first 2 hours after P^{32} injection is responsible for development of the peak in DNA-P specific activity found in peripheral blood leukocytes.

1. Howard, A., Pelc, S. R., *Exp. Cell Research,* 1951, v2, 258.
2. Lajtha, L. G., Oliver, R., Ellis, F., *Brit. J. Cancer,* 1954, v8, 367.
3. Osgood, E. E., Li, J. G., Tivey, H., Duerst, M. L., Seaman, A. J., *Science,* 1951, v114, 95.
4. Ottesen, J., *Acta Physiol. Scand.,* 1954, v32, 75.
5. Osgood, E. E., Tivey, H., Davison, K. B., Seaman, A. J., Li, J. C., *Cancer,* 1952, v5, 331.
6. Andreasen, E., Ottesen, J., *Acta Physiol. Scand.,* 1945, v10, 258.
7. Kline, D. L., Cliffton, E. E., *Science,* 1952, v115, 9.
8. Craddock, C. G., Perry, S., Lawrence, J. S., *J. Clin. Invest.,* 1956, v35, 285.
9. Coassin, N., Kline, D. L., *Am. J. Physiol.,* 1957, v190, 147.
10. Perry, S., Craddock, C. G., Lawrence, J. S., *J. Lab. Clin. Med.,* 1958, v51, 501.
11. ———, ———, Ventzke, L., Crepaldit, G., Lawrence, J. S., *Blood,* 1959, v14, 50.
12. Walker, R. I., Herion, J. C., Palmer, J. G., *Anal. Biochem.,* 1960, v1, 382.
13. ———, ———, ———, *Am. J. Physiol.,* 1961, in press.
14. Marshak, A., *J. Gen. Physiol.,* 1941, v25, 275.
15. Hull, W., Kirk, P. L., *ibid.,* 1949, v33, 335.
16. Taylor, J. H., *Exp. Cell Research,* 1954, v4, 164.
17. Brues, A. M., Tracy, M. M., Cohn, W. E., *J. Biol. Chem.,* 1944, v155, 619.
18. Hughes, W. L., *The Kinetics of Cellular Proliferation,* 1959, Grune and Stratton, New York, p. 83.
19. Athens, J. W., Mauer, A. M., Ashenbrucker, H., Cartwright, G. E., Wintrobe, M. M., *Blood,* 1959, v14, 303.

Received Sep. 5, 1961. P.S.E.B.M., 1961, v108.

Pyelonephritis. III. Observations on the Association between Chronic Pyelonephritis and Hypertension in the Rat.* (26976)

LUCIEN B. GUZE AND GEORGE M. KALMANSON
(Introduced by R. Goldman)
Medical Service, Veterans Administration Center and Department of Medicine, University of California Medical Center, Los Angeles

The relationship between hypertension and pyelonephritis has not been clearly defined. Various clinical studies have suggested: 1) pyelonephritis can cause hypertension; 2) pyelonephritis can aggravate a pre-existing hypertension and result in "malignant hypertension"; and 3) there is no relationship between renal infection and elevated blood pressure. Experimental consideration of this problem has been somewhat limited by the lack of suitable laboratory model of pyelonephritis. Studies performed in animals with "obstructive" pyelonephritis have with one exception(1) failed to reveal sustained hypertension(3). Similar findings have been recorded in experiments when renal infection was produced by various other manipulative procedures(2,4).

With the availability of a chronic, progressive pyelonephritis in the rat, produced without ureteral obstruction, experiments were designed to study the possible etiologic relationship between kidney infection and hypertension.

Methods. White, male Wistar rats were used. Previous studies have shown that following intravenous injection of a standard inoculum of *Str. faecalis* pyelonephritis uniformly resulted(5). This infection was characterized by the persistence of bacteria in relatively constant numbers in the kidney during the period when the disease progressed from the acute to the chronic stage histologically. In other experiments, microorganisms were found in the majority of rat kidneys

* Supported by grants from American Heart Assn. and U.S. Public Health Service. Presented in part at the International Symposium, Biology of Pyelonephritis, Henry Ford Hosp., Detroit, Mich., Oct., 1959.

