

Review

Relationship and Interaction between Sodium and Potassium

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Compared with the Stone Age diet, the modern human diet is both excessive in NaCl and deficient in fruits and vegetables which are rich in K^+ and HCO_3^- -yielding organates like citrate. With the modern diet, the K^+/Na^+ ratio and the HCO_3^-/Cl^- ratio have both become reversed. Yet, the biologic machinery that evolved to process these dietary electrolytes remains largely unchanged, genetically fixed in Paleolithic time. Thus, the electrolytic mix of the modern diet is profoundly mismatched to its processing machinery. Dietary potassium modulates both the pressor and hypercalciuric effects of the modern dietary excess of NaCl. A marginally deficient dietary intake of potassium amplifies both of these effects, and both effects are dose-dependently attenuated and may be abolished either with dietary potassium or supplemental $KHCO_3$. The pathogenic effects of a dietary deficiency of potassium amplify, and are amplified by, those of a dietary excess of NaCl and in some instances a dietary deficiency of bicarbonate precursors. Thus, in those ingesting the modern diet, it may not be possible to discern which of these dietary electrolytic dislocations is most determining of salt-sensitive blood pressure and hypercalciuria, and the hypertension, kidney stones, and osteoporosis they may engender. Obviously abnormal plasma electrolyte concentrations rarely characterize these dietary electrolytic dislocations, and when either dietary potassium or supplemental $KHCO_3$ corrects the pressor and hypercalciuric effects of these dislocations, the plasma concentrations of sodium, potassium, bicarbonate and chloride change little and remain well within the normal range.

The Issue of Ionic Dominance in Electrolytic Determinacy

Given the sodium-dominated context in which it appears, the assigned title "Relationship and Interaction Between Sodium and Potassium" might suggest that dietary "potassium" only modulates an always dominant dietary "sodium" in these ions' joint determinacy of blood pressure, including that in the hypertensive range, calcium-containing kidney stones and osteoporosis. The title might further suggest that only the cationic components of the dietary salts of sodium and potassium contribute importantly to that determinacy. Indeed, the determinacy is traditionally represented as the dietary (and urinary) Na^+/K^+ ratio. In fact, that ratio associates positively and predictively with blood pressure, including that in the hypertensive range [1] and the frequency of kidney stones [2].

However, recent reports indicate that dietary potassium not only dose-dependently counters, but in some instances also abolishes potentially pathophysiological effects of the modern dietary excess of NaCl, e.g. hypercalciuria and normotensive salt-sensitivity, a likely precursor of hypertension [3]. In the case of hypercalciuria, such a dose-dependent sodium-countering effect of dietary potassium depends on its major conjugate anion, bicarbonate (as a dietary precursor like citrate) [4].

The Electrolytic Mismatch Between the Modern Diet and the Ancient Kidney

That the determinacy of dietary potassium can be so dominant, vis a vis dietary NaCl, accords with the fact that human biological machinery evolved to process dietary potassium in amounts many times those of sodium, and several times those present in the

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modern diet. The ancient human diet contained little of the then scarce Na^+ (2–3 mmol/day) but relatively large amounts of K^+ (>200 mmol/day) [5]. Foods rich in K^+ , like fruits and vegetables, are usually rich in HCO_3^- -yielding precursors like citrate, but contain little Cl^- and virtually no Na^+ , virtually all Cl^- like Na^+ , being ingested as NaCl . Accordingly, in the modern diet, which dates from the Industrial Revolution some 200 years ago, not only is the content of Na^+ and Cl^- much higher, but that of K^+ and HCO_3^- -yielding substances much lower. Indeed, with the advent of the modern diet both the K^+/Na^+ and $\text{HCO}_3^-/\text{Cl}^-$ ratio have become reversed. Yet, the renal machinery that evolved to process the ancient diet remains largely unchanged, genetically fixed in Paleolithic time. Thus, the electrolytic mix of the modern diet is profoundly mismatched to its genetically determined processing machinery, and the extent of this diet-kidney mismatch increases with age, largely because the contemporary dietary intake of potassium decreases with age, at least as recently measured in Caucasian-Americans and African-Americans [6]. Because of the mismatch, those eating the modern diet are not only overloaded with Na^+ and Cl^- , but also deficient in K^+ and HCO_3^- .

