Pulmonary Function in Normal Subjects and Patients with Sarcoidosis after Bronchoalveolar Lavage*

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To determine if fiberoptic bronchoscopy (FOB) with bronchoalveolar lavage impairs pulmonary function in normal subjects or those with sarcoidosis, we measured flow-volume loops, thoracic gas volume, and single breath carbon monoxide diffusing capacity before, one half hour and 24 hours after lavage. We studied 12 normal subjects; six underwent a large volume lavage (approximately 500 ml saline instilled), and six underwent a small volume lavage (approximately 175 ml). Five subjects with sarcoidosis also had a small volume lavage. Six control subjects underwent FOB without lavage. The FOB alone produced no significant changes in pulmonary function one half hour after the procedure. Small volume lavage in normal subjects produced no change except for a 16.3±5.1 percent (mean±SEM) decline in peak expiratory flow rate (p<.05) one half hour postlavage which returned to normal by 24 hours. This contrasts with sarcoidosis subjects in whom forced expiratory volume in one second, peak expiratory flow rate, and vital capacity declined by 20±4.8 percent, 26.7±7.3 percent, and 15.2±4.1 percent, respectively, (all p<.05) one half hour postlavage. No change occurred in total lung capacity or diffusing capacity. Only with large volume lavage did decrements in lung function occur in normal patients that were comparable to those seen in the sarcoidosis subjects. Our findings suggest that bronchoalveolar lavage in normal patients can be associated with a significant and volume-related decline in pulmonary function and that in subjects with sarcoidosis, the deterioration is more pronounced.

Bronchoalveolar lavage through the fiberoptic bronchoscope is frequently employed to evaluate patients with lung disease. Several studies have shown that fiberoptic bronchoscopy alone is associated with small declines in forced expiratory volume in 1 second (FEV1), vital capacity (VC), and peak expiratory flow rate (PEFR) which can be prevented by the use of atropine prior to bronchoscopy. Overall, fiberoptic bronchoscopy has been extensively studied and found to be a relatively safe procedure. However, few studies have carefully evaluated the potential additional complications of bronchoalveolar lavage. Strumpf et al noted no major complications among 119 subjects with interstitial lung disease who had 281 lavage procedures. However, pulmonary function tests following lavage were not reported. Burns et al did measure the effect of lavage on lung function in a study of normal volunteers who were lavaged with 1,000 ml of saline solution. They used a fiberoptic bronchoscope with a cuff inflated in the right lower lobe. They found ventilation and/or perfusion defects on lung scan in the lavaged region, transient hypoxemia, and declines of 20 percent in total lung capacity (TLC) and 30 percent in VC. There was an increase in residual volume (RV) of 10 percent and no change in FEV1.

The study of Burns et al provides important data on the physiologic effects of very large, strictly regional lavage on normal subjects. However, the usual lavage volume used clinically is much smaller, and the bronchoscope is typically wedged in the right middle lobe bronchus rather than balloon occluded in the right lower lobe. In addition, the subjects most likely to have lavage are not normal, but have interstitial lung disease. Therefore, we evaluated a group of subjects with sarcoidosis and a mild restrictive defect. To investigate the importance of lavage volume, we studied the effects of different volumes of lavage on two groups of normal subjects.

METHODS

Subjects

Two groups (six in each group) of young, nonsmoking, normal subjects and five subjects with sarcoidosis underwent bronchoalveolar lavage. The five subjects with sarcoidosis had no history of asthma. Six subjects undergoing bronchoscopy without lavage served as control subjects. The diagnoses among the control subjects included hemoptysis in two, persistent cough in two, right middle lobe obstruction in one and a solitary pulmonary nodule in one. None of the control subjects had a history of asthma. The study was approved by the Human Studies Committee of the Massachusetts General Hospital, and informed consent was obtained. All subjects received intravenously administered atropine (0.4 to

