9275 P

Influence of Diet on the Course of Nephrotoxic Nephritis in Rats.

LEE E. FARR AND JOSEPH E. SMADEL. (Introduced by D. D. Van Slyke.)

From the Hospital of the Rockefeller Institute for Medical Research, New York.

While numerous investigations concerning the effect of diet on Bright's disease have been reported, the laboratory approach to this problem has been criticized on the ground that experimental nephritis usually fails to correspond closely with the disease as it occurs in man. The chronic nephritis induced by Masugi[1] in rabbits with anti-kidney serum has reawakened a general interest in nephrotoxins; and with suitable nephrotoxic sera we[2, 3] have induced nephritis in rats, which, in clinical course, disturbance of renal function, and development of pathological picture, resembles human Bright's disease closely enough to permit it being used as a tool for evaluating the effects of diet on the course of nephritis.

Forty-eight young rats were fed a purified diet while renal function studies, plasma protein and hemoglobin determinations, and urinalyses were made by the methods previously employed.[2, 4] Then severe nephritis was induced uniformly in all animals by intravenous injections of anti-kidney serum given on 3 successive days. The animals were divided into 3 comparable groups and fed isocaloric diets. Each diet contained 27% fat, 4% salt mixture and vitamins with the following variations: diet No. 1, 64% carbohydrate and 5% protein; diet No. 2, 51% carbohydrate and 18% protein; diet No. 3, 29% carbohydrate and 40% protein. Lactalbumin served as the protein, Crisco as the fat, and dry Karo powder with cane sugar as the carbohydrate. Observations were continued for 11 months after injection of nephrotoxic serum. Urea clearance determinations and plasma protein values were obtained every third week, hemoglobin values at 3- to 6-week intervals and urine analyses and body weights were recorded weekly.

The course of the nephritis in all 3 groups was parallel for the first month; severe albuminuria and cylindruria appeared and persisted, anasarca was present for from a few days to several weeks; plasma protein values were temporarily depressed; neither the blood

[1] Masugi, M., *Beitr. path. Anat. u. allg. Path.*, 1933, **92**, 429.

[2] Smadel, J. E., and Farr, L. E., *J. Exp. Med.*, 1937, **65**, 527.

[3] Smadel, J. E., *J. Exp. Med.*, 1937, **65**, 541.

[4] Farr, L. E., and Smadel, J. E., *Am. J. Physiol.*, 1936, **116**, 349.

urea nor the urea clearance was significantly altered except in those animals (one in each group) that succumbed during the acute phase.

In the second month evidences of nephritis diminished greatly or disappeared in all but 2 animals on diet No. 1 (low protein). The sudden death of these 2 rats in the fifth month, without antecedent renal failure, seemed attributable to severe acute liver necrosis of unexplained origin. Eight and a half months after injection none of the 13 surviving rats fed diet No. 1 had elevated blood urea or depressed urea clearance values; moreover only one animal had urine abnormalities of even moderate degree. At this point 5 of the apparently recovered rats were changed from diet No. 1 to diet No. 3 and, in the ensuing 2 months, 3 of the animals developed moderate albuminuria with some casts, but neither the urea clearance, blood plasma nor hemoglobin were depressed. Growth was retarded in the animals on diet No. 1 and was never as great as in rats on the other diets.

Every animal fed diet No. 3 developed progressive nephritis. Only 2 animals, both in terminal phases of the disease, were still alive when the experiment was stopped; the rest died of apparent renal failure, averaging 6 months survival after injection.

Of the rats fed diet No. 2, one recovered completely during the second month, 6 had abnormal urinary findings throughout the period; 8 of the 15 rats that survived the acute phase of the disease died of apparent kidney failure; the time of death averaged 5½ months after the initial injury.

Diagnosis of renal failure was based on progressive fall of the urea clearance and rise in the blood urea levels. Terminally the majority of the rats with progressive nephritis showed also anemia, polyuria, and weight loss.

Pathological lesions found in nephritic rats fed diet No. 2 were practically identical with those previously described[3] in rats with this type of nephritis kept on an ordinary mixed diet. Renal scarring was more intense in the group fed diet No. 3 while the rats that received diet No. 1 and recovered clinically had slight renal damage represented by old scarring. Generalized vascular lesions resulting in secondary degenerative changes, especially in the heart, occurred in most of the animals with progressive nephritis.

Conclusions. 1. Under certain conditions chronic progressive nephritis follows a *single* insult to the kidney. 2. The course of nephrotoxic nephritis in rats can be markedly influenced by diet.