Interactive Electrolytic Dislocations

We contend that over time interactions between these electrolytic dislocations can critically determine the expression of hypertension, kidney stones and osteoporosis (Fig. 1), and that increasing the dietary intake of K^+ (as precursors of KHCO_3) can dose-dependently delay, dampen or prevent the expression of these diseases [3,7–9]. A question immediately arises: If

interactions between these dietary electrolytic dislocations have such pathogenic potential, and KHCO_3 is so pointedly interdicting, why have these dislocations and their interactions not been identified and interdicted before, given that the field of fluid/electrolyte-acid/base metabolism is so mature and the diseases at issue so important? In large part, the answer lies with the ways in which these dietary electrolytic dislocations differ from traditionally defined clinical “electrolyte disorders”. The plasma concentrations of the electrolytes dislocated by diet are usually not outside their clinically adjudged “normal” ranges. The clinical, physiologic and biochemical consequences of the electrolytic dislocations are rarely acute. Indeed, their existence may only be demonstrated by the metabolic and physiological consequences of either their pointed mitigation or amplification. Further, with dietary correction of the electrolytic dislocations and the pathogenic disturbances they induce, the plasma concentrations of all electrolytes predictably remain well within their normal limits.

Both the severity and apparent benignity of these electrolytic dislocations are consequences of the still ancient renal machinery for processing dietary NaCl and dietary potassium and bicarbonate (and hence of processing increased acid).

Dietary Potassium Deficiency

Because the GI tract absorbs some 80 to 90% of dietary K^+ , and the kidney provides for almost all of its excretion, the dietary intake of K^+ and its renal excretion jointly determine the external balance of K^+ , and by so doing determine its body

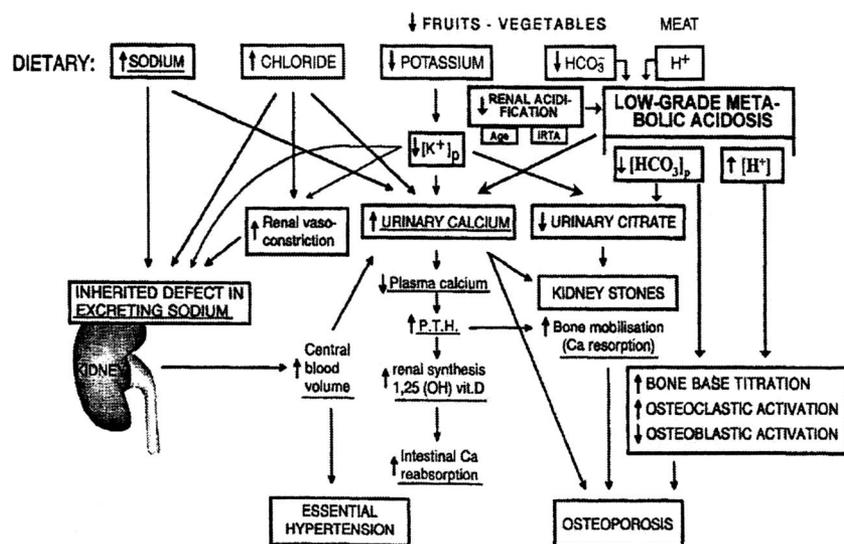


Fig. 1. Hypothesized relationships between certain dietary inorganic electrolytes and bicarbonate, the kidney, essential hypertension, kidney stones, and osteoporosis: the modern diet’s excessive dietary sodium and chloride and deficient dietary potassium and bicarbonate precursors as determinants of salt-sensitive blood pressure, low-grade metabolic acidosis and hypercalciuria and thereby hypertension, kidney stones and osteoporosis. As formulated, the acidosis can be amplified by impaired renal acidification that occurs as part of the “incomplete syndrome of renal tubular acidosis” (iRTA), an age-related decline in renal function (“age”), or both. The underlined dietary determinants and pathogenic events are those originally hypothesized and depicted. In this scheme, the word “osteoporosis” replaces the term “bone mineralization” specified in the depiction of the original formulation. (Modified from MacGregor and Cappuccio [30] by Morris RC et al. [8].)

