Early 24-Hour Blood Pressure Elevation in Normotensive Subjects With Parental Hypertension

Antonella Ravogli, Silvia Trazzi, Alessandra Villani, Emanuela Mutti, Cesare Cuspidi, Lorena Sampieri, Luigi De Ambroggi, Gianfranco Parati, Alberto Zanchetti, and Giuseppe Mancia

Subjects with a family history of parental hypertension are reported to have a slightly higher office blood pressure in the prehypertensive stage. Whether this reflects a hyperreactivity to blood pressure measurement or a more permanent blood pressure elevation, however, is not known. In the present study, blood pressure was measured in 15 normotensive subjects whose parents are both hypertensive (FH++), 15 normotensive subjects with one hypertensive parent (FH+-), and 15 normotensive subjects whose parents are not hypertensive (FH--); among the three groups, subjects were matched for age, sex, and body mass index. The measurements were made in the office during a variety of laboratory stressors and during a prolonged resting period, and for a 24-hour period (ambulatory blood pressure monitoring). Office blood pressure was higher in the FH++ group than in the FH-- group (p<0.05). The pressor responses to laboratory stressors were similar in the two groups, but the FH++ group had higher prolonged resting and 24-hour blood pressure than the FH-- group; the difference was always significant (p<0.05) for systolic blood pressure. The FH++ group also had a greater left ventricular mass index (on echocardiographic examination) than the FH-- group (p<0.01). The blood pressure values and echocardiographic values of the FH+- group tended to be between those of the other two groups. Thus, the higher blood pressure shown by individuals in the prehypertensive stage with a family history of parental hypertension does not reflect a hyperreactivity to stress but an early permanent blood pressure elevation. Because blood pressure is related to cardiovascular disease even within the normotensive range, we can speculate that these individuals are at increased risk even before hypertension develops. (Hypertension 1990;16:491-497)

Several studies have reported that office blood pressure is slightly elevated in subjects with a family history of parental hypertension even before overt hypertension develops.1-4 However, these subjects have also been shown to be hyperreactive to stress.5-11 This raises the possibility that the blood pressure elevation represents only a transient event and that no permanent abnormality characterizes the prehypertensive stage of these individuals.

We addressed this issue in healthy normotensive subjects with a family history of parental hypertension in whom office blood pressure was measured for a prolonged resting period and for a 24-hour period. The results were compared with those of healthy normotensive subjects with a negative family history of hypertension.

Methods

Our study included 45 subjects whose office blood pressure was less than 140/90 mm Hg at three visits performed over a 2-month period. All subjects were healthy high school or university students from the Milan area and were identified from a population of 1,500 students recruited for an epidemiological survey of blood pressure values in the young Milanese population. In all subjects, familial hypertension or normotension was established by measurement of the
parents' blood pressure in the outpatient clinic; recorded values greater than 160/95 mm Hg in the parents indicated a family history of hypertension, and values less than 140/90 mm Hg indicated a negative family history of hypertension. Parental hypertension was also inferred from a history of antihypertensive treatment. There were 15 subjects whose parents were both normotensive (FH—), another 15 subjects who only had one hypertensive parent (FH+−), and the remaining 15 subjects whose parents were both hypertensive (FH++). The three groups were matched for age (22.1±1, 21.8±1, and 22.8±1 years, respectively, mean±SEM), body mass index (2.2±0.1, 2.1±0.2, and 2.0±0.1 g/m²), and sex (10 women and five men in each group). There were two smokers in the FH—, four in the FH+—, and five in the FH++ group. The subjects were included in the study after giving informed consent.

Measurements

Office blood pressure was measured in the morning by a sphygmomanometer, using the first and the fifth Korotkoff sounds to identify systolic and diastolic blood pressure, respectively. Measurements were made in the sitting position at the beginning and at minutes 5 and 10 of the doctor's visit. After each measurement, heart rate was assessed over a 30-second period by the palpatory method.

In addition, blood pressure was monitored by a noninvasive device (Finapres, Ohmeda 2300, Ohmeda, Englewood, Colo.), which allows a reliable blood pressure signal to be obtained on a beat-to-beat basis, thereby obtaining a beat-to-beat pulse interval as well. The monitoring was carried out during a 30-minute rest period and during the following laboratory stressors: 1) mental arithmetic (56 subjects of varied complexity within 3 minutes), 2) mirror drawing test (reproduction of a geometric drawing as reflected by a mirror within 3 minutes), 3) handgrip (30% of subjects' maximal strength for 1 half minute), and 4) cold pressor test (hand immersion in ice water for 1 minute). Each stressor was repeated twice. The four stressors were randomly applied and separated from the following and the preceding one by an interval of 5 minutes.

