problem. These results are very similar to what was observed in the guinea pig (10) where it was shown that both the γG1 and γG2 antibodies are transmitted from mother to fetus.

Summary. Passively transmitted homologous γG1 and γG2 antidinitrophenyl antibodies to pregnant mice near term pass into the circulation of fetuses. With the amounts of antibodies used, γG1 and γG2a are detected in the sera of fetuses 6 hr after intravenous injection of the mothers.

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Uric Acid Nephropathy: An Experimental Model (33593)

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In a previous paper[1] it was shown that oxonic acid is a potent *in vivo* inhibitor of uricase. This compound, administered orally or intraperitoneally to rats, gave rise to a marked increase in plasma and urine uric acid levels with a concomitant decrease in urinary allantoin. A greater than twentyfold increase in urinary uric acid with deposition of uric acid in the kidney tubules was observed in rats maintained on a diet containing both oxonic acid and uric acid. The associated nephropathy, which in several respects resembles uric acid nephropathy in the human (1–3), is described in the present paper.

Methods. Male rats (175–200 g) of the Wistar strain were used. The control group was fed a diet of commercial rat cubes pulverized in a mechanical blender. The second, third, and fourth groups were fed the same diet into which was blended 5% oxonic acid; 1% uric acid; and 5% oxonic acid plus 1% uric acid, respectively. Water was freely available. The rats were on test for varying periods of time up to 28 days.

Histologic sections. The kidneys were exposed under deep ether anesthesia and removed for histologic study. After clamping the right renal artery and vein with a hemostat, the right kidney was removed and placed in 10% formal saline solution. The posterior vena cava was then severed, a needle was inserted into the aorta at the bifurcation of the iliac arteries, and 10% formal saline was used as a perfusate for the left kidney. Formalin-fixed tissues were stained

[1] Johnson, W. J., Starvic, B., and Chartrand, A. P.S.E.B.M. (in press, April 1969, 33791).

with hematoxylin–phloxine and saffron. Sections from frozen kidney were stained with Paragon multiple stain and examined microscopically under polarized light for evidence of uric acid crystallization.

Results. The kidney uric acid content of control rats and those receiving 1% uric acid or 5% oxonic acid in the diet for a period of 23 days was in the order of 5 mg/100 g (wet wt.) of tissue[1]. In the rats consuming the diet which contained 5% oxonic acid plus 1% uric acid the urinary uric acid output was 46.6 mg/24 hr (22 times control) by day 20. The kidney content of uric acid was 72 mg/100 g (wet wt.) of tissue. In view of the fact that the stable solubility of urate in the serum is 6.5 mg/100 ml, and allowing for some degree of supersaturation, it would be physically impossible for a uric acid concentration of 72 mg/100 g to be present in the kidney wholly in soluble form. Consequently, it was anticipated that histological examination would reveal uric acid crystallization in the kidneys.

Gross pathology. The kidneys from all rats except those on the diet containing 5% oxonic acid plus 1% uric acid were normal in appearance. The kidneys of the latter were enlarged, and weighed 20% more than the controls. They were irregularly discolored with light and dark mottling. The capsule was easily removed. Sagittal sections revealed multiple straight, white or yellow radiating streaks in the medulla, sometimes extending to the inner cortex (Fig. 1). This had the effect of markedly delineating or accentuating the medullary striations. Wedge-shaped areas of erythema alternating with ischemic areas were occasionally seen in the medulla and cortex. The ureters and pelvis were examined with the aid of a stereoscope; calculi were not observed in these structures in animals on test up to 28 days.

