Fractional Distribution of Right Ventricular Output in the Lungs of Dogs


Although under certain circumstances it is known that the perfusion of lung tissue may be radically reduced, for example in atelectasis, we are not familiar with any measurements of perfusion rates of different lobes of lung in normal animals. It has been speculated, on the basis of pathological evidence, and on the basis of the relation between the position of lung tissue and the pressure available for its perfusion, that the apical portions of the lungs are poorly perfused in man.1,2

The present study, utilizing the intravenous injections of microspheres, 53 μ in diameter and labeled with scandium40, makes possible the fractionation of right ventricular output to various lobes of lung in dogs.

The principle is as follows: A tracer dose of labeled microspheres is injected into a blood vessel (jugular vein) which delivers them into the blood supply of the lung. The microspheres are chosen to be of such size that they will not traverse pulmonary capillaries, i.e., they will have an extraction ratio of 1.00. Assuming that the microspheres are well mixed by the time they reach the pulmonary artery, and that they are completely extracted from the flowing blood by impaction in the pulmonary capillaries while the blood continues to circulate through nonimpacted channels, it must necessarily follow that their delivery to, and location in, pulmonary tissue will correspond precisely to the flow of blood to the various portions of the lung. It cannot be overemphasized that, although the microspheres originally label blood, the fact that they are trapped in the pulmonary capillaries results in their ultimate location in accordance with blood flow rather than blood volume at the time of their movement. This would not be true if the microspheres were not extracted by pulmonary tissue but circulated freely through the pulmonary and systemic capillaries. In such a case, the distribution of the microspheres would correspond to the distribution of blood volume, but in that case they would have an extraction ratio of zero.

The basic principles underlying the manner in which indicators carried by the bloodstream are distributed were originally described by Kety.3 The behavior of indicators with high extraction ratios has been described and discussed by Black, Davies, and Emery,1 by Sapirstein,6,7 and by Sapirstein and Mandel.7

The purpose of this paper is to report the distribution of scandium40-labeled microspheres following intravenous injection in healthy dogs.

Methods

Seven mature, healthy mongrel dogs, weighing between 10 and 15 Kg., were anesthetized, intravenously, with pentobarbital sodium, 35 mg. per Kg. body weight. One dog was laid on its right side, two on their left sides, and four animals were placed in dorsal supine recumbency.

Ceramic microspheres,* 53 ± 7 μ in diameter and labeled with scandium40, were injected into the jugular vein. The specific activity of the microspheres was 1.5 mc. per Gm. Approximately 10 mc. of microspheres containing 15 μc. were diluted in 2 ml. of saline. Because of the relatively high density of the microspheres (3.0 Gm. per ml.), they were extremely difficult to keep suspended in the saline and would settle out on the

*The microspheres were supplied by Minnesota Mining and Manufacturing through the courtesy of Mrs. T. N. Lahr and J. P. Ryan.
lowest portion of the syringe used for injection. A plastic syringe with a rubber plunger was selected for the injection to avoid crushing the microspheres. The syringe was rinsed with blood 10 times following the initial injection of microspheres to insure complete ejection of its contents.

One minute following the last rinse, the animals were killed with saturated potassium chloride injected into the left ventricle. The thoraces were opened, and the lobes of lung were carefully removed and labeled.

Each lobe of lung was counted for one minute in a large well scintillation detector which was capable of holding up to 4 Kg. of tissue.* Background counts were taken repeatedly throughout the counting periods.

The microsphere content per gram of lung tissue was calculated for each lobe from the total count rate and the weight of each lobe. The standard deviation and coefficient of variation of this value were determined for each lobe.

In order to determine the extraction ratio of the lungs for the microspheres used in these experiments, we could have sampled arterial blood during the period when the microspheres were being carried to the lungs by way of their arterial inflow. A more convenient method of making an analogous determination was the measurement of the microsphere content of an organ with a large blood supply, viz., the kidneys. As will be shown herein, the microsphere content of these organs was negligible so that it was not necessary to quantitate the renal blood supply.

### Results

The results of this study are summarized in table 1. The counts per minute per gram of each lobe of lung from each animal are recorded. The mean coefficient of variation for all animals is 23.9 per cent. The range of the coefficients of variation is 15.8 to 37.0 per cent, with a standard deviation of 6.4 per cent.

The animal lying on its left side has no greater proportion of microspheres in the left lobes of lung than in the right. The animals lying on their right sides had no greater proportion in the right lobes of lung than in the left. Although the coefficient of variation for animal 3, lying on its right side, was the greatest observed (37.0 per cent), the left lobes of lung received the greatest proportion of microspheres.

*The scintillation detector was manufactured by Nuclear Ohio Enterprises, Bay Village, Ohio.

No lobe of lung retained per gram, uniformly, either a greater or a lesser proportion of the microspheres. Although the intermediate lobes of lung received the greatest number of microspheres per gram in three cases, they also received the least number in two animals.

In each of seven experiments in which the microsphere content of the kidney was estimated, the counts obtained from these organs were at, or even below, background levels.

### Discussion

One of the requirements for the label used in this study was that it be largely or completely extracted by lung tissue. As has been noted previously, a label not so extracted might correspond in its distribution to the distribution of blood volume rather than blood flow.

