Salt and Blood Pressure
Population and Individual Perspectives

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The need to reduce the amount of salt in the diet has remained a very controversial issue in spite of strong evidence from animal experimental and human studies that increased salt intake is associated with increased blood pressure levels. The fundamental problem is the confusion between clinical, preventive medicine, and public health approaches. Reducing salt intake is not as effective as drug therapy to treat hypertension (clinical model). Individual preventive medicine approaches aimed at high risk populations are effective, but the efficacy is limited by the size of the population at risk and the intensity of the intervention. The public health approach to gradual reduction of available salt in the diet is likely to result in decreased morbidity and mortality with little inconvenience to the public. Am J Hypertens 1997;10:29S–36S © 1997 American Journal of Hypertension, Ltd.

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The association between the amount of salt (NaCl) consumed, blood pressure levels, and risk of cardiovascular disease (CVD) and other diseases has been known for at least 50 years.1 Studies by Dahl,2 Meneely,3 and others documented the association between estimated population consumption of salt and elevated blood pressure, as well as the association between salt intake and blood pressure in animal models, rats. Further ecological studies by Page et al4 documented the high correlation between level of salt intake of the population and prevalence of hypertension. More recent ecological studies5 have further documented the association of salt intake, blood pressure, and stroke mortality rates (Figure 1).6 Short-term human experimental feeding studies clearly showed that increases or decreases in salt intake resulted in either an increase or decrease in blood pressure.7 The effects of change in salt intake are rapid and predictable in relationship to the changes in salt consumption. There is little evidence of a unique distribution of the responses to salt intake. In spite of what appears to be overwhelming evidence that higher salt intake results in higher blood pressure levels, there remains a continued belief by some that salt in the diet is of little importance. The scientists who support this few are unfortunately wrong. Their vocal opposition to the need to lower the salt consumption of the U.S. population, as well as active opposition by part of the food industry have slowed a much needed reduction in the amount of salt consumed by the U.S. population, as well as that in other countries. Much of the controversy related to the association of salt intake and blood pressure is due to misinterpretation of the concepts of clinical and preventive medicine and public health.

CLINICAL PERSPECTIVE

The clinician can use very effective drugs to treat hypertension. Reduction of salt in the diet results in a relatively small decrease in blood pressure. For example, a 100 mmol decrease would result in perhaps 6 to 7 mm decrease in systolic blood pressure, and 3 to 4 mm decrease in diastolic blood pressure.8–10 These
reductions in blood pressure are clearly not as great as can be accomplished by relatively small doses of diuretics or other drugs. Furthermore, maintaining 100 mmol decrease is very hard and even a 50 mmol decrease is difficult given the large amount of added salt in the food chain. The clinician therefore presumes that the amount of salt in the diet is of relatively little importance. In some ways the clinician is correct. The Trial of Mild Hypertension Study (TOMHS) evaluated both drug therapy and nonpharmacological therapy in a randomized blinded trial. The nonpharmacological therapies included exercise, lower salt intake, and weight loss, and was very successfully implemented. However, the nonpharmacological therapy with placebo was not nearly as effective in reducing blood pressure over 48 months, compared to the combination of nonpharmacological therapy and a variety of antihypertensive medications. Furthermore, the participants on drug therapy had lower risks of subsequent CVD and less symptomatology, than those who had a combination of nonpharmacological therapy and placebo. The extent of lowering the blood pressure is clearly a major determinant of risk of stroke, other hypertensive complications, and atherosclerotic diseases, such as myocardial infarction. The TOMHS study included both drugs and nonpharmacological intervention. Nonpharmacological interventions are probably no substitute for drug therapy for most hypertensives. However, the combination of nonpharmacological treatments and drugs may be better than drug therapy alone. The clinicians’ observation that nonpharmacological therapy does not lower the blood pressure in hypertensives as much as drug therapy, and therefore may not be as beneficial to the patient may be correct. It is also very difficult to maintain nonpharmacological intervention as compared to taking a pill. This, however, does not mean that lowering the amount of salt in the diet of the population is ineffective. Stopping smoking after the onset of lung cancer or even in the few years prior to the onset of lung cancer is not a very effective intervention. Drug therapy, surgery, and radiation are clearly more effective in treating lung cancer. Smoking cessation before the development of lung cancer or...
better yet total life time abstinence will substantially reduce the risk of lung cancer, a far more preferable approach than the treatment of lung cancer.

Lipid lowering drugs are more effective than diet alone for lowering LDL cholesterol (LDLc) for most patients with coronary heart disease (CHD) and elevated LDLc. This, however, does not mean that dietary approaches to lowering LDLc in the population are ineffective. In fact, the reduction of LDLc levels in the entire population, through dietary modification, is probably having a bigger overall effect on reduction of CHD than drug therapy for lowering LDLc for those who already had a heart attack or have very high LDLc.

