Bronchoalveolar Lavage in Liquid Paraffin Pneumonitis*

Dominique Lauque, M.D.;† Georges Dongay, M.D.;† Thierry Levade, M.D.;‡ Claude Caratéro, M.D.;§ and Pierre Carles, M.D., F.C.C.P.†

We evaluated cells and lipids recovered in the bronchoalveolar lavage fluid from seven patients with liquid paraffin pneumonitis. For each patient, the BALF was whitish with oil droplets on the surface. Alveolar macrophages contained numerous, large vacuoles that did not react with May-Grunwald-Giemsa, Papanicolaou, or periodic acid-Schiff but were stained in black with Sudan B, orange with Sudan III and red with oil Red O. Liquid paraffin was identified on thin layer chromatography of BALF-extracted lipids as a very hydrophobic compound migrating on the solvent front as control liquid paraffin. This abnormal spot was definitely identified as liquid paraffin by infrared spectros-

copy and gas liquid chromatography for the first patient. The number and percentage of AMs were largely decreased in the BALF of each patient, whereas the number of neutrophils, eosinophils and lymphocytes was increased. These findings suggest that this cell-mediated inflammatory response plays a role in the development of interstitial fibrosis at late stages of liquid paraffin pneumonitis. (Chest 1990; 98:1149-55)

BALF = bronchoalveolar lavage fluid; AM = alveolar macrophages; PAF = pulmonary alveolar proteinosis; PAS = periodic acid-Schiff; TLC = thin layer chromatography

Laughlen first reported in 1925 four cases of lipid pneumonitis following the use of mineral oil for nose drops or laxatives. Three of his cases occurred in young children and one in an adult with soft palate and vocal cord paralysis. Two years later, Pinkerton described six children with lipid pneumonitis following the use of mineral, animal (cod liver oil) or vegetable (milk fat) oil. Then the number of reported cases increased during the next years. Large series of lipid pneumonitis mainly due to mineral oil used as laxative or intranasally, or to cod liver oil were reported in adults or children. Then the hazard of oil aspiration was emphasized leading to a decrease in the use of mineral oil for nose drops or as laxative, and to a probable decrease in the incidence of mineral oil pneumonitis. However, cases reported since 1970 stress the persistence of mineral oil pneumonitis and the delay of diagnosis often made on post mortem study or at an advanced stage of respiratory failure. An earlier diagnosis in the course of mineral oil pneumonitis is not easy because the history of ingestion of mineral oil is not readily ascertained, the symptoms appear at an advanced stage of the disease, and the biologic, radiologic, and functional features are not specific of the disease. Chemical analysis of lung surgical biopsy specimen or sputum cytology have been proposed for the diagnosis but the finding of lipophages in the sputum is inconsistent, and lung biopsy may be a risked procedure in these often critically ill patients.

We report the cytologic and biochemical results of BALF analysis from seven patients with chronic liquid paraffin pneumonitis seen in our department from September 1981 to March 1989. To our knowledge, this is the first report showing that BALF analysis is a useful tool for the diagnosis of liquid paraffin pneumonitis.

METHODS

Patient Population

A bronchoalveolar lavage was performed in seven patients with liquid paraffin pneumonitis, seven patients with pulmonary alveolar proteinosis, and ten healthy nonsmoker subjects.

Bronchoalveolar Lavage

Bronchoalveolar lavage was performed (after informed consent) with five successive fractions of 50 ml saline solution injected at room temperature through a fiberoptic bronchoscope. The small amount of fluid recovered from the initial aliquot was discarded. The return of fluid from subsequent aliquots was pooled, placed on ice, and analyzed for cell content in the following hours. The lavage was performed in the right middle lobe for six patients, or in the left lower lobe for patient 3.

