Regulation of Regional Perfusion Distribution in the Lungs. Experimental Model and Effect of Alveolar Pressure

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ISAWA, T., TESHIMA, T., HIRANO, T., SHIRAISHI, K., MATSUDA, T. and KONNO, K. Regulation of Regional Perfusion in the Lungs. Experimental Model and Effect of Alveolar Pressure. Tohoku J. exp. Med., 1978, 124 (1), 33–46 — An experimental model for studying changes in regional perfusion distribution in the lungs of a dog was described. The right upper lobe was separated in vivo from the rest of the lungs by a balloon catheter and gas exchange of the lobe was artificially done asynchronously with the rest of the lungs by using a gas of interest at a prescheduled alveolar pressure. 99mTc-albumin microsphere was the agent of choice for multiple sequential studies in one dog. Alveolar gas composition reached a plateau after the 4th inflation of the right upper lobe. Effect of alveolar pressure on regional perfusion distribution was studied by using nitrogen and air as exchange gases. Perfusion distribution in the right upper lobe was the least at the maximal alveolar pressure of 14 to 19 cm H$_2$O, while it was the greatest at the tidal maximal alveolar pressure of 1 to -1 cm H$_2$O with either gas. Alveolar hyperinflation in a localized lung region due to the increase in regional alveolar pressure reduced regional perfusion distribution. —— regional perfusion distribution; alveolar pressure; alveolar hyperinflation; 99mTc-albumin microsphere

An experimental model to study the change of perfusion distribution in a localized lung region in vivo without disturbing perfusion distribution in other parts of the lungs as a whole would facilitate studying regional pulmonary perfusion changes under an experimental condition of interest.

Lung inflation due to increased alveolar pressure, for example, has been known to cause collapse of the small vessels or capillaries in the excised dog lung preparations (Harasawa and Rodbard 1961; Proctor and Yamabayashi 1961; Riley 1962), but little in vivo study has been made regarding perfusion distribution in a localized lung region with alveolar hyperinflation in relation to perfusion distribution in other parts of the lungs.

The purpose of this paper is to describe an experimental model which we have established to study changes in regional perfusion in the living dog lungs and to assess the effect of different alveolar pressure levels on regional perfusion distribution by using this model.

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MATERIALS AND METHODS

The adult mongrel dogs weighing 15 to 25 kg were anesthetized with intramuscular Ketalar* (ketamine hydrochloride, 100 to 150 mg) followed by intravenous Nembutal† (pentobarbital sodium, 25 mg/kg) to the depth that respiratory rate was between 10 to 16 per min, and Nembutal was added as required. Following endotracheal intubation with the dog in the supine position, a balloon catheter was inserted into the orifice of the right upper lobe bronchus under fiberoptic bronchoscopic guidance and the orifice was sealed by inflating the balloon. The right upper lobe was thus isolated in vivo from the rest of the lungs and its gas exchange was done artificially by using different gases to a prescheduled alveolar pressure level, while the rest of the lungs maintained a spontaneous breathing of ambient air.

The balloon catheter was hand-made by using a Cook catheter of Fr. 9 in size with a balloon part made from a latex contraceptive condom to which a tube of Fr. 4 in size was attached for inflating the balloon. The catheter end distal to the balloon was previously heat-bent 3 to 5 cm from the tip so that the catheter portion was propped up against the bronchial wall close to the carina and the balloon was snugly positioned inside the orifice of the right upper lobe bronchus and was inflated with 2 to 2.4 ml of air. The end of the catheter proximal to the balloon was end- and side-holed. The external end of the catheter was connected to a water manometer and two syringes for exchanging gas of the isolated right upper lobe (Fig. 1). Complete sealing of the right upper lobe bronchial orifice was ascertained not only bronchoscopically but also by checking whether pressure in the right upper lobe dropped or not after filling it with air to a pressure of 17 to 20 cm H2O. If the pressure of the right upper lobe was elevated above 27 cm H2O, a part of the balloon tended to be popped out of its orifice.

