

Beyond office sphygmomanometry: Ways to better assess blood pressure

■ ABSTRACT

To diagnose and manage hypertension optimally, we may need to do more than measure the patient's blood pressure in the office using traditional sphygmomanometry. A variety of devices—some already available, validated, and reimbursable, some still in development—provide more information and give us a better picture of the patient's true hypertensive status, degree of blood pressure control, and risk of end-organ damage.

■ KEY POINTS

Traditional office blood pressure measurements have diagnostic limitations, since they are only snapshots of a very dynamic variable.

Ambulatory 24-hour blood pressure monitoring is a useful and proven tool and can reveal nocturnal hypertension, a possible new marker of risk.

Automatic devices can be used in the clinician's office to minimize the "white coat effect" and measure blood pressure accurately.

Pulse-wave analysis provides physiologic data on central blood pressure and arterial stiffness. This information may help in the early identification and management of patients at risk for end-organ damage.

Hypertension is difficult to diagnose, and its treatment is difficult to monitor optimally on the basis of traditional office blood pressure measurements. To better protect our patients from the effects of undiagnosed or poorly controlled hypertension, we need to consider other options, such as ambulatory 24-hour blood pressure monitoring, automated measurement in the office, measurement in the patient's home, and devices that analyze the peripheral pulse wave to estimate the central blood pressure and other indices of arterial stiffness.

■ MANUAL OFFICE MEASUREMENT HAS INHERENT LIMITATIONS

Office blood pressure measurements do provide enormous information about cardiovascular risk and the risk of death, as shown in epidemiologic studies. A meta-analysis¹ of 61 prospective observational studies that included more than 1 million patients showed that office blood pressure levels clearly correlate with increased risk of death from cardiovascular disease and stroke.

But blood pressure is a dynamic measure with inherent minute-to-minute variability, and measurement will not be accurate if the correct technique is not followed. Traditional office sphygmomanometry is a snapshot and does not accurately reflect a patient's blood pressure in the real world and in real time.

Recently, unique patterns of blood pressure have been identified that may not be detected in the physician's office. It is clear from several clinical trials that some patients' blood pressure is transiently elevated in the first few minutes during office measurements (the "white coat effect"). In addition, when office measure-

Medical Grand Rounds articles are based on edited transcripts from Education Institute Department of Medicine Grand Rounds presentations at Cleveland Clinic. They are approved by the author but are not peer-reviewed.

doi:10.3949/ccjm.76gr.0409

ments are compared with out-of-office measurements, several patterns of hypertension emerge that have prognostic value. These patterns are white coat hypertension, masked hypertension, nocturnal hypertension, and failure of the blood pressure to dip during sleep.

■ WHITE COAT EFFECT

The white coat effect is described as a transient elevation in office blood pressure caused by an alerting reaction when the pressure is measured by a physician or a nurse. It may last for several minutes. The magnitude of blood pressure elevation has been noted to be higher when measured by a physician than when measured by a nurse. Multiple blood pressure measurements taken over 5 to 10 minutes help eliminate the white coat effect. In a recent study,² 36% of patients with hypertension demonstrated the white coat effect.

In a study by Mancia et al,³ 46 patients underwent intra-arterial blood pressure monitoring for 2 days, during which time a physician or a nurse would check their blood pressure repeatedly over 10 minutes. This study found that most patients demonstrated the white coat effect: the blood pressure was higher in the first few measurements, but came down after 5 minutes. The white coat effect was as much as 22.6 ± 1.8 mm Hg when blood pressure was measured by a physician and was lower when measured by a nurse.

■ WHITE COAT HYPERTENSION

In contrast to the white coat effect, which is transient, white coat hypertension is defined as persistent elevation of office blood pressure measurements with normal blood pressure levels when measured outside the physician's office. Depending on the population sampled, the prevalence of white coat hypertension ranges from 12% to 20%, but this is understandably difficult or almost impossible to detect with traditional office blood pressure measurements alone.⁴⁻⁷

■ MASKED HYPERTENSION

Patients with normal blood pressure in the physician's office but high blood pressure dur-

ing daily life were found to have a higher risk of cardiovascular events. This condition is called masked hypertension.⁸ For clinicians, the danger lies in underestimating the patient's risk of cardiovascular events and, thus, undertreating the hypertension. Preliminary data on masked hypertension show that the rates of end-organ damage and cardiovascular events are slightly higher in patients with masked hypertension than in patients with sustained hypertension.

