Sodium excess or potassium lack as a cause of hypertension: a discussion paper¹

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Studies on twins and investigations into the family history of patients with hypertension have conclusively shown that heredity is a determinant of blood pressure. However, the prevalence of hypertension varies within a given race according to certain, possibly environmental factors: geographical location within a country, for example in Japan (Takahashi *et al.* 1957), urban or rural location within the same geographic region, and the socioeconomic status of the patients (Hypertension Detection and Follow-up Program 1977). Variation in the prevalence of hypertension between countries also appears to be greater than would be expected on the grounds of genetic differences alone. Langford and colleagues (1979) have reviewed these findings and concluded that diet may explain these differences. The editor's summary of their review states: 'A very low sodium intake may prevent hypertension; a very high intake may directly cause hypertension'. This hypothesis is supported by many animal experiments, but in man there are other possibilities apart from diet, and these include environmental temperature, poisoning from metals such as lead and cadmium, alcohol consumption, mental 'stress' and lack of exercise. Moreover, the effect of diet may be mediated by a dietary constituent other than sodium, and this paper considers whether diet is important and whether an excess of sodium or a lack of potassium can be causally related to the development of hypertension.

Is diet the most likely environmental factor?

Blood pressure is associated strongly with obesity and the relationship is independent of age. This fact does not automatically incriminate diet as a cause of hypertension as obesity indicates only an excess of calorie intake over output over a period of time, and this excess is affected by exercise and metabolic rate. In addition, a subject with a genetic predisposition to obesity may also be prone to hypertension, leading to a non-causal relationship. However, it is tempting to conclude that the relationship between obesity and hypertension supports a role for diet in producing hypertension. In a recent review, total calories, sodium, potassium and fibre were considered as possible aetiological agents (Amery *et al.* 1980). The present paper considers only if sodium excess or potassium lack can explain geographic (between-population) differences in blood pressure; within-population differences; and experimental studies in animals and man. Finally, the mechanisms whereby these factors could influence blood pressure are briefly summarized.

Dietary factors producing between-population differences in blood pressure

Many dietary constituents are closely related to one another. For example, total calories, carbohydrate, fat, sodium and potassium consumption are all interrelated and the results of studies examining only one factor must be considered with caution.

Unacculturated (isolated) societies have been surveyed in many parts of the world, including representatives of several different races, and the results have been reviewed by Dahl

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(1977) and Gleibermann (1973). The study of these populations reveals not only a lack of obese subjects and hypertensive persons but also a lack of subjects over the age of 60 years. Sodium consumption is low in these isolated societies and blood pressure fails to rise with age. This may be due to the paucity of salt in the diet, and it has therefore been suggested that a low sodium intake will prevent the development of hypertension in industrialized societies. This may be true, but it must be admitted that the diet of these isolated societies does not lead to a prolongation of life in this situation. They appear to die from conditions unrelated to hypertension.

It must also be remembered that a low sodium intake is not only characteristic of these isolated societies. They may have a diet low in total calories, containing an excess of potassium and lacking poisons such as cadmium and lead. Moreover, the subjects may take more exercise or suffer from gastrointestinal and other infections. In addition, isolated societies are popularly supposed to avoid psychological 'stress'.

Figure 1 correlates the level of blood pressure with sodium and potassium excretion in two studies where methods were held constant and subjects of a similar age were studied. One study compared blood pressure and electrolyte excretion in Belgian subjects and in two areas of South Korea (Kesteloot *et al.* 1980). The other study compared blacks and whites in Evans County, Georgia, USA (Grim *et al.* 1980). The populations with the greatest intakes of sodium had the highest average blood pressures, but those with the greatest intakes of potassium had the lowest blood pressures. These studies do not distinguish between the relative importance of sodium excess or potassium lack, but the inverse relationship between blood pressure and potassium excretion is at least as good as any positive association between sodium and pressure. Comparisons between several populations generally support a role for sodium in raising blood pressure, but too few measurements of potassium intake have been made to allow any conclusion about whether this substance can lower pressure.

Dietary factors producing within-population differences in blood pressure

Current evidence suggests that patients with established hypertension take less salt than their normotensive counterparts (Miall 1959, Dawber *et al.* 1967, Berglund *et al.* 1976, Beevers *et al.* 1980, Fodor & Rusted 1980). This finding does not support the hypothesis that an excessive sodium intake produces hypertension. However, there are at least two reasons why

Figure 1. Relationship between blood pressure and urinary excretion of sodium and potassium in two studies (Kesteloot *et al.* 1980, Grim *et al.* 1980). × Men in Belgium and two areas of South Korea. ○ Women in Belgium and two areas of South Korea. △ White men in Evans County. ▲ Black men in Evans County. □ White women in Evans County. ■ Black women in Evans County

the hypothesis cannot be rejected. Hypertensive patients may reduce their intake of sodium after the development of hypertension and yet an excess of sodium in early life may have caused their hypertension. This could arise if patients with severe hypertension have a decreased appetite for salt, but the opposite may be true (Schechter *et al.* 1973). Also, such patients may have a deficient absorption of sodium from the gut. However, one study found an excessive sodium excretion in hypertensive patients (Doyle *et al.* 1976).

Three explanations suggest themselves for these conflicting results. The variability of measures of sodium excretion may mask a correlation between this estimate of sodium intake and blood pressure (Liu *et al.* 1979), but such a variability did not mask the negative (and one positive) associations reported above. Similarly, not all subjects are expected to be genetically sensitive to salt and their variability of response may mask an association. Also, within a population the range of sodium intake may not be large and it is possible that a very low excretion would be associated with lower blood pressures (Freis 1976). However, the range of sodium excretion is often considerable (Simpson 1979).