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### Table 1—Baseline Data*

<table>
<thead>
<tr>
<th></th>
<th>Normal Subjects</th>
<th>Sarcoid (n=5)</th>
<th>Bronchoscopy Control Subjects (n=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Small (n=6)</td>
<td>Large (n=6)</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>27.7 ± 1.6</td>
<td>24.7 ± 1.2</td>
<td>39 ± 5.9</td>
</tr>
<tr>
<td>Sex</td>
<td>4F, 2M</td>
<td>6F</td>
<td>2F, 3M</td>
</tr>
<tr>
<td>Smoker</td>
<td>0</td>
<td>0</td>
<td>1/5</td>
</tr>
<tr>
<td>FEV&lt;sub&gt;1&lt;/sub&gt;</td>
<td>99.2 ± 4.9</td>
<td>104.8 ± 3.8</td>
<td>66.7 ± 8.4</td>
</tr>
<tr>
<td>VC</td>
<td>102.3 ± 2.9</td>
<td>106.2 ± 3.1</td>
<td>66.7 ± 6.6</td>
</tr>
<tr>
<td>PEFR</td>
<td>101 ± 12.2</td>
<td>105.2 ± 9.8</td>
<td>86.2 ± 11.4</td>
</tr>
<tr>
<td>TLC</td>
<td>105.3 ± 3.5</td>
<td>100 ± 3.8</td>
<td>66.4 ± 3.0</td>
</tr>
<tr>
<td>RV</td>
<td>113.7 ± 13.4</td>
<td>89.2 ± 14.6</td>
<td>70.2 ± 9.4</td>
</tr>
<tr>
<td>DCO&lt;sub&gt;55&lt;/sub&gt;</td>
<td>94.3 ± 5.7</td>
<td>97.2 ± 7.2</td>
<td>58.3 ± 5.8</td>
</tr>
<tr>
<td>V&lt;sub&gt;n&lt;/sub&gt;</td>
<td>4.1 ± .46</td>
<td>4.43 ± .59</td>
<td>1.25 ± .59</td>
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</table>

*All pulmonary function data are percent predicted except V<sub>n</sub> (flow rate in liters/second at constant volume 60 percent TLC).

†p<.05 vs control subjects.

0.6 mg) and comparable premedication including meperidine and/or diazepam and topical xylocaine. Oxygen was administered by nasal cannula. The bronchoscope was passed transorally and wedged in the right middle lobe. Aliquots of approximately 35 ml of room temperature saline solution were infused and recovered after each infusion with gentle suction (80 to 100 mm Hg). A total of approximately 175 ml or 500 ml was instilled for small volume and large volume lavage respectively.

### Pulmonary Function Tests

Pulmonary function tests were performed prelavage (prior to any premedication), one half hour postlavage, and 24 hours postlavage on normal subjects. On subjects with sarcoidosis and bronchoscopic control subjects (no lavage), these tests were performed prelavage and one half hour postlavage only. We used a 12-L rolling seal spirometer and an on-line computer. The loop with the highest sum of FEV<sub>1</sub> and VC was analyzed. The FEV<sub>1</sub>, VC, FEV<sub>1</sub>/VC ratio, and PEFR were recorded, and flow rate at constant volume 60 percent total lung capacity (V<sub>n</sub>) was derived and used as an indicator of small airways dysfunction. The functional residual capacity (FRC) was measured in a variable pressure body plethysmograph. The RV and TLC were derived with the expiratory reserve volume and VC obtained from the rolling seal spirometer. To evaluate pulmonary gas exchange, single breath carbon monoxide diffusion capacity (DCO<sub>55</sub>) was measured in duplicate and the mean value recorded using a transfer test module. Predicted values were hemoglobin corrected. The prediction equations of Crapo et al<sup>12</sup> were used for all spirometric tests except V<sub>n</sub>. For lung volume, the equations of Goldman et al<sup>4</sup> were used and for DCO<sub>55</sub>, we used the equations of Crapo et al.<sup>14</sup> All pulmonary function tests are expressed as percent predicted.

