antagonizes sulfonamide activity[5] and whole blood and serum up to 25%.

The antimycobacterial activity of 5-amino-2-butoxypyridine and its derivative is primarily bacteriostatic rather than bactericidal. (We hold the term bactericidal in its strictest sense, *i.e.*, complete sterilization of a sizable inoculum in a culture medium which, when free of inhibitory compounds, supports vigorous growth). Concentrations of 5-amino-2-butoxypyridine 1,000 times the minimum tuberculostatic concentration do not consistently render the system free of viable organisms.

The fact that these compounds are bacteriostatic rather than bactericidal and strikingly specific for the acid-fast group of organism suggest a mechanism of action involving the interference with some essential metabolic process common to species of Mycobacterium but which is lacking, has readily available alternatives or is nonessential in other genera of organisms.

[5] Lockwood, J. S., and Lynch, H. M., *J. A. M. A.*, 1940, **114**, 935.

15531

Bilateral Nephrectomy in Rats: Blood Chemistry, Longevity and the Effect of Aluminum Hydroxide.

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In the hypocalcemic tetany of the uremic patient aluminum hydroxide reduces the tendency towards convulsions by elevating the serum calcium[1] presumably by preventing the absorption of the phosphate ion.[2] Subsequently, these studies were initiated in order to observe the effect of aluminum hydroxide gel on the survival time and on the blood levels of sulphates, phosphates, calcium, urea and cholesterol in rats following bilateral nephrectomy.

Method and Material. A total of 108 rats were used in this study. Fifty-one rats were employed in the longevity study of which 26 (16 males and 10 females) served as controls and 25 (15 males and 10 females) as experimental animals. The males weighed 400 to 500 g and the female rats 250 to 300 g. Both kidneys were removed by a transperitoneal approach through a midline ventral incision under ether anaesthesia. Sterile technic was utilized throughout. Each of the animals in the experimental group was given 5 ml of 4% aluminum hydroxide gel by stomach tube. An analgesic dose of ether was administered prior to the passage of the stomach tube in order to permit intubation without the use of a gag. The aluminum hydroxide was given once daily for 2 days prior to nephrectomy, then 4 to 6 hours after surgery, and thereafter once every 24 hours until the animals expired. The survival time of these rats was compared with the control group.

For the study of variations in blood chemistry, 28 non-nephrectomized male rats were anaesthetized with ether after which the abdominal aorta was exposed through a midline ventral incision. Blood was then aspirated from the aorta by means of a 26-gauge needle and a 2-ml hypodermic syringe. Seventeen male rats were nephrectomized and 48 to 50 hours postoperatively blood was withdrawn from the abdominal aorta as described above. In addition, 11 male rats were nephrectomized but were given aluminum hydroxide by stomach tube. These animals were also sac-

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[1] Personal observation, unpublished data.

[2] Evans, G. T., and Flink, E. B., *Modern Med.*, 1945, **13**, 63; Fauley, G. B., Freeman, S., Ivy, A. C., Atkinson, A. J., and Wigodsky, H. S., *Arch. Int. Med.*, 1941, **67**, 563.

rificed 48 to 50 hours postoperatively in order to obtain blood from the abdominal aorta. The bloods were analyzed for serum inorganic sulphates, serum inorganic phosphates, serum calcium, whole blood urea and whole blood cholesterol.

Serum calcium was determined by the Clark-Collip[3] modification of the Kramer-Tisdall method and serum inorganic phosphates by the Lowenberg and Mattice[4] modification of the Benedict-Theis[5] method. Blood serum was analyzed for inorganic sulphates according to the method of Power and Wakefield.[6] The procedure of Myers[7] was used for the estimation of whole blood urea nitrogen. The whole blood cholesterol was determined by the method of Sackett.[8] Since the amount of blood withdrawn from the abdominal aorta of any one rat was frequently insufficient for complete studies, several samples were mixed thoroughly by gentle shaking and an aliquot portion of this pooled blood was used.

Results. Of 26 control rats, 14 or 54% expired on the 3rd day following bilateral nephrectomy while 12 (46%) died on the 4th day. The sex of the animal was not an influencing factor. In 25 nephrectomized rats receiving aluminum hydroxide, 12 (48%) expired on the 3rd day, 7 or 28% on the 4th day, while 20% lived beyond the control survival time (4 for 5 days and 1 for 6 days).

The average whole blood urea nitrogen of 28 normal rats was found to be 17.3 mg % (range 14-20.5), average serum calcium 9.5 mg % (range 8.4-10.4), average serum inorganic phosphates 6.9 mg % (range 4.5-9.2), average serum inorganic sulphates 2.97 mg % (range 2.70-3.49) and whole blood cholesterol 55.5 mg % (range 42-70). The 17 nephrectomized rats which did not receive aluminum hydroxide had an average urea nitrogen of 194 mg % (range 130-250), calcium 10.4 mg % (range 9.4-12.0), phosphates 8.1 mg % (range 6.5-10.8), sulphates 23.2 mg % (range 15-28.8) and cholesterol 70.8 mg % (range 60-96) 48 to 50 hours postoperatively. Bilateral nephrectomy, therefore, caused a marked retention of urea nitrogen and sulphate and a somewhat smaller rise in calcium, phosphate and cholesterol. The 11 nephrectomized rats receiving aluminum hydroxide showed an average urea nitrogen of 182 mg % (range 150-203), calcium 9.5 mg % (range 8.2-9.8), phosphates 7.9 mg % (range 6.1-9.4), sulphates 21.6 mg % (range 14.1-26.3) and cholesterol 65.5 mg % (range 60-69) 48 to 50 hours postoperatively. Apparently, the administration of aluminum hydroxide to bilateral nephrectomized rats was accompanied by slight decreases in each of the chemical constituents studied.