We may conclude that within-population studies neither support nor refute the salt hypothesis. However, two recent within-population studies failed to find a positive relationship between sodium excretion and blood pressure but did find a negative association between potassium excretion and pressure (Walker *et al.* 1979, Staessen *et al.* 1981). A further study found a negative association between plasma potassium and blood pressure that was marginally stronger than a positive association between plasma sodium and pressure (Bulpitt *et al.* 1981).

Experimental evidence in man and animals

In 1904 Ambard & Beaujard suggested that a reduction in salt intake would lower blood pressure. Kempner devised his strict rice diet in 1944 and this low salt diet lowered blood pressure even in patients with malignant hypertension. More recently, four controlled clinical trials have been reported in hypertensive patients showing, on average, a fall in systolic and diastolic blood pressure of about 10 mmHg for a reduction in sodium intake of 100 mmol a day (Amery *et al.* 1980).

The possibility that potassium intake may be negatively associated with blood pressure was suggested by Addison as long ago as 1928. He reported: 'One has forced on one the concept that the prevalence of arterial hypertension on this continent is in large part due to a potash poor diet and an excessive use of salt'. In recent studies Parfrey and his colleagues (1981*a,b*) have shown that an increased intake of potassium in hypertensive patients may be associated with a fall in blood pressure. However, the fall was very modest at 4 mmHg systolic and 2 mmHg diastolic and the effect of a high potassium diet was confounded by some reduction in sodium intake. In control subjects for the hypertensive patients and in medical students with no family history of hypertension, the high potassium diet was associated with small rises in blood pressure. When the medical students had a family history of hypertension small falls in pressure were observed. Priddle (1962) also considered that a high potassium diet lowers the blood pressure in hypertensive patients and the diet appears to increase sodium excretion in the short term (Brunner *et al.* 1970).

Experimental evidence thus suggests that a reduction in sodium intake or an increase in potassium can lower blood pressure in hypertensive patients. The body of evidence is stronger for the effect of lowering sodium intake, but less experiments have been performed using high potassium diets.

Hypertension can also be induced by salt in certain strains of rats. Dahl *et al.* (1962) selectively bred rats who were sensitive to salt and developed hypertension, and rats who were resistant and remained normotensive. These experiments showed the importance of both dietary and genetic factors in these animals, and it has been argued that the normotensive subject on a high salt diet is the human equivalent of the 'salt resistant' rat. Meneely & Ball (1958) also reported that a high potassium diet modified the increase in pressure in salt-sensitive rats.

Mechanisms whereby sodium excess or potassium lack can raise blood pressure

Mechanisms are known whereby sodium excess may increase blood pressure. These have been grouped into deficient renal sodium excretion, expansion of the extracellular fluid space, increase in sodium content of the vascular wall, increase in peripheral vascular resistance and hormonal changes (Amery *et al.* 1980). Suffice it to say that there are several plausible mechanisms whereby sodium can raise blood pressure, and recent work has suggested that hypertensive subjects have a renal abnormality and are unable to excrete sodium as effectively as normal subjects (Bianchi *et al.* 1974, Dahl *et al.* 1967, 1974). Hypertensive patients may show a generalized membrane depression of sodium pump activity (Garay & Meyer 1979, Edmondson *et al.* 1975) and have a compensatory circulating substance which promotes sodium excretion and which may cause their hypertension (Bianchi *et al.* 1975, Clarkson *et al.* 1979).

There are also mechanisms whereby potassium can influence blood pressure. A review by Tan & Mulrow (1977) emphasized the fact that the potassium ion can act as a vasodilator (Overbeck *et al.* 1974) and that potassium repletion can increase sodium diuresis and reduce plasma renin activity (Brunner *et al.* 1970).

Concluding remarks

Over the years the 'salt hypothesis' has become the 'salt-genetic' hypothesis, implying that in genetically salt-sensitive subjects the excess of sodium that is present in the diet of industrialized nations will lead to a rise in blood pressure with age. There is much evidence to support this view and many have argued in favour (Freis 1976, Morgan *et al.* 1979) and a few against (Simpson 1979). The purpose of the present paper is not to review all the evidence incriminating sodium but to examine whether potassium lack can be considered as an equal contender for an aetiological role, i.e. whether or not there is a case for a potassium-genetic hypothesis.

Some diets may be relatively low in potassium and evidence comes from studies in Glasgow (Beevers *et al.* 1980) and in Evans County (Grim *et al.* 1979) where potassium excretion is lower than in Belgium (Staessen *et al.* 1981). It is possible to raise the dietary consumption of potassium by an increased intake of vegetables, meat and fruit and this would be little affected by a reduction in bread consumption. However, the average diet of industrialized societies contains a ten-fold excess of sodium intake over physiological requirement and the evidence linking sodium with hypertension appears somewhat stronger than for potassium. It is possible that the effects of sodium excess and potassium lack are complementary and that the ratio of sodium intake to potassium intake is important.

At present it would appear reasonable to modify the dietary habits of hypertensive patients with a view to lowering their blood pressure. As reported above, reduction of sodium intake from 200 mmol to 100 mmol can be expected to lower systolic pressure by 11 mmHg and diastolic pressure by 10 mmHg (Amery *et al.* 1980). Similarly, it may be important to increase potassium intake, especially as hypokalaemia due to diuretics has been suggested as a cause of arrhythmias (Surawicz 1966).

Evidence is lacking that the general population would benefit from a decreased consumption of sodium or an increased dietary intake of potassium. Large intervention trials are required to provide solid scientific evidence for benefit from such changes and to refute the possibility of any adverse effect. We cannot decide whether, on a population basis, we should advise a reduction in sodium intake, an increase in potassium intake, or both.

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