with the collaboration of Mangun and Reichle[3] involving the simultaneous determination of creatine, phosphorus, and potassium, but the observations are as yet too few to warrant additional conclusions.

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## Experiments on Ligation of Renal Vein.

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The effect of partial or complete obstruction of the renal vein on the secretion of urine and the histology of the kidney has been investigated repeatedly. Conflicting results reported in the literature have been reviewed by Rowntree, Fitz and Geraghty,[1] Orofino,[2] and Nicastro.[3] Little has been added to the histological description of such kidneys since Buchwald and Litten's[4] report. The outstanding feature is degeneration and atrophy of the tubules with apparently relatively normal glomeruli. Other studies have been concerned with the development of an adequate collateral circulation to maintain the functional capacity of the kidney. This is apparently much better in dogs than in either cats or rabbits, and Alesandri,[5] Rowntree, Fitz and Geraghty were able to maintain dogs in excellent condition for a time even when one kidney had been removed and the other renal vein ligated. Usually, however, even in the dog when the renal vein has been ligated a progressive atrophy of the kidney follows with decrease and finally cessation of all urinary secretion. In cats and rabbits this is the constant finding.

Orofino found that from 5 to 20 days after ligation of one renal vein in dogs, the urine from that kidney was decreased in amount, and contained lower concentrations of urea and chloride but more albumin than the urine from the normal kidney. Dicker and Demoor[6] found the volume of urine from the ligated kidney greater

[3] Myers, V. C., Mangun, G., and Reichle, H. S., unpublished observations.

[1] Rowntree, L. G., Fitz, R., and Geraghty, J. T., *Arch. Int. Med.*, 1913, **11**, 121.

[2] Orofino, A., *Ann. Ital. di Chirur.*, 1932, **11**, 924.

[3] Nicastro, G., *Il Morgagni*, 1927, **69**, 2001.

[4] Buchwald, A., and Litten, M., *Virchow's Arch.*, 1876, **66**, 145.

[5] Alesandri, quoted by Orofino.

[6] Dicker, E., and Demoor, J., *Compt. Rend. Hebdomadaires Soc. de Biol.*, 1930, **103**, 503.

(2 to 3 times) than from the normal side 6 to 8 weeks after operation, while the concentration of urea was reduced, that of chloride was increased. These experiments suggested that the effect of temporary obstruction to the renal vein and the resulting anemia of the kidney produces its greatest effect on the highly specialized epithelium of the renal tubules. It seemed that if the renal vein could be clamped for a sufficient length of time to produce a severe asphyxial injury, and then the normal circulatory channels reestablished, an opportunity should be afforded to study the urine formed after such damage as well as the pathological process of degeneration, or degeneration and repair. The development by Goldblatt[7] of an ingenious clamp which easily and accurately can be tightened and loosened seemed to afford a suitable means of temporarily obstructing the renal vein with a minimum chance of producing thrombosis.

Rabbits were used entirely. They were anesthetized with sodium pentobarbital and the left renal vein exposed through a lumbar incision. The clamp was then put on the vein, tightened, and the wound closed. After from 6 to 72 hours, the wound was reopened and the clamp loosened. After from 1 to 16 days the animal was anesthetized again, the abdomen opened, the stomach and intestinal tract removed, and then cannulae inserted in both ureters. Urine flow from the injured kidney was usually very small—frequently only a few drops could be obtained even after the intravenous injection of physiological salt solution or hypertonic sodium sulphate. In a few experiments, sufficient urine was obtained for analysis. At the end of the experiment, the kidneys were removed, weighed, and blocks fixed in formalin for histological study. All experiments in which thrombus formation in the renal vein or its branches could be detected have been discarded.

Urine was obtained in acute experiments from each of 3 rabbits after the vein had been clamped for 30 minutes. The volume per minute was greatly reduced, and the urine contained albumin and red cells. The volume was not sufficient for chemical analysis. Sufficient urine for analysis was obtained in 2 of 3 animals in which the vein had been clamped 6 hours, in 1 of 3 clamped 24 hours, in none of 8 clamped 48 hours, and in 1 of 2 clamped 72 hours. Blood was drawn from the carotid artery at the end of the urine collection. The outstanding change in the urine from the injured kidney was that in spite of the smaller volume, its composition more nearly

[7] Goldblatt, H., *et al.*, *J. Exp. Med.*, 1934, **59**, 347.

approached that of the plasma. The greatest differences were in the concentrations of chlorides and urea nitrogen, the former being higher and the latter lower than from the normal side. Estimations of creatinine were probably unreliable because of the low concentrations and the fact that no account was taken of interfering chromogenic substances in the plasma. The small volume of dilute urine is at variance with the normal rabbit, in which the greater the diuresis the nearer does the urine approach an ultrafiltrate of plasma in composition.

These findings suggest that in the injured kidney, the function of the tubule cells had been seriously impaired. The low volume of urine might be due to a diminished volume of filtrate formed, if many glomeruli were occluded, or to the reabsorption *in toto* of a large part of the filtrate by the osmotic pressure of plasma proteins in the peritubular capillaries through functionally dead tubule cells.

The histological changes seen after 30 minutes' occlusion resembled those found by Huber[8] to follow obstruction to both artery and vein for a similar length of time. There was marked hyperemia, subcapsular and peritubular hemorrhages, and swelling of the tubular epithelium. The glomeruli appeared relatively normal. Occlusion of the renal vein for from 6 to 72 hours produced histological changes most marked in the proximal convoluted tubules, less in the loop of Henle, and inconspicuous in the distal convoluted and collecting tubules. The glomeruli were as a rule remarkably well preserved. The changes were in general similar to those described by Zeckwer[9] in the cat, except that the evidences of regeneration are more marked.

There were no striking differences in the histological picture of kidneys from which urine had been obtained and those from which it had not. This simply brings out again the difficulty of interpreting functional capacity from histological appearance. In all sections, there was marked difference in the apparent involvement of different tubules. This suggests the possibility that the postglomerular circulation, including the collateral channels of Huber, may vary considerably for different tubules. It would seem proper to believe that the urine obtained was derived from the less damaged nephrons, while in spite of apparently relatively normal glomeruli, the majority of nephrons were functionless.

[8] Huber, A., *Arch. f. klin. Clin.*, 1926, **141**, 51.

[9] Zeckwer, I. T., *Am. J. Path.*, 1926, **11**, 57.