Regional Lung Function of Non-smokers with Healed Spontaneous Pneumothorax

A Physiologic and Emission Radiologic Study*

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This study is based on investigations of 11 nonsmokers with healed spontaneous pneumothorax. Physiologic, scintigraphic and radiologic examinations were performed to determine whether they had any impairment of overall or regional lung function. Posteroanterior and lateral chest radiographic examinations revealed no abnormality. Forced expirographic study was normal, but the residual volume was increased. Ventilation was impaired and perfusion decreased in the apical region of the lungs, also the most common location of spontaneous pneumothorax. Findings are consistent with the presence of regional airway obstruction, which may cause, or at least contribute to, development of this condition.

Spontaneous pneumothorax (SP) is generally considered to be due to the rupture of an emphysematous bulla, but the occurrence of airway occlusion with consequent inhibition of pressure equilibration over the alveolar wall. Conventional single spirometric and clinical examinations, however, have not revealed any distinct ventilatory abnormalities in SP patients other than some minor subjective complaints. These patients have therefore been considered apparently healthy.

The aim of the present investigation was to determine whether patients who have suffered from SP have any impairment of ventilation and perfusion in areas previously affected by this condition. Such patients were therefore submitted to chest x-ray examination and lung function measurements eight months or more after the latest episode of SP. All examinations and measurements in each subject were concluded within a two-week period.

Materials and Methods

The subjects consisted of eight men and three women who had been treated for SP. Detailed information concerning the patients is given in Table 1. Mean age at the time of the first treatment was 31 years. One male patient received treatment in 1975, the others between 1979-84. The patients were selected because they were apparently healthy non-smokers. The women were not suffering from cataract, other pulmonary diseases, and none of the patients had any other cardiopulmonary diseases. SP had been confirmed in each case by posteroanterior and lateral chest x-ray examinations. Lungs were regularly reexamed at a repeat x-ray study after the acute phase. The patients had no symptoms or signs of infection, or of systemic or malignant disease. Length of time between diagnosis of SP and the present investigation ranged from eight months to seven years.

Two women and three men provided control values for the lung function measurements. They were all healthy non-smokers and were similar in height and weight to the SP patients (Table 1). In addition, another 17 women and seven men with height similar to that of the SP patients were studied with regard to lung height on x-ray film (see below).

Written consent to participate in this study was obtained from the patients and the control subjects.

Chest X-ray Findings

Posteroanterior and lateral chest x-ray films were obtained in each subject one to two weeks before the lung function study. (Normal chest x-ray film was a prerequisite for the subsequent lung function measurements.) Lung height, ie, the distance between the apex and the phrenocostal sinus, was measured on either side on the frontal radiographic films.

Regional Lung Function

Patients were seated in a semirecumbent position, leaning back at an angle of 15° towards a large-field-of-view gamma camera (General Electric Giga camera) connected on line to a computer (Digital Equipment PDP 11/44).

In the ventilation study, serial scintigrams were recorded for 4-s periods during eight minutes following an inhaled bolus of 370 MBq 133Xe. A standard rebreathing bag system (Atomic Products Corporation) filled with 5 L of oxygen was used.

The patient was instructed to exhale completely and to make a maximal slow inspiration while the radioactive bolus of 133Xe was
injected into the mouthpiece, then to hold his breath for at least 16 s (single breath phase). Distribution of the radioactivity recorded during this phase (summed over four scintigraphic studies) gives a measure of the regional ventilation (V) during deep breath. The patient then breathed into the bag until the regional activity had reached a steady state, approximately three to four min after the injection. Distribution of the radioactivity recorded in the steady state phase (summed over 25 scintigraphic studies) is a measure of the regional ventilated volume (V) of the lungs. Five minutes after the injection, the patient was switched from the rebreathing system to an exhaust system (washout phase) for a further three min, during which time the regional activity was continuously measured. This permitted calculation of the effective half-time of the washout of the radioactive gas (T ½), which can be considered a measure of the regional ventilatory efficiency during quiet breathing.

Perfusion (Q) study was performed immediately after ventilation study with the patient in exactly the same position. Perfusion scintigraphic results were accumulated over a period of 100 s following IV injection of 60 MBq 99mTc-macroaggregated albumin.