The claim that reducing salt intake only lowers blood pressure a few millimeters and therefore is ineffective compared to drugs, really has no importance in evaluating the need to reduce salt consumption for the “population.”

PREVENTIVE MEDICINE APPROACH

The preventive medicine, as well as the clinical approaches, assumes that hypertension is a unique disease. The population can be divided into hypertensives and nonhypertensives. The Fifth Joint National Committee Report (JNC V) has partially modified the traditional classification of hypertension. The preventive medicine approach assumes that a unique high risk subpopulation of hypertensives can be identified and this subgroup has unique genetic (host susceptibility), and/or environmental exposures including high salt intake, obesity, heavy alcohol consumption, etc. The goal therefore is to identify the at-risk hypertensives and prevent hypertension and its complications.

Specific interventions that are proposed include reduction of salt intake, which can be tailored to this high risk population. Several of the recent clinical trials in nonhypertensives, but high risk individuals, have focused as one of their goals the prevention of hypertension. In the recently completed phase two of the Trial of Hypertension Prevention (TOHP), is probably the best example of the prevention trials. The trial randomized 2,382 men and women aged 30 to 54 not taking antihypertensive medication. Diastolic blood pressures for entry to the study were between 83 to 89 mm Hg and systolic pressure < 140 mm Hg. The study compared weight loss, weight loss and sodium reduction, and sodium reduction alone, versus a control group. The goal was to reduce sodium to less than 80 mmol/day, around 5 g of salt. An initial observation in this study was the very high salt intake in the population based on 24 h urines of 188 mEq in the controls or about 11 g of salt in the diet.

The trial results are similar to those of TOHP in that it was possible to reduce salt consumption, especially in the short-term. Sodium was reduced 78 mEq in the urine at 6 months and 51 mEq at 36 months. The participants, even in the sodium reduction arm, were still consuming around 130 mEq of salt or close to 8 g of salt, approximately 2 g above the U.S. recommended levels of salt intake, even after the intervention at 6 months.

Change in blood pressure was very consistent with the effects of reduced salt intake. Compared with the usual care, there was a 2.9 mm decrease in systolic blood pressure at 6 months, 2 mm at 18 months, and 1.2 mm at 36 months. All were significant, P < .03 at 36 months. The study required fairly intensive nutritional and behavioral intervention to reach even these modest goals of sodium reduction. In TOHP, the decrease in blood pressure was directly related to the amount of reduced sodium in the urine. Similar analysis has not been completed for TOHP II.

In TOHP II the salt reduction and weight loss arm, as well as the combined sodium and weight loss, was associated with a substantial decrease in the incidence of hypertension. At 48 months, the incidence of hypertension was about 38% in the weight loss, sodium reduction and weight loss, and sodium group as compared to about 44% cumulative incidence in the usual care, P = .02 to .06. Similar results for the prevention of hypertension and reduced sodium intake were noted in the TOHP I study. The results are impressive and important by clearly documenting the effects that salt reduction does lower blood pressure in this high risk population. The decrease in blood pressure noted in these studies is fairly consistent with the estimated 7 mm decrease in systolic blood pressure for 100 mEq change in sodium, ie, about 3 to 3.5 mm for a 50 mEq decrease versus the 3 mm for a 50 mEq decrease in the TOHP II intervention compared to control groups at 6 months.

There are, however, three major problems associated with the preventive medicine approach. First, the size of the at-risk population is huge. By age 70, 40% of the U.S. population is expected to be hypertensive. Second, the intensity of the intervention required for any individual is obviously very extensive, and it is hard to believe that there is enough nutritional and behavioral intervention, personnel and resources available to generalize the individual or group approach for the entire population at risk of hypertension. Even with the high quality personnel such as in TOHP I and II and other intervention studies, the effectiveness of the intervention is modest because of the very high amount of salt in the diet, ie, 10 to 11 g at baseline, and the fact that the majority of salt is in processed food, 70% to 80%. Decreasing the amount of added salt in cooking or in table salt has only a modest effect on salt intake. The third problem is that long-term adherence to a low salt intake is difficult.
By 48 months, even with the continued intervention, it would appear that about one-quarter of the salt reduction may have been lost in TOHP II. In TOHP I the effect of salt reduction was pretty well maintained for 18 months, however, there is relatively little data about change in salt intake over several years, especially cessation of active intervention. The basic problem is not the effectiveness of the low salt diet in reducing blood pressure, but the efficacy of the application to the large population of individuals at risk.

Several related aspects of the prevention approach need to be considered. First is the concept that only a percentage of this high risk population is “salt sensitive” and needs to have a lower salt intake. Weinberger et al have described laboratory methods for the measurement of salt sensitivity. The approach is to see the effects on blood pressure, salt excretion and various biochemical, physiological parameters of a rapid increase in sodium followed by a rapid decrease the next day. A 10 mm decrease in blood pressure between the sodium loading and depletion was considered a positive response and 6 to 9 mm in determinant.

