Abnormalities in Lung Elastic Properties and Surfactant Function in Adult Respiratory Distress Syndrome*

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We have examined the lungs from five patients who died with the adult respiratory distress syndrome (ARDS). Pressure volume curves were obtained and bronchoalveolar lavage fluid was studied on a surface balance. The pressure volume curves revealed reduced compliance compared to normal or near normal lungs. A significant loss of volume was also found. The data obtained from the surface balance studies show a normal range of minimum surface tension when compared to "normals," but the ARDS lung lavage fluid revealed an increase in surface film compressibility relative to "normal." The increased compressibility may be an important factor contributing to the stiff lungs of patients with the adult respiratory distress syndrome.

We have reported previously on abnormalities of human surfactant in a lung from a patient with the adult respiratory distress syndrome (ARDS) following trauma and shock. The lung with ARDS was compared to three normal lungs obtained from transplant donors. An abnormal static pressure-volume curve indicated reduced compliance and abnormally high surfactant film compressibility was found, but the minimum surface tension of material obtained by bronchoalveolar lavage was within the normal range.

Since that report was published, we have had the opportunity to study five additional specimens from patients with ARDS following a variety of different catastrophic events resulting in ARDS. The spectrum of abnormalities of surfactant function from these lungs compared to normal or nearly normal lungs without ARDS is the subject of this report.

MATERIALS AND METHODS

All patients were previously healthy and fulfilled the definition of the adult respiratory distress syndrome. The first specimen was obtained from a transplantation donor with brain death following massive trauma. Details of this case and the surfactant abnormalities found have been reported elsewhere. Five additional specimens were obtained from autopsy specimens. The salient clinical details from these five cases as well as the first reported case are summarized in Table 1.

All lungs were studied within 48 hours after death except for patient 6, whose lungs were studied 80 hours after death. The right lung or both lungs were studied in a manner described in the earlier report. Each lung was removed carefully and weighed immediately (Table 2).

A pressure-volume curve was obtained from each lung.

<table>
<thead>
<tr>
<th>Case, Age, Sex</th>
<th>Cause</th>
<th>Acute Lung Injury</th>
<th>PEEP</th>
<th>CTP</th>
<th>Interval onset ARDS to Autopsy (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1, 24, M</td>
<td>Hemorrhagic shock</td>
<td>0.6 to 1.0</td>
<td>10</td>
<td>20</td>
<td>4</td>
</tr>
<tr>
<td>2, 30, F</td>
<td>Septic shock</td>
<td>1.0</td>
<td>20</td>
<td>24</td>
<td>5</td>
</tr>
<tr>
<td>3, 28, F</td>
<td>Drug overdose shock aspiration</td>
<td>0.4 to 1.0</td>
<td>12</td>
<td>20</td>
<td>2</td>
</tr>
<tr>
<td>4, 59, M</td>
<td>Hemorrhagic shock aspiration</td>
<td>1.0</td>
<td>*</td>
<td>28</td>
<td>7</td>
</tr>
<tr>
<td>5, 59, M</td>
<td>Hemorrhagic shock</td>
<td>0.7 to 1.0</td>
<td>10</td>
<td>23</td>
<td>11</td>
</tr>
<tr>
<td>6, 29, F</td>
<td>Hemorrhagic shock</td>
<td>0.4 to 1.0</td>
<td>12</td>
<td>35</td>
<td>21</td>
</tr>
</tbody>
</table>

*Use of PEEP unsuccessful due to refractory shock.

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Table 2—Morphologic Parameters of ARDS and Control Lungs at Autopsy

