SPECIAL ARTICLE

Salt, Volume and the Prevention of Hypertension

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SUMMARY **The evidence supporting the thesis that hypertension can be prevented by eliminating salt from the diet is based on four principal sources: (1) epidemiological studies in unacculturated peoples showing that the prevalence of hypertension is inversely correlated with the degree of salt intake; (2) hemodynamic studies suggesting that the development of chronic experimental hypertension is a homeostatic response to a maintained increase in extracellular fluid volume (ECF); (3) evidence that the ECF of "salt eaters" is expanded in comparison to that of "no-salt eaters"; and (4) investigations in hypertensive patients receiving either diets greatly restricted in salt or continuous diuretic therapy which correlate the fall in blood pressure with a reduction in ECF. Although this mechanism of essential hypertension is still obscure the evidence is very good if not conclusive that reduction of salt in the diet to below 2 g/day would result in the prevention of essential hypertension and its disappearance as a major public health problem.**

This special article is designed to correlate data obtained from various lines of investigation to support a concept bearing on the pathogenesis and prevention of essential hypertension. In essence, the concept indicates that essential hypertension is a disorder of acculturated peoples and is caused specifically by the acquired habit of eating salt. The supporting evidence will use data from three principle sources: 1) epidemiological studies in unacculturated peoples showing that the prevalence of hypertension is inversely correlated with the degree of salt intake; 2) hemodynamic studies suggesting that the development of chronic experimental hypertension is a homeostatic response to a maintained increase in extracellular fluid volume (ECF); and 3) investigations in hypertensive patients receiving either diets greatly restricted in salt or continuous diuretic therapy which correlate the fall in blood pressure with a reduction in ECF.

The importance of salt in the pathogenesis of hypertension was emphasized as early as 1904 by Ambard and Beaujard[1] and later by Allen,[2] Meneely[3] and Dahl.[4] The hemodynamic changes relating an increase in ECF as the initiating factor in a sequence of events leading to chronic hypertension were shown by Ledingham,[5] Borst,[6] Guyton[7] and Tobian.[8] Using a systems analysis approach, Guyton in particular provided a conceptual framework integrating the various mechanisms for controlling blood pressure and indicated the overriding importance of the relationship between arterial blood pressure and renal functional capacity to handle excess sodium in determining the presence or absence of hypertension. The crucial role of the ECF in the reduction of blood pressure with dietotherapy was emphasized by Murphy[9] and Watkin,[10] and with diuretics by Dustan[11] and Wilson and Freis.[12] It is not the purpose of this article to reemphasize such pioneering observations. Rather it is to combine these and other related studies in order to present a comprehensive picture of the role of salt in the pathogenesis of essential hypertension and to indicate how these observations point the way toward prevention.

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Salt and Hypertension in Unacculturated Peoples

It is a striking fact that hypertension is not found in unacculturated societies nor does the blood pressure rise with age as occurs in all "civilized" populations. Obviously, there must be some environmental factor which accounts for the difference. The hypotheses that have been advanced to explain the lack of hypertension in unacculturated peoples include 1) debility produced by parasitic or other diseases, 2) a simple, slow-paced and noncompetitive way of life, 3) lack of obesity and 4) a low intake of salt. The evidence suggests that it is the latter factor which accounts for the virtual absence of hypertension among primitive peoples.

An absence of hypertension and a failure of the blood pressure to rise with age has been observed in unacculturated populations from widely different parts of the world including New Guinea,[13] the highlands of Malaysia,[14] the Easter Islands,[15] the Amazon Basin,[16] the San Blas Islands of Panama,[17] rural Uganda,[18] and the Kalahari Desert of Africa.[19] Whereas malaria and other parasitic diseases are endemic in some of these areas,[14] this is not the case in all. The desert living Kalahari bushmen were free of these diseases and were in physically excellent condition, being able to run for long distances in pursuit of game.[19] Inhabitants of some of the more remote South Pacific islands such as Pukapuka in the Cook Islands[20] or the Easter Islands[15] also were in excellent health and had little or no hypertension. A recent survey of six Solomon Island societies indicated that the lower blood pressure among the less acculturated peoples could not be ascribed to disease or malnutrition.[21]

