GLOMERULAR LESIONS PRODUCED IN THE RABBIT BY PREDNISONE AND PREDNISOLONE

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After administration of cortisone to rabbits for short periods, kidney lesions with some morphologic features of diabetic glomerulosclerosis have been described by Rich and his co-workers,2 by Bloodworth and Hamwi,3,4 and by Wilens and Stumpf.5 The histologic changes consist of striking glomerular capillary dilatation and nodular glomertular lesions which stain positively with periodic acid-Schiff (PAS) stain, fat stains, and fibrin stains. Deeply staining amorphous casts are frequently noted in various portions of the renal tubular system. In the course of studies on the nature and significance of these lesions the effects of steroids other than cortisone on rabbit kidney morphology were investigated. This report deals with experiments carried out using the,1 synthetic steroids, prednisone and prednisolone)1 These substances are reported to have greater anti-inflammatory activity than cortisone, while exerting negligible effects on carbohydrate or electrolyte balance.6

Material and Methods

Twenty-four male New Zealand white rabbits were employed. Six were normal animals, and ten had been made diabetic six weeks previously with a single intravenous dose of alloxan monohydrate. The left kidney of each of these 16 animals was removed with use of pentobarbital (Nembutal) and ether anaesthesia to serve as control material.

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Results

The animals were maintained on Sherwood feed unsupplemented by cyanocohalamin (vitamin B12) or chlortetracycline (Aureomycin) and were provided with 1% sodium
chloride solution as drinking water. The diabetic group received 10 mg. of prednisone suspension intraperitoneally each day and the nondiabetic group, 5 mg. Wherever the condition of the animal permitted the steroid was continued for a period of 21 days.

A further group, of eight rabbits, received a daily intraperitoneal injection of 5 mg. of prednisolone suspension. After 21 days the left kidney was removed, and the animals continued to be given 15 mg. of prednisone intraperitoneally each day for a further 21 days. These animals were maintained on a similar feed but were provided with ordinary tap water ad libitum.

In all groups, body weight, nonfasting blood glucose, and 24-hour urine glucose were measured twice weekly. Blood pressure was measured in the prednisone-treated nondiabetic group by auscultation over the aorta below a pediatric sphygmomanometer cuff. Kidney slices were fixed in formol and Zenkerformol, sectioned at 2.5µ, and stained with hematoxylin, phloxine, and saffron. Additional sections were stained with PAS, oil red 0, masson richrome, and phosphotungstic acid and hematoxylin.

Results

The blood sugar level in the diabetic rabbits ranged between 200 and 570 mg. per 100 cc. and was unaffected by prednisone administration. The blood sugar level of the nondiabetic animals receiving either prednisone or prednisolone remained within normal limits. In all cases the body weight remained essentially unchanged throughout the experiment. The nondiabetic rabbits given Prednisone were found to have a mean maximum blood pressure increase of 31 mm. of mercury systolic and 33 mm. of mercury diastolic. All animals were noted to excrete
amber urine containing a large quantity of sediment. The urine was not found to react with benzidine.

The kidneys removed at time of autopsy presented a petechial mottling on the capsular and cut surfaces of the cortex; no other gross alteration was observed. All animals which had received prednisone and/or prednisolone for 21 days showed characteristic alterations indistinguishable from those observed with cortisone by ourselves anti others \(^2\text{-}^5\) (Figs. 1 and 2). Kidneys from the diabetic group of animals presented, in addition, evidence of acute pyelonephritis and tubular-cell calcium accumulation.

While the effects of prednisolone and cortisone were similar, those of prednisone at the dosages employed were more numerous and severe. Preexisting diabetes and the presence of hypertension had no significant influence on the severity or frequency of lesions.

**Comment and Conclusions**

Our own histologic studies have led us to agree with those authors \(^2\text{-}^1\text{,}^8\) who find that the cortisone-induced lesions of the rabbit kidney resemble those of human diabetic glomerulosclerosis. A relationship is suggested too by recent studies of Sommers and Haley,\(^9\) who have demonstrated in the glomeruli and arterioles of nondiabetic humans and animals treated with cortisone the presence of an abnormal
substance identical in ultraviolet absorptive properties with the nodules of human intercapillary glomerulosclerosis. The present study demonstrates that the, substituted steroids, prednisone and prednisolone, can produce similar kidney damage to that observed in our cortisone studies. It is particularly significant that these lesions occur in nondiabetic animals and are not influenced by alloxan diabetes or experimental hypertension.

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REFERENCES