<table>
<thead>
<tr>
<th>Case, Age, Sex</th>
<th>Lung Weight (gm)</th>
<th>Pneumonia*</th>
<th>Edema**</th>
<th>Hemorrhage*</th>
<th>Hy. Memb.**</th>
<th>Emphy†</th>
</tr>
</thead>
<tbody>
<tr>
<td>1, 24, M</td>
<td>780</td>
<td>5%</td>
<td>+</td>
<td>10%</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>2, 30, F</td>
<td>860</td>
<td>0</td>
<td>0</td>
<td>40%</td>
<td>+</td>
<td>0</td>
</tr>
<tr>
<td>3, 28, F</td>
<td>980</td>
<td>40%</td>
<td>0</td>
<td>0</td>
<td>++</td>
<td>0</td>
</tr>
<tr>
<td>4, 59, M</td>
<td>1130</td>
<td>5%</td>
<td>++</td>
<td>0</td>
<td>+</td>
<td>15%</td>
</tr>
<tr>
<td>5, 59, M</td>
<td>1151</td>
<td>0</td>
<td>0</td>
<td>20%</td>
<td>++</td>
<td>10%</td>
</tr>
<tr>
<td>6, 29, F</td>
<td>1310</td>
<td>20%</td>
<td>++</td>
<td>30%</td>
<td>++</td>
<td>0</td>
</tr>
<tr>
<td>7, 19, F</td>
<td>240</td>
<td>0</td>
<td>0</td>
<td>&lt;5%</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>8, 19, F</td>
<td>225</td>
<td>5%</td>
<td>0</td>
<td>5%</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>9, 45, F</td>
<td>459</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>&lt;5%</td>
<td>CLE</td>
</tr>
<tr>
<td>10, 24, M</td>
<td>438</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>11, 62, M</td>
<td>422</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>5%</td>
</tr>
<tr>
<td>12, 58, M</td>
<td>440</td>
<td>&lt;5%</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>&lt;5%</td>
</tr>
</tbody>
</table>

* = Approximate percentage of lung volume involved, based on gross and stratified micro sections.
** = Subjective assessment based on microscopic sections.
+ = Slight
++ = Moderate
+++ = Severe
CLE = Centrilobular emphysema

After standardizing the volume history by inflations with air to a pressure of 20 to 22 cm of H2O. Pressure-volume curves were constructed by inflating the lung with air to +20 cm H2O and removing air in 2 cm H2O decrements. The pressure-volume curves of the three ARDS lungs were compared to curves obtained in the same manner from normal lungs obtained from transplant donors. Three men aged 24, 62 and 58 years served as normal controls for men, and three women, two age 19 and one age 45, were female controls for the study reported here.

As with the first ARDS specimen,1 all the lungs were subjected to bronchoalveolar lavage with normal saline solution and this material was rendered acellular with a 850 xg spin. The acellular bronchial-alveolar lavage (ABAL) material was then examined on a Kimray-Greenfield surfactometer for surface tension (γ)-area (A) behavior at 23°C. The ABAL was placed directly in the trough and allowed to age 0.5 hour before compression to 7.0 cm² and re-expansion to 57.5 cm² at a cycling rate of 1.5 minute per cycle. Surface compressibility was calculated from (1/A) (dA/dγ) at γ = 18 mN/m.

After lavage, the lungs were fixed in 1.8 percent isomolar neutral buffered glutaraldehyde. All lungs were studied grossly and microscopically by a pathologist (RES) with no prior knowledge of the clinical history or parameters of surfactant function using our standard postmortem techniques.3

Results

Figure 1 presents the mean static deflation pressure volume curves as a percentage of the measured total lung capacity (TLC) for all ARDS lungs compared to six control lungs studied in identical fashion. Reduced compliance is present from 10 to 2 cm H2O pressure (P < 0.05). Figure 2 shows the mean static deflation pressure volume curves presented as a percentage of predicted TLC. The total lung volumes were compared with predicted values by converting the total lung volume of a single lung assum-
ing the left lung represented 45 percent and the right lung 55 percent of the total volume of both lungs. The predicted values of Goldman and Becklake were used for women, and for men, the values of Boren, Kory and Syner were used. There was a large loss of volume (P < 0.05) at all pressures examined.

Table 2 presents the gross and microscopic pathologic changes noted including extent of pneumonia, alveolar edema, hemorrhage, hyaline membrane formation and destructive emphysema. A marked difference in gross weight of the ARDS lung versus the controls is noted in Table 2. Hyaline membranes were also present in all six ARDS cases compared to no hyaline membranes in the controls.

Table 3 presents data on minimal surface tension and surface compressibility in all six ARDS specimens. A marked increase in surface film compressibility relative to “normals” is the most notable finding. As in our first report, the stiffening of the ARDS lungs appears to result from a loss of film elasticity (reciprocal of compressibility).

**Comment**

Data from five additional lung specimens obtained fresh after varying intervals following the initial lung injury and the onset of ARDS appear to confirm our earlier report. Again we found abnormal PV curves as in the original study. The magnitude of the increase in surface compressibility was of similar degree in all six ARDS specimens. The statistical significance of this increased compressibility was borderline.

