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A New Endpoint for Blood Pressure Determination in the Rat's Tail.*

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The indirect plethysmographic method for the measurement of systolic blood pressure in the caudal artery of the rat by the method of Byrom and Wilson,[1] as adapted by Williams, Harrison, and Grollman,[2] and also by other workers,[3] has found widespread application. Among the difficulties encountered in the use of this method is the occasional appearance of equivocal endpoints. We wish to describe a device which may be used in place of the plethysmograph and which we believe gives more reliable endpoints in trained rats.

In the plethysmographic method a change in volume of the tail occurs when the pressure in an inflated cuff at the base of the tail is allowed to drop to the arterial pressure. This small change in volume of the tail is conducted through a thin rubber membrane to a rigid water system and thence to a capillary tube where it is noted as a rise in the water level, and is regarded as the endpoint for the determination. In the device which we have constructed, this same change in volume of the tail is mechanically transferred to develop a pressure on a carbon telephone transmitter button. This increased pressure on the button results in an approximate 75% decrease in its electrical resistance which may be observed on a continuously-indicating ohmmeter circuit.

Mechanically, the device (Fig. 1) consists of an H-shaped figure formed of balsa wood, the upright on the left being hinged at its middle to one end of the crosspiece, the other end of the crosspiece being rigidly fixed to the righthand upright. Thus a lever is formed whose action is similar to a nasal speculum. At the upper end of the lever and in a plane perpendicular to it, are secured flat plates of light sheet metal. The inner edges of these plates are straight, 5.5 cm long, and parallel. A cloth band is glued between the upper surfaces of these plates and allows a 1.5 cm separation of their inner edges. At the lower end of the H-shaped lever is secured a carbon telephone transmitter button, the flat grounded portion of the button being placed against the righthand upright. At the lower end of the lefthand upright, and mounted on the lower part of the hinge is an adjusting screw. This screw is so placed that it may be adjusted to touch the center, ungrounded, diaphragm portion of the button at any degree of separation of the upper plates. The overall height of the device is 7 cm, the fulcrum of the hinge is 4 cm from the upper surface of the plates, and the uprights are separated by the 2.5 cm crosspiece.

Electrical connections are made to the grounded and to the ungrounded portion of the button with the most flexible wire that is consistent with strength. The wires may be soldered directly to the button. The wire from the ungrounded, diaphragm portion is mechanically secured to the righthand upright to prevent transmission of wire movements to this sensitive portion of the button.

The electrical leads from the device may be connected to a simple ohmmeter circuit capable of indicating 0-300 ohms continuously without electrical adjustments. A wide dial instrument is obviously desirable. We prefer, however, to use a simple wheatstone bridge circuit, the first 2 arms of which are formed by a 400-ohm radio type potentiometer, the third arm by a 200-ohm fixed carbon

* We will be pleased to loan, for a short period of time, a sample device to any interested individuals.

Supported by a grant from the Smith, Kline, and French Company, Philadelphia, Pa.

1 Byrom, F. B., and Wilson, C., *J. Physiol.*, 1938, **93**, 301.

2 Williams, J. R., Jr., Harrison, T. R., and Grollman, A., *J. Clin. Invest.*, 1939, **18**, 373.

3 Kemph, G. F., and Page, I. H., *J. Lab. Clin. Med.*, 1942, **27**, 1192.

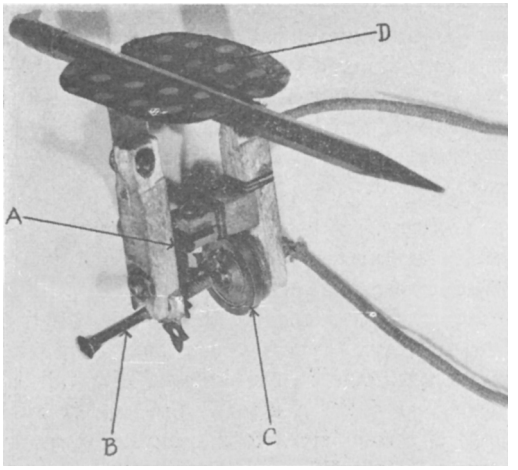

FIG. 1.
Photograph of endpoint device for indirect blood pressure measurement in the rat's tail. "A" is a hinge. "B" is an adjusting screw touching diaphragm portion of carbon button "C." "D" is one of 2 metal plates covered and joined with a cloth band. The pencil shows the position occupied by the rat's tail.

resistance, and the fourth arm by the device itself. As a balance indicator we use a 0-150 microammeter, and as a source of current, a 1.5-volt dry cell in series with a 5000-ohm variable resistance. In this circuit the setting of the variable resistance controls the sensitivity, while the setting of the potentiometer controls the working range. It is not necessary at any time to "balance" the bridge accurately since only changes in the resistance of the button are desired and not the actual resistance.