■ NOCTURNAL HYPERTENSION

Elevated nighttime blood pressure ($>125/75$ mm Hg) is considered nocturnal hypertension and is generally considered a subgroup of masked hypertension.⁹

In the African American Study of Kidney Disease and Hypertension (AASK),^{10,11} although most patients achieved their blood pressure goal during the trial, they were noted to have relentless progression of renal disease. On ambulatory 24-hour blood pressure monitoring during the cohort phase of the study,¹⁰ a high prevalence of elevated nighttime blood pressure (66%) was found. Further analysis showed that the elevated nighttime blood pressure was associated with worse hypertension-related end-organ damage. It is still unclear if lowering nighttime blood pressure improves clinical outcomes in this high-risk population.

■ DIPPING VS NONDIPPING

The mean blood pressure during sleep should normally decrease by 10% to 20% compared with daytime readings. "Nondipping," ie, the lack of this nocturnal dip in blood pressure, carries a higher risk of death from cardiovascular causes, even if the person is otherwise normotensive.^{12,13} Nondipping is commonly noted in African Americans, patients with diabetes, and those with chronic kidney disease.

A study by Lurbe et al¹⁴ of patients with type 1 diabetes mellitus who underwent ambulatory 24-hour blood pressure monitoring found that the onset of the nondipping phenomenon preceded microalbuminuria (a risk factor for kidney disease). Data from our institution¹⁵ showed that nondipping was associated with a greater decline in glomerular

On ambulatory
24-hour
monitoring,
normal is
125/80 to
130/80 mm Hg,
rather than
140/90

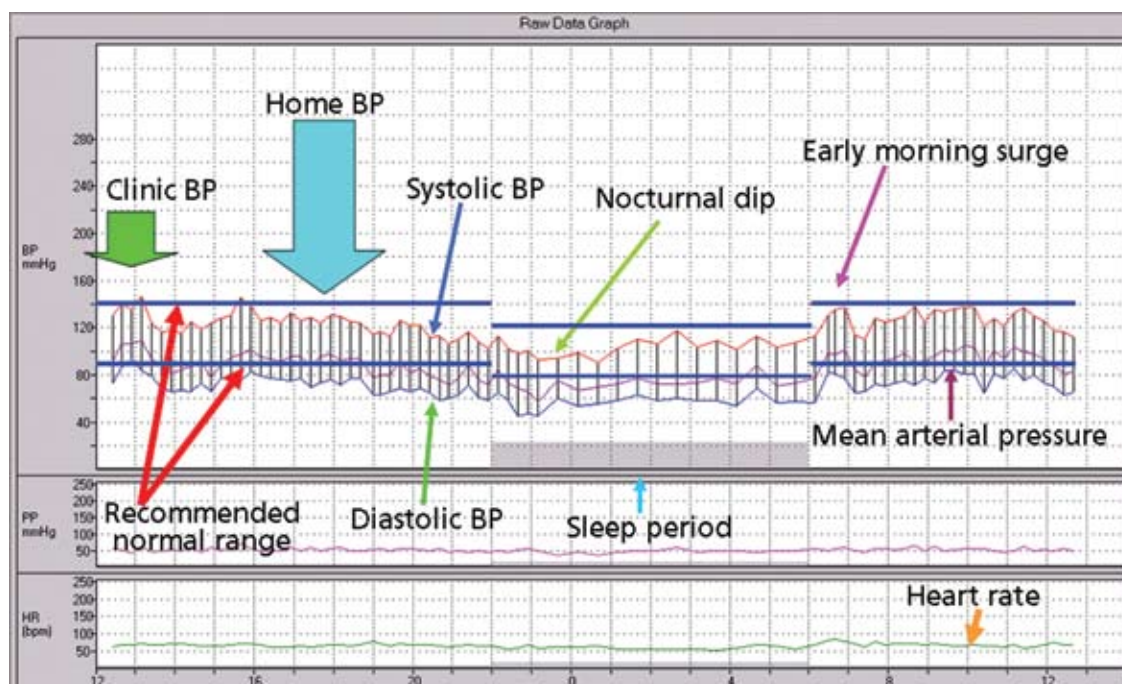


FIGURE 1. Graph of ambulatory 24-hour blood pressure readings, with nocturnal dip.

filtration rate when compared with dipping.