The dog was placed under a specially designed wooden table with a large central hole in

![Diagram of lung anatomy](image)

Fig. 1. Experimental model. Actually another tube is in the right intermediate bronchus to collect expired gas from the RML, RLL and RCL. RUL: Right upper or apical lobe. RML: right middle or cardiac lobe. RLL: right lower or diaphragmatic lobe. RCL: right cardiac or intermediate lobe. LUL: left upper or apical lobe. LML: left middle or cardiac lobe. LLL: left lower or diaphragmatic lobe.

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* Ketalar: Ketamine hydrochloride injection, Parke-Davis-Sankyo Ltd., Tokyo, Japan
† Nembutal: Pentobarbital sodium, Abbott Laboratories, Chicago, U.S.A.
Fig. 2. Experimental apparatus consisting of an animal table, a wooden table with a central hole, lead shields and a detector of a scintillation camera facing the central hole of the wooden table. An overview of the dog lungs from the detector is shown on the left hand side. (See text for further explanation).

the supine position with the four extremities tied and fixed to the animal table (Fig. 2). The detector of a scintillation camera* faced the animal from immediately above the central hole of the table and the geometry of measurement was kept constant throughout a series of experiments.

Gas exchange of the right upper lobe was artificially done through the catheter slowly by using different gases each mixed with a trace amount of helium, while the rest of the lungs maintained a spontaneous air breathing. Prior to each experiment, the right upper lobe was filled with air to a pressure of 17 to 20 cm H₂O for at least 30 seconds to prevent it from collapsing, and then the catheter end was left open for 10 to 15 seconds. The right upper lobe was artificially inflated with an exchange gas to a prescheduled alveolar pressure level and was left at the pressure level for 10 seconds and then the gas was removed as much as possible. The maneuver of inflation and removal of gas or gas exchange was repeated until the alveolar gas concentrations of helium, oxygen and carbon dioxide reached a plateau at the given alveolar pressure. Gas exchange of the lobe was repeated at prescheduled different maximal alveolar pressure levels ranging from −9 through 19 cm H₂O.

After discarding the initial 10 ml of the gas from the right upper lobe, the gas was sampled through the catheter each time until no further gas was removable or in other words to the approximate level of residual volume of the right upper lobe. The gas removed from the right upper lobe was called alveolar gas of the same lobe and was analyzed for helium, oxygen and carbon dioxide concentrations by gas chromatography†.

Helium concentration in the alveolar gas was expressed as relative percentage of its concentration to that of the inspired gas, and oxygen and carbon dioxide concentrations were expressed in actual concentration in percent in the sampled gases. Another catheter was placed in the intermediate bronchus of the right lung just distal to the bifurcation

* Scintillation camera RC-IC-1205. Hitachi Medical Corporation, Tokyo, Japan.
† Gas chromatography GC-1B, Shimadzu Seisakusho, Ltd., Kyoto, Japan.
of the right upper lobe bronchus and expired gas was sampled to see if helium was detected. If helium was detected, it indicated the presence of either leakage from around the balloon or collateral ventilation.

As a tracer agent, $^{99m}$Tc-albumin microsphere was used. Comparative studies were made beforehand between $^{99m}$Tc-MAA† and $^{99m}$Tc-albumin microsphere regarding radioactive decay patterns in the lungs following injection.

In order to determine how often gas exchanging maneuvers should be repeated before the alveoli of the right upper lobe reached a uniform concentration of alveolar gas, nitrogen, air and 100% oxygen each mixed with a trace amount of helium were used as exchange gases. The right upper lobe was inflated with each exchange gas both to the maximal alveolar pressure level of +14 to +19 cm H$_2$O and to the tidal alveolar pressure range of +1 to -1 cm H$_2$O. Collected alveolar gas samples were analyzed for helium, oxygen and carbon dioxide concentrations.

Because it was learned as shown later that the alveolar gas concentration in the right upper lobe became nearly uniform after 4th gas exchange, $^{99m}$Tc-albumin microsphere approximately 500 µCi in a volume of 0.5 ml or less, was injected intravenously 10 seconds after the 7th inflation of the right upper lobe with the exchange gas.