Several studies have suggested that older individuals, blacks, those who have low-renin hypertension, and high sympathetic activity have a greater frequency of salt-sensitive hypertension. In an extensive study of 309 whites and 81 blacks, Luft et al reported that 32% of blacks and 30% of whites who were normotensive were also salt sensitive, as compared with 73% of black and 55% of white hypertensives. Salt sensitivity in both groups were significantly related to age.

Sullivan et al used a different approach to measure salt sensitivity. They defined salt sensitivity as a 5% increase in blood pressure from a change in 10 to 200 mEq of sodium in the diet, holding potassium constant at 60 mEq. They determined that 29% of white and 50% of black borderline hypertensives were salt sensitive. The distribution of change in blood pressure was normally distributed. There was no evidence of bimodality or a unique salt sensitive population in their study. Similarly in the Luft and Weinberger studies, there is little evidence of unique salt sensitive individuals. The cutoff points for blood pressure change are arbitrary to define “salt sensitivity.” The reproducibility of these measures over time is also a major issue. An individual may be salt sensitive at one test, but not 6 months or 1 or 2 years later.

It is very likely that there are individuals more salt sensitive in terms of an increase in blood pressure than other individuals. It is likely that certain characteristics can define who will be more salt sensitive, including age, black race, low renin, high end tidal CO₂ and mild acidosis, psychosocial stresses, insulin resistance and higher sympathetic activity.

Presume that there really was a unique salt sensitive population. If 40% of the population is hypertensive and therefore at high risk, then there are probably 50 to 60 million at-risk individuals. If 30% were salt sensitive, there would be about 20 million salt sensitive individuals. There would therefore be two obvious problems. First the cost of finding all of these individuals, and second, the difficulties of developing a unique low salt dietary approach for approximately 20 million people. Clearly, neither approach is feasible. Salt sensitivity is furthermore not an all or nothing phenomenon. It is a continuous variable consistent with a variety of host-environmental interactions.

There are probably a few individuals who are extremely salt sensitive, and probably at the other extreme individuals who are completely not salt sensitive. This is characteristic of the interrelationship between many environmental exposures and the host susceptibility, ie, cholesterol levels, weight, etc. Organizing a high risk preventive approach for these 20 million salt sensitive individuals is just not feasible. Such an approach is similar to trying to identify the 10% of cigarette smokers likely to get lung cancer and presuming that the rest of the population could continue to smoke cigarettes.

The next high risk approach is to identify the specific genes that cause hypertension. Genotyping the population to identify the susceptible from non-susceptible so that the intervention can be limited to susceptible has great intuitive appeal and has generated a substantial amount of research dollars. Unfortunately, the approach is based on false premises and will fail. Hypertension is an arbitrarily defined disease. The distribution of blood pressure in the population is continuous. There are no genes for hypertension because there is no disease hypertension. The search for hypertensive genes is like searching for genes for the “soul.” There are many biochemical and physiological determinants of blood pressure levels. The mechanistic modelers of hypertension are determined to identify everyone of the pathophysiological determinants of blood pressure, and then working with geneticists, to identify the specific genes, ie, polymorphisms, that contribute to the variations in blood pressure level. It is very likely that the genes, especially combinations of genes, will provide a better understanding of the grade of susceptibility to environmental exposures, such as salt, obesity, alcohol intake, other nutrients, and blood pressure levels. Unique genes have been identified, which account for a relatively small percentage of elevated blood pressure in the population. The genetic disorders are important for the understanding of the pathophysiology of hypertension, but contribute little to the overall prevalence of hypertension in the population. Similarly, within pedigrees, it is probable that specific genetic polymorphisms, as well as environmental exposures,
account for the high familial aggregation of blood pressure levels. However, it is extremely unlikely that specific genes or several genes will be identified that will make it possible to identify individuals likely to develop elevated blood pressure, hypertension, from those that will not. It may be possible to identify high relative risk, but the attributable risk will be extremely small. The search for the genes for elevated blood pressure have been remarkably unrewarding to date. It is almost certain, however, that specific genetic polymorphisms will be identified that affect blood pressure levels and susceptibility to salt in the diet. However, it is also almost certain that the genetic polymorphisms will not separate the population into high and low risk, but rather a continuous distribution of risk of hypertension. The gene for eating salty pretzels is unlikely to be found.

