The diagnostic and prognostic significance of eosinophilic pleural effusions remains controversial despite a century of observation and discussion. Eosinophilic effusions, defined as 10% or more eosinophils, account for between 5 and 8% of exudative pleural effusions. Pulmonary textbooks state that eosinophilic pleural effusions denote a favorable prognosis, based on their association with benign diagnoses. Specifically, eosinophilic effusions are held to be associated only rarely with malignant pleural diseases. These conclusions are based almost entirely on retrospective case series of pleural effusions. Furthermore, such findings may not be applicable to patient populations with high prevalences of malignancy.

Therefore, to determine whether eosinophilic pleural effusions are less likely to be malignant and are associated with a better prognosis, we prospectively studied the causes and clinical outcomes of 777 consecutive pleural effusions diagnosed over 5 years at the Minneapolis Veterans Affairs Medical Center.

**Materials and Methods**

**Selection of Cases**

All patients who underwent thoracentesis and had analysis of pleural fluid between September 1990 and September 1995 at the Minneapolis Veterans Affairs Medical Center were identified prospectively by the hematology, chemistry, and cytology laboratory services. Patient clinical and demographic data, pleural fluid analyses, and cytology reports were obtained from the hospital computer database.

Presumptive clinical diagnoses for pleural effusions were determined by the primary physicians, based on history and physical examination, ancillary laboratory data, chest radiographs, and results of pleural fluid studies. Effusions were classified as confirmed malignant when pleural fluid cytologic findings were diagnostic for malignancy. Effusions were attributed to cancer if confirmed malignant or if exudative in a patient who had a known lung neoplasm without any other etiology revealed by diagnostic studies. Effusions were classified as idiopathic if no etiology could be assigned at either the initial or subsequent evaluations.

Eosinophilic pleural effusions were defined as 10% or more eosinophilic leukocytes on differential cell count. Effusions were classified as transudates or exudates using the criteria of Light.

Date last seen alive or date of death was obtained by scanning the hospital computer database for hospital admissions, outpatient visits, and dates of death. For patients who could not be clearly identified from the hospital computer records as alive (outpatient or inpatient visit within the last 2 months) or dead, the Veterans Af-

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CHEST / 110 / 5 / NOVEMBER, 1996 1271
Table 1—Etiologies of Pleural Effusions

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Total (n=476)</th>
<th>Non eosinophilic (n=432)</th>
<th>Eosinophilic (n=44)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer*</td>
<td>128 (26.9)</td>
<td>118 (27.3)</td>
<td>10 (22.7)</td>
<td>0.51</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>127 (26.7)</td>
<td>121 (28.0)</td>
<td>6 (13.6)</td>
<td>0.04</td>
</tr>
<tr>
<td>Parapneumonic</td>
<td>61 (12.8)</td>
<td>57 (13.2)</td>
<td>4 (9.1)</td>
<td>0.44</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>46 (9.6)</td>
<td>35 (8.1)</td>
<td>11 (25.0)</td>
<td>0.001</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>19 (4.0)</td>
<td>16 (3.7)</td>
<td>3 (6.8)</td>
<td>0.40</td>
</tr>
<tr>
<td>Empyema</td>
<td>17 (3.6)</td>
<td>17 (3.9)</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>Postsurgical</td>
<td>19 (4.0)</td>
<td>14 (3.2)</td>
<td>5 (11.4)</td>
<td>0.02</td>
</tr>
<tr>
<td>Sepsis</td>
<td>10 (2.1)</td>
<td>10 (2.3)</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>11 (2.3)</td>
<td>9 (2.1)</td>
<td>2 (4.5)</td>
<td>0.27</td>
</tr>
<tr>
<td>Serositis</td>
<td>8 (1.7)</td>
<td>6 (1.4)</td>
<td>2 (4.5)</td>
<td>0.16</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>8 (1.7)</td>
<td>8 (1.9)</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>Traumatic</td>
<td>7 (1.5)</td>
<td>7 (1.6)</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>4 (0.8)</td>
<td>4 (0.9)</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>Asbestos</td>
<td>4 (0.8)</td>
<td>4 (0.9)</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>Pulmonary embolus</td>
<td>4 (0.8)</td>
<td>4 (0.9)</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>Atelectasis</td>
<td>3 (0.6)</td>
<td>2 (0.5)</td>
<td>1 (2.3)</td>
<td>0.25</td>
</tr>
</tbody>
</table>

*Includes confirmed malignant and unconfirmed cancer etiologies; see “Materials and Methods” section for description.

Baird Beneficiary Identification and Records Locator System database was used to ascertain dates of death.

Statistical Analysis

Associations between categorical variables were analyzed with χ² analysis and continuous variables with unpaired Student’s t test. Survival curves were calculated by the Kaplan-Meier method and compared with the log rank test. A Cox proportional hazards model, incorporating age and clinical diagnoses as covariates, was used to determine the independent association between pleural fluid eosinophilia and survival. Calculations were performed using software (SPSS for Windows; release 6.1; Chicago). All p values are two-tailed.

