Although dietary salt restriction is often valuable as sole or adjunctive therapy of hypertensive disorders, it is abundantly clear that hypertensive patients comprise a heterogeneous group with regard to salt sensitivity of blood pressure. This is apparent despite the many methodological obstacles to defining salt sensitivity in an individual patient. Currently, dietary trial is the only sure means of defining a given patient as responsive to salt restriction. Easily definable markers of salt sensitivity would allow appropriate targeting of this rather ponderous therapy. Promising leads include the assessment of membrane ion transporters such as sodium-lithium exchange and of the activity of the renin-angiotensin system, including the phenomenon of “non-modulating” hypertension and other volume regulatory hormones such as atrial natriuretic factor. Although less intensively studied than in hypertensive patients, the blood pressure response of normal subjects to salt restriction is also marked by great variability. Given the possibility of deleterious consequences of population-wide salt restriction for at least some people in a setting such as the United States, it seems imprudent to recommend such a policy before its proven worth has been demonstrated by clinical trial. Pending such evidence and the development of markers, salt restriction should be reserved for those in whom it is of demonstrated efficacy.

Since the introduction of dietary sodium chloride restriction as a therapy of essential hypertension, it has been recognized that hypertensive patients comprise a heterogeneous group with regard to the property of salt sensitivity of blood pressure, a fact amply borne out by animal models of hypertension. The basis of this heterogeneity among patients with essential hypertension is poorly understood, and we have only a limited ability to select salt-sensitive and salt-resistant individuals without rigorous clinical trial. The definition of salt sensitivity itself is not clear and may be different for different purposes. As with blood pressure in the general population, the distribution of changes in blood pressure with changes in dietary salt, while markedly skewed, is not bimodal, and any cutoff criterion must be dictated by other than physiological considerations. It is also not clear whether defining salt sensitivity in short-term studies identifies the same subjects as those who are responders to long-term therapy. Given the methodological difficulties of definition and the biases inherent in the selection of subjects for study combined with the intrinsic heterogeneity of essential hypertension, it becomes quite difficult to ascertain the incidence of this phenomenon in the general hypertensive or normotensive population.

A universally acceptable definition, together with the development of markers of this phenomenon, would be of great value not only for targeting this rather ponderous diet therapy but also for obtaining pathophysiological insight into its mechanisms. Among the potential markers with some promise are those evaluations of the renin-angiotensin-aldosterone system that define low renin hypertension, perhaps including plasma prorenin levels as an additional, more reliable indicator, or non-modulating hypertension. Atrial natriuretic factor is part of a volume-sensing and volume-regulating hormonal system whose assessment may also provide an indicator of salt sensitivity. Assessment of the activity of ion transport systems is another area of research that may prove useful in identifying salt-sensitive people. Of these, sodium-lithium exchange activity seems to be promising, and importantly is not dependent on salt intake (A. Weder, personal communication, December 1989).

The existence of significant salt sensitivity among normal subjects, short of the extremes of shock with volume depletion and toxic levels of salt, is uncertain. Intervention studies of normal subjects show variable, usually small changes in blood pressure with some experiencing a decline and others a rise. The reproducibility of these changes in a given individual is uncertain, and some of the changes may reflect...
variability of blood pressure. However, several studies show that changes in blood pressure in both directions exist even with intra-arterial monitoring under controlled circumstances, suggesting that both pressor and depressor responses to short-term (1–2 weeks) salt loading indeed occur in normotensive subjects. Beyond individual variability, there is also very likely to be considerable heterogeneity in the response of populations to changes in salt intake based on adaptations to differing environments. 

In addition to the heterogeneous responses to salt restriction, a second aspect of the heterogeneity of hypertension of potential significance to the phenomenon of salt sensitivity is the variability in prognosis. In the recent past the ability to stratify patients as to prognosis has improved greatly. Factors other than blood pressure per se, such as left ventricular mass, microalbuminuria, plasma renin, fasting blood sugar, lipid profile, previous heart attack, or tobacco use, have been shown to have an important influence on the outcome of patients with hypertension. In this context, it is important to know whether types of hypertension characterized by the presence or absence of salt sensitivity have any unusual prognostic features, as is suggested by some studies showing better prognosis in patients with lower renin values, who are more likely to be salt-sensitive.

