number of sodium salts, such as sodium citrate, sodium nitrite, sodium phosphate, or sodium benzoate. To date, the authors have only shown that a mixture of sodium bicarbonate and sodium amino acids does not cause hypertension in the Dahl S rat. On the basis of these findings and those of Kurtz and Morris in their study on uninephrectomized rats treated with deoxycorticosterone (8), one could also conclude that sodium raises blood pressure, but that this effect is canceled out by a hypothetical depressor effect of the bicarbonate ion.

We have no problem accepting the results of the two studies. We point out, however, that the effect that they demonstrate may be difficult to reproduce regularly. When Abernethy and one of us (H.G.L.) demonstrated that pressure elevation from sodium bicarbonate-ace
tate mixtures caused less of an increase in blood pressure than sodium chloride, the rats also gained less weight. When pairing was done so that there was no difference in the gain in weight, there was no difference in the gain in blood pressure (9). For the moment, we think that the safest interpretation of these studies is that the use of an anion other than chloride in experimental hypertension in the rat may, in some yet-to-be defined circumstance, be able to block the blood pressure-raising effects of sodium, probably by decreasing tubular reabsorption of sodium.

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References
10. 18 September 1984; accepted 29 January 1985.

Liebman and Langford (1) raise several different issues, not all of which are directly related to our study of Dahl salt-sensitive (Dahl S) rats fed diets containing high concentrations of sodium, with or without chloride (2).

We previously reported that dietary sodium loading with anions other than chloride (either bicarbonate alone or a combination of anions including bicarbonate, phosphate, glycinate, glutamate and aspartate—referred to as NaAA) did not produce hypertension in the Dahl S rat (2, 3). We have recently extended these observations to another model of salt-sensitive hypertension—unineph
trectomized rats treated with deoxycorticosterone acetate (DOCA) (4). Blood pressures were higher in rats fed sodium chloride than in rats subjected to comparable sodium loading by means of NaAA. These observations led us to conclude that the full expression of salt-sensitive hypertension in these models is not dependent on dietary sodium alone.

In developing the NaAA diet, we combined a variety of sodium compounds so that, when compared to a high sodium chloride diet, the equivalent sodium loading without chloride would not result in differences in weight gain, arterial pH, net sodium and potassium balance, and plasma concentrations of sodium, potassium, and ionized calcium. At the dietary intakes required, sodium citrate chelates calcium, sodium nitrate results in decreased weight gain, sodium phosphate causes diarrhea, and sodium benzoate is a gastrointestinal irritant. After considerable trial and error, we arrived at the NaAA diet. To determine if lower blood pressures in the NaAA-treated animals might be related to a nonspecific effect of the NaAA diet itself, we studied Sprague-Dawley rats using the “one-kidney, one-clip” model of hypertension (one kidney removed and partial occlusion of the renal artery of the remaining kidney). Groups of these rats received either a high sodium chloride diet or a high NaAA diet (4). Over a 17-day period, both diets caused comparable increases in blood pressure. We therefore conclude that in the Dahl S rat and the DOCA-salt hypertensive rat the absence of hypertension in NaAA fed animals is specifically related to the lower intake of dietary chloride rather than to some other effect of the NaAA diet itself.

We have also evaluated the effects of selective chloride loading (without sodium) on the development of hypertension in the Dahl S rat (4). Blood pressure increased gradually in animals fed 4 percent sodium chloride but did not increase in animals fed equivalent amounts of chloride provided as glycine chloride. We therefore conclude that in this model the development of hypertension is dependent on the concomitant administration of sodium and chloride.

Our studies are not in conflict with the observations of others that a high dietary potassium intake tends to lower blood pressure, an effect generally attributed to potassium, not chloride. Our observations have implications for the mechanism by which sodium chloride produces hypertension in susceptible hosts.

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Liebman and Langford (1) imply that we, and others, hold that chloride is the pressor component of sodium chloride in the diet. In fact, we proposed the possibility that the anionic component of the sodium salt consumed can be a critical pathogenetic determinant of “sodium-dependent” hypertension. Given our finding that, in rats given deoxycorticosterone (DOC), provision of dietary sodium as sodium chloride induced hypertension whereas provision of dietary sodium as sodium bicarbonate did not, we concluded that it seemed prudent to speak of sodium chloride–dependent hypertension rather than “sodium-dependent” hypertension. We suggested that the pathogenesis of the DOC model of hypertension and other models of “sodium-dependent” hypertension might depend on the chloride component of sodium chloride.

In one sense, Liebman and Langford appear to agree with our suggestion that the anion of a dietary sodium salt can determine the extent to which that sodium salt induces an increase in blood pressure. They “feel that the safest interpretation of these studies [ours (2, 3), and those of Whitescarver et al. (4, 5)] is that the use of an anion other than chloride in experimental hypertension in the rat may, in some yet-to-be defined circumstance, be able to block the blood pressure-raising effects of sodium, probably by decreasing tubular reabsorption of sodium.” This formulation, however, assumes that the pressor effect of a sodium salt resides with the sodium ion alone and is critically dependent on its increased renal reabsorption.

In presupposing that sodium is the
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Science 228 (4697), 352.
DOI: 10.1126/science.228.4697.352

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