Distribution of Myocardial Blood Flow in the Rat

By Edward J. Hershgold, M.D., Sheldon H. Steiner, M.D., and Leo A. Sapirstein, Ph.D., M.D.

Rubidium$^{86}$ distribution was used to estimate the distribution of myocardial blood flow in albino rats. The results indicate that the perfusion rates of the left ventricle, apex and interventricular septum are all substantially identical, averaging 2.6 to 2.9 ml./Gm. of tissue/min. The value for the right ventricle is 3.2 ml./Gm./min. The implications of these findings for the measurement of coronary blood flow by the nitrous oxide method are discussed.

A METHOD which has been described previously$^1$ can be applied to the measurement of myocardial blood flow in each part of the heart available for dissection. Basically, the method estimates the blood flow fraction to an organ by estimating its uptake of a label given in a single intravenous injection at a time when venous drainage of label is very small in relation to arterial delivery. This value can be determined from observations made at later times by extrapolation of such observations to the moment of arterial delivery. When either K$^{42}$ or Rb$^{86}$ is the label, the extrapolation to the moment of arterial delivery is simplified because of the exceedingly slow changes in label content with time displayed by most organs. Previous studies have shown that extrapolation can be carried out to the moment of injection rather than to the moment of arterial delivery without visibly influencing the results. When the zero time situation can be described by extrapolation, the fraction of the label contained in the organ corresponds to its fraction of the cardiac output. Thus, from a knowledge of organ label content over an interval of time and knowledge of the cardiac output, one can calculate the actual organ blood flow. The theory of the method, its limitations and some applications to the measurement of regional blood flow have been described elsewhere.$^2$-$^8$ This method has the advantage of measuring functional blood flow and does not measure the flow through nonexchanging channels such as arteriovenous anastomoses.

Despite the extensive use of the nitrous oxide method for the estimation of myocardial blood flow,$^9$-$^{12}$ there seems to be considerable uncertainty regarding the significance of the flow value obtained. This results from the fact that the flow value obtained is in units of flow per gram of tissue drained by the vein sampled (in this case the coronary sinus). Studies indicating uniformity of blood flow to the various parts of the heart drained by the coronary sinus appear to be lacking. It has been shown$^{12, 13}$ that nonhomogeneity of perfusion in an organ may vitiate the application of the nitrous oxide method. The present studies were originally undertaken to determine whether myocardial perfusion was, in fact, uniform.

METHODS

A detailed description of the method has been given elsewhere.$^1$ Young adult albino female rats weighing between 170 and 260 Gm. were used. They had fasted for 18 hours prior to use, but were allowed water ad lib. The indicator material was Rb$^{86}$Cl obtained from the Oak Ridge National Laboratory. The dose was 2-3 $\mu$C in a volume of 0.2 ml.
The animals were anesthetized with pentobarbital sodium, 40 mg./Kg., injected intraperitoneally. A femoral vein was exposed and the isotope injected using a 0.25 ml. syringe. Time for injection was less than 0.5 sec. The rats were killed by transection of the thorax just below the axillae with a mallet-driven axe. The killing time post-injection for one half the group was 10±1 sec., and 20±1 sec. for the other half. The heart was removed and a through and through section taken from the lateral wall of each ventricle, the apex and septum. These were weighed immediately on a Roller-Smith torsion balance. The Rb 86 content of each part was then determined in a well-type scintillation detector, Nuclear-Chicago Model DS5-5, which displayed its counts in a Nuclear-Chicago Model 132 computer-analyzer.

Table 1.—Distribution of RVCl to Portions of Rat Myocardium as a Function of Time After Injection

<table>
<thead>
<tr>
<th>Killing Time</th>
<th>Right ventricle</th>
<th>Left ventricle</th>
<th>septum</th>
<th>apex</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 sec.*</td>
<td>6.5±1.8</td>
<td>5.9±1.2</td>
<td>6.0±1.2</td>
<td>5.7±1.0</td>
</tr>
<tr>
<td>X</td>
<td>12</td>
<td>12</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>20 sec.</td>
<td>6.8±1.8</td>
<td>5.7±1.3</td>
<td>6.0±1.8</td>
<td>5.4±1.2</td>
</tr>
<tr>
<td>X</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
</tbody>
</table>

*The differences between the 10 and 20 second values for each portion are not statistically significant.

Table 2.—Distribution of Cardiac Output to Myocardium

<table>
<thead>
<tr>
<th>Per gram of tissue per minute</th>
<th>Right ventricle</th>
<th>Left ventricle</th>
<th>Septum</th>
<th>Apex</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of observations</td>
<td>22</td>
<td>22</td>
<td>22</td>
<td>22</td>
</tr>
<tr>
<td>Flow ml./Gm./min.</td>
<td>3.2</td>
<td>2.6</td>
<td>2.9</td>
<td>2.7</td>
</tr>
<tr>
<td>S.D.</td>
<td>.7</td>
<td>.4</td>
<td>.6</td>
<td>.5</td>
</tr>
</tbody>
</table>

RESULTS

The results in 22 animals are presented in table 1. It will be noted that there is no significant change with time in any portion of the heart examined. In this circumstance, the extrapolation to zero time can be safely used to describe the situation of zero venous drainage. Since in this condition the extrapolated value is simply the average of all observed values, the blood flow calculation was made as indicated above and presented in table 2.

