Two major research strategies have emerged for investigating the role of psychosocial stress in the development of hypertension. The first is to carry out population-based assessments of associations between stress exposure and future hypertension or increases in blood pressure using standard observational epidemiological methods. Such studies provide evidence for a relationship between stress and the development of clinical hypertension but supply limited information about the pathways involved. The second more mechanistic strategy is to measure physiological reactions to acute psychological stress. Extensive work was carried out in the 1980s and 1990s comparing hypertensive subjects with normotensive subjects, people with high and low blood pressure in the reference range, and individuals with positive and negative family histories of hypertension, assessing whether the higher-risk group shows greater physiological stress reactivity. The clinical significance of acute stress reactions has been questioned, so longitudinal follow-up studies have been conducted to establish whether people who show heightened acute stress reactivity are at greater risk for the development of hypertension.

In this issue of Hypertension, Flaa et al² present an important longitudinal study of the prognostic significance of individual differences in reactions to psychological stress. The study has several strengths. First, the follow-period of 18 years is longer than in most previous work, and the proportion of the original participants who were reassessed was high (82%). Second, a population-based sampling strategy was used, recruiting participants from young Norwegian men being examined before military service. Military service is obligatory in Norway, so the 19-year-olds tested in this study were selected from the general population. Many studies in this field have involved nonrepresentative convenience samples of college students.

The third unusual feature of this study is that the investigators measured arterial catecholamine responses to stress. Most studies have only measured cardiovascular reactivity, testing whether blood pressure or heart rate stress responses predict future blood pressure levels. The assessment of plasma catecholamines provides direct evidence about the contribution of sympathetic nervous system activity. Venous catecholamines are more commonly measured but are strongly influenced by local tissue activity; it has been estimated that half of the norepinephrine in a venous sample from the forearm is derived from sympathetic nervous activity in the arm itself. Arterial samples provide more robust indicators of whole body output. An additional feature of the study by Flaa et al² is that participants were not aware of their blood pressure status at the time of stress testing. It has been shown previously by this group that individuals who knew that they had moderately elevated blood pressure showed greater stress reactivity than people with similar blood pressure who were not informed of their blood pressure levels, and this is an important factor that is rarely taken into account in this area of research.

Flaa et al² have demonstrated that systolic blood pressure at 18-year follow-up is predicted by resting blood pressure on entry, a positive family history of hypertension, and by systolic pressure and catecholamine responses to mental stress. The effects are substantial, with systolic pressure during stress explaining 9.4% of the variance in follow-up blood pressure and plasma catecholamines during stress an additional 12.7%. Interestingly, effects were more marked when reactions to mental stress, rather than the cold pressor test, were assessed. The cold pressor was the original “stressor” used in early research on stress reactivity and blood pressure but elicits pressor responses underpinned by α-adrenergically mediated vascular changes rather than β-adrenergic cardiac responses. This result, therefore, supports the notion that catecholamine responses to psychological stress drive a hyperkinetic hemodynamic profile that contributes to hypertension risk.

The theory underlying the use of acute psychophysiological stress testing is that these short-term responses reflect stable individual differences in physiological reactivity. Hyperreactive people will experience repeated episodes of elevated catecholamines and blood pressure as they go about their everyday lives, so that over the course of time their tonic blood pressure will rise. The results of this study are consistent with the hypothesis, but not all hyperreactive people show progression of blood pressure toward hypertension. One important issue may be whether the individual is exposed to challenges in everyday life that elicit appropriate stress reactions; a person could be hyperreactive yet manifest little rise in blood pressure because they lead tranquil lives. Thus, Light et al⁶ demonstrated that high stress reactivity predicted increases in tonic blood pressure over a 10-year period only if it was associated both with a positive family history and with high levels of daily stress. It is also possible that, over time, some people learn to cope more effectively with behavioral and emotional challenges, thereby reducing the frequency of hyperreactive episodes. Adding measures of stress exposure and coping during the follow-up period
may increase the strength of the prediction of future blood pressure.

Studies of this type do not establish causality. There could be underlying factors, such as genetic disposition, that influence both physiological stress reactions and blood pressure changes over time. In addition, raised catecholamine and blood pressure reactions to acute stress may be markers for other processes that contribute to the development of hypertension. For example, both interleukin-6 and fibrinogen responses to stress have been shown to predict increases in ambulatory pressure prospectively, independent of baseline ambulatory pressure and other covariates. Stress-induced lymphocyte adhesion is elevated in hypertension, and inflammatory stress responses are associated with arterial stiffness in older adults.

The study by Flaa et al was limited to young white men, and there is evidence for ethnic and gender differences in the prognostic significance of stress reactivity. The magnitude of the physiological reaction is only 1 aspect of the stress response, and response duration and rate of poststress recovery may be equally significant. In this respect, it is notable that slow recovery back to baseline blood pressure levels after stress predicts increases in tonic pressure levels over time independent of reactivity effects. Other aspects of autonomic function, such as vagal withdrawal, may contribute to hypertension risk independent of sympathetic activation. Nevertheless, the longitudinal study by Flaa et al provides important evidence in support of a role for sympathetic nervous system hyperreactivity in hypertension, adding to the accumulated data from epidemiological and clinical studies endorsing the influence of psychological stress on the development of high blood pressure.

Source of Funding
This work was supported by the British Heart Foundation.

Disclosures
None.

References

Source of Funding
This work was supported by the British Heart Foundation.
Psychophysiological Stress Reactivity and Hypertension
Andrew Steptoe

Hypertension. 2008;52:220-221; originally published online June 23, 2008;
doi: 10.1161/HYPERTENSIONAHA.108.115477

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2008 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://hyper.ahajournals.org/content/52/2/220

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published
in Hypertension can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial
Office. Once the online version of the published article for which permission is being requested is located,
click Request Permissions in the middle column of the Web page under Services. Further information about
this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Hypertension is online at:
http://hyper.ahajournals.org//subscriptions/