"White Coat" Versus "Sustained" Borderline Hypertension in Tecumseh, Michigan

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During a survey of young subjects not receiving treatment for hypertension in Tecumseh, Michigan, clinic and self-monitored blood pressures taken at home (14 readings in 7 days) were obtained in 737 subjects (387 men, 350 women, average age 31.5 years). Hypertension in the clinic was diagnosed if the clinic blood pressure exceeded 140 mm Hg systolic or 90 mm Hg diastolic. In the absence of firm criteria for what constitutes hypertension at home, subjects whose average home blood pressure was in the upper decile of the whole population were considered to have hypertension at home. By these criteria, 7.1% of the whole population had "white coat" hypertension (i.e., high clinic but not elevated home readings). The prevalence of "sustained" hypertension (i.e., high readings in the clinic and at home) was 5.1%. Subjects with white coat and sustained borderline hypertension in Tecumseh were very similar. Both groups showed, at previous examinations (at ages 5, 8, 21, and 23 years), significantly higher blood pressure readings than the normotensive subjects. As young adults (average age 33.3 years), the parents of both hypertensive groups had significantly higher blood pressure readings than the parents of normotensive subjects. Both hypertensive groups had faster heart rates, higher systemic vascular resistance, and higher minimal forearm vascular resistance. Both hypertensive groups were more overweight, had higher plasma triglycerides, insulin, and insulin/glucose ratios than normotensive subjects. The white coat hypertensive group also had lower values of high density lipoprotein than the normotensive group. White coat hypertension is a frequent condition. In regards to excessive risk of hypertension (past blood pressures, parental blood pressures, weight, and heart rate), excessive risk for atherosclerosis (triglycerides and insulin), and hemodynamic parameters (vascular resistance and minimal forearm resistance), the white coat and sustained hypertensive groups are similarly different from the normotensive group. These findings do not support the accepted practice of using home blood pressure determination to distinguish groups of borderline hypertensive subjects with a lesser or greater clinical problem. (Hypertension 1990;16:617–623)
blood pressure trends in patients with borderline hypertension and suggested that such readings can be used to assist in therapeutic decisions.4

The Tecumseh Blood Pressure Study is a research project on precursors of hypertension in subjects living within a 25-mile radius of Tecumseh, Mich., whose present age ranges from 18 to 42 years (average 32.9±3.2) and who are not receiving antihypertensive medication. Previous blood pressure readings for the majority of these subjects and their parents are available.

In the present study, we report on white coat hypertension in Tecumseh, Mich. The results indicate that 1) white coat hypertension is present in about 7.1% of the general population; 2) white coat hypertension is a stable condition (subjects in this group show higher office blood pressure readings from childhood, through young adulthood, to their present age); 3) subjects with white coat hypertension come from families with higher blood pressure levels; 4) the cardiovascular risk profile in white coat hypertension is significantly abnormal; and 5) the white coat hypertension group is not different from the group with sustained borderline hypertensive readings with regard to past blood pressure measurements, family background, cardiovascular risk factors, and underlying hemodynamics.

These findings call for reexamination of accepted clinical practice regarding white coat hypertension.

Methods

The Tecumseh Blood Pressure Study investigated subjects aged 18–42 years. None of the subjects received antihypertensive treatment. The study protocol called for measurement of home blood pressures and a visit to the field office in Tecumseh. First, the subjects were visited in their homes, taught to measure their own blood pressures, and given an appointment for a visit to the clinic office. The instruction in home blood pressure measurement was given by a trained technician. The subjects and the technician auscultated through a "Y"-connected stethoscope, and a subject was considered properly trained when the subject's and the technician's readings were within 5 mm Hg. The coefficient of variation of the 14 home readings (i.e., 7 days of taking readings twice daily, morning and evening) was 4.4% for the systolic and 6.3% for the diastolic. In a separate test of the validity of home blood pressure readings, 133 subjects repeated home blood pressure readings after 1 year, and the correlation coefficient of two readings for mean blood pressure was 0.71.

Subjects brought to the clinic records of home blood pressure readings, were given a physical examination, and underwent a battery of laboratory tests. During the clinical examination, a physician took sitting blood pressure measurements after a minimal accommodation of 2 minutes. Two readings were recorded and averaged. This report is based on 737 subjects (387 men, 350 women) with complete clinic and home blood pressure records. Another 86 subjects were examined in the clinic but did not have home blood pressure readings, and their results are not reported in this paper.