RESULTS

Between September 1990 and September 1995, 777 thoracenteses were performed on 572 patients. Differential cell counts were reported for 655 pleural fluids from 476 patients. Virtually all of the patients were men (470 of 476), with a mean age of 67.4±11.3 years (range, 22 to 95 years).

Eosinophilic pleural effusions (≥10% eosinophils) were identified in 44 of 476 patients (9.2%). Eosinophilic effusions were significantly more often exudative than were noneosinophilic effusions (81 vs 52%; p<0.001). Compared with noneosinophilic pleural effusions, pleural eosinophilia was significantly more likely to be idiopathic or due to thoracic surgery (Table 1). There was no significant difference in proportions of eosinophilic or noneosinophilic effusions associated with cancer or with congestive heart failure. In addition, none of the effusions attributed to empyema, sepsis, tuberculosis, trauma, pancreatitis, asbestos, or pulmonary embolism were eosinophilic.

Because exudative pleural effusions were attributed to concomitant lung cancer in many cases without cy-
shown). In addition, pleural fluid eosinophilia did not correlate with peripheral blood eosinophilia (results not shown).

A favorable prognosis has been attributed to eosinophilic pleural effusions in previous retrospective studies, based on the association of such effusions with benign diagnoses, but the actual prognosis of eosinophilic and noneosinophilic effusions has not been determined prospectively. In our total study population, survival after the initial thoracentesis was unexpectedly short, with a median survival of only 8.4 months. Patients with eosinophilic pleural effusions had a significantly better survival than those with noneosinophilic effusions, with a median survival of 16.8 months compared with 7.7 months (p=0.017) (Fig 1). This difference in survival was not explained by differences in the ages of patients with eosinophilic compared with noneosinophilic effusions (67.5±11.7 vs 67.4±11.2), and eosinophilia independently predicted survival when adjusted for age. Similarly, the association between pleural fluid eosinophilia and survival remained significant when age and the major diagnoses for effusions (malignancy, congestive heart failure, idiopathic, and parapneumonic) were entered into a Cox proportional hazards model. Thus, pleural fluid eosinophilia appeared to be associated with a better prognosis for survival after thoracentesis, independent of age and of underlying etiology for the effusion.

**DISCUSSION**

This large prospective study of consecutive thoracenteses performed over a 5-year period refutes previous assertions that eosinophilic pleural effusions are unlikely to be malignant. Based on the low prevalence of eosinophilia in malignant effusions, previous reports have falsely inferred the converse, that the prevalence of malignancy in eosinophilic effusions is low. In agreement with previous series,\(^1,2,5\) we found that the prevalence of eosinophilia among malignant effusions was low (7.8%). However, eosinophilic effusions were as likely to be malignant as were noneosinophilic effusions in our population (20.5% vs 20.1%, respectively, for cytologically confirmed malignant effusions). Although the probability of malignancy in eosinophilic pleural effusions is dependent on the underlying prevalence of malignancy in the population studied,\(^2,13\) the prevalence of malignant effusions in our population was similar to or less than that in other reports.\(^1,2,5,11,12\) Thus, physicians should not be deterred from pursuing a diagnosis of malignancy in a suspicious effusion simply on the basis of pleural fluid eosinophilia.

Our results also challenge the conventional wisdom that repeated thoracenteses produces pleural fluid eosinophilia, presumably through the occult introduction of air into the pleural space.\(^2,11\) A single repeated thoracentesis within 2 to 12 weeks produced an eosinophilic effusion in only 2.3% of patients, and more often actually reduced the pleural eosinophilia.

Finally, to our knowledge, our study provides the first documentation of a significant association between eosinophilic effusions and improved survival. This association remained significant after adjustment for age and underlying diagnosis. Thus, pleural fluid eosinophilia may be a marker for a more favorable immune or inflammatory response to pleural disease. Although an association between pleural eosinophilia and pleural lymphocytosis was recognized previously,\(^11,12\) the local secretion of interleukin 5 by helper T lymphocytes within the pleural space has only recently been identified as the mechanism underlying post-traumatic pleural fluid eosinophilia.\(^17\) Although helper T lymphocytes outnumber suppressor T cells in pleural fluid regardless of the etiology of the effusion,\(^3\) further study is required to determine whether an active pleural helper T lymphocyte response correlates with better prognosis in pleural diseases.

In summary, our prospective study of consecutive thoracenteses suggests that pleural fluid eosinophilia is not a helpful diagnostic finding; in particular, it should not be interpreted as reducing the likelihood of malignancy as the underlying cause of the effusion. Nevertheless, pleural fluid eosinophilia does appear to be associated with improved survival, independent of diagnosis.

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