SODIUM and chloride have an important role in regulating the volume of extracellular fluid. Herbivorous mammals living away from the sea may have difficulty in obtaining enough sodium and chloride and have developed a salt appetite and powerful mechanisms to conserve both sodium and chloride in urine and sweat.1 When humans found that salt had the almost magical property of preserving food, salt became of great economic, and in some cultures, religious importance. The ability to obtain salt cheaply from mines and the sea increased the consumption of sodium from 1 to 10 mmol during evolution to our present consumption, which in most communities varies between 100 and 400 mmol/day. Several lines of evidence suggest that this very high consumption of salt is an important predisposing factor to the development of essential hypertension.

Epidemiological Evidence

Sodium

Many studies have demonstrated that blood pressure rises with age in societies where salt is added to food. In populations that do not add salt to food, however, blood pressure does not rise with age (Figure 1).2,3 When dietary sodium intake has been assessed by either estimating intake or measuring 24-hour urinary sodium excretion, a significant relationship between both systolic and diastolic pressure and salt intake has been found (Figure 2).4-16 Simpson17 has recently confirmed and updated these findings in men and women. The slope of the regression line he found showed that an increase in sodium intake of 100 mmol caused an increase in systolic pressure of 12 mm Hg and diastolic pressure of 7 mm Hg. As Simpson and others have pointed out, the conclusions of some of these studies can be criticized; for instance, dietary recall and measurement of 24-hour urinary sodium excretion pose difficulties. Most studies have had inadequate controls, and protein, calcium, and saturated fat intake tend to increase as salt intake increases, whereas potassium and fiber intake tend to decrease.

Most within-population studies have found no relationship between a person's sodium intake or excretion and blood pressure.9,18-30 This finding is not unexpected since the range of intrapersonal salt intake in most Western countries is small (e.g., in the United States
approximately 100–200 mmol of sodium per day) and individual sodium intakes may vary to the same extent from day to day. The measurement of 24-hour urinary sodium excretion in a group will therefore reflect quite accurately the average intake for the population but will not characterize accurately individual salt intake. Furthermore, it will not relate to individual sodium intake over the last 20 to 50 years or during the first few years of life.

The tendency to develop essential hypertension appears to be inherited, therefore, a subgroup of the population may well be more susceptible to the effects of salt. The Framingham (MA) survey in the United States showed that when subjects were grouped according to sodium excretion, the prevalence of high blood pressure increased as sodium excretion increased, but no intraindividual relationship between blood pressures and sodium excretion was found. When communities have been studied in which there is a wider range of salt intake and each individual’s intake is more consistent (e.g., Korea, Japan, and Kashmir, India), direct relationships have been shown between 24-hour urinary sodium excretion and blood pressure. These findings demonstrate that sodium intake may play an important role in determining the difference in the prevalence of high blood pressure between different communities.

Calcium

In contrast to sodium, there is no published work on calcium intake and the prevalence of high blood pressure in unacculturated societies compared to Western communities. However, in the United States, McCarron et al. have claimed that hypertension may be related to a small reduction in calcium intake. Some unacculturated societies, however, are likely to have much lower calcium intakes (i.e., < 200 mg/day). Denton has suggested that one reason for the practice that some primitive tribes have of eating cremated ashes of their deceased relatives, and perhaps even cannibalism, is their need for minerals, particularly calcium. This situation contrasts to that in the West, where there is a much greater consumption of dairy products, with an average calcium intake between 600 to 1400 mg/day. Although more direct evidence is required, this circumstantial evidence suggests that there may be a positive relationship between calcium intake and blood pressure between different communities throughout the world.
McCarron et al. claim that there is an inverse relationship between calcium intake and hypertension is based on their analysis of the U.S. National Health and Nutrition Examination Survey, 1971–1973. Their deduction, that subjects with high blood pressure eat too little calcium, must be examined with caution. If it is true, it suggests that Americans with hypertension inherit an associated genetic distaste for calcium or milk products.