The measurement of cardiac output after 30 minutes of rest in recumbency is based on two-dimensional echocardiographic assessment of the aortic root diameter and a Doppler recording of the aortic flow velocities, using an ATL Ultramark IV, Advanced Technology Laboratories, Bellevue, Wash. Two-dimensional images of the aortic root were recorded in the long axis view using a 2.25 mHz transducer. The aortic root diameter was measured from the two-dimensional image at the level of the aortic leaflets during mid-systole, and the aortic cross-sectional area was calculated. Aortic outflow measurements were obtained from the suprasternal notch with a continuous-wave Doppler transmitter operating at 3.0 mHz. The cardiac output and stroke volume measurements were calculated using a computer-interfaced digitizing tablet and Doppler analysis program (Freeland Medical Systems, Indianapolis, Ind.). The average of eight consecutive cardiac cycles was taken, and only those Doppler recordings that showed maximal flow velocities and exhibited the "cleanest" envelopes were chosen. The flow velocity integral or the area under the velocity curve was determined by tracing from the baseline around the maximal velocity curve. Heart rate was measured from the R-R interval of the simultaneously recorded electrocardiogram. Stroke volume was calculated using the formula:

\[
SV (\text{ml}) = FVI (\text{cm}) \times CSA (\text{cm}^2)
\]

where SV is stroke volume, FVI is flow velocity integral, and CSA is cross-sectional area. The cardiac output was calculated by multiplying the stroke volume and the heart rate. Ninety-five percent of the recordings were done by one technician (L.K.).

In a previous study, we demonstrated that cardiac output determined by Doppler echocardiogram, when done under controlled laboratory conditions, correlates well with dye dilution.5 We have confidence in our readings obtained in this field study. The primary variable, stroke volume, correlated positively with the body weight \(r=0.47; p<0.001\). This correlation is of a similar order of magnitude as we obtain in the invasive laboratory with dye dilution \(r=0.50; n=267; p<0.0001\).

Forearm plethysmography was performed using a mercury-in-Silastic strain gauge (D.E. Hokanson, Inc., Issaquah, Wash.). The temperature in the room was kept at a constant 70° F with the subject in the recumbent position. To measure minimal forearm vascular resistance, subjects first performed rhythmic contractions of the forearm muscles while an inflated tourniquet interrupted the forearm blood flow for 10 minutes. The cuff was then released and the flow measured during the ensuing maximal hyperemia. During such postischemic reperfusion, the arterioles are entirely relaxed, and the resistance to flow reflects the structural property of the vessels (the wall
of a thicker blood vessel impinges on the lumen and causes higher resistance).

Subjects were classified as having hypertension if the clinic reading exceeded 140 mm Hg systolic or 90 mm Hg diastolic. Hypertension at home was defined as having an average of 14 home blood pressure readings in the upper 10% of the values of the whole population studied. Based on these criteria, those who were hypertensive in the clinic were subdivided into two groups. Subjects were considered to have "sustained" hypertension if the average clinic blood pressure exceeded 140 mm Hg systolic or 90 mm Hg diastolic and the home blood pressure value was in the upper decile of the distribution. Subjects who had hypertension in the clinic but whose home blood pressure was not in the upper 10% were considered to have white coat hypertension. It must be pointed out that the term "hypertension" is used for the sake of brevity but that both the sustained and white coat groups had, on average, only a borderline blood pressure elevation. The normotensive group consisted of subjects whose clinic blood pressure did not exceed the 140 mm Hg systolic or 90 mm Hg diastolic limit.

While the subject was in a recumbent position after 20 minutes of rest, all blood samples were drawn, quickly processed, placed in a cooler, and delivered to the laboratory in Ann Arbor. The majority of subjects (70.1%) fasted 12 hours or more before blood was drawn for insulin testing. The rest fasted between 6 and 11 hours before blood was drawn. The mean insulin and insulin/glucose ratio of the two groups (i.e., fasted more than 12 hours and fasted less than 12 hours) were not different. Lipid values and plasma insulin were analyzed in the Michigan Diabetes Research and Training Center research laboratories. Insulin was measured by radioimmunoassay, using the iodinated anti-pork insulin as tracer and human insulin as standard. A second antibody was used to separate the bound and free fractions.6

The percentage over ideal body weight was calculated using Metropolitan Life Insurance tables for age and sex.