It will be noted that the values for the left ventricle, intraventricular septum and apex are all substantially the same. The value for the right ventricle is greater (3.2 ml./Gm./min.). Comparison of the value for the right ventricle with those of the left ventricle and the apex revealed the differences to be significant (p < .02). No other significant differences were revealed by similar comparisons of the other parts of the heart with each other.

DISCUSSION

These findings show that Rb 86 is distributed nearly homogeneously throughout the mass of ventricular tissue. The lateral wall of the right ventricle, on a weight basis, takes up slightly, but significantly, more of this isotope than other ventricular tissues. This indicates that the perfusion rate of the right ventricle is a little greater than that of the left.

The absolute value for perfusion rate is considerably greater in the rat heart than has been reported for either the dog or the human heart. The value for dog heart is of the order of 0.7 ml./Gm./min.; that for the human heart is also approximately 0.7 ml./Gm./min. The values for rat heart are about four times as great.

A possible reason for this discrepancy is revealed by consideration of the ratio between the perfusion (flow/gram) and work load per gram in each of these species. In a man, a 300 Gm. heart serves to eject approximately 6 L. of blood/min. against a mean pressure of 90 mm. Hg. In a 20 Kg. dog, a 175 Gm. heart will eject 3.6 L./min. against approximately the same pressure. In a 200 Gm. rat,
a 0.6 Gm. heart ejects about 45 ml./min. against the same pressure. In terms of the work of the heart per unit mass and disregarding the kinetic factor, the human heart produces 0.27 joules/Gm./min., the dog heart 0.27 joules/Gm./min., and the rat heart 1.00 joules/Gm./min. (In this calculation both the work and the mass of the right heart have been neglected.) There is, therefore, a rough proportionality between blood flow per gram and work per gram of myocardium in the three species.

At first sight, it would seem peculiar that the exceedingly rapid rat heart should have a work : blood flow ratio similar to that of the dog, since it has been shown that the dog heart decreases the work : blood flow ratio with increasing rate. At a rate of 300 beats/min., the dog heart would be expected to increase its coronary flow 60 per cent above that at 100 beats/min. This value is calculated from the formula presented by Laurent et al. The fourfold difference in the perfusion rate of the rat myocardium cannot be explained solely on the basis of rate differences between the species. The finding that the work : blood flow ratio is roughly the same for rat, dog, and man suggests that the normal rapid rate of the rat heart is not associated with the same metabolic alterations which develop in abnormal tachycardia in the dog.

The relative constancy of the work : blood flow ratio appears also in the behavior of the right and left heart. Although precise data are not available, Clark has shown that the lateral wall of the right ventricle makes up about one sixth the mass of the ventricles in the rat. Presumably, the right heart in the rat as in other animals has approximately one sixth the work load of the left heart. The smaller mass and smaller work load of the right heart are almost in proportion; it is not surprising, therefore, that the perfusion rate per gram is almost the same in the right ventricle as in the remainder of the heart.

The significance of these findings as far as the application of the nitrous oxide method to the measurement of coronary blood flow is concerned, lies in the fact that, though the perfusion rate of the right side of the heart is greater than that of the left, it is not much greater. Further, the perfusion rate on the left side of the heart is substantially the same throughout. It seems probable, therefore, that samples taken from the coronary sinus, though they cannot be considered perfectly representative of the whole heart, probably come quite close to describing the venous drainage from the whole heart. The nitrous oxide method would, therefore, appear to be adequate for the measurement of total coronary blood flow.

**SUMMARY**

The isotope fractionation technic for the measurement of regional blood flow has been applied to the measurement of myocardial perfusion rates in various parts of the rat heart. The perfusion rates of the left ventricle, apex and intraventricular septum are about 2.7 ml/Gm./min. This value is considerably higher than that found in dogs and men, but correlates with the larger work load per gram of tissue. The right ventricle has a perfusion rate somewhat higher than the left. The values are not, however, sufficiently different from those observed in other parts of the heart to vitiate flow determinations by the nitrous oxide method which are based on the assumption of flow homogeneity throughout the heart.

**SUMMARIO IN INTERLINGUA**

Le technica del fractionation a isotopos pro le mesuration de fluxos regional de sanguine eseva applicate al mesuration del intensitate del perfusion myocardial in varie partes del corde del ratto. Le intensitate del perfusion in le ventriculo sinistre, le apice, e le septo interventricular in le ratto es circa 2.7 ml/g/min. Iste valor es considerabilemente plus alte que illo trovate in canes e humanos, sed illo se trovo in correlacion con le plus grande carga de labor per gramma de histo. Le ventriculo dextere ha un intensitate de perfusion un peuco superior a illo del ventriculo sinistre. Tamen, le valores non differe sufficientemente ab illos observate in alte partes.
del corde pro vitiar le determinationes del fluxo per le metodo a oxydo nitrose le qual es basate super le premissa que le fluxo es homogenee in omne partes del corde.

REFERENCES

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