

A Simplified Procedure for Inducing Chronic Renal Hypertension in the Mammal.*

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Recent interest in experimental hypertension makes a simple procedure for inducing this condition in laboratory animals highly desirable. The present paper describes a method which, in our experience, is simpler in technic and gives a higher incidence of chronic hypertension than those previously used. We have applied it with equal success to the mouse, rat, dog, and rabbit, and it is apparently applicable to any of the mammalian forms commonly used in the laboratory.

The 3 principal methods for inducing chronic renal hypertension in present use are based on the original procedures of (1) Chanutin and Ferris,¹ which involved partial ablation of the kidneys and was applicable only to the rat; (2) that of Goldblatt,² which had as its basis constriction of the renal artery, and (3) that of Page,³ involving the application of a cellophane or silk capsule to the kidney. Other methods based on the use of toxic agents (metal salts, sera or other nephrotoxins), operations on the nervous system, ureteral ligation, irradiation of the kidneys by X-rays, etc., although of theoretical interest, are unsuitable for maintaining a colony of hypertensive animals.

In our earlier work on the rat, we utilized the procedure of Chanutin and Ferris.¹ Only a minority of the animals subjected to this procedure develop chronic hypertension, since many die of renal insufficiency when the operation is of sufficient severity to induce

hypertension or, if the operation is not severe enough, fail to develop an elevation in blood pressure. It is difficult in all of the above-mentioned methods to avoid a fatal ischemia of the kidney while inducing enough interference with normal renal function to cause the animal to develop chronic hypertension.

The method of Goldblatt *et al.*,² although of greatest importance in advancing our recent knowledge, is not readily applicable to smaller mammals and is much more difficult to apply to the dog—for which it was primarily intended—than the application of a silk, colloidion, or cotton capsule to the kidney. The latter method suffers from the disadvantage that infection is relatively frequent and when applied to the rat, the incidence of hypertension is not satisfactorily great.⁵ Although the application of these foreign bodies to the surface of the kidney sometimes evokes an inflammatory invasion of the cortex,^{3,6} we have observed that hypertension develops in the absence of such a perinephric reaction.⁷ It occurred to us, therefore, that the observed hypertension was caused by compression of the renal parenchyma without necessitating the formation of a fibrous capsule around this organ. This led to the adoption of a procedure which during the past 2 years has been found to be more satisfactory than those previously available.

The method has been used successfully in the mouse, rat, rabbit, and dog and consists essentially in passing a cotton thread or tape

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¹ Chanutin, A., and Ferris, E. B., *Arch. Int. Med.*, 1932, **49**, 767.

² Goldblatt, H., Lynch, J., Hanzal, R. F., and Summerville, W. W., *J. Exp. Med.*, 1937, **59**, 227.

³ Page, I. H., *J. Am. Med. Assn.*, 1939, **113**, 2046.

⁴ Drury, D. R., *J. Exp. Med.*, 1938, **68**, 693.

⁵ Remington, J. W., Cartland, G. F., Drill, V. A., and Swingle, W. W., *Am. J. Physiol.*, 1944, **140**, 627.

⁶ Friedman, B., Jarman, J., and Klemperer, P., *Am J. Med. Sci.*, 1941, **202**, 20.

⁷ Grollman, A., and Williams, J. R., *Am. J. Med. Sci.*, 1942, **204**, 73.

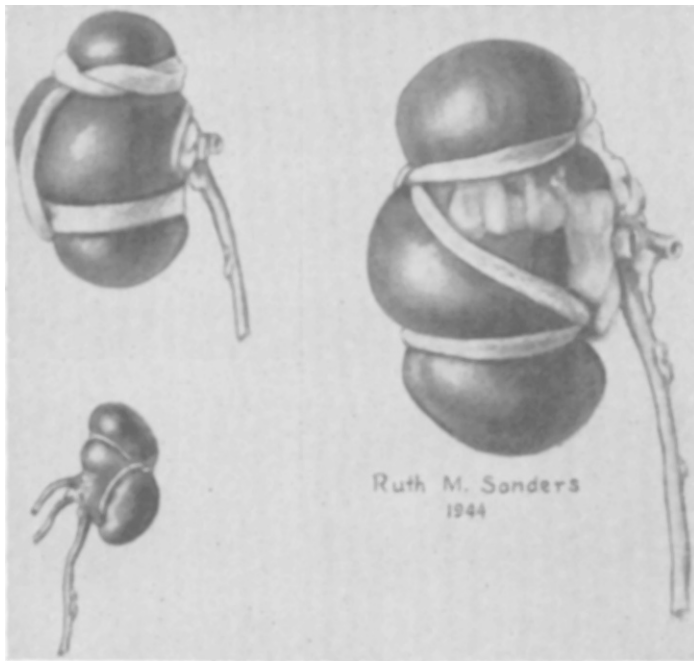


FIG. 1.

