

HISTOLOGICAL CHANGES IN THE KIDNEYS IN PROLONGED ALLOXAN PREDIABETES AND IN LATENT AND MANIFEST DIABETES

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Histological investigation of rat kidneys 14-18 months after administration of alloxan revealed changes corresponding to diffuse glomerulosclerosis of varied severity, irrespective of the form of insular insufficiency - prediabetes, latent and manifest diabetes.

KEY WORDS: alloxan diabetes; kidneys; glomerulosclerosis.

There is much evidence in the literature on changes in the kidneys in manifest diabetes mellitus in man [1, 4, 9, 13, 14], whereas kidney lesions in latent diabetes and, in particular, in prediabetes have been inadequately studied [7-9]. However, the study of these early stages is particularly important for the institution of prophylactic measures. Since one of the earliest stages of diabetes (prediabetes) is diagnosed retrospectively in man, its experimental study is of undisputed interest. Changes corresponding to diffuse and nodular diabetic glomerulosclerosis in man have been described in monkeys [10], dogs [6, 12], and hamsters [5, 11] in the course of prolonged alloxan diabetes.

The effect of different degrees of insufficiency of the islet-cell system of the pancreas on the development of changes in the kidneys was studied.

EXPERIMENTAL METHOD

Experiments were carried out on 36 sexually immature female Wistar rats. In order to produce diabetes alloxan was injected subcutaneously in a dose of 170-500 mg/kg by a scheme developed by the writers. The blood sugar was determined by the Somogyi-Nelson method and the 24-hour excretion of glucose in the urine was determined polarimetrically. The period of observation lasted 14-18 months. A glucose tolerance test was carried out (400 mg/100 g body weight by mouth, in a fasting state, followed by determination of the blood sugar 1 and 2 h later) on the animals in which the hyperglycemia and the glucosuria disappeared soon after the experiment began.

The group of animals with prediabetes included 10 rats in which transient alloxan diabetes had been present at a sexually immature age (duration 5-27 days, blood sugar 184-305 mg %, excretion of glucose in the urine 0.8-1.9 g daily), after which a normal blood sugar level and normal glucose tolerance tests had been found. The group of animals with latent diabetes contained nine rats in which persistent normal blood sugar levels and absence of glycosuria also had developed, but the glucose tolerance was disturbed (the blood sugar 1 h after loading was 170 mg % or more, and 130 mg % or more 2 h after loading). In the animals with manifest diabetes (11 rats) there was persistent hyperglycemia (200-360 mg %) and glucosuria (1.5-3.2 g excreted daily).

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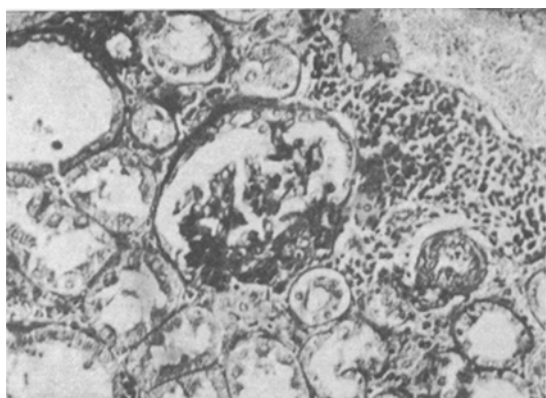


Fig. 1. Kidney in prediabetes. Glomerulus with massive deposition of PAS-positive masses in the mesangium in the center; accumulation of PAS-positive material also in Bowman's capsule; exudate present inside the cavity of the capsule. PAS reaction, 100 \times .