stores and plasma concentration [10]. Because humans evolved from ancestors who habitually consumed large amounts of uncultivated plant foods that provided substantial amounts of potassium, the human kidney developed a highly efficient capacity to excrete potassium. In consequence, the normal human kidney efficiently dumps potassium when its dietary intake is great enough to increase its plasma concentration even slightly, but does not efficiently conserve potassium when its dietary intake and plasma concentration are reduced. Thus, normal renal function prevents body potassium overload and the occurrence of pathogenic hyperkalemia even when dietary potassium is greatly increased. However, when dietary potassium is even slightly reduced, relative to the modern usual dietary intake of K^+ , 40–80 mmol/d, an already extant body potassium deficiency is amplified [10]. Yet, with an increasingly severe dietary deficiency of potassium, the decrease in plasma concentration of potassium induced is attenuated both by a renal conserving mechanism, however inefficient, and the release of intracellular potassium from somatic muscle (but not from the brain or heart) [11]. As a consequence, plasma potassium, while progressively decreasing, is still maintained within its “normal” limits until there results a substantial tissue deficiency of potassium. Thus, in most instances, deficient dietary potassium and consequent tissue deficiency of potassium is not characterized by clinically defined hypokalemia, i.e. a plasma concentration of K^+ less than 3.5 mmol/L.

Dietary Bicarbonate Deficiency (Metabolic Acidosis)

That the modern Western diet could induce a low-grade metabolic acidosis that in turn could induce bone demineralization and ultimately osteoporosis has long been formulated and recently supported by the results of a variety of epidemiological and metabolic studies [8,12–16]. Non-carbonic acid is generated from both vegetable and animal protein, e.g. in both, sulfuric acid is generated from the metabolism of sulfur-containing amino acids. But unlike fruits and vegetables, meat contains few precursors of HCO_3^- , like citrate. Thus, the modern diet is a net producer of non-carbonic acid, not because of the large amount of acid-generating animal protein, but because of its deficient content of HCO_3^- precursors. In fact, the ancient diet contained considerably larger amounts of meat than does the modern diet, but the large amounts of HCO_3^- generated from that diet’s abundance of fruits and vegetables renders it a net producer of HCO_3^- [4,17,18]. Accordingly, the ancient renal machinery still persisting in normal humans evolved to excrete large loads of HCO_3^- and K^+ , not the large net acid loads chronically generated by the modern diet (or its excess of NaCl). In fact, the renal acidification process of the normal human does not completely excrete the modern acid load [17–20]. Though ever mounting, the acid thereby retained does not titrate plasma HCO_3^- to ever lower levels, but rather to sustained levels only slightly lower than those otherwise occurring. This is because the retained H^+ not only exchanges

with bone Na^+ and K^+ , but also titrates, and is buffered by, basic salts of bone [21]. Although preventing the occurrence of frank metabolic acidosis, the acid titration of calcium-containing carbonates and hydroxyapatite mobilizes bone calcium, promotes hypercalciuria and over time dissolves bone matrix.

Thus, the human adaptation to the modern diet’s deficiencies of both potassium and bicarbonate involves classic biologic trade-off. In “compensation” for the limited capacity of ancient renal machinery to regulate plasma concentrations of potassium and bicarbonate (and thereby arterial pH), these concentrations are maintained at clinically near “normal” levels at the expense of tissue losses of potassium and basic calcium salts, respectively. To a considerable extent, K^+ lost from cells is replaced with H^+ , which has its own biological consequences. Such “intracellular acidosis” in the renal tubule may account in part for the capacity of seemingly mild potassium deficiency to enhance the renal reclamation of NaCl and citrate, reduced urinary excretions of which are potentially pathogenic of kidney stones (vide infra).