The method of compressing the kidney. In the upper left corner is the compressed kidney of a rabbit, below it, that of a rat, and at the right, that of a dog. Note the distortion of the kidney and the relation of the ligature to the hilus and poles of the kidney. The ureter, renal artery and vein are shown emerging from the hilus.

over the pole and body of the kidney and drawing it taut, as shown in Fig. 1.

After exposing the kidney by the usual lumbar incision the adrenal is pushed away from its attachments to the kidney. The latter is now brought through the incision. In the case of the rat, the renal capsule must be removed by gentle traction with the finger. Unless this is done the thread tends to slip. In the case of the dog, the tape (as shown in Fig. 1) is passed through the connective tissue which is adherent to the under surface of the kidney and is thus held firmly in position. Care is taken to avoid the ureter and blood vessels emerging from the hilus. In the case of the rat, cotton thread (No. 8 gauge) is used; for the dog or rabbit, umbilical tape has been found satisfactory since this does not cut into the renal tissues when tightened sufficiently to deform the normal ellipsoidal shape of the kidney.

The subsequent operations to be performed after compressing one kidney depend upon the

type of hypertension desired and the rapidity with which it is to develop. As previously reported for the rat and rabbit, some animals (about 10 to 20%) develop a moderate degree of hypertension following the compression of a single kidney, leaving the other intact. This may require 3 to 6 months, however. If the second kidney of such animals as fail to develop hypertension in this time, be now compressed, about half the animals will be found to ultimately develop hypertension. Such animals as fail to develop the desirable rise in pressure following another interval of several months are then subjected to a unilateral nephrectomy. By following this procedure it is possible to obtain ultimately a high percentage of animals with hypertension which is relatively stable and does not rise rapidly as is the case when a more intensive form of surgical procedure is used. Animals prepared in this way are more suitable for assays and other studies in which a constant pressure is desirable over a long period of time.

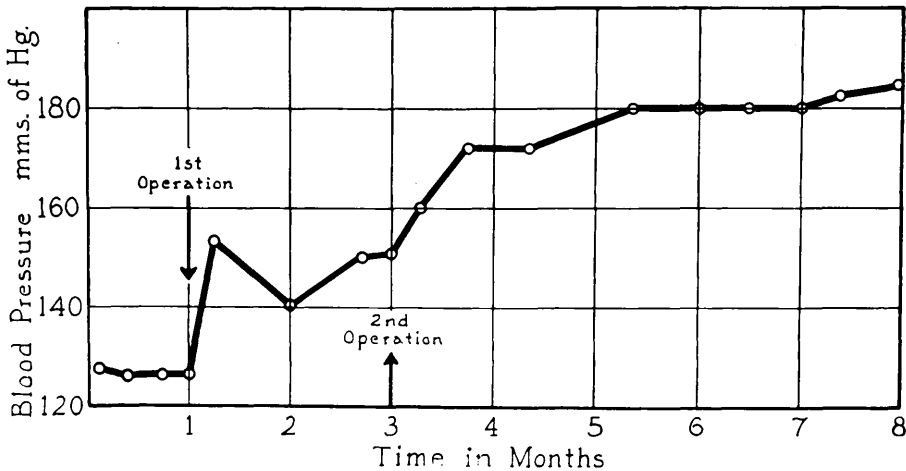


FIG. 2.

The blood pressure of a dog following compression of the kidneys. At ↓ the right kidney was compressed; at ↑, the left was similarly treated. The mean pressures as determined by direct arterial puncture and measured on a mercury manometer are given as ordinates.

If a rapidly developing hypertension is desired, the second kidney may be compressed or removed about 10 days after the first operation. Many animals thus treated will develop a rapidly progressive malignant hypertension.

In Fig. 2 is shown a typical response of the blood pressure of a dog to the bilateral compression of the kidneys. One year following the first operation, the blood pressure had gradually risen to 200 mm Hg., at which level it remained during the next 8 months during which the animal was under observation.

Summary. A relatively simple and easily applicable procedure is described for inducing chronic hypertension in the mouse, rat, rabbit, dog, or other laboratory mammal. The method in our experience results in a higher percentage of chronically hypertensive animals, is simpler in application than the procedures involving constriction of the renal artery or the application of silk or cellophane to the kidney, and is less apt to result in an interference with the renal excretory function or the development of a rapidly fatal malignant form of hypertension.

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Salmonella loma-linda: A New Type Isolated from Meningitis.*

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Salmonella loma-linda was isolated by Dr. T. F. Judefind of the College of Medical Evangelists, Loma Linda, California, from the

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spinal fluid of a baby that died of meningitis. The clinical and pathological aspects of the infection will be described by Dr. Judefind and his associates who recognized the organism as an unusual *Salmonella* type. The organism was a motile bacillus which possessed the usual cultural and biochemical