The evidence that salt is an important aetiological agent, if not the cause, of hypertension

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Summary

1. Salt intake and the incidence of hypertension correlate between populations.
2. Salt intake within a population may correlate with the incidence of hypertension.
3. Disorders that lead to retention of salt cause hypertension.
4. Modest salt restriction reduces blood pressure in many patients.
5. Reducing salt balance and preventing the compensatory rise in angiotensin II controls blood pressure in most patients.
6. Salt is the probable cause of the epidemic of hypertension in the Western world; this could be prevented by salt restriction.

In this review I wish to discuss the evidence that salt causes hypertension, from three viewpoints: 1, epidemiological; 2, specific forms of hypertension; 3, essential hypertension—evidence from therapy.

The evidence from interpopulation studies that hypertension and salt intake are linked is impressive though capable of other interpretations. I wish to refer to four papers in this connection. First there is the study by Prior, Evans, Harvey, Davidson & Lindsey (1968) in Polynesian populations. These populations are genetically similar and as they move towards civilization the incidence of hypertension increases. This increase correlates with an increased intake of salt. However, many other factors also change and absolute conclusions cannot be drawn. A second study, by Lowenstein (1961) in South America, examined two populations. The degree of urbanization of one of these groups is greater than the other though still primitive, and this group has a higher blood pressure than the other group. An important change is that the group who are 'civilized' now use salt (sodium chloride) while the others use plant ashes (potassium chloride). Shaper (1972) in Africa and Maddocks (1967) in New Guinea have shown that as a population or a group of individuals change their dietary habits by ingesting salt, the blood pressure rises. This rise takes place progressively over 2-6 years. However, not only does salt intake increase, the weight also goes up, though various features make it more likely to be that salt increase is the cause of the rise in blood pressure. Many of these studies have inadequate data regarding level of salt intake and do not dissect out other influences. If we combine these and other reports (Sasaki, 1964) we obtain a close correlation. Most populations fit along this line but I am certain there can be exceptions.

In the groups that have been studied in primitive societies on a low salt-high potassium intake blood pressure does not rise with age. This is an aspect of considerable importance and I will return to it later.

Intra-population studies have supported this thesis. The paper by Dahl & Love (1957) showed that if the population were divided up on the basis of salt intake then the people with a greater salt intake had higher blood pressure. Miall (1959) in a Welsh community did not find this correlation. However, inside his own study he showed that dietary history did not correlate with sodium excretion whereas in Dahl's study it did, and thus it was invalid to draw conclusions regarding salt intake and blood pressure. He did divide a sub-group of postmenopausal women into hypertensive and normotensive, and showed no correlation with salt intake. Such a correlation is not required if the theory is that it is the salt balance of the body that is important.

However, Doyle, Chua & Duffy (1976) have shown that hypertensive patients have a higher salt intake than normotensive subjects in a study in Australia. Simpson, Nye, Bolli, Waal-Manning,
Goulding, Phelan, De Hamel, Stewart, Spears, Leek & Stewart (1978) failed to show such an effect in New Zealand. A difficulty, however, now is that many people have already been identified as being hypertensive and are excluded. Thus due to the excellent work of Smirk, Doyle and Simpson at Dunedin I suspect that all the people likely to have blood pressure elevation in Milton (Simpson et al., 1978) had already been identified and it is not surprising that no correlation was seen in the rest. In these various reports the correct way of analysing the results is to divide a population where nobody is on treatment for blood pressure into groups according to their salt intake and determine the incidence of hypertension in each salt intake group. Such a survey with good estimations of salt intake has not and probably cannot now be performed in the Western world.

The importance of salt intake (or better the body content of salt or control of salt balance) is shown in certain states. Thus patients with hyperaldosteronism have hypertension which is salt-dependent. The blood pressure can be controlled by altering salt balance. Experimentally Perera & Blood (1947) showed this by their finding that DOCA would not induce elevated blood pressure in people on a low salt diet. The blood pressure of people with renal impairment can similarly be controlled by altering salt intake. This is seen in people with moderate impairment of renal function and also in patients on dialysis.

However, these are unusual causes of hypertension. Does the same apply to people with essential hypertension? Severe essential hypertension has been successfully treated in the past by a very low salt diet with marked success. Perrera & Blood (1947) showed that this was a continuous variable and changing salt intake to three levels respectively of 10, 70 and 200 mmol/day caused the blood pressure to alter significantly. Parijs, Joossens, Van Der Linden, Verstreken & Amery (1973) and more recently Morgan, Gillies, Morgan, Adam, Wilson & Carney (1978) have shown that modest salt restriction does reduce blood pressure in people with mild hypertension. This fall in blood pressure may take a considerable time to be fully expressed. The question will be asked: ‘why does not everyone respond to a low salt diet?’ This is the same as a wish that stopping cigarette smoking may cure bronchitis. Other factors have come into play that prevent this response.

Recent work with the converting enzyme inhibitor captopril, however, has emphasized the importance of salt. Consider that there are two major arms controlling blood pressure, which ideally for good control would be of equal importance. In a primitive society salt intake is low and the salt force controlling blood pressure is small but the angiotensin ‘arm’ can compensate. In our Western society the salt intake is high, and in most of us the angiotensin ‘arm’ falls to low levels and hypertension does not develop. However, in some people this ‘arm’ cannot fall as much as is desired and thus hypertension results. If we reduced salt intake alone we should reduce blood pressure. However, the reduction in salt intake in some people stimulates an increase in angiotensin II and blood pressure is not controlled. Captopril alone will control blood pressure in such people where the angiotensin ‘arm’ predominates. The real importance is that the combination of sodium depletion with captopril does control blood pressure in most people. This is probably the first truly rational drug therapy for high blood pressure.