Discussion. The survival time of bilateral nephrectomized rats in this series is consistent with that of other investigations.[9] The increase of 20% in the longevity rate by the administration of aluminum hydroxide is difficult to explain, although it is conceivable that aluminum hydroxide may adsorb some of the toxic metabolites excreted into the intestinal tract (Adams).[10] It is universally appreciated that a moderate or severe acidosis develops in retention uremia;[11] the retention of the acid sulphate ion is probably the most important factor in the production of the acidosis. Aluminum hydroxide does not influence the acidosis directly since it is insoluble and nonabsorbable.[12] One may postulate that this aluminum compound interrupts, temporarily, the vicious cycle which might exist in nephritic acidosis, namely, the continued resecretion of high concentrations of

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[4] Lowenberg, C., and Mattice, M. R., *J. Lab. and Clin. Med.*, 1930, **15**, 598.

[5] Benedict, S. R., and Theis, R. C., *J. Biol. Chem.*, 1924, **61**, 63.

[6] Power, M. H., and Wakefield, E. G., *J. Biol. Chem.*, 1938, **123**, 665.

[7] Myers, V. C., *Practical Chemical Analysis of Blood*, St. Louis, C. V. Mosby, 1924, p. 45.

[8] Sackett, G. E., *J. Biol. Chem.*, 1925, **64**, 203.

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[10] Adams, W. L., *Arch. Int. Med.*, 1939, **63**, 1030.

[11] Marriott, W. M., and Howland, J., *Arch. Int. Med.*, 1916, **18**, 708; Holt, L. E., and McIntosh, R., *Holt's Diseases of Infancy and Childhood*, 10th ed., D. Appleton-Century, 1934.

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acid into the stomach, by adsorbing total and free acid.[2,11,13]

The increase in inorganic acids of the blood is perhaps more important than the retention of nitrogenous products particularly insofar as acid-base balance is concerned. Denis[14] has demonstrated an increase of the blood sulphate level in patients with chronic nephritis and Macy[15] has shown an impaired clearance of sulphates in this disease. The present study shows that sulphate retention is appreciable in the nephrectomized rat.

No significant changes either in phosphates or serum calcium levels were noted in the nephrectomized rat. In the presence of prolonged acidosis and proteinuria (calcium adsorbed to protein) such as is found in chronic nephritics one might expect changes in serum calcium; in this study the element of time was too short and the factor of proteinuria absent.

Conclusions. 1. The longevity of the bilateral nephrectomized rat was 3 to 4 days. 2. The oral administration of aluminum hydroxide increased the survival time of 20% of nephrectomized rats to 5 or 6 days. 3. Bilateral nephrectomy resulted in a marked elevation of urea nitrogen and inorganic sulphate in the blood whereas the retention of inorganic phosphate, calcium and cholesterol was insignificant. 4. The oral administration of aluminum hydroxide in the bilateral nephrectomized rat produced a slight decrease in the degree of retention of each of the various blood constituents studied.

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[15] Macy, J. W., *Arch. Int. Med.*, 1934, **54**, 389.

15532 P

Reproduction in Chickens on Synthetic B-Complex Supplement.

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Reproduction in rats on a diet containing the B-factors in synthetic form was previously reported.[1] However, it was not possible to rear chickens on a diet of this type until synthetic pteroylglutamic acid became available.[2] Day-old New Hampshire chicks were placed on the following diet: glucose (cerelose) 58.5 g, purified casein (Labco) 20 g, gelatin 8 g, calcium gluconate 5 g, cystine 0.4 g, choline chloride 0.2 g, inositol 0.1 g, bone ash 2 g, NaCl 0.6 g, KH_2PO_4 0.45 g, K_2HPO_4 0.6 g, $MgSO_4$ 0.25 g, $MnSO_4,4H_2O$ 0.05 g, ferric citrate 0.05 g, $CuSO_4,5H_2O$ 2 mg, $Al_2(SO_4)_3,18H_2O$ 1.6 mg, zinc acetate 1.4 mg, KI 0.6 mg, cobalt chloride 0.4 mg, nickel chloride 0.2 mg, calcium pantothenate 5 mg, niacinamide 5 mg, riboflavin 1 mg, pyridoxine HCl 1 mg, thiamine HCl 1 mg, *p*-aminobenzoic acid 1 mg, pteroylglutamic acid 0.5 mg, 1-acetoxy-2-methyl-4-naphthyl sodium phosphate 0.5 mg, (dl) biotin .04 mg, to which were added vitamin A 1500 U.S.P. units, vitamin D 200 A.O.A.C. units, mixed tocopherols 34 mg, dissolved in corn oil (Mazola) to a total of 3 g. The birds were kept in metal cages with wire floors. In this diet, the fat-soluble factors were fed in a crude form but the water-soluble vitamins, except inositol, were all synthetic and were fed at levels which appeared to be more than sufficient in each

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