Blood Pressure in the Unanesthetized Rat. I.

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Methods of indirectly determining blood pressure in the rat are reviewed and their drawbacks noted. A new method is described which has the advantage of objectivity and provides permanent graphic record of each determination. The end point used is the reappearance of pulsation in the foot distal to a slowly deflating leg cuff. Application of the method is described and its use compared with tail plethysmography.

Of the many methods devised for the measurement of blood pressure in small animals, the most accurate is the high frequency manometer with arterial cannulation. The necessary operative procedure and anesthetics may, however, disturb arterial pressure unpredictably, and such observations can not be repeated over long periods. Indirect methods have therefore been developed.

These are based on the detection of arterial inflow distal to a slowly deflating cuff on the foot, tail or ear of the animal. Thus Kunstmann observed the color change in the foot as was described for the human finger by Gärtner. Bonsman utilized photoelectric transmittance of the rat tail. Moberg, with a special viewing and occluding capsule, observed the resumption of the blood flow in the ear of anesthetized rats. Griffith used as an end point the inflow in the capillaries of the interdigital web. This method was later used by Rubin, Fasciolo and Duncan. Unfortunately, it requires both microscopy and anesthesia. A simpler but more traumatic method was used by Diaz. This consisted of snipping a small piece of the tail and noting the appearance of blood flow at the wound as the occluding cuff pressure was lowered. The number of measurements possible is self limited.

Byrom devised a sensitive water plethysmograph for use on the tail of the anesthetized rat. This instrument was modified for use in unanesthetized animals by Harrison, Grollman, and Williams, Kempf and Page and Sobin. Electrical modifications were described by Skeggs and Leonards, Friedman and Freed.

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and Grimson. In one form or another this method has been widely used in the study of experimental hypertension in rats.

At normal room temperatures, tail arterial inflow is small, and caudal arterial pressure low, but with heating at about 40 C. for about 10 minutes, the tail artery dilates, its pressure rises to that in the femoral or carotid arteries, and the increased volume flow facilitates plethysmographic measurements. Thus Harrison, Grollman and Williams stated they used ambient temperatures, which increased rectal temperature to 40 C. Neuman, Proskauer, and Graef have since shown, however, that such vigorous heating increases arterial pressure. To offset this disadvantage of body heating, Sobin and Landis described a modification of the tail apparatus in which heat (40 to 42 C.) was applied to the tail only for 10 or 15 minutes. They did not describe the effect of such heating on body temperature. As we show below, it is appreciable.

Kersten and his co-workers, using the plethysmographic principles of Hurthle, and Kunstmann and Bonsman, devised a photo-electric foot plethysmograph, an appropriate rat holder, and an accurate but fragile occluding cuff. Systolic flow was detected from an ammeter needle connected by a direct current amplifier to a phototube which received variations in transmitted light caused by volume change. The advantage of such measurements in the foot as compared to those in the tail, lies in the avoidance of heating.

A drawback in all those methods is the imprecision of the end point, which is easily obscured by animal movement. Another disadvantage is the tendency toward subjective errors, for the operator must at the same time

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control cuff pressure, observe its level and receive some signal of arterial inflow.

We therefore proposed to develop a procedure with a graphically recorded end point. The end point used was noted by Vierordt in the last century as the obliteration of return of pulse wave under proximal compression. In this report we shall describe this method, demonstrate its accuracy, and compare the results obtained with the results of tail plethysmography.

METHOD

Three methods of detection of pulse wave were tested; the mechanical, the audiometric and one dependent on change of electrical impedance (Nyboer). In the audiometric method used, artefacts of animal movement and microphone "noise" interfered seriously. Resistance changes due to animal movement, electrode contact change, and complexity of the apparatus are disadvantages of the impedance method. The mechanical transducer with vacuum tube amplification was therefore selected.

The pulse in the rat's foot can be detected by an unbonded strain gage bridge (Statham), and amplified output can be observed on a suitable oscillograph. Interferences from respiratory and animal movements make it desirable to record the output with a direct writing oscillograph, such as the Brush Penmotor, so that the characteristic rhythm of the pulse may be noted. Cuff pressure is simultaneously recorded on the paper trace. The record obtained is permanent and the measurements are truly objective. Rapid inflation and slow deflation of the cuff is made semiautomatic. The cuff used is not as exactly proportioned as that described by Kersten and co-workers but it is rugged and can be rapidly applied.

The holder (fig. 1) is similar to that of Kersten and associates. Rubber is used instead of leather for the flexible hind part. The animal's position is made horizontal, and an oil cloth strap applied over the lower leg is connected to the strain gage and acts both as pickup and foot retractor. To facilitate placing the animal in a natural position, the lucite foot platform is mounted at an angle of 45 degrees on a heavy metal slab which may be moved horizontally to any position.

