Effects of Surface-Active Aerosols and Pulmonary Congestion on Lung Compliance and Resistance

By RICHARD A. OBENOUR, M.D., HERBERT A. SALTZMAN, M.D., HERBERT O. SIEKER, M.D., AND JAMES L. GREEN, B.S.

LUNG blood volume and surface tension forces are known factors contributing to the mechanical cost of breathing. In experimental and clinical states, pulmonary compliance decreases with lung congestion and increases with a reduction in pulmonary blood volume.\(^1\)\(^2\) Surface tension forces have been known to influence respiratory mechanics since the work of von Neergaard,\(^3\) who demonstrated that more pressure was required to inflate air-filled than fluid-filled lungs. Subsequent observations have confirmed the mechanical importance of surface tension produced by an alveolar air-liquid interface, which includes a lipoprotein alveolar lining material that stabilizes surface forces.\(^4\)\(^6\)

This study was designed to evaluate the relative contribution of surface forces and pulmonary congestion to the mechanics of breathing in man. Pulmonary compliance and resistance were determined before and after the nebulization of surface active agents in normal and abnormal hemodynamic states. Ethyl alcohol was used as an aerosol because of its low surface tension and beneficial effect reported in pulmonary edema.\(^7\) A superinone respiratory detergent containing silicone (Defomaire) was chosen for comparison because of the unique surface effects of silicones. This report indicates that surface active aerosols alter respiratory mechanics significantly in normal man, but will not modify lung compliance in the presence of pulmonary congestion.\(^*\)

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Methods

Pulmonary compliance and resistance were measured under the following conditions: 69 studies in 12 normal trained volunteers to determine control values, 14 studies to evaluate the effect of alcohol aerosols, and seven experiments to assess the action of a siliconized respiratory detergent. Nebulization of distilled water served as a control for these studies of surface-acting aerosols. The response to nebulized alcohol was determined after inducing pulmonary vascular congestion by application of counterpressure with a capstan-type altitude suit and rapid infusion of saline in five additional studies. Finally, observations were made with alcohol aerosols in 10 patients with congestive heart failure and pulmonary edema before and after antieongestive therapy. All observations were made with the subject in the seated position.

Surface-active agents were administered from an air-driven nebulizer, using 3 ml. of the material during a 6-minute period. Although nebulizations do not penetrate pulmonary tissues in a complete or uniform manner, comparable aerosols have been demonstrated to enter the alveolar air spaces and pulmonary circulation in significant quantities.\(^8\) The subjects were instructed to take occasional deep inspirations during the inhalation period and two maximum inspirations at the termination of nebulization just prior to measurement of compliance.

Lung compliance was determined by measuring the volume and intrathoracic pressure changes for each respiration at a time of zero airflow velocity. Inspiratory volumes were kept in the tidal range during measurement, and expiration was terminated at the resting functional residual capacity. A mean value for between 8 and 15 volume-pressure complexes was obtained for each compliance determination. All measurements were made immediately after completing two maximum

inspirations, with the subject seated and breathing quietly. This procedure was followed because earlier studies indicated that the prior state of lung expansion influenced the reproducibility as well as the magnitude of compliance measurement. Respiratory volumes were determined from the pressure change produced by breathing into a closed tank system as recorded by an air differential strain gage. The subject breathed through a low-resistance valve with a screen pneumotachograph from which airflow velocity was determined. Intrathoracic pressure change was recorded as the pressure difference between the mouth and a polyethylene esophageal balloon catheter. The esophageal balloon was passed 35 to 45 cm. from the anterior nares using a constant level for each subject. All pressures and flows were recorded electronically in scalar or vectorial forms.

Pulmonary resistance was calculated by the method of von Neergaard and Wirz,3 which gives a value representing the sum of airway and lung tissue resistance. Pulmonary resistance = Pr/\( \Delta \nu \), where Pr is the resistive component of the pressure difference between the pleural space and mouth during inspiration and \( \nu \) is the simultaneous airflow. Pr was measured at a \( \nu \) of 0.57 L per second, by subtracting the pressure necessary to distend the lung statically (\( \Delta \) Pe) from the pressure difference between the mouth and esophagus. \( \Delta \) Pe was calculated from the change in lung volume at 0.57 L per second airflow divided by pulmonary compliance as previously determined. Individual resistance values represent the mean of measurements from the same 8 to 15 respirations used to calculate compliance.

