ered negative with a possible error of 5%, and that a titre above 146% for the clot formation method and above 130% for the spectrophotometric method could be considered as indicative of malignant neoplasia with a possible error of 5%. With the clot formation method, titres between 112.5% and 146% and with the spectrophotometric method titres between 103% and 130% must be considered of doubtful significance.

These results indicate that this spectrophotometric method may be as satisfactory for the detection of patients with malignant neoplasia as the previously reported method.

False positive results with the spectrophotometric method fall in the same groups as with the clot formation method, *i.e.* those patients with acute infectious diseases, especially streptococcal infections, those with advanced tuberculosis of the lungs and those recently subjected to major operations.

Summary. A spectrophotometric method of assay of antiproteolytic material in the serum, using inhibition of trypsin digestion of fibrinogen, has been described. Results obtained in 250 sera by this method have been analyzed statistically and have been found to show a close correlation with the clot formation method.

17028

Microphonic Manometer for Indirect Determination of Systolic Blood Pressure in the Rat.*

MEYER FRIEDMAN AND S. CHARLES FREED.

From Harold Brunn Institute for Cardiovascular Research, Mount Zion Hospital, San Francisco.

Although the plethysmographic method for the indirect measurement of systolic pressure in the rat[1] has been improved by modifications devised later by other workers,[2-5] it has not been adopted universally. This has been due primarily to technical difficulties and errors encountered in any method employing plethysmographic changes for determination of blood pressure.

We have devised a method, however, of obtaining the systolic blood pressure of the rat which is similar in principle to that employed in the indirect measurement of systolic blood pressure in man,—namely, the detection of sound at the exact time that the arterial pressure of the caudal artery exceeds the pressure of the occluding cuff. This method was found to be accurate, simple, and rapid.

The apparatus consists essentially of a carbon type of microphone (3 cm in diameter) to the diaphragm of which is attached a thin copper trough (1.5 cm in length and 0.6 cm in diameter). The microphone is connected to a specially designed, low frequency (100 c.p.s.) sound amplifier† operated by direct current supplied by three dry cells. This amplifier affords a voltage gain of approximately 3000. The energy changes obtained by the amplifier may be detected by ordinary earphones or oscilloscope.

In order to take blood pressure readings, a

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5 Skeggs, L. T., Jr., and Leonards, J. R., PROC. SOC. EXP. BIOL. AND MED., 1946, **63**, 294.

† Further details of the construction of this apparatus and the electrical circuit will be furnished by the authors upon request. The microphonic manometer itself may be obtained from Charles Calvert of the Pacific Industrial Electronics Company, San Francisco, Calif.

rat is placed for 10 minutes in a wood box (55 x 25 x 25 cm) having sliding doors at each end and a glass top. The temperature of the box is maintained at approximately 39°C. The tail of the rat is led through a 10 mm pressure cuff and the segment of the tail immediately distal to the cuff is placed in the trough. The pressure of the cuff is raised to a point above the expected blood pressure and slowly released. At the point at which the cuff pressure becomes less than the caudal arterial pressure, one *immediately* hears in the ear phones a rhythmical succession of sounds reflecting at exactly the same rate the transmitted pulsatile variations of the caudal artery. If the amplifier is connected to an oscilloscope, one sees at this same critical point an intense and abrupt change in the contour and frequency of the preceding waves. It should be stressed that the regularity and actual rate of these sounds do not allow their confusion with any possible extraneous movements of either the body or tail of the rat. As the cuff is deflated further, the sounds attain their greatest intensity at the expected diastolic level, although this increase in intensity is too gradual to allow precise determination of the diastolic pressure. The sounds continue even with the cuff completely deflated. No preliminary venous drainage of the tail is necessary as the method does not depend upon gradual increase in tail volume but upon the almost instantaneously transmitted pulsatile variations which occur when the cuff pressure is overcome. Blood pressure determinations can be made at intervals of 15 to 30 seconds.

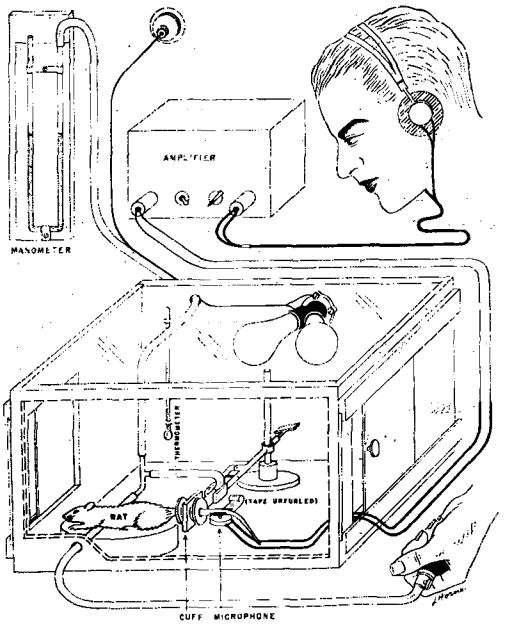

FIG. 1.