Significance of difference between the groups was calculated by analysis of covariance (ANCOVA) adjusting for sex, as the groups differed significantly in regards to their male/female composition.

The study was approved by the Institutional Review Board, and all the subjects signed an informed consent form.

Results

The general characteristics and blood pressure values for the three groups are given in Table 1. All groups were of similar age. Both hypertensive groups were heavier than the normotensive group: +10 kg in the white coat group and +18 kg in the sustained hypertensive group. The average clinic blood pressure of the white coat hypertensive group was 128/93 mm Hg; the average home readings were 7/17 mm Hg lower and clearly fell in the normotensive range. Nevertheless, the home reading of 121/75 mm Hg in the white coat hypertensive group was significantly higher than 115/71 mm Hg observed in the normotensive group. The sustained hypertensive group had significantly higher clinic blood pressure values than the white coat group and, by definition, their home blood pressure readings were more elevated.

Cardiovascular risk factors for the two groups are given in Table 2. Both hypertensive groups had faster heart rates and higher levels of cardiovascular risk factors. The plasma insulin, triglycerides, and insulin-to-glucose ratio were significantly higher in both hypertensive groups. The white coat group had significantly lower high density lipoprotein (HDL) values than the normotensive group.

Table 2 also shows the hemodynamic findings in the three groups. Both hypertensive groups had a significant elevation of vascular resistance, whereas the cardiac output values were not different from the normotensive group. The values for vascular resis-
tance in both hypertensive groups were similarly elevated. Both hypertensive groups had elevated minimal forearm vascular resistance.

Records of previous blood pressure readings are available for many of the participants in the present Tecumseh Study. These readings were obtained when the subjects were children and later when they became young adults. Previous average blood pressure measurements for the three groups are reconstructed in Figure 1. Both hypertensive groups had similar and significantly elevated blood pressures as children. As young adults, both groups continued to show significantly higher pressures than the normotensive group, but by age 21 the white coat hypertension group tended to have higher values than the sustained group. However, at only two (ages 21 and 22.6) of the possible eight points of comparison was the blood pressure in the white coat group significantly higher than in the sustained hypertensive group (p < 0.05).

Blood pressure readings of parents in our study subjects were also on record. At the time of those exams the average age of the mothers was 32 years and 35 years for the fathers. Results are shown in Figure 2. The diastolic blood pressure of parents of both hypertensive groups was significantly elevated. Parental systolic blood pressure also tended to be elevated, but the difference reached significance only in fathers of the sustained hypertension group.

Discussion

We want to emphasize that study subjects called hypertensive, based on a clinic reading exceeding 140 mm Hg systolic or 90 mm Hg diastolic, in fact have borderline hypertension; the average diastolic reading is slightly above 90 mm Hg and the systolic blood pressure is below the 140 mm Hg value. The term hypertension in this report is used for the sake of convenience, to avoid repeated use of the cumbersome term borderline hypertension; the average diastolic reading is slightly above 90 mm Hg and the systolic blood pressure is below the 140 mm Hg value. The term hypertension in this report is used for the sake of convenience, to avoid repeated use of the cumbersome term "borderline hypertension" and "sustained borderline hypertension." To stress the nature of blood pressure elevation in this study, the term borderline hypertension is used in the title of the paper.