Interactive Electrolytic Dislocations: Consequent Disturbances and Diseases

Dietary deficiencies of both potassium and bicarbonate interact with dietary NaCl overload to induce physiologic and metabolic disturbances that over time can determine the expression of hypertension, kidney stones and osteoporosis (Fig. 1). Therein resides the critical importance of these electrolytic dislocations, and the near unique capacity of increasing dietary $KHCO_3$ to interdict their pathogenic interaction. Thus, low-grade potassium deficiency interacts with dietary NaCl-overload to induce the expression of salt-sensitive blood pressure, which over time engenders salt-sensitive hypertension and stroke [22–24]. Low-grade deficiencies of both potassium and bicarbonate interact with each other and with dietary NaCl-overload to induce hypercalciuria and hypocitraturia, [3,8,19,25], metabolic disturbances which over time can engender the expression of kidney stones [26]. Presumably in part by inducing hypercalciuria and negative external calcium balance, all three dislocations interact to induce bone demineralization, diminished bone formation and increased bone resorption, metabolic disturbances that over time could engender the expression of osteoporosis [8,14,15,21,27–29].

Dietary Potassium and Bicarbonate as Dominant Joint Determinants of Urinary Calcium

Although the dietary intakes of sodium and calcium are said to be “the two major determinants of urinary calcium excretion” [30], and the urinary excretion of Ca^{++} is well documented to vary directly with that of Na^+ [31,32], the hypocalciuric effect of supplemental $KHCO_3$ can override the hypercalciuric effect of dietary NaCl-loading, even as such supplementation further increases the urinary excretion of Na^+ . In a recently reported metabolic study of middle-aged normal

men fed a diet marginally deficient in both K^+ , 30 mmol/d, and Ca^{++} , 14 mmol/d, increasing dietary NaCl from 15 to 250 mmol/d induced a 50% increase in urinary calcium that supplemental $KHCO_3$ either reversed or abolished, depending on whether it was supplemented to 70 or 120 mmol/d, mid- and high-“normal” intakes, respectively [7]. In post-menopausal women fed a “normal” potassium diet, supplementing dietary potassium with potassium citrate prevented not only the hypercalciuria otherwise induced by dietary NaCl-loading, but also the increase in biochemical markers of bone resorption otherwise induced [4]. In another study of post-menopausal white women who continued to eat their regular diet, supplementing $KHCO_3$ over a period of up to three years induced a sustained reduction in urinary Ca^{++} [33]. The hypocalciuric effect of $KHCO_3$ presumably reflects the fact that both K^+ [34] and HCO_3^- [35,36] act jointly on the renal tubule to increase its renal reclamation of calcium. Even a mild deficiency of potassium evokes hypercalciuria [37] as does mild metabolic acidosis [38]. Neither $NaHCO_3^-$ [2] nor KCl [39] has a hypocalciuric effect, at least in adults who ingest normal amounts of NaCl. Neither K^+ nor HCO_3^- reduces the intestinal absorption of Ca^{++} , and HCO_3^- possibly enhances it. Thus, deficiencies of K^+ and HCO_3^- in the modern diet may be as powerfully hypercalciuric as is its excess of NaCl, and the hypercalciuric effects of all of these electrolytic dislocations may summate to increase the likelihood of occurrence of osteoporosis. Conversely, as pointed out by Lemann and his associates [28], since both ionic components of supplemental $KHCO_3$ participate in its sustained reduction of urinary Ca^{++} , “diets containing relatively more potassium” (and hence also more HCO_3^- precursors) “would serve to protect skeletal mass”. Thus, correcting the modern diet’s deficiencies of K^+ and HCO_3^- , either with an increased intake of fruits and vegetables, or with supplemental $KHCO_3$, or both, may be more effective than, and possibly synergistic with, moderately restricting dietary NaCl in reducing not only the renal excretion of Ca^{++} , but also the level of blood pressure [3,7], and hence the expression of hypertension [7,40] as well as that of osteoporosis and kidney stones [3,7].