Finally, blood pressure and heart rate were recorded for 24 hours by a noninvasive automatic portable monitoring device (Spacelabs 5300). The recording was started at the end of the laboratory session (approximately at noon), and the automatic measurements were taken at 10-minute intervals from 6:00 AM to midnight and at 20-minute intervals from midnight to 6:00 AM. During the recording, the research subjects were allowed to return to their usual daily life.

Left ventricular wall thickness was assessed by measuring septal and left posterior wall thickness with M-mode echocardiography. The level at which the measurements were made was standardized by B-mode echocardiography (ATL Ultramark 8, 3 MHz probe, Advanced Technology Laboratories, Bothell, Wash.), and the data were collected over five cardiac cycles. Left ventricular mass index was calculated from the wall thickness and the left ventricle diameters according to the formula of the Penn Convention. All echocardiographic measurements were made by the same operator. The operator was unaware of both the family history and the blood pressure values of the subjects examined.

Data Analysis

Beat-to-beat blood pressure data were stored on a tape recorder (Racal Thermonics, store 4, Racal Recorders, Ltd., Hythe, Southampton, England) and sent to a computer (Digital PDP 11/23, Digital Equipment Corp., Maynard, Mass.) which was programmed to sample the signal at 165 Hz. The signal was digitized into 12 bit, and systolic, diastolic, and mean blood pressures were computed for each pulse wave. Corresponding heart rate values were derived from the reciprocal of interbeat intervals.

Data were averaged for the 30-minute resting period and the corresponding standard deviations were taken as measures of blood pressure and heart rate variability. The beat-to-beat signal was also displayed on a Grass polygraph (Grass Instruments, Quincy, Mass.) to allow blood pressure and heart rate changes induced by laboratory stressors to be calculated as the difference between the average values of the 30 seconds before and of 1) the final 30 seconds of the stressor (handgrip, cold pressor test) or 2) the 30 seconds of the stressor during which maximal blood pressure or heart rate changes were observed (mental arithmetic, mirror image).

Data obtained by 24-hour ambulatory blood pressure recording were edited for artifacts, and the average systolic blood pressure, diastolic blood pressure, mean blood pressure, and heart rate were calculated for the 24-hour period and then separately for 2-hour periods of the daytime (7:00 AM to 10:00 PM) and the nighttime when the subjects were asleep (2 hours selected between midnight and 6:00 AM). The standard deviations of the 24-hour values were taken as additional measures of blood pressure and heart rate variability.

Individual blood pressure and heart rate data were averaged to obtain mean±SEM for the FH++, FH+—, and FH— groups. Linear regression analysis was used to determine the relation of blood pressure to left ventricular mass index and wall thickness. The intergroup differences in mean values were assessed by Student's paired t test according to the Bonferroni correction. A value of p<0.05 was taken as the level of statistical significance.

Results

Office Blood Pressure

Confirming previous findings, office systolic, diastolic, and mean blood pressures (mean of the three office measurements) were slightly but significantly higher in FH++ than in FH— subjects. Office
**FIGURE 1.** Bar graphs showing cuff values for systolic (SBP), diastolic (DBP), and mean (MAP) blood pressure and heart rate (HR) measured during the doctor’s visit. Data obtained at the beginning and at minutes 5 and 10 of the visit were averaged and shown as mean±SEM for the FH—, FH++, and FH+ + groups. Asterisks refer to the statistical significance of the differences between groups. FH—, neither parent is hypertensive; FH+, one parent is hypertensive; FH++, both parents are hypertensive.

Blood pressure of FH+- subjects tended to be in between those of the other two groups, and the diastolic and mean values of this group were also significantly greater than those of FH— subjects. In contrast, office heart rate values were less in FH++ subjects than in the other two groups (Figure 1).

**Prolonged Resting and 24-Hour Blood Pressure Monitoring**

As shown in Table 1, average systolic, diastolic, and mean blood pressure obtained by beat-to-beat monitoring of a 30-minute resting period were higher in FH++ than in FH— subjects, although only the difference in systolic blood pressure reached statistical significance. The average 30-minute blood pressure of FH+- subjects tended again to fall in between the other two groups, but the values were not significantly different from those of FH++ subjects. Average 30-minute heart rate was similar in the three groups.

