

Noninvasive Blood Pressure Determination in the Rabbit with a Doppler Ultrasound Probe (40564)

PATRICIA B. WILLIAMS, HERBERT SCHAPIRO, AND PATRICIA E. YEISER

Departments of Pharmacology and Anatomy, Eastern Virginia Medical School, Box 1980, Norfolk, Virginia 23501

Reliable measurements of blood pressure in rabbits have long been necessary in studies of cardiovascular disease and also in the study of drug effects on the cardiovascular system. In acute studies, direct arterial cannulation is an accurate method for blood pressure determination. In chronic studies, blood pressure determinations have proved to be more difficult and less reliable, although several methods have been employed (1-4). Described here is a rapid, reproducible, noninvasive technique for blood pressure determination which detects both systolic and diastolic pressures with minimal agitation of the rabbit.

Materials and methods. White New Zealand rabbits weighing 2.6 to 3.3 kg were studied. Normotensive and surgically induced hypertensive rabbits were included. In all animals, blood pressure was measured in the following manner. The unanesthetized rabbit was gently restrained in the supine position. A pediatric blood pressure cuff (Roche Laboratories) was fitted around the upper thigh and connected to an aneroid sphygmomanometer, calibrated regularly against a mercury manometer. A Doppler ultrasound probe (Parks Electronics Laboratories) was placed over the femoral artery and used to determine the systolic and diastolic blood pressures upon inflation of the cuff (Fig. 1). The beginning of the equivalent of the Korotkoff sounds and their muffling were recorded as the systolic and diastolic blood pressures, respectively, as described by Hochberg and Solomon (5).

Direct, acute determinations of blood pressure were also obtained by the cannulation of the abdominal aorta. The rabbits were anesthetized with ether and the abdominal aorta was exposed and cannulated with a 1.5-mm polyethylene cannula. These cannulae were connected to a Beckman 8503-4M11 blood pressure transducer and pressures recorded on a Beckman Dynograph R611.

Some rabbits in the study had surgically

induced hypertension. Under ether anesthesia either the left kidney was removed or the left renal artery was partially ligated to reduce blood flow. The partial ligation was accomplished by tying a 0.8-mm stainless-steel rod to the artery and slipping the rod out from under the suture.

All data were expressed as the mean \pm standard error of the mean (\pm SE). Statistical comparisons were made using *t* tests for unpaired or independent means (6). The level of significance was $P < 0.05$.

Results. Blood pressures obtained by means of the Doppler ultrasound method were compared with direct blood pressure recordings obtained by cannulation of the abdominal aorta. Both before and during ether anesthesia, the rabbit's blood pressure was determined using the Doppler ultrasound probe. The abdominal aorta was then cannulated and the blood pressure again measured. Pressures obtained by the Doppler ultrasound probe before and during ether anesthesia were $118 \pm 6/65 \pm 2$ and $117 \pm 9/67 \pm 3$ mm Hg, respectively ($n = 6$). Pressures obtained from cannulation of the abdominal aorta during ether anesthesia were $110 \pm 8/68 \pm 5$ mm Hg ($n = 6$). Comparisons of the indirect blood pressure determinations, preinduction and during anesthesia, showed no significant differences from those obtained through direct cannulation of the aorta.

Blood pressures were determined with the Doppler ultrasound probe in a large series of normotensive and renal hypertensive rabbits (Table I). There was little variation in the blood pressures recorded from normotensive rabbits. There was, however, a significant difference in the pressure between the normotensive and hypertensive rabbits. This method was less effective in detecting and measuring blood pressure in hypotensive rabbits. After the intravenous administration of either pentobarbital (30 mg/kg) or 1.0 ml of absolute ethanol the diastolic pressure fell to

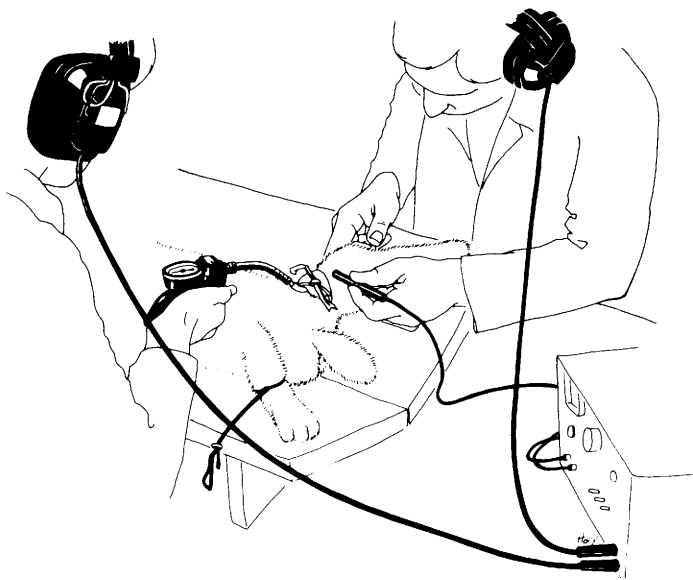


FIG. 1. Apparatus for blood pressure determination in the unanesthetized rabbit by means of the Doppler ultrasound probe.

