casein level exerts on the skin lesions produced in the vitamin B_6 deficient rat not receiving desoxypyridoxine(8). The results obtained with the methionine supplement are not surprising in view of our observations on rats(9) which clearly showed the deleterious effect of sulfur amino acids on the vitamin B_6 deficient animal.

In contrast to the anti-vitamin action shown by desoxypyridoxine, methoxypyridoxine exhibits pyridoxine activity in the mouse. Thus, the mouse differs from the chick in its reaction to this analogue. The results of Porter and co-workers(3) are of interest in this connection in that they give evidence for both a vitamin and anti-vitamin action of this compound in rats. Results of experiments now in progress in our laboratory indicate that methoxypyridoxine is not quantitatively cleaved to pyridoxine in the mouse, since injection of an amount equivalent to 2 γ pyridoxine (which gives a fairly good growth response in the vitamin B_6 deficient mouse (Table III)) is without effect.

Summary. (1) Desoxypyridoxine has been shown to exert a powerful antipyridoxine effect in the mouse. With the aid of this substance, typical symptoms of vitamin B_6 deficiency (acrodynia) have been produced in this species. (2) A high casein level in the diet was found to have a detrimental effect on the acrodynia thus produced, but not to the same extent as that observed in the case of the acrodynia of vit. B_6 deficient rats, not receiving desoxypyridoxine. Methionine, in amounts equivalent to those present in the casein, had a corresponding detrimental effect. (3) The pyridoxine requirement of the mouse was found to be, under the conditions of our experiments, between 1 and 2 γ per day. (4) For mice receiving 2 γ pyridoxine per day, the inhibition index of desoxypyridoxine was found to be 10. (5) Methoxypyridoxine acts as a pyridoxine precursor in the mouse.

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8. Cerecedo, L. R., and Foy, J. R., *Arch. Biochem.*, 1944, v5, 207.

9. Cerecedo, L. R., Foy, J. R., and De Renzo, E. C., *Arch. Biochem.*, 1948, v17, 397.

Hypoalbuminemia and Renal Lesions in Experimental Hyperglobulinemia.* (17682)

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Recent observations have stimulated interest in the role of proteins in the pathogenesis of renal disease(1-5). This report is concerned with changes in blood serum and kidneys which occur after the intraperitoneal injection of normal rabbit globulin. When the rabbit antipneumococcic serum† employed was subjected to chemical and electrophoretic analysis, it was found to be a 10% globulin solution with a salt content of 0.9% at pH 7.4 consisting chiefly of gamma and traces of beta globulin preserved in 0.4% phenol and 1:50,000 phenyl mercuric borate.

Method. Rabbits weighing 2 to 3 kg were fed pellets, lettuce and water. Fifty to 60 cc of the test material were injected intraperi-

* Work done under a grant from the Joseph and Helen Yeamans Levy Foundation established in memory of their daughter, Miriam Levy Finn.

1. Bywaters, E. G. L., and Beall, D., *Brit. M. J.*, 1941, v1, 427.

2. Flink, E. B., *J. Lab. and Clin. Med.*, 1947, v32, 223.

3. Lucke, B., *Military Surgeon*, 1946, v99, 371.

4. Adams, W. S., Alling, E. L., and Lawrence, J. S., *Am. J. Med.*, 1949, v6, 141.

5. Sussman, R. M., and Kayden, H. J., *Arch. Int. Med.*, 1948, v82, 598.

† Through the courtesy of the Lederle Laboratories Division of the American Cyanamid Corporation.

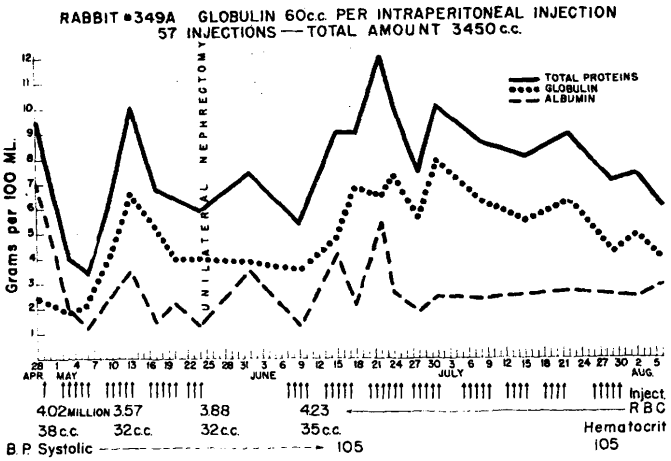

FIG. 1.