The second possibility, that the absence of hypertension in unacculturated peoples is due to lack of economic stress, racial or ethnic tensions, urban way of living, noise, and fast pace of life is more difficult to examine. However, the life of primitive man is not always idyllic or free from anxiety. On the other hand, among the native population of the Virgin Islands where racial tensions are low, the blacks are in the majority and the pace of life is relaxed, there is a very high prevalence of hypertension.[22] Nor does urban living seem to be an important factor since the prevalence of hypertension in the United States is considerably higher among rural

southern blacks than among blacks living in large cities.[23] Therefore, crowding, competition, noise and other forms of urban socioeconomic stress show no direct correlation with the presence of hypertension.

Although a relationship between body weight and hypertension is well established in this country[24] such a correlation does not seem to hold among less acculturated populations. Prior[20] compared the less acculturated Pukapukans who exhibit little hypertension with the more acculturated Raratongans in whom hypertension is common. He found that the difference in blood pressure between the two societies could not be attributed to differences in body weight. Similarly, Page[21] in his studies of six Solomon Island populations could find no correlation between body weight and systolic blood pressure. Page observed a rise of blood pressure with age in the relatively acculturated societies but not in the unacculturated peoples. However, the rise in the former groups could not be attributed to differences in body weight. The available evidence, therefore, does not support the concept that the lack of hypertension in unacculturated populations is due to their leaner bodily habitus as compared to acculturated peoples.

On the other hand, a number of studies suggest that it is the lack of salt in the diet which accounts for the virtual absence of hypertension in unacculturated peoples. Lowenstein surveyed two neighboring tribes living in the Amazon Basin, the Mundurucus and the Carajos.[16] The former had been converted to Christianity by missionaries who also introduced them to the use of table salt. Although still living under relatively primitive conditions, the members of this tribe showed a rise of blood pressure with age and some had hypertension. The Carajos, on the other hand, who spurned all contact with civilization including the use of table salt, exhibited no change in blood pressure with increasing age and hypertension was absent. In their investigation of six Solomon Island societies, Page and his associates[21] found a rise in blood pressure with age in the three most acculturated societies and no rise in the three most unassimilated peoples. The differences correlated best with the intake of salt, the ingestion of which was substantially greater in the more acculturated populations. In another part of the world, Shaper carried out investigations of the nomadic peoples of Uganda over a period of many years.[18] He consistently observed that the tribes without hypertension were those with a low salt intake. In tribes with hypertension, the salt intake had increased markedly.

Further evidence is provided by Prior and his associates[20] who measured blood pressure and estimated salt intake from both dietary samples and urine collections in two ethnically similar groups of Polynesians in the Cook Islands. There were no significant differences in height, weight or general health among the two populations. In the more acculturated Rarotongans, sodium intake averaged about 125 mEq per day and hypertension was common. Among the Pukapukans, however, sodium intake averaged 60 mEq per day and hypertension was rare. A blood pressure of 160/95 mm Hg or higher was observed in 28% of Rarotongan males and in only 3% of Pukapukan males. While the Pukapukans used no salt in cooking, they sometimes ate canned beef which may account for the occasional cases of hypertension observed among them.

Further evidence for a relationship between salt ingestion and the presence of hypertension is provided by two additional studies, one of the Yanomamo Indians of Brazil[25] and another of a native population in the highlands of New Guinea.[26] In the former, the urinary excretion of sodium was only 1.0 mEq per 24 hours while in the latter it was approximately 15 mEq. Hypertension was absent among the Yanamamo Indians and was present in only 3% of the New Guinea adult population. When it was found, the hypertension was practically limited to the 20 to 40 year age group in contrast to acculturated populations where the prevalence of hypertension increases with age.