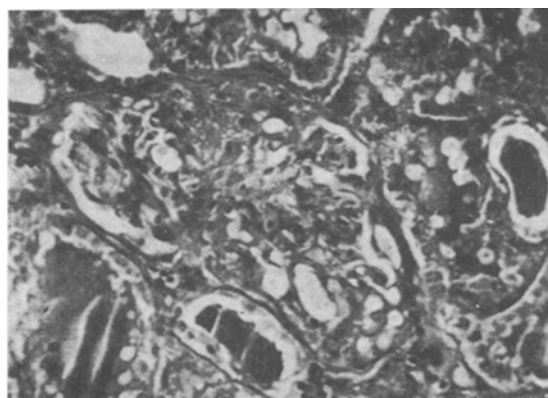


Fig. 2. Kidney in latent diabetes. Large glomerulus in center; lumen of Bowman's capsule is absent; massive accumulation of homogeneously lamellar masses in mesangium. Stained by Van Gieson's method and for elastic fibers, 200 \times .

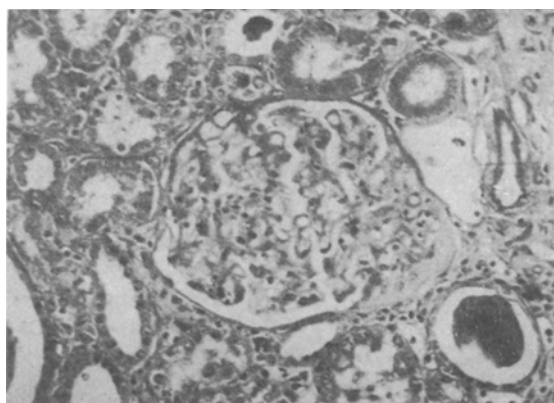


Fig. 3. Kidney in manifest diabetes. Deposits of PAS-positive masses mainly in "handles" of Bowman's capsule and also in mesangium; some loops of capillaries are grossly dilated. Stained by Van Gieson's method and for elastic fibers, 100 \times .

periphery of the lobules, where they formed thickenings. Sometimes deposits of PAS-positive material began at the "handles" of the glomerulus and then spread to all the glomeruli. Bowman's capsule of some glomeruli was thickened as a result of accumulation of PAS-positive masses, and its lumen was frequently filled with similar masses.

Deposition of PAS-positive material could sometimes be seen in the wall of the vessels in the "handle" of the glomeruli. In the diffuse thickening of the mesangium in the glomeruli greatly dilated capillaries with a thin wall were frequently found. When marked changes were present in the kidneys, thickening of the basement membranes was observed in some places in groups of tubules. Degenerative changes were observed in the epithelium of the tubules. If damage to the glomeruli was considerable, the cytoplasm of the tubular epithelium was swollen and granular, no nuclei could be seen in many cells, the tubules were greatly dilated, their epithelium was flattened, and cysts containing strongly PAS-positive casts, staining green or yellowish green by Van Gieson's method and not staining with alcian blue, in their lumen appeared. Usually extensive foci of infiltration by small cells were present in the cortex and medulla of such kidneys. Small foci of small-cell infiltration also were found when the changes in the kidneys were of slight severity.

Sections through the kidneys for histological study were stained with hematoxylin-eosin, by Van Gieson's method, and for elastic fibers, and for fat by Sudan and oil red. The PAS reaction and the reaction with alcian blue were carried out.

EXPERIMENTAL RESULTS

Changes in the kidneys were found in 8 of the 11 rats with manifest diabetes, in 7 of the 9 rats with latent diabetes, and in 7 of the 10 rats with prediabetes and they were similar in character (Figs. 1, 2, and 3). In the case of severe lesions changes were found in a larger number of glomeruli.

Diffuse thickening of the mesangium took place on account of accumulation of PAS-positive material in the glomeruli, which frequently were large. The deposits in the glomeruli stained pinkish-yellow by Van Gieson's method. Considerable deposits in the glomeruli did not stain with alcian blue. The largest accumulations of PAS-positive material were found at the

In all three forms of alloxan diabetes studied, changes corresponding to diffuse glomerosclerosis were detected. Later the nodules typical of diabetic lesions of the kidneys [1, 4-6] may have been formed from the thickenings (resulting from massive deposition of PAS-positive material) at the periphery of the lobules.

Similar changes in the kidneys have also been found in diabetes in man. Such changes give no manifest clinical effects and they are not progressive if the diabetes is well compensated [2, 3].

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