Blood pressure values recorded throughout the day and night tended to be lowest in FH—, intermediate in FH+-, and highest in FH++ subjects (Figure 2). Average 24-hour, daytime, and sleep systolic blood pressure were significantly greater in FH++ as compared with FH— subjects. This was the case also for average 24-hour and daytime mean blood pressure, whereas the 24-hour, daytime, and sleep differences in diastolic blood pressure between the two groups were not statistically significant. The differences in ambulatory blood pressure between FH— and FH++ or FH— subjects were also not statistically significant (Figure 3). Ambulatory heart rate values were similar in the three groups (Figures 2 and 3).

Systolic, diastolic, and mean blood pressure variability were similar in FH++, FH+-, and FH— subjects either when measured by the standard deviation of all 30-minute resting values and when measured by the standard deviation of the 24-hour values. This was the case also for heart rate variability (Figure 4).

**Laboratory Stressors**

All laboratory stressors caused a significant increase in mean blood pressure and heart rate (p always <0.01). With the exception of the blood pressure response to mental arithmetic (increase less in FH++ than in FH— subjects) the magnitude of the pressure or the tachycardic responses was similar in FH++, FH+-, and FH— subjects (Figure 5).

**Echocardiographic Data**

Septal wall thickness, left posterior wall thickness, and left ventricular mass index tended to be lowest in FH—, intermediate in FH+-, and highest in FH++ subjects. For all echocardiographic variables, mean values were significantly greater in FH++ and FH— than in FH— subjects, whereas the differences between the FH++ and FH— groups were not statistically significant (Figure 6).

The left ventricular mass index showed a significant linear relation with blood pressure values. The correlation coefficient was higher for systolic than for diastolic blood pressure and for average 24-hour blood pressure than for office blood pressure. In no instance, however, did the coefficient exceed 0.47 (Figure 7).

**Discussion**

Our data confirm previous observations that in the prehypertensive stage, subjects with hypertensive parents have higher office blood pressure than subjects with normotensive parents. They also provide multiple evidence that this does not result from a hyperreactivity to the emotional stress induced by the doctor’s visit. First, subjects with hypertensive and normotensive parents had similar pressor and tachycardic responses to laboratory stressors. Furthermore, behaviorally modulated phenomena such as blood pressure and heart rate variability were also similar in the two groups. Finally, and more importantly, in the subjects with hypertensive parents blood pressure was higher over a prolonged period of rest and showed slightly but significantly elevated

---

**Table 1. Blood Pressure and Heart Rate Values During a Thirty-Minute Resting Period**

<table>
<thead>
<tr>
<th>Measurements</th>
<th>FH—</th>
<th>FH+</th>
<th>FH++</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP (mm Hg)</td>
<td>120.8±3.5*</td>
<td>128.2±2.5</td>
<td>133.1±4.6*</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>57.0±2.3</td>
<td>61.8±2.2</td>
<td>62.3±2.7</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>75.6±9.0</td>
<td>79.8±2.4</td>
<td>81.8±3.4</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>69.6±2.8</td>
<td>70.8±2.3</td>
<td>67.8±2.1</td>
</tr>
</tbody>
</table>

Average data from a beat-to-beat monitoring period. Values given are mean±SEM for each of the three groups. FH—, neither parent is hypertensive; FH+, one parent is hypertensive; FH++, both parents are hypertensive; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; HR, heart rate.

*p<0.05.
FIGURE 2. Bar graphs showing 24-hour ambulatory blood pressure monitoring values for systolic (SBP), diastolic (DBP), and mean (MAP) blood pressure and heart rate (HR) in FH−−, FH+-, and FH++ subjects. Data are shown as mean±SEM for the whole 24-hour period, the daytime period, and for a 2-hour nighttime period of sleep. FH−−, neither parent is hypertensive; FH+-, one parent is hypertensive; FH++, both parents are hypertensive.

FIGURE 3. Line graphs showing systolic (SBP), diastolic (DBP), and mean (MAP) blood pressure and heart rate (HR) values of 2-hour subperiods within the 24-hour ambulatory blood pressure monitoring period. Data are shown as mean±SEM for the FH−−, FH+-, and FH++ groups. Large symbols at right of each panel refer to 24-hour average values. FH−−, neither parent is hypertensive; FH+-, one parent is hypertensive; FH++, both parents are hypertensive.
values also during the 24-hour monitoring period. Interestingly, even during sleep (i.e., during a condition free from emotional and physical stress) systolic blood pressure was higher in subjects with parental hypertension compared with those with no parental hypertension. All this leaves no doubt that in individuals with a strong genetic hypertensive background the prehypertensive phase is characterized by a permanent and not merely a transient and stress-related abnormality in blood pressure.