The lack of reproducibility of a person's dipping status has been a barrier in relying on this as a prognostic measure. White and Larocca¹⁶ found that only about half of the patients who appeared to be nondippers on one 24-hour recording still were nondippers on a second recording 4 to 8 weeks later. Compared with nondipping, nocturnal hypertension is a more stable blood pressure pattern that is being increasingly recognized in patients undergoing 24-hour blood pressure monitoring.

■ AUTOMATIC BLOOD PRESSURE DEVICES

An automated in-office blood pressure measurement device is one way to minimize the white coat effect and obtain a more accurate blood pressure assessment. Devices such as BpTRU (BpTRU Medical Devices Ltd, Coquitlam, BC, Canada) are programmed to take a series of automatic, oscillometric readings at regular intervals while the patient is left alone in a quiet room. BpTRU has been validated in several clinical trials and has been shown to overcome the white coat effect to some extent. Myers et al¹⁷ compared 24-hour blood pressure readings with those obtained by a family physician, by a research technician,

and by the BpTRU device and found that the BpTRU readings were much closer to the average of awake blood pressure readings on 24-hour blood pressure monitoring.

■ AMBULATORY 24-HOUR BLOOD PRESSURE MONITORING

Ambulatory blood pressure monitoring provides average blood pressure readings over a 24-hour period that correlate more closely with cardiovascular events when compared with office blood pressure readings alone. The patient wears a portable device that is programmed to automatically measure the blood pressure every 15 minutes during the day and every 30 minutes during the night, for 24 hours. These data are then transferred to a computer program that provides the average of 24-hour, awake-time, and sleep-time readings, as well as a graph of the patient's blood pressure level during the 24-hour period (FIGURE 1). The data provide other valuable information, such as:

- Presence or absence of the nocturnal dip (the normal 10% to 20% drop in blood pressure at night during sleep)
- Morning surge (which in some studies was associated with higher incidence of stroke)

Nondipping is common in African Americans, patients with diabetes, and patients with chronic kidney disease

- Supine hypertension and sudden fluctuations in blood pressure seen in patients with autonomic failure.

Studies have shown that basing antihypertensive therapy on ambulatory 24-hour blood pressure monitoring results in better control of hypertension and lowers the rate of cardiovascular events.^{18,19}

Perloff et al¹⁸ found that in patients whose hypertension was considered well controlled on the basis of office blood pressure measurements, those with higher blood pressures on ambulatory 24-hour monitoring had higher cardiovascular morbidity and mortality rates.

More recently, Clement et al¹⁹ showed that patients being treated for hypertension who have higher average ambulatory 24-hour blood pressures had a higher risk of cardiovascular events and cardiovascular death.

After following 790 patients for 3.7 years, Verdecchia et al²⁰ concluded that controlling hypertension on the basis of ambulatory 24-hour blood pressure readings rather than traditional office measurements lowered the risk of cardiovascular disease.

'Normal' blood pressure on ambulatory 24-hour monitoring

It should be noted that the normal average blood pressure on ambulatory 24-hour monitoring tends to be lower than that on traditional office readings. According to the 2007 European guidelines,²¹ an average 24-hour blood pressure above the range of 125/80 to 130/80 mm Hg is considered diagnostic of hypertension.

The bottom line on ambulatory 24-hour monitoring: Not perfect, but helpful

Ambulatory 24-hour blood pressure monitoring is not perfect. It interferes with the patient's activities and with sleep, and this can affect the readings. It is also expensive, and Medicare and Medicaid cover it only if the patient is diagnosed with white coat hypertension, based on stringent criteria that include three elevated clinic blood pressure measurements and two normal out-of-clinic blood pressure measurements and no evidence of end-organ damage. Despite these issues, almost all national guidelines for the management of hypertension recommend ambulatory 24-hour blood pressure monitoring to improve

cardiovascular risk prediction and to measure the variability in blood pressure levels.

■ USING THE INTERNET IN MANAGING HYPERTENSION

Green et al²² studied a new model of care using home blood pressure monitoring via the Internet, and provided feedback and intervention to the patient via a pharmacist to achieve blood pressure goals. Patients measured their blood pressure at home on at least 2 days a week (two measurements each time), using an automatic oscillometric monitor (Omron Hem-705-CP, Kyoto, Japan), and entered the results in an electronic medical record on the Internet. In the intervention group, a pharmacist communicated with each patient by either phone or e-mail every 2 weeks, making changes to their antihypertensive regimens as needed.