Numeration and Morphologic Evaluation of Cells from BALF

Total cell count was done with a hemocytometer on the unconcentrated BALF and expressed as total cell number recovered from the whole fluid. The differential count was made from a cytocentrifuged preparation stained with May-Grunwald-Giemsa, Papanicolaou, periodic acid-Schiff, and Perls. In order to assess the composition of the lipids present in the AMs, cytocentrifuged preparations were also stained with Sudan B, Sudan III, and oil

*From the †Service de Medecine Interne, ‡Laboratoire de Biochimie, and §Laboratoire de Cytologie, Toulouse, France. Manuscript received January 19; revision accepted April 27.
Reprint requests: Dr. Lauque, Medecine Interne (Batillon Senac), CHU Purpan, 31059 Toulouse Cedex, France

CHEST / 98 / 5 / NOVEMBER, 1990 1149
Electron microscopic examination was performed after fixation of the cell pellet for one hour with 3 percent glutaraldehyde and washing in phosphate buffer pH 7.3. The cells were subsequently postfixed in 2 percent osmium tetroxide in phosphate buffer pH 7.3. Ultrathin sections of representative regions chosen from semithin sections were prepared and examined using an electron microscope after staining with uranyl acetate and lead citrate.

**BALF Lipid and Protein Analysis**

Ten milliliters of the BALF of each patient were analyzed for protein and lipid contents. Protein concentration was determined by the method of Bradford. Lipids were extracted according to Bligh and Dyer, dried under a stream of nitrogen, and analyzed. Phospholipid content was determined by the phosphorus content of each lipid extract, assuming that the mean molecular weight of phospholipid was 650.

One dimensional thin layer chromatography (Silica gel 50 plates) of each extract dissolved in chloroform/methanol (2:1, by vol) was performed using two solvent systems to separate phospholipids (chloroform/methanol/acetic acid/water: 75 + 45 + 12 + 6, by vol) and neutral lipids (petroleum ether/diethyl ether/acetic acid: 80 + 20 + 1, by vol). Spots were visualized under iodine vapors and compared to various control liquid paraffin preparations.

**Statistical Methods**

All results were expressed as mean ± standard deviation. Statistical comparisons were made using the Student's two-tailed t-test. A p value less than 0.05 was considered as significant.

**RESULTS**

**Patient Population with Liquid Paraffin Pneumonitis**

The seven nonsmokers (four women and three men) between 56 and 87 years old (mean 69) were hospitalized for chronic pneumonitis (Table 1). None had any known respiratory disease in their past medical history. A neurologic or psychiatric disorder was present in four of them: chronic psychosis treated with neuroleptic drugs (patient 1); severe Parkinson disease treated with levodopa (patient 2) or bromocriptine mesylate (patient 5); and persistent palatal paresis and difficulties for swallowing (patient 3). Patient 6 had a chronic aggressive hepatitis, thyroiditis, and Sjögren's syndrome.

Only one patient complained of marked dyspnea. The others acknowledged slight or no dyspnea in spite of extensive pulmonary disease for patients 1 and 2. All but one patient had frequent cough but were not able to raise any sputum. Most of them had anorexia, asthenia, and were underweight. Chest auscultation found fine crackles rales on posterior and lateral bases. There was no clubbing, but cyanosis was noted in

**Table 1—Clinical Features, Chest X-Ray Findings and Blood Gas Analysis in Patients with Liquid Paraffin Pneumonitis**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age</th>
<th>Predisposing Factors</th>
<th>Dyspnea</th>
<th>Cough</th>
<th>Sputum</th>
<th>Crackles</th>
<th>Chest X-ray Findings</th>
<th>PaO₂, mm Hg</th>
<th>PaCO₂, mm Hg</th>
<th>Follow-up</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>56</td>
<td>Chronic psychosis</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>++</td>
<td>Diffuse</td>
<td>48</td>
<td>38</td>
<td>7 yr</td>
<td>Stable</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>73</td>
<td>Parkinson disease</td>
<td>−</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Diffuse</td>
<td>39</td>
<td>47</td>
<td>2 mo</td>
<td>Death (Parkinson disease)</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>65</td>
<td>Membranous palate paralisi</td>
<td>+</td>
<td>+</td>
<td>−</td>
<td>++</td>
<td>LLL</td>
<td>53</td>
<td>40</td>
<td>4 yr</td>
<td>Death (Myocardial infarction)</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>87</td>
<td>Reflux esophagitis</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Diffuse</td>
<td>36</td>
<td>43</td>
<td>1 mo</td>
<td>Death (Intestinal infarction)</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>64</td>
<td>Parkinson disease</td>
<td>+</td>
<td>+</td>
<td>−</td>
<td>++</td>
<td>RML</td>
<td>55</td>
<td>38</td>
<td>1 yr</td>
<td>Stable</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>60</td>
<td>Reflux esophagitis</td>
<td>+</td>
<td>+</td>
<td>−</td>
<td>+</td>
<td>Diffuse</td>
<td>－</td>
<td>－</td>
<td>4 yr</td>
<td>Stable</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>75</td>
<td>Reflux esophagitis</td>
<td>+</td>
<td>+</td>
<td>−</td>
<td>++</td>
<td>RML, RLL</td>
<td>－</td>
<td>－</td>
<td>1 yr</td>
<td>Death (cardiac and respiratory failure)</td>
</tr>
</tbody>
</table>