Salt-Sensitive Blood Pressure: The Determinacy of Dietary Na^+/K^+

Salt-Sensitive Hypertension

In the first strain of rats Dahl bred for the trait of “salt-sensitive” hypertension, he observed that the severity of hypertension induced by a given dietary load of salt varied inversely with the dietary intake of potassium. When the molar intake of dietary potassium was increased to that of NaCl, by supplementing dietary potassium with KCl, blood pressure increased only minimally [41]. Conversely, Ganguli and Tobian observed that the salt-loaded spontaneously hypertensive rat (Okamoto strain) (SHR) could be rendered salt-sensitive by restricting its dietary intake of potassium, if only to an amount still within the

normal range. Thus, the dietary molar ratio of Na^+/K^+ can be determining of salt-sensitivity [42]. The essential hypertension of the older and the elderly and of African-Americans is characteristically salt-sensitive [40,43–45]. In an outpatient study of white men with salt-sensitive essential hypertension, aged 55–70 years, in whom a basal urinary excretion of K^+ of 41 mmol/day presumably reflected a just adequate dietary intake of potassium, Morgan demonstrated that supplementing dietary potassium with KCl, 70 mmol/day for four weeks, attenuated “the blood-pressure raising effect of NaCl” [43]. In a subsequent outpatient study of similarly old white men with essential hypertension, Morgan et al [40] observed that in the 17 whose blood pressure decreased to normal values with NaCl restriction, supplementing dietary potassium with KCl, 48 mmol/day, for two weeks prevented the otherwise significant increase in blood pressure induced by a high salt diet. Morgan further observed that the blood-pressure lowering response to potassium in supine systolic and diastolic blood pressures was critically dependent upon the sodium intake. In those patients on a low salt diet, supplemental potassium did not significantly reduce blood pressure in either salt-sensitive or salt-resistant patients.

Although the mechanisms by which supplemental potassium attenuates hypertension are not well understood, the attenuation has been demonstrated most consistently [40,46] in affected patients on a normal or high-NaCl diet. In two well done studies, supplementing dietary potassium with KCl was without effect in patients with essential hypertension in whom moderate salt restriction had already induced attenuation of hypertension [40,46]. For many years, potassium salts of several acids have been known to be natriuretic. In normal human subjects studied under controlled metabolic conditions, the potassium salts, $KHCO_3$ and KCl, both have a substantial and comparable natriuretic effect [47]. Conversely, potassium deficiency impairs the natriuretic response to dietary NaCl loading in the normal human [48].

The mechanism by which supplementing dietary potassium induced natriuresis is incompletely understood. In the rat, administration of KCl into the renal artery induces natriuresis [49]. Since potassium loading increases the plasma concentration of potassium, and thereby that of aldosterone, the antinatriuretic effect of this hormone limits the extent of natriuresis induced by potassium loading in the intact mammal. In micropuncture studies, potassium inhibits reabsorption of sodium in the proximal tubule [50], and the thick ascending limb [51]. In vesicles prepared from luminal membranes of the distal tubule, potassium inhibits transport of sodium [34].

By reducing extracellular volume and blood volume, the natriuretic effect of potassium is generally considered to be an important component of its antihypertensive effect. In 29 Japanese men with essential hypertension studied under controlled metabolic conditions, Fujita [52] demonstrated that supplementing dietary potassium with KCl (96 mmol/day) to a total intake of 146 mmol/d prevented the increase in blood pressure

that otherwise occurred when NaCl loading (250 mmol/day over 6 days) followed NaCl restriction. The prevention could be related to the greater natriuresis that occurred with KCl and consequent attenuation of the NaCl-induced positive sodium balance, and increase in blood volume and cardiac output. In an earlier study of 20 Japanese men with “mild or moderate” essential hypertension also investigated under controlled metabolic conditions, Iimura et al [53] observed the effect on blood pressure of changing dietary potassium from a normal level (75 mmol/day for a 2-week period) to both higher and lower levels (175 and 25 mmol/day for 10 day periods). In a cross-over design, 10 patients first increased, and 10 first decreased dietary potassium while the dietary intake of NaCl was maintained constant at 260 mmol/day. Increasing dietary potassium was attended by a decrease in mean arterial blood pressure of 11 mm Hg, an increase in urinary excretion of sodium, and a decrease in plasma volume, cardiac output and body weight. Decreasing dietary potassium had opposite effects.