When unacculturated peoples who are free of hypertension adapt modern ways of life, blood pressure rises and hypertension appears. At the same time, their salt intake increases dramatically. Maddox investigated five populations in New Guinea.[13] In the highland regions where salt or salty foods were not used, no hypertension was found and blood pressure did not rise with age. However, in a coastal fishing population, blood pressure rose with age and hypertension was present. The coastal peoples ate salted canned foods in contrast to the highlanders who did not, a fact confirmed by the finding of a considerably higher sodium-potassium ratio in the urine of the coastal population. The urban Zulu exhibits hypertension while the nonsalt eating rural Zulu does not.[27] Semiacculturated Cook Islanders have more hypertension than their more primitive neighbors.[20] In every epidemiological study of this type, when salt is not added to the diet hypertension is low or absent, and when salt is used the prevalence of hypertension is high. In almost every recent epidemiological survey of unacculturated peoples, the importance of salt has been emphasized as the leading possibility for determining the presence or absence of hypertension.[16, 20, 21, 25, 26]

The evidence for the role of salt in the development of hypertension is admittedly circumstantial. Obviously, many social, economic and dietary factors change with acculturation. Yet the evidence points away from other factors such as pace of life, crowding and improved general health as being important factors. The observation of Lowenstein of the two tribes in the Amazon basin indicates that urbanization is not the important factor since both groups lived in essentially the same environment except for their diet. The considerably higher prevalence of hypertension in rural southern blacks as compared to those who migrated to the large cities of the north indicates that urbanization, *per se*, is not an important influence. Of the various changes that are brought about with acculturation by far and away the most important seems to be an increase in the intake of dietary salt.

Role of the ECF in Blood Pressure Regulation

Salt ingested in the diet is distributed predominantly to the extracellular space. Excess amounts of salt or water are eliminated primarily through the kidneys. Over the past 20 years, there has been a growing realization of the importance of the relationship between extracellular fluid volume (ECF) and arterial blood pressure.[5-10] Ledingham in 1953 called attention to the fact that prior to the development of hypertension, the ECF increased in rats subjected to renal arterial constriction.[5] Floyer and Richardson concluded that the relationship between the blood volume and capacitance vessels was important in the blood pressure control of

parabiotic rats with experimental hypertension.[28] These observations caused Ledingham to investigate the cardiac output changes in rats during the development of experimental renovascular hypertension.[29] The rise in extracellular volume in the early period following renal arterial constriction was accompanied by an increase in cardiac output and a rise in blood pressure. The elevated extracellular volume then receded due to diuresis and cardiac output fell while total peripheral resistance increased to maintain the hypertension. Ledingham postulated that the increased cardiac output led to autoregulation of the resistance vessels so that the peripheral resistance increased. The resulting further rise in blood pressure increased left ventricular afterload and, thereby, returned cardiac output to normal. Thus, the chronic stage of the hypertension was represented by a normal cardiac output and an increased peripheral resistance.

The ability of the tissues to autoregulate blood flow by local changes in resistance is clearly demonstrated in patients with coarctation of the aorta.[30] Despite widely differing blood pressures above and below the coarctation, blood flows in the arm and leg are similar. This nice regulation of blood flow must be accomplished by appropriate and strictly local changes in peripheral vascular resistance.

Borst, in studies on licorice-induced hypertension in man, postulated that the elevated blood pressure results from circulatory adjustments that occur in response to an increase in extracellular volume.[6] He found that venous filling pressure rises and is followed by an increase in cardiac output and a rise of blood pressure. As a result of the increased blood pressure, the kidney is able to excrete the increased volume (see below). To explain the occurrence of hypertension in some individuals and not in others, Borst postulated an unknown renal defect requiring a higher than normal blood pressure to excrete the increased salt and water load, a remarkably prophetic insight in view of later developments.