* = absent; +, slight; + +, moderate; + + +, marked; LLL, left lower lobe; RML, right middle lobe; RLL, right lower lobe.

**Figure 1.** Posterioranterior chest roentgenogram of patient 1 with liquid paraffin pneumonitis.
patient 4.

Roentgenographic examination revealed bilateral dense alveolointerstitial infiltrates of the inferior, middle lobes and lingula in four patients (Fig 1). The roentgenographic abnormalities were more spread than expected on symptoms. The three other patients had more limited infiltrates to the left lower lobe (patient 3), right middle lobe (patient 5), right middle and lower lobe (patient 7).

The sedimentation rate was increased between 37 and 76 (mean 55) for the seven patients. Serum protein analysis, electrolytes, hepatic and renal test results were normal. The tests for immune complexes and markers of autoimmune disease were negative except for patient 6 with chronic aggressive hepatitis. The PaO₂ measured for five patients was markedly decreased between 36 and 56 mm Hg (mean 46.2). The PaCO₂ was normal or mildly increased (mean 41.2 mm Hg).

The intake of paraffin oil was known only after the results of BALF analysis for four patients. Furthermore, patient 1 with chronic psychosis did not acknowledge any paraffin oil intake in spite of BALF results.

The chronic aspiration of mineral oil was explained by a massive but asymptomatic esophageal reflux (patient 1, 4, 6, 7) or by difficulties in swallowing and false passages (patient 2 and 3) (Table 1). Parkinson disease was the sole possible predisposing factor for patient 5.

After the diagnosis had been made, all patients were advised to stop mineral oil intake. Four patients died between two months and four years after the diagnosis (Table 1). The death was attributed to the Parkinson disease (patient 2), a myocardial infarction (patient 3), an intestinal infarction (patient 4), and cardiac and respiratory failure (patient 7). Patients 1, 5, and 6 were in rather good physical condition and their

---

### Table 2—Numbers and Types of Cells Recovered in the Bronchoalveolar Lavage Fluid of Patients with Liquid Paraffin Pneumonitis and Ten Control Subjects

<table>
<thead>
<tr>
<th>Patient</th>
<th>Percent Recovery Fluid</th>
<th>Total Cells × 10⁶</th>
<th>Macrophages × 10⁶</th>
<th>%</th>
<th>Lymphocytes × 10⁶</th>
<th>%</th>
<th>Neutrophils × 10⁶</th>
<th>%</th>
<th>Eosinophils × 10⁶</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>60</td>
<td>30</td>
<td>8.7</td>
<td>29</td>
<td>4.8</td>
<td>16</td>
<td>15.3</td>
<td>51</td>
<td>1.2</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>47</td>
<td>22</td>
<td>12.3</td>
<td>56</td>
<td>1.1</td>
<td>5</td>
<td>7.5</td>
<td>34</td>
<td>1.1</td>
<td>5</td>
</tr>
<tr>
<td>3</td>
<td>60</td>
<td>17</td>
<td>10.2</td>
<td>60</td>
<td>3.4</td>
<td>20</td>
<td>2.7</td>
<td>16</td>
<td>0.68</td>
<td>4</td>
</tr>
<tr>
<td>4</td>
<td>44</td>
<td>56</td>
<td>11.2</td>
<td>20</td>
<td>7.8</td>
<td>14</td>
<td>32.5</td>
<td>58</td>
<td>4.5</td>
<td>8</td>
</tr>
<tr>
<td>5</td>
<td>42</td>
<td>20</td>
<td>14.6</td>
<td>73</td>
<td>4.0</td>
<td>20</td>
<td>1.4</td>
<td>7</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>53</td>
<td>29</td>
<td>6.8</td>
<td>23</td>
<td>7.1</td>
<td>24</td>
<td>15.1</td>
<td>51</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>40</td>
<td>4.8</td>
<td>3.1</td>
<td>65</td>
<td>0.5</td>
<td>11</td>
<td>0.6</td>
<td>12</td>
<td>0.5</td>
<td>12</td>
</tr>
</tbody>
</table>