Many criticisms have been made of the analysis performed by McCarron and colleagues. 1) It excluded the majority of the hypertensive subjects from the data analyzed. 2) It used only systolic pressure to define high blood pressure and used variable cutoff points in parts of the paper for this definition (e.g., a group was defined as hypertensive with a systolic blood pressure of only 130 mm Hg, whereas another group was defined as hypertensive only if their systolic pressure exceeded 190 mm Hg). 3) It contains unstandardized differences between these so-called hypertensive and normotensive subjects. Using the unstandardized data, they found that the most important relationship to calcium intake (assessed by dietary recall only) was body mass index with a negative correlation of 0.588. This finding might indicate that overweight Americans consume less dairy products in an attempt to lose weight. If this assumption is correct, it would have a markedly confounding effect on any analysis of the relationship between calcium intake and blood pressure. 4) The National Health and Nutrition Education Survey was partly designed to study poverty in relation to diet in the United States and is therefore biased toward poorer families, a point not mentioned by McCarron et al.

The absolute standardized difference in calcium intake found by McCarron between the normotensive and hypertensive subjects was only 60 mg of calcium per day, which represents a difference of less than one quarter of a cup of milk. Feinleib et al. reanalyzed the same data using a more appropriate sample weighting adjustment, particularly for age, and failed to duplicate the findings of McCarron’s group. Harlan et al. using a smaller sample of the NHANES in which more detailed studies had been undertaken, found what they described as a “fragile” negative relationship between blood pressure and calcium intake but a “more robust and consistent” positive relationship between plasma calcium level and blood pressure.

At present it would be premature to ascribe any role to calcium intake in relation to blood pressure levels. More evidence is needed, particularly between different communities with different levels of calcium intake, and a more accurate method of assessing calcium intake other than dietary recall must be used in these studies.

**Intervention Studies in Humans**

**Sodium**

Several studies in which salt intake has been altered demonstrate that salt may play an important role in determining blood pressure levels within a community. For instance, when Samburu soldiers in Kenya were given a daily 16-g salt ration, blood pressure rose. An ongoing study of an African rural tribe reported that when tribe members migrate to cities, their urinary sodium excretion rises, their potassium excretion falls, and their blood pressure increases. Government campaigns in two countries have resulted in a reduction in salt consumption. In Japan, there was a fall in daily salt consumption from 14.5 to 12.5 g from 1971 to 1981. This reduction in salt intake was accompanied by a decreased prevalence of high blood pressure and a decrease in cerebrovascular mortality. Belgium also waged a successful campaign to lower salt intake, and salt consumption fell from 15 to 9 g per day from 1968 to 1981. During this time, stroke mortality also declined.

In Holland, Hofman et al. randomly allocated 476 newborn babies into two groups, one of which had a normal sodium intake and the other, a low sodium intake. The mothers were provided with all the nutrients and did not know in which group their child had been placed. The study demonstrated a progressively increasing difference in systolic blood pressure between the two groups so that at 6 months of age the babies on the normal sodium intake had a mean systolic pressure 2.1 mm Hg higher than those on the low sodium intake (p < 0.01). The study was discontinued when the infants were 6 months old. This carefully controlled study clearly demonstrates the important role of salt intake in determining blood pressure levels in early life in humans. This type of study should be extended, but there are obvious practical difficulties of maintaining differences in sodium intake for the 20 to 30 years that would be needed to prove beyond doubt that salt does cause or predispose to essential hypertension.

Lowering salt intake in a predominantly adult population may be much less effective than if it is started in the first few weeks of life. Careful observation of the communities in which intake of sodium is being reduced, for instance, Japan, Belgium, and more recently, the United States, may retrospectively provide the evidence to justify the reduction. Public health decisions in the past have often been based on circumstantial evidence (e.g., vaccination for smallpox and provision of clean water and drainage during the 19th century cholera and typhoid epidemics in Europe).

**Calcium**

There are no intervention studies with calcium comparable to those with sodium. Worldwide, however, Finland has one of the highest cardiovascular mortalities and one of the highest dairy product intakes, with an average calcium intake of approximately 1400 mg/day. Coincident with a government campaign to cut back on the consumption of fat, dairy products, and salt, cardiovascular mortality has decreased.

**Studies in Animals**

**Normal Animals**

In the 1950s, Ball and Meneely demonstrated that blood pressure in ordinary 9-month-old laboratory rats varied with the amount of salt in the diet (Figure 3).
Blood pressure in baboons and sheep also rises with an increase in salt intake. Grollman and Grollman demonstrated that an increase in salt intake in pregnant rats resulted in offspring with higher blood pressure than was found in offspring of pregnant rats that were given less sodium. No comparable work on the effects of altered calcium intake in normal animals has been done.