Observational studies comparing the relation of salt intake with blood pressure in different populations have suggested that effects of salt intake on mean blood pressure or on the increase of blood pressure with age, although statistically significant, are small. These relations weaken further when analyses of variables such as body mass index or alcohol intake are included. Thus, the INTERSALT study, the most comprehensive cross-cultural study of salt excretion and blood pressure, suggests that a reduction of salt intake of 100 mmol/day would lower the mean systolic pressure of a population by 2 mm Hg and the diastolic pressure by 0.1 mm Hg. Projections that even these small changes in blood pressure could have profound effects on the incidence of cardiovascular disease in the United States raise the possibility that universal salt restriction would result in a dramatic decrease in cardiovascular disease. Several scientific and legislative committees have already suggested that all Americans reduce their salt intake to less than 3 g (105 meq) per day (see Reference 16). The INTERSALT data have led some investigators to suggest that such reductions in salt intake should be even more stringent.

We believe that universal salt restriction is inappropriate for several reasons. The magnitude of benefits remains uncertain despite the multiple attempts made to quantify them. Biological meaning rests on more than statistical correlation. In this regard, the trials of the treatment of mild hypertension are instructive in that actual benefits regarding coronary protection fell far short of statistical projections based on epidemiological studies.

Furthermore, the failure of most people to benefit becomes important when the discomforts and possible dangers of salt restriction are taken into consideration. It is routinely assumed that the marvelous capability of the kidneys to attain external sodium balance over wide ranges of intake make salt restriction a therapy without significant hazard and thus universally applicable as a preventive measure. We believe that this view is unproven and that there are several important cautions in this regard.

Sodium chloride is the major currency of the extracellular fluid (ECF) volume, and external sodium balance in the face of changes in salt intake is accompanied by fluctuations in the ECF volume. The ability to adapt to very low salt diets is usually studied in healthy young people or observed in non-Western, traditionally living people whose lifestyles and life expectancy differ substantially from our own. This ability does not appear to be uniform even within our society. For example, age appears to have an important influence on the ability to conserve sodium. Healthy older people have greater negative sodium balance and take longer when coming into sodium balance than do younger persons.

Decreased availability of salt in the diet would have at least two potentially detrimental effects beyond "quality of life" issues. First, a person on a low salt diet might be closer to a critical deficit of ECF and therefore have less reserve in the face of a salt-depleting stress. Second, a persistent low salt diet would make it more difficult to reconstitute losses after an acute salt-depleting stress.

Such stresses are not rare and include many acute, otherwise self-limited illnesses accompanied by diarrhea, vomiting, or fever with anorexia and diaphoresis. The seriousness of these illnesses is most often related to circulatory derangements caused by salt deficits. The very young and elderly are particularly vulnerable. The marked vulnerability of even the healthy elderly person to salt depletion was demonstrated in a study of healthy young and old men, in which both groups tolerated 60° head-up tilt when salt replete, but only the young subjects tolerated the stress after short-term salt depletion. The older subjects all had pronounced falls in pressure and half fainted under the latter condition.

Another large group of people who may be vulnerable to salt depletion are healthy persons who exercise intermittently, especially in hot weather. Weekend warriors who spend most of their time in temperature-controlled environments may have large sodium losses in sweat. Few follow regimens rigorous enough to provide maximal acclimatization, and even with acclimatization, sodium losses in sweat can be considerable, up to 10–25 meq/hr. Salt depletion in this setting may predispose to heat stress, in addition to the other problems associated with hypovolemia. Rhabdomyolysis and acute renal failure are well described consequences of exertion in the context of hypovolemia.
These important derangements come to medical attention only in their most severe form, and the treatment is saline administration. The value of liberal dietary salt intake in buffering these problems is poorly researched but may be quite important in maintaining people during milder versions of these stresses and preventing them from coming to medical attention.

In addition to these conditions, several investigators have suggested that liberal salt intake may afford protection from toxemia and is advantageous in several medical conditions, including poorly controlled diabetes mellitus, adrenal insufficiency, and some forms of chronic renal insufficiency.

These dangers of salt restriction, while extremely well-known qualitatively, have not been subject to quantitation in a population such as ours. Given the broad variety of dietary habits in the population, even a policy of universal moderate salt restriction achieved by markedly restricting the salt content of prepared foods may subject large numbers of people to diets severely restricted in salt. Thus, problems related to salt depletion may well exist even with a program of moderate salt restriction.

Therefore, it would seem appropriate to recommend universal salt restriction only after its benefits have been proven and carefully weighed against its other costs to society as well as its dangers, to which even cursory analysis reveals that large groups of people may be susceptible. This should involve carrying out the same type of rigorous trials to which antihypertensive medications have been subject in both hypertensive and normotensive people. Meanwhile, the pending development of markers of salt sensitivity, salt restriction as a safe and effective treatment of hypertension should be reserved for those hypertensive subjects in whom it has been demonstrated by clinical trial to be effective. Its use for the prevention of hypertension in the general population must remain an interesting speculation without enough evidence to justify its inclusion as part of a national program.

References


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