Since the foot pulse voltage from the gage is of the order of 33 microvolts, a high gain amplifier is connected to the gage output. The circuit used (fig. 2) gives a 3 cm. deflection for a 50 microvolt square wave input (a gain of $6 \times 10^6$). The frequency response to a sine wave falls off rapidly below 5 cycles per second and above 35 cycles per second. The apparatus responds to the rising systolic phase of the transmitted pulse and not to the pulse wave as a whole. The systolic signal in the rat has a duration of the order of one thirty-fifth of a second. The amplifying system is thus adapted to the signal desired, while other signals are to an extent obscured. Unblocking circuits are provided in the amplifier because of the surge currents caused by animal movement.
The pulse recorder is a Brush Pennotor mounted at one side of a standard two channel chassis. This provides an 8.5 cm. width for recording cuff pressure, and allows space for the cuff pressure recorder. This is a reector Selsyn motor controlling a pen moving normal to the direction of the paper travel. The drive Selsyn motor is mounted separately from the Brush chassis and is activated by a 4 inch sylphon bellows opposed by a helical spring. The pressure range of bellows and spring is 0 to 250 mm. Hg. The motors are General Electric #2JIF1, 110 volt, 400 cycles per second, run by 25 volts, 60 cycles per second. The pen trace is calibrated by step pressure applied to the bellows.

The cuff consists of a 1 inch length of ½ inch Penrose tubing, backed by a layer of heavy dental dam. Air is supplied through a length of fine plastic tubing. Air pressure is reduced from laboratory air lines and is controlled by a special valve (fig. 3).*

The action of this valve is such that pushing the control disc down inflates the cuff, and releasing it starts a gradual leak from the system, finely regulatable by rotation of the control disc. Two sphygmograms are shown in figure 4; B from a quiet animal, A from a more restless one. In spite of the restlessness and movements of the animal, and resulting dysrhythmic pen swings, the point of the pulse return is clear.

Satisfactory use of the method depends, as with other procedures, on practice and training of animals and operator. Proper adjustment of tension and placing of the foot strap are learned with practice. While useful records can often be obtained from untrained animals, their habituation to the procedure greatly speeds the reliability and rate of measurement. For clear recordings, the unanesthetized rat should be kept at about 30 C. for an hour or more.

* Construction by the MicroMetric Company.

**Accuracy of Method**

Seventy-five simultaneous direct Hamilton manometer and indirect foot pulse determinations were made under pentobarbital anesthesia and recorded photographically as in figure 5. The comparison of direct and indirect methods is graphed in figure 6, in which the 45 degree slope represents ideal correlation of methods. In the lower ranges (56 to 100 mm. Hg) indirect measurements indicate a lower pressure than direct, but in the higher ranges (130 to 180) there is a tendency toward the reverse. A similar swing about a point of maximum accuracy was noted by Hamilton21 in comparing optically and plethysmographically recorded tail pressures. The average deviation from the mean carotid systolic pressure for the entire series is 5.6 mm. Hg.

**Comparison with Tail Plethysmography**

A group of 10 adult rats, normal and hypertensive, whose pressures ranged from 122 to 216 mm. Hg, were kept in a room at 30 C. Pressure determinations were made daily for 10 days by tail plethysmography,13 and by the present method. The daily measurements were made in
rapid sequence. The foot pulse record was made first. The animal was then preheated for three minutes at 45°C and tail and body kept at 40°C. Measurement used was the mean of two close sequential observations. With both methods, a considerable daily variation was noticed. A striking example of this is shown in figure 7. The mean of the 100 foot measurements was 158.3 mm Hg ($\sigma = \pm 14.5$) and that of measurements from the tail, 166 mm Hg ($\sigma = \pm 16.6$).

In comparison to tail plethysmography, foot pulse pressure records can be made at intervals as short as 10 seconds, and can be repeated for as long as the rat will tolerate restraint. The apparatus described above permits observation of concurrent changes in pulse and respiratory rates.

**Summary**

A method is described for the graphic registration of systolic arterial pressure in unanesthetized rats. It depends upon detection and amplification of the mechanical pulse wave in the foot distal to an inflatable cuff, and simultaneous ink recording of pulse signal and cuff pressure. The method is compared with tail plethysmography, and no important difference of pressure found, although the electrical foot method has other inherent advantages.

The method is accurate and objective. Values obtained agree well with those found by foot plethysmography. Sequential determinations can be made at intervals of 10 seconds.

**REFERENCES**

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