even though the amount of vit. B_{12} in the yolk was greater than that found by Elam *et al.*(4) in eggs that hatched satisfactorily. There is, thus, a contradiction between the vit. B_{12} content of the egg yolk by microbiological analysis and the amount required for hatchability.

Summary. An experiment was conducted with White Leghorn pullets to determine the effect of feeding terramycin alone and in combination with vit. B_{12} on egg production and hatchability. The results obtained indicate that terramycin had little or no effect on egg production and gain in weight. In the absence of vit. B_{12}, hatchability of fertile eggs was definitely improved by feeding terramycin. There was an indication that terramycin fed in combination with vit. B_{12} further improved hatchability.

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Proteinuria in Experimental Renal Hypertension.* (19339)

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Recently the rate of development of proteinuria in three-quarters nephrectomized rats was reported(1). Removal of both adrenals after the proteinuria was well-developed did not significantly alter the rate of protein excretion although Addis and his coworkers have shown that adrenalectomy abolishes the proteinuric action of renin and decreases the rate and amount of excretion of intraperitoneally injected protein. Administration of cortical hormones restores the proteinuric effect of renin and increases the rate and amount of excretion of intraperitoneally injected protein(2-4). The purpose of the present paper is to report on the rate of development of proteinuria in rats made hypertensive by the removal of one kidney and constriction of the other, and its relationship to growth of the remaining renal tissue, development of hypertension and development of renal lesions. Since the renin-angiotonin pressor system is probably involved in the pathogenesis of constrictive renal hypertension and since not only renin but angiotonin as well(2) will induce proteinuria in the rat the possibility exists that the proteinuria of the hypertensive rat is to be explained on this basis. On the other hand the proteinuria might be a consequence of a renal lesion. Study of the time relationships should throw some light on the pathogenesis of the proteinuria.

Methods. 24 male albino rats of the Stanford colony, weighing close to 150 g each at the start of the experiments were divided into 2 equal groups. A base line of protein excretion was established by 4, and a base line of blood pressure by 2, observations. Following one-stage operative procedures on the kidneys these measurements were repeated bi-weekly. In the first group of rats one kidney was removed and the other exposed, handled and replaced. In the second group one kidney was removed and the other constricted by a figure-of-eight silk ligature, according to the technic of Grollman(5). Measurements of protein excretion were carried out by placing the rats in metabolism cages at 4 p.m., col-

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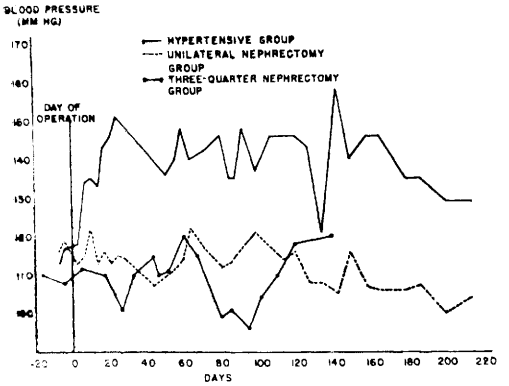

FIG. 1.

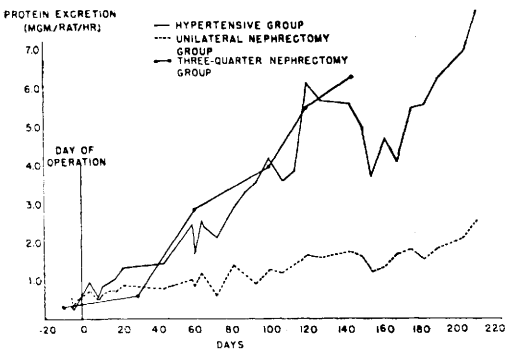

FIG. 2.

lecting for the next 16 hours and analyzing pooled specimens by the Shevky-Stafford technic as described in a previous paper(2). Systolic blood pressure was measured in the tail with the Friedman-Freed microphonic manometer(6) according to a procedure previously described in detail(7). The rats were kept on a stock diet containing 17% protein and 0.3% NaCl. Two of the rats died after unilateral nephrectomy and 3 shortly after renal constriction. The survivors were killed on the 210th day.