In each experiment initial perfusion study was made following artificial ventilation of the right upper lobe with nitrogen. Now the lower edge of the right upper lobe that was well demarcated as an area of reduced perfusion with nitrogen as an exchange gas was adjusted to the transverse diameter (x-x’) of the hole of the specially designed wooden table which was in turn adjusted to the corresponding diameter of the detector and the right and left lungs were separated by the longitudinal diameter (y-y’) of the hole of the table which was adjusted to the corresponding longitudinal dividing line of the detector.

After waiting for 2 min after injection of $^{99m}$Tc-albumin microsphere for complete mixing and distribution in the pulmonary vascular beds, radioactivity of the right upper lobe (Ru), right lower half (Rl) and the entire right lung (Ru+1) and their counterparts of the left lung was measured by the scintillation camera, respectively as shown in Fig. 3. The liver, the spleen and the very bases of the right and left lungs were shielded by a lead shield attached beneath the wooden table. When radioactivity of the Ru and its corresponding region of the left lung was to be measured, the Rl and its counterpart of the left lung were covered by another lead shield on the table, adjusting the upper margin of the lead shield to the line x-x’ and radioactivity of the Ru and its counterpart of the left lung was measured with the detector crystal in a divided mode. The lead shield was then slid upward on the table to adjust the lower margin of the lead shield to the line x-x’, and was removed when radioactivity of the lower lung fields (Rl and its counterpart of the left lung) was measured. Then radioactivity of Ru+1 and the entire left lung was measured without the lead shield. Radioactivity of Ru+1 roughly corresponded to a summation of radioactivity of Ru and Rl. If this was not the case, it indicated that the measurement of radioactivity or positioning of the animal was not properly done. Net radioactivity in each region was

\[
\begin{align*}
\text{Ru vs. Lu.} & \quad \text{Rl vs. Ll.} & \quad \text{Ru + l. vs. Lu + l.}
\end{align*}
\]

![Diagram of measuring radioactivity](image1)

N$_2$ in RUL

Fig. 3. A diagram to show the sequence of measuring radioactivity of each lung region in one study.

* $^{99m}$Tc-albumin microsphere TCK-5, SORIN, Saluggia, Italy.
† $^{99m}$Tc-MAA Daiichi Radioisotope Laboratories, Tokyo, Japan.
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expressed in percentage of total net radioactivity of the $R_{+1}$ and the entire left lung. Perfusion percentage of each lung region was indicative of perfusion distribution under an experimental condition.

In order to see the effect of placing a balloon catheter and artificial ventilation of the right upper lobe through the catheter on regional perfusion distribution in the right upper lobe, perfusion studies were made with and without the balloon catheter in the right upper lobe orifice in eleven normal dogs.

In order to compare the experimental results obtained from different dogs at different times, the perfusion percentages in the right upper lobe, right lower half and the entire lung at each different alveolar pressure level in the right upper lobe were divided by the respective perfusion percentage obtained at the tidal alveolar pressure range (maximal alveolar pressure of +1 to -1 cm H$_2$O) of the same dog at the same study. The maximal alveolar pressure was defined as the alveolar pressure at the end of expiration of the spontaneously breathing dog; the alveolar pressure of the right upper lobe fluctuated between +1 to 0 and -1 to -3 cm H$_2$O, corresponding respectively to end-expiration and end-inspiration during tidal breathing. Calculated values were called perfusion ratios; naturally the perfusion ratio in each lung region was 1 when the right upper lobe was artificially ventilated at the tidal alveolar pressure range. For statistical analysis, a paired $t$-test was employed.

RESULTS

Analysis of alveolar gas samples

The results of analysis of the sampled alveolar gases at each artificial gas exchange of the right upper lobe for helium, oxygen and carbon dioxide are shown in Figs. 4 and 5.