Inherited Hypertension in Rats

By selectively inbreeding rats for five to seven generations, Dahl's group produced strains that were either highly susceptible or resistant to the effect of salt. They found that the young salt-sensitive rats go through a phase in which they are more susceptible to the effects of salt. Furthermore, they showed that feeding salt-sensitive rats the then-available commercial baby food induced hypertension and increased the death rate. Parabiotic experiments between the two strains of rats demonstrated that the rise in blood pressure was due at least in part to a blood-borne factor. Kidney cross-transplantation between the two strains of rats before high blood pressure had developed clearly demonstrated that the kidney carried the underlying genetic message for the high blood pressure. Tobian et al. subsequently demonstrated in isolated kidneys of the normotensive salt-sensitive and salt-resistant rats that the salt-sensitive kidneys excreted less sodium than the salt-resistant kidneys.

Large increases in calcium intake in the spontaneously hypertensive rat have been reported to blunt the expected rise in blood pressure. Careful balance studies by Lau et al. have shown that such increases in calcium intake cause phosphate depletion and that blood pressure rose when intravenous phosphate was given. Such changes in calcium intake would correspond in humans to a change from around 500 mg to 15 g of calcium a day.

Experimental Hypertension

Increasing salt intake in all forms of experimental hypertension causes a rise in blood pressure. Large increases in calcium intake have been claimed to blunt the rise in blood pressure that occurs in the deoxycorticosterone-acetate-salt form of experimental hypertension. It is not known whether this effect is also due to phosphate depletion.

Abnormalities of Sodium Metabolism in Human Essential Hypertension

Several different abnormalities of sodium transport have now been described in the red blood cells of persons with essential hypertension. More consistent results have been obtained in studies of white blood cells, in which persons with hypertension have been shown to have an increase in white blood cell sodium concentration that is related to a reduction in the ouabain-sensitive component of the sodium pump. This latter finding is consistent with either an inborn abnormality of the cell membrane or an increase in the levels of a circulating inhibitor of the sodium pump. Several studies have now demonstrated a raised plasma level of an inhibitor of sodium transport in many persons with essential hypertension by incubating leukocytes from normotensive subjects in plasma from hypertensive subjects. When incubated in hypertensive subjects' plasma, the normotensive subjects' white blood cells experienced the same reduction in the ouabain-sensitive component of sodium transport as the hypertensive subjects' white blood cells. Furthermore, this reduction in white blood cell sodium efflux rate constant that occurs with incubation has been shown to be related to the blood pressure level of the subject from which the plasma was obtained. A reduction in the ouabain-sensitive white blood cell sodium efflux rate constant has also been found in normotensive relatives with a family history of high blood pressure. Treatment with diuretics causes a fall in blood pressure as well as an increase in the white cell efflux rate toward the normal range in both hypertensive subjects and those with a family history of high blood pressure, which suggests that alterations in sodium balance can affect the sodium efflux rate constant.

Cross-incubation studies of red blood cells from normotensive subjects in plasma from hypertensive subjects have not shown the same transference of abnormalities. This result may be due to the slower rate of sodium transport in red blood cells or to some other difference between the sodium transport characteristics of red and white blood cells. Based on the results of a cytochemical bioassay for the ability of plasma to inhibit guinea pig renal Na,K-ATPase, plasma taken from normotensive persons on a high salt diet had a greater ability to inhibit Na,K-ATPase in living cells than did plasma taken from the same normotensive subjects on a low sodium diet. Using a similar cytochemical bioassay but measuring...
the ability of plasma to stimulate guinea pig renal glucose-6-phosphate-dehydrogenase, which has been shown to relate inversely with the inhibition of renal guinea pig Na,K-ATPase, it was found that plasma from hypertensive subjects had increased ability to stimulate glucose-6-phosphate-dehydrogenase, which suggests an increased ability to inhibit Na,K-ATPase. Using an enzyme-coupled assay, Hamlyn et al. demonstrated that hypertensive subjects have a raised level of a purified preparation of Na,K-ATPase that was significantly correlated with the blood pressure level. Devynck et al. have also shown that plasma from hypertensive subjects contains a substance that displaces ouabain from red blood cells of normotensive subjects to a greater extent than occurs with plasma from normotensive subjects.