PUBLIC HEALTH APPROACH
The final model is the public health approach to reducing salt in the diet. The public health model is based on the observation that salt intake in the population is a continuous distribution and that the majority of the population is consuming more than 4 to 6 g of salt per day in the United States. The sources of salt in the diet are from mainly processed foods, not just from table salt or salt added for cooking. The distribution of blood pressure levels are continuous in the population with some skewing to higher levels. The risk of CVD, especially stroke and CHD is probably linearly related to the levels of blood pressure, from relatively low diastolic and systolic blood pressure. For example, among the Multiple Risk Factor Intervention Trial (MRFIT) screenees the risk increases from a systolic blood pressure of around 120 mm Hg and a diastolic blood pressure < 80 mm Hg. Most of the population is at risk even those considered at higher risk than the lower levels of blood pressure, even those considered normotensive. The increased risks have been reported for different ethnic and racial groups and also in other studies for women.

FIGURE 2. Estimated number of coronary heart disease (CHD) events prevented per 100,000 with the given reductions in diastolic blood pressure (DBP) in a population previously untreated for hypertension.
The extrapolation of the risk of CHD and stroke from observational studies such as the MRFIT screeners have shown that an average 2 mm decrease in blood pressure, equivalent to perhaps a 30 to 40 mEq decrease in salt intake, would reduce CHD mortality by 4%, stroke mortality by 6%, and total mortality by 3%, that is, a reduction of possibly 12,000 deaths per year in the 45 to 64 year old age group.33

A further analysis of the potential reduction in risk was done by Cook et al., using data from the Framingham Study. They estimated that a 2 mm decrease in blood pressure over a 2 year period would decrease the number of CHD events per 100,000 population by 45.8 for those who had a blood pressure of 70 to 79 mm Hg, 67 for those with a blood pressure 80 to 89 mm Hg, and 33.3 for those with a blood pressure of 90 to 94 mm Hg, and 64.6 for those with a blood pressure = 95 mm Hg (Figure 2). A 2 mm decrease in blood pressure for those with diastolic pressure <= 95 mm Hg would decrease coronary events by 146/100,000, while treatment for blood pressure for those with a diastolic reading of 95 mm Hg would decrease the events by 214.5/100,000.

There is substantial tracking or correlation of blood pressure from childhood and young adult life into adult life.35 Thus, prevention of the increase in blood pressure over time would have major public health benefit. The public health approach therefore proposes a shift in the population distribution of blood pressure by preventing the rise in blood pressure with increasing age through a decrease in sodium in the diet. If 100 mEq decrease of sodium resulted in a 7 mm decrease in blood pressure, then reducing salt intake from 10 g, about 171 mEq to 6 g, about 100 mEq should reduce blood pressure by about 5 mm and possibly total mortality in the 45 to 64 age group of 28,000 per year or about 7% overall.

The success of the public health approach requires a decrease in the amount of salt that is added to processed food and a change in food selection by consum-
ers. The most important change, however, is in the amount of salt added to processed food so that the average consumption of salt in the diet would be reduced to about 6 g or 100 mEq. Further reductions over time would also be of substantial benefit.

The public health approach does not assume that every single individual’s blood pressure would decrease 2 mm Hg, or that the lower consumption of sodium greatly affects any individual hypertensive patient or for that matter any person. The public health approach also does not presume that reducing salt is the only change necessary to reduce the high prevalence of hypertension, and CVD in the population (Figure 3). Thus, the approach does not preclude increasing exercise, and weight loss, decreased alcohol intake, increased potassium or other nutrients that may be related to risk of hypertension and CVD.

The public health approach does, however, presume that salt is a necessary if not sufficient cause of hypertension and that the high prevalence of hypertension can not be substantially reduced by other preventive approaches without reducing salt intake. A vocal group who oppose the reduction of salt in the diet argue that changes in other risk factors such as moderation of obesity, or perhaps increasing other nutrients instead of a decrease in salt in the diet, can prevent hypertension and therefore reduction of salt consumption is not necessary. The ecological and animal experimental studies are not consistent with this premise. In the past we have hoped to develop a safe cigarette or presume that smokers who consume large amounts of vitamins such as beta carotene would avoid the risks of lung cancer. The approach has failed.

The public health approach does require a modification of food production in the United States. Such a model is not unique. We have recently added folic acid to bread in order to reduce a relatively small number of cases of spina bifida and perhaps, although unproven, coronary heart disease and stroke. Iodine has been added to salt. Fortification of other substances with multiple vitamins has been done, such as vitamin D in milk. Recently there has been a substantial effort to reduce the amount of fat and especially saturated fat and calories in food, by substitution of various nonfat and noncaloric substitutes. The reduction of the amount of salt added to processed foods would obviously have to be gradual in order to be acceptable to the consumer.

Given the continued high prevalence of elevated blood pressure and hypertension in the United States and the high risk and costs of CVD, a major effort must be made to prevent hypertension. There are a few alternatives to the reduction of salt in the diet. We could for example provide low dose diuretic therapy for most of the population so that they could continue to consume their high salt diet and excrete the salt load with the help of the diuretic. Such an approach seems less appealing than reduction of salt in the diet.

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