TABLE I. BLOOD PRESSURE DETERMINATION IN UNANESTHETIZED NORMOTENSIVE AND HYPERTENSIVE RABBITS WITH A DOPPLER ULTRASOUND PROBE.^a

	Blood pressure	<i>n</i> ^b
Normotensive	132 ± 3/65 ± 1*	93
Nephrectomy	142 ± 8/82 ± 5**	18
Partial renal artery ligation	156 ± 5/88 ± 3**	10

^a These readings reflect the average of two consecutive determinations of the blood pressure in each of a large group of unanesthetized rabbits. Blood pressure is expressed in mm Hg.

^b The number of rabbits is represented by *n*.

* Mean ± SE.

** Significantly different from normotensive, *P* < 0.05.

30 ± 5 mm Hg (range 25 to 40). Detection of the diastolic pressure in this range was often obscured by the stronger signal for venous pressure picked up from the adjacent vein. However, the method is capable of accurately recording blood pressures in normotensive and hypertensive rabbits.

Blood pressures were also taken over an extended period of time (Fig. 2). With the Doppler ultrasound method, it was possible to detect increasing blood pressures in the renal hypertensive rabbits while those in the control animals remained unchanged. It was also possible to demonstrate the difference between the unilateral nephrectomized rab-

bits and those rabbits with unilateral partially ligated renal arteries (Table I). After nephrectomy or partial renal artery ligation, diastolic and systolic pressures increased rapidly. The diastolic pressure remained elevated for at least 5 weeks. The systolic pressure in the nephrectomized rabbits peaked at 1 week and decreased to a lower but still significantly elevated level. The systolic pressure after partial ligation of the renal artery remained elevated. The difference between nephrectomy and partial renal artery ligation may reflect the ability of the remaining kidney to partially compensate for the loss of the contralateral kidney. It is believed the kidney as a result of the partial ligation perceived the reduced blood flow as a hypotensive state. The kidney reacted physiologically by secreting endogenous compounds such as renin in an attempt to increase blood pressure.

Due to unavoidable personnel changes during the course of this study, it was possible to measure variations in the subjective determination of the beginning of the equivalent of the Korotkoff sounds and of their muffling by different observers. For normotensive rabbits, the variation between observers was 1.0 ± 2.8 mm Hg for systolic pressures and 0.8 ± 1.4 mm Hg for diastolic pressures (*n* = 5). Each observer determined the pressure in at least nine different rabbits. A Duncan's mul-

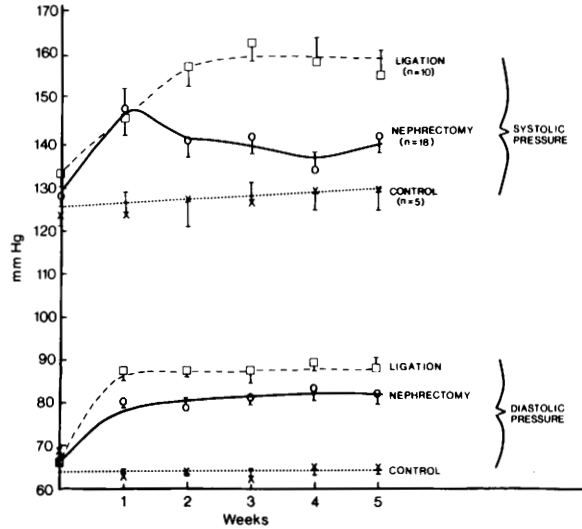


FIG. 2. Blood pressures were measured weekly in the control, nephrectomized, and partial renal artery ligated (referred to above as ligation) rabbits. Pressures recorded for each rabbit were the average of two determinations. The number of rabbits is presented by *n*. The vertical bars represent the standard error.

tiple range test indicated no significant differences between the values for any of the observers. Similar results were obtained upon analysis of the blood pressure determined in the unilateral nephrectomized rabbits and in the rabbits with a partially ligated renal artery.

Discussion. The use of an ultrasound beam to measure the movement of the arterial wall when a deflating occlusive cuff has been applied was suggested by Ware (7) and by Kirby and associates (8). In humans the audible signal generated by this method correlated well with the Korotkoff sounds and direct arterial methods of blood pressure measurement (5). Blood pressure determination by this method has also been used coupled with the tail cuff method in rats (9), and also in the small arteries of the hind limb of the dog proximal to the tarsal joint (10). Good correlation between this indirect method and direct intraarterial recordings were obtained in the dog, but not in the rat, possibly due to the preheating necessary in the tail-cuff determination method on rats.