Patients in the intervention group had an average reduction in blood pressure of 14 mm Hg from baseline, and their blood pressure was much better controlled compared with the control groups, who were being passively monitored or were receiving usual care based on office blood pressure readings.

■ MEASURING ARTERIAL STIFFNESS TO ASSESS RISK OF END-ORGAN DAMAGE

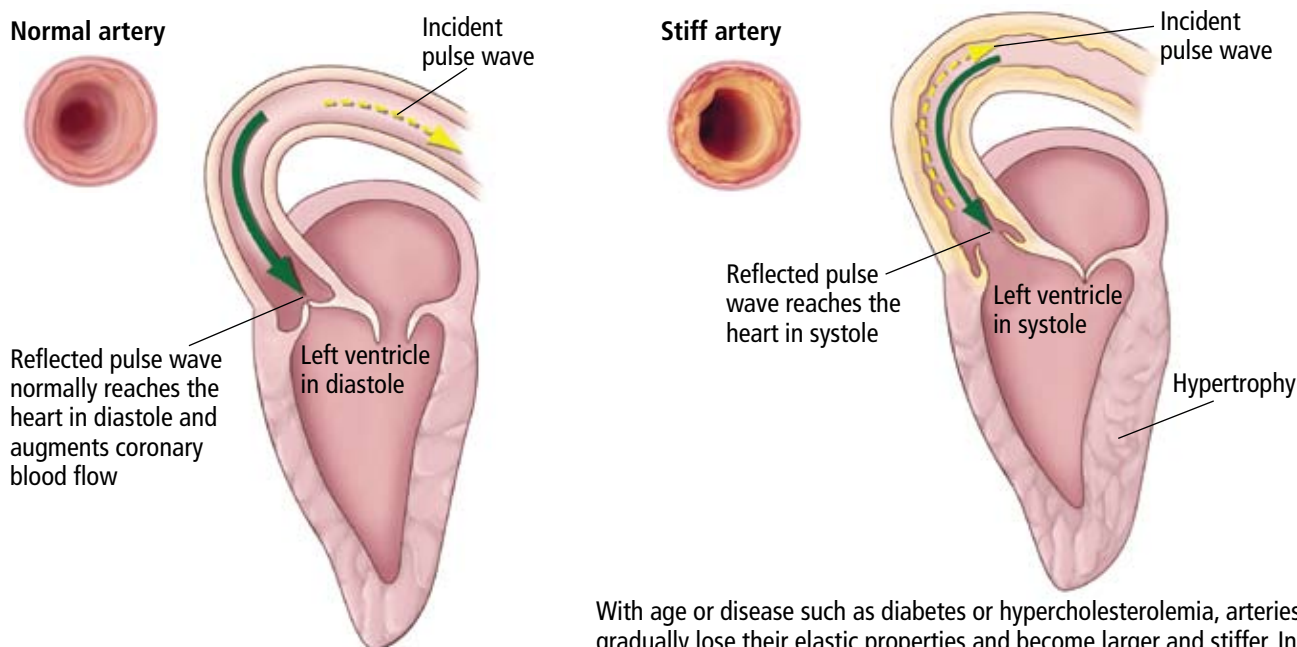
Mean arterial blood pressure, derived from the extremes of systolic and diastolic pressure as measured with a traditional sphygmomanometer, is a product of cardiac output and total peripheral vascular resistance. In contrast, central aortic blood pressure, the central augmentation index, and pulse wave velocity are measures derived from brachial blood pressure as well as arterial pulse wave tracings. They provide additional information on arterial stiffness and help stratify patients at increased cardiovascular risk.

The art of evaluating the arterial pulse wave with the fingertips while examining a patient and diagnosing various ailments was well known and practiced by ancient Greek and Chinese physicians. Although this was less recognized in Western medicine, it was the pulse wave recording on a sphygmograph that was used to measure human blood pres-

Nondippers have a higher risk of cardiovascular death, microalbuminuria, and decline in glomerular filtration rate

Pulse-wave patterns in normal and stiff arteries

The left ventricle contracts during systole, generating a pulse wave that propagates forward into the peripheral arterial system. This wave is reflected back to the heart from the branching points of peripheral arteries.



With age or disease such as diabetes or hypercholesterolemia, arteries gradually lose their elastic properties and become larger and stiffer. In these arteries, the reflected wave returns faster and merges with the incident wave in systole. This results in a higher left ventricular afterload and decreased perfusion of coronary arteries, leading to left ventricular hypertrophy and increased arterial and central blood pressure.