For evaluation of the test results, each lung was divided into three equally sized regions of interest—apical, middle, and basal. Regional percentages of activity for Q, V and V were calculated. Finally, distribution ratios (V/V, Q/V, V/Q) were calculated for each region.

Conventional Spirometry

The resting lung volume was measured by means of body plethysmography (variable pressure box) as described by Dubois et al. The frequency of panting against the occluded shutter was 1 Hz, as guided by a metronome. After the shutter had been released, the subject made a maximum inspiration for assessment of the total lung capacity (TLC) and a maximum expiration for calculation of the vital capacity (VC) and residual volume (RV). Lung volume measurements and forced expiratory recording were performed three to five times with the subject in the sitting position. The best results for each variable were selected, even if this meant that results had to be obtained from different recordings. The following variables were measured: forced expiratory vital capacity (FVC), forced expiratory volume in 1 second (FEV1), FEV1 divided by FVC (FEV1/FVC), and forced expiratory flow at 50 percent of FVC (FEF50). A low-resistive bellows spirometer was used (Ohio 840); the output signal was treated on-line by a computer (PDP/1160) at a sampling frequency of 60 Hz. For calculation of reference values, the multiple regression equations proposed by Fridrikson and co-workers were used for men, and those of Berglund et al8 and Grimby and Soderholm8 for women.

### Transfer Factor for CO

The transfer factor for carbon monoxide was measured using a single breath technique as described by Cotes.8 A double bag-in-box system was used, and the second expired liter was collected for gas analysis, helium measured by a mass-spectrometer (Centronic MGA200) and carbon monoxide by an infra-red meter (UNOR). Reference values presented by Cotes (men)8 and Billiet et al (women)8 were used.

### Lung Mechanics

Transpulmonary pressure was measured as mouth minus esophageal pressure, the latter recorded via an esophageal balloon catheter positioned in the lower third of the esophagus. The balloon was 10 cm long and 3 cm in circumference and was filled with 0.5 ml of air. The lung volume was measured in conjunction with the body plethysmographic recording (see above). Normal values presented by Jonson8 were used as reference.

### Statistics

Student's t-tests were used for comparing the lungs which had been affected by SP with the unaffected lungs of the patients and the controls.

### RESULTS

### Radiologic Examinations

Frontal and lateral chest radiographic examinations of the patients obtained eight months or more after SP were scrutinized by three independent interpreters and judged to be normal.

The apex-sinus distance (x ± SD) (Table 1) in the affected lung, measured on the posteroanterior radiographic films, was 35.6 ± 2.0 cm for the men and 32.3 ± 1.5 cm in the women. Corresponding distances in the unaffected lungs of the patients were 35.1 ± 2.1 cm and 31.5 ± 1.7 cm, respectively. The apex-sinus distance was not significantly shorter in the two shortest men. Individual patient data are given in Table 1. The apex-sinus distance in the control subjects was 31.5 ± 2.0 cm in the women (n = 17, mean of both

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**Table 1—Data at Time of Study**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age (yrs)</th>
<th>Height (cm)</th>
<th>Weight (kg)</th>
<th>SP</th>
<th>Affected side</th>
<th>Apex-base distance (cm)</th>
<th>Time after SP (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>34</td>
<td>170</td>
<td>55</td>
<td>1</td>
<td>R</td>
<td>35</td>
<td>34</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>26</td>
<td>193</td>
<td>93</td>
<td>1</td>
<td>R</td>
<td>37.5</td>
<td>37</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>45</td>
<td>169</td>
<td>63</td>
<td>3</td>
<td>R</td>
<td>32.5</td>
<td>33</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>35</td>
<td>172</td>
<td>67</td>
<td>1</td>
<td>L</td>
<td>32.5</td>
<td>41</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>41</td>
<td>167</td>
<td>65</td>
<td>2</td>
<td>L</td>
<td>34</td>
<td>106</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>20</td>
<td>189</td>
<td>64</td>
<td>1</td>
<td>R</td>
<td>36.5</td>
<td>36</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>41</td>
<td>172</td>
<td>59</td>
<td>1</td>
<td>RL</td>
<td>34</td>
<td>12</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>48</td>
<td>188</td>
<td>80</td>
<td>4</td>
<td>R</td>
<td>34.5</td>
<td>-</td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>45</td>
<td>166</td>
<td>78</td>
<td>1</td>
<td>R</td>
<td>31.5</td>
<td>32</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>19</td>
<td>186</td>
<td>79</td>
<td>1</td>
<td>L</td>
<td>38.5</td>
<td>36</td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>23</td>
<td>189</td>
<td>85</td>
<td>1</td>
<td>L</td>
<td>38</td>
<td>37.5</td>
</tr>
</tbody>
</table>