Mean ± SD

<table>
<thead>
<tr>
<th></th>
<th>49.4 ± 8.3†</th>
<th>25.5 ± 15.8</th>
<th>9.6 ± 3.8†</th>
<th>46.6 ± 21.9†</th>
<th>4.1 ± 2.8*</th>
<th>15.7 ± 6.4*</th>
<th>10.7 ± 11*</th>
<th>32.7 ± 21†</th>
<th>1.1 ± 1.5*</th>
<th>4.7 ± 4.3†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal volunteers</td>
<td>73.5 ± 12</td>
<td>20.3 ± 6.1</td>
<td>18.2 ± 6.0</td>
<td>99.7 ± 6.5</td>
<td>1.6 ± 1.4</td>
<td>9 ± 6.5</td>
<td>.4 ± .3</td>
<td>2.3 ± 1.8</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

N = 10

* p<0.05.
† p<0.01 compared to normal volunteers.

---

The BALF recovered from the seven patients with liquid paraffin pneumonitis was whitish and turbid with many oil droplets on the surface. The percentage of recovery was greater than 40 percent of the injected fluid for the seven patients (Table 2). The mean total cell count in the BALF from these seven patients was not significantly increased as compared to the nonsmoker control subjects (respectively [25.5±15.8] x 10⁶ vs [20.3±6.1] x 10⁶, p>0.1) (Table 2). However, the distribution of the cell popu-
lations was modified in mineral oil pneumonitis. There was a large decrease in the mean AM number and percentage as compared to the control group (9.6 ± 3.8) × 10⁶ vs (18.2 ± 6) × 10⁶, p < 0.01; and 46.6 ± 21.9 percent vs 89.7 ± 6.5, p < 0.001 respectively. The mean neutrophil count (10.7 ± 11.3) × 10⁶ and percentage (32.7 ± 21.1 percent) of the patient group were increased as compared to the mean control number (0.42 ± 0.32) × 10⁶, p < 0.02 and percentage (2.3 ± 1.8 percent). The lymphocyte and eosinophil numbers were also significantly higher in the patient BALF, but not at a level as high as that of neutrophils.

Morphologic and Histochemical Evaluation of Alveolar Macrophages

The AM from liquid paraffin pneumonitis demonstrated morphologic abnormalities. Nearly all the AM had a foamy appearance because the cytoplasm was full of numerous, large, rounded vacuoles (Fig 2). These optically empty vacuoles were not stained with the May-Grünwald-Giemsa, Papanicolaou or PAS. Vacuoles were weakly stained in black with Sudan B and in orange with Sudan III. Oil Red O intensively stained in red nearly all the AM, supporting the presence of neutral lipids as the main constituent of the vacuoles.

The cytoplasm of AM from normal subjects was basophil, microvacuolated in relation to the lysosomes and phagosomes, but never displayed large empty vacuoles such as those found in liquid paraffin pneumonia. The AM of patients with PAP displayed a foamy cytoplasm but the vacuoles were smaller and contained amorphous material which was strongly PAS-positive and dark stained with Oil red O. Their nuclei often were pyknotic, and they were surrounded by an abundant extracellular proteinaceous material, also PAS-positive.

Electron microscopic evaluation of the AM from liquid paraffin pneumonitis confirmed the existence of large, numerous, empty vacuoles throughout all the cytoplasm and surrounded by a thin osmiophil line (Fig 3). Few areas of normal cytoplasm were present between these large vacuoles and the number of intracellular organelles was reduced. The size of the AM appeared to be in the normal range. Their plasma membranes were very irregular with many pseudopodes. Some AM exhibited smaller vacuoles containing slightly osmiophil and partially retracted material.