Fig. 4. Concentration of helium (He), oxygen (O$_2$) and carbon dioxide (CO$_2$) in the alveolar gas obtained at the end of each inflation of the right upper lobe to the maximal alveolar pressure of +14 to +19 cm H$_2$O with 100% O$_2$ (●, $n=5$), air (▲, $n=3$) and nitrogen (○, $n=3$).
Fig. 5. Concentration of helium (He), oxygen (O₂) and carbon dioxide (CO₂) in the alveolar gas obtained at the end of each inflation of the right upper lobe at the tidal pressure with 100% O₂, (●, n=11), air (▲, n=16) and nitrogen (○, n=17)

As shown in Figs. 4 and 5, the concentrations of helium, oxygen and carbon dioxide in the alveolar gas became nearly uniform after the 5th or 6th alveolar gas sampling; i.e., the 4th or 5th gas exchange. In the case of nitrogen as an exchange gas for the right upper lobe, the helium concentration in the alveolar gas reached 90% levels both at the maximal alveolar pressure of 14 to 17 cm H₂O and 1 and -1 cm H₂O after the 5th inflation and the oxygen and carbon dioxide concentration remained between 5 and 6% and between 4 and 5% throughout at either maximal alveolar pressure level, respectively.

In the case of air as an exchange gas, the alveolar helium concentration reached 90 to 100% after the 5th gas exchange and the oxygen concentration was from 9 to 11% after the 2nd gas exchange and carbon dioxide concentration remained 6 to 7% throughout.

In the case of 100% O₂ as an exchange gas, the helium concentration reached 99 to 100% at the maximal alveolar pressure of 14 to 17 cm H₂O and 120 to 124% at the maximal alveolar pressure of 1 to -1 cm H₂O and the oxygen concentration was close to 70 to 80% after the 4th gas exchange and the carbon dioxide concentration remained constant at 6 to 7% throughout.

From these results, it was decided to exchange the gas of the right upper lobe 7 times in the subsequent experiments, and an injection of the tracer agent was made 10 seconds following the end of the 7th inflation of the right upper lobe with the gas of interest. The alveolar gas samples from the right upper lobe were collected immediately before the first artificial gas exchange; i.e., after filling the
right upper lobe with air to the pressure of 17 to 20 cm H₂O, and at the end of the 4th, 5th and 6th inflations of the lobe with the exchange gas to a prescheduled pressure level. The mean concentrations of helium, oxygen and carbon dioxide of the alveolar gas samples collected 10 seconds following the end of the 4th, 5th and 6th inflation of the right upper lobe with the exchange gas were assumed to represent the concentrations of the alveolar gases at the time of perfusion study.

Selection of a radioactive tracer material

In order to choose a suitable tracer agent to be used in the present experiment, both ⁹⁹ᵐTc-MAA and ⁹⁹ᵐTc-albumin microsphere were tested.

Each agent was intravenously injected sequentially multiple times, and radioactivity of the lungs was measured externally. Measured radioactivity was replotted on semilogarithmic paper and the traced radioactivity curve was visually separated into two components, when possible. An exponential curve for the second or slow component \( y = a e^{bx} \) was calculated by the least squares fit of pairs of data points of time versus radioactivity. Coefficient of determination \( r^2 \) was more than 0.98. An exponential curve for the initial or fast component was calculated by using data points of time versus radioactivity corrected by subtracting radioactivity contributed by the slow component. Half-time \( (T_{1/2}) \) was calculated by the formula \( T_{1/2} = \ln 2 / b \). At the initial injection, two components were discernible in all five dogs to which ⁹⁹ᵐTc-MAA was injected but in only two of the four dogs injected with ⁹⁹ᵐTc-albumin microsphere. From the time after the second superimposed injection, replotted radioactivity curve was practically straight either with ⁹⁹ᵐTc-MAA or ⁹⁹ᵐTc-albumin microsphere.

As indicated in Table 1, radioactivity decayed in the lungs with a shorter \( T_{1/2} \) following injection of ⁹⁹ᵐTc-MAA, while \( T_{1/2} \) following injection of ⁹⁹ᵐTc-albumin microsphere was almost 5 times longer than the volume with ⁹⁹ᵐTc-MAA.