Mean ± SD 34.5 ± 10.3 178 ± 11 71.6 ± 12
Table 2—Spirometry and Single Breath CO Transfer Data (X ± SD)

<table>
<thead>
<tr>
<th></th>
<th>TLC (L)</th>
<th>VC (L)</th>
<th>RV (L)</th>
<th>FEV$_1$ (L)</th>
<th>FEV%</th>
<th>FEF$_{50}$ (L/s)</th>
<th>TLCO (mL/mm Hg/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measured</td>
<td>7.62</td>
<td>5.16</td>
<td>2.29*</td>
<td>4.25</td>
<td>83.0</td>
<td>5.16</td>
<td>31.4</td>
</tr>
<tr>
<td>± 1.12</td>
<td>± 1.10</td>
<td>± 0.48</td>
<td>± 0.85</td>
<td>± 0.80</td>
<td>± 1.05</td>
<td>± 0.50</td>
<td>± 8.4</td>
</tr>
<tr>
<td>Reference†</td>
<td>7.30</td>
<td>5.27</td>
<td>1.82</td>
<td>4.19</td>
<td>79.7</td>
<td>4.99</td>
<td>30.0</td>
</tr>
<tr>
<td>± 1.24</td>
<td>± 1.10</td>
<td>± 0.20</td>
<td>± 0.91</td>
<td>± 1.4</td>
<td>± 0.50</td>
<td>± 5.7</td>
<td></td>
</tr>
</tbody>
</table>

*Significantly different from reference value, p < 0.05.
†Reference values from Fridriksson et al., Berglund et al., Grimby and Soderholm, Cotes, and Billiet.

Regional Lung Function

Perfusion. The perfusion of the apical region was significantly lower and that of the basal region significantly higher in the affected lungs than in the healthy control lungs (p<0.01 in both cases) (Table 3). In the unaffected lungs in the patients, fractional perfusion of the upper lung region was lower and fractional perfusion of the lower region higher than in the control subjects, but only the apical difference was statistically significant. These observations indicated an increased vertical gradient of perfusion in the pneumothorax lung, and a tendency to a similar increase in the unaffected lung, compared with the lungs of the control subjects.

Ventilation. The fractional ventilation of the apical region of the affected lung in the pneumothorax patients was slightly but significantly lower than that of their unaffected lung (p<0.05) but did not differ from the fractional ventilation of the corresponding lung region in the control subjects (Table 3). T½ was significantly longer in the apical region of the affected lung than that of the unaffected lung (p<0.05).

It was also 17 percent higher than in the apical region of the control lung, but this difference was not statistically significant. There were no differences in

Table 3—Radiospirometric Data of Eleven Patients with Healed Spontaneous Pneumothorax and Five Control Subjects