Results. Fig. 1 shows the curve of the mean of the systolic blood pressures in the 2 groups of rats. For purposes of comparison the blood pressure mean of a group of three-quarters nephrectomized rats, previously reported(1), is included. The mean pressure rose rapidly and became stabilized after about 3 weeks in the rats with constricted kidneys, while no elevation occurred in the 2 other groups. Expressed as a percentage of the predicted value based on heart weight/body weight tables for this colony(8), the mean heart weight of the hypertensive group was 141 $\pm$ 12 (stand. error), of the unilaterally nephrectomized group 106 $\pm$ 2, and of the three-quarters nephrectomized group 105 $\pm$ 2.4. The corresponding mean weights for kidney tissue were 85 $\pm$ 4.4, 81 $\pm$ 2, and 70 $\pm$ 4.6. Fig. 2 shows the protein excretion expressed as milligrams per rat per hour during the 16-hour collection period. *Renal lesions*: in the rats with constricted kidneys lesions similar to those described in the three-quarters nephrectomized rats were present in variable degree. Intercapillary and extracapillary proliferative and sclerosing alteration with irregular thickening of the basement membrane, irregular distribution of hyaline droplets in the proximal tubule cells and occasionally in the capsular epithelium, were the characteristic features, and did not seem to be related to the constricting band or to the development of pyelonephritis. In a previously studied group of rats with renal constrictive hypertension these lesions were not present nor were they seen in three-quarters nephrectomized rats. Apparently this was because both groups were killed only 50 days after the operative procedures. The delayed development of renal lesions of the type described appears to be characteristic(1,11,12). When hypertension does develop in three-quarters nephrectomized rats it does not manifest itself until a month or more after the operation while in the rat made hypertensive by removal of one kidney and constriction of the other elevation of the blood pressure occurs within a day or two.

Discussion. The development of hypertension and proteinuria under these conditions appear to be independent processes. The blood pressure rises rapidly and levels off while the proteinuria shows a linear increase with time. The proteinuria of the non-hypertensive three-quarters nephrectomized rats roughly parallels that of the hypertensive rats. No relation exists between the hypertrophy of remaining renal tissue and the development of proteinuria. Addis(9) found that by the 20th post-operative day the remaining kidney of the unilaterally nephrectomized rat reached 73% of the predicted 2-kidney weight and for the next 60 days the

weight of the kidney did not change. Constriction of the remaining kidney with a figure-of-eight ligature after contralateral nephrectomy seems to have no adverse effect on its growth although if the contralateral kidney is not removed the constricted kidney is thereafter stunted(7). Addis found(10) that the growth of the stump after three-quarters nephrectomy was rapid, reaching 55% of the predicted 2-kidney weight by the 20th day. Thereafter there was a slow increase in weight of the stump which, however, seems to be dependent on the renal lesion described above. Part of the weight increase is due to distension of the renal tubules with protein-containing fluid.

The immediate loss of renal tissue, drastic though it seems, does not produce pronounced proteinuria. The significance of the renal lesion with regard to the proteinuria is difficult to assess. There is no direct evidence that the lesion is the cause of the proteinuria or that it precedes it. Increased permeability of the glomeruli may be present but cannot be presumed on the basis of the proteinuria alone since the value of the tubular resorptive factor is not known. Measurement of the hemoglobin and creatinine clearances as carried out by Monke and Yuile(13), Lippman, Ureen, and Oliver(14), and Brandt, Frank, and Lichtman(15) might provide data from which to estimate the relative roles of glomerular permeability and tubular resorption. Athrocytic phenomena in the tubule cells probably indicate overloading of a tubular mechanism for absorbing and disposing of protein, but whether this is a consequence of increased filtration of protein cannot be answered at present.

Summary. Rats made hypertensive by the removal of one kidney and constriction of the other show a linear increase in urine protein paralleling the rate and magnitude of increase in urine protein excretion shown by non-hypertensive three-quarters nephrectomized rats. The development of proteinuria is independent of the development of hypertension. No apparent relationship exists between the proteinuria and hypertrophy of remaining kidney. Glomerular and tubular lesions are present in most of the proteinuric rats.

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