A direct relationship between arterial blood pressure and urine volume was first clearly demonstrated by Selkurt[31] and has since been confirmed by many different investigators. The important relationship between ECF and arterial blood pressure has been elegantly presented by Guyton and his associates[7] and by Tobian.[8] Guyton produced a continued expansion of ECF by salt and water loading animals with reduced renal mass. He observed the same sequence of hemodynamic events leading to hypertension which included a temporary rise in cardiac output followed by an elevated total peripheral resistance. An increase in urinary output and reduction in ECF accompanied the rise in blood pressure. As a result of these and other experiments involving additional blood pressure control mechanisms, Guyton constructed systems-analysis type of flow diagrams to demonstrate the interrelationships of the various feedback loops involved in the regulation of blood pressure. He concluded that the common denominator in the development of any chronic elevation of blood pressure is the need for the kidney to increase urine volume and sodium excretion, that is, to prevent a chronically expanded ECF. The level of blood pressure required to produce the diuresis will depend upon the ability of a particular kidney to excrete an excess of sodium which varies from one individual to another. The gradient of the curve which relates urinary output to arterial blood pressure will depend on the intrinsic functional capacity of the kidney; the more impaired the function, the steeper the slope of the curve modified by other influences as described below including the renin-angiotensin-aldosterone mechanism, the sympathetic nervous system, ADH secretion and probably other factors.

It is frequently noted in hypertensive patients that continuous reduction of blood pressure with antihypertensive agents other than diuretics will result in an accumulation of extracellular fluid.[32, 33] In this case, the arterial blood pressure apparently has been forced below a level at which the hypertensive kidney can maintain homeostasis of the ECF.

Of great interest has been the demonstration in rats that the predisposition to hypertension is inherited and at least in some strains, seems to reside in the kidneys. Dahl selectively inbred hypertension-prone strains and hypertension-resistant strains of rats.[4] The hypertension-prone strain regularly developed hypertension with any of the usual experimental maneuvers including renal arterial constriction and high salt feeding, while the hypertension-resistant strain seldom exhibited hypertension following these maneuvers. Bianchi also produced a hypertensive strain of rats by selective inbreeding.[34] In a brilliant surgical *tour-de-force* he succeeded in transplanting the kidneys of the hypertensive rats into normotensive rats. The normotensive rat with hypertensive kidneys then became hypertensive. Transplantation of the kidneys of normotensive rats into hypertensive rats led to a reduction of blood pressure in the latter. Similar observations have been made by Dahl.[35]

In the light of the various experimental and clinical observations cited above, it is possible to reemphasize the following hypothesis of the pathogenesis of hypertension.[5-8] Homeostasis of the ECF is maintained by a balance between salt and water intake and urinary output. The latter depends in part on the level of arterial blood pressure and this relation will differ from individual to individual depending on the intrinsic renal functional capacity to handle salt and water loads. If the ECF expands as in primary aldosteronism or excessive licorice ingestion, venous filling pressure will increase and a series of hemodynamic events will occur resulting in a rise of blood pressure sufficient to increase urine volume and sodium excretion by the amount necessary to prevent edema. In experimental renovascular hypertension, a similar sequence of events has been shown to occur possibly through activation of the renin-angiotensin-aldosterone system. In essential hypertension, it is suggested that there is an inherited defect in the handling of sodium such that the kidney requires a higher than normal perfusion pressure to maintain ECF homeostasis in the presence of a high sodium intake.[7]

While the renal functional ability to handle an increased ECF load appears by this theory to be the crucial pathogenetic determinant of hypertension, it is also probable that the expanded ECF of acculturated peoples increases the pressor responses to other, more short-term pressor stimuli. For example, the pressor response to infusion of norepinephrine in man is greater when the ECF is "normal" than when it is reduced by the administration of a diuretic.[36] Also, salt loaded rats exhibit an enhanced pressor response to angiotensin whereas ECF depletion has the opposite effect.[37]

There also is evidence that frequently repeated elevations of blood pressure will eventually lead to structural changes in the resistance vessels so that the wall is thickened and the

lumen is correspondingly narrowed. Folkow demonstrated structural changes in the resistance vessels of spontaneously hypertensive rats during the period in which they developed hypertension.[38] He postulated that the hypertension seen in these rats is the result of a vicious circle in which frequent, probably neurogenically mediated, pressor reactions lead to structural alterations of the resistance vessels and a rise in basal blood pressure. Further pressor stimuli will then result in even higher blood pressures and greater thickening of the arterial walls, a vicious circle resulting in progressive structural changes and elevations of blood pressure. If essential hypertension is of similar origin, it would follow that the pressor influences, neurogenic or otherwise, would be amplified in the presence of an expanded ECF such as is present in acculturated peoples but not in unacculturated populations.