**Results**

Control studies on normal subjects at rest and immediately following two respirations are shown in table 1. Following deep inspiration mean compliance increased significantly from 0.201 to 0.229 L/cm. H\(_2\)O (\( p < 0.01 \)) and airway and tissue resistance decreased from 22.3 to 19.1 cm. H\(_2\)O/L/sec. (\( p < 0.01 \)). Measurements made after deep inspiration did not vary significantly when repeated during a 30- to 60-minute control interval. Analysis of the 10 to 15 consecutive respirations used for each measurement revealed that compliance decreased insignificantly from 0.230 in the initial two breaths after deep breathing to 0.220 in the terminal complexes. Because of these findings our studies included two deep inspirations as an integral part of preparation for measurement of pulmonary mechanics.

Figure 1 presents graphically the effect of nebulized 30 per cent alcohol upon pulmonary compliance and resistance in 14 studies. There is a significant increase in mean compliance from 0.212 to 0.275 L/cm. H\(_2\)O (\( p < 0.01 \)) and a decrease in mean resistance from 20.9 to 17.5 cm. H\(_2\)O/L/sec. (\( p < 0.01 \)).

**Table 1**

| Pulmonary Compliance and Resistance in Normal Subjects after Deep Breathing |
|-------------------------------|-----------------|-----------------|
|                               | Number of studies | During quiet respiration | After 2 deep inspirations |
| Mean pulmonary compliance     | 69               | 0.201 ± 0.005*       | 0.229 ± 0.006            |
| Mean pulmonary airway and tissue resistance | 34               | 22.3 ± 1.0         | 19.1 ± 1.0               |

*Standard error.*

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Figure 2
Pulmonary compliance decreases and resistance usually increases after a siliconized superinone nebulization.

2 indicates the effect of siliconized superinone aerosols upon pulmonary compliance and resistance. Nebulization resulted in a significant decrease of mean compliance from 0.233 to 0.207 L/cm. H₂O (p < 0.05) and an increase of mean resistance from 19.0 to 21.0 cm. H₂O/L/sec. (p < 0.05). Nebulization of distilled water also reduced lung compliance, from a mean of 0.233 to 0.216 L/cm. H₂O in five studies.

In order to investigate the relative contribution of surface-tension forces and pulmonary blood volume to respiratory mechanics, pulmonary congestion was produced in normal subjects by the application of external counterpressure with a capstan-type altitude suit and the rapid intravenous infusion of 1,000 mL of saline, with a resultant mean rise in peripheral venous pressure to 227 mm. H₂O. Under these conditions mean pulmonary compliance was 0.124 L/cm. H₂O and decreased after alcohol nebulization to 0.107 L/cm. H₂O pressure in five studies (table 2). In 10 patients with congestive heart failure and pulmonary edema, pulmonary compliance averaged 0.075 L/cm. H₂O before and 0.067 after two deep inspirations. Nebulization with 30 per cent alcohol decreased mean compliance insignificantly to 0.063 L/cm. H₂O (table 2). Studies were repeated in eight subjects after successful anticongestive therapy. At this time, pulmonary compliance averaged 0.088 L/cm. H₂O pressure at rest, increased to 0.095 after two deep inspirations and increased further to 0.108 after 30 per cent alcohol nebulization and two deep inspirations.

Discussion
The tendency for compliance to increase and resistance to decrease following deep inspiration is of considerable importance. Paired studies of respiratory mechanics require control of ventilatory volume if reproducible measurements are desired even for short periods of time. These studies confirm previous observations in animals and man concerning the effects of deep inspiration upon lung mechanics.10-13 The normal values reported in this study of 0.201 during quiet respiration and 0.229 after two deep inspirations

