Chloride: Effect on Morphology of Heart, Kidney, and Testis in Potassium-Deficient Rats (36892)

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The experiments described here showed that dietary chloride deficiency modifies the histological changes encountered in potassium-deficient rats.

Morphological changes in potassium-deficient rats have been studied repeatedly (1–3). If the diet is deficient only in potassium, kidneys show characteristic tubular lesions and appear swollen and pale. In one paper, it was reported that, if chloride was also omitted from the diet, kidneys were more normal in appearance and tubular lesions were much less severe (4).

A recent review (5) states that until recently, "anions in general, and chloride in particular, have been considered physiologically indifferent," but more recent work has shown "that under many physiological and clinical conditions anion characteristics have considerable influence on both the reabsorption of bicarbonate and the secretion of potassium." Most such studies have been concerned with acid–base equilibria and the physiological effects of anions on alkalosis. In this paper, the influence of chloride on the morphology of kidney, heart, and testis will be reported.

Matching groups of male Charles River CD rats (initially, average weight approximately 100 g) were fed K-, Na-, and Cl-deficient diets containing 30% vitamin-free casein, 44% dextrose, 20% lard, 2% cellulose, and 4% of a salt mixture containing no potassium, sodium, or chloride;[1] all vitamins were added to the diet. One of the following supplements was added to a diet when desired: 1.32% $NaHCO_3$ (+ Na); 1.16% $CaCl_2 \cdot H_2O$ (+ Cl); 0.92% NaCl (+ Na, + Cl); 1.58% $KHCO_3$ (+ K); 1.18% KCl (+ K, + Cl); 0.92% NaCl + 1.58% $KHCO_3$ (+ K, + Na, + Cl).

The rats were housed individually on wire screen to facilitate measurement of their food intakes and were given distilled water to drink. They were sacrificed after 34–36 days on the diet and their livers, kidneys, hearts, testes, adrenals, and thyroids were weighed and fixed in Bouin's solution for histological examination.

Survival rates, average weekly food intakes, and terminal body weights are given in Table I. The highest mortality occurred in the groups given the potassium-deficient diets containing sodium (with or without chloride). Mortality was significantly lower when the K-deficient diets did not contain sodium (Chi Square = 8.8; $p < .01$).

Within each experiment, the food intakes of the K-deficient groups did not differ significantly regardless of other electrolyte supplements; the groups receiving potassium had significantly higher food intakes and body weights.

The kidneys of the rats deprived only of potassium (*i.e.*, given NaCl) were heavier than in any other group, including the controls. These swollen kidneys were pale and showed the microscopic lesion described by Follis: extreme tubular dilatation with the tubules lined with flattened epithelium and containing cellular debris and hyaline casts. No glomerular or vascular lesions were noted. Figure 1 shows a section of such a kidney. All kidney sections were evaluated in a blind test and the lesions graded on a scale of 0–4+.

[1] Composition of Salt Mixture Deficient in K, Na, and Cl.

	Parts		Parts
$CaHPO_4$	620	$MnSO_4 \cdot H\ O$	7
$CaCO_3$	230	MgI_2	1.3
$MgSO_4 \cdot 7\ H_2O$	202	$ZnSO_4 \cdot 7\ H_2O$	1
Fe citrate	55	$CuSO_4 \cdot 5\ H_2O$	0.6

TABLE I. Effects of Feeding Electrolyte-Deficient Diets to Young Male Rats for Five Weeks.

	Survival	Food intake (gm/day)	Terminal body wt (gm)	Kidneys		Hearts		Testes	
				Weight (mg)	4+ Lesions	Weight (mg)	4+ Lesions	Weight (mg)	4+ Lesions
Experiment I									
K, Na, Cl-deficient	10/12	7.0 ± 0.50	94 ± 3.5	1790 ± 65	6/10	368 ± 18	2/10	1080 ± 108	6/9
+ Na	7/12	6.7 ± 0.20	104 ± 3.3	1940 ± 90	1/7	520 ± 30	1/6	620 ± 86	5/5
+ Na + Cl	6/12	6.7 ± 0.25	105 ± 5.0	2720 ± 270	4/5	399 ± 34	1/5	1260 ± 146	1/5
+ Cl	10/12	6.7 ± 0.69	89 ± 3.0	1840 ± 86	7/10	289 ± 16	0/10	1600 ± 80	0/10
+ K + Cl	11/12	12.4 ± 0.60	154 ± 6.8	1580 ± 177		474 ± 21		2700 ± 77	
Controls (+ K, Na, Cl)	9/10	13.2 ± 0.50	289 ± 14.9	2020 ± 78		843 ± 40		2950 ± 91	
Experiment II									
K, Na, Cl-deficient	8/8		103 ± 2.8	2200 ± 144	1/4	433 ± 24	1/4	697 ± 48	4/4
+ Na	10/16	6.8 ± 0.36	105 ± 4.4	1840 ± 102	0/8	529 ± 33	2/10	605 ± 49	10/10
+ Na + Cl	11/16	6.2 ± 0.17	121 ± 4.4	2730 ± 155	8/11	433 ± 22	2/11	1340 ± 116	0/11
+ Cl	8/8		100 ± 2.2	1950 ± 82	2/8	304 ± 8	0/8	1470 ± 95	0/8
+ K	8/8		174 ± 6.3	1720 ± 45	0/8	476 ± 16	0/8	2610 ± 147	0/8
+ K + Cl	8/8		167 ± 6.0	1690 ± 57	0/8	466 ± 17	0/8	2640 ± 164	0/8
Controls (+ K, Na, Cl)	6/6		302 ± 7.6	2310 ± 79	0/6	857 ± 25	0/6	3000 ± 50	0/6

