THE EFFECT OF TESTOSTERONE ON THE KIDNEY

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In the course of our experiments with testosterone, we became aware of the fact that the kidneys of mice receiving large doses of this hormone are usually greatly enlarged. Perusal of the literature revealed no relevant papers except a communication of Korenchevsky and Dennison (1934) who claimed that the kidneys of castrate male rats are slightly subnormal in weight and that treatment with commercial androgenic extracts (method of preparation not stated) may restore their size toward normal. We decided to make a systematic study of the effect of testosterone on the kidney and the present report summarizes our observations on this subject.[1]

In the first experiment, 6 normal adult female albino mice were treated with 0.5 mg. of testosterone propionate in 0.1 cc of Mazola oil daily subcutaneously during 10 days. Then the dose was doubled, 1 mg. being injected during a further period of 6 days. On the seventeenth day, all these animals and 6 controls were killed. Table 1 shows the great increase in the weight of the kidneys of the treated animals in comparison with the controls.

In order to see whether other strains of mice would respond in a similar manner, a group of 7 adult grey females of the Bar Harbor dba strain were treated with 5 mg. of testosterone propionate in 0.2 cc of Mazola oil daily subcutaneously during a period of 20 days. On the twenty-first day, these and 6 untreated controls were sacrificed and the weights of their kidneys are shown in table 2.

It is clear that under the experimental conditions of this second group, testosterone also caused a marked increase in kidney weight but although these animals received much higher doses of the hormone, the average weight increase was not larger (in fact, it was somewhat less pronounced) than in the previous group.

[1] The expenses of this investigation were defrayed in part through a grant in aid received from the Schering Corporation, Bloomfield, N. J. The author is especially endebted to Drs. G. Stragnell and E. Schwenk of the above Corporation for the testosterone propionate used in these experiments.

Note: Since this report went to press, we were able to show that testosterone exerts a similar action on the rat kidney. It was found furthermore that in mice, desoxycorticosterone and progesterone likewise cause kidney enlargement, although their effect is not as marked as that of testosterone.

TABLE 1

UNTREATED CONTROLS			TESTOSTERONE-TREATED ANIMALS		
No. of animals	Body weight	Kidney weight	No. of animals	Body weight	Kidney weight
	gm.	*mg.*		*gm.*	*mg.*
1	24	300	1	32	640
2	31	540	2	26	610
3	36	562	3	28	710
4	27	384	4	32	690
5	30	410	5	26	680
6	28	290	6	26	590
Average	29.3	414.3	Average	28.3	653.3

TABLE 2

UNTREATED CONTROLS			TESTOSTERONE-TREATED ANIMALS		
No. of animals	Body weight	Kidney weight	No. of animals	Body weight	Kidney weight
	gm.	*mg.*		*gm.*	*mg.*
1	21	380	1	23	568
2	26	484	2	24	700
3	26	530	3	20	558
4	25	406	4	21	610
5	26	490	5	21	552
6	30	486	6	23	636
7	35	532	7	24	644
Average	25.5	472.6	Average	22	609.7

TABLE 3

CHOLESTEROL-TREATED ANIMALS			TESTOSTERONE-TREATED ANIMALS		
No. of animals	Body weight	Kidney weight	No. of animals	Body weight	Kidney weight
	gm.	*mg.*		*gm.*	*mg.*
1	15	422	1	20	562
2	20	288	2	20	562
3	17	282	3	23	450
4	21	320	4	24	442
5	18	320	5	22	430
6	21	282	6	20	560
7	20	314			
8	25	402	Average	21.5	501
9	23	324			
10	12	314			
11	18	312			
12	18	312			
Average	19	324.3			

The question arose whether this action on kidney tissue is a specific property of testosterone or whether it could also be obtained with other sterols. We, therefore, selected a group of 6 young female mice who re-

FIG. 1

FIG. 2

FIG. 1. Cross section through kidney of untreated mouse. (Magnification 12×.)
FIG. 2. Cross section through kidney of mouse which received 20 daily injections of 5 mgs. of testosterone propionate. Note marked enlargement of renal cortex. (Magnification 12×.)

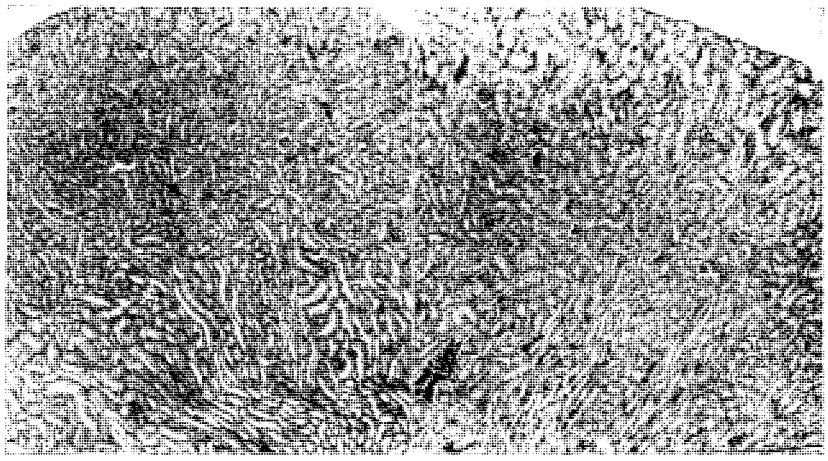

FIG. 3 FIG. 4

FIG. 3. Portion of renal cortex of an untreated mouse. (Magnification 50×.)
FIG. 4. Portion of renal cortex of mouse shown in figure 2. Note hypertrophy of various convoluted tubules. (Magnification 50×.)

ceived 3 mg. of testosterone propionate in 0.2 cc of Mazola oil subcutaneously daily during a period of 14 days while 12 controls were treated with the same amount of cholesterol administered in the same solvent during the same length of time. Table 3 summarizes our findings.

