The Epidemiology of Diet and Blood Pressure
Francesco P. Cappuccio, MBBS, MD

Hence if too much salt is used in food, the pulse hardens..."—Huang Ti Nei Ching Su Wen (1000 BC), from the translation by Wang Ping (AD 762).

The relation between diet and blood pressure has been generally recognized since ancient times, but it was not until the 20th century that the first proposals were made of a possible relation between some dietary components and the pathogenesis of hypertension. In 1904, Ambard and Beaujard related sodium chloride ingestion to high blood pressure; in 1926, Donaldson reported an increase in blood pressure in college students after a high meat protein diet; in 1928, Addison suggested the possible hypotensive effect of potassium salts; and in 1930, Saile reported that among German monks, those who were lacto-ovo-vegetarian had lower blood pressure than those who were meat eaters. Ever since, possible relations between nutrients and blood pressure have received much attention in epidemiological and clinical research. In this context, the study by Ascherio and colleagues, published in the present issue of Circulation, is of great interest. They studied a large cohort (n=30,681) of predominantly white U.S. male health professionals aged 40–75 years without diagnosed hypertension. These men received a detailed postal questionnaire both in 1986 and in 1990. The authors found an inverse association between dietary fiber, potassium and magnesium intake (estimated by self-administered semiquantitative food frequency questionnaire in 1986), and both the 4-year incidence of hypertension and the self-reported blood pressure. These associations were independent of age, relative weight, alcohol consumption, central adiposity, physical activity, and smoking. The relative risks (RR) of hypertension in the bottom quintiles compared with the top quintiles of daily intakes (and 95% CI) were 1.49 (1.15–1.92) for magnesium, 1.54 (1.19–1.96) for potassium, and 1.57 (1.20–2.05) for fiber. When these associations were also adjusted for magnesium, potassium, and fiber, only the association with fiber maintained statistical significance (RR=1.46, 1.09–1.96). These results were confirmed in multiple linear regression (MLR) analysis using self-reported blood pressure as continuous variable. No significant predictive value was observed for sodium intake.

In different communities, there is a direct relation between the amount of salt consumed in the diet and the prevalence of hypertension. From cross-cultural comparisons, blood pressure levels tend to rise with age in societies where salt is added to food, whereas in populations that do not add salt to their food, blood pressure does not increase with age. Some pitfalls in the interpretations of ecological associations have been overcome by the INTERSALT study carried out in 10,079 men and women sampled from 52 centers around the world and studied with standardized methods. The cross-center analysis showed that the rise in both systolic and diastolic blood pressure with age was directly and significantly related to the average sodium excretion (reflecting sodium intake) after adjustment for confounders. If the relation were causal, it would imply that for 100 mmol sodium/day less intake, the increase in blood pressure from age 25 to age 55 years in a population would be less by 9.0 mm Hg systolic and 4.5 mm Hg diastolic. In view of the imprecision of measurements of the exposure factor (i.e., sodium intake) by a single 24-hour urinary sodium excretion, the association of blood pressure and the rise in blood pressure with age with sodium intake is substantially larger than has been generally appreciated, particularly when studied within a population where the variability in sodium intake and urinary sodium excretion within an individual is equal to or greater than that between individuals. A reduction in salt intake prevents the rise in blood pressure in newborn babies within the first 6 months of life, and a reduction of sodium intake reduces blood pressure in hypertensives and, to a lesser degree, in normotensives.

Why, then, did Ascherio and colleagues fail to detect this association and to estimate the relative contribution of salt intake as a predictor of hypertension? The estimate of sodium intake was obtained from the reported amount of salt added during cooking and from the number of shakes of salt added to food at the table. This only considers the discretionary salt that accounts for 20–40% of the total daily intake. About 30–70% of salt intake, at least in industrialized countries, comes from processed food, and a tiny amount naturally occurs in food. The lack of association, therefore, may just reflect the inaccuracy in measuring dietary salt intake. Ascherio and colleagues report, if anything, a negative association between their estimate of salt intake and blood pressure, and this in part supports their concern that some men may have reduced their discretionary

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From the Blood Pressure Unit, Department of Medicine, St. George's Hospital Medical School, London.
Address for correspondence: Francesco P. Cappuccio, MBBS, MD, Blood Pressure Unit, Department of Medicine, St. George's Hospital Medical School, Cranmer Terrace, London SW17 ORE, UK.
salt intake in response to the knowledge of their higher blood pressure values.