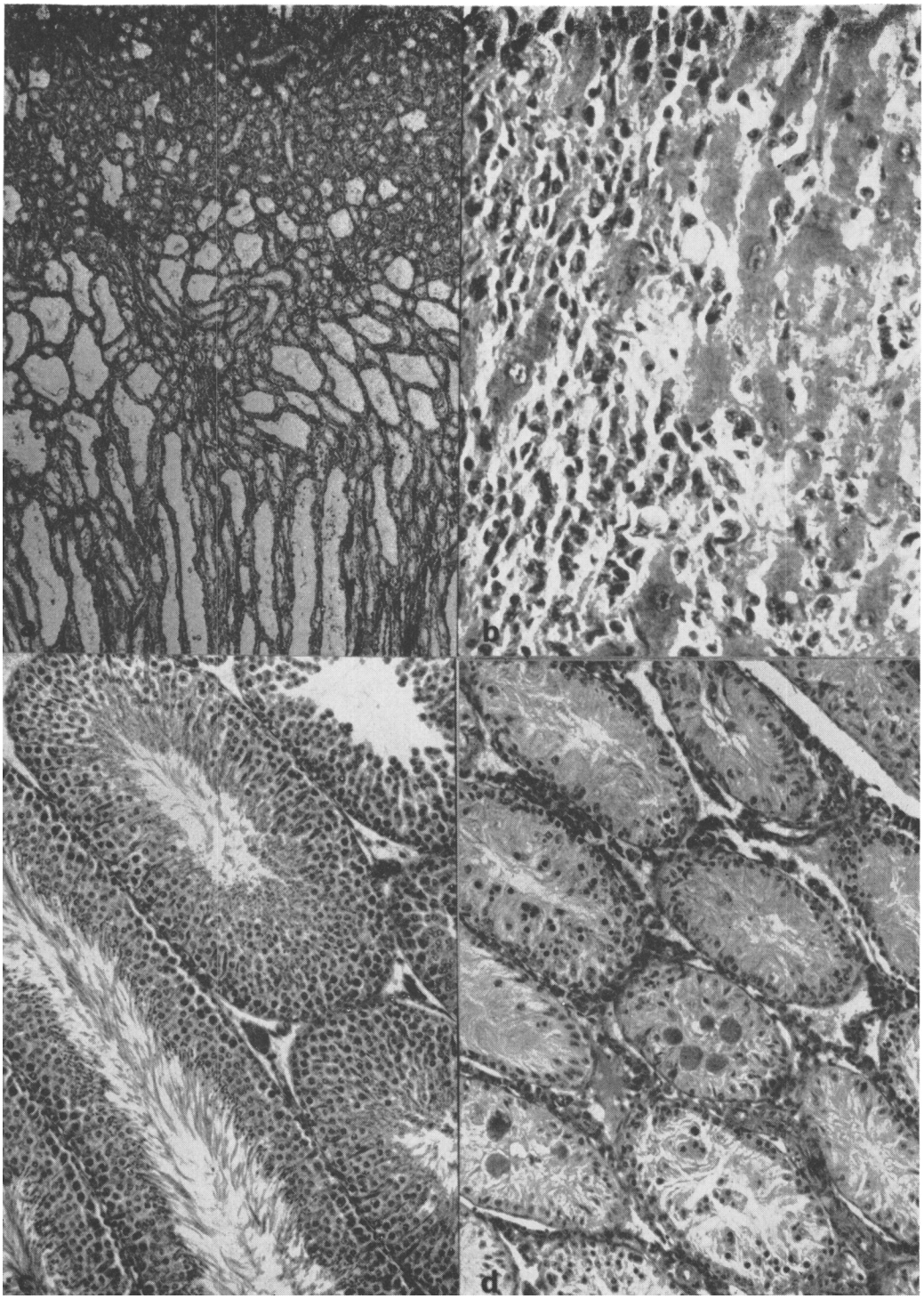

FIG. 1. Microscopic sections of organs from potassium-deficient rats. a. Kidney of rat given NaCl. Tubules dilated with flattened epithelium and containing cellular debris. b. Heart of rat given NaCl. Unspecific myocarditis with focal necrosis of muscle fibers and infiltration of interstitial spaces by inflammatory cells. c. Testis of rat given NaCl. Essentially normal. d. Testis of rat given $NaHCO_3$. Advanced atrophy of seminiferous tubules; spermatogenesis absent; ghosts of spermatozoa and degenerating giant cells in tubular lumina.

The incidence of 4+ lesions is shown in Table I.

When chloride was omitted from the K-deficient diet, kidneys were significantly lighter ($p < .02$ and .001 in Exp. I and II, respectively) and were a deep brown color. The lesions described were seen much less frequently. These lesions would seem to be due, in large part, to the presence of chloride in the absence of potassium because, when chloride was fed alone (without sodium), kidneys had severe lesions in 7/10 and 2/8 instances whereas, when sodium was fed alone, there were essentially no severe lesions, and the kidneys were a dark brown color. Rats given potassium had essentially normal kidneys.

The hearts of the K-deficient rats also showed the effects of chloride. The heaviest hearts were found in the groups given only sodium. When chloride was added to sodium, the hearts were approximately equal in weight to those animals given neither sodium nor chloride. Supplementation with chloride alone resulted in much lighter hearts ($p < .01$ and .001). Histologically, heart muscles in all K-deficient groups showed signs of an unspecific myocarditis characterized by focal necrosis of muscle fibers and infiltration of the interstitial spaces by leucocytes. This has been described by Follis (1). A section of such a heart is shown in Fig. 1. Evaluation of the lesions in a blind test did not reveal any marked differences among the K-deficient groups (Table I).

The testis was particularly affected by the presence or absence of chloride in the diet of K-deficient rats. Absence of chloride, regardless of whether sodium was present or not, brought about advanced testicular degeneration (Table I). Testes of rats given only sodium weighed less than half those of the K-deficient rats given NaCl. Addition of chloride alone, increased testicular weight more than did NaCl.

