Salt Sensitivity: Trophic Effect of Growth and Vasoactive Factors

To the Editor:

The nexus between salt (sodium chloride) intake and essential hypertension is not simple. (For a recent review, see Reference 1). Population studies have demonstrated a positive correlation between increased dietary salt intake and the incidence of essential hypertension, whereas intrapopulation studies have not always shown this relation. Established essential hypertension is not simple. (For a recent review, see Reference 1).

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Great numbers of vasoactive agents and growth factors stimulate the peripheral circulatory system. Thus, the high incidence of essential hypertension in populations consuming large quantities of sodium chloride is likely to reflect the chronic influence of a high salt intake on the cardiovascular system. This phenomenon is probably related to enhanced growth of the vascular media and peripheral vasoconstruction, both of which produce narrowing of the vascular lumen. However, a substantial increase of vascular smooth muscle (VSM) mass is unlikely to result from a brief exposure to a high salt intake. Yet, to characterize the nature of "salt-sensitivity," most investigations have monitored the blood pressure response in individuals subjected to an increased intake of salt for short periods ranging from days to months. A significant elevation of blood pressure in association with increased sodium intake was thus considered as indicative of salt-sensitivity.

A recent insight into cellular mechanisms that mediate alterations of the PVR suggests that underlying causes for the increased incidence of essential hypertension in populations habitually consuming a high salt diet results from additional pathophysiological processes to those responsible for blood pressure elevation during short periods of exposure to increased salt intake. A great number of vasoactive agents and growth factors stimulate pathways in VSM cells that may lead both to vasoconstruction and enhanced growth. These factors usually increase the cytosolic free calcium in concert with a greater stimulation of the sodium-proton exchange by factors in serum than do skin fibroblasts from whites. Similar tendencies in VSM cells would favor an increased sensitivity of VSM cells to these factors, or both. Such a concept is compatible with recent observations that structural vascular alterations in animal models of hypertension may not solely relate to the elevated blood pressure level but to the trophic influences of vasoactive hormones (for example, see Reference 8).

These findings suggest the concept that a chronic increase of salt intake in susceptible subjects is associated with increased VSM growth due to altered levels of vasoactive and growth factors, increased sensitivity of VSM cells to these factors, or both. However, short periods of salt loading may identify individuals whose salt-sensitivity is expressed primarily by acute or subacute hemodynamic mechanisms. These individuals may represent a different group or only a segment of the population responding to a chronic increase in salt intake by increased growth of the VSM. In fact, subjects reacting to a chronic increase in sodium intake primarily by accelerated growth of the vascular media would not demonstrate a significant blood pressure response to short-term alterations in sodium intake inasmuch as changes in the vascular media are unlikely to occur over a short span. Nonetheless, these subjects must also be considered salt-sensitive.

As a group, blacks manifest more salt-sensitivity and a greater propensity to the development of essential hypertension than do whites. Thus, racial (black versus white) differences in cellular sodium and calcium regulation may shed light on the nature of salt-sensitivity. Such an idea is strengthened by our recent observations that skin fibroblasts from blacks show a higher elevation of cytosolic free calcium in concert with a greater stimulation of the sodium-proton exchange by factors in serum than do skin fibroblasts from whites. Similar tendencies in VSM cells would favor an increase in the propensity for VSM growth in blacks.

I propose that future research into the question of salt-sensitivity in essential hypertension will focus not only on the impact of a brief change in salt intake on blood pressure levels, but also on the influence of a long duration of altered dietary salt intake on the interplay of growth factors and vasoactive agents that can stimulate VSM growth.

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References


Single Versus Triplicate Measurements: A Commentary on Fagan et al.

In an article published in this journal, Fagan et al concluded that duplicate or triplicate measurements of blood pressure are neither more accurate nor less variable than single measurements and that the additional measurements are of no value in evaluating the effects of antihypertensive medications or other interventions on blood pressure. This conclusion was based on a study of 40 patients who were withdrawn from antihypertensive medications...
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