<table>
<thead>
<tr>
<th>Injection</th>
<th>MS</th>
<th>MAA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st</td>
<td>( 53.2\pm28.3 ) (( n=2 ))</td>
<td>( 10.3\pm2.1 ) (( n=5 ))</td>
</tr>
<tr>
<td>2nd</td>
<td>( 146.5\pm7.6 ) (( n=4 ))</td>
<td>( 48.5\pm15.2 ) (( n=5 ))</td>
</tr>
<tr>
<td>3rd</td>
<td>( 203.5\pm31.8 ) (( n=4 ))</td>
<td>( 69.8\pm7.4 ) (( n=5 ))</td>
</tr>
<tr>
<td>4th</td>
<td>( 369.5\pm46.5 ) (( n=2 ))</td>
<td>( 67.2\pm4.3 ) (( n=3 ))</td>
</tr>
</tbody>
</table>

| Mean±S.E.M. |          |          |

It seemed, therefore, that once injected, ⁹⁹ᵐTc-albumin microsphere trapped in the pulmonary vascular beds remained there for a fairly long time, certainly much longer than the period necessary for gas exchanging maneuver in this experiment. The time required for one experimental procedure of gas exchanging 7 times was 10 min at most or less and radioactive decay during that period was practically
negligible. In other words, if $^{99m}$Tc-albumin microsphere was used as a tracer agent, calculation of net radioactivity was possible by simply subtracting radioactivity of the previous injections from radioactivity currently measured. Thus $^{99m}$Tc-albumin microsphere was exclusively used in the present experiments.

**Effect of a balloon catheter in the right upper lobe on regional perfusion**

In all eleven dogs studied, perfusion distribution in the right upper lobe decreased after artificial ventilation through the balloon catheter as shown in Table 2. Under air breathing without the balloon catheter in the right upper lobe orifice in place, perfusion distribution averaged $22.7\pm2.2$ (s.e.m.)%, and it decreased to $12.4\pm1.7\%$ when the right upper lobe was artificially ventilated through the catheter with air asynchronously with the rest of the lungs which breathed ambient air. The difference was statistically significant ($p<0.002$).

**TABLE 2. Perfusion distribution in the right upper lobe before and after a balloon catheter placement**

<table>
<thead>
<tr>
<th>Dog</th>
<th>Before (%)</th>
<th>After (%)</th>
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<tbody>
<tr>
<td>1</td>
<td>26.2</td>
<td>6.6</td>
</tr>
<tr>
<td>2</td>
<td>21.1</td>
<td>17.7</td>
</tr>
<tr>
<td>3</td>
<td>32.7</td>
<td>6.6</td>
</tr>
<tr>
<td>4</td>
<td>13.2</td>
<td>13.1</td>
</tr>
<tr>
<td>5</td>
<td>18.0</td>
<td>14.7</td>
</tr>
<tr>
<td>6</td>
<td>20.5</td>
<td>15.7</td>
</tr>
<tr>
<td>7</td>
<td>22.3</td>
<td>8.1</td>
</tr>
<tr>
<td>8</td>
<td>19.1</td>
<td>17.5</td>
</tr>
<tr>
<td>9</td>
<td>11.3</td>
<td>5.0</td>
</tr>
<tr>
<td>10</td>
<td>32.9</td>
<td>22.5</td>
</tr>
<tr>
<td>11</td>
<td>25.8</td>
<td>8.7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>S.D.</th>
<th>S.E.M.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before (%)</td>
<td>22.7</td>
<td>7.3</td>
<td>2.2</td>
</tr>
<tr>
<td>After (%)</td>
<td>19.4</td>
<td>5.7</td>
<td>1.7</td>
</tr>
</tbody>
</table>

**Effects of alveolar pressure on regional perfusion distribution**

*Nitrogen as an exchange gas.* Perfusion ratios in the right upper lobe and the entire right lung are presented in Figs. 6 and 7. As shown in Fig. 6, perfusion ratio was the least when the right upper lobe was inflated with nitrogen to the maximal alveolar pressure of 14 and 19 cm H$_2$O, while it was the greatest at the maximal alveolar pressure of $-2$ to $-5$ cm H$_2$O, and 1 to $-1$ cm H$_2$O or at the tidal pressure range. There was a statistical significance ($p<0.0001$) in the difference between the perfusion ratios at the maximal alveolar pressure of 14 to 19 cm H$_2$O and at the tidal pressure range. Perfusion ratios were slightly diminished at the maximal pressure levels of 5 to 7 cm H$_2$O and at $-5$ to $-9$ cm H$_2$O as compared with that at the tidal pressure range, and the difference between perfusion ratios at the maximal alveolar pressure of 5 to 7 cm H$_2$O and at the tidal pressure range was statistically significant ($p<0.05$).
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Fig. 6. Regional perfusion ratio in the right upper lobe versus alveolar pressure change in the same lobe, when the right upper lobe was artificially ventilated with nitrogen (N₂).