CCF
Medical Illustrator: Beth Halasz ©2009

FIGURE 2

sure in the 19th century.²³ In the early 20th century, this art was lost with the invention of the mercury sphygmomanometer.

With age or disease such as diabetes or hypercholesterolemia, arteries gradually lose their elastic properties and become larger and stiffer. With each contraction of the left ventricle during systole, a pulse wave is generated and propagated forward into the peripheral arterial system. This wave is then reflected back to the heart from the branching points of peripheral arteries. In normal arteries, the reflected wave merges with the forward-traveling wave in diastole and augments coronary blood flow.²⁴ In arteries that are stiff due to aging or vascular comorbidities, the reflected wave returns faster and merges with the forward wave in systole. This results in a higher left ventricular afterload and decreased perfusion of coronary arteries, leading to left ventricular hypertrophy and increased arterial and central blood pressure (FIGURE 2).

Arterial stiffness indices—ie, central aortic blood pressure, the central augmentation index, and pulse wave velocity—can now

be measured noninvasively and have been shown to correlate very well with measurements obtained via a central arterial catheter. In the past, the only way to measure central blood pressure was directly via a central arterial catheter. New devices now measure arterial stiffness indices indirectly by applanation tonometry and pulse wave analysis (reviewed by O'Rourke et al²⁵).

Several trials have shown that these arterial indices have a better prognostic value than the mean arterial pressure or the brachial pulse pressure. For example, the Baltimore Longitudinal Study of Aging²⁶ followed 100 normotensive individuals for 5 years and found that those with a higher pulse wave velocity had a greater chance of developing incident hypertension. Other studies showed that pulse wave velocity and other indices of arterial stiffness are associated with dysfunction of the microvasculature in the brain, with higher cardiovascular risk, and a higher risk of death.

A major limitation in measuring these arterial stiffness indices is that they are derived values and require measurement of brachial blood

pressure in addition to the pulse wave tracing.

Recent hypertension guidelines^{21,27,28} released during the past 2 years in Europe, Latin America, and Japan have recommended measurement of arterial stiffness as part of a comprehensive evaluation of patients with hypertension.

■ EXCITING TIMES IN HYPERTENSION

These are exciting times in the field of hypertension. With advances in technology, we

have new devices and techniques that provide a closer view of the hemodynamic changes and blood pressures experienced by vital organs. In addition, we can now go beyond the physician's office and evaluate blood pressure changes that occur during the course of a usual day in a patient's life. This enables us to make better decisions in the management of their hypertension, embodying Dr. Harvey Cushing's teaching that the physician's obligation is to "view the man in his world."²⁹ ■