Several other results of our study deserve to be discussed. First, although still definable as normal, the septal wall thickness, posterior wall thickness, and left ventricular mass index were greater in subjects whose parents were both hypertensive. This may suggest that even an increase in cardiac afterload confined within the normal range acts as a hypertrophic stimulus to the heart. However, in experimental models of hypertension cardiac weight has been found to be already increased at birth.22-24 Thus, the reverse explanation is also possible (i.e., that a genetically determined tendency for cardiac hypertrophy to develop precedes and possibly leads to a blood pressure increase.25 This may be supported by the fact that, if anything, the differences in left ventricular mass index among the three groups were more evident than the differences in 24-hour blood pressure.

Second, the blood pressure and cardiac alterations discussed above involved to some extent the subjects

![Graph 1](image1)

**Figure 4.** Bar graphs showing laboratory stressors. Increase in mean (MAP) blood pressure and heart rate (HR) induced by mental arithmetic test (MA), mirror image drawing test (MI), cold pressor test (CPT), and handgrip test (HG) laboratory stressors (see Methods). Data are shown as mean±SEM for the FH−−, FH−+, and FH++ groups. FH−−, neither parent is hypertensive; FH−+, one parent is hypertensive; FH++, both parents are hypertensive.

![Graph 2](image2)

**Figure 5.** Scatterplots showing systolic (SBP), diastolic (DBP), and mean (MAP) blood pressure and heart rate (HR) variability assessed by standard deviations of 24-hour values (upper panels) and of beat-to-beat analysis during a 30-minute resting period (lower panels). Individual data from FH−−, FH−+, and FH++ subjects are shown. Horizontal bars refer to average group values. FH−−, neither parent is hypertensive; FH−+, one parent is hypertensive; FH++, both parents are hypertensive.

![Graph 3](image3)

**Figure 6.** Bar graphs showing echocardiographic parameters of left ventricular mass index (LVMI), interventricular septum thickness (IVS), and left posterior wall thickness (PW) in FH−−, FH−+, and FH+++ subjects. Data are shown as mean±SEM. FH−−, neither parent is hypertensive; FH−+, one parent is hypertensive; FH++, both parents are hypertensive.
in whom hypertension was present in one parent only. Thus, in individuals in whom the genetic background for hypertension is less pronounced the prehypertensive phase may not be entirely immune from hemodynamic and structural abnormalities. This has obvious relevance to clinical practice because monoparental hypertension is much more common than biparental hypertension.20

Third, in subjects with one or both parents hypertensive the blood pressure and heart rate responses to stress were similar to those of control subjects. This was clarified with the use of a variety of stress testing maneuvers and by the precise estimate of hemodynamic changes provided by beat-to-beat blood pressure and heart rate monitoring. It was further emphasized by the fact that phenomena with a behavioral component such as blood pressure and heart rate variability did not differ among the various groups when measured either in the laboratory or in real life. Thus, the hyperreactivity to stress described in earlier studies in subjects whose parents were hypertensive5-11 may not always be manifest.27

Finally, in our study left ventricular mass index was better correlated to systolic than to diastolic blood pressure and to 24-hour than to office blood pressure. This agrees with previous observations in subjects with essential hypertension. 28-33 It further shows that these two variables are also associated within a normal blood pressure range. It should be emphasized, however, that the correlation coefficients were never greater than 0.47. This suggests that factors other than the pressure load to the heart are involved in cardiac cell growth.34-36

In conclusion, our results demonstrate that, in subjects with a strong genetic predisposition to hypertension, the prehypertensive stage is characterized by an elevation in prolonged resting and 24-hour blood pressure. To a lesser extent, a blood pressure elevation also occurs in subjects in whom the genetic hypertensive background is less pronounced. Although these individuals escape recognition until the blood pressure values at which the diagnosis of hypertension is made are reached, this elevation in blood pressure may be clinically important because blood pressure is related to cardiovascular disease even within the normotensive range.37

References


KEY WORDS: stress • ambulatory blood pressure monitoring • echocardiography • blood pressure • genetic hypertension
Early 24-hour blood pressure elevation in normotensive subjects with parental hypertension.
A Ravogli, S Trazzi, A Villani, E Mutti, C Cuspidi, L Sampieri, L De Ambroggi, G Parati, A Zanchetti and G Mancia

_Hypertension_. 1990;16:491-497
doi: 10.1161/01.HYP.16.5.491

_Hypertension_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1990 American Heart Association, Inc. All rights reserved.
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:
http://hyper.ahajournals.org/content/16/5/491

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Hypertension_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Hypertension_ is online at:
http://hyper.ahajournals.org//subscriptions/