1955, v182, 131.

4. Marriott, W. M., and Howland, J., *Arch. Int. Med.*, 1918, v22, 477.

5. Salter, W. T., Tarquharson, R. F., and Tibbetts, D. M., *J. Clin. Invest.*, 1932, v11, 391.

6. Conway, E. J., *Microdiffusion Analysis and Volumetric Error*, 3rd ed., 1950, London, C. Lockwood.

7. Peters, J. P., and Van Slyke, D. D., *Quantitative Clinical Chemistry, v2 Methods*, 1932, Baltimore, Williams and Wilkins.

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A New Simple Method for Indirect Determination of Blood Pressure in the Rat.* (22948)

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Technics generally used for indirect determination of blood pressure in the rat's tail have one or more of the following disadvantages: 1) they are cumbersome, 2) they require complex apparatus, or 3) they are relatively inaccurate. The older plethysmographic methods(1,2,3) have been further complicated by adapting them to electronic devices in order to increase their sensitivity (4). The photoelectric tensometer depends upon change in transmission of a light beam incident on a small area of the rat's tail(5) or foot(6). Friedman and Freed(7) described what is called a microphonic manometer which, according to these observers, operates by amplifying the pulsatile vibrations of the caudal artery in the tail similar to that noted in the indirect recording of blood pressure in the human brachial artery. A graphic method of recording these tail vibrations has been reported to yield greater accuracy than that obtained with the microphonic manometer(8).

The present report is concerned with the relationship of these pulsatile vibrations, as seen by the naked eye, to blood pressure in the rat's tail as measured by other standard procedures. Thus, by simply observing the characteristic pattern of vibration in the tail, the indirect systolic pressure may quickly be determined without the use of expensive or complex equipment. This report also deals with comparative measurements of blood pressure after whole body warming versus tail warming, the influence of cuff length on blood pressure readings, and difficulties encountered following the use of vaso-constrictor agents.

Materials and method. 1. Description of the Visual Method. When the rat's tail is warmed for 5-10 minutes or the rat itself is placed in a ventilated incubator at 39°C for 15 minutes and a 20 mm cuff attached to a manometer is placed on proximal part of tail, pulsatile vibrations can readily be seen along the entire length of the tail. These movements are of maximal amplitude at the distal end of the tail which must be allowed to hang freely. If the cuff is then inflated to a pressure exceeding the systolic pressure, the vibrations cease. With slow deflation of the cuff the vibrations suddenly reappear and increase in amplitude as the cuff pressure approaches zero. The pressure at which the pulsations make their first reappearance is taken as the systolic endpoint. This point is sharp, reproducible within narrow limits, and easily seen by the inexperienced observer. Often the endpoint is heralded by an arching upward of the end of the tail, after which the vibrations immediately appear. Observations of minimal vibrations are facilitated by use of darkened room with a lamp placed so that a sharp shadow of the tail is cast on a white background one or two cm behind the tail. To avoid struggling and to limit extraneous movements, the animals are confined in a

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TABLE I. Blood Pressure Determination in Normal and Hypertensive Rats by 4 Different Methods.

Wt range, g	No. of rats	Visual method* Avg	Visual method* Range	Audiometric method* Avg	Audiometric method* Range	"Cut tail" method† Avg	"Cut tail" method† Range	Aortic mean‡ Avg	Aortic mean‡ Range
		mm Hg							
		Normotensive rats							
200-275	24	115 ∓ 10.6	92-132	112 ∓ 10.4	92-131				
275-350	20	125 ∓ 10.9	108-140	122 ∓ 16.4	103-158	117 ∓ 13.7	90-135	88 ∓ 19.7	62-113
350-475	20	124 ∓ 9.7	108-142	119 ∓ 11.5	100-143	121 ∓ 10.8	100-140	104 ∓ 14.6	75-122
		Hypertensive rats§							
335-444	9	165 ∓ 16.9	143-187	151 ∓ 18.8	130-183	153 ∓ 17.7	130-180	149 ∓ 9.3	136-166

* 4-6 observations/rat by visual and audiometric methods.
† Single observation/rat.
‡ " " " at time of sacrifice under light ether anesthesia.
§ Animals subjected to prolonged desoxycorticosterone trimethylacetate administration and increased salt intake.

container during the study. Suitable containers may be made simply and inexpensively by telescoping 2 empty tin cans from which the bottoms have been removed but with the conical tops left intact. Different sized cans may be selected to accommodate virtually any size rat. Measurements should be made immediately after removal from incubator since cooling results first in diminution and later complete disappearance of the vibrations. Pulsations reappear upon re-heating the animal or its tail.

