Pulmonary Regional Ventilation-Perfusion Relationships in Chronic Cardiopulmonary Disorders

II. Scintiscanning Method

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SUMMARY

This is the study attempting to clarify quantitatively the regional disturbance of ventilation-perfusion relationships in pulmonary diseases. Measurements were made on 7 normal subjects, 16 cases with pulmonary parenchymal diseases and 4 cases with pulmonary vascular diseases. Perfusion and inhalation scintigrams were taken in sitting position and were divided into 9 horizontal zones in order to know relative values of regional pulmonary blood flow \( Q \) and alveolar ventilation \( V_A \). Cardiac output and minute alveolar ventilation were also obtained at the same time. Using these data, absolute values of regional \( V_A/Q \) of 9 zones were analyzed from the base to the apex of both lungs.

In 7 normal subjects the average regional \( V_A/Q \) ratio was 0.64 at the base and increasing 1.35 at the apex. In 20 patients the ratio ranged between 0 and 11.2, and even in the parts of parenchymal disorders the ratio was generally higher than normal since the decrease of regional perfusion was more remarkable than that of regional ventilation.

Discussions were made on the usefulness as well as limitations of this scintiscanning method in approaching ventilation-perfusion unevenness topographically and quantitatively.

Additional Indexing Words:
Pulmonary perfusion scintiscanning  Inhalation scintiscanning
Influence of body position  Hypoxia  Gas exchange  Ultrasonic nebulizer

VENTILATION-PERFUSION unevenness is one of the causes of hypoxemia and the abnormality of which has been studied as a whole lung in various ways, but the topographical analysis of the unevenness has been difficult to study until the recent advances of radioisotope techniques. In the previous paper\(^b\) we reported a study of regional ventilation-perfusion relationship using radioac-
tive rare gases. In this paper we will report the analysis of regional ventilation and perfusion using inhalation and perfusion scintiscanning method. The method, the results and the limitations of our study are presented.

**METHODS AND MATERIALS**

Twenty-seven patients were studied. Seven of them were normal control having no evidence of cardiopulmonary diseases confirmed both by clinical and laboratory examinations including chest X-ray films. The other 20 cases had various pulmonary diseases, 16 with parenchymal diseases and 4 with pulmonary vascular diseases. All the 20 cases studied were listed in Table I with the diagnosis and the results of arterial blood gas analysis.

For the study of the regional ventilation, inhalation scintiscanning, which is similar to Alterbrunn’s and Taplin’s method, was tried using 1.5–2.0 mCi of Au$^{198}$ colloid aerosol. Inhalation of the aerosol was assisted by the use of respirator which was set at the positive pressure of 8 cm H$_2$O. The expired gas was collected in the bag and was released into the atmosphere after the decline of the radioactivity to avoid the contamination of the room. Regional perfusion study was done according to the reported methods with $^{131}$I-macroaggregated albumin ($^{131}$-MAA)

<table>
<thead>
<tr>
<th>No.</th>
<th>Name</th>
<th>Age</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>$P_{O_2}$ mm Hg</th>
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<tr>
<td>1</td>
<td>J. T.</td>
<td>78</td>
<td>M</td>
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<tr>
<td>5</td>
<td>H. K.</td>
<td>51</td>
<td>F</td>
<td>Pulmonary cysts of the right lung</td>
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<tr>
<td>6</td>
<td>H. H.</td>
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<td>M</td>
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<tr>
<td>7</td>
<td>Y. M.</td>
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<td>M</td>
<td>Vanishing lung</td>
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<tr>
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<td>9</td>
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<td>M</td>
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<td>M</td>
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<td>16</td>
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<td>F</td>
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<tr>
<td>17</td>
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<td>F</td>
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<td>18</td>
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<td>M</td>
<td>Fibroplastic sarcoma of pulmonary artery</td>
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<tr>
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<td>F</td>
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<td>20</td>
<td>M. S.</td>
<td>16</td>
<td>F</td>
<td>Pseudotruncus arteriosus communis</td>
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Table II. $\dot{V}_A$, $\dot{Q}$, $\dot{V}_A/\dot{Q}$ Ratio Abnormalities Seen in Parenchymal and Pulmonary Vascular Diseases

<table>
<thead>
<tr>
<th>$\dot{V}_A/\dot{Q}$</th>
<th>$\dot{V}_A$</th>
<th>$\dot{Q}$</th>
<th>Pulmonary parenchymal disorders</th>
<th>Pulmonary vascular disorders</th>
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</thead>
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<td>↓</td>
<td>↓</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>~</td>
<td>↓</td>
<td>↓</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>↓</td>
<td>↓↓</td>
<td>↓</td>
<td>4</td>
<td>0</td>
</tr>
</tbody>
</table>

