CHRONIC RENAL DISEASE IN RATS FOLLOWING A TEMPORARY DEFICIENCY OF POTASSIUM

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FOLLIS, Orent-Keiles and McCollum (1942) described lesions in the heart and kidneys of rats killed while on a potassium-deficient diet. The present experiment was carried out to discover what happened to these lesions if the rats were allowed to recover from their deficiency of K.

METHODS

The " experimental " group contained twelve young inbred black and white hooded rats of a strain obtained from the Lister Institute. Their starting weight was 180–250 g. and they were given a diet consisting of rice (87 per cent), casein (10 per cent) and arachis oil (3 per cent) to which were added cod liver oil, yeast, aneurin and a K-free salt mixture. The diet contained 0·014 per cent of K. For 10 days in every fortnight an ammoniated exchange resin (Zeokarb 225) was incorporated in the diet in the proportion of 20 g. resin to 100 g. diet. The resin removes K from the body; it also produces an acidosis, but the rats were able to correct their acidosis during the 4-day intervals when resin was not given, whereas the diet contained too little K to enable them to restore this deficit.

The first control group consisted of an equal number of animals who received the same food and vitamins, but they were given no resin, and their salt mixture contained enough K to provide 0·07 g. per 100 g. diet.

The second control group of 12 animals received the same diet with K in the salt mixture, but with the addition of 3 g. NH_4Cl per 100 g. diet for 10 days in every fortnight. This amount of NH_4Cl provided the same quantity of H^+ ions as the ammoniated resin, and the object of including this group of animals was to find out if any of the lesions found in the K-deficient animals could be attributed to an intermittent acidosis.

The resin and the experimental diets were given in the way described over a period of 8 consecutive weeks. During this period 6 animals in each group were killed, 4 of them after 6, and the remaining 2 after 8 weeks; they were killed in the intervals when animals were not receiving resin or NH_4Cl. All the animals remaining at the end of 8 weeks were given the stock diet of rat pellets. After 3 months on this diet 3 in each group were killed, and the remaining 3 in each group after they had had the diet for 7 months. The rats were killed under anaesthesia by bleeding them from the aorta. In some of the animals the percentage of K in the heart, the kidneys, the brain and the adductor muscles of the thigh was measured by the method of Mudge and Vislocky (1949). The hearts and kidneys were fixed in Heidenhain's *susa* fixative and stained with haematoxylin and eosin, van Gieson's, Weigert's elastic and picro-Mallory stain. During the course of the experiment the percentage of urea was estimated by the method of Lee and Widdowson (1937) in blood drawn from the rats' tails, and the urinary excretion of urea was measured when the animals were in metabolism cages by the same method.

RESULTS

Killed after 6 or 8 weeks

The rats deprived of K did not grow and even lost weight. The concentration of K in their serum was 2·5–3 mEq. per l., compared with 4 to 5 mEq. per l.

in both groups of control animals. The concentration of K in their muscle was reduced (Table). The analysis of other organs of the K-deficient rats showed that in the heart and kidney the loss of K was only slight and there was no depletion in the brain. The amount of urea excreted in the urine was similar in all groups, but the blood urea of the K-deficient rats rose to about 60 mg. per 100 ml. and in some animals much higher, while in all the others the blood urea remained at the normal level of about 30 mg. per 100 ml. The kidneys in all the K-deficient rats showed degenerative changes, mostly necrotic in type and usually limited to a short length of the ascending loop of Henle. The kidneys of both control groups were normal.

Killed 3 months after K deficiency had been corrected

These rats had restored their serum and their muscle K to normal, but their serum still contained about 60 mg. urea per 100 ml. There were degenerative changes, vacuolation, granularity of the cytoplasm, and pyknotic nuclei in most parts of the renal tubules. A further change, probably regenerative rather than degenerative, was the presence of clumps of up to a dozen closely clustered nuclei in the ascending loop of Henle. The kidneys of both control groups were normal.

Killed 7 months after K deficiency had been corrected

The blood urea remained about 60 mg. per 100 ml. in one rat ; it had risen to 150 mg. in another and to 290 mg. in the third. The urine contained albumen and was of greater volume and lower specific gravity than in the control rats. All the control rats still had a normal blood urea, although, as frequently happens in older rats, they also now had some albumen in the urine. In the two rats with a high blood urea the hearts were larger than in both the groups of controls.

The kidney of the rats which had been made K-deficient had finely granular surfaces and were two to three times larger (Fig. 1) than the kidneys of the rats in the first control group (Fig. 2) or of those receiving NH_4Cl, which were all normal. The enlarged kidneys contained grossly dilated tubules, maximum in the proximal convoluted segment, with flattening of their epithelium and eosinophilic casts in their lumina (Fig. 3). Between the dilated tubules there were strands of reticulin and collagen, broader in the medulla than in the cortex (Fig. 3) containing occasional remains of degenerate tubules. Most of the glomeruli were atrophic and showed hyaline change. For the first time the kidneys of both control groups showed changes, namely, slight dilatation and flattening of epithelium in an occasional tubule, usually the proximal convoluted tubule. Lesions in the heart of the K-deficient rats were found but were not materially different from the description given by French (1952).

DISCUSSION

The experiments show that a temporary deficiency of K can lead to progressive renal damage in the rat. No claim is made that the final histological picture is peculiar to K deficiency. Apparently similar lesions appear in much older animals with advancing age (Saxton and Kimball, 1941), can be provoked by

giving a large excess of phosphate in the diet (Gough, Duguid and Davies, 1933; Duguid, 1933–34; MacKay and Oliver, 1935), or by the administration of desoxycorticosterone with an anterior pituitary extract (Selye, 1951), but in this case a deficiency of K may be responsible for the lesions (Durlacher, Darrow and Winternitz, 1942).