Sections of testes of rats fed the K-deficient diets supplemented with sodium only and with sodium + chloride are shown in Fig. 1. In the rats receiving $NaHCO_3$, the seminiferous tubules of the atrophic testes were greatly reduced in diameter; spermatogenesis had ceased, with only Sertoli cells and a few pycnotic cells remaining. Ghosts of spermatozoa and numerous degenerating giant cells were found within the tubular lumina. Leydig cells appeared more numerous because of the condensation of the parenchyma. In the animals given NaCl, testes were more or less normal, as had been observed by others studying potassium deficiency. Testes in the potassium-deficient rats given chloride without sodium were essentially normal.

The modification of the histological lesions occurring in potassium deficiency by chloride are probably related to the functional changes produced by chloride on electrolyte and acid–base balance and fluid distribution. At least in the testis, the absence of chloride would appear to have intensified the degree of potassium deficiency. In any event, the biological antagonism between potassium and sodium is strongly modified by chloride.

Summary. Effects of dietary chloride, with and without sodium, in potassium-deficient rats were studied in two experiments with similar results. The rats were sacrificed after five weeks on the experimental diets. Exclusion of chloride from potassium-deficient diets modified some of the histological findings in the potassium-deficient rats. Renal lesions were much less pronounced, but hearts were abnormally heavy when chloride was omitted. Testes were normal in the presence of chloride but markedly atrophic in its absence. Potassium obliterated these effects of chloride deficiency.

1. Follis, R. H., Orent-Keiles, E., and McCollum, E. V., Amer. J. Pathol. **18**, 29 (1942).

2. Kornberg, A., and Endicott, K. M., Amer. J. Physiol. **145**, 291 (1946).

3. Macpherson, C. R., and Pearse, A. G. E., Brit. Med. Bull. **13**, 19 (1957).

4. Kaunitz, H., Lab. Invest. **5**, 132 (1956).

5. Schwartz, W. B., de Strihou, C. van Ypersele, and Kassirer, J. P., New Eng. J. Med. **279**, 630 (1968).

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