In order to take blood pressure readings the tail of the rat is led through a 20 mm pressure cuff[4] and thence into a tube fashioned of wire screen which simply supports the tail in a horizontal position. A gap of approximately 6.5 cm is left between the cuff and the tail holder. The endpoint device is clamped to the tail in this gap by forming the cloth band like a sling around the tail from below and setting the adjusting screw up against the center of the carbon button so that the parallel edges of the metal plates approach on the upper side of the tail. The pressure with which the device is clamped to the tail is entirely noncritical with respect to obtaining endpoints and need only be sufficient that there be no danger of its becoming detached. The carbon button proper is then tapped lightly which loosens the carbon particles and increases their resistance to approximately 200 to 300 ohms. The pressure in the cuff is then rapidly elevated to a point above the expected blood pressure of the animal and slowly lowered. At the endpoint, at which the arterial pressure fills the tail with blood, the indicator of the ohmmeter will commence a characteristic smooth movement in the direction of decreasing resistance. If further fall in cuff pressure be prevented at this point the movement will continue until a resistance value of 20 to 50 ohms is obtained. Should the cuff pressure be allowed to fall without interruption this characteristic movement of the ohmmeter indicator will occur much more rapidly. When this low resistance value has been obtained one may, in a sense, confirm his reading by allowing the cuff pressure to fall rapidly below the venous pressure of the rat and observing the return of the ohmmeter indicator to its former value. Undue movements of the rat will result in sharp, jerky, nonpersistent movements of ohmmeter indicator. There is no difficulty in differentiating these movements from the true endpoint.

It has been shown by Sobin[5] that the accuracy of the indirect plethysmographic method of blood pressure measurement may be greatly increased by local warming of the tail. We have accordingly mounted the pressure cuff, endpoint device and tail holder in a warm air chamber controlled thermostatically to 43°C ± 1°C. The rat's body is enclosed in a wire screen holder on the outside of the chamber. We have found that after placing a rat in this apparatus, at least 5 to 15 minutes are necessary in order to secure a maximum reading. Better results are obtained if the entire rat is first warmed at 40-42°C for 10 minutes according to the method of Williams, Harrison and Grollman.[2] However, in this case, as

[4] Schuler, R. H., Kupperman, H. S., and Hamilton, W. F., *Am. J. Physiol.*, 1944, **141**, 625.

[5] Sobin, S. S., *Am. J. Physiol.*, 1946, **146**, 179.

shown by Proskauer *et al.*[6] one must accept the possibility of a systemic error due to elevation of the rats' body temperature.

In order that we might compare the 2 methods we have replaced the tail holder with a simple plethysmograph and have simultaneously recorded cuff pressures by both carbon button and plethysmographic endpoints. Over a large number of trials we have found general agreement within 5 to 15 mm, the carbon button endpoint nearly always being the higher. Often the readings were identical.

Discussion. The method described may be used on either anesthetized or unanesthetized animals. If anesthesia is not objectionable a very satisfactory endpoint may be more simply obtained by inserting 26-gauge syringe needles about 3 cm apart into the tail distal to the pressure cuff. These needles serve as electrodes and are connected to a sensitive direct current wheatstone bridge. Thus the actual resistance of the rat's tail is measured and is found to decrease when blood flows into it.

Summary. A new endpoint for the indirect measurement of systolic blood pressure in the caudal artery of the rat has been described. The change in volume of the rat's tail which occurs when the pressure in an inflated cuff at the base of the tail is allowed to drop to arterial pressure is mechanically transferred to develop pressure on a carbon telephone transmitter button. The electrical resistance of the button is continuously observed, a decrease in resistance indicating the endpoint for the blood pressure measurement.

[6] Proskauer, G. G., Neumann, C., and Graef, I., *Am. J. Physiol.*, 1945, **143**, 290.

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Chemotherapeutic Action of Various Forms of Penicillin on Hemolytic Streptococcal Infections in Mice.*

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The existence of at least 4 distinct forms of penicillin was first revealed in 1945.[1,2] The various penicillins differ widely in biological activity as evidenced by the fact that their potency varies from approximately 900 to 2300 Oxford units per mg when assayed *in vitro* against a standard strain of *Staphylococcus aureus*. Differences in the biological activity of these penicillins *in vivo* have also been reported recently by Eagle and Musselman[3] and by Coghill, Osterberg, and Hazel.[4] The penicillin in clinical use during the past 4 years has contained varying proportions of these penicillins as well as varying amounts of unidentified impurities.[5] It has been suggested by Dunham and Rake[6] and by Lewis[7] that the impurities in commercial penicillin may play a role in the total efficacy of the drug *in vivo*.

In 1943 it was observed by one of us

* This work was presented at a Penicillin Conference held under the auspices of the U. S. Public Health Service, Food and Drug Administration, and National Research Council, Washington, D.C., on March 26-27, 1946.

[1] Dale, Sir Henry, *Science*, 1945, **101**, 23.

[2] Report by the Committee on Medical Research, O.S.R.D., Washington, and the Medical Research Council, London, on Chemistry of Penicillin, *Science*, 1945, **102**, 627.

[3] Eagle, H., and Musselman, A., *Science*, 1946, **103**, 618.

[4] Cogill, R. D., Osterberg, A. E., and Hazel, G. R., *Science*, 1946, **103**, 709.

[5] Coghill, R. D., *Chemical and Engineering News*, 1945, **23**, 2310.

[6] Dunham, W. B., and Rake, G., *Am. J. Syph.*, 1945, **29**, 214.

[7] Lewis, M. R., *Science*, 1944, **100**, 314.