Whether the inhibitor of sodium transport found in persons with essential hypertension affects sodium transport in arteriolar smooth muscle is not known. Ouabain increases the reactivity of isolated arteries to agonists such as norepinephrine and oral digoxin for 4 days in normotensive subjects increased the blood pressure response to both infused norepinephrine and infused angiotensin II. Whether this is a direct effect on arteriolar smooth muscle cells or is mediated by the sympathetic nervous system is not known.

A Potential Mechanism

Kidney cross-transplantation experiments in inherit-ed hypertension in rats has clearly demonstrated that the kidney carries the message for the high blood pressure. The isolated kidney of the Dahl salt-sensitive, normotensive rat has a reduced ability to excrete sodium, which indicates that the inherited renal abnormality responsible for this rat model’s high blood pressure is likely to be a difficulty in excreting sodium.

Kidney transplantation in humans also suggests that the kidney is responsible for the rise in blood pressure in essential hypertension. Guidi et al. have shown that the donor’s family history of hypertension plays an important role in determining subsequent blood pressure in the renal transplant recipient. Curtis et al. reported that kidney transplantation eliminated high blood pressure in patients who experienced renal failure secondary to essential hypertension without malignant hypertension.

In 1969, Dahl’s group proposed that the rise in arterial pressure in salt-sensitive rats might be due to an increase in levels of a sodium-excreting hormone. Haddy and Overbeck and Blaustein subsequently applied this idea to volume expanded hypertension and humans with essential hypertension. Blaustein suggested a mechanism whereby a raised level of a sodium transport inhibitor could increase vascular reactivity by slowing down sodium-calcium exchange across arteriolar smooth muscle. Subsequently, de Wardener and MacGregor suggested that their finding of a raised level of the sodium transport inhibitor in patients with essential hypertension was secondary to an inherited difficulty in the kidney’s ability to excrete sodium. They suggested that the level of this inhibitor and, with time, the severity of the blood pressure would depend on salt intake and the extent of the defect in the kidney’s ability to excrete sodium. These suggestions provide a potential mechanism whereby a high salt intake coupled with an inherited abnormality in the kidney’s ability to excrete sodium could cause a rise in blood pressure. They could also account for many other related abnormalities that are known to occur in human essential hypertension.

Abnormalities of Calcium Metabolism

Persons with essential hypertension have an increase in urinary calcium excretion. Although this finding appears to be unrelated to sodium intake, it is known that alterations in sodium balance play an important role in determining urinary calcium excretion. A similar increase in calcium excretion has been shown in dogs when reabsorption of sodium in the distal tubule is enhanced by the administration of deoxycorticosterone acetate.

Total plasma calcium concentration is also increased in persons with essential hypertension. and one large study in Belgium showed a significant positive correlation with blood pressure levels. There are differing reports concerning ionized calcium levels. McCarron found that ionized calcium levels are reduced by approximately 0.1 mmol/L in most persons with essential hypertension. This finding of a low ionized calcium level is difficult to reconcile with a raised total plasma calcium concentration. Resnick et al. found that ionized calcium levels are only reduced in persons with low renin hypertension. Overall, they found no difference in calcium levels between hypertensive and normotensive subjects. Two other studies found no difference in ionized calcium levels between normotensive and hypertensive subjects. Apperently, none of these studies measured the serum pH when the ionized calcium was measured. Ionized calcium must be measured in conjunction with serum pH because overbreathing causes an alkalosis and could reduce ionized calcium levels. This omission may explain part of the discrepancies in the results to date. In addition, some hypertensive persons have a raised level of parathyroid hormone, the significance of which is not clear.

At present, therefore, the abnormalities of calcium metabolism in persons with essential hypertension form no coherent pattern. They provide no rational explanation for the claim by McCarron et al. that very small reductions in dietary calcium intake can cause high blood pressure in humans. It is difficult to see how a lower calcium intake could be associated with an increase in urinary calcium excretion and a raised total but lowered ionized level of calcium in the plasma. There would need to be a change in calcium absorption or an abnormality of vitamin D metabolism. In spite of the claims of McCarron et al. to the contrary, calcium balance studies comparing hypertensive subjects with normotensive subjects have not yet been performed.

