**Dr. Brigham:** We have not done that measurement. However, we did not observe infection in any of the animals. Blood cultures the next day were all sterile and none of the animals had persistent fevers.

**Dr. Lauweryns:** Assuming lymphatic endothelium was not affected by the Pseudomonas as shown, were there any intracellular gaps among the cellular junctions? In particular, was there evidence of damage to the anchoring filaments of the cells?

**Dr. Brigham:** I have no information in this regard.

**Dr. Greenfield:** This work corresponds well to work we have reported in the isolated lung with live organisms which also showed early increase in the size of perivascular lymphatic spaces. Can you relate this to the problem when clearance is ineffective and there is protein stasis which probably contributes to the difficulty with recruiting that edema fluid out of the lung with agents such as diuretics or osmotics?

**Dr. Brigham:** The only evidence which I can address to that question is that in the two animals that died, the lymph flow was among the highest we had seen. So the fact that pathologic changes occurred does not mean that lymph function was diminished but that the capacity was overwhelmed.

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**The Hemodynamics of Experimental Fat Embolism and Associated Therapy**

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Pulmonary fat embolism continues to be a significant cause of morbidity and mortality in the multiple trauma victim. Respiratory failure plays a leading role in the clinical course of this entity. Numerous theories have attempted to explain the pathogenesis of fat emboli. It is now generally accepted that following severe trauma small fat particles enter the blood stream and are transported to the lung. Most investigators currently believe that these particles initially block many of the small pulmonary vessels and are then hydrolyzed into chemically active fatty acids by the action of pulmonary lipase. These free fatty acids (FFA) may cause localized pulmonary inflammatory damage, leading to respiratory distress. Numerous studies have shown elevation of FFA in clinically evident fat embolism. It was shown experimentally that catecholamines mobilize free fatty acids from the fat stores by increasing activated lipase. There are two possible sources of circulating FFA: (1) those due to hydrolysis of neutral fat in the lung; and (2) those mobilized from systemic sources. Laboratory animals reveal an increase in pulmonary lipase following neutral fat emboli. Following severe fat embolism, blood lipase levels are elevated in a significant number of patients. Of the many entities implicated in the post-traumatic respiratory distress syndrome, fat emboli are felt to play a significant role. It is assumed that the pulmonary capillary bed receives most of the damage. Experimental hemodynamic and pathologic studies demonstrating the changes in the region of the pulmonary capillary bed following experimental fat embolism have not been previously performed. Our work was designed to study the hemodynamic and pathologic changes in this region following experimental fat embolism. We have also assessed two different modes of treatment of this entity.

**METHODS**

Four groups of artificially ventilated anesthetized mongrel dogs were utilized. The control group consisted of 11 dogs with catheters which measured pulmonary artery pressure (PA), pulmonary artery wedge pressure (PAW), pulmonary venous wedge pressure (PVW), small pulmonary vein pressure (SPV) and left atrial pressure (LA). These catheters completely surrounded the pulmonary capillary bed (Fig 1). Oleic acid (0.07 ml/kg) was injected through a femoral vein. Cardiac output, systemic pressure, pulmonary compliance, arterial blood gas values, hematocrit levels and hemoglobin values were measured over a three-hour period. The second group of six dogs received methylprednisolone sodium succinate (30 mg/kg) intravenously after the oleic acid injection. The third group of six dogs had 15 cm of positive end-expiratory pressure (PEEP) superimposed on the positive end-inspiratory pressure (PEEP)...

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**Figure 1. Placement of catheters to completely surround pulmonary capillary bed.**

**Figure 2. Demonstration of preservation of compliance by PEEP as compared to other two groups.**

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A significant finding in the experiment was the development of a pressure gradient of 3.6 mm between the PAW and LA (p<.05). No significant gradient in this area developed in the steroid or PEEP groups (Fig 4).

All groups demonstrated a mean fall in cardiac output of approximately 200 ml/min, but this did not prove statistically significant.

The hematocrit level rose nine points in the control group (p<.001), six points in the steroid group (p = NS) and seven points in the PEEP group (p<.02).

Cinemicrophotography revealed increasing interstitial and intra-alveolar edema following the oleic acid injection. There was marked slowing of pulmonary capillary blood flow and evidence of erythrocytary clumping.

**DISCUSSION**

There is little doubt that in experimental animals fatty acid emboli cause marked changes in the region of the pulmonary capillary bed. These changes undoubtedly account for the severe hypoxemia shown. Intrapulmonary shunting, perfusion and, presumably, diffusion defects at the alveolar level account for this change. Treatment with positive end expiratory pressure presumably brings about significant improvements by decreasing the amount of physiologic shunting and increasing diffusion capacity by a reduction in interstitial edema.

Clinically, severe fat embolism has responded well to increased inspired oxygen concentration, positive end expiratory pressure and steroid therapy. Judicious use of diuretics and volume expanders in the form of albumen and plasma are also important. Excessive use of crystalloid solutions should be avoided. We have had no morbidity or mortality in the last 13 cases of severe fat embolism treated in this manner.