<table>
<thead>
<tr>
<th></th>
<th>Spontaneous pneumothorax patients</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Affected lungs</td>
<td>Non-affected lungs</td>
<td>Control subjects</td>
</tr>
<tr>
<td>Upper</td>
<td>n = 13</td>
<td>n = 9</td>
<td>n = 10</td>
</tr>
<tr>
<td>Q</td>
<td>0.31 ± 0.11*</td>
<td>0.32 ± 0.08*</td>
<td>0.41 ± 0.07</td>
</tr>
<tr>
<td>V</td>
<td>0.78 ± 0.11†</td>
<td>0.85 ± 0.06</td>
<td>0.80 ± 0.14</td>
</tr>
<tr>
<td>T½†</td>
<td>42.9 ± 11.6†</td>
<td>33.8 ± 8.5</td>
<td>36.8 ± 7.6</td>
</tr>
<tr>
<td>Middle</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q</td>
<td>1.05 ± 0.04</td>
<td>1.02 ± 0.10</td>
<td>1.11 ± 0.15</td>
</tr>
<tr>
<td>V</td>
<td>0.96 ± 0.12</td>
<td>0.97 ± 0.08</td>
<td>1.02 ± 0.16</td>
</tr>
<tr>
<td>T½</td>
<td>26.2 ± 6.9</td>
<td>28.4 ± 5.3</td>
<td>30.6 ± 5.6</td>
</tr>
<tr>
<td>Lower</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q</td>
<td>1.54 ± 0.18*</td>
<td>1.47 ± 0.15</td>
<td>1.30 ± 0.15</td>
</tr>
<tr>
<td>V</td>
<td>1.18 ± 0.09</td>
<td>1.21 ± 0.24</td>
<td>1.17 ± 0.14</td>
</tr>
<tr>
<td>T½</td>
<td>26.2 ± 6.9</td>
<td>25.2 ± 7.2</td>
<td>23.7 ± 6.8</td>
</tr>
</tbody>
</table>

*Significantly different from control value, p < 0.01.
†Significantly different from non-affected value, p < 0.05.
‡Effective half time of the wash-out of inhaled radioactive gas.

FIGURE 1. Static transpulmonary pressure (P$_{1p}$) volume (in percent predicted TLC) curves of the lungs in six patients. The normal range according to Jonson has been shown as horizontal bars. Note the essentially normal slope of the pressure volume curves, except in patient no. 5 who showed slightly steeper than normal slope around FRC.
washout times between the affected lung and either the unaffected or control lungs in the middle and lower lung regions.

Discussion

There appear to have been no previous reports on the perfusion and ventilation of lungs in patients with healed spontaneous pneumothorax.

In our investigation, we found that non-smokers with healed SP had a slightly elevated residual volume, decreased perfusion and ventilation, and prolonged TV5, mostly in the apical part of the affected lung.

Material

All together, 305 patients were treated at this hospital for SP from 1975 to 1984. Most of these patients were heavy smokers. Non-smokers constituted 5 percent of the total, which is remarkably low when compared with the fraction of non-smokers in the Swedish population, namely 40 percent.16 We selected patients who had never smoked and who had not had SP for at least eight months prior to that study, so as to eliminate the effects of smoking and acute pathophysiologic changes of the lungs. The aim was to study all non-smoking SP patients treated during the preceding ten-year period. However, five women were not included. Two of them refused to participate. The three other were excluded because of suspicion of catamenial pneumothorax, which may have a different pathophysiologic background.17-19 The 11 participating non-smoking patients were considered apparently healthy on the basis of clinical, chest x-ray and spirometric examination.

One female patient, however, complained of inability to perform physical work, but at several examinations no objective abnormality was found. In addition, the two shortest male patients had a height of 167 and 170 cm, respectively, but the apex-sinus distances of their pleural cavities were not significantly shorter than those of the other patients. The other patients fulfilled the conventional clinical and constitutional criteria of being "young, tall, slim, and apparently healthy."6

Previous Results

Only a few publications have dealt with SP in the acute phase of the disease. Anthonisen16 performed scintigraphic examination in patients with extensive SP. He noted that the vertical perfusion and ventilation gradient was reduced or absent in the affected lung and that the airway closure phenomenon was uniformly distributed all over the lung, which he considered responsible for the development of SP.

In two studies, lung scintigraphy was performed to study pulmonary edema immediately after re-expansion, and showed decreased perfusion in the affected lung.20-22 In two further studies, perfusion and ventilation scintigraphic examination disclosed defects in otherwise lung-healthy SP patients.23-24

Present Results

Perfusion distribution. In the present investigation a lower perfusion was observed in the apical region of both the affected and unaffected lungs of the SP patients than in the corresponding region in the control subjects. An increased vertical height of the lung will reduce the perfusion of non-dependent regions (ie, apical regions in the upright position) but the difference in this height between the SP patients and control subjects was less than 1 cm at maximum inspiration. Such a small difference can hardly account for the diminished apical perfusion in the SP patients. A general reduction of the pulmonary arterial pressure would also result in reduced perfusion of the apical lung regions. However, cardiac catheterization was not performed in this study, and there are no reports available in the literature after the acute phase of the condition.