BALF Biochemical Analysis

After overnight decantation or low-speed centrifugation, the BALF from the patients with liquid paraffin
Table 3—Phospholipid (PL) and Protein Content of BALF from Seven Patients with Liquid Paraffin Pneumonitis, Seven Patients with Pulmonary Alveolar Proteinosis and Ten Control Subjects

<table>
<thead>
<tr>
<th>Patients</th>
<th>Phospholipids, mg/ml</th>
<th>Proteins, mg/ml</th>
<th>Phospholipids/Proteins</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.10</td>
<td>0.60</td>
<td>0.16</td>
</tr>
<tr>
<td>2</td>
<td>0.03</td>
<td>0.22</td>
<td>0.12</td>
</tr>
<tr>
<td>3</td>
<td>0.03</td>
<td>0.49</td>
<td>0.06</td>
</tr>
<tr>
<td>4</td>
<td>0.02</td>
<td>0.18</td>
<td>0.14</td>
</tr>
<tr>
<td>5</td>
<td>0.14</td>
<td>1.89</td>
<td>0.08</td>
</tr>
<tr>
<td>6</td>
<td>0.03</td>
<td>0.29</td>
<td>0.11</td>
</tr>
<tr>
<td>7</td>
<td>0.05</td>
<td>1.05</td>
<td>0.04</td>
</tr>
<tr>
<td>M ± SD</td>
<td>0.06 ± 0.04</td>
<td>0.67 ± 0.61*</td>
<td>0.10 ± 0.04</td>
</tr>
<tr>
<td>PAP (n = 7)</td>
<td>0.13 ± 0.09†</td>
<td>5.17 ± 4.15*</td>
<td>0.03 ± 0.02†</td>
</tr>
<tr>
<td>Controls (n = 10)</td>
<td>0.03 ± 0.02</td>
<td>0.20 ± 0.15</td>
<td>0.20 ± 0.15</td>
</tr>
</tbody>
</table>

*p<0.05.
†p<0.01 compared to control subjects.

Pneumonitis often was separated into an upper oily layer and a lower clearer phase. The upper layer represented a small fraction, less than 20 percent of the 10 ml aliquot protein. Protein content was increased in the lower phase of patients 1, 5, and 7, and was in the normal range (mean ± SD) for the other patients (Table 3). Phospholipids also were increased in the lower phase of patients 1 and 5.

The TLC of the BALF-extracted lipids showed, for each patient with liquid paraffin pneumonitis, sphingomyelin, phosphatidylcholine and phosphatidylethanolamine migrating as the control spots in the solvent system for phospholipids (Fig 4, left). An abnormal hydrophobic compound migrating on the solvent front as the control paraffin was found for each patient. This abnormal spot was very slightly stained by iodine vapor. In the solvent system for neutral lipids, this abnormal compound still migrated on the solvent front as did the control paraffin and was well separated from the other neutral lipids (Fig 4, right). This abnormal spot isolated by TLC was definitely identified as liquid paraffin by comparative infrared spectroscopy and gas liquid chromatography for patient 1.

The BALF from the seven patients with PAP contained large amounts of proteins as compared to the control subjects (p<0.01) or to the patients with liquid paraffin pneumonitis (p<0.05) (Table 3). The amounts of total phospholipid were also increased as compared to the control subjects (p<0.01), but a spot migrating as control paraffin was never seen on TLC.

**DISCUSSION**

These seven cases of liquid paraffin pneumonitis show that the disease still occurs and that its diagnosis can be made by cytologic and biochemical analysis of

![Figure 4](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21620/ on 04/19/2017)

