relate positively with the degree of artherosclerotic involvement. Regarding the local proatherogenic effects of the 2 classes of immunoactive molecules, those of the complement system are likely to be much more powerful. Here we refer to the recent commentary by Niculescu and Rus[5] and to a novel alternative hypothesis for the pathogenesis of atherosclerosis in which complement activation in the arterial wall is given the central role.[6] Finally, regarding the suggestion by Muscari and Puddu that the "increased immunoglobulin levels in subjects at risk for myocardial infarction are an epiphenomenon of C3 complement elevation, which in turn is the true independent indicator of the risk," we would add that definition of true risk factors for future ischemic events is impaired by the complexities of the disease process itself. For example, C-reactive protein and fibrinogen, like C3 complement, are acute-phase reactants. They are all synthesized in the liver as a response to similar molecular signals generated in distant inflammatory (infectious) tissue sites. Moreover, C-reactive protein, fibrinogen, and C3 complement all are deposited in the arterial wall (like immunoglobulins), and an increased concentration of any of them is a good predictor of a future coronary event. Which one is the true predictor and which one is an epiphenomenon? At present, it is too early to decide.

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Reliability of Self-Measured Blood Pressure for Research Purposes

Thijs and coauthors[1] recently proposed reference values for self-recorded blood pressure (BP). Brody and colleagues[2] examined the test-retest reliability of at-home self-measured BP with an automatic device (AUD). These authors concluded that the at-home AUD measurements may be reliable when multiple readings are taken by trained patients and that the use of AUDs may be adequate for clinical and research purposes.

Before recommending that this technique be used in research, several points deserve emphasis. First, the accepted standard device used[3] for noninvasive BP measurement is the mercury sphygmomanometer. An AUD may be a convenient surrogate for self-measurement of BP for patients who have difficulty in achieving skill and accuracy with a mercury sphygmomanometer. Second, when choosing an AUD for clinical use or for research, preference should be given to devices that have been authorized by a regular validation procedure.[4,5] However, the accepted validation protocols are time consuming and expensive because a large number of subjects are tested across a wide range of BPs, which requires the employment of many well-trained observers.[4,5] At present, manufacturers have no obligation to have AUDs validated independently, even though there has been a call for such action.[4] Third, the AUD needs to be periodically recalibrated during the course of prolonged studies.

Fourth, in addition to recalibration, each AUD should be periodically reassessed to ascertain that its validity has not changed during long-term use. Conventional procedures for validation are too cumbersome and expensive to be used for in-field monitoring of accuracy. Recently, a rapid and inexpensive method for evaluation of AUDs has been proposed, based on numerous BP measurements at rest and during a standardized postural challenge in a small number of subjects with a wide range of BPs.[6] The latter method could be used for the periodic reassessment of the validity of AUDs.

Accuracy of BP measurements is of critical importance in BP research and for the evaluation of antihypertensive medications. Regular self-monitoring of BP at home could be very useful if the appropriate AUD is chosen and if the validity of the instrument and measurement technique is supervised. Unfortunately, most studies have not met these requirements.[1,2] Self-monitoring of at-home BP measurements could be deceiving if any of the conditions specified above are ignored.

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In reply

Dr Naschitz and colleagues have raised a number of issues in relation to the reliability of the self-measurement of BP, many of which are presently under consideration by the Working Group on Blood Pressure Monitoring of the European Society of Hypertension. The conclusions of 2 recent meetings held under the auspices of the group may, therefore, be of interest.

At the First Consensus Conference on the Self-Measurement of Blood Pressure held in Paris, France, on June 4, 1999, the participants would not have shared the opinion of Naschitz and colleagues that application of the technique should be restricted to clinical research. In fact, the conference, in keeping with the Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure guidelines,[1] advocated self-monitoring of blood pressure, as an accessory to conventional sphygmomanometry, with a broad role in day-to-day clinical practice. Blood pressure measurement outside the medical environment provides valuable information for the initial evaluation of hypertensive patients and for monitoring the response to treatment. Self-measurement makes it possible to distinguish patients with white-coat hypertension from those with sustained BP elevation.[2] This technique also has the potential of improving patient adherence to antihypertensive medication and of reducing the costs of caring for hypertensive patients.[1] There is almost general consensus that, for now, at-home BP readings of 135 mm Hg systolic and/or 85 mm Hg diastolic, or greater, should be considered elevated.[1-3] Prospective epidemiologic studies[4] and clinical trials[5] to validate these thresholds in terms of target organ damage or morbidity and mortality are under way. Useful though the technique may be, it does have limitations, and these have been aired recently in the correspondence columns of the American Journal of Hypertension.[6]

The Working Group also held a workshop at the European Society of Hypertension Scientific Meeting in Milan, Italy, on June 15, 1999, at which it was reiterated that manufacturers of AUDs must follow the internationally agreed-on validation protocols of either the British Hypertension Society[7] or the Association for the Advancement of Medical Instrumentation.[8] These quality standards are equally important for clinical practice and research, because a patient's life or well-being may depend on the accurate assessment of his BP outside the clinic environment. We would agree that the British Hypertension Society and Association for the Advancement of Medical Instrumentation protocols are complex and expensive to perform. However, in the past year, both the British Hypertension Society and Association for the Advancement of Medical Instrumentation have had a number of meetings with the purpose of not only harmonizing the 2 protocols, but also of simplifying the validation procedures.

The British Hypertension Society protocol recognizes the need for evaluating accuracy after a device has been in use and incorporates an "in-use phase" for this purpose. Naschitz and colleagues rightly draw attention to the impossibility of regularly performing validation assessments on devices in use. However, most AUDs are dependent on an algorithm, which is unlikely to develop inaccuracies with use, though the components of the device, such as the cuff and tubing, may become faulty and cause inaccuracy. Simple calibration checks may suffice with most AUDs, and BP simulators can have a role in this regard. Naschitz and colleagues advocate a rapid and inexpensive procedure for the in-field monitoring of the accuracy of devices. While their still unpublished proposals may be of value, they will have to be viewed as a further means of assessing the reliability of devices that have been in regular use and cannot be substituted for the formal validation procedures described above to which all devices should be subjected initially.

We foresee that with the banning, for environmetal reasons, of the mercury sphygmomanometer in many European countries,[9] and with the introduction of fully automated and properly validated machines for self-measurement,[10] most based on an oscillometric algorithm with data storage and printout facilities, the Riva-Rocci/Korotkoff[11] technique will soon lose its status as the standard method for noninvasive BP measurement.[9]

We agree with the recommendation that governments should urgently regulate manufacturers. Some companies betray the public by advertising nonvalidated devices or machines that sometimes measure BP at anatomical sites other than the brachial artery, a procedure prone to error and far from generally endorsed.[1] Other commercial interest groups, regardless of whether devices have been validated, sell machines for the self-measurement of BP via public outlets without providing any proper training to patients or information on the limitations of their use. Furthermore, users' instructions should be better standardized, include guidelines for calibration, and state a guaranteed lifetime of accurate use.

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Drug-Associated Agranulocytosis: Experience at Strasbourg Teaching Hospital

We read with great interest the study by van der Klauw et al[1] of drug-associated agranulocytosis in a Dutch hospital. We agree with their conclusions (the highest risks of drug-induced agranulocytosis occur with thyroid inhibitors, the combination drug sulfamethoxazole-trimethoprim, sulfasalazine, clomipramine hydrochloride, and dipyrone com-