These figures show that cholesterol does not have the same action on the kidney as testosterone propionate. We must assume, therefore, that the male hormone exerts a specific action on kidney tissue.

Histological studies of the kidneys (figs. 1 to 8) of testosterone-treated mice showed that most of the increase in the weight of these organs is due to marked hypertrophy of the epithelial cells of the proximal and

FIG. 5

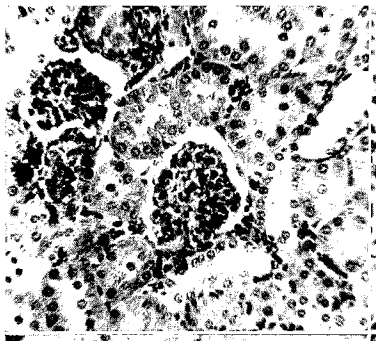

FIG. 6

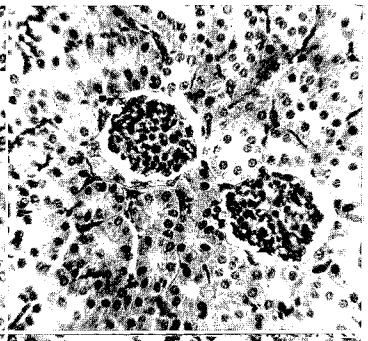

FIG. 7

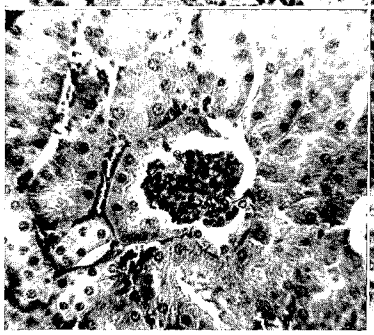

FIG. 8

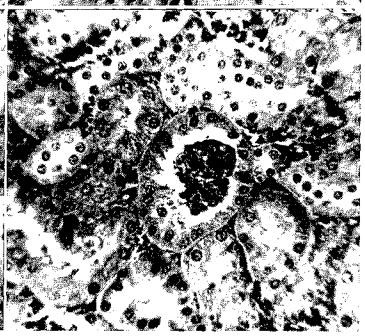

FIG. 5. Glomerulus from kidney of normal mouse. Note flat endothelium-like lining of the parietal lamina of Bowman's capsule. (Magnification 250×.)

FIG. 6. Two adjacent glomeruli from kidney of normal mouse. Epithelium lining parietal lamina of Bowman's capsule of left glomerulus in this picture was highest observed in this kidney. (Magnification 250×.)

FIG. 7. Glomerulus from kidney shown in figure 2. Note hypertrophied capsular epithelium which shows a well developed brush border. (Magnification 250×.)

FIG. 8. Glomerulus from kidney shown in figure 2. Capsular epithelium in this case is also unusually high and free surface rather irregular. (Magnification 250×.)

distal convoluted tubules. As a result of this enlargement, the cortex of the kidney is greatly thickened. The glomeruli themselves, show no very striking deviation from the normal but the normally thin layer of epithelium which lines the parietal lamina of Bowman's capsules shows marked signs of hypertrophy. These lining cells are usually so flat that it is quite difficult to see them under low magnification except in the immediate vicinity of their transition into the proximal convoluted tubules.

In the testosterone-treated animals, on the other hand, these cells are usually greatly enlarged and assume the appearance of a high cuboidal or low cylindric epithelium with a brush border similar to that seen in the proximal convoluted tubules themselves. Degenerative lesions or any other changes suggestive of kidney damage were never observed in the testosterone-treated mice.

While there appears to be no doubt about the fact that testosterone exerts a characteristic and specific action on kidney tissue, it is difficult to evaluate the significance of this finding. It is possible that the male hormone causes such metabolic changes as would necessitate increased kidney function. In this case, the changes in the kidney would have to be considered as secondary in nature. On the other hand, it is also possible that the hormone exerts a specific physiological trophic influence on kidney tissue. If the latter assumption be correct, it might be possible to improve kidney function by the administration of this substance.

SUMMARY

Experiments in the mouse indicate that testosterone propionate given during a period of 2 to 3 weeks causes marked enlargement of the kidneys in the mouse. Histologically such kidneys are characterized by pronounced hypertrophy of the epithelium of the proximal and distal convoluted tubules and of the epithelium lining the parietal lamina of Bowman's capsules.

REFERENCE

KORENCHEVSKY, V., AND M. DENNISON: Biochem. J. **28:** 1486, 1934.