Drawing depicts entire apparatus. The rat is placed on a pad of sponge rubber. The cuff is inflated by hand bulb and air pressure is measured by manometer. As the air is released, the cuff pressure falls below that in tail artery and the pulsatile vibration instantly detected by the microphone is amplified into rhythmic audible signals heard by the observer.

Results. A. *Blood Pressure of the Normal Rat* (1) *Unanesthetized Rats.* Twelve albino rats weighing between 150-200 g were given 0.02 mg of Intracostrin (Squibb) per 100 g of body weight. This amount of curare, although insufficient to produce paralysis, did subdue the rats sufficiently that they remained relatively quiet when wrapped loosely in a cloth binder. The average systolic blood pressure of these rats as determined by the microphonic manometer was 98 mm of Hg. (Range: 82 to 120 mm Hg). Repeated daily determinations of the same animal rarely deviated more than 4-10 mm of Hg from the initial reading. These determinations are comparable to those obtained by previous investigators.[1,2]

(2) *Anesthetized Rats.* Twenty rats similar to those above were anesthetized by intraperitoneal injection of pentobarbital sodium. The average systolic blood pressure of these rats was 90 mm of Hg (Range: 70 to 104 mm of Hg). Later subsequent determinations of the same animals did not deviate more than 4-8 mm of Hg from the initial value.

B. *Blood Pressure of Rat after Injection of Epinephrine and Renin.* Five anesthetized rats whose average initial pressure was 91 mm of Hg (Range: 82 to 102 mm of Hg) were given 0.2 mg of epinephrine in oil by subcutaneous injection. Thirty minutes later, the average pressure was 180 mm of Hg (Range: 144 to 208 mm of Hg).

Twelve anesthetized rats were given one mg of purified hog renin by intravenous injection. The pressure of each rat was de-

termined immediately and continuously after the injection. It was observed that the average pressure of 88 mm of Hg before injection increased to a maximal average of 170 mm of Hg approximately two minutes after injection. Similar to the pressor response of the dog to renin, the pressures of the injected rats gradually fell after maintaining a plateau for approximately five minutes after injection. The pressures usually reached the control levels about 20 minutes after injection. Again similar to the dog, the rat was observed to develop tachyphylaxis rather quickly to injections of renin. Thus successive injections of the same amount of renin effected progressively smaller and more evanescent pressor effects and the third or fourth successive injection usually caused little or no rise in pressure.

Summary. The ability of the microphonic manometer to measure rapidly and simply not only the pressure of the intact rat but also of the rat made hypertensive by the injection of the vasoconstrictor substances, epinephrine and renin, indicates that it might be of considerable usefulness in studies necessitating frequent or successive blood pressure determinations in the rat.

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17029

Kinetics of Distribution of Inulin Between Two Body Water Compartments.

MARIO GAUDINO.* (Introduced by Homer W. Smith.)
From the Department of Physiology, New York University College of Medicine, New York City.

The kinetics of distribution of inulin between the intravascular and the interstitial compartments after its introduction into the circulatory system is of interest in relation to the use of this substance as a measure of the extracellular volume.[1,2]

The present paper concerns the distribution of any substance with the properties of inulin between two fluid systems representing schematically the intravascular and interstitial compartments of the body.

Let V_1 be the volume† of the intravascular compartment (I) and V_2 the volume of the interstitial compartment (E), both of which will be assumed to remain constant during the experimental procedure. It is further supposed that the rate of mixing of the substance in each of these compartments is rapid compared to simple diffusion. If the concentration of the substance in I is represented by $c_1(t)$, the concentration in E by $c_2(t)$, the concentration in the urine (assumed to be the only route of elimination) by $c_3(t)$, and if the flow (q_1) of the liquid that is being interchanged between the two compartments is assumed to be constant, q_2 being the urine flow, then, $c_1(t)V_1$ is the amount of substance accumulated in I at any instant, $c_2(t)V_2$ the amount accumulated at any instant in E, $[c_1(t)—c_2(t)]\ q_1$ the rate of interchange of the substance between I and E, and finally, $c_3(t)\ q_2$ is the rate of elimination. In the case under consideration, the substance (inulin) is eliminated only by glomerular filtration, and if the renal clearance at any instant is q_3, then $c_3(t)\ q_2 = c_1(t)\ q_3$. The substance will be introduced into the system in the form of a chemical solution with a rate CQ, where C is its concentration and Q is the rate of infusion, both C and Q being kept constant experimentally.

Under these conditions, the rate of accumulation of the substance in the vascular compartment will be:

$$V_1 \frac{dc_1}{dt} = QC - q_1(c_1 - c_2) - q_3c_1 \qquad (1)$$

* Dazian Foundation Fellow.

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2 Gaudino, M., Levitt, M. F., *Am. J. Physiol.*, 1949, in press.

† Volumes are expressed in cc of fluid, independently of any volume effects of protein, flows in cc per minute, concentrations in mg per cc.