### Data Analysis

Following analysis of variance (ANOVA), paired and unpaired student’s t-tests were applied where appropriate. All values are expressed as the mean ± standard error of the mean (SEM) and significance accepted when p was <.05.

### Table 2—Saline Instilled and Recovered

<table>
<thead>
<tr>
<th></th>
<th>Normal Subjects</th>
<th></th>
<th>Sarcoid</th>
<th>Bronchoscopy Control Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Large Lavage</td>
<td>Small Lavage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saline instilled, ml</td>
<td>540 ± 18†</td>
<td>161 ± 9</td>
<td>178 ± 9</td>
<td></td>
</tr>
<tr>
<td>Saline recovered, ml</td>
<td>339 ± 29†</td>
<td>84 ± 7</td>
<td>80 ± 13</td>
<td></td>
</tr>
<tr>
<td>Percent recovered</td>
<td>68 ± 4</td>
<td>53 ± 4.6</td>
<td>44 ± 7.2</td>
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</table>

†p<.05 from small lavage or sarcoid lavage.

### Results

There were no significant differences between the two groups of normal subjects (Table 1). The sarcoid subjects were approximately ten years older than the lavage control subjects and had a moderate restrictive defect. The bronchoscopy control subjects were significantly older than the normal patients and were mostly smokers. Their baseline pulmonary function was on the low side of normal and included slight but significant reductions in FEV<sub>1</sub> and VC compared to the normal subjects.

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normal subjects and subjects with sarcoidosis (Fig 4). Figure 5 illustrates the greater decrement in VC with a larger amount of saline solution instilled for one subject who had both a small and large volume lavage. Figure 6 shows that the change in VC is comparable to the change in RV for normal subjects who had a large volume lavage and subjects with sarcoidosis who had a small volume lavage. The DCOs was unaffected by lavage in any group.

All normal subjects and control subjects tolerated the procedure well without complications. However, among the subjects with sarcoidosis, two were markedly dyspneic after the lavage. One required supportive treatment in the emergency room while the other subject was observed in the bronchoscopy suite for several hours. Both returned home the same day.

**DISCUSSION**

Our data demonstrate that bronchoalveolar lavage despite atropine pretreatment is associated with a significant deterioration in pulmonary function (Fig 1 and 2). Lavage produced declines in lung function in the normal subjects that increased with the volume of lavage (Fig 2 and 5). In the sarcoidosis subjects, the table 2 illustrates the amount of saline solution instilled, recovered, and the percentage recovered for the three groups. There were no significant differences among groups in the percentage of lavage recovered.

Bronchoscopy alone did not alter pulmonary function (control subjects in Fig 1 and 2). Small volume lavage did cause a transient fall in FEV1, VC, and PEFR (Fig 1) which returned to normal by 24 hours (Fig 2). Only the change in PEFR of approximately 16 percent was significant compared to control subjects. With large volume lavage, there were significant declines compared to control subjects of approximately 20 percent in FEV1 (Fig 1 and 2), VC, PEFR (Fig 2), and V̇e (4.4 ± 0.6 L/s to 3.5 ± 0.7). In the sarcoidosis patients who underwent a small volume lavage, there was a dramatic deterioration in flow rates and VC compared to control subjects equivalent to those seen with large volume lavage in the normal subjects (Fig 1 and 3). The declines in the large volume lavage group as well as in the subjects with sarcoidosis were not significantly greater than the small changes noted in the small volume lavage group. The decline in VC was significantly larger than the unrecovered lavage for the

**FIGURE 2.** Mean percentage of decrement in FEV1, VC, and PEFR, one half hour post lavage, for normal subjects who underwent either large (open bars) or small (hatched bars) volume lavage compared to control subjects (solid bars). Significant decrements in FEV1, VC, and PEFR occurred in the large lavage group while only PEFR significantly declined in the small lavage group (* = p < .05 vs control subjects).