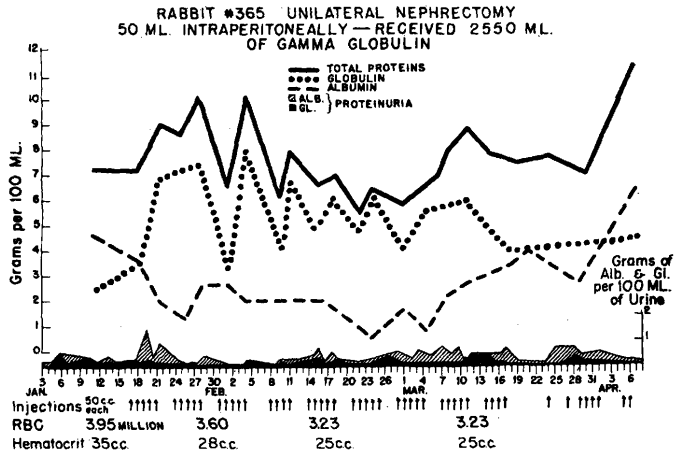

FIG. 2.

The blocked areas represent levels of proteinuria. Urine globulin levels are in black; urine albumin levels are hatched.

toneally daily with interruption over Saturday and Sunday. Nine animals were given globulin and one Ringer's solution. Total daily urine output was recorded 5 days weekly; weekend urine was collected Monday. Unilateral nephrectomy was performed in 4 instances. Four to 5 cc of blood were withdrawn from an ear or by cardiac puncture twice weekly. Serum protein, albumin, globulin(6), blood urea N, cholesterol, hematocrit and erythrocyte counts were estimated, in addition to serum sodium, potassium and cephalin flocculation. The urine total protein, albumin, globulin, urea and chlorides were determined 5 days weekly.

Results. There was a rise in the serum globulin and a fall in the serum albumin in all 9 animals receiving the globulin intraperitoneally for 4 or more days. This was usually sustained for the period during which injections were continued. While there was often a slight rise in the total protein, it rarely approached the marked ascent observed in the globulin level. (Fig. 1,2). As may be seen in Table I, the maximum globulin level was 8.15 g per 100 cc rising from an initial level of 2.54 g per 100 cc. The minimum albumin level was 0.64 g per 100 cc. The mean maxi-

6. Looney, J. M., and Walsh, A., *J. Biol. Chem.*, 1939, v130, 635.

TABLE I.

Globulin received, cc	Initial total protein, g/100 cc	Max. total protein, g/100 cc	Initial globulin, g/100 cc	Max. globulin, g/100 cc	Initial albumin, g/100 cc	Min. albumin, g/100 cc
450	6.40	7.62	1.62	4.75	4.78	1.75
2800*	5.70	10.40	1.37	5.34	4.33	1.56
400	5.82	6.90	1.98	4.85	3.84	2.05
550	5.96	7.88	2.08	5.84	3.88	2.04
600	8.40	8.40	1.97	5.43	6.42	1.56
2850*	7.20	10.16	2.54	8.15	4.65	0.64
350	7.50	5.86	1.56	4.20	5.95	1.66
1100†	8.46	9.58	2.72	6.23	5.73	2.10
3450*	9.48	12.00	2.40	7.81	7.07	1.83
950	8.12	11.60	3.04	6.98	5.08	2.60
Control Ringer's sol.						
1750	5.68	6.42	1.84	1.93	3.84	3.57

* Glomerular and tubular changes.
† Tubular changes only.

mum globulin rose to 2.64 times its original level in the serum, whereas the original albumin level was 2.8 times higher than the mean minimum recorded. In contrast to these findings there was no significant change in the protein levels observed in the control animal which received 27 injections of Ringer's solution. Blood cholesterol, blood urea N, serum sodium and potassium revealed no persistent abnormalities. The rise in globulin could not be associated with changes in the hematocrit or red blood counts.

Urine. The was no constant increase in either albumin or globulin excretion, the average total protein being 0.4 g/100 cc, of which 0.13 g were globulin and 0.27 g albumin. (Fig. 2). Urea content was 0.4 to 2.8%. Chlorides from 0.1 to 1.6%. Daily benzidine tests were constantly negative.

Glomerular Findings. Whereas no characteristic morphologic alterations were observed in animals receiving smaller amounts of globulin, all of the 3 rabbits which received globulin in amounts of 2500 cc or more showed a characteristic lesion in many glomeruli (Fig. 3) consisting of a homogenous nodular coagulum of varying size reminiscent of intercapillary glomerulosclerosis (Kimmelstiel-Wilson)(7). In no instance did these nodules give the tinctorial reactions for amyloid when stained with congo red, methyl violet and iodine.