The ECF is "normal" in patients with essential hypertension.[39, 40] This finding, however, is not inconsistent with the volume-load hypothesis because the kidney maintains ECF homeostasis by reason of the fact that the blood pressure is elevated. Nevertheless, the ECF probably is expanded by the standards of unacculturated peoples and also by that of our primitive forebears. The evidence for this statement, which is presented more fully below, includes the following: 1) nonedematous hypertensive patients consuming diets containing less than 10 mEq sodium per day maintain a reduction of approximately 15% of their ECF. While ECF has not been measured directly in unacculturated peoples, there is no reason to believe they would behave any differently from hypertensive patients. 2) Unacculturated peoples exhibit characteristics usually associated with ECF "depletion" including elevated plasma renin activity and urinary aldosterone excretion despite low normal levels of blood pressure. Therefore, in addition to the constant stress placed on the sodium excretory mechanisms, the relatively expanded ECF would also enhance the effects of all pressor stimuli as compared to primitive man.

Relationships Between Dietary Sodium, ECF and Blood Pressure

The importance of dietary sodium in the maintenance of the ECF has been known for many years.[41] Murphy in 1950 measured the changes in plasma volume and ECF in hypertensive patients treated with the Kempner rice diet.[9] This diet is very low in sodium containing less than 8 mEq per day. While there was no change in serum sodium concentration, plasma volume decreased 10% and ECF fell 12% over a three-week period. This was accompanied by a reduction in arterial blood pressure. Watkin and his associates found similar changes in patients treated with the rice diet.[10] Plasma volume was reduced 9% and ECF 15%. A fall in blood pressure accompanied the reductions in volume. The volume changes correlated significantly with changes in body weight suggesting that the weight loss was due primarily to the reduction in ECF. The addition of 3.0 gm of salt daily restored the plasma volume and this was accompanied by a partial rise of the blood pressure toward control levels. Addition of 1.0 g of salt only slightly raised plasma volume and did not increase blood pressure. Thus, the critical level of salt ingestion for re-expansion of the ECF was between 1 and 3 g per day. In discussing the degree of sodium restriction required for effective treatment, Watkin commented, "The critical level of sodium intake with respect to hypertension appears to be extremely low; at least in many patients with advanced stages of hypertension a sodium intake above the critical level causes a more or less prompt return of hypertensive manifestations."

Similar changes have been observed following the continuous administration of thiazide diuretics. Plasma volume and ECF fall by nearly identical percentages as with the rice diet.[11, 12] Right heart filling pressures and cardiac output decrease.[11, 42] Responses to depressor agents such as adrenergic blocking drugs or vasodilator agents are enhanced while the effects of pressor stimuli are depressed.[36] Although it is generally taught that ECF returns to normal after several weeks of diuretic treatment, the burden of evidence strongly indicates the contrary. All studies except one[43] indicate that plasma volume and ECF remain reduced after long periods of treatment.[12, 44, 45] Furthermore, discontinuation of the diuretic after prolonged treatment results in a prompt rebound of these volumes indicating that they had remained depressed during the treatment period.[12, 45] These observations are important because they indicate that a continued reduction in volume is required to maintain the antihypertensive effect of the diuretic agents. Further evidence against a vasodilator action of the thiazides is indicated by the fact that the drug exerts no antihypertensive effect in nephrectomized animals.[46]

Only one well controlled trial has claimed an antihypertensive effect from moderate as opposed to severe sodium restriction.[47] In this trial in patients with mild hypertension, a degree of sodium restriction was imposed sufficient to decrease the 24 hour excretion of sodium from 191 to 93 mEq per day. The blood pressure fell minimally, the reduction being only 7.7/4.4 mm Hg as compared to a fall of 16.1/8.1 mm Hg in the same patients given thiazide diuretics. Plasma or ECF volumes were not measured.