Microscopic pathology. Histologic alterations were present in the rats on the oxonic–uric acid diet after 2 weeks on test. Uric acid was identified in frozen sections, examined under polarized light, as multiple granular birefringent crystals concentrated mainly within the medullary tubules (Fig. 2). No

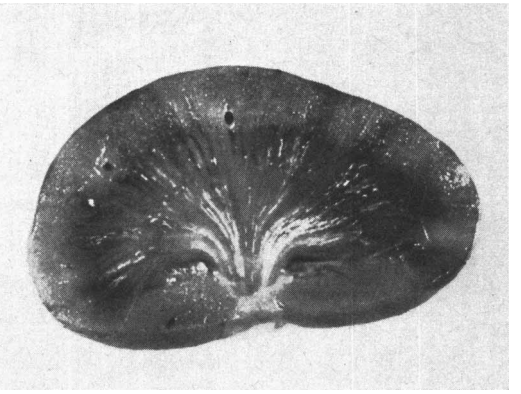

FIG. 1. Hemisected kidney from a rat fed 5% oxonic acid and 1% uric acid in diet. White radiating streaks in the medulla extending into outer cortex can be seen.

such crystals were present in the kidneys of the rats fed the diet containing oxonic acid or uric acid individually. The crystals were lost in routinely processed formalin-fixed material and alterations consisted principally in a distention of the collecting tubules of the medulla. The greatest distention was in the tubules of the outer medulla, but those of the inner medulla and inner and outer cortex were also affected (Fig. 3). The epithelial cells lining the tubules were generally flattened and were absent from some tubules, leaving only the basement membrane. In other tubules the epithelial cells appeared hyperplastic. Some tubules contained nonrefractile debris in which the ghost outline of the epithelial cells could be recognized. In other tubules there were aggregates of polymorphonuclear leukocytes. Interstitial infiltration of leukocytes was quite marked in some areas (Fig. 4), and was confined to the medullary region.

At 3 weeks there were no remarkable changes beyond those previously noted, the difference being quantitative rather than qualitative. Kidneys from animals killed at 4 weeks had more advanced changes. Collections of leukocytes were seen in the cortical tubules and the interstitial areas of the cortex, as well as in the medulla. Some proliferation of fibrous tissue was evident in the medulla, and collecting tubules were more tortuous. Atro-