Fig. 1. Pulmonary scintigrams of a normal subject sitting upright, (a) perfusion scintigram, (b) inhalation scintigram.

which was injected 100-200 μCi intravenously. The studies were done in the sitting position in all cases. Inhalation and perfusion scintiscannings were done with several days interval considering the effect of residual background. Shimazu SCC-30 scintiscanner (3"φ×2" crystal) was used, which has multichannel 37 holes focusing collimator with the focusing distance of 10 cm. The collimator was set anterior to the chest wall 10 cm. from the plane of the anterior axillary line and regional dot countings were recorded. The lower edge of the clavicle and the fifth intercostal space were chosen as the upper and lower border of the lung field and recorded on the scintigram. Later chest X-ray film was superimposed on the scintigram to divide the lung field into 9 equal zones from the apex to the base (Fig. 1). The dots were counted in the each zone and the background counts were substracted. The values were further corrected according to the thickness of the lung and the response curve of the collimator. Thus the relative regional ventilation and perfusion were obtained. In the normal subjects regional alveolar P02, Pco2 and R.Q. were calculated using the O2-CO2 diagram of Rahn and Fenn.6) Here total alveolar ventilation and ventilation-perfusion ratio were assumed 5 L./min. and 0.85 respectively. For the calculation, P02 and Pco2 of the mixed venous blood were assumed 40 and 46 mm. Hg respectively. Diffusion gradient was not taken into consideration. In some of the patients with pulmonary diseases, cardiac output was measured by Fick's method during cardiac catheterization. To obtain the total alveolar ventilation, the calculation was done from the equation $\dot{V}_A=\dot{V}_{CO2}/F_ACO2$ for the cases who had the expired gas analysis, and for the rest the calculation was done from the values of
the tidal volume assuming anatomical dead space equal to the weight in pounds.\(^7\)

Thus the absolute values of zonal \(\dot{V}_A\), \(Q\) and \(\dot{V}_A/Q\) ratio were calculated and the values were tabulated. The mathematical equations used for the calculations are as follows.

\[
\frac{\dot{V}_A}{Q_i} = \frac{a_i}{b_i} \times \frac{\text{a.v.}}{\text{c.o.}}
\]

\[
a_i = \frac{(d_{hi} - c) \times f_i}{\sum_{i=1}^{18} [(d_{hi} - c) \times f_i]}
\]

\[
b_i = \frac{(d_{pi} - c') \times f'_i}{\sum_{i=1}^{18} [(d_{pi} - c') \times f'_i]}
\]

- \(d_h\): counts of inhalation scintigram
- \(d_p\): counts of perfusion scintigram
- \(c, c'\): counts of background
- \(f, f'\): correction factor for the thickness of pulmonary tissue
- \(\text{a.v.}\): alveolar ventilation of total lung
- \(\text{c.o.}\): cardiac output

**RESULTS**

1. **Regional ventilation and perfusion in normal subjects sitting upright**

Seven normal subjects were studied. \(\dot{V}_A\), \(Q\) and \(\dot{V}_A/Q\) values were tabulated in Fig. 2 and were mapped in Fig. 3. The amount of both ventilation...
and perfusion were smaller in the upper zone compared to those in the lower zone, while the values of $V_A/Q$ ratio ranged from 1.35 in the upper zone to 0.64 in the lower zone since the rate of decrease from the apex to the base was more prominent for perfusion than for ventilation. Using these values, alveolar-arterial gradient of $P_{O_2}$ and $P_{CO_2}$ were calculated and the results were 5 mm.Hg for oxygen and $-0.3$ mm.Hg for carbon dioxide which are within reasonable ranges compared to the values obtained by others.

2. Regional ventilation and perfusion in various pulmonary diseases

The values of regional $V_A$, $Q$ and $V_A/Q$ ratios were mapped in various lung diseases and are seen in Fig. 4.

Case 1 and case 2: bronchogenic carcinoma. In both cases bronchogram revealed compression of the left main stem bronchus and sign of local infiltrations. Both ventilation and perfusion were reduced in the involved side. Since the depression of perfusion was more marked, the calculated $V_A/Q$ ratio became high.