The increase in vascular smooth muscle cell reactivity and contraction that eventually is responsible for the increase in peripheral resistance and therefore high
blood pressure is likely to be mediated through some calcium-dependent process of the smooth muscle cell. Blaustein has suggested that the rise in intracellular calcium is due to diminished sodium-calcium exchange secondary to a rise in intracellular sodium caused by the raised level of the circulating sodium transport inhibitor.

In the spontaneously hypertensive rat, ATPase-dependent calcium accumulation is reduced in cell membranes and microsomes of aortic and mesenteric smooth muscle cells. There is also some evidence to suggest that cell membrane binding to calcium is reduced in the spontaneously hypertensive rat and in humans with essential hypertension. Both of these abnormalities potentially could lead to an increased concentration of free calcium within the smooth muscle cell (for a review, see ref. 87a). External calcium concentration also may be important in smooth muscle cell reactivity. Overbeck has demonstrated in spontaneously hypertensive rats that small infusions of calcium cause vasodilatation. This finding, however, contrasts with his earlier work in which similar calcium infusions caused vasoconstriction in dogs and humans. Phillips and Robinson have shown that local infusion of calcium into the forearm, which causes a rise of approximately 0.5 mmol/L, leads to a significant reduction in the dilatory response of verapamil in normotensive subjects and a normalization of the previously abnormal response in subjects with high blood pressure.

**Does Reducing Sodium Intake Lower High Blood Pressure?**

Many early studies (1904–1950) clearly demonstrated that restriction of sodium intake to the same level as that eaten during evolution (i.e., around 10 mmol/day) caused a substantial fall in blood pressure in subjects with severe or malignant hypertension. This fall in blood pressure was accompanied by decreases in morbidity and mortality with no adverse effects except in subjects with preexisting severe renal failure. Unfortunately, such a diet was monotonous and some subjects found it difficult to adhere to the diet for long periods. Increasing sodium intake from 10 mmol/day to 25 to 35 mmol/day caused the blood pressure to return toward, but not reach, pretreatment levels. It was therefore assumed that less severe sodium restriction would not lower blood pressure. With the advent of the diuretics in the late 1950s, sodium restriction was abandoned by most physicians.

More recent evidence has shown that less severe restriction of sodium intake (i.e., to around 80 mmol/day) also causes a fall in blood pressure, even in persons with less severe essential hypertension, and that its effect is additive to that of blood pressure lowering drugs.

Of the 20 published studies I have been able to find in which pretreatment or control blood pressures and the fall in blood pressure with sodium restriction alone are given, it can be seen that the higher the blood pressure, the greater the effect of salt restriction irrespective of the degree of sodium restriction or the duration of sodium restriction (Figure 4). Several studies have suggested that the blood pressure fall with sodium restriction is mediated by a diminished renin response in the hypertensive subjects.

To examine this relationship further, we studied 103 subjects, including normotensive and hypertensive subjects who had not been treated for 2 months. They were studied 1) while receiving their normal sodium diet (approximately 150 mmol/day), 2) after 5 days of a high salt diet (approximately 350 mmol/day), and 3) after 5 days on a low sodium diet (10 mmol/day); no subject was admitted to hospital. The fall in blood pressure that occurred from the normal to the low sodium diet or from the high sodium to the low sodium diet was related to the pretreatment blood pressure (Figure 5). These individual results show a remarkably similar relationship to that found when the results of all the sodium restriction studies are plotted (see Figure 4).

These types of correlation may, under certain circumstances, be statistically invalid. However, when the log of the pretreatment systolic pressure was plotted against the log of the achieved blood pressure, the
FIGURE 5. Fall in supine systolic blood pressure on fifth day of a 10 mmol/day sodium diet plotted against systolic blood pressure on normal diet in 103 normotensive and hypertensive subjects. (Data from MacGregor et al.120)

slopes of the lines, 0.80 and 0.78, respectively, were significantly \( p < 0.001 \) less than the slope of the line of identity. This confirms that as blood pressure rises, the effectiveness of salt restriction increases.120 In a subgroup of 29 subjects, saralasin (a competitive inhibitor of angiotensin II) was infused on the fifth day of the low sodium diet. The fall in blood pressure that occurred with saralasin on the fifth day of the low sodium diet was inversely correlated with the fall in blood pressure that occurred with the sodium restriction \( r = -0.52; p < 0.005 \). These results demonstrate that the blood pressure fall that occurs with sodium restriction is, at least in part, directly related to the blunted response of the renin system as blood pressure rises.121 Unsurprisingly, therefore, persons with low renin hypertension have a greater fall in blood pressure with salt restriction. All of the blood pressure lowering drugs are additive to sodium restriction, particularly those drugs that inhibit the renin-angiotensin system (i.e., \( \beta \)-blockers and converting enzyme inhibitors). Persons receiving blood pressure lowering drugs should therefore be instructed on how to restrict their sodium intake, and those not receiving drug treatment should undergo a trial of moderate sodium restriction.