Normotensive Salt-Sensitive Blood Pressure

The phenomenon of salt-sensitivity, even in those who are non-hypertensive, has been found to confer its own cardiovascular risks, including incident hypertension and cardiovascular death [24,54]. Salt-sensitivity occurs with greater frequency and severity in non-hypertensive African-Americans than in non-hypertensive whites [7,55]. This question was recently asked: Does dietary potassium determine whether salt-sensitivity is expressed in most or few African-Americans and in more African-Americans than whites? In a metabolic study of 38 healthy, non-hypertensive men (24 African-Americans and 14 whites) fed a basal diet with low but not unusual levels of K⁺ (30 mmol/day) and Na⁺ (15 mmol/day), the modulating effect of potassium supplementation on the pressor effect of dietary NaCl loading (250 mmol/day) was investigated [7] (Fig. 2).

Before potassium was supplemented, 79 percent of the African-American men and 26 percent of the white men were termed salt sensitive, as defined by a NaCl-induced increase in mean arterial pressure of at least three mm Hg. Salt-sensitivity was defined as “severe” if NaCl induced an increase in mean arterial pressure of 10 mm Hg or more, an increase observed only in African-American men. When dietary potassium was increased with KHCO₃ from 30 to 70 mmol per day, over half of the African-American men, but only one-fifth of the white men, remained salt-sensitive. In the African-Americans with severe salt-sensitivity, increasing dietary potassium to an intake of 120 mmol/day reduced the frequency of salt-sensitivity to 20 percent, the same percentage as that observed in white subjects when their potassium intake was increased to only 70 mmol/day. In another metabolic study of 16 mostly non-hypertensive African-American subjects loaded with 250 mmol of NaCl per day, increasing dietary potassium as KHCO₃ to an intake of 170 mmol/day abolished the salt-sensitivity of all subjects [56]

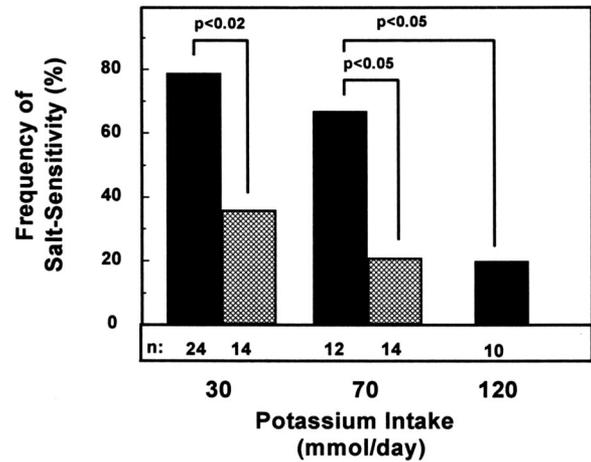


Fig. 2. Effect of potassium intake on frequency of salt-sensitivity in non-hypertensive African-American men (solid bar) and white men (cross-hatched bar). No white men were tested with 4.7 g/day (120 mmol/day) of potassium. Throughout an initial 7-day period of salt loading in all study subjects, potassium intake as potassium bicarbonate was set at 1.2 g/day (30 mmol/day), then increased to a total of either 2.7 or 4.7 g/day (70 or 120 mmol/day) for a subsequent 7-day period of salt loading.

and their NaCl-induced hypercalciuria. Predictably, the serum concentration of potassium remained well within normal limits.