2. Experimental procedures. The blood pressure was determined in male rats of the Sprague-Dawley strain fed a fox chow diet *ad lib*. Their weights ranged from 200-475 g. Measurements were made as described previously. Where measurements were made with the microphonic manometer, the microphone was placed just distal to the cuff allowing the rest of the tail to hang freely. Simultaneous measurements were made by 2 observers independently, one recording the blood pressure by the visual method as noted above, while the other employed the microphonic manometer (audiometric method) essentially as described by Friedman and Freed(7).‡ In a preliminary experiment involving 13 normal rats, blood pressure measurements by the visual method were made with and without the microphone suspended from the tail to determine if weight of microphone dampened the vibrations. In no instance did the readings differ significantly. In 3 of the 4 groups of normal rats, 2 additional methods were used to measure blood pressure as soon as visual and audiometric readings were completed. With the cuff inflated beyond the systolic pressure level as previously determined, the distal 2-3 mm of the tail was amputated with a sharp scissors. The cuff was then slowly deflated until the first drops of blood spurted from the cut end. This was recorded as systolic pressure by the "cut tail" method. Blood loss was minimized by securing prompt hemostasis with an elastic band positioned just proximal to the cut end. The animal was then removed from the container, lightly anesthetized with ether, and the abdomen was opened along a midline incision. A 20 gauge needle was inserted into the abdominal aorta at its bifurcation and the pressure was recorded with the aid of a Statham strain gauge transducer connected to a Sanborn recorder. The latter was equipped with an electrical integrator which was used to obtain direct mean aortic pressure. Limitations of the recording apparatus available did not permit accurate measurement of systolic pressures. Two cuffs, 20 and 7 mm in length, were designed for comparison of blood pressure values as a function of compressed tail length. The cuffs were made of one half inch Penrose drain incorporated into a rigid receptacle allowing for inflation with air. The cuff was connected to either a mercury or aneroid type

‡ An additional amplifier permits more accurate readings. In some cases a Stethotron was used in conjunction with apparatus.

TABLE II. Influence of Cuff Size on Blood Pressure Measurement.

Wt, g	Cuff size, mm	Visual method* Avg	Visual method* Range	Audiometric method* Avg	Audiometric method* Range	"Cut tail" method†
330	20	145	144-145	140	140-140	135
	7	230	220-240	210	200-220	
310	20	134	132-136	154	145-158	118
	7	175	175-175	192	185-195	118
326	20	130	126-135	136	134-138	135
	7	150	145-152	151	150-152	140
286	20	133	130-136	134	132-135	140
	7	173	170-175	167	164-170	136
323	20	138	134-144	139	136-144	
	7	175	170-180	174	170-178	
	20	147	145-148	155	152-158	140
340	20	114	108-120	142	140-144	
	7	183	180-185	182	180-184	
	20	123	115-130	146	144-148	125
305	20	128	125-130	130	126-132	
	7	188	185-190	182	178-185	
	20	125	125-130	127	122-132	116
288	20	114	110-118	110	108-112	
	7	150	135-160	—	over 300	
	20	123	120-125	121	117-125	115
272	20	119	118-120	101	95-108	
	7	134	125-140	142	140-144	
	20	125	124-125	108	105-111	118

* Avg of 2-3 observations/rat.
† Single observation.

manometer. The experiments in which only the tail of the animal was heated were performed a few days after the blood pressures were determined in the usual way, *i.e.* after the animal had been kept in an incubator for 15-20 minutes at 39°C. The tail was heated by means of a light bulb situated at a variable distance from it and measurements were made as soon as vibrations appeared.

Results. 1. Comparison of indirect and direct methods. As shown in Table I, blood pressures determined by the 3 indirect methods—visual, audiometric, and "cut tail method" were approximately the same for normal rats weighing 200-475 g. The direct aortic mean pressure was definitely lower than the value obtained by indirect methods in the case of normal rats. In the hypertensive range, however, the direct measurements approximated those obtained by indirect means. Two other observations are of special interest: 1) In comparative studies in which movement of the tail was almost completely prevented by holding the tip of the tail gently with a forceps the microphonically audible sounds disappeared or were markedly diminished. 2) In some rats systolic pressure could not be determined with the microphonic technic because the sound persisted with no change in its character up to pressures of 300 mm of mercury.