It is suggested on the basis of the various lines of evidence presented that the antihypertensive effect of either sodium restriction or diuretic therapy depends upon the maintenance of a reduced ECF. The decreased volume load permits the hypertensive kidney to operate at a lower level of arterial blood pressure and still maintain homeostasis of the ECF. The studies that have been done indicate that a reduction of salt intake to about 1 gm or 17 mEq per day is required to produce more than a minimal reduction of blood pressure.[10, 47]

The above considerations explain much of the discrepancy that exists in the literature concerning the relationship between dietary sodium and hypertension. The evidence from unacculturated peoples which was reviewed above indicated an absence of hypertension when no salt was added to the diet. The level of dietary intake of sodium was such that a contraction of the ECF would be expected as compared to salt eating populations. On the other hand, significant differences in ECF in peoples who ingest canned goods and other salted foods would not be expected regardless of different degrees of additional salting of food. Salt is added to almost all processed foods, even to bread, so that ECF is expanded in all "civilized" peoples compared to man living under primitive conditions. Therefore, the hypertensive stimulus of a relatively expanded ECF will be present regardless of use of a salt shaker. It is not surprising, therefore,

that neither Dawber and associates[48] nor Miall[49] found any correlation between sodium intake and blood pressure in acculturated Western populations. They evaluated salt intake primarily on the basis of whether a salt shaker was used in cooking and/or at the table. Even their low-salt group, however, must have been ingesting enough salt to expand the ECF. On the other hand, severe salt restriction results in a significant fall in blood pressure.[9, 10, 50, 51]

The surveys of Dawber and Miall indicate that within the range of intake encompassed by the ordinary Western diet which is about 5 to 15 grams of salt per day there is little influence on blood pressure. Beyond this range of salt intake, however, there is some evidence to suggest that an excess of hypertension may appear. For example, in the northeastern district of Japan, the daily intake of salt averages about 25 grams per day.[52] The prevalence of hypertension in the fifth decade was found to be 30 to 40%, significantly higher than in most parts of the world. Such high levels of sodium ingestion must greatly stress the homeostatic control mechanisms and a high level of arterial blood pressure could well be required by the kidney to handle the ECF load. Possibly, there are critical levels of sodium ingestion which cause the blood pressure to rise with age and for some to develop hypertension. With sodium intakes below 10 mEq per day, ECF is contracted (by our standards) and hypertension is absent. In the range of 10 to 70 mEq per day, a few cases of hypertension will appear as in the Pukapukans,[20] while in the range of 70 to 350 mEq per day, about 15% of adults will exhibit hypertension, the percentage rising with age. When salt intake rises above 350 mEq per day, hypertension may be found in about 30% of the population.[52]

The inference from these considerations with respect to the prevention of hypertension would now be fairly obvious. The level of ECF which we call normal probably is an expanded one compared to our primitive forebears. This condition has arisen because acculturated man has developed a taste for salt. Its elimination from the diet and a return to natural, unsalted foods will, by contracting ECF, reduce the stimulus to develop hypertension that presently exists in our society.

Other ECF Control Mechanisms

This discussion would not be complete without considering the role of the renin-angiotensin-aldosterone system in the pathogenesis of hypertension. Certainly, it is a subject of great current interest.[53] However, with respect to the present discussion, the role of this system seems to be of secondary importance. While the renin-angiotensin-aldosterone system is involved in the homeostatic control of the ECF, the ability of this mechanism to cope with a continued increase in ECF appears to be rather limited.[7] As Guyton has pointed out, the renin feedback loop does not have the infinite gain provided by the arterial blood pressure-urine volume relationship. Although it aids and abets the kidney in control of volume, the renin-angiotensin-aldosterone system is incapable of maintaining *for long periods* homeostasis of the ECF in the presence of a high salt intake and a reduced intrinsic functional capacity of the kidney to excrete salt and water loads at normal levels of blood pressure.

There is no increase in renin, angiotensin nor aldosterone levels in mild or moderate essential hypertension.[52] In fact, many hypertensive patients exhibit reduced plasma renin activity (PRA).[54] While this observation appears at first glance to be paradoxical, it is, in fact, consistent with the renal-body fluid pressure control theory of hypertension. A reduction in the activity of renin feedback system would be expected as an additional compensatory reaction in individuals who have a reduced renal functional capacity for handling excess salt and water loads.