Case 3–7: cystic diseases of the lung. The relationship between ventilation and perfusion in this disorder was found to be various. In case 3, where the left lung was mainly involved, the decrease of both ventilation and perfusion was quite impressive with the predominant disturbance of the latter. Similar results were observed in other cases (case 4 and case 6) though the areas involved were different in each case. In case 5, where right middle and lower lobes were the site of major involvement, the decrease of ventilation and perfusion was found almost the same degree, thus maintaining normal $V_A/Q$ ratio. In case 7, there was a formation of an abscess in the cyst which was located in the left lung. The impairment of perfusion was found more predominant over the involved area, while in the right upper zone, where cystic lesions were also present, the impairment of ventilation was more predominant.

Case 8–13: chronic pulmonary emphysema. In some cases (case 8 and case 9) there was a marked regional decrease of ventilation, while in others (case 10–13) the changes were more or less diffuse without regional differences.
In the former group, there were formation of giant bullae in the right upper lobe which prevented the normal ventilation resulting in low $V_A/Q$ values. A compensatory increase of ventilation was also seen in the left lung of case 9.

Case 14: Kartagener's syndrome. In this case bronchiectatic changes were seen in both lower lobes, especially predominantly in the right side, and

Fig. 4. Regional ventilation and perfusion in various pulmonary diseases.
there was a poor development of the left upper lobe, producing an expansion and elevation of the left lower lobe. The study showed a decrease of ventilation and perfusion in the left upper zone (Fig. 4). The pattern was similar in the right lower zone but the decrease of perfusion was found to be more predominant.

Case 15. In this case the scintigram did not reveal any significant abnor-
malities, though the patient had an atelectasis of right lower lobe after bronchopneumonia. Probably the abnormality was masked by the expanded right middle and upper lobe over the atelectatic area.

Case 16. In this case the scintigrams showed almost no ventilation and perfusion to the left lower zone which was thought to be due to the shift of the heart to the left. The patient had pulmonic regurgitation with the ectasia of pulmonary artery compressing left main stem of bronchus. There was also a pleural adhesion due to old pleuritic changes. Calculated $V_A/Q$ over the left zone was 0.69, indicating the more predominant ventilatory impairment. In the next 4 cases, pulmonary vessels are the sites of major involvement.

Case 17. This is the case of pulmonary hypertension probably caused by multiple pulmonary emboli. Both ventilation and perfusion were reduced almost the same degree.

Case 18. Pulmonary embolism was suspected clinically, but postmortem examination revealed fibroblastic sarcoma involving pulmonary artery. Prominent decrease of perfusion to the right lower zone was seen in the scintigram. Since there was no parallel decrease of ventilation $V_A/Q$ ratio became as high as 5.7.

Case 19. Poor development of right pulmonary artery was demonstrated by pulmonary arteriogram. Ventilation of the right lung was relatively normal but perfusion to the apex, middle and lower lobes were poor resulting in an unusual configuration in the figure of regional mapping of $V_A/Q$ ratios. Drop of $V_A/Q$ ratio in the left middle zone is probably explained by the compensatory shift of blood flow from the right lung to the left lung.

Case 20. Pseudotruncus arteriosus communis and hypoplasia of the left lung. Prominent decrease of perfusion to the hypoplastic lung was seen. Ventilation was also decreased but is a lesser degree.

We have divided the abnormal zones into 3 groups depending on the values of regional ventilation-perfusion ratio, that is high, normal, or low. When $V_A/Q$ ratio of a certain zone is within one standard deviation from the mean of the $V_A/Q$ ratios of this zone in the normal control, we have accepted the $V_A/Q$ ratio of this zone as normal. Out of 19 abnormal zones in the 16 cases of parenchymal lung diseases, $V_A/Q$ was higher than normal in 9, normal in 6 and lower in 4. In 4 cases of pulmonary vascular diseases high $V_A/Q$ ratio was found in 3 cases and normal in 1. None had the values lower than normal (Table II).

Next we have tried to see the relationship between the arterial Po$_2$ and the variance of $V_A/Q$ ratio. The variance was calculated as the deviation of the $V_A/Q$ ratios of the each zone from the mean of the corresponding zones in the normal expressed in logarithmic scale. The formula used for the cal-
The variance of $\frac{\bar{V}_A}{\bar{Q}}$ ratio is as follows.

$$\text{The variance of } \frac{\bar{V}_A}{\bar{Q}} \text{ ratio} = \sqrt{\frac{\sum_{i=1}^{18} \left[ \log \left( \frac{\sum_{i=1}^{18} V_{Ai}}{\sum_{i=1}^{18} Q_i} \right) - \log \left( \frac{V_{A1}}{Q_1} \right) \right]^2}{18}}$$

In Fig. 5 indices of $\frac{\bar{V}_A}{\bar{Q}}$ variance were plotted in the abscissa and the values of arterial Po2 in the ordinate to see the correlation between the two. The plottings show the presence of a negative correlation; in other words, the higher the variance, the lower the arterial Po2.

