Withholding treatment in white-coat hypertension: wishful thinking

J. David Spence, MD

"Measurement" of blood pressure is in many ways a mug's game. At best, a single blood pressure recording in the doctor's office gives only a rough estimate of a person's usual blood pressure; such a reading has only a tenuous relation to the true state of affairs. Cuff size in relation to arm size, pseudohypertension and cuff artifact caused by stiffness of the arteries,[1,2] the technique of measurement, and loss of calibration of aneroid devices constitute only part of the problem. Perhaps one of the most important difficulties is that a single reading in the office is like a single frame of a movie. Sir George Pickering introduced that concept to the world in his classic monograph a quarter century ago.[3] His illustration of a 24-hour intra-arterial blood pressure recording in one of his young assistants showed that the blood pressure was remarkably low during sleep, rose abruptly while he rushed to catch the bus in the morning, and dropped again while he nodded off during ward rounds, rising remarkably when the head sister stuck him with a pin to waken him! Floras and colleagues[4] and Perloff and associates[5] contributed early on to the evidence that ambulatory monitoring might be useful in identifying patients at high risk for hypertension.

The term "white-coat syndrome" was coined in 1983, when Mancia and colleagues[6] reported, on the basis of continuous intra-arterial blood pressure recordings, that systolic and diastolic blood pressure rose on average by 27 and 15 mm Hg respectively and heart rate increased by 16 beats/minute when a doctor entered the patient's hospital room. Now we are faced with "white-coat response," "white-coat effect" and "white-coat hypertension," the whole while having no idea what we should do about it.

In this issue MacDonald and colleagues[7] report on the prevalence and determinants of the white-coat response. They found that 20% of the men and 54% of the women in their sample were either reclassified from hypertensive to normotensive (because their mean daytime ambulatory blood pressure was 139/89 mm Hg or less) or had mean ambulatory systolic and diastolic readings 20 and 15 mm respectively below the clinic readings (their definitions of the white-coat response). For women, perceived level of stress and time since diagnosis of hypertension predicted the white-coat response, whereas for men depression was a predictor.

The problem we are left with is what to do about such information. White-coat hypertension is defined as high blood pressure occurring in a medical setting despite normal ambulatory pressure; a key issue is therefore the definition of "normal" ambulatory pressure. The 6th report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment (JNC VI) recently recommended that normal blood pressure be defined as mean daytime systolic pressure less than 135 mm Hg and mean daytime diastolic pressure less than 85 mm Hg,[8] but the choice of these cut-off values appears to have been rather arbitrary[9] (Canadian Hypertension Society guidelines on this subject should be available soon). The best information about this issue comes from the prospective studies of Verdecchia and colleagues,[10,11] who recommended a highly restricted definition of white-coat hypertension. They reported that cardiovascular morbidity did not differ between people with normal ambulatory blood pressure (daytime pressure below 130/80 mm Hg) and "office normotensive" patients, defined as those whose blood pressure was below 140/90 mm Hg on at least 3 visits on different days. However, the rate of cardiovascular events was higher among those with white-coat hypertension defined more liberally, specifically those with ambulatory blood pressure between 130/80 and 131/86 (for women) or 136/87 (for men). Cardiovascular morbidity was the same in this group as in those with ambulatory hypertension (greater than those limits).

Ambulatory blood pressures between 130/80 and 140/90 mm Hg present a murky area of confusion. Ambulatory pressures in that range appear to be equivalent to early hypertension and are associated with end-organ manifestations intermediate between those of hypertensive and normotensive people. For example, Glen and collaborators[12] found that patients with white-coat hypertension were intermediate between normotensive and hypertensive people with respect to carotid stiffness and left ventricular relaxation. Similarly, Cerasola and associates[13] and Weber and colleagues[14] found that white-coat hypertension is a variant of hypertension. In fact, white-coat hypertension is probably a variant of a rise in blood pressure during stress, as shown by Trenkwalder and collaborators.[15] Alderman and associates[16] found that patients in whom physician-measured diastolic blood pressures were at least 4 mm Hg higher than pressures measured by nurses were at greater risk of myocardial

infarction; however, as Pickering[17] pointed out, ambulatory pressures were not measured in that study. We have shown in prospective studies[18,19] that the magnitude of the rise in blood pressure during mental stress predicts progression of atherosclerosis more strongly than baseline blood pressure, cholesterol level or smoking history, and that the height of systolic pressure during mental arithmetic is a stronger predictor of an increase in left ventricular mass over 2 years than either ambulatory or clinic readings.

The widespread assumption that it is not necessary to treat office hypertension in patients with "normal" ambulatory blood pressures, although attractive, is an unwarranted, untested assumption that amounts to wishful thinking. High blood pressures in the office are the basis of the evidence that hypertension is harmful, and office pressures are the basis of the evidence that treatment of hypertension is beneficial.[20–23] To date there has been no evidence that it is safe to withhold treatment of office hypertension on the basis of normal ambulatory blood pressure.

If measurement of blood pressure in the office is a mug's game, white-coat hypertension is a dog's breakfast. What we need, to do a better job of preventing heart attacks and strokes (which, after all, is the object of the exercise), is a randomized study in which treatment for hypertension is initiated on the basis of either office or ambulatory measurements. Blood pressures measured at home could be used for the ambulatory group, since they mirror closely the results of ambulatory recordings.[20] Once we know that it is safe to withhold treatment in patients with high office pressure and normal ambulatory blood pressure and that diagnosing and treating high blood pressure on the basis of ambulatory blood pressure is as good as or better than the established practice, we will know what to make of this phenomenon. Until then, it's all wishful thinking.

Dr. Spence is with the Stroke Prevention and Atherosclerosis Research Centre, Siebens-Drake/Robarts Research Institute, London, Ont.

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Correspondence to: *Dr. J. David Spence, Stroke Prevention and Atherosclerosis Research Centre, Siebens-Drake/Robarts Research Institute, 1400 Western Rd., London ON N6G 2V2; dspence@rri.on.ca*