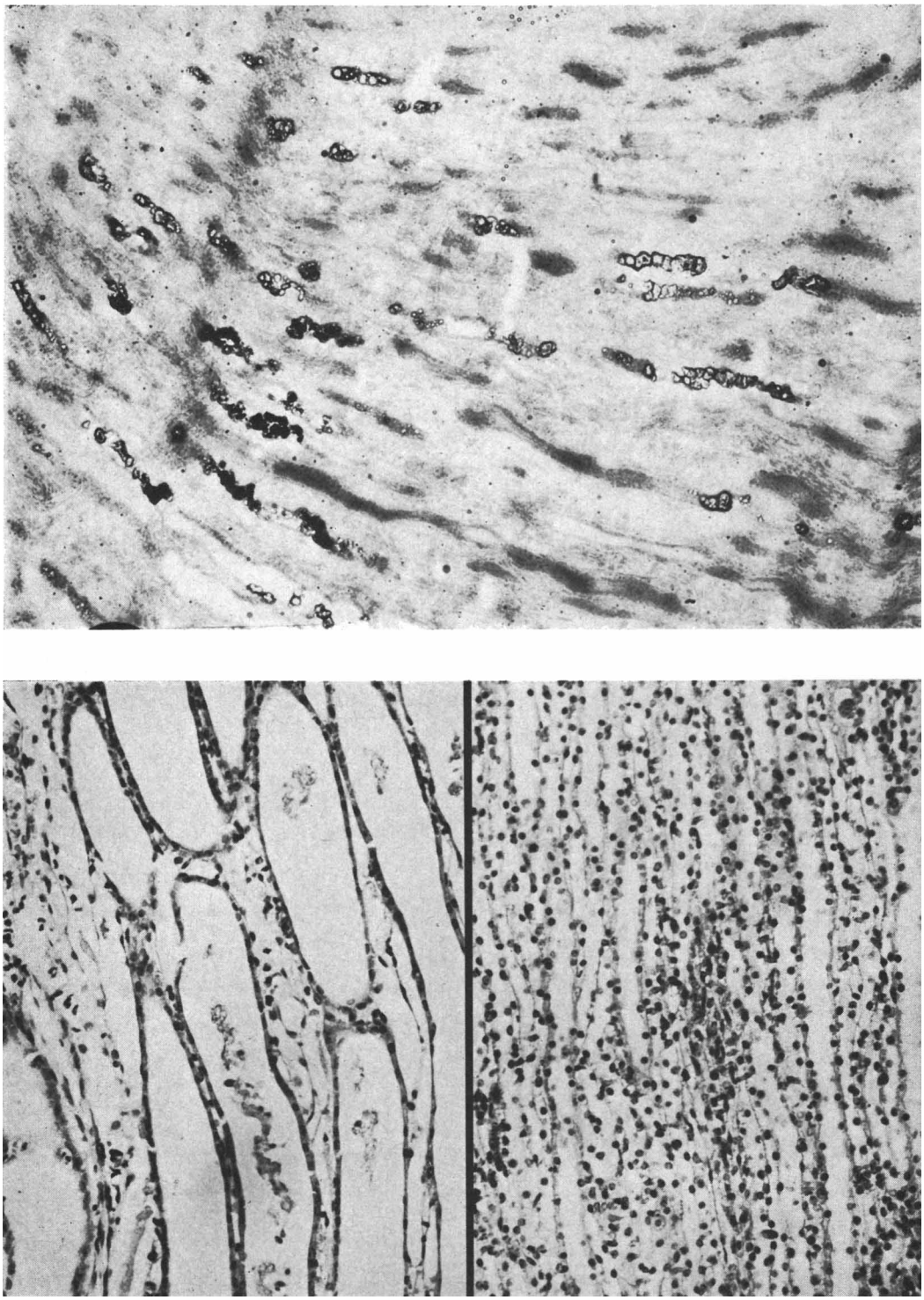

FIG. 2. (top) Section through medulla of kidney shown in Fig. 1. The birefringent crystals are contained mainly within the medullary tubules; frozen section, polarized light; ×40.

FIG. 3. (bottom) Section through medulla of a control rat (right) and a rat fed 5% oxonic acid and 1% uric acid in the diet (left). The distention of medullary tubules in the kidney from treated rats is apparent; hematoxylin–phloxine–saffron stain: × 50.

phic, degenerative changes, and loss of tubular epithelium was evident.

Discussion. Grimes (4) found no deposition of uric acid in the kidneys of rats fed 1 g of uric acid/day for 21 days. In the present study, extensive uric acid deposition occurred on a uric acid intake of 200 mg/day, but only when oxonic acid was present as uricase inhibitor. Duncan *et al.* (5) produced a remarkably similar uric acid nephropathy in rats by giving daily intravenous injections of large doses (500 mg/kg) of uric acid for 3 consecutive days. The major damage appeared to be due to precipitation of urates in the collecting tubules and distal convoluted tubules, causing mechanical blockage. Proximal tubular dilation and epithelial cell damage appeared to be secondary effects. These effects, it should be noted, were produced by flooding the kidneys with sudden large concentrations of uric acid. However, our experiments show that similar lesions can be produced in rats by chronic exposure of the kidneys to lower concentrations of uric acid, which more closely resemble the human hyperuricosuric condition.

These studies tend to support the concept, now widely held, that the nephropathy of gout is caused by the deposition of urates resulting from an increased filtered load of uric acid by the kidneys, and that the associated pyelonephritis is secondary to the obstruction of collecting tubules by urate deposits (1, 2, 6, 7).

