TABLE I.

Min. after insulin injection	Arterial-Venous O_2 Difference Vol.%	Blood Sugar mg%	Alpha Frequency per second	Delta-Index, cm
0	9.0	89	9.5	0.5
70	—	—	7.0	16.0
90	2.8	22	0.0	21.0
175	—	—	0.0	22.0
252	1.6	23	0.0	20.0
10 (After sugar)	4.5	45	7.0	—
30 " "	6.3	57	8.8	2.0

were made. The first group of symptoms appeared while the oxygen uptake fell from 9.0 volumes % to 2.8 volumes %. The second, third, and fourth groups developed in turn as oxygen uptake decreased further to 1.6 volumes %. The administration of sugar was followed by a rapid reversal of the symptoms and the blood picture. In view of the fact that there may be no significant change in cerebral blood flow during hypoglycemia uncomplicated by convulsions[3] it may be concluded that (a) there is a progressive decrease in cerebral metabolism as indicated by the diminution in the arterial-venous oxygen difference, (b) this decrease in oxygen consumption may be correlated with a lessening frequency and final disappearance of the alpha waves as well as an augmentation of the delta index, and (c) the progress of the symptoms through the 4 stages is also associated with an ever-deepening depression of cerebral metabolism. Thus a parallelism is revealed in the metabolic, electrical, and clinical changes resulting from the injection of insulin.

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An Indirect Method for Repeated Determinations of Blood Pressure of Rats.

J. T. DIAZ* AND SANFORD E. LEVY.† (Introduced by J. C. Burch.)

From the Departments of Obstetrics and Gynecology, and Surgery, Vanderbilt University School of Medicine, Nashville, Tenn.

A frequently used method for recording approximate mean blood pressures in rats is the insertion into the aorta, or other large vessels,

3 Leibel, B. S., and Hall, G. E., PROC. SOC. EXP. BIOL. AND MED., 1938, **38**, 894.

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† National Research Fellow in the Medical Sciences.

of a needle which is connected to a mercury manometer. However, the animal must usually be sacrificed after such a procedure. An entirely satisfactory method which permits repeated determinations of blood pressure of rats has not been devised. Any improvement in the method now available is therefore desirable.

Recently described indirect methods are those of Griffith[1] and Bonsmann.[2] The use of the hypodermic needle and the optical manometer described by Hamilton, *et al.*,[3] is not simple technically, although it has many advantages. It was used by Woodbury and Hamilton[4] for recording the systolic and diastolic blood pressures in small animals. The method is not well adapted, however, for making repeated observations in small animals such as the rat, in which the blood vessels to be punctured must be exposed surgically at each determination.

In the present publication, an indirect method is described for making repeated determinations of blood pressure in rats. The results obtained with the indirect method are compared with pressures in the aorta recorded with the mercury manometer and needle.

Two methods of determination of blood pressure were used in these experiments. Direct determinations of the aortic pressure with a needle and mercury manometer were used to check the blood pressures obtained by the indirect method. The principle of the indirect method employed was the compression of the rat's tail by a cuff of a special design (Fig. 1). This cuff consists of a rigid outer cone of glass (approximately 3 cm in diameter and 7 cm in length) closed at each end with rubber stoppers. The stoppers each have a central hole. A tube of thin rubber (such as Penrose tubing) connects the holes in the stoppers. The pressure in the space between the outer glass tube and the inner rubber tube is regulated by a blood pressure bulb and mercury manometer. Anesthesia is induced by nembutal administered intraperitoneally. The rat's tail is placed through the central tube of thin rubber, which is of course open at both ends.

In order that the blood pressure be determined, the tail is adjusted so that a short length projects through the central tube. The pressure in the cuff is raised well above the systolic level. The tip of the tail is then snipped off with a pair of scissors and immediately immersed in a 0.2% solution of sodium citrate to avoid clotting. There is an initial flow of blood following the severing of the tail which diminishes until little or no blood oozes from the cut end.

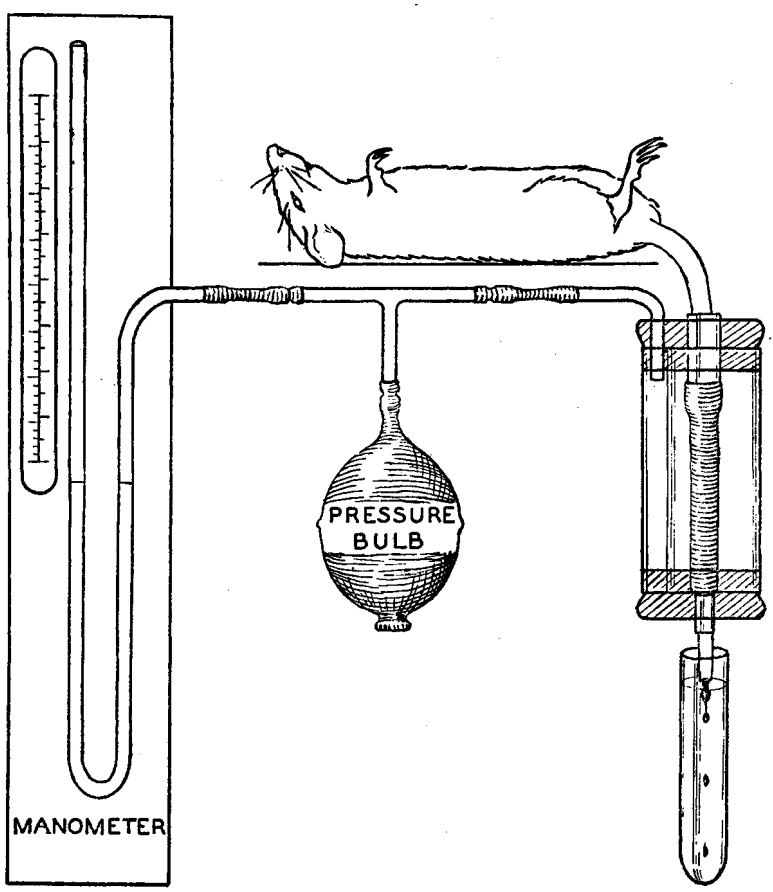
1 Griffith, J. Q., Jr., PROC. SOC. EXP. BIOL. AND MED., 1934-35, **32**, 394.