Vascular abnormalities in the apical regions could, in theory, restrict blood flow, but as yet there is no evidence of such changes. Another possible cause of the reduced apical perfusion may be a redistribution of perfusion away from less well-ventilated regions. However, the fact that the blood flow was decreased to a similar extent in the affected and unaffected lungs, whereas the ventilation was lower in the apical region of the affected lung, is not consistent with a redistribution caused by hypoxic vasoconstriction.

Thus, there are several conceivable causes of decreased apical perfusion, but it is not possible from our data to identify the responsible factor. Interestingly, perfusion reduction was more pronounced than ventilatory impairment. Whether this indicates that the obstruction of blood flow in some way contributes to SP, rather than being a consequence of it, is at present only a matter of speculation.

Ventilation distribution. Forced expiratory measurements displayed no impairment, FEV1 and FEF25, being well within the normal limits. Thus, the overall measurements provided no indication of airway obstruction. These measurements were apparently not sensitive enough to detect regional abnormalities. However, the finding that the ventilation of the apical region of the affected lung was lower than that of the unaffected one may fit in with localized airway obstruction in the SP lung.

To our knowledge, this is the first observation that points to regional airway obstruction as a likely contributor to SP. The abnormality must, however, be very localized or very minor because the deviation in apical ventilation from the normal is much smaller than the normal vertical ventilation gradient.23 The cause of
such airway obstruction can only be speculated upon. It can hardly be attributed to "airway closure" in the sense of passive collapse of the airway, which rather occurs in dependent lung regions where pleural and extrabronchial pressure may become positive, relative to atmospheric pressure. Whether there are morphologic changes causing occlusion of the airway remains to be shown. However, the idea that airway obstruction may be a precipitating factor of SP is strengthened by the report of Popovich and Babcock, who described a case of intrabronchial blood clot causing recurrent SP.

Smoking

The possibility that airway obstruction may contribute to SP also gains support from the fact that smoking is much more common among SP patients than in the average Swedish population. Ninety percent of those who became ill abruptly were heavy smokers, and 5 percent were moderate smokers. Thirty-two percent of those in whom the symptoms had a more insidious onset were heavy smokers, and 23 percent were moderate smokers. In a study of the first SP, Bense et al found that smoking increased the incidence of SP 17.5 times among males and 8.5 times among females.

Fall in Atmospheric Pressure

Another observation of pertinence to the discussion on SP and airway obstruction is that pneumothorax has frequently been observed during decompression in naval and air space medicine. The rate of hospital admissions for SP has also been found to increase after a fall in atmospheric pressure of at least 10 MB/24 h. This suggests that a possible cause of SP might be a previously higher atmospheric pressure is maintained in a lung region which is completely sealed off from the atmosphere by airway obstruction. The falling atmospheric pressure would lead to an increasing tension and eventually cause a rupture of the alveolar wall.

Gas Resorption

If an intraalveolar pressure higher than the atmospheric pressure were to be maintained in obstructed lung regions, this would imply that no, or only minimal, gas resorption would take place. If, then, 1 to 2 percent of the oxygen trapped in an obstructed region of the lung were to diffuse into the surrounding tissue or into the circulating blood, the intraalveolar pressure would decrease by 10 to 20 MB. Concomitantly, a certain amount of carbon dioxide might diffuse into the enclosed area, but this amount would normally be smaller than the amount of oxygen that escaped. It is obvious that a decrease in the blood flow of the obstructed lung region will reduce the possibility of gas diffusion between the enclosed area and the surroundings.

Apical lung regions are less well-perfused than the basal ones, especially under resting conditions when the perfusion pressure is low. In conclusion, we suggest that the tendency for apical lung regions to suffer from SP is possibly due to increased stress (upright position) in combination with airway obstruction and reduced perfusion.

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