducive to hypertension) could further increase a child’s tendency to become hypertensive. Heritability measures how much of family aggregation is due to genetic factors. Studies showing heritability estimates of BP to be higher when based on ambulatory than on office BP suggest that the relationship between ambulatory BP and family history demonstrated in this article supports the role of genetic factors in hypertension.

Among the positive aspects of this study is a sizeable sample of healthy men and women of varied ethnicity, whose family history information was verified by subjects’ parents. Rather than studying positive family history of hypertension as a single variable, individuals were separated into groups with one and with two hypertensive parents. Finally, the use of ambulatory BP monitoring provided multiple daytime and night-time measurements of BP in the natural environment during 2 separate days. Nevertheless, it is important to note that our results may not generalize to all populations. The subjects were primarily college-educated men and women, the majority of whom worked in professional and skilled jobs in a large university. By excluding hypertensive individuals from the study, we may have excluded people most likely to have
two hypertensive parents, thereby decreasing the strength of our findings relating BP in offspring to parental hypertension.

Unlike investigations using only casual BP measures, the current findings of elevated BP in offspring of hypertensive parents are not the result of a white coat response to one or two office visits. Instead, elevated BP throughout the day and night appears to be characteristic of individuals with a strong hypertensive family history. The results underscore the value of differentiating between individuals with one and with two hypertensive parents and of focusing on sex differences in BP. Studying healthy offspring can provide a unique opportunity to investigate the precursors of hypertension in drug-free individuals before a diagnosis of hypertension has been made. Moreover, the ability to identify individuals at greatest risk for hypertension enables one to intervene early in life by means of diet and lifestyle changes, resulting in a potential decrease in the incidence of hypertension. Because hypertension is predictive of future coronary heart disease, stroke, and renal disease, lowering BP of possible hypertensive individuals could decrease morbidity and mortality rates.

References