Surface compressibility (C), C = (1/A)dA/dy, or its reciprocal which is surface elastance is an expression of the resistance of the surface film to compression at any given area. In this study, the films from ARDS lungs had a high value of compressibility which demonstrates that these films were unable to adjust rapidly to stress, in contrast to the normal films with low values of C, ie, rapid response to stress. These findings are similar to the studies by Hallman and Gluck who compared fetal and postnatal surfactants from rabbit lung. Their study revealed that although minimum surface tensions were similar, the compressibilities were different; fetal surfactant had high surface compressibility compared to postnatal compressibility.

The relationship between surface tension and surface elastance has been presented by Clements and co-workers who pointed out the importance of both for the maintenance of alveolar stability. Stability is confirmed on alveoli by having low surface tension and high surface elastance (or low compressibility).

Lungs of infants who have died of respiratory disease syndrome (IRDS) have a high minimum surface tension and low surface elastance. Collapse of alveoli is the primary pathologic feature of the disease.

Our findings in ARDS lungs of a normal surface tension, when compared to controls, but increased surface compressibility further underscore the importance of surface compressibility and its role in

![Figure 2. The mean (± SE) static deflation pressure volume curve of all ARDS lungs (solid line), of six control lungs (dashed line) are shown where volume is expressed as a percentage of predicted total lung capacity (TLC) and static lung recoil is expressed in cm H2O. The predicted values of Goldman and Becklake were used for women, for men the values of Boren, Kory and Syner were used.](image)

**Table 3—Surface Properties from Six Normal Lungs and Six ARDS Lungs**

<table>
<thead>
<tr>
<th></th>
<th>Minimum Surface Tension mN/m</th>
<th>Compressibility cm/dyne</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARDS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>22.1</td>
<td>0.45</td>
</tr>
<tr>
<td>SD</td>
<td>2.2</td>
<td>0.33</td>
</tr>
<tr>
<td>SEM</td>
<td>0.9</td>
<td>0.14</td>
</tr>
<tr>
<td>n = 6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean</td>
<td>23.3</td>
<td>0.14</td>
</tr>
<tr>
<td>SD</td>
<td>1.5</td>
<td>0.07</td>
</tr>
<tr>
<td>SEM</td>
<td>0.6</td>
<td>0.03</td>
</tr>
<tr>
<td>n = 6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Statistical comparison Not significant P = 0.051 by t-test for independent samples

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stabilizing the alveoli. This factor alone, we feel, is
the primary factor contributing to the stiffness of the
lungs of ARDS patients.

Clearly these surfactant abnormalities are the re-
sult and not the primary cause of ARDS which
begins as a catastrophic pulmonary insult. Once
present, alveolar instability due to altered surfactant
function may result in hydrostatic tissue forces
which explain the reduced compliance observed in
bedside measurements and the abnormalities in
pressure volume curves demonstrated in these six
cases. It remains a reasonable hypothesis that sur-
factant abnormalities in ARDS play a secondary role
in the pathogenesis of the clinical syndrome through
the mechanism of encouragement of further intra-
alveolar fluid sequestration, further alteration in
lung mechanics, and reduced functional residual
capacity resulting in a vicious circle leading to shunt-
ing and refractory hypoxia.

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International Symposium on Pulmonary Circulation

The International Symposium, Pulmonary Circulation III, will be held in Prague,
Czechoslovakia, July 2-4. It is sponsored by the Societas Europaea Physiologicae Clini-
cae Respiratoriae and the European Society of Cardiology, and organized and hosted
by the Czechoslovak Society for Respiratory Physiology and Pathology, and Czecho-
slovak Society for Cardiology. For information, please write the Czechoslovak Medical
Society, International Symposium Pulmonary Circulation III, Sokolska 31, 120 26
Prague 2, Czechoslovakia.

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Canadian Lung Association

The 79th Annual Meeting of the Canadian Lung Association and the Canadian Thoracic
Society, Canadian Nurses' Respiratory Society, and the Physiotherapy Section, will
be held June 25-27 at the Sheraton Centre, Toronto, Ontario. For information, contact
Mr. H. E. Drouin, Executive Secretary, 75 Albert Street, Ottawa, Ontario K1P 5E7,
Canada.