Tubular Findings. The cells of the proximal convoluted tubules were laden with droplet material (Fig.(3) which represented tubular reabsorptive activity for protein as revealed by the Gram stain(8).‡

Discussion. These data may explain the frequent occurrence of hypoalbuminemia in diseases characterized by hyperglobulinemia such as multiple myeloma, kala-azar, malaria and others. Previous experiments by Dick and Leiter(9) with a rabbit plasma globulin were associated with amyloidosis but no correlation between the total amount of globulin administered and such deposits was evident, the amyloid deposits having been attributed to the denatured globulin. The recent production of glomerulonephritis by the intravenous injection of bovine gamma globulin(10) in rabbits was not paralleled in any of the 9 rabbits. That globulin may be concerned with the Kimmelstiel-Wilson lesion is reflected by the findings of others(11,12) who observed hyper-

7. Kimmelstiel, P., and Wilson, C., *Am. J. Path.*, 1936, v12, **83.**

8. Oliver, J., *J. Mt. Sinai Hosp.*, 1948, v15, 175.

‡ Through the kindness of Professor Jean Oliver, Department of Pathology, Long Island College of Medicine, to whom we are indebted for much guidance.

9. Dick, G. F., and Leiter, L., *Am. J. Path.*, 1941, v172, 741.

10. More, R. H., and Waugh, D., *J. Exp. Med.*, 1949, v89, 541.

11. Schneider, R., Lewis, L. A., and McCullagh, E. P., *Am. J. Med. Sci.*, 1946, v212, 462.

12. Lewis, L. A., Moses, J., and Schneider, R. W., *Am. J. Med. Sci.*, 1947, v213, 214.

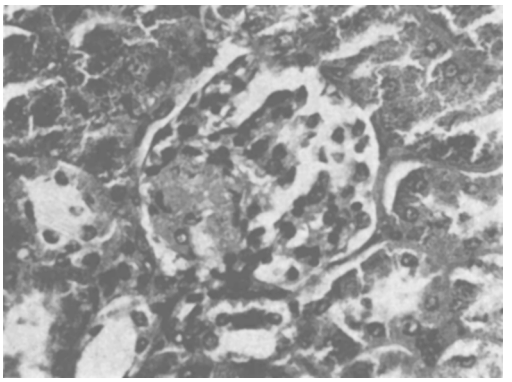

FIG. 3.
Rabbit No. 349 A.
Note the eccentric globoid blomerular lesion. The cells of the proximal convoluted tubules are laden with droplet material of protein origin.

beta-globulinemia and hypoalbuminemia in alloxan treated rabbits and in diabetic humans. This supports the statement of Blackman *et al.*, that hyaline coagula seen in the kidney, not identifiable as fibrin consist chiefly of precipitated globulins.(13)

Summary. (1) Homologous gamma globulin injected intraperitoneally elevated the level of serum globulin and depressed the albumin without inducing significant albuminuria.

(2) Characteristic glomerular and tubular changes occurred in the animals in which protracted hyperglobulinemia was produced.

(3) Serum protein levels reverted to normal when injections were discontinued.

(4) Glomerulonephritis was not present.

(5) The resemblance of the glomerular lesions to the nodular lesion of intercapillary glomerulosclerosis is noteworthy.

13. Blackman, S. S., Jr., Barker, W. H., Buell, M. V., and Davis, B. D., *J. Clin. Invest.*, 1944, v23, 163.

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Effect of Single Inocula of *Endamoeba histolytica* Trophozoites on Guinea Pigs.*† 17683)

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Guinea pigs are very susceptible to infections with *E. histolytica* of human origin. Carrera and Faust(1) reported that 33 out of 34 guinea pigs inoculated into the terminal ileum with doses of 200,000 or more amebae developed typical amebic lesions. Taylor and coworkers(2) found an infectivity rate of 58%, which could be increased up to 100% with certain dietary modifications. In order to study further certain aspects of this host-parasite relationship the following experiments were carried out.

Materials and Methods. A total of 84 guinea pigs of both sexes and of approximately the same weight and age were kept in separate cages through the experiments and were fed mixed Rabbit and Guinea Pig Diet. The operative procedure was the same as that described by Carrera and Faust(1) except that the inoculum was injected directly into the cecal pouch. Aseptic technic was used throughout the operation. A clone which had been isolated some months previously from our strain no. 22 was maintained, together with the bacteria associated with the parent strain, by serial passage every 48 hours in Balamuth's medium(3). The trophozoites used for inoculation were collected by pooling the content of several flasks which had been

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† Thanks are extended to Dr. Huldah Bancroft, Professor of Biostatistics in our Department, for checking our statistical interpretations.

1. Carrera, G. M., and Faust, E. C., *Am. J. Trop. Med.*, 1949, v29, 647.

2. Taylor, D. J., Greenberg, J., and Coatney, G. R., *J. Parasit.*, 1949, v35, 24.

3. Balamuth, W., *Am. J. Clin. Path.*, 1946, v16, 380.