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Sodium Chloride–Dependent Hypertension

TO THE EDITOR:

In a letter recently published in Hypertension, Dr. Mordecai P. Blaustein comments that “two recent studies . . . have been interpreted as showing that salt-dependent hypertension in some animal models can be ‘dissociated from the intake of sodium’ and may, at least in part, be attributable to Cl–.” This sentence might suggest that we, the authors of one of the studies cited,2 hold that salt-dependent hypertension can be dissociated from the intake of sodium. We do not hold this position. Rather, we concluded that “it seems prudent to speak of ‘sodium chloride–dependent’ hypertension rather than ‘sodium-dependent’ hypertension.”2 This conclusion was based in large part on our finding that in rats given deoxycorticosterone, provision of dietary sodium as sodium chloride induced hypertension whereas provision of dietary sodium without chloride did not. As recently reiterated, we have not contended that chloride is the pressor component of sodium chloride nor have we proposed use of the term chloride-dependent hypertension.

Dr. Blaustein states that “the decision as to whether to use the term Na+-dependent hypertension or Cl–-dependent hypertension might appear to be semantic. Since Na+ is the actively transported ion and is the primary ion affected by mineralocorticoids, it seems most appropriate to define mineralocorticoid hypertension as Na+ dependent on the basis of the underlying physiology. . . .” We believe that neither “sodium-dependent” hypertension nor “chloride-dependent” hypertension is the optimal term. We prefer to speak of mineralocorticoid hypertension as “sodium chloride-dependent” since induction of the hypertension, whatever its mechanism, appears to depend on the provision of both sodium and chloride.2,4 We have recently found that supplementing the dietary sodium intake of rats given deoxycorticosterone with sodium bromide and sodium iodide combined can induce increases in blood pressure.5 Thus, the deoxycorticosterone model might also be referred to as “sodium-halide-dependent hypertension.” In this regard, it seems relevant that in 1928 Addison6 reported that oral loading with either sodium chloride or sodium bromide induced blood pressure increases in five hypertensive patients.

Dr. Blaustein states that “when an appropriate anion, such as Cl–, is limiting, net reabsorption of Na+ will be restricted as will the attendant expansion of the ECF [extracellular fluid] volume.” He continues, “Retention of Na+ and ECF volume expansion play a key role in the development of mineralocorticoid hypertension.” In presupposing that chloride merely permits the kidney to reabsorb more sodium than it otherwise would, Dr. Blaustein does not appear to allow for the possibility that some effect of chloride might contribute to the pathogenesis of sodium chloride–dependent hypertension through a mechanism involving something more than the renal retention of sodium and expansion of ECF volume.

Because of the controversy that surrounds the role of ECF volume expansion in the pathogenesis of mineralocorticoid hypertension,7–10 and because chloride and other electrolytes can have important biological effects in brain, kidney, and smooth muscle,11–18 it would seem prudent to allow for the possibility that various substances (e.g., chloride, calcium, potassium) might affect blood pressure independent of, or in addition to, their effects on sodium balance and ECF volume. The recent provocative finding of McCarron et al.19 that blood pressure of spontaneously hypertensive rats is lower with a high calcium, high sodium diet than with a high calcium, low sodium diet would suggest that the effects of dietary substances on blood pressure are much more complex than previously recognized.

Dr. Blaustein and we appear to be in agreement that the anionic components of the sodium salts consumed can be determinants of the extent to which, or whether, a given dietary intake of sodium induces an increase in blood pressure. Unlike Dr. Blaustein, however, we are not certain that anions affect blood pressure only by affecting “net (renal) reabsorption of Na+” and thereby ECF volume.20

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AUTHOR’S RESPONSE:
In my recent letter,1 I tried very carefully to indicate that I believe McCarron et al.2 have misinterpreted the reports of Kurtz and Morris3 and of Whitescarver et al.4 by suggesting that “salt-dependent hypertension in some animal models can be ‘dissociated from the intake of sodium.’”5 I did not mean to imply that the authors of these articles3,4 hold such views; indeed, I am pleased that Kurtz and Morris also take issue with McCarron’s interpretation of their data.

Current views regarding the mechanism of action of mineralocorticoids on salt reabsorption are briefly summarized in my letter6 and need not be repeated here. The evidence supplied by Kurtz and Morris that other halide ions can substitute for chloride in enabling the mineralocorticoid-dependent retention of sodium and generation of hypertension does not conflict with my view7 that sodium retention is required for the development of mineralocorticoid-salt hypertension.

Although there may be disagreement about the relationship between extracellular fluid volume expansion and hypertension,8 there seems to be general agreement that 1) mineralocorticoids act on the renal sodium transport systems and induce salt (NaCl) and water retention (the attendant volume expansion is primarily extracellular) and 2) mineralocorticoids apparently do not induce hypertension when salt intake is restricted. The question of whether the hypertension is due to the volume expansion per se or can be better correlated with the natriuretic (and diuretic) escape from the salt and water retention9 requires further study.

The foregoing considerations, and those mentioned by Kurtz and Morris appear to reinforce my main conclusion “that it may be misleading to infer pathophysiological mechanisms in the development of hypertension on the basis of dietary studies alone”10.

References

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