High potassium excretion (approximate index of intake) is inversely associated with blood pressure.7 Potassium supplements lower blood pressure in hypertensive patients and, to a lesser extent, in normotensive individuals.13 A moderate increase in potassium intake, as that obtained with potassium supplements, can be achieved by increasing the intake of potassium-rich foods (fruit, vegetables, legumes) with a significant reduction in the need for antihypertensive therapy in hypertensive patients.14 Ascherio and colleagues report an increased RR (1.54) in those in the bottom quintile of potassium intake (<2.40 g/day) compared with those in the top quintile (≥3.60 g/day), and this is in line with the available evidence.

The relation between dietary divergent cations such as calcium and magnesium and blood pressure has become of interest since the reports in the 1960s of an inverse association between drinking water hardness and cardiovascular mortality. Ascherio and colleagues found an inverse association between magnesium intake and incidence of hypertension, whereas no relation seemed to be found with calcium intake in the cohort as a whole. The epidemiological evidence of such associations is, however, inconsistent and controversial.15 Magnesium supplements, at least in the short term, do not lower blood pressure.16 Calcium supplements, both in the short and in the longer term (up to 6 months), do not lower blood pressure in hypertensive patients,15,17,18 and the predisposition of such patients to kidney stones19 offsets any real application of calcium supplementation in high-risk patients and may constitute a potential hazard in primary prevention.

The more interesting finding in the study by Ascherio et al is the independent inverse relation between dietary fiber from fruit and the incidence of hypertension. The possible causality is unclear and, so far, there are no obvious mechanisms by which dietary fiber might lower blood pressure.20 Siani and colleagues14 have recently reported that a diet enriched in potassium-rich foods (increasing potassium intake from 2.76 to 4.35 g/day) led to a 36% reduction in the use of drug therapy in hypertensive patients over 1 year. However, it is noteworthy that the same diet also increased fiber intake from 24 to 36 g/day. The differences in potassium and fiber were similar to the differences between bottom and top quintiles in the Ascherio U.S. cohort.

This clearly illustrates one of the pitfalls that may in some circumstances lead to erroneous conclusions being drawn from studies of relation between diet and blood pressure in populations. Many of these problems have been satisfactorily and commendably dealt with by Ascherio and colleagues. It is important, however, to cite some of the difficulties in carrying out such studies and in interpreting their results. People eat foods rather than individual nutrients. There is a high degree of association of nutrients in many types of foods, i.e., potassium, magnesium, and fiber in fruit and vegetables. It can therefore be very difficult to isolate effects of one food component from another and to attribute specificity to any one association. Assuming the association found were specific for any one nutrient, is it strong enough to be considered quantitatively important? Importance or significance can be statistical or biological. From the statistical viewpoint, probability values may lead us to consider some factor to be of great importance when it really is not. Its significance arises from either a large sample size or a small variability in the measurements or both21—but not necessarily from an important quantitative distinction. This can, in turn, produce distortions or deceptions in the mathematical inference (statistical process).

The results reported by Ascherio et al are undoubtedly of great interest. Nevertheless, many of the associations of nutrients are weak although statistically highly significant and nearly four times weaker than that of Quelet's index. Indeed, men eating <12 g/day of fiber had an RR of 1.46 of developing hypertension in the subsequent 4 years compared with those who ate ≥24 g. By contrast, the RR of men with a Quelet's index ≥32 kg/m² was 4.59 compared with those with an index <23. Moreover, from MLR analyses (Tables 3 and 4),4 it can be derived that a 12-g difference in fiber intake predicted 0.37 mm Hg difference in systolic and 0.13 mm Hg difference in diastolic blood pressure over 4 years, whereas for a 9-kg/m² difference in Quelet's index, there would be 2.63 mm Hg and 1.82 mm Hg difference in systolic and diastolic blood pressure, respectively, over the same 4-year period. Therefore, without questioning the validity of the findings, one should always interpret the associations between nutrients and blood pressure with caution and within a broader context of practical importance. In this respect, the article by Ascherio and colleagues is a fine example of balanced appraisal of nutritional epidemiological data. What, then, could an alternative approach to the study of the relation between diet and blood pressure be in an epidemiological context? The answer is far from being available, but one exploratory approach could be the use of principal component analysis to group together as factors those nutrients that covary and then to use the resultant factor scores as independent predictors of change in blood pressure.22

Summary

Epidemiological studies of diet and blood pressure support the concept that some dietary nutrients are strongly related to blood pressure and are amenable to modifications, with a likely impact on the incidence of hypertension and of related vascular events.13 For other potential nutrients, the evidence is more difficult to obtain. Further studies are required to establish 1) the practical value of assessment of individual nutrients versus dietary patterns in risk prediction, 2) the effects of changes of these individual nutrients versus dietary patterns on blood pressure, and 3) whether long-term changes in these individual nutrients or dietary patterns reduce the incidence of hypertension and can be implemented at a population level.

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F P Cappuccio

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