As shown in Fig. 7, perfusion ratios in the entire right lung, when the right upper lobe was ventilated at various maximal alveolar pressure levels, were nearly equal to each other, indicating that the perfusion ratios in the lower half of the right lung was the greatest when the right upper lobe had the least perfusion. There was no statistical significance in the difference between perfusion ratios of the entire right lung at various alveolar pressure levels of the right upper lobe.

The result of analysis of the exchange gas and the alveolar gas samples of the right upper lobe when it was ventilated at different maximal alveolar pressure levels is shown in Fig. 8. The helium concentration of the alveolar gas was the closest to that of the exchange gas at the maximal alveolar pressure of +14 to +19 cm H₂O, indicating the least dilution of the alveolar gas at this pressure level. No helium was detected in the gas samples obtained from the right intermediate bronchus just distal to the bifurcation of the right upper lobe bronchus.

Air as an exchange gas. When air was used as an exchange gas of the right upper lobe at the different maximal alveolar pressure levels, perfusion ratios in the right upper lobe and the entire right lung were as shown in Figs. 9 and 10, respectively.
In the right upper lobe, perfusion ratios were the least at the maximal alveolar pressure of 14 to 19 cm H$_2$O as in the case of nitrogen as described previously, and the difference was statistically significant as compared with perfusion ratios at other alveolar pressure levels ($p<0.002$). Perfusion ratios in the entire right lung were also similar to each other, notwithstanding differences in the maximal alveolar pressure levels in the right upper lobe as observed with nitrogen as an exchange gas. There was no statistical significance in the difference between them.

The result of the analysis of inspired and alveolar gases at different alveolar pressure levels is shown in Fig. 11. There was no statistical significance in the
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**Fig. 10.** Regional perfusion ratios in the right whole lung versus alveolar pressure change in the right upper lobe, when the right upper lobe was artificially ventilated with air.

**Fig. 11.** Alveolar pressure in the right upper lobe versus concentrations of helium (He), oxygen (O₂) and carbon dioxide (CO₂) in the same lobe, when air was used as an exchange gas for the right upper lobe. ☐, inspired gas; ☑ alveolar gas.

difference in helium concentration. The alveolar oxygen concentration was the greatest and the alveolar carbon dioxide concentration was the least at the maximal alveolar pressure of 14 to 19 cm H₂O, indicating that at this maximal alveolar pressure level perfusion distribution in the right upper lobe was the least as compared with that at other alveolar pressure levels. Again no helium was detected in the gas samples obtained from the right intermediate bronchus distal to the bifurcation of the right upper lobe.
DISCUSSION

The experimental model we have described here is useful in studying perfusion distribution in a localized lung region in vivo under various experimental conditions such as at different alveolar pressure levels as reported in this paper. The effect of different oxygen and carbon dioxide concentrations in the alveolar gas on regional perfusion or drug effects are also studied by using this model (Isawa et al. 1977). In this model, gas is artificially exchanged in the right upper lobe in which any change in perfusion distribution is the subject of study, while the rest of the lungs maintains a spontaneous air breathing.

Probably because of a relatively small contribution of the right upper lobe with a balloon catheter in place to the total lung perfusion as shown in Table 2, perfusion change in that lobe can be studied without greatly disturbing perfusion distribution in the entire right lung as a whole but still in relation to perfusion distribution in the rest of the lungs. The facts that no helium was detected in the gas samples obtained from the right intermediate bronchus immediately distal to the bifurcation of the right upper lobe bronchus and that the alveolar pressure of the right upper lobe remained almost constant following filling it with air to 17 to 20 cm H₂O indicate that there was no collateral ventilation between the right upper lobe and the rest of the right lung. Examination of the lungs of 3 dogs autopsied showed that the right upper lobe was either completely separated from the other lobes or connected only by fibrous tissue. The visceral pleura was intact.