Table 2
Pulmonary Congestion, Alcohol Nebulization, and Pulmonary Compliance

<table>
<thead>
<tr>
<th></th>
<th>Number of studies</th>
<th>Mean pulmonary compliance L/cm. H₂O Pressure</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td>During quiet respiration</td>
</tr>
<tr>
<td>Normal subjects with pulmonary congestion</td>
<td>5</td>
<td>0.156 ± 0.017*</td>
</tr>
<tr>
<td>Congestive heart failure with pulmonary edema</td>
<td>10</td>
<td>0.075 ± 0.012</td>
</tr>
<tr>
<td>Congestive heart failure after anti-congestive therapy</td>
<td>8</td>
<td>0.088 ± 0.005</td>
</tr>
</tbody>
</table>

*Standard error.
tions fall within the normal range for dynamic compliance as previously reported by a variety of techniques.\textsuperscript{14-16} Time studies of the deep-breathing effect suggest that compliance will fall if the depth of respiration is kept in the normal tidal range. However, significant change did not occur in the 12 to 15 consecutive respiratory complexes following deep breathing although values were slightly lower for the final as compared to the initial complexes.

In the present studies, we have attempted to demonstrate surface tension phenomena by observing the effect of surface active aerosols upon pulmonary compliance and resistance. In order to relate surface tension to the mechanics of breathing, the Laplace equation has been used after making the assumption that the alveolus has the physical properties of a bubble.\textsuperscript{17-19} Simply stated, this relationship means that the internal pressure of a bubble is directly proportional to twice its surface tension divided by its radius. If this relationship is true for the lung, an agent that lowers surface tension in the alveoli should cause an increase in compliance, since less pressure would be required for maintenance of any given volume. The converse would also be true. Our compliance data for alcohol is consistent with such a theory and is similar to studies reported in animals.\textsuperscript{20} However, the simultaneous resistance change suggests that the nebulized aerosols may increase alveolar recruitment through a direct endobronchial or endobronchial mucosal secretion effect and, thereby, also increase the lung volume change for a given decrease in intrapleural pressure. If this were the case, the compliance change would be secondary to improved endobronchial function and alveolar delivery of air.

The experimental production of pulmonary vascular congestion in normal subjects reduced lung compliance and inhibited the anticipated response to alcohol nebulization. Similar results were noted in patients with congestive heart failure and pulmonary edema. Moreover, some responsiveness to the alcohol aerosol returned in the same patients after effective anticongestive therapy. These observations do not indicate a large contribution by surface forces to altered lung mechanics in congestive heart failure. Furthermore, the reported improvement in pulmonary edema patients with alcohol nebulization cannot be readily explained on the basis of surface-tension effects. These observations indicate that with a normal lung and pulmonary circulation aerosols can significantly modify pulmonary mechanics by altering alveolar surface forces or endobronchial function. Specifically, alcohol increased compliance significantly, a response not observed with other aerosols tested. However, when pulmonary hemodynamics were altered so that the lungs were engorged or edematous, alcohol as a surface-active nebulization did not modify compliance.

Summary

Pulmonary compliance and resistance were studied in normal subjects after quiet respiration, deep breathing, and the nebulization of surface-active agents. Deep breathing resulted in a significant rise in pulmonary compliance and decrease in airway and tissue resistance. Alcohol nebulizations increased compliance and decreased resistance in normal subjects. Siliconized superinone and water nebulizations had an opposite effect.

Simulated pulmonary congestion in normal subjects and congestive heart failure with pulmonary edema inhibited the anticipated response to alcohol aerosols. Responsiveness returned in part to patients with congestive heart failure after restoration of cardiac compensation. These observations suggest that pulmonary vascular congestion is a major cause of altered respiratory mechanics in heart failure. In the presence of pulmonary congestion, surface-active aerosols do not demonstrably affect compliance.

References

Application of Physical Diagnostic Methods

The real study of heart disease began only after percussion had been applied in diagnosis and Laennec had shown the scope of auscultation. When that was done a period of active application of physical diagnostic methods began and the steady round of discoveries in the diagnosis and pathology of valvular disease may have diverted attention from the less objective signs of angina pectoris. At all events, interest in the coronary arteries waned and interpretations of angina as a nervous disease began to multiply, although the real study of diseases of the nervous system had hardly passed the stage it was in while Laennec was alive.—GEORGE Dock, M.D. “Historical Notes on Coronary Occlusion: From Heberden to Osler. Frank Billings Lecture.” J.A.M.A. 113: 563, August 12, 1939.
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