9059

Cytotoxic Glomerular Nephritis in Rabbits—a Non-Allergic Condition.

W. E. EHRICH. (Introduced by E. B. Krumbhaar.)

From the Department of Pathology, School of Medicine, University of Pennsylvania.

The important discovery of Masugi[1] that in rabbits and rats glomerular nephritis can be produced by intravenous injections of anti-kidney serum has been confirmed by Fahr[2] and his pupils Hemprich[3] and Weiss,[4] in rabbits; by Arnott, Kellar and Matthew,[5] in rabbits; and by Farr and Smadel,[6, 7] in rats. It has been shown that the animals develop albuminuria (up to 30%, Esbach), hematuria, cylindruria, lipuria, moderate oliguria or occasionally anuria (in acute stages), moderate edema, rise in blood urea (up to 224 mg. %), rise in blood pressure, cardiac hypertrophy, and anemia, and that at autopsy the kidneys exhibit extensive glomerular lesions which closely resemble those of human glomerular nephritis.

Masugi injected 10 cc. of a 10 to 30% suspension of blood-free kidney juice of rabbits in saline solution into the peritoneal cavity of ducks, and that 18 to 30 times at intervals of about 5 days. Five to 8 days after the last injection serum was prepared, and after inactivation by heating to 56°C. for 30 minutes, was injected intravenously once or repeatedly into rabbits in doses of 5 to 15 cc. Most rabbits received more than 15 cc. of serum. Hemprich suspended the juice of 2 kidneys in 100 cc. of saline solution. Of this suspension, 10 cc. were injected into ducks 9 to 22 times at 4 to 8 days' intervals. The serum of these animals was injected into rabbits in doses of 3.5 to 26 cc. Most rabbits received more than 10 cc. of serum. Weiss improved the method by thoroughly squeezing the remnants of the ground up kidneys while preparing the juice. He produced glomerular nephritis already with doses of 3 to 7 cc. of ducks' serum, in most cases with 4 to 5 cc. Arnott, Kellar and Mat-

1 Masugi, M., *Beitr. Path. Anat.*, 1933, **91** 82; 1934, **92**, 429.

2 Fahr, Th., *Verh. Deutsch. Path. Ges.*, 1935, **28**, 179; *Klin. Wchnschr.*, 1936, **15**, 505.

3 Hemprich, R., *Z. ges. exp. Med.*, 1935, **95**, 304.

4 Weiss, A., *Beitr. Path. Anat.*, 1935, **96**, 111.

5 Arnott, W. M., Kellar, R. J., and Matthew, G. D., *Edinburgh Med. J.*, 1936, **43**, 217.

6 Farr, L. E., and Smadel, J. E., *J. Clin. Invest.*, 1936, **15**, 449.

7 Smadel, J. E., *Am. J. Path.*, 1936, **12**, 742.

TABLE I.
The Production of Glomerulonephritis by Antikidney Serum in Rabbits.

Preparation of Serum					Production of Glomerulonephritis					
Duck No.	Duck weight (gm.)	Dose of kidney juice (cc.)	No. of doses given	No. of days treated	Rabbit No.	Rabbit weight (gm.)	Dose of serum (cc.)	Killed days after injection	Glomerulo-nephritis	No. of Glomeruli affected %
1	2400	5	16	60	93	1550	7	93	+	13
2	2450	5	20	77	36	1880	3.5	47	+	82
					34	2000	7	Died within 24 hours		
4	2270	10	16	60	94	1560	3.5	63	+	84
					42*	1540	5.0	14	+	68
					96	1480	7.0	Died within 24 hours		
3	2750	10	20	77	35	1660	3.5	63	+	8
					33	2040	7.0	47	+	42

*Injected with a serum which was preserved by the lyophile process of Mudd (*J. Immunol.*, 1935, **29**, 389), and kept for 80 days.

thews, using the original method of Masugi, injected the ducks 25 to 40 times.

Since the experimental production of glomerular nephritis is an actual problem, additional information may be welcome. It may be permitted, therefore, to present the following preliminary data:

The kidneys of a freshly killed rabbit were perfused *in situ* with sterile saline solution until they appeared to be free of blood. Then they were ground in a mortar and the juice thus prepared was diluted with 60 cc. of sterile saline solution. After centrifugation, the ground kidney remnants were thoroughly squeezed with 2 forceps, and their juice added to the supernatant fluid of the centrifugate. The suspension then was injected intraperitoneally into Peking ducks in doses of 5 or 10 cc. at intervals of 4 to 5 days for 60 to 77 days (16 to 20 injections). Four days after the last injection the ducks were decapitated, the blood collected, and the serum inactivated by heating to 56 C. for 30 minutes. The serum then was injected intravenously into rabbits in doses of 3.5 to 7 cc., each rabbit receiving one injection only.