Fig. 5. Relationship between the $P_{ao2}$ and the variance of $\frac{\bar{V}_A}{\bar{Q}}$ ratio.

**DISCUSSION**

Since the report of the Björkman in 1934 there have been many studies which states the decrease of both ventilation and perfusion in the upper part compared to the lower part of the lung and inequal ventilation-perfusion ratios between the upper and lower segments. Various methods have been used for the study. In our study both inhalation scintiscanning and perfusion scintiscanning were applied using Au198 colloid aerosol in the former and I131-MAA in the latter. The entire lung fields were divided into 9 horizontal belts. The $\frac{\bar{V}_A}{\bar{Q}}$ ratio ranged between 1.35 and 0.64, the values being higher in the upper zone.
The differences of $V_{\text{A}}/Q$ ratio between the upper and lower zones are smaller here compared to those reported by the others.\textsuperscript{10-13} This difference can be related to the methodological differences. In our method, $I^{131}$-MAA or $Au^{198}$ colloid aerosol was given in the sitting position, while the counting was done in the supine position. It is quite possible that the zone of our scintigram does not necessarily corresponds to the same zone in the chest film taken upright. For instance the area under clavicle in the scintigram may correspond actually to the zone below the clavicle in the chest film. Also in the supine position the amount of pulmonary tissue which lies under the zone of the fifth intercostal space will become decreased due to the elevation of the diaphragm. All these geometrical relationships may influence the values of $V_{\text{A}}/Q$ ratios in our calculation.

In our method, the difference in regional ventilation or perfusion can be picked up more precisely compared to the method which uses $CO_{2}$\textsuperscript{18} or radioac-

K. A. 34 yrs. \textsuperscript{♂}  
I. multiple pulmonary cysts

Inhalation Scan

with pressure-cycled respirator with ultrasonic nebulizer

Fig. 6. Comparison of the 2 inhalation scintiscanning methods.
tive rare gases. But there is a methodological weakness in that the measurements of ventilation and perfusion should be done separately; in other words, there was a time lag between the 2 measurements. The next argument is the validity of our measurement of regional ventilation. For the measurement of regional ventilation, Au 198 colloid aerosol was inhaled under low positive pressure breathing which may disturb the pattern of spontaneous breathing. Later, we have tried the use of ultrasonic nebulizer for inhalation scintiscanning, since we can eliminate the influence of positive pressure breathing in this method. Fig. 6 illustrates the difference in the inhalation scintiscanning in both methods done in a patient with multiple pulmonary cysts. After several more studies, it was found that there is not a significant difference in the inhalation scintigram obtained in both methods.

There have been few studies done on the actual distribution of V_A/Q ratios in the patients of pulmonary diseases using such a method. It has been said that in cystic lung disease ventilation and perfusion decrease in parallel, while in chronic bronchitis or emphysema the change in V_A/Q ratio is variable but generally tends to decrease more or less. In our study there were many cases where the V_A/Q ratios were normal or even higher than normal over the diseased area, though the basic diseases in our study were not the same as those reported by others. Our results are in agreement with our previous study using radioactive rare gases.

Since the unevenness of ventilation-perfusion ratio is one of the cause of hypoxemia, we have calculated the variance of V_A/Q ratios in each case and plotted against the values of arterial oxygen tension to see the correlation between the two. There was a negative correlation though the correlation was rather poor, which is rather expected since the variance of V_A/Q ratios is not the only cause of hypoxemia and our method does not necessarily reflect the V_A/Q abnormality at the alveolar level.

For the actual performance of the measurement, it was hard to correct the counting according to the thickness of the lung and locate the exact position in the apex. Also at the base the respiratory motion of the diaphragm interferes with the regional geometry. For these reasons, we have discarded the measurement of the zones above clavicle and below sixth rib. It is possible that the difference in V_A/Q ratios becomes higher between the apex and the base if we included these two zones for the study. The lesion located just below the chest wall and the one located posteriorly close to the back were not treated equally in our study due to the response of the collimator used, and the regional differences in relation to the anteroposterior axis cannot be measured in our study, though these two drawbacks are inevitable in the other studies using CO 2 or radioactive rare gases at present.
The measurements of cardiac output and alveolar ventilation were done separately and the difference of cardiac output in relation to the change in position was not taken into consideration in our study. The overcoming of these methodological limitations and the correction of the possible errors remain for our future effort.

REFERENCES