2. Blood pressure measurements as a function of cuff size. As seen in Table II, visual and audiometric blood pressure readings obtained using the 7 mm cuff far exceeded those obtained with the 20 mm cuff in every case. However, in the case of the 3 rats studied with the "cut tail method" blood pressure values were independent of cuff size.

3. Whole body warming versus tail warming. It is evident from Table III that blood pressure readings were almost the same regardless of which warming method was used.

4. Studies with epinephrine. Each of 5 rats was injected subcutaneously with 0.2 mg of epinephrine in oil. Blood pressure readings by the indirect methods were obtained 30 minutes and 2 hours after the injection after preliminary whole body warming at 39°C for 15 minutes. Seven other animals received 0.05 mg of aqueous epinephrine subcutaneously and were then warmed in a similar manner. Blood pressure readings were made at 15-minute intervals for 2 hours. No sig-

TABLE III. Blood Pressure Measurements after Whole Body and Tail Warming.*

	Visual method				Audiometric method			
	Body warming		Tail warming		Body warming		Tail warming	
Wt, g	Avg	Range	Avg	Range	Avg	Range	Avg	Range
204	116	110-122	112	110-115	107	100-118	107	104-110
212	120	114-125	118	112-120	118	112-124	114	110-116
214	122	112-130	121	116-126	115	105-122	115	114-118
233	104	104-104	114	110-118	98	95-100	116	110-118
249	113	110-120	123	120-125	107	106-108	120	118-122

* Avg of 2-3 observations/rat.

nificant effect on blood pressure was noted in either of these experiments. The experiment was then repeated using aqueous epinephrine in doses of 0.2 mg subcutaneously. This resulted in extreme excitability and marked blanching of the peripheral parts including the ears, feet, and tail. Despite warming, tail vibrations were not visible, and no sound could be heard with the microphonic manometer.

Discussion. Measurement of rat blood pressure by the visual observation of tail vibrations as a systolic endpoint as described herein has the advantage of simplicity, low cost, and accuracy when compared to other indirect methods.

Since the sounds heard with the microphonic manometer are abolished or markedly decreased by holding the tail rigidly in position, it is apparent that these sounds are related directly to the tail vibrations rather than to the direct transmission of sound from the arterial pulsations. In those cases where sound can be heard far beyond the systolic pressure level, it would appear that the sound is due to the impact of blood striking the compressed segment of artery just under the proximal end of the cuff. This would also explain why the latter sound is also synchronous with the pulse. It is not clear why this sound is heard only occasionally and only in the case of certain animals. Its presence might be due to such factors as the location of the caudal artery in relation to the position of the microphone and to the thickness of the tail itself. It would appear that the pulsatile vibrations which can be seen with the naked eye, graphically recorded or amplified in the microphonic manometer into recognizable sound are one and the same. The similar values for systolic pressure by the visual and audiometric methods also support this view. In general, blood pressure measurements made by observation of blood flow after amputating the tip of the tail compared favorably with those made by the other 2 indirect methods when the 20 mm cuff was used. This holds true even for the hypertensive range.

The importance of the tail temperature, cuff width, and cuff position on the simultaneous measurement of indirect and direct arterial pressure has been pointed out by Sobin(9) and others(8,10,11). The data in Tables II and III are in agreement with the published observations concerning cuff size.

A serious limitation of indirect blood pressure measurements using the tail occurs when there is severe peripheral vasoconstriction. Thus, when hypertension is associated with vasoconstriction, the tail cannot be used to measure blood pressure by either the visual or audiometric methods. Indeed, the initial heating is necessary in order to overcome the normal vasoconstrictive tone present in the caudal artery. The heating maneuver, however, apparently fails to produce this effect when there is a powerful vasoconstrictor agent, such as aqueous epinephrine, exerting its influence. In the doses used in this study, epinephrine in oil was found to have no such pressor effect. This is in contrast with the findings of Friedman and Freed(7) who reported that 0.2 mg of this drug in oil resulted in doubling the systolic pressure as measured by the microphonic manometer. However, Del Greco *et al.*(8) found that even a much larger dose of this drug dissolved in oil, one milligram, resulted in widely variable blood pressure readings, and they further commented on the reduced tail vibration making it impossible to take readings in some cases.

