Blood Pressure in the Unanesthetized Rat

II. Spontaneous Variations and Effect of Heat

By Frederick Olmsted, A. C. Corcoran, M.D., and Irvine H. Page, M.D.

Heating is commonly used in indirect determinations of blood pressure in the rat. Its effect on arterial pressure is determined at short sequential intervals by a method which permits rapid measurements. Spontaneous variations in the rat’s blood pressure are noted and analyzed. A plan is suggested which minimizes the effect of these variations by setting up criteria of significance of blood pressure change as between control and experimental periods.

Estimates of the normal rat’s blood pressure have varied widely from one laboratory to another. Arterial pressure is variously stated to be consistent from day to day, or to extend over a wide range. Most determinations are made by procedures in which the animal is heated in various ways.

Our purpose is to describe the effect of heating on the blood pressure of intact, unanesthetized rats as determined by an objective method.1 We have also analyzed day to day fluctuations of blood pressure in these animals.

I. Effect of Heating

Method

A group of 10 rats, normal and hypertensive, whose control pressures by the foot pulse method ranged from 80 to 172 mm. Hg were maintained in a room at 30 C. The control levels of pressure at 30 C. were recorded from readings which had stabilized for at least one minute. The animals were then heated by a gentle current of air, electrically warmed and thermostatically controlled. For tail heating alone, the tail was placed in an electrically warmed tube maintained at 45 C. Rectal temperatures were measured with a thermocouple thermometer.

Three schedules of warming were tested. In one, 45 C. heat was applied for 10 minutes. The second simulated the plethysmographic routine of this laboratory, where rats are preheated at 45 C. for three minutes, and then placed in a tail plethysmograph apparatus at 40 C. The third followed the Sobin procedure in which the tail only is warmed for 15 minutes at 45 C.

Results

Blood pressures were recorded at 30 and rectal temperatures at 60 second intervals. Minute averages for these functions are shown in figure 1. Pulse rates were determined from the recordings of the 45 C. group. They did not correlate with changes in blood pressure or body temperature.

The rats heated at 45 C. for 10 minutes exhibited a steady rise in blood pressure. At 10 minutes the mean increment was 42 mm. Hg (+ 33 per cent of the control mean). Those heated at 45 C. for three minutes and then at 40 C. attained a pressure rise of 20 mm. Hg after the three minutes at 45 C., which is equal to the increase in the 45 C. group at this time. Pressure stabilized at about this level during exposure to 40 C. Those animals whose tails only were heated for 15 minutes at 45 C. exhibited a similar slow rise. In 15 minutes they attained about the same pressure levels as the second group. Most of the pressure rise in the tail-heated series occurred in the first six minutes.

To compare effects of heating in normotensive rats, the animals heated at 45 C. were divided into two groups. One group had control readings below 120 mm. Hg (averaging 100) and the other had control determinations above 140 mm. Hg (averaging 158). The average rises in each group are graphed in figure 2. The increment in the normotensive group at 10 minutes is 49 mm. Hg (+ 49 per cent), that of the hypertensive group is 40 (+ 25 per cent). For the first three minutes, the normotensive group increased 25 and the hypertensive 10 mm. Hg. The increase of pressure caused by heating was consistently less in hypertensive than in normal rats.

It was observed that during heating runs, the amplification could be gradually reduced

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several fold without decreasing the amplitude of the recorded pulse stroke. This is interpreted as evidence of arterial vasodilation in the foot.

Fig. 1. Comparison of foot pulse recorded arterial pressures (left ordinate) at one-minute intervals (abscissa) in groups of rats heated by methods noted in text to various levels of rectal temperature (right ordinate).

Fig. 2. Comparison of mean effect of heating on arterial pressure in normotensive and hypertensive groups.

II. Variability of Arterial Pressure

Method

Ten normal rats weighing from 125 to 175 Gm. were housed at 30 C. Blood pressure measurements were made by the foot pulse method daily for 10 days. Values recorded were those measured after the pressure had stabilized for at least one minute.