**Calcium**

A recent South American study showed that when large amounts of calcium (1000 mg/day), were given to normotensive subjects, there was a small but significant fall in diastolic pressure, which appeared to take many weeks to reach a maximum compared with that in a group given a placebo.122 The findings that the fall in diastolic pressure was greater in the lying and standing position than sitting and that falls in systolic pressure were not significant for men but were significant for women are also difficult to interpret. These findings contrast with that of McCarron and Morris (unpublished results, 1985), who studied normotensive subjects given 1000 mg of calcium in the form of calcium carbonate. In this double-blind study, no change in either supine or standing systolic or diastolic pressure was noted. In subjects with untreated essential hypertension, however, they did find a small but significant fall in blood pressure with calcium supplementation. The greatest change in blood pressure occurred in standing systolic blood pressure after 8 weeks of the treatment: systolic blood pressure increased in 16 subjects and decreased in 31. Changes in supine systolic blood pressure and diastolic blood pressure were smaller throughout the study and on the whole failed to reach statistical significance.

Another study found no overall fall in blood pressure with calcium supplementation in subjects with essential hypertension but reported a significant fall in those subjects with low plasma renin activity.123 These contradictory results in both normotensive and hypertensive subjects do not allow any conclusions to be drawn (Figure 6). Even if it were confirmed that an additional 1000 mg of elemental calcium does lower blood pressure in some persons with essential hypertension, it would be difficult to do this by dietary means without a large increase in dairy product consumption, for instance, approximately 2 pints of milk per day. This diet modification would entail a large increment in saturated fat, calorie, and salt intake and might paradoxically increase rather than decrease cardiovascular mortality.

**Figure 6** Standing systolic blood pressure of subjects receiving calcium supplementation plotted against standing systolic blood pressure of subjects on a normal diet. (Data obtained from Belizan et al.,122 McCarron DA, Morris GD, unpublished results, 1985.)
References


62. de Wardener HE, MacGregor GA. The relation to a circulating transporter (the 'natriuretic hormone') to hypertension. Medicine 1985:62:310–326
Discussion

Dr. Eduardo Slatopolsky (Washington University, Barnes Hospital, St. Louis, Missouri): Dr. McCarron, I entirely agree with your recommendation that we should ingest 1 to 1.2 g of calcium per day. As you realize, the differences in plasma ionized calcium and parathyroid hormone (PTH) concentrations you have shown in your studies are very small. Therefore, the methods are critical. What method did you use to assay PTH in the rat?

Dr. McCarron: We used two different assays from the Nichols Institute that were performed under research conditions. One was an N-terminal assay and one was a C-terminal assay. Regarding plasma ionized calcium concentration, we have employed a technique that corrects for pH and temperature. Using this method, we have found that the observations in the spontaneously hypertensive rats (SHR) are consistent. When the SHR are followed longitudinally, low values of extracellular fluid space in hypertensive subjects. J Clin Invest 1950;29:912–917


105 Miller JZ, Daugherty SA, Weinberger MH, Grim CE, Christian DEBATE DISCUSSION 637

107. Mark AL, Lawton WJ, Abboud FM, Fitz AE, Connor WE, Heis-

tad BD. Blood pressure response to dietary sodium restric-


treatment of hypertension in normotensive subjects and pa-


110. MacGregor GA, Markandu ND, Sagnella GA. Dietary sodium restriction for mild hypertension in general prac-

113. Fujita T, Henry WL, Barter SC, Lake CR, Delea CS. Factors influencing blood pressure in salt sensitive patients with hyperten-

114. Pavek K. Potassium supplements and hypertension. Lancet


Sodium is more important than calcium in essential hypertension.
G A MacGregor

Hypertension. 1985;7:628-640
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