**REFERENCES**

3 Hunninghake DB, Azarnoff DI: Clofibrate effect on catecholamine-induced metabolic changes in humans. Metabolism 17:588, 1968

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**CHART 3.** Marked fall in PaO₂ in both control and steroid groups compared to no essential change in PEEP group.

**CHART 4.** Comparison of pressure gradients, which developed between PAW and LA in all groups.
methylprednisolone sodium succinate has any effect over six hours after oleic acid injection. However, if the animals are placed back in their cages and studied on the second and fourth days after the initial experiment we find that arterial Po2 and shunt return to normal. This is in marked contrast to dogs which did not receive steroid. Eighty percent of these animals died within 12 hours after completing the initial study whereas all the steroid treated group survived, and the 20 percent that did survive failed to show any significant improvement in gas exchange over the four day post-oleic acid period. Because of this we feel that steroids are of benefit in the treatment of oleic acid induced pulmonary edema. It

appears that greater time is required to produce these salutary effects than was allowed in your study and in that cited by Dr. Ashbaugh.

Dr. Neff: We see from your data that the hematocrit increased in your animals. We see clinically a probable hemolytic anemia later in the course. Did you follow these animals long enough to evaluate this?

Dr. Parker: No. We observed them only for a matter of hours.

Dr. Branscomb: At what volume was compliance measured?

Dr. Parker: At the relaxation point.

**SESSION V—INJURY VIA INHALATION AND INFECTION**

**Sputum Cell Population Measurements in Bronchial Injury: Observations in Acute Smoke Inhalation**

L. J. Faing, M.D., T. C. Medici, M.D., and S. Chodosh, M.D.

Exfoliative cytologic examination of sputum permits the qualitative and quantitative determination of the bronchial epithelial cells exfoliated in various bronchial disorders. The extent and severity of the specific injury can be objectively estimated and serial observations of the pathologic changes carried out in the living human subjects. In this study, measurements of populations of exfoliated bronchial epithelial cells and several parameters of pulmonary function were made in patients with and without underlying chronic obstructive lung disease (COLD) associated with one identifiable harmful stimulus: namely, acute smoke inhalation.

**MATERIAL AND METHODS**

As part of a larger study on acute smoke inhalation in the absence of significant body burns, 29 patients had determinations of sputum volume and cytology, spirometric function, arterial blood gas and admission carboxyhemoglobin levels. Baseline clinical features are presented in Table 1.

For each 24-hour period (generally 9:00 AM to 9:00 AM) during their hospitalization, the patients were instructed to collect in a glass jar all the sputum they raised. During the first hospital day, however, the collection was started at the time of admission and the subsequent volume obtained corrected to reflect a 24-hour period. For example, if the patient was admitted at 9:00 PM, the 12-hour volume was measured the following morning and multiplied by a factor of 2.

Cytologic examination was carried out on each 24-hour sputum specimen, according to the methods of Chodosh1 and the number and percentage of bronchial epithelial cells as well as its subtypes: (basal, degenerated basal, ciliated, degenerated ciliated, goblet and metaplastic) were calculated.

The three subgroups were reasonably similar as to the number of subjects, age, sex and duration of hospitalization. Virtually all patients had smoke inhalation in the absence of skin burns (the one exception had burns < 2-3 percent of body surface area) and were subjected to a closed space exposure (97 percent). The majority of patients (69 percent) had their exposure during two specific fires: one in a hotel and the other in an underground subway. All but one of the remaining patients were involved in apartment fires. Unfor-

Table 1—**Baseline Clinical Classification of Patients with COLD Chronic Obstructive Lung Disease**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Moderate to severe</th>
<th>Minimal</th>
<th>None</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject, No.</td>
<td>9</td>
<td>8</td>
<td>12</td>
</tr>
<tr>
<td>Age, Mean</td>
<td>60</td>
<td>50</td>
<td>51</td>
</tr>
<tr>
<td>Sex, % male</td>
<td>78</td>
<td>75</td>
<td>75</td>
</tr>
<tr>
<td>Duration of hospitalization</td>
<td>4.8</td>
<td>5.9</td>
<td>3.4</td>
</tr>
<tr>
<td>History of cigarette smoking, %</td>
<td>100</td>
<td>75</td>
<td>54.5</td>
</tr>
<tr>
<td>Known history of pulmonary disease, %</td>
<td>100</td>
<td>37.5**</td>
<td>8+</td>
</tr>
<tr>
<td>Baseline productive cough, %</td>
<td>100</td>
<td>37.5</td>
<td>8+</td>
</tr>
<tr>
<td>Baseline dyspnea on exertion, %</td>
<td>100</td>
<td>37.5</td>
<td>8+</td>
</tr>
<tr>
<td>Chronic pulmonary changes on chest x-ray film, %</td>
<td>89</td>
<td>12.5</td>
<td>8</td>
</tr>
</tbody>
</table>

*Two patients with bronchial asthma, one with recurrent acute bronchitis.
**Secondary to chronic left ventricular failure in two of three patients.
+History of childhood asthma in one patient.