The primary indirect method of blood pressure determination in the rabbit has been the Grant-Rothschild capsule (3) or its modifications (11-13). However, because the blood vessels in the rabbit ear are important for heat dissipation or conservation, under ordinary conditions these vessels constrict or

dilate intermittently. Similar blood vessel activity is also seen in response to excitement. Therefore, to obtain an adequate flow in the vessels the whole body or ear of the animal is warmed altering the pressure and flow characteristics which may contribute to the discrepancies in the central arterial pressure. An alternative method is denervation of the central ear artery. It is also possible by means of complex formulae and tables to relate the ear artery pressure to the central arterial pressure. However, it is still difficult to obtain a diastolic pressure reading with the ear capsule method. McGregor (4) described an auscultatory approach for the indirect determination of blood pressure in the rabbit. An inflatable cuff was wrapped around the abdomen and the Korotkoff sounds were utilized to determine the systolic and diastolic pressures. The major disadvantage of this procedure was the tendency to cause serious vasomotor disorders negating its reliability.

Several methods have been described for repeated direct determination of arterial blood pressure, however, problems of trauma and clotting remained. The most common method involved repeated cannulation of the ear artery which was compromised by spontaneous alterations in blood flow to this region. Goldblatt (2) repeatedly cannulated the femoral artery by insertion of a needle through the skin. Indwelling catheters have

been utilized (1) but the risk of infection and clotting remains.

In comparison to the methods of measuring blood pressure in rabbits discussed above, the modified auscultatory method using the Doppler ultrasound probe described here has several advantages when blood pressure determination must be made over an extended period of time. This method is accurate with respect to central arterial pressure and does not require complex computations to correct the directly obtained values. Pressures can be reproducibly determined and elevations of pressure accurately measured. The inter- and intra-rabbit variations are small and although subjective endpoints are involved, the variation between observers has been small.

A major advantage of the method described here is the ability to reliably determine both the systolic and diastolic pressures. This is particularly important in the study of hypertension and in an analysis of the effects of drugs on blood pressure, where it is vital to be able to evaluate the diastolic pressure. There is some elevation of systolic pressures in normal rabbits possibly due to handling, but diastolic pressures remain within normal limits. In addition, this method induces no alterations in blood flow such as are produced by denervation of the artery or by warming the animal. The major disadvantage associated with the blood pressure determination by means of the Doppler ultrasound probe is the inability to quantify pressures below 45 mm Hg. They are also difficult to differentiate from venous sounds which begin at 30 to 40 mm Hg.

Summary. A rapid, reproducible, noninvasive technique which allows repeated determinations of blood pressure in the rabbit is described. With the rabbit in the supine position, hind legs extended, a pediatric blood pressure cuff was placed around the upper thigh. A Doppler ultrasound probe, placed over the femoral artery, was used to deter-

mine the systolic and diastolic pressures. The average pressures obtained were $132 \pm 3/65 \pm 1$ mm Hg (\pm SEM) ($n = 93$). These correlated well with direct intraarterial recording of the blood pressure. This technique was also used to measure the elevated pressures in hypertensive rabbits. Pressure measurements varied very little from one observer to another. Repeated determinations from the same rabbit were also relatively constant. This modified auscultatory method provides an efficient method for blood pressure determination in the rabbit over a period of time.

The authors wish to acknowledge the assistance of Patricia Morris, Marie Tulou, Valerie Lawwill, Susan Levy, Vicky Snyder, and Tina McKimmey for their technical assistance on this project. This study was partially supported by the Tidewater Heart Association. A preliminary report of these results was presented at the 1977 American Society of Pharmacology and Experimental Therapeutics in Columbus, Ohio, August, 1977.

1. Brooks, B., and Muirhead, E., *Arch. Pathol.* **93**, 464 (1972).
2. Goldblatt, H., *Proc. Soc. Exp. Biol.* **105**, 213 (1960).
3. Grant, R., and Rothschild, P., *J. Physiol.* **81**, 265 (1934).
4. McGregor, L., *Arch. Pathol.* **5**, 630 (1928).
5. Hochberg, H., and Solomon, H., *Curr. Ther. Res.* **13**, 129 (1971).
6. Steel, R., and Torrie, J., "Principles and Procedures of Statistics," p. 73. McGraw-Hill, New York (1960).
7. Ware, R., Presented at the 3rd National Biomedical Sciences Instrumentation Symposium (Instrument Society of American EM-65). Dallas, Texas (1965).
8. Kirby, R., Kemmerer, W., and Morgan, J., *Anesthesiology* **31**, 86 (1969).
9. Bunag, R., Muetting, N., and Riley, E., *J. Appl. Physiol.* **39**, 724 (1975).
10. Frenlich, J., Detweiler, D., and Hance, H., *Curr. Ther. Res.* **14**, 73 (1972).
11. Wilson, D., Romero, G., Strong, C., Lea, K., and Schriver, S., *J. Lab. Clin. Med.* **86**, 1032 (1975).
12. Thind, G., *Curr. Ther. Res.* **14**, 540 (1972).
13. Landis, E., Montgomery, H., and Sparkman, D., *J. Clin. Invest.* **17**, 189 (1938).

Received October 31, 1978. P.S.E.B.M. 1979, Vol. 161.