Clinical Significance of “White Coat” Hypertension

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This issue of *Hypertension* includes a report by Julius and colleagues on a topic of great importance for the diagnosis of hypertension, that is, the alerting reaction and blood pressure rise triggered by blood pressure measurements and commonly referred to as the “white coat” phenomenon.2

The first observation that blood pressure measurement may trigger an alerting reaction and a pressor response in the patient was made by Riva-Rocci in his original report on the sphygmomanometric technique, which was published near the end of the last century. This pressor response was then described in several other papers and quantified in subjects in whom sphygmomanometric assessment of blood pressure by the physician was obtained during prolonged intra-arterial ambulatory blood pressure monitoring. The data showed that the peak increase in intra-arterial systolic and diastolic blood pressure occurring during the procedure was so pronounced that it averaged 27/14 mm Hg. However, although a blood pressure rise was observed in most subjects, the pressor response showed a pronounced interindividual variability, with the maximal increase in mean arterial pressure ranging from 2 to 53 mm Hg.

The large database available on the white coat phenomenon has always been regarded as leaving many important questions unanswered. For example, it is not yet established how often the blood pressure rise associated with the blood pressure measurement is responsible for a false diagnosis of hypertension or whether its occurrence in a given individual can be predicted by his or her response to standardized stressful stimuli elicited in the laboratory. Furthermore, it is not clear whether the pressor response remains constant or whether repetition of the physician’s visit leads to its decline and final disappearance. Finally, and most importantly, there is uncertainty as to the prognostic significance of the white coat rise in blood pressure. This originates from the somewhat conflicting evidence provided by epidemiological and interventional studies. Epidemiological studies show that casual blood pressure (i.e., an isolated blood pressure reading inclusive of the white coat effect) is predictive of cardiovascular morbidity and mortality. On the other hand, interventional studies suggest that hypertensive patients showing a spontaneous decline in blood pressure after the first visit have a favorable prognosis when compared with hypertensive subjects with the same blood pressure level on an antihypertensive drug regimen. The uncertainty over the prognostic value of this phenomenon has an obvious implication for the decision of whether white coat hypertensive patients should or should not be treated.

The report by Julius et al describes the results of the Tecumseh study in which clinic blood pressure measurements were associated with repeated self-measurements of blood pressure at home, that is, in a circumstance devoid of the white coat effect. This allowed identification of subjects with sustained hypertension as those having high clinic and high home blood pressures and subjects with white coat hypertension as those having high clinic and low home blood pressures. The results are of great interest because the number of white coat hypertensive subjects was found to be as high as 55% of the hypertensive group. Furthermore, blood pressure measurements performed over many years documented that in the white coat hypertensive group, clinic blood pressures had been higher than normal since childhood and that the parents of these individuals also displayed somewhat elevated blood pressure values. Finally, white coat hypertensive subjects shared with sustained hypertensive subjects an elevation in body weight, plasma triglycerides, and plasma insulin levels, a reduction in high density lipoprotein cholesterol, and an increase in an index of vascular hypertrophy such as minimal forearm vascular resistance. This suggests that white coat hypertension is an exceedingly common event. It also suggests that this hypertension is not a diagnostic error that can be avoided by repeated blood pressure measurements, but rather represents a persistent and perhaps genetically determined feature. Finally, white coat hypertension appears to be associated with the hemodynamic abnormalities typical of sustained hypertension and also with the metabolic alterations that have recently been shown to be more frequent in subjects with higher than normal blood pressure levels.

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pressure.\textsuperscript{14,15} This calls into question the clinical "innocence" of this phenomenon.

Should we then definitely conclude that white coat hypertension is common, that it is risky, and that thus the physician should deal with it as with hypertension "tout court"? There is no doubt that the study of Julius et al\textsuperscript{1} scores significantly in this direction. Yet the preceding complexity of the issue does not allow all problems to be thoroughly resolved. For example, lack of a large published database forced the authors of this study to adopt an arbitrary though reasonable criterion to define home blood pressure normalcy and thus distinguish among the individuals with a high clinic blood pressure those having white coat hypertension. In other studies,\textsuperscript{16,17} this condition was diagnosed by the combination of a high clinic and a normal ambulatory blood pressure, the latter also somewhat arbitrarily defined. Thus, determining the prevalence of white coat hypertension is methodologically difficult, and this may explain why the data available in the literature are different. Another explanation for these differences is the dynamic nature of the pressor response to the blood pressure assessment (i.e., the fact that the blood pressure rise reaches a peak within 4 minutes from the beginning of the visit and then declines at a variable rate).\textsuperscript{8,9} This means that early clinic blood pressure measurements may result in a greater prevalence of white coat hypertension than late clinic blood pressure measurements.

The mechanisms of the possible adverse impact of white coat hypertension on the cardiovascular system also remain uncertain. A widely held and attractive hypothesis is that this phenomenon reflects a tendency to hyperreact to any kind of stress and thus to display a greater number of blood pressure peaks and an enhanced blood pressure variability during a 24-hour period. This is in line with the important evidence of the Tecumseh study that in the subjects with white coat hypertension, the increased pressor response to the stress elicited by blood pressure assessment was a persistent and not a transient feature. It is also in agreement with evidence that in hypertension, 24-hour blood pressure variability is related to target organ damage.\textsuperscript{18,19} However, no relation has been found between the pressor response to clinic blood pressure assessment, the cardiovascular reactivity to other stressful stimuli, and the 24-hour or daytime blood pressure variability in studies based on accurate intra-arterial blood pressure measurement.\textsuperscript{10} This leaves the hypothesis of hyperreactivity to stress still unproven.

Finally, the adverse prognostic significance of a blood pressure elevation limited to the clinic environment requires serious consideration because it involves many individuals largely regarded as deserving long-term observation but no treatment. In this context, the results of Julius and colleagues\textsuperscript{1} are unique in that they provide large and consistent evidence that this condition is hemodynamically more similar to sustained hypertension than to normotension. It also reveals several metabolic abnormalities that make sustained hypertension a multifactorial source of cardiovascular risk. This justifies the suggestion advanced by the report of Julius et al\textsuperscript{1} that this condition may not be as harmless as it is often thought.

However, in our opinion, the issue is not definitely settled for two reasons. One, in the white coat hypertensive subjects of the Tecumseh study, home blood pressure was lower than that of sustained hypertensive subjects, but a few millimeters of mercury higher than that of the control normotensive population. This raises the possibility that the group characterized by a clinic blood pressure elevation was not entirely devoid of a small blood pressure abnormality of the sustained type as well. Two, the data described in the paper of Julius et al\textsuperscript{1} are cross-sectional, and it is obvious that a clinically vital question such as the prognostic significance of white coat hypertension must ultimately rely on a controlled prospective morbidity and mortality study.

An important merit of the report by Julius and colleagues\textsuperscript{1} is that it offers a rationale for planning a controlled prospective morbidity and mortality study. It may also offer, through the longitudinal nature of the Tecumseh investigation, the structure to make it feasible.

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