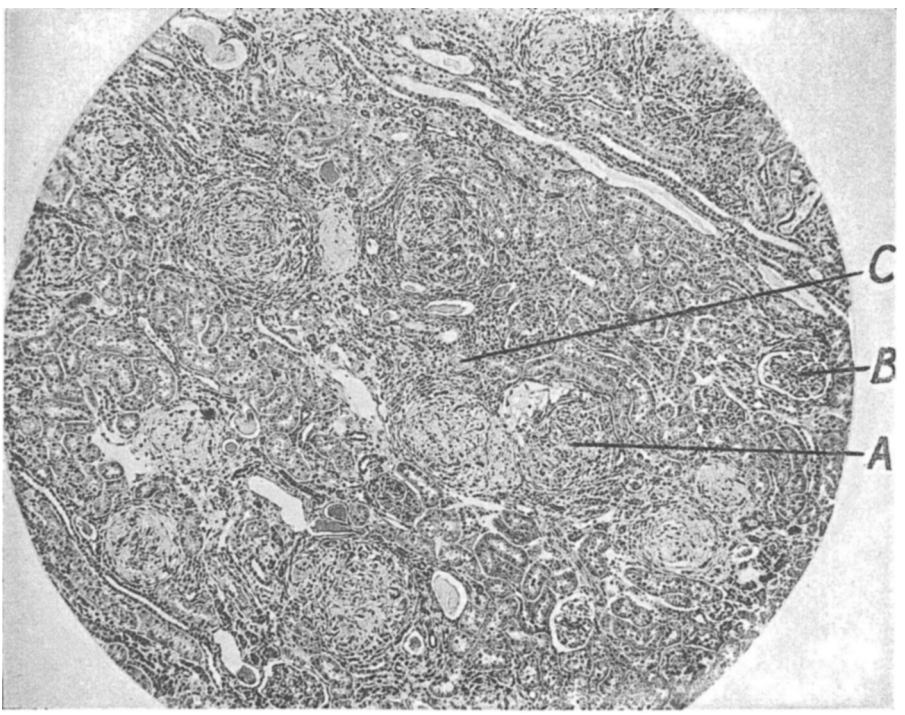

FIG. 1.

Experimental glomerular nephritis. Hematoxylin-Eosin, × 70. Most glomeruli are much enlarged and badly damaged (A); some appear to be normal (B); many tubules contain casts (C).

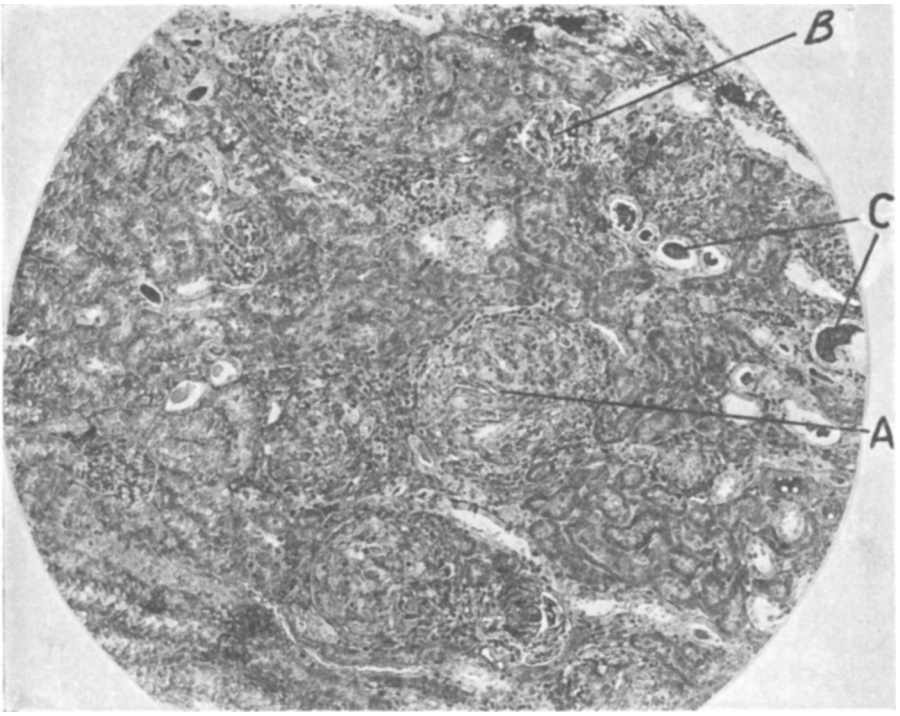

FIG. 2.
Experimental glomerular nephritis. Azur II, × 100. For description see Fig. 1.

The results of the experiments are given in Table I. With the exception of 2 rabbits which died within 24 hours after the injection, all rabbits developed glomerular nephritis. The larger the dose injected and the more powerful the serum, the greater the number of glomeruli affected. That the histological changes closely resemble those of human glomerular nephritis, is shown in Figures 1 and 2. The clinical findings were: albuminuria, oliguria, temporary rise in blood urea, temporary anemia and edema. The urinary sediment and the blood pressure were not studied.

Concerning the nature of the nephritis produced, it should be noted that the lesions were focal in all instances. As compared with human glomerular nephritis, the changes resembled not so much those of diffuse hemorrhagic glomerular nephritis as those of focal glomerular nephritis as observed in bacterial endocarditis. Concerning the etiology of our disease, it may be emphasized that all the rabbits received one injection only. This glomerular nephritis, therefore, can not be looked upon as an allergic disease, as done by Masugi and others; it rather should be classified as a toxic disease, the toxin being a specific antibody, a so-called cytotoxin.