Summary. A nephropathy was experimentally induced in rats by feeding a diet con-

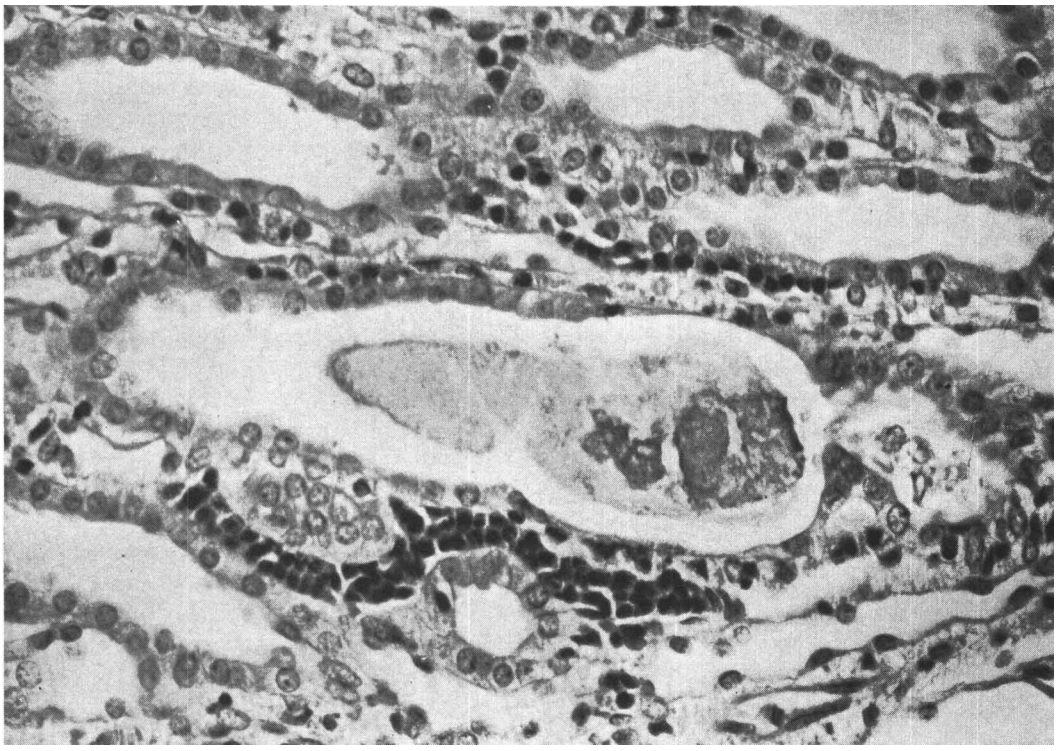

FIG. 4. Section through medulla of a rat fed 5% oxonic acid and 1% uric acid in the diet. Amorphous granular debris contained in a distended tubule; epithelial cells lining the tubule are flattened in one area; inflammatory cells are present in the interstitium; hematoxylin–phloxine–saffron stain; ×100.

taining uric acid and oxonic acid, a uricase inhibitor. It was characterized by hyperuricemia, hyperuricosuria, deposition of uric acid in the kidney tubules, distention of tubular lumens, and early tubular and interstitial nephritis, and thus could serve as a useful experimental model for uric acid nephropathy.

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Heterologous Transfer of Amyloid—Human to Mouse* (33594)

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Isologous (1–4) and homologous (4) transfer of amyloid in mice was recently reported. These studies indicated that casein-sensitized donor spleen cells whether living or dead can induce amyloidosis in recipient mice within 3–7 days following intravenous or intraperitoneal injection. In addition, serum from sensitized isogenic donor mice was also reported to accelerate induction of amyloidosis in the X-irradiated recipient model (4). The sum total of the above experiments has been (a) the introduction of the concept of a transfer factor in the spleen homogenate or serum of the donor which is responsible for accelerated induction of amyloidosis, and (b) greater interest in its isolation and characterization in an attempt to understand further the pathogenetic mechanism of this disease, a disorder of increasing clinical and investigative significance (5,6). We recently confirmed many of the above facts. From our experiments, however, it was apparent that use of immunosuppressive agents may be unnecessary in this transfer system whereas both of the recipient models reported to date were treated with immunosuppressive agents, viz., X-irradiation or nitrogen mustard (1–4). This new recipient model without use of immunosuppressive agents may be more useful for the study of the nature of amyloid transfer factor, because it removes variables that were already shown to enhance amyloidosis in the induction model (6–8). This communication reports the successful heterologous transfer—human to mouse—of amyloid, again using a recipient model untreated by immunosuppresive agents.

Materials and Methods. Three human spleens were obtained at autopsy from patients with primary, secondary, and myeloma-associated amyloidosis respectively, and were stored at —10°. One nonamyloidotic human spleen was used as a control. 1.0 g (wet wt.) of spleen was homogenized in 2.0 ml of cold physiological saline solution with a Potter–Elvehjem homogenizer. One-ml ali-

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