Results

The range of pressure recorded was from 70 to 175 mm. Hg. The mean of the 100 determinations was 114 mm. Hg. The standard deviation for the group was ±16.3 mm.

Similarly, the pressures of 7 hypertensive rats whose group average was 184 mm. Hg ranged from 100 to 228 mm. Hg. The standard deviation was ±17.1 mm. Hg.

Day to day fluctuations apart, animals recently handled or inadequately habituated to the apparatus commonly show rapid variations of as much as 30 mm. Hg. These changes take place in a few seconds and emphasize the desirability of the repetition of observations in the selection of base line for blood pressure study.

Table 1.—Solutions of Equation 2 for Groups of Varying Size, Observed Daily for Five Days

<table>
<thead>
<tr>
<th>Difference between average pressure of two groups (mm. Hg)</th>
<th>Minimum number of animals per group for significant data</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>42</td>
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<tr>
<td>10</td>
<td>11</td>
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<td>15</td>
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<td>30</td>
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Discussion

Effect of Heating

Our data confirm the tail plethysmograph observations of Proskauer, Neumann and Graef,² and extend them by demonstrating the sequence and regularity of pressure change in heated rats. The need for systematic control of heating technics is apparent. When conditions are closely controlled, such methods can yield useful comparative values, since the sequence of heat-induced pressure change in a group is regular. Measurements made after heating the tail at 45 C. for 15 minutes and those obtained by our more convenient plethysmographic routine are substantially the same.

We have no adequate explanation of the rise in blood pressure which results from heating in rats. Heating has been observed to cause renal vasoconstriction in man.³ ⁴ During heating the
increased peripheral blood flow must be provided for by splanchnic vasoconstriction, increased cardiac output, or both. The absence of a relationship between pulse rate and blood pressure change might suggest that in the rat splanchnic vasoconstriction is the principal cause of the pressure rise. However, since cardiac output is a function of metabolic rate, and the rat is known to alter metabolism with shifts of external temperature away from 28 or 29 C.,

the pressure rise may be cardiogenic. The proportionally smaller and slower rise of pressure in hypertensive as compared to normal rats is of interest since it suggests that the pressor mechanisms which operate during heating are either less responsive in renal hypertension or already submaximally engaged.

The day to day variability of pressure in the rat imposes a certain requirement as to the number of animals and successive daily measurements needed to obtain significant data. When the standard deviations of each animal in the groups of normal or hypertensive rats are graphed against duration of measurement in days, it is evident that the variability does not diminish after five successive days in groups of four or more. Seventeen mm. Hg can be taken as the usual variability of the rat's blood pressure.

The standard deviation of the difference between the averages of two groups is equal to

\[
\sqrt{\frac{(\sigma \text{ control group})^2}{n - 1} + \frac{(\sigma \text{ experimental group})^2}{n - 1}}
\]

or

\[
\sqrt{\frac{2(17)^2}{n - 1}} \quad \text{or} \quad \sqrt{\frac{578}{n - 1}}
\]

where \(n\) = number of determinations.

For a probability of 500 to 1 that a difference between the arithmetic means of pressures of two groups of animals is significant, this difference should be equal to or greater than three times the standard deviation of the difference. In Table 1 is shown the solution of equation 2 (after five successive daily determinations) for the differences of the averages of pressures, in two groups. Obviously, a 5 mm. Hg pressure change, to be significant, requires an impractical number of animals. However, the group size is reasonable for the difference of 10 mm.

**Summary**

1. The effect of various modes of heating on the graphically recorded blood pressure of the rat is regularly and sequentially pressor in proportion to the amount of heating applied.

2. Careful control of the warming of rats in blood pressure determinations which involve heating is essential for accuracy.

3. The occasional rapid variability of the rat's blood pressure is noted. The day to day variations are analyzed to determine a minimum experiment group for five successive daily measurements.

**REFERENCES**


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