Summary. A new indirect method for measuring systolic pressure in the rat's tail has been described. It depends upon the visual recognition of pulsatile vibrations which are obliterated by inflating of the cuff to a pressure exceeding the systolic pressure. As the cuff is slowly deflated the vibratory motion reappears, the amplitude of the vibration increasing to a maximum as the cuff pressure approaches zero. The reappearance of the persistent vibration is taken as the systolic endpoint. The accuracy of the method was checked by comparing measurements with values recorded with the microphonic manometer, blood flow after amputating the tip of the tail, and in some instances by direct mean aortic pressure measurements in normal and hypertensive rats. No data were obtained in

hypotensive animals. The advantages and limitations of the visual method have been discussed. The effect of cuff size and preliminary warming of the whole animal or only the tail have been studied.

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1. Byrom, F. B., and Wilson, C., *J. Physiol.*, 1938, v93, 301.

2. Griffith, J. Q., Jr., PROC. SOC. EXP. BIOL. AND MED., 1934, v32, 394.

3. Williams, J. R., Harrison, T. R., and Grollman, A., *J. Clin. Invest.*, 1939, v18, 373.

4. Chittum, J. R., Hill, H. C., Jr., and Grimson, K. S., PROC. SOC. EXP. BIOL. AND MED., 1947, v66, 486.

5. Bonsmann, M. R., *Arch. f. exp. Path. U. Pharmakol.*, 1934, v176, 460.

6. Kersten, H., Brosene, W. G., Jr., Ablondi, F., and Subbarow, Y., *J. Lab. and Clin. Med.*, 1947, v32, 1090.

7. Friedman, M., and Freed, S. C., PROC. SOC. EXP. BIOL. AND MED., 1949, v70, 670.

8. Del Greco, F., Olmsted, F., Masson, G. M. C., and Corcoran, A. C., *J. Lab. and Clin. Med.*, 1953, v41, 729.

9. Sobin, S. S., *Am. J. Physiol.*, 1946, v146, 179.

10. Proskauer, G. G., Neumann, C., and Graef, I., *ibid.*, 1945, v143, 290.

11. Shuler, R. H., Kupperman, H. S., and Hamilton, W. F., *Am. J. Physiol.*, 1944, v141, 625.

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An Experimental Aortic Valve. (22949)

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The correction of aortic valvular insufficiency remains a problem that has not been adequately solved. The insertion of a plastic ball valve by Hufnagel(1) has received the greatest trial, both experimentally and clinically. More recently Silen and his associates (2) attempted to create a competent aortic valve in experimental animals by intussusception of the aorta in its thoracic portion. However, this ingenious method seems to create some degree of constriction. The present report describes experiments in animals, attempting to produce an aortic valve by creation of a flutter valve in the thoracic aorta.

Methods. Mongrel dogs weighing 14-25 kg were anesthetized with nembutal or with ether. Hypothermia (rectal temperature 22-28°C) was induced with an ice bath. Aseptic technics were employed. The left thoracic cage was opened through the fifth intercostal space and the aorta mobilized from the left subclavian artery to the diaphragm. The ad-

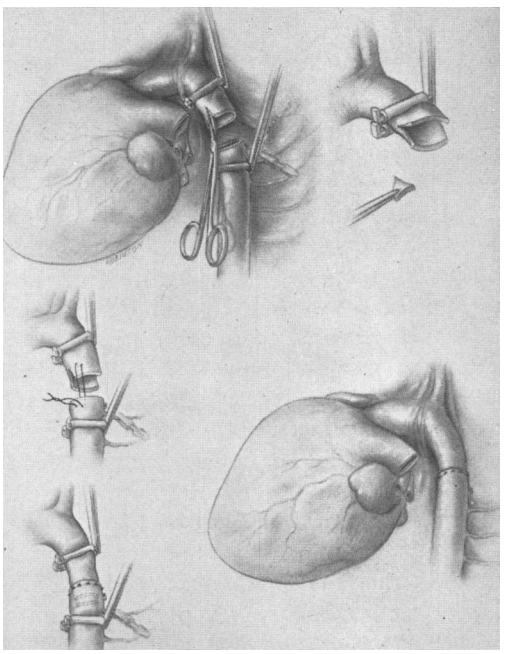

FIG. 1. Steps utilized to create aortic valve.