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al11 reported that of all blood pressure measurements taken during 24-hour monitoring, the blood pressure readings during work correlated mostly closely to the peak readings shown in the physician's office, there are also some dissenting views. Recently Devereux et al10 who found that subjects with white coat hypertension did not manifest left ventricular hypertrophy. Although these studies suggest that morbidity is chiefly related to the average blood pressure obtained by ambulatory monitoring and not so much to peak readings shown in the physician's office, there are also some dissenting views. Recently Devereux et al10 reported that of all blood pressure measurements taken during 24-hour monitoring, the blood pressure readings during work correlated mostly closely to the left ventricular mass. The authors speculated that mental stress at work may cause both higher blood pressures and enhanced sympathetic activation. Similarly, the Milan group recently reported that blood pressure variability assessed from intra-arterial recordings, independent of blood pressure levels, predicts cardiovascular damage.12 Again, the most likely cause for increased blood pressure variability are periods of sympathetic (emotional or physical) activation. There is also some evidence that sympathetic stimulation may be an independent "trophic" factor for cardiac myocytes13,14 and for the blood vessels.15 Because some papers suggest that the morbidity of hypertension is related to the average blood pressure level1,9 and others find it related to certain pressor episodes11 or to overall blood pressure variability,12 the practicing physician is left in a quandary. From a large pool of subjects with borderline hypertension vying for limited resources, should the physician temporarily eliminate the white coat hypertensive individuals and concentrate on the subjects with sustained and therefore more severe hypertension? Findings reported in the present study do not support such an approach. White coat hypertensive subjects come from families with higher blood pressure levels, show high blood pressure readings very early in life, and continue to maintain elevated readings from childhood through young adulthood to adulthood. Present and past blood pressure levels of the sustained hypertension and the white coat hypertension groups are similar.

The hemodynamic comparison of the two hypertensive groups also leaves no room for speculation that white coat hypertension requires less medical attention. In both groups, the elevation of blood pressure was due to a high vascular resistance. Elevated vascular resistance is the hemodynamic hallmark of established essential hypertension.16 Minimal forearm resistance of both groups was equally elevated. We accept Folkow's concept that minimal forearm vascular resistance is a measure of vascular hypertrophy in the forearm.17 After ischemic reper-
fusion, vessels in the forearm are maximally dilated and the resistance entirely depends on the physical properties of the vessels; hypertropic vessels cause higher resistance. A recent challenge to that concept has been adequately refuted by Folkow. Higher minimal forearm vascular resistance in very mild hypertension is considered an early sign of pressure-related structural changes.

Another reason not to take solace from the normal blood pressure readings at home in subjects who have high readings in the clinic is found in their cardiovascular risk profile. These risk factors can be divided into the risk of developing "true" treatment-requiring hypertension and the risk for development of atherosclerosis.

There are only a few known risk factors for development of hypertension. Both hypertension groups in the present study had faster heart rates than the normotensive group. Fast heart rate in youth is an independent predictor of future hypertension. Subjects who have both an elevation of heart rate and a blood pressure increase in youth later develop hypertension three times as frequently as the subjects who have only borderline blood pressure elevation. Both hypertensive groups in this study were overweight. Overweight and gain of weight are an independent risk factor for the development of future hypertension. Family history is also considered a risk factor for future hypertension. Both parents of both hypertensive groups in Tecumseh had elevated blood pressure readings.

Both hypertensive groups in this study also had an undesirable constellation of risk factors for atherosclerosis. Plasma insulin, insulin-to-glucose ratio, and triglycerides were significantly elevated in both hypertensive groups. The white coat group had significantly lower HDL values, triglycerides and HDL cholesterol are well-recognized traditional risk factors. Recent evidence shows plasma insulin to be an independent atherosclerotic risk factor. The fact that borderline hypertension rarely comes in isolation and is intimately intertwined with other cardiovascular risk factors is not sufficiently appreciated in clinical practice. All of these risk factors can be modified, and it behooves the practicing physician to attempt to modify them before submitting the patient to antihypertensive medication. The presence of other risk factors is probably the strongest argument against dismissing white coat hypertension as a clinical condition of little importance.

In summary, the Tecumseh study indicates that white coat hypertension is frequent and that it does not appear to be particularly different from sustained borderline hypertension. Consequently, the usefulness of ambulatory blood pressure monitoring solely to identify white coat hypertension must be questioned. It is conceivable that future, longitudinal research will justify the use of home blood pressure monitoring as a better predictor of hypertension. At present, it seems to us prudent to stop considering the subjects with high clinic and normal ambulatory pressures as not having a clinical problem. Such patients should be monitored and counseled on nonpharmacological methods of blood pressure and atherosclerotic risk factor control.

References


**KEY WORDS** • risk factors • heart rate • cardiac output • epidemiology • borderline hypertension • insulin • obesity • white coat phenomenon
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