■ REFERENCES

- Lewington S, Clarke R, Qizilbash N, Peto R, Collins R. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet* 2002; 360:1903–1913.
- Culleton BF, McKay DW, Campbell NR. Performance of the automated BpTRU measurement device in the assessment of white-coat hypertension and white-coat effect. *Blood Press Monit* 2006; 11:37–42.
- Mancia G, Parati G, Pomidossi G, Grassi G, Casadei R, Zanchetti A. Alerting reaction and rise in blood pressure during measurement by physician and nurse. *Hypertension* 1987; 9:209–215.
- Mancia G, Sega R, Bravi C, et al. Ambulatory blood pressure normality: results from the PAMELA study. *J Hypertens* 1995; 13:1377–1390.
- Ohkubo T, Kikuya M, Metoki H, et al. Prognosis of "masked" hypertension and "white-coat" hypertension detected by 24-h ambulatory blood pressure monitoring 10-year follow-up from the Ohasama study. *J Am Coll Cardiol* 2005; 46:508–515.
- Kotsis V, Staboulis S, Tzouanidis S, et al. Target organ damage in "white coat hypertension" and "masked hypertension." *Am J Hypertens* 2008; 21:393–399.
- Obara T, Ohkubo T, Funahashi J, et al. Isolated uncontrolled hypertension at home and in the office among treated hypertensive patients from the J-HOME study. *J Hypertens* 2005; 23:1653–1660.
- Pickering TG, Rafey MA, Schwartz J, Gerin W. Masked hypertension: are those with normal office but elevated ambulatory blood pressure at risk? *J Hypertens* 2002; 20(suppl 4):176.
- Pickering TG, Hall JE, Appel LJ. Recommendations for blood pressure measurement in humans and experimental animals: part 1: blood pressure measurement in humans: a statement for professionals from the Subcommittee of Professional and Public Education of the American Heart Association Council on High Blood Pressure Research. *Circulation* 2005; 111:697–716.
- Pogue V, Rahman M, Lipkowitz M, et al. Disparate estimates of hypertension control from ambulatory and clinic blood pressure measurements in hypertensive kidney disease. *Hypertension* 2009; 53:20–27.
- Agodoa LY, Appel L, Bakris GL, et al. Effect of ramipril vs amlodipine on renal outcomes in hypertensive nephrosclerosis: a randomized controlled trial. *JAMA* 2001; 285:2719–2728.
- Ohkubo T, Hozawa A, Yamaguchi J, et al. Prognostic significance of the nocturnal decline in blood pressure in individuals with and without high 24-h blood pressure: the Ohasama study. *J Hypertens* 2002; 20:2183–2189.
- Brotman DJ, Davidson MB, Boumitri M, Vidt DG. Impaired diurnal blood pressure variation and all-cause mortality. *Am J Hypertens* 2008; 21:92–97.
- Lurbe E, Redon J, Kesani A, et al. Increase in nocturnal blood pressure and progression to microalbuminuria in type 1 diabetes. *N Engl J Med* 2002; 347:797–805.
- Davidson MB, Hix JK, Vidt DG, Brotman DJ. Association of impaired diurnal blood pressure variation with a subsequent decline in glomerular filtration rate. *Arch Intern Med* 2006; 166:846–852.
- White WB, Larocca GM. Improving the utility of the nocturnal hypertension definition by using absolute sleep blood pressure rather than the "dipping" proportion. *Am J Cardiol* 2003; 92:1439–1441.
- Myers MG, Valdivieso M, Kiss A. Use of automated office blood pressure measurement to reduce the white coat response. *J Hypertens* 2009; 27:280–286.
- Perloff D, Sokolow M, Cowan R. The prognostic value of ambulatory blood pressures. *JAMA* 1983; 249:2792–2798.
- Clement DL, De Buyzere ML, De Bacquer DA, et al. Prognostic value of ambulatory blood-pressure recordings in patients with treated hypertension. *N Engl J Med* 2003; 348:2407–2415.
- Verdecchia P, Reboldi G, Porcellati C, et al. Risk of cardiovascular disease in relation to achieved office and ambulatory blood pressure control in treated hypertensive subjects. *J Am Coll Cardiol* 2002; 39:878–885.
- Mancia G, De Backer G, Dominiczak A, et al. 2007 ESH-ESC Guidelines for the management of arterial hypertension: the task force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *Blood Press* 2007; 16:135–232.
- Green BB, Cook AJ, Ralston JD, et al. Effectiveness of home blood pressure monitoring, Web communication, and pharmacist care on hypertension control: a randomized controlled trial. *JAMA* 2008; 299:2857–2867.
- Mohamed F. On chronic Bright's disease, and its essential symptoms. *Lancet* 1879; 1:399–401.
- Liew Y, Rafey MA, Allam S, Arrigain S, Butler R, Schreiber M. Blood pressure goals and arterial stiffness in chronic kidney disease. *J Clin Hypertens (Greenwich)* 2009; 11:201–206.
- O'Rourke MF, Pauca A, Jiang XJ. Pulse wave analysis. *Br J Clin Pharmacol* 2001; 51:507–522.
- Najjar SS, Scuteri A, Shetty V, et al. Pulse wave velocity is an independent predictor of the longitudinal increase in systolic blood pressure and of incident hypertension in the Baltimore Longitudinal Study of Aging. *J Am Coll Cardiol* 2008; 51:1377–1383.
- Sanchez RA, Ayala M, Baglivo H, et al. Latin American guidelines on hypertension. *J Hypertens* 2009; 27:905–922.
- Japanese Society of Hypertension. The Japanese Society of Hypertension Committee for Guidelines for the Management of Hypertension: Measurement and clinical evaluation of blood pressure. *Hypertens Res* 2009; 32:11–23.
- Dubos RJ. *Man Adapting*. New Haven, CT: Yale University Press, 1980.

ADDRESS: Mohammad Rafey, MD, Department of Nephrology and Hypertension, Glickman Urological and Kidney Institute, Q7, Cleveland Clinic, 9500 Euclid Avenue, Cleveland, OH 44195; e-mail rafeym@ccf.org.