2 Bonsmann, M. R., *Arch. Exp. Path. u. Pharm.*, 1934, **176**, 460.

3 Hamilton, W. F., Woodbury, R. A., Harper, H. T., *J. A. M. A.*, 1936, **107**, 153.

4 Woodbury, R. H., and Hamilton, W. F., *Am. J. Physiol.*, 1937, **119**, 663.

FIG. 1
BLOOD PRESSURE CUFF AND MANOMETER
WITH RATS TAIL IN PLACE



As the pressure in the cuff is slowly released, the character of the stream of blood may be noted to change at 2 points. These points may be called "systolic" and "diastolic", although it is open to question whether this designation would be strictly correct. The "first point" is marked by the appearance of jets of blood which have the appearance of beads as they fall through the citrate solution. The flow of blood gradually grows larger as the cuff pressure is reduced. Suddenly there is a striking increase in the stream of blood. This is quite definite in most animals and is the "second point." The pressure in the cuff is raised again and the procedure repeated. After

the final reading, the end of the tail is ligated to prevent further bleeding.

Comparisons of blood pressure determinations by the indirect and direct methods were made, the latter being determined immediately after the former method.

Results. The results of determinations of blood pressures in 53 normal rats are shown in Table I. It was found that 87% of the "first point" pressures were between 101 and 130 mm mercury and 90.6% of the "second point" pressures were between 41 and 80 mm mercury. These pressures determined by the tail method vary less than those reported by Leiter[5] in a series of 131 rats in which the direct carotid artery method was used. He states: "Sixty-nine percent of the initial values fell between 101 and 140 mm Hg, 20% were above 140 mm Hg, and only 11% were below 101 mm Hg." A direct aortic blood pressure was obtained in 35 animals. The aortic pressures averaged approximately 10 mm Hg above our calculated mean of the "pulse pressure" (one-half of "pulse pressure" added to "second point" pressure). It is our impression that the so-called "second point" pressure appears to be less variable than the "first point" when compared with the blood pressure in the aorta obtained with mercury manometer and needle. The latter pressures agree with those reported by Leiter[5] and Durant,[6] who used the carotid artery. They also agree with the aortic pressures determined in 1,207 normal rats by Williams, Weigreia and Harrison,[7] who found that 94% of the pressures were between 90 and 140 mm Hg.

That the cuff readily detects changes in blood pressure produced by an injection of epinephrine is illustrated by the following experiments, 2 of which were performed. The control pressures were 160 "first point" and 90 "second point." At 3 and 5 minutes after the injection of epinephrine, the blood pressure had risen to 210 "first point" and 140 "second point." Thirteen minutes following the injection, the tail pressure had fallen to 180 "first point" and 120 "second point."

The indirect method described for taking blood pressures is similar to the one Chanuten and Ferris[8] attempted to use but discarded as unsatisfactory. The design of the cuff used in our experiments is probably the factor which has made the tail method satisfactory in our hands.

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[5] Leiter, L., *Arch. Int. Med.*, 1936, **57**, 729.

[6] Durant, R. R., *Am. J. Physiol.*, 1927, **81**, 679.

[7] Williams, J., Weigreia, R., and Harrison, T. R., in press.

[8] Chanuten, A., and Ferris, E. B., *Arch. Int. Med.*, 1932, **49**, 767.

TABLE I.
Blood Pressures of Rats Determined by the Indirect Cuff Method and Direct Aortic Needle Puncture.
Normal Rats.

No. of Animals	Indirect Cuff Method						Mean Blood Pressure Calculated from "First Point" and "Second Point"	Direct Aortic Needle Method		
	"First Point"			"Second Point"						
	Avg	Min.	Max.	Avg	Min.	Max.		Avg	Min.	Max.
53	118	90	140	66	40	95	92	110	93	125

As previously mentioned, the points at which a change is noted in the character of the flow of blood from the cut end of the tail are designated as "first point" and "second point" for convenience. The so-called "second point" is usually extremely sharp and easily observed. It also appears to be less variable, when compared with the aortic blood pressure determined by the direct method of needle puncture. However, the "first point" pressure can be determined, we believe, particularly after some experience has been acquired with the same method. The "pulse pressures" we obtained in the present experiment are of the same order as those reported by Woodbury and Hamilton.[4] Both "first point" and "second point" pressures, particularly the "second point", are somewhat lower than the systolic and diastolic pressures given by Woodbury and Hamilton, but the fact that the tail vessels are quite distant from the heart may account for the lower values obtained. Direct pressures in the tail have not been recorded to our knowledge, so that the exact pressure in these vessels is not known.

Since the "second point" pressures we obtain can be determined easily, this figure alone, although perhaps somewhat low, would be useful in many types of experiments in which it is desirable to determine pressures at intervals for comparison. Landis believes that by heating the animal (*i. e.*, raising its body temperature) the tone of the vessels is lowered and, therefore, the blood pressure can be detected at a higher point. If this is the case, heating the animal, then, could supplement the method of blood pressure determinations reported here.

Summary. A method has been described for obtaining repeated determinations of blood pressure in rats. The blood pressures obtained with the indirect method agree with those obtained by the direct method of aortic cannulation.