There are also other inconsistencies in relating the renin-angiotensin-aldosterone system to the pathogenesis of essential hypertension. Normalization of blood pressure with certain antihypertensive agents such as diuretics[55] or vasodilator drugs[56] leads to a rise in PRA, that is, blood pressure falls despite an increase in PRA. Furthermore, in no-salt cultures, a chronic elevation of PRA is associated with an absence of hypertension. In Oliver's studies[25] on the blood pressure, sodium excretion, PRA and urinary aldosterone excretion of the unacculturated Yanomamo Indians of Brazil, the urinary excretion of sodium was extraordinarily low averaging 1 ± 1.5 mEq per 24 hours. Blood pressure, which averaged below 110/70 mm Hg, did not rise with age and hypertension was completely absent. On the other hand, PRA and urinary aldosterone excretion were abnormally elevated according to our standards of normalcy. Although ECF was not measured, it undoubtedly was reduced because of the extremely low intake of salt in the diet.[9, 10] Needless to say, such findings are hardly consistent with the hypothesis that elevated renin or aldosterone secretion rates are important factors in the pathogenesis of hypertension.

Unlike no-salt cultures, the blood pressures of all populations which use salt as a condiment rise with age. Perhaps the ability of the human organism to handle a chronically increased ECF load diminishes with age and a rise of blood pressure occurs as a compensatory reaction for maintaining homeostasis of the ECF. A decreased ability to maintain ECF homeostasis in the face of a high salt intake could occur via several mechanisms. First, the intrinsic functional capacity of the kidney to handle excess salt and water may deteriorate gradually with age. Second, the various other supportive processes could begin to fail. An increased salt intake leads to inhibition of renal sympathetic nerve stimulation, ADH secretion, and the renin-angiotensin-aldosterone activity.[7] These homeostatic mechanisms for the control of the ECF support the renal-body fluid system in the control of the ECF and ultimately in the control of the blood pressure. However, if they should fail, the kidney must rely more on the blood pressure-urine volume relationship and hypertension could result. The curve relating renal arterial perfusion pressure and urine volume is much steeper in the isolated kidney than in the intact organism where all of the other homeostatic mechanisms can exert their effects.[7]

Role of Inheritance

That there may be inherited differences in the intrinsic renal functional capability for handling a salt load is suggested by the already alluded to transplantation experiments of Bianchi[34] and Dahl.[35] At least in the rat a higher blood pressure seems to be required by some kidneys than by others and this function is inherited. This hypothesis would explain the mechanism for the inherited tendency toward es-

sential hypertension in man. Also, an inherited defect in one or more of the ancillary feedback mechanisms for maintaining homeostasis of the ECF would equally explain the familial trend in essential hypertension. However, there is as yet little more than suggestive evidence to support any of these hypotheses.

Whether due entirely to an inherited renal functional deficiency in handling an excessive ECF load or to a volume-induced increased responsiveness to other pressor influences, the difference in the prevalence of essential hypertension between acculturated and unacculturated societies appears to be due to the amount of dietary salt. Nature did not intend for us to handle a chronically expanded ECF. In congenitally predisposed individuals, the mechanisms for handling the increased load may deteriorate with aging so that a higher than normal blood pressure is required to maintain homeostasis of the ECF. If so, essential hypertension is a comparatively new disease in the history of man.

Unacculturated peoples have demonstrated that even with severe physical exertion in tropical climates, the addition of salt to our food is not essential for good health and physical performance. Salt is an acquired taste inculcated at a very early age by flavoring infant foods. The infant who is not exposed will not develop this habit. On the basis of present knowledge, it would seem wise for individuals with a family history of essential hypertension to accustom themselves to a truly salt free diet (less than 1 gm of salt or 15 mEq of sodium per day) and to prevent their children from acquiring the habit of eating salted foods. While this is difficult at present, an increased variety of unsalted foods would be made available if there were sufficient public demand. It is quite possible, if not probable, that we already have the knowledge to prevent essential hypertension and its various complications.

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