Stress mechanisms in hypertension

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Summary: Recent studies of stress mechanisms in hypertension have focussed on the cardiovascular and neuroendocrine reactions to challenging or threatening psychosocial stimuli. Fixed hypertension may develop in some animal models following chronic exposure to psychosocial conflict. Acute experiments in humans show that marked sympathetically-mediated cardiovascular reactions accompany the performance of challenging tasks. Responses are more accentuated in hypertensives and in people at high risk for developing the disorder. The working hypothesis to emerge is that the haemodynamic responses that accompany attempts to cope with challenging environments may promote the spiral towards sustained hypertension in susceptible individuals.

Essential hypertension is a multifactorial disorder in which several pathophysiological mechanisms are implicated at various stages in its progression. Among the many processes considered relevant to pathology are disturbances in fluid volume regulation, structural changes in the vasculature, the action of a circulating natriuretic factor, and dysregulation of the renin-angiotensin system. The purpose of this paper is to argue that psychosocial stress and the way in which people cope with aversive environments also plays a part in the development of hypertension in susceptible individuals. In order to make a case for the role of stress, it is necessary to take account of a range of empirical data, from studies of pathophysiology through experimental investigations of the responses to stress in the laboratory, to clinical assessments of patients with high blood pressure (Steptoe, 1981). The manner in which these various lines of research converge on stress mechanisms in hypertension will be briefly described.

Physiological stress mechanisms

When considering the processes underlying hypertension, it is useful to make a distinction between initiating and maintaining factors (Korner, 1982). Several mechanisms such as the resetting of the baroreceptor reflexes and 'structural autoregulation' in the peripheral vasculature may operate to sustain blood pressure (BP) at a high level once it is raised, but account less convincingly for the initial elevation. However, if psychosocial factors are involved in the development of hypertension, they are likely to be linked with the early, triggering stages of the patho-

physiological sequence. There is considerable evidence that heightened autonomic nervous system activity may be present early in the aetiology of hypertension. Studies of circulating plasma catecholamines suggest that concentrations are elevated among young hypertensives (Goldstein, 1983). In addition, investigations of the haemodynamics of mild hypertension show that cardiac output is often raised, in contrast to the pattern of raised total peripheral resistance observed in established cases (Korner, 1982). This haemodynamic disturbance can be reversed by autonomic blockade in many patients (Julius & Esler, 1975).

It has become clear over recent years that autonomic regulation of the cardiovascular system is not confined to the brain stem cardiovascular control 'centres', but is organized longitudinally within the central nervous system, with higher cortical and subcortical regions having an important influence (Hilton & Spyer, 1980). This may provide the substrate through which psychophysiological factors play a part in hypertensive aetiology. The general hypothesis to emerge is that autonomically-mediated cardiovascular reactions to psychosocial challenges may initiate the progression towards sustained hypertension in susceptible individuals.

Experimental studies of stress in hypertension

These notions have been studied extensively in animal experiments, in which the sustained influence of psychosocial stress may be evaluated under carefully controlled conditions (reviewed by Campbell & Henry, 1983). Although negative results have been reported (Harrap *et al.*, 1984), sustained elevations in BP have been observed in many species. Hypertension is particularly common following the imposition of

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non-habituating psychosocial challenges or aversive conflicts that must be resolved by adaptive behaviour on the part of subjects. Evidence for the involvement of the autonomic nervous system in these patterns has also been obtained with measures of enzyme activity in the adrenal glands, plasma catecholamines and reversal of responses following autonomic blockade. In contrast, hypertension is less frequently produced by 'passive' stressors such as footshock and restraint.

The scope for experimental studies in humans is of course very much restricted, so investigations have largely been confined to assessments of acute reactions to stress in the laboratory. Since the classic work of Jan Brod (1960), a considerable literature has accumulated, and with it a growing awareness of the methodological problems accompanying such experiments (Steptoe *et al.*, 1985). Although many researchers have reported that hypertensives display greater haemodynamic reactions to experimental stress than normotensives, this finding is again by no means universal. An appraisal of the literature suggests that the nature of the challenge may be important, with hypertensives being especially reactive under conditions provoking effortful, active coping with the environment. A study of cardiovascular reactions among normotensives and mild hypertensives recruited from factories in South London indicated that heightened blood pressure reactions were present when subjects were required to cope with active challenges (a problem-solving task and competitive game), but not during exposure to the more passive stress of the disturbing film (Steptoe *et al.*, 1984).

Studies of this kind corroborate the role of psychosocial stress in hypertension, but do not provide direct aetiological evidence. An alternative explanation of results is that heightened responsivity is an effect of the circulatory disturbance present in hypertensives, and follows rather than precedes the disorder. Recent years have therefore witnessed an effort to study cardiovascular reactivity in healthy normotensive people who are nevertheless at risk for hypertension. Experiments involving the normotensive offspring of hypertensive parents (known to be at high risk) show that they too manifest exaggerated BP reactions to active psychological challenge. Their exaggerated reactions are probably mediated by heightened activity in the cardiac sympathetic nerves (Schulte & von Eiff, 1985). An interesting study by Light *et al.* (1983) demonstrated that reactive high risk subjects

showed sodium and fluid retention following behavioural stress, implicating a renal mechanism in the process as well. Prospective studies are now required to test the importance of these mechanisms on a longitudinal basis, while establishing the relevance of laboratory reactivity patterns to the behaviour of blood pressure in everyday life.

Clinical implications

Laboratory studies of the type described here permit cardiovascular reactivity to psychosocial stress to be evaluated in a controlled fashion, but provide limited information about the real world. Recent developments in the technology of direct and indirect ambulatory recording now make it possible to study fluctuations in BP under the conditions of everyday life. It has been known for many years that BP is highly variable both in hypertensives and normotensives, and that it responds to the physical and psychological demands of the environment (Conway *et al.*, 1984). What has proved more difficult to establish are methods of quantifying both psychosocial demands and BP variability, so as to assess the relationship between the two. It is to be hoped that studies in the future will be able to evaluate the association between acute psychosocial stress during everyday life with variations in cardiovascular activity, linking natural observations with more detailed studies in the laboratory.

An alternative approach to evaluating the clinical implications of stress hypotheses is to predict which members of the population will be at risk for hypertension. The possibility emerging from laboratory studies is that people may be at heightened risk if they are persistently exposed to challenging environments, particularly if they strive actively to cope with these conditions. Such circumstances may arise at work, and it is interesting that Theorell *et al.* (1985) have recently reported especially high levels of BP at work among people at risk for hypertension whose jobs are rated as 'hectic' and 'strain' occupations. Other data from epidemiological surveys indicates that the incidence of hypertension is related to a complex interaction between psychosocial stimulation and psychological coping style (e.g. Gentry, 1985). It is out of the multidisciplinary approach outlined here that firm statements about stress mechanisms in hypertension will emerge over the next few years.

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