These observations document that supplemental KHCO₃ mitigates the pressor effect of dietary NaCl in a dose-dependant fashion, just as it mitigates the hypercalciuric effect of dietary NaCl. Furthermore, these trials highlight the potential benefit of increased potassium intake in African-Americans, who have a higher prevalence of hypertension and of salt-sensitivity and a lower intake of potassium than non-African-Americans [57]. It seems likely that by suppressing the expression of salt-sensitivity, increasing dietary potassium to values within its real normal range can prevent or delay the occurrence of hypertension [6,7,24,58].

The DASH Diet: The Issue of Correcting Interactive Electrolytic Dislocations

The observations that demonstrate the capacity of dietary KHCO₃ to dose-dependently mitigate and abolish the pressor and hypercalciuric effects of dietary NaCl seem relevant to recent observations made in normotensive and hypertensive subjects ingesting the DASH diet [59]. In this study, the “control” diet was “low in fruits and vegetables and dairy products” and hence deficient in potassium, bicarbonate-precursors and calcium. After a three week run-in on the control diet, the study subjects were randomly assigned to receive for eight weeks the control diet, a diet rich in fruits and vegetables, or a “combination” diet rich also in low-fat dairy products with reduced saturated and total fat. All diets were designed to provide a constant intake of NaCl of approximately 140 mmol/d. Both enriched diets, which increased the mean intake of potassium from approximately 50 (control) to 130 mmol/d [61], induced

substantial reductions of blood pressure, the greater reduction occurring with the combination diet. It was also observed that the “fruits and vegetables” diet induced a reduction in urinary calcium, and that the combination diet did not induce an increase in urinary calcium, despite its high calcium content. It seems safe to assume that the fruits and vegetables provided in the DASH diet increased the metabolic generation of an amount of bicarbonate that could have increased the renal reclamation of calcium. A greater retention of dietary calcium so afforded may have accounted in part for the greater reduction in blood pressure observed with the combination diet [7].

In the second DASH study [60], the investigators sought to determine the extent to which graded dietary restriction of NaCl might enhance the hypotensive effect of both the control and the combination diet (hereafter referred to as the DASH diet). Three intakes of NaCl were investigated, 150, 100 and 65 mmol/d. It was again demonstrated that the DASH diet has a robust hypotensive effect, about six mm Hg. With both the control and DASH diets, NaCl restriction had a dose-dependent hypotensive effect. Combining the DASH diet with the greater NaCl restriction induced the greatest hypotensive effect. However, the hypotensive effects of NaCl restriction were far greater with the control diet than with the DASH diet, i.e., when dietary K^+ was “low”, 50 mmol/d. In fact, NaCl restriction only modestly amplified the hypotensive effect of the relatively high-potassium DASH diet, systolic blood pressure decreasing by 1.3 and 1.7 mm Hg with intakes of NaCl of 100 and 65 mmol/d, respectively. It seems likely that the hypotensive effect of the DASH diet is to a considerable extent determined by its relatively high potassium intake, and possibly to some extent by a greater renal calcium retention thereby induced.

Accordingly, the question becomes: Would the hypotensive and renal calcium-retaining effects of the DASH diet be importantly amplified by supplemental potassium bicarbonate (or citrate), even though the potassium content of the DASH diet is already substantially enriched relative to that of the control diet. In a recent study of 14 English patients with mild to moderate hypertension, 151/93 mm Hg, and in whom baseline urinary excretions of Na^+ and K^+ were 161 and 81 mmol/d, respectively, He and MacGregor and their associates performed a crossover trial comparing both the hypotensive and hypocalciuric effects of K-citrate and KCl, 96 mmol/d, each for one week [62]. With either potassium supplement, the urinary excretion of potassium doubled to a value twice that observed with the DASH diet, but similar to that observed in NaCl-loaded normotensive, salt-sensitive African-Americans in whom dietary potassium was supplemented with $KHCO_3$ to a level of 170 mmol/d for one week. With the augmented dietary intakes of potassium, systolic blood pressure decreased 10–12 mm of Hg in the hypertensive English patients, and 18 mm of Hg in the normotensive, NaCl-loaded, salt-sensitive African-Americans [56]. These antipressor effects are considerably greater and