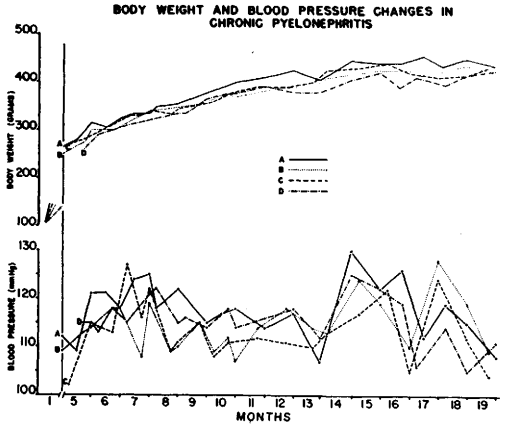

FIG. 1. Body weight and blood pressure recorded in rats with chronic pyelonephritis. Group A—Chronic enterococcal pyelonephritis. Group B—Chronic enterococcal pyelonephritis with acute exacerbations of enterococcal infection. Group C—Chronic enterococcal pyelonephritis with acute exacerbations of *E. coli* infection. Group D—Uninfected controls.

examined 2 years after injection(6).

Four groups of rats were studied in the present experiments. *Group A-Chronic enterococcal pyelonephritis:* Animals received one injection of *Str. faecalis* intravenously. *Group B-Chronic enterococcal pyelonephritis with acute exacerbations of enterococcal infection:* Animals received one injection of *Str. faecalis* intravenously and after an interval of 6 months were given 4 repeated injections of *Str. faecalis* at 2-month intervals. *Group C-Chronic enterococcal pyelonephritis with acute exacerbations of E. coli infection:* Animals were treated as Group B with the exception that the repeated infections were produced by injection of a strain of *E. coli*. *Group D-Controls:* Uninfected animals.

Animals were observed for 20 months. During this time, blood pressures were recorded monthly under light ether anesthesia by the tail plethysmograph method of Williams *et al.*(7). At conclusion of the experiment, rats were sacrificed and weighed. Organs were removed aseptically and prepared for bacteriological or histological study by previously described methods(5).

In the original design of the experiment, 50 animals were included in Group A, 25 each in Groups B, C and D. At the end of the study period there were 33 rats remaining in Group A, 16 in Group B, 21 in Group C, and 16 in Group D. This high mortality noted was not attributed to the renal infection produced or its sequelae, since other studies have shown that rats tolerate this infection well for periods up to 2 years. The majority of deaths in this study occurred in the 24 hours following blood pressure recordings and were therefore attributed to the anesthesia or complications arising therefrom.

Results. Fig. 1 shows the blood pressure and body weight data recorded in these experiments. The animals tolerated the infection well, as noted by normal weight gain. No difference in blood pressure was noted between any of the groups. This failure to measure hypertension was confirmed at autopsy by the finding of normal body weight/heart weight ratios.

The bacteriological data obtained at autopsy are presented in Table I. These results are consistent with those previously published and confirm the persistence of renal infection and the tendency for bacteria gradually to disappear from the liver and spleen following the injection of *Str. faecalis*. The comparatively larger numbers of microorganisms isolated from the organs of Group B animals may be explained by the accumulative effects of the repeated injections of *Str. faecalis* which these rats received. The majority of kidneys examined in Groups A, B and C had macroscopic scars on the cortical surfaces. Histologically these consisted of areas of loss of renal parenchyma, presence of fibrous tissue, mononuclear cell infiltration, dilated tubules filled with "colloid" casts, and

TABLE I. Bacteriological Data Obtained at Autopsy.