We had a priori reason to suspect that microspheres 53 μ in diameter would be completely extracted by the pulmonary circulation. However, to be certain that the extraction of the microspheres used in our experimental circumstances was complete, we felt it necessary to establish that they did not appear on the systemic arterial side of the circulation. In order to calculate the extraction ratio of microspheres by the lungs, it would have been necessary to divide the difference between the pulmonary arterial and systemic arterial microsphere concentration by the pulmonary arterial microsphere concentration. Clearly, the determination of systemic arterial microsphere concentration by organ sampling would require the division of organ microsphere content by organ blood flow. If, however, as was the case, the organ microsphere content was zero, then the statement could be made with assurance that the extraction ratio for microspheres by the lung was 1.00 without any knowledge of organ blood flow, provided that organ blood flow was substantial. Thus, we felt our finding that the renal content of microspheres was zero was incontrovertible evidence that the pulmonary extraction of microspheres was complete.
DISTRIBUTION OF OUTPUT IN LUNGS

TABLE 1

Counts per Gram Lung per Minute (in Thousands)

<table>
<thead>
<tr>
<th>Lobe of lung</th>
<th>(1) Left lateral</th>
<th>(2) Right lateral</th>
<th>(3) Right lateral</th>
<th>(4) Supine</th>
<th>(5) Right Supine</th>
<th>(6) Left Supine</th>
<th>(7) Left Supine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right apical</td>
<td>10.5</td>
<td>37.4</td>
<td>30.8</td>
<td>2.07</td>
<td>3.23</td>
<td>2.79</td>
<td>8.59</td>
</tr>
<tr>
<td>Right cardiac</td>
<td>3.9</td>
<td>38.3</td>
<td>31.3</td>
<td>1.85</td>
<td>2.57</td>
<td>2.12</td>
<td>11.3</td>
</tr>
<tr>
<td>Right diaphragmatic</td>
<td>9.7</td>
<td>35.0</td>
<td>28.0</td>
<td>1.86</td>
<td>4.47</td>
<td>2.50</td>
<td>5.14</td>
</tr>
<tr>
<td>Intermediate</td>
<td>12.5</td>
<td>24.2</td>
<td>17.3</td>
<td>2.29</td>
<td>3.29</td>
<td>2.47</td>
<td>11.5</td>
</tr>
<tr>
<td>Left apical</td>
<td>9.1</td>
<td>33.3</td>
<td>54.5</td>
<td>1.02</td>
<td>2.42</td>
<td>2.73</td>
<td>8.43</td>
</tr>
<tr>
<td>Left cardiac</td>
<td>9.9</td>
<td>25.7</td>
<td>24.0</td>
<td>2.02</td>
<td>2.86</td>
<td>1.85</td>
<td>11.2</td>
</tr>
<tr>
<td>Left diaphragmatic</td>
<td>9.2</td>
<td>35.4</td>
<td>29.6</td>
<td>2.03</td>
<td>4.17</td>
<td>2.02</td>
<td>5.91</td>
</tr>
</tbody>
</table>

| Σ S               | 64.8             | 230.3             | 215.5             | 13.1       | 23.0             | 16.5           | 65.3           |
| S                 | 9.3              | 29.0              | 30.8              | 1.88       | 3.29             | 2.35           | 9.33           |
| S/Σ × 100 = C%     | 15.8             | 24.2              | 37.0              | 22.0       | 24.0             | 22.2           | 22.3           |

In these experiments, the outstanding finding was the relative homogeneity of microsphere distribution in lung tissue (mean coefficient of variation is 23.9). Since following the intravenous injection of scandium-46 labeled microspheres the radioactivity per gram of lung tissue is nearly constant for all lobes of lung, it is likely that the indicator was homogeneous (completely mixed with the blood) and that the right ventricular outflow was fractionated proportional to the weight of lung tissue it perfused. It is of course possible that the results might have been a consequence of unequal perfusion coupled with an equal and opposite nonhomogeneity of microsphere in blood concentration, but this appears to be exceedingly unlikely. We must, therefore, accept the more rational explanation that the overall homogeneity is compounded of individual homogeneities.

One would anticipate that the microspheres would be retained in greater proportions by lobes of lung in the hemithorax upon which the animal lay. Such was not the case. It may at first appear puzzling that the portions of the lungs which lie above the pulmonary conus should be as well perfused as those which are dependent with respect to it. The difference in height between the highest and lowest portions of the lungs is approximately 10 cm., which corresponds to 8 mm. Hg, more than 50 per cent of the mean pulmonary arterial pressure of the dog. One might argue from this that the pressure available for the perfusion for pulmonary tissue ranges from 7 to 23 mm. Hg, and that there should therefore be a 300 per cent range in flow, assuming homogeneous pulmonary arteriolar resistance. This argument neglects the fact that the pulmonary veins return through precisely the same distance as the pulmonary artery, and that the pressure difference, between the entrance to, and the exit from, any closed fluid system, which is not collapsed, is more important in determining flow than is the midpoint in space of the entire system. Although the pulmonary vessels may be collapsible, there is no evidence that they are collapsed. Our findings argue that the siphon is a complete one and that perfusion rates are, therefore, independent of the position of lung tissue with respect to the pulmonary artery.

Summary

Microspheres, approximately 50 μ in diameter and labeled with scandium-46, were injected into the jugular vein of seven anesthetized dogs. Each lobe of lung contained nearly equal counts per minute per gram of tissue. This suggests that the indicator was completely mixed with the blood by the time it arrived in the pulmonary artery, and that the perfusion rate of blood per gram of lung is nearly identical for all lobes.
Acknowledgment
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References
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