Session 1: Morphology

Pathology of Interstitial Lung Diseases, with Particular Reference to Terminology, Classification and Trephine Lung Biopsy

Brian E. Heard, M.D.*

The adjective, interstitial, which you have chosen to use in the title of this conference, is probably the best word available at the present time to indicate diseases which affect predominantly the pulmonary connective tissue. The tissue is distributed to all parts of the lung, and communicates continuously from the alveolar wall to the hilum. At this conference, our interest will be focused mainly on the most peripheral and delicate connective tissue that runs in the alveolar walls. It is affected by many diseases of known and unknown cause, and serious abnormalities in lung function may result.

In the alveolar walls, the interstitial connective tissue forms a thin but complex layer lying between the alveolar epithelial cells and the capillary endothelial cells. In the normal lung, the tissue appears very scanty and is poorly seen by the light microscope. By the electron microscope, however, the separate components are seen clearly and include fibers of collagen, reticulin and elastin, basement membranes and ground substance, and small numbers of cells of several types such as primitive mesenchymal cells, fibroblasts, fibrocytes, mast cells, histiocytes, neutrophils, eosinophils, lymphocytes and plasma cells. Some histologists restrict the term interstitium only to the material lying between cells (on etymologic grounds), but most of them in practice include the cells as well under the term, for example von Hayek,1 who uses the term interstitial connective tissue throughout his book. The interstitial tissue of the alveolar walls communicates directly with that of the adjacent bronchioles, and of the interlobular septa.

In describing pathologic processes in the lungs, pathologists commonly use the word interstitial to refer to changes in alveolar walls and intra-alveolar for, of course, changes in the contents of the lumen of the alveolus. The barrier between these sites is the single layer of alveolar epithelial cells (types I and II). It is useful in diagnostic work to distinguish between interstitial fibrosis and intra-alveolar fibrosis, the latter being seen classically in unresolved pneumonia, in which fibroblasts invade unusually persistent inflammatory exudate by passing between the epithelial cells into the lumen. In interstitial fibrosis, the alveolar walls become thickened and encroach upon the alveolar spaces. As long as the alveolar epithelium preserves even a small alveolar space, the fibrosis is still termed interstitial.

The several terms for types of interstitial pneumonia recognized by Liebow2 have been adopted widely almost throughout the world, but there are one or two problems that have to be faced about the word interstitial that you may find of interest. One is that both interstitial and intra-alveolar sites are usually involved in conditions labelled only interstitial. In fact, in desquamative interstitial pneumonia, the most striking feature is the immense number of cells in the intra-alveolar spaces. The pulmonary fibrosis occasionally observed in the lungs of patients under treatment with busulphan was originally described as interstitial,4 but we found that most of the new fibrous tissue was actually intra-alveolar in position. Conversely, no one would describe pneumococcal pneumonia as an interstitial lung disease, and yet the intra-alveolar changes are obviously secondary to a profound acute interstitial inflammation.

In recent years, some new terminology has been devised by colleagues at the Brompton and London Chest Hospitals, and I believe you at this conference may be interested in it so that you may compare it with terminology used in the United States. The British term that has found widest favor is "diffuse fibrosing alveolitis." It was introduced by Scadding5 in 1964 to label a histologic appearance with two defining features—cellular thickening of the alveolar walls with a tendency to fibrosis, and large mononuclear cells within the alveoli. The term thus indicates both interstitial and intra-alveolar changes. In the United States, Liebow and co-workers4 named a histologic pattern with many intra-alveolar cells: desquamative interstitial pneumonia. Scadding and Hinson7 fitted this to their terminology as the desquamative type of fibrosing alveolitis. They contrasted it with a mural type in which there was much fibrosis of the alveolar walls. Cases of very cellular desquamative histologic type have been found likely to respond favorably to treatment with steroids, whereas the fibrotic mural type are not.8 In fact, serial biopsies have shown cellular patterns that later changed to fibrotic patterns, so it is quite reasonable anyway to expect a better response to steroids in the earlier active stage of the disease before fibrous scarring has become established.

Although our terms are different, the only real discrepancy in meaning between the two schools is that my colleagues and I feel that the desquamative pattern merges into the mural pattern merely according to the stage of development, whereas Carrington (personal communication, 1975) is convinced that desquamative interstitial pneumonia is a separate entity from usual interstitial pneumonia. We now plan to carry out a cooperative study to try to reach agreement on this point.

As regards the classification of interstitial lung diseases, Scadding8 has recently produced a table of diagnostic categories of pulmonary alveolar fibrosis that can be employed usefully for the present purpose. In the first group are all those diseases that can be defined etiologically: a) asbestosis, silicosis, etc due to inhaled mineral dusts; b) farmer's lung, bird-fancier's lung, etc due to...
inhaled organic dusts (also known as forms of extrinsic allergic alveolitis\(^1\)); c) busulfan lung, etc due to ingested toxic substances; and d) tuberculosis and other infections. In a second group are those conditions of, as yet, unknown cause that can be defined histopathologically, as we did with emphysema in earlier Aspen conferences. There are two subdivisions of this group: a) conditions such as sarcoidosis and eosinophilic granuloma, which are each part of a separate systemic disease with a fairly characteristic histologic pattern, and b) fibrosing alveolitis, defined as a pulmonary disease only (see foregoing definition above). The last-mentioned group could be expanded further using the histologic variants suggested by Liebow as varieties of interstitial pneumonia, ie usual, desquamative, lymphoid and giant cell, and also the lymphoplasmacytic type described by Greenberg.\(^1\) To match fibrosing alveolitis, one could suggest the terms diffuse lymphoid alveolitis, diffuse giant cell alveolitis and diffuse lymphoplasmacytic alveolitis.

**TREPHINE LUNG BIOPSY**

The diagnosis of interstitial lung diseases is sometimes not possible without biopsy of the lung. Physicians vary greatly in their attitudes to lung biopsy, and particularly to needle or trephine lung biopsy. Some insist on open biopsy, some use trephine or needle biopsy, and a few are against lung biopsy altogether, being concerned in case of complications. Those who favor lung biopsy must choose between a trephine biopsy on the ward, causing minor discomfort to the patient, but yielding a small sample of lung, or an open biopsy in an operating theater, yielding a larger, better sample of lung.

At the London Chest Hospital, Steel and Winstanley\(^1\) use a large trephine which they designed, measuring 7.5 cm long, 3.0 mm in external diameter and 2.1 mm internally, and an air drill. Table 1 shows the number of investigations carried out by Steel to a recent date, and gives an idea of the considerable proportion of cases in which a successful diagnosis has been achieved. In his hands, the procedure has proved safe and useful, and although pneumothorax has been found afterwards in about 25 percent, this has cleared quickly and nothing more serious has been encountered. Mild hemoptysis occurs in about 15 percent.

The procedure is undoubtedly a valuable diagnostic one in patients with persistently problematic diffuse pulmonary shadowing. However, because the sample is small, and sometimes very small, there are limits to the value of the procedure for research, and it may not be possible always to gain enough information histologically to identify with certainty whether the cellular or fibrotic elements predominate. For example, cells can be lost from the lumina of the alveoli, especially near the surface of the sample. Nevertheless, the procedure has proved its diagnostic value in practice