**Figure 4.** Thin layer chromatography of lipids extracted from BALF of a patient with liquid paraffin pneumonitis. **Left,** Solvent system for phospholipid separation (chloroform/methanol/acetic acid/water: 15+45+12+6, by vol). The plate was stained by iodine vapor. BALF (2) has an abnormal spot very slightly stained by iodine vapor and migrating as the control liquid paraffin (5). Control sphingomyelin (1), phosphatidylcholine (3), phosphatidylethanolamine (4), phosphatidylserine and phosphatidylinositol (6), origin (o) and front (f) of migration. B is solvent system for neutral lipid separation (petroleum ether/ diethyl ether/acetic acid: 80+20+1, by vol). BALF (MC) still has the abnormal spot migrating as control liquid paraffin (p) on the solvent front (f). Control monoglycerides (mg), diglycerides (dg), triglycerides (tg), free cholesterol (fc), cholesterol ester (ce), and fatty acid (fa).
BALF. The macroscopic aspect of the BALF with oily substances floating on its surface may first evoke the diagnosis. Microscopic examination of the cell pellet showed that almost all the AM had a typical abnormal foam appearance due to empty vacuoles not stained with the usual dyes. Positive staining of AM with dyes specific for lipids, Sudan B, Sudan III, and oil red O showed that the material contained in the vacuoles was made of neutral lipids. Ultrastructural examination of these macrophages showed the presence of many clear vacuoles occupying a large part of the cytoplasm. The vacuoles were empty because liquid paraffin was extracted during fixation and staining. The vacuoles appeared to be within phagosomes because they were bound in place by a single membrane.

These large amounts of vacuolated material within the AM are similar to the previous histologic findings of liquid paraffin pneumonia.6,9 These foamy macrophages with large cytoplasmic vacuoles are suggestive of liquid paraffin pneumonitis but must be distinguished from the vacuolated AM found in PAP.14 in cholesterol pneumonia,15 after exposure to silicone,16 or exposure to polyvinylpyroldione.17 In active PAP, there are a few alveolar macrophages, and their nuclei are often piknotic and the vacuoles are much smaller than in paraffin loaded AM. The abundant intracellular and extracellular material is strongly stained with PAS.14 In the case of cholesterol pneumonia, which usually occurs distal to an obstructing bronchial lesion,15 AM inclusions are deeply stained with dyes for lipids and give a positive PAS reaction.8

Since the paraffin-loaded AM have suggestive but nonspecific histochemical features, liquid paraffin must be identified by TLC of the BALF lipid extract. Liquid paraffin was identified for the seven patients as a very hydrophobic compound migrating on the front in the solvent systems used for phospholipid or neutral lipid separation. This abnormal compound was faintly stained by iodine vapor and was identified as liquid paraffin by comparison with medicinal liquid paraffin deposited on the same plate. Furthermore, since cholesterol ester and paraffin spots were not completely separated in the solvent system for neutral lipid, the resolution was further improved by replacing this solvent system by pure hexane when the solvent front reached the three fourths of the plate. Therefore, cholesterol ester spot did not move anymore, whereas the paraffin spot continued to migrate with the solvent front, allowing better distinction between these two compounds. The paraffin nature of the abnormal spot was confirmed for patient 1 by comparative infrared spectroscopy and gas liquid chromatography10 of the spot. Liquid paraffin was never found by TLC in the BALF from the patients with PAP.

Most cases of liquid paraffin pneumonitis are diagnosed at necropsy.6,7 following operations for suspected bronchial carcinoma8 or after open lung biopsy.8 Transthoracic needle biopsy has been used for diagnosis of lipoid pneumonitis, but false negative results are possible.19 Histologic changes are dominated by large amounts of vacuolated macrophages in the alveoli and to a lesser extent, in the interstitium and bronchial lymph nodes.2,9 Inflammatory cells, multinuclear giant cells, and various degrees of interstitial fibrosis are also present. The vacuoles of macrophages are empty on conventionally fixed sections and only slightly stained by the specific dyes for lipids, Sudan III, Sudan IV, and Black Sudan on fresh frozen sections.8 Liquid paraffin may finally be identified in the lung specimen by gas chromatography6,20 or infrared spectroscopy.8 Cytologic examination of the sputum for paraffin-laden macrophages5 and gas chromatography of the sputum after lipid extraction20 have been proposed for a noninvasive diagnosis of paraffin pneumonitis. However, positive sputa are not constantly found because expectoration of lipid material may be sporadic or intermittent.