sooner occurring than those usually observed with lesser supplements of potassium [9,63]. Further, despite the “relatively high” dietary intake of potassium at baseline, supplemental K-citrate, but not KCl, induced a significant reduction of urinary calcium. The percent reduction, about 15, [62] is similar to that observed with the DASH diet when dietary NaCl was restricted from the “higher” intake (150 mmol/d) to the “lower” intake (50 mmol/d) [64]. The urinary excretion of K^+ observed by He and MacGregor at base line, 81 mmol/d, is identical to that observed with the DASH diet, and the urinary excretion of Na^+ at baseline is similar to that observed with the DASH diet at the “higher” intake of NaCl. Thus, supplementing the DASH diet with K-citrate might substantially enhance its capacity to lower blood pressure and urinary calcium, if the amount of potassium supplemented approached that employed by He and MacGregor, and as a consequence the intake of K^+ approached 190 mmol/d. It is apparent that by either so supplementing potassium or so restricting sodium, the dietary Na^+/K^+ ratio is greatly decreased, as is the Cl^-/HCO_3^- ratio.

In a recent editorial, “Potassium intake and blood pressure”, He and MacGregor state that “The epidemiological and clinical evidence for potassium is now as convincing as that for salt. The whole population, including those with high blood pressure, would benefit from a reduction in salt intake and an increase in potassium intake” [65]. This may well be true, but the question remains: If the K^+ intake attained with a DASH type diet were amplified to levels of 170–190 mmol/d, as with supplemental K-citrate or $KHCO_3$, would salt-restriction confer further benefits. We believe this to be an important question.

Salt Restriction Versus Potassium Bicarbonate as a Treatment of Kidney Stones

Dietary salt restriction has also been recommended for the prevention and treatment of kidney stones, based on the fact that dietary NaCl is an important determinant of the urinary excretion of calcium, and hypercalciuria is generally accepted as an important risk factor for calcium-containing kidney stones [30]. But again the question can be asked: Is salt restriction as likely to be as availing as supplementing dietary potassium with an alkaline salt, e.g. $KHCO_3$, to the currently recommended level of 120 mmol/d? It has been reported that the occurrence of kidney stones in both sexes is highly related to the urinary Na^+/K^+ ratio [2,66]. In a recent epidemiological study of 51,529 men conducted prospectively over four years, the incidence of symptomatic kidney stones did not correlate with dietary Na^+ , but did not correlate strongly and negatively with dietary K^+ over a broad but normal range, 67–113 mmol/d [67]. In a 12-year prospective study of an even larger number of women nurses, the incidence of stone formation also correlated inversely with dietary K^+ over an even broader but normal range, 54–120 mmol/d [68]. The incidence of kidney stones in the men, and likely also that in the women, correlated directly with the dietary intake of meat. An increase dietary

intake of meat has long been recognized as a risk factor for kidney stones, presumably in part because of the acid load imposed by meat and the well documented determinacy of the magnitude of that load on the urinary excretion of calcium [69].

By increasing acid load, an increased intake of animal protein also induces a decrease in the urinary excretion of citrate, a major risk factor for the formation of kidney stones [70]. Urinary citrate chelates urinary calcium in a soluble form. Both hypocitraturia and hypercalciuria occur with even modest potassium deficiency. Administration of KHCO_3 or K-citrate induces an increase in the urinary excretion of citrate, as well as a reduction in the urinary excretion of calcium. Neither the citraturic effect of K-citrate, nor its hypocalciuric effect, is greater than that of KHCO_3 , presumably because these salts induce similarly small increases in the plasma concentration of bicarbonate. In a double-blinded, placebo-controlled study conducted over three years, Pak and his colleagues demonstrated that the administration of K-citrate, 60 mmol/d, induced a highly significant reduction in the occurrence of kidney stones, along with a urinary excretion of K^+ of about 100 mmol/d and a substantial increase in urinary pH [71]. Similar results have been recorded in uncontrolled trials of K-citrate. We know of no comparable studies with NaCl restriction.

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