vascular bed is under active vasomotor control.[13] A reduction in the amount of blood pumped from the venous to the arterial side of the circulation would lower arterial pressure while tending to elevate venous pressure.[1,2,5] It seems possible, therefore, that whenever cardiac output is inadequate, reflex peripheral autonomic mechanisms are called into play. These would maintain arterial pressure by arteriolar constriction and tend to increase cardiac output by further increasing the venous filling pressure. Venous filling pressure might be elevated by an increased tone in the large veins or by a redistribution of blood resulting from constriction of smaller peripheral vessels. These experiments do not exclude the possibility that other factors such as increased blood volume or tissue fluid pressure may also play major roles in the maintenance of the elevated venous pressure of congestive failure.

Finally, it should be pointed out that only the peripheral venous pressure was measured in these experiments. It is possible, particularly in subjects without venous hypertension, that pressure changes in the central veins and right atrium were not closely reflected by changes in the peripheral venous pressure.

Summary. Tetraethylammonium chloride given intravenously to 9 normotensive patients in congestive failure caused a precipitous fall in venous pressure and a significant decrease in arterial pressure in every case. Compensated cardiacs and non-cardiac normotensive controls showed no fall in venous pressure and a much smaller change in arterial pressure. Following digitalization, 2 cardiac subjects in failure lost some of their initial responsiveness to TEAC.

[13] McDowall, R. J. S., *Phys. Rev.*, 1935, **15**, 98.

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Survival of Rats After Temporary Complete Renal Ischemia.*

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It has been shown that rats generally survive bilateral interruption of the renal circulation for periods lasting up to one hour.[1] With longer intervals of complete ischemia, the mortality rises sharply. Cessation of blood flow to both kidneys for two hours is uniformly fatal; there is progressive elevation of BUN and death occurs in uremia within a few days.

The principal lesion produced by temporary periods of complete renal ischemia is necrosis of the proximal convoluted tubules.[1] In rats with a one hour period of bilateral ischemia, the necrosis is followed by repair and survival of the animals. Rats with a 2 hour period of ischemia evidently die in uremia before regeneration is effective.

In order to determine whether the renal lesion produced by periods of ischemia longer than those in the preceding experiments was subject to repair and would permit survival of the rats, unilateral ischemia was produced. The left main renal artery and vein of 50 adult white rats were occluded with a bulldog clamp for periods ranging from 2 to 4 hours. A 5 hour period was unsatisfactory because of the frequent occurrence of renal infarction. Heparin was given intravenously before clamping, and in some instances during clamping, to retard intrarenal thrombosis. The right kidney was intact. The animals were sacrificed at various intervals up to 5 months after removal of the clamps.

Results. Tubular necrosis was followed by

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1 Koletsky, Simon and Gustafson, G. E., *J. Clin. Invest.*, 1947, **26**, 1072.

TABLE I.
Mortality in 75 Rats After Complete Ischemia of Left Kidney and Subsequent Resection of the Right Kidney.

Duration of left renal ischemia, hrs	No. of rats	No. of rats which died	Mortality, %
1½	15	0	0
2	15	1	7
3	15	6	40
3½	15	9	60
4	15	13	87

repair in all rats. At the end of one week the tubules were largely cleared of necrotic débris and were lined by a newly formed epithelium. However after one week there was progressive and profound renal atrophy so that at 3 weeks the kidney, although completely repaired, was reduced to approximately one half to one third the normal size. Both glomeruli and tubules were atrophic and the interstitial fibrous stroma increased in amount. The tubular lumens were narrow or closed and the lining cells small. Further observations showed that the atrophy resulting from temporary ischemia persisted indefinitely as long as the complete opposite kidney was intact.

The functional capacity of the small atrophic kidney resulting from temporary interruption of blood flow was then investigated. Clamps were applied to the left main renal artery and vein of 75 adult rats divided into 5 groups of 15 rats each, with the following periods of occlusion respectively, *i.e.*, 90 minutes and 2, 3, 3½, and 4 hours. The right kidney was resected 3 weeks after removal of the clamp. BUN was determined by the method of Ormsby[2] before and after release of the clamps and at regular intervals following resection of the right kidney. Heart's blood was obtained for BUN in rats which died in uremia. Surviving animals were sacrificed from 3 to 5 months after the right kidney was removed.

Results. The mortality among the 5 groups of rats is shown in Table I. In the rats which died the BUN usually rose rapidly and death occurred within 1 or 2 weeks after resection of the right kidney. Terminal BUN values ranged from 220 to 764. Four animals developed chronic uremia with BUN levels up to 300 and marked weight loss, and these died from 4 to 11 weeks after resection of the right kidney.

All rats in the 90 minute group and 14 of 15 in the 2 hour group survived. In the 3 and 3½ hour groups, 9 and 6 animals survived respectively as compared to only 2 survivals in the 4 hour group. All surviving rats were in good condition and either maintained or gained weight. However, except for most animals in the 90 minute and 2 hour group, the BUN subsequent to resection of the right kidney was permanently elevated. The levels were usually below 100 mg per 100 cc with ischemia up to 3 hours' duration and above 100 in the animals with 3½ and 4 hour periods of ischemia. Two of the 6 surviving rats with 3½ hour renal ischemia, after being in good condition for 4 months, had a sudden rise in BUN and developed uremia. At autopsy the kidneys were the seat of necrotizing arteriolitis, especially the glomeruli, and also acute pyelonephritis.

In all surviving rats resection of the right kidney was followed by marked compensatory hypertrophy of the left kidney. The latter was large, usually exceeding normal size, and both glomeruli and tubules were hypertrophic. In contrast the rats which died following removal of the right kidney had a small atrophic left kidney with minimal or no compensatory hypertrophy.

Conclusion. These experiments indicate that if the period of complete ischemia does not exceed 2 hours, the rat kidney can regain enough function to permit survival. With complete ischemia of 3 hours' duration chance of survival is reduced to about half. Cessation of renal blood flow for more than 3 hours usually results in loss of capacity for compensatory hypertrophy and hence may be considered irreversible.

2 Ormsby, A. A., *J. Biol. Chem.*, 1942, **146**, 595.