**FIGURE 3.** Mean percentage of decrement in FEV1, VC, and PEFR, one half hour post lavage, for subjects with sarcoidosis (hatched bars) is comparable to normal subjects who underwent large volume lavage (open bars).
changes were more pronounced than in the normal subjects and occurred after only small volumes of lavage were instilled (178 ± 9 ml, Table 2).

The fall in VC was not due just to volume replacement with saline solution, since the decline in VC was much greater than the volume of unrecovered lavage (Fig 4). The decline in VC was probably due to airway obstruction since RV increased proportionately (Fig 6) and TLC was unchanged. The mechanism of the increased airway obstruction is unclear. The obstruction may have involved large airways as manifested by the fall in FEV₁ but also small airways as shown by the fall in V₉₀ and VC. These changes suggest that the increased airway obstruction was not confined solely to the right middle lobe and cannot be explained on the basis of local trauma to the area. Mucosal edema may contribute to the obstruction, since some lavage fluid may well extravasate around the wedged bronchoscope into the right lower lobe or, less likely, leak into the upper lobe through collateral channels. The volume of lavage that could leak out through collateral channels is
probably small since it has been reported that the right middle lobe collateral ventilation is characterized by high resistance and a long time constant. Vagally mediated bronchospasm is another possibility. While these subjects were pretreated with atropine in a dose sufficient to prevent the usual deterioration in pulmonary function seen with bronchoscopy alone, this dose of atropine may have been insufficient to meet the more severe challenge to the airways of lavage. Lavage may have altered surfactant function and surfactant may play a role in maintaining small airway patency. Finally, among the group of sarcoïd subjects, some of the decline in flow rates may be accounted for by the fact that some patients with sarcoïdosis exhibit hyperactive airways in response to methacholine challenge.

Since we did not perform FOB alone on our sarcoïdosis subjects, we cannot be absolutely sure that the lavage alone was responsible for the decline in lung function. Our control group was composed of mostly smokers with mild airways disease. There was no change in their pulmonary function, and since we have no evidence to suggest that the sarcoïd subjects had any more airway obstruction, we suspect bronchoscopic lavage in sarcoïdosis patients premedicated with atropine would have produced little or no change in lung function.

Burns et al noted a decline in lung volume as well as changes consistent with increased small airway obstruction two to four hours after they lavaged subjects with 1,000 ml of saline solution using a fiberoptic bronchoscope with an inflatable cuff wedged in the right lower lobe. The increase in obstruction in small airways was similar to our findings. In addition, they noted a decline in total lung capacity. This may reflect bronchoscopic technique (inflatable cuff) in the right lower lobe vs wedging the tip in the right middle lobe), the timing of the post-bronchoscopy pulmonary function tests (two to four hours vs 30 minutes), or volume of lavage used. Rankin et al used volumes of saline solution (300 ml) that were intermediate between our small and large volumes and similar bronchoscopic technique in a recent investigation of lung function after bronchoalveolar lavage in normal subjects and subjects with asthma. When we analyzed their data by paired rather than unpaired Student's t-tests, the mean percentage of declines in FEV₁ and VC of approximately 12 percent for normal subjects and 8.3 and 11.3 percent for asthmatic patients were significant at the p<.05 level. These data are comparable to our own reported here.

When bronchoalveolar lavage is performed in normal subjects with the bronchoscope wedged in the right middle lobe and 200 to 500 ml of saline solution instilled, there is a decline in pulmonary function related to the amount of saline instilled. Broncho-

alveolar lavage in normal subjects is well tolerated even though transient declines of 20 percent or more in lung function were noted. However, in subjects with interstitial lung disease and a mild restrictive defect, one needs to proceed cautiously when lavage is performed even with less than 200 ml since a 20 percent reduction in pulmonary function in these subjects can, in certain cases, be poorly tolerated.

References
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