The experiments raise the question whether in man, as in rats, the renal lesions of K deficiency may lead to a progressive change and whether some of the renal lesions in so-called potassium-losing nephritis (Evans and Milne, 1954) may be the result and not the cause of the K deficiency (Conn, 1955).

SUMMARY

Rats were made K-deficient by diet and exchange resin for 6–8 weeks and they were then allowed to recover from their deficiency.

In the ensuing months lesions in their kidneys which were small in extent at the time of recovery became progressively more extensive.

After seven months, the rats had a high concentration of urea in their blood and their kidneys were enlarged with gross dilatation of tubules, and atrophy of most of the glomeruli.

The experiments show that a temporary deficiency of K can lead to progressive renal change in the rat.

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TABLE—*The K Content of Muscle in mEq./100g. Fat Free Dry Muscle of K-Deficient Rats and Controls*

Duration of exp. diet in weeks.	K-deficient group.	Control groups. Normal salt mixture.	Control groups. Normal salt mixture + NH_4Cl.
6	37.7	44.5	44.3
8	25.1	47.1	48.5
Duration of recovery stock diet in weeks.			
12	48.2	48.0	—
28	46.5	46.6	—

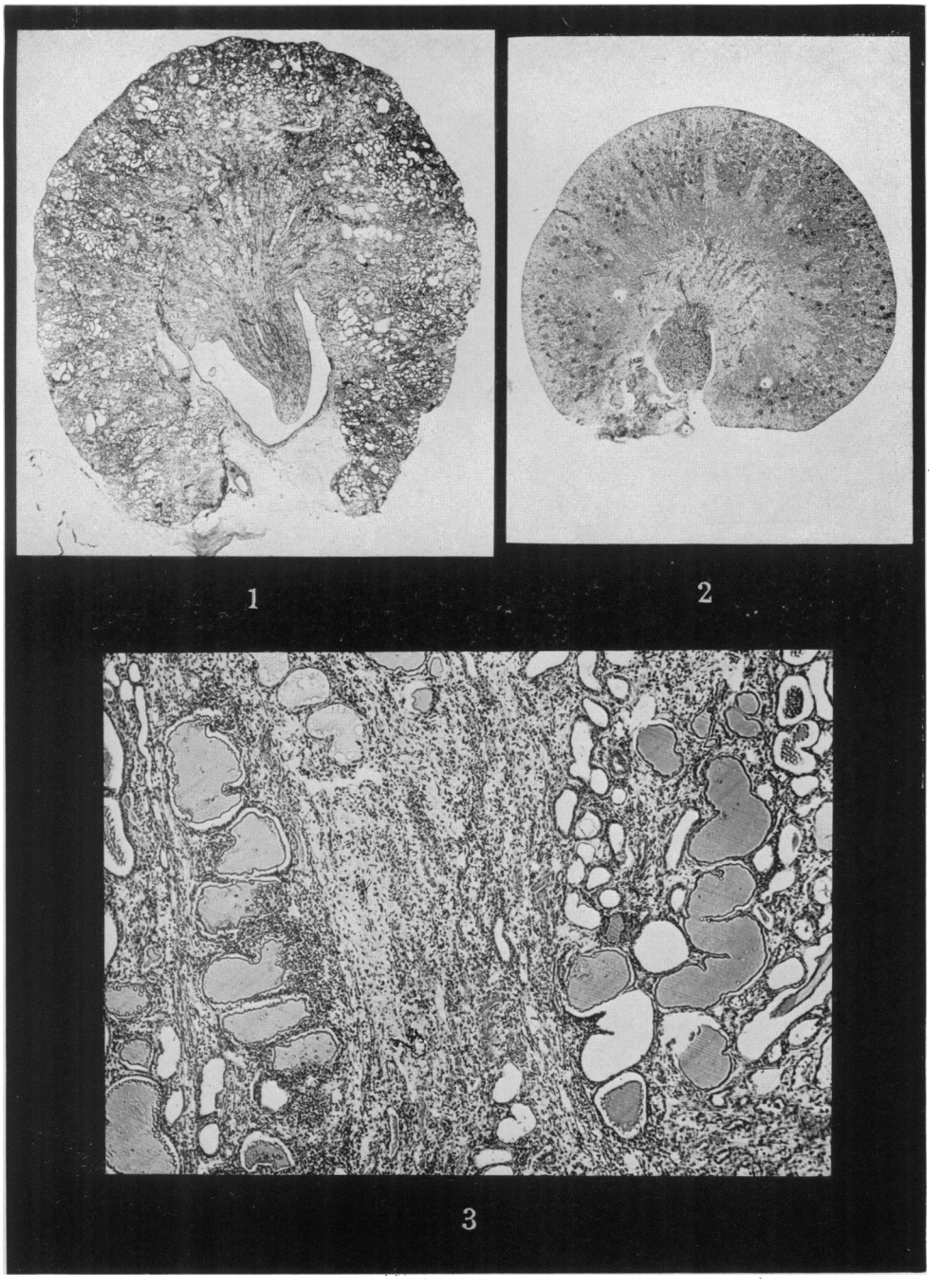
Figures represent means of determinations of 2 animals.

EXPLANATION OF PLATE

FIG. 1.—Enlarged kidney with dilatation of tubules from a rat on normal diet for seven months after an initial period of K-deficient diet. H. & E. × 8.

FIG. 2.—Normal-sized kidney of rat from first control group for comparison with Fig. 1, same magnification. H. & E. × 8.

FIG. 3.—Medulla of the same kidney as in Fig. 1 showing a band of reticulin and collagen fibres between dilated tubules with flattened epithelium. H. & E. × 73.



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