Many studies which claim that salt reduction is not effective have failed to ascertain whether their patients are compliant or have not continued therapy for a long enough period of time. In Western society and societies with a salt intake of 70 mmol/day or more, the blood pressure rises with age. Renal function deteriorates as a person ages. Young people with normal renal function can tolerate a high salt intake and not become hypertensive. As they age the normal mechanisms can no longer excrete their salt load and thus hypertension develops. It is not argued that salt causes all forms of hypertension, but it is believed that the body has a series of controls that allow it to excrete salt. If the capacity of these controls is exceeded by excess intake or if their performance is impaired (as in hyperaldosteronism and renal failure) then the patient develops hypertension to maintain the body’s salt content in the normal range. In our society the high salt intake together with the decrease in renal function with age causes an increased incidence of hypertension in the elderly. This is also accentuated by the secondary development of vascular disease.

Salt restriction is not advocated as the treatment for established hypertension though certain individuals respond dramatically to modest salt restriction. However, it is believed that reduction of salt intake to 70 mmol/day would halt the epidemic of hypertension that envelops the Western world and would be a more suitable solution than the alternative of treating 20% of our population with antihypertensive drugs.

I shall know if this talk has been successful if no
one uses the salt shaker at the dinners of this Society!

References


DISCUSSION

Robertson: Thank you very much, Dr Morgan. Dr Lever, would you like to comment on the relationship between total exchangeable sodium and angiotensin II in essential hypertension?

Lever: Dr Morgan, you suggested that angiotensin II might be high in relation to total exchangeable sodium in essential hypertension. We examined this some years ago. Plasma angiotensin II levels are distributed continuously, but more widely, in essential hypertension than in normal subjects (British Medical Journal, 1977, i, 415). Mean plasma angiotensin II is low in relation to exchangeable sodium in essential hypertension (Lancet, 1974, ii, 308); however, there is a significant correlation between arterial pressure and exchangeable sodium (Journal of Endocrinology, 1979, 81, 79p).

Morgan: This is what I would have predicted in essential hypertension. The normal mechanisms regulating sodium and angiotensin II have been disturbed and hypertension therefore results.

Skrabal: I don’t want to make the matter more complicated than it is already by bringing another organ into the game. However, the colon is the only structure equipped with mineralocorticoid receptors that is easily accessible in human subjects. As you see in Fig. 1, there is a good correlation between the prevailing plasma aldosterone concentration and the electrical asymmetry of the human colon measured in vivo (Lancet, 1978, i, 298). If you can accept this as a model which is comparable to the distal tubules of the kidney, I can show you (Fig. 2) the relationship in normal subjects between 24 h urinary sodium excretion, as a measure of sodium intake, and the electrical asymmetry of epithelia involved in external sodium homeostasis. As you can see in Fig. 2, at the usual levels of sodium intake of between 100 and 300 mmol/day, the electrical asymmetry is already

FIG. 1. Relation of plasma aldosterone to mineralocorticoid activity in vivo as measured by subtraction potential difference (Skrabal et al., 1978; Lancet, i, 298) in patients with essential hypertension and low (●), normal (○) and high (▲) plasma renin activity compared with patients with adrenocortical insufficiency (▼) and patients with primary (Δ) or secondary (◇) hyperaldosteronism (means ± SEM, numbers of observations in parentheses). Regression line and confidence limits are shown, from normal subjects in whom endogenous aldosterone was varied by different levels of sodium intake or tetracosactrin injection. Mean mineralocorticoid activity in vivo in patients with essential hypertension is comparable with that found in normotensive controls and appropriate for the prevailing plasma aldosterone concentration (from Skrabal, 1979, Journal of the Proceedings of the Royal Society of Medicine, 72, 252).
FIG. 2. Relation between 24 h urinary sodium excretion and mineralocorticoid activity in vivo as measured by subtraction potential difference in normal subjects on their usual sodium intake of between 6 and 18 g of salt/day (•) and after being equilibrated for 1 week on low (<4 g of salt/day, ▼) and high (>18 g of salt/day, □) salt intakes. Note that electrical asymmetry of epithelia involved in external sodium balance is already completely suppressed at the usual levels of sodium intake (from Skrabal, 1979, Journal of the Proceedings of the Royal Society of Medicine, 72, 252).

completely suppressed, with no further suppression at higher sodium intakes than 300 mmol/day. Only below a sodium intake of 50 mmol/day is electrical asymmetry stimulated. This means that sodium excretion in normal human subjects can only be regulated by the adrenal gland and trans-epithelial transport processes if sodium intake is lower than 50 mmol/day. These data suggest that the human race was originally designed for sodium intakes of below 50 mmol/day, corresponding to about 3 g of sodium chloride. Any excess of intake above that level apparently cannot be dealt with by trans-epithelial transport, and needs a rise of arterial pressure for elimination. A sodium intake of 50 mmol/day or less, therefore, should be recommended by the International Society of Hypertension for hypertensive patients and subjects who have a family history of hypertension.

Hornych: I am not completely convinced that it is valid to consider only angiotensin II and sodium balance as the dominant factors regulating blood pressure when salt intake is varied. Surely it is necessary to admit other factors, for example, prostaglandins?

Morgan: I agree that there are other factors. Nevertheless, I believe there are people who may not get a good hypotensive response to a reduced sodium intake because their plasma angiotensin II levels may rise. If one uses a converting enzyme inhibitor, such as captopril, to prevent this rise of angiotensin II, then 90–95% of hypertensive patients can be controlled with the combination of captopril and reduced sodium intake. Thus you do not have to postulate that there are other very important factors controlling the vascular response.

Robertson: Obviously there are many other points which we can take up later in the discussion. I think, however, that it is appropriate that Dr Simpson now gives his presentation.