These findings are in agreement with the observation that atelectasis occurred in dog lungs when the lobar bronchus was obstructed but that the occluded parts remained filled with air when the obstruction was in a segmental bronchus (Macklem 1971). These observations have been confirmed recently by Effman and others by using radioactive xenon gas in the living dog (Effman et al. 1972).

The right upper lobe occupies the upper third of the right hemithorax and shows the least overlapping with the other lobes. The absence of collateral ventilation with other lobes and its anatomical location make the right upper lobe a suitable experimental model to study changes in regional perfusion distribution by external counting. Furthermore, ⁹⁹ᵐTc-albumin microsphere once injected remained in the lungs during one experiment of less than 10 minutes’ duration without significant decay in radioactivity and was the agent of choice which enabled multiple repeated studies in a dog at one time.

From the present studies, it has become certain that the distribution of regional perfusion is reduced when the alveoli are inflated with the increase in alveolar pressure, while regional perfusion distribution was the greatest at the tidal alveolar pressure range or its vicinity.

In clinical lung imaging, it is an everyday experience that regional perfusion distribution in the lungs is uneven or even deficient in pulmonary emphysema, bronchitis or bronchial asthma in which air trapping occurs (Lopez-Majano et al. 1966; Rogers and Kuhl 1966; Woolcock et al. 1966; Henderson et al. 1967; Mishkin and Wagner 1968; Isawa et al. 1970; Yamazaki 1972). Especially in bronchial
asthma, regional perfusion distribution pattern is ever changing (Yamazaki 1972); the underlying mechanism for such perfusion abnormalities may be due to increased alveolar pressure and hypoventilation of a localized lung region where air trapping occurs secondary to bronchospasm and/or mucus plugging (Woolcock et al. 1966). Besides regionally increased alveolar pressure as a cause of decreased perfusion distribution as shown in this paper, regional hypoventilation due to bronchial occlusion, hypoxia and hypercarbia have been known to induce regional decrease in perfusion distribution (Isawa et al. 1967, 1971, 1977; Fishman 1976). In bronchial asthma, however, Henderson and others think that regional hypoxia due to bronchospasm and mucus plugging plays a more important role than increased alveolar pressure does in reducing regional perfusion distribution (Henderson et al. 1967).

It is easily conceivable that the regionally increased alveolar pressure may induce alveolar hyperinflation. Alveolar hyperinflation may in turn mechanically compress the vascular lumens of the small vessels and/or the capillary beds which exist in the interstitial space between the hyperinflated alveoli. What we observed in the present in vivo experiment by using the right upper lobe is nothing but the reflection of what actually happened in the living lung region when exposed to various alveolar pressures. Harasawa and Rodbard have shown that positive intrapulmonary air pressure increases the resistance to blood flow through the lobe of the excised dog lung (Harasawa and Rodbard 1961). The capillaries collapse when the pressure in the capillaries is held constant relative to the pressure in the alveoli during inflation of the excised lung (Riley 1962). Proctor and Yamabayashi have shown that the excised lung lobes of a dog inflated with 25–28 cm H₂O not uncommonly show compressed small vessels and that open capillaries are not found. In two lobes from the same dog treated in identical fashion, there is much more capillary filling in the lobe inflated with 5 cm H₂O than that inflated with 25 cm H₂O (Proctor and Yamabayashi 1961). Takaro (1958) used a tracheal divider to separate the right and left lungs and inflated one lung to 15 cm H₂O while the other lung was inflated to 20 cm H₂O or higher and demonstrated angiographically that the lung inflated with a higher pressure showed hypovascularity as compared with the lung which was inflated to 15 cm H₂O. In this sense the lung areas with a high alveolar pressure may become the so-called zone 1 physiologically (West et al. 1964). It is also interesting to find from a teleological stand point that perfusion distribution in a localized lung region is the greatest when the regional alveoli are ventilated at the tidal pressure range.

Acknowledgments

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References