Most of the recently reported cases of mineral oil pneumonitis have been due to liquid paraffin taken by mouth as laxative.7,8,10,19 In the past, liquid paraffin formed the base of nose drops and throat sprays, but is now rarely used for this purpose. Chronic aspiration of mineral oil is facilitated by deglutition abnormalities; central nervous system diseases such as stroke, Parkinson disease, systemic sclerosis;9 or esophageal diseases, such as gastroesophageal reflux, achalasia, and megaesophagus, and diverticula.10 Mineral oil pneumonitis also occurs in aged, debilitated or bedridden patients with central nervous or gut disorders. In such patients, mineral oil is often used at bedtime as laxative: reflux and chronic aspiration are facilitated by decubitus and decreased vigilance during sleep. Quinn and Meyer21 demonstrated that iodized oil introduced into the nostril of sleeping patients easily and silently entered the bronchial tree without exciting reflex inhibition. Large amounts of oil were found in the dependent regions of the lung by chest roentgenograms the next morning.

Once in the bronchial tree, liquid paraffin is removed by mucociliary transport only with difficulty. In 1939, Proetz22 showed that liquid petroleum hinders the flow of mucus transported in vivo on rabbit nasal epithelium. More recently, King et al23 found that viscous substances, such as oils, are not or are slowly transported in vitro on the ciliated epithelium of frog palate.23 Thus, aspirated liquid paraffin could depress the bronchial mucociliary transport by altering the viscoelastic properties of secretions.

Once in the alveolar spaces, mineral oil is emulsified and engulfed by the AM. Although some paraffin-laden AM may penetrate into the interstitial tissue
and reach the peribronchial lymphatics and hilar lymph nodes, most of the mineral oil remains within the alveoli, free or in the AM. 7 Since the macrophages cannot metabolize the chemically inert, nonsaponifiable oil, they disintegrate after some time and liberate the intracellular oil into the alveoli. This alveolar free liquid paraffin cannot be removed up to the pharynx by the depressed mucociliary transport and a vicious circle is set up which accounts for the chronicity of this disease, even several years after discontinuation of the liquid paraffin intake.3

In order to further investigate the inflammatory response induced by liquid paraffin in the lung, we have also examined the different types of cells recovered in the BALF from these seven patients. The numbers of lymphocytes, eosinophils, and neutrophils were increased on the surface of the lower respiratory tract. These findings support that a local cell-mediated inflammatory response induced by liquid paraffin may be important for the development of interstitial fibrosis in liquid paraffin pneumonitis. Fibrosis of the interstitium is usually associated with the paraffin-laden AM on the lung biopsy of patients with liquid paraffin pneumonitis.7 Since neutrophils may induce a lung cell injury through their secreted proteases and oxygen radicals,44 it could be speculated that the neutrophil alveolitis seen in our patients may control the development of interstitial fibrosis present at late stages of liquid paraffin pneumonitis. No correlation was found between BALF cell, phospholipid or protein changes, or between BALF changes and hypoxia, but such relations could not be excluded because of the small study group.

These seven cases of liquid paraffin pneumonitis seen in our department since 1981 show that the disease still occurs although the risk of chronic aspiration of mineral oil is known. This may be explained in France because this laxative is purchased without medical prescription. In Sweden, 12,000 L of liquid paraffin were sold in the pharmacies in 1981.8 In the United States, the Food and Drug Administration advised in 1975 against the use of mineral oils for persons at risk for inhalation such as young children, bedridden or aged patients, persons with difficulty in swallowing, but listed mineral oils among the safe and effective laxatives.25

In conclusion, liquid paraffin pneumonitis must be clinically suspected on the basis of several facts as follow: chronic pneumonitis of the lower or middle lobes with crackles; known intake of liquid paraffin; and a potential risk for inhalation. In this context, the histochemical and biochemical analysis of the BALF, demonstrating the presence of liquid paraffin, is very useful for the diagnosis and avoids more invasive procedures such as lung surgical biopsies for these often critically ill patients.

REFERENCES
4 Sweeney WJ. Intranasal medication with oils. Eye Ear Nose throat Mon 1943; 22:335-38
8 Fox B. Liquid paraffin pneumonia with chemical analysis and electron microscopy. Virchows Arch (A) 1979; 382:339-46
22 Proetz AH. The effects of certain drugs up on living nasal ciliated epithelium. Ann Otol Rhin Laryngol 1934; 43:450-63

CHEST / 98 / 5 / NOVEMBER, 1990 1155