Group	No. animals studied	Avg. Log. No. bacteria (per g tissue) kidney	spleen	liver
A	33	3.7	.7	.8
B	16	5.6	1.1	1.2
C	21	2.9*	.2	.4
		2.1**		
D	16	0	0	0

(*) and (**) represent the average Log. No. of *Str. faecalis* and *E. coli* colonies cultured respectively. Only *Str. faecalis* was isolated from liver and spleen of these animals. Total and differential bacterial counts in this group were obtained by using various inhibitory media; quantitative dilutions were incorporated into agar plates containing Polymyxin, 10 μg/ml, or Vancomycin, 10 μg/ml.

occasionally, minimal to moderate periglomerular fibrosis. Limited alterations were noted in the arteries and arterioles. For the most part these latter were sclerotic changes associated with aging processes and were similar in all groups studied. In a few scarred areas, perivascular fibrosis and mononuclear cells within the vessel wall were noted. These infrequent findings were thought to represent direct extension of the parenchymal inflammatory process to the wall of the arteriole.

Discussion. These results are consistent with most reports concerning the relationship between experimental pyelonephritis and hypertension(2,3,4). Exception to this was noted by Spitznagel and Schroeder(1) who produced pyelonephritis in the rat by intravenously injecting *E. coli* into animals with unilateral ureteral obstruction. Elevated blood pressures were recorded in many of these animals and the authors noted the occurrence of "vascular changes" in the kidneys. This finding may account for discrepancies with other published data. Other investigators have commented upon the absence of significant arteriolar nephrosclerosis and have postulated that this could explain the failure to note hypertension. This was noteworthy in the experiments described here.

Our observations and those recorded in the literature suggest that pyelonephritis does not cause hypertension in experimental animals despite the occurrence of progressive infection, marked tissue destruction and uremia. Whether this represents an animal specie variation is not known. It has suggested an alternative hypothesis to explain the clinically reported increased association between pyelonephritis and hypertension; that hypertension *per se* predisposes to renal infection. Experimental confirmation of this in rats has been reported(8).

Summary. Chronic, progressive, non-obstructed, enterococcal pyelonephritis in the rat is not associated with hypertension. It is suggested that this may be related to the absence of significant arteriolar nephrosclerosis.

1. Spitznagel, J. K., Schroeder, H. A., PROC. SOC. EXP. BIOL. MED., 1951, v77, 762.
2. Heptinstall, R. H., Gorrill, R. H., *J. Path. Bact.*, 1955, v69, 191.
3. Shapiro, A. P., Braude, A. I., Siemienski, J., *J. Clin. Invest.*, 1959, v38, 1228.
4. ———, Kobernick, J. L., *Circulat. Res.*, 1959, v7, 936.
5. Guze, L. B., Goldner, B. H., Kalmanson, G. M., *Yale J. Biol. Med.*, 1961, v33, 372.
6. ———, Kalmanson, G. M., unpublished data.
7. Williams, J. R., Jr., Harrison, T. R., Grollman, A., *J. Clin. Invest.*, 1939, v18, 373.
8. Woods, J. W., *ibid.*, 1960, v39, 1813.

Received Sep. 5, 1961. P.S.E.B.M., 1961, v108.

An Antigen for Detection of Hypersensitivity to *Cryptococcus neoformans.* (26977)

S. B. SALVIN AND R. F. SMITH
(Introduced by C. L. Larson)
U. S. Department of Health, Education, and Welfare, P.H.S., Nat. Inst. Health, Nat. Inst. of Allergy and Infectious Diseases, Rocky Mountain Laboratory, Hamilton, Mont.

Cryptococcus neoformans exists as a saprophyte in soils of various areas(1,2). The fungus has also been isolated from many specimens of pigeon droppings and nests(3-5), although the organism was not cultured from the internal organs of 20 pigeons(3). The possibility arises, therefore, that a reservoir for human infection can exist in pigeon excreta, for "pigeon" strains and "human" strains possess similar properties of virulence in mice(5).

Human cryptococcosis is world-wide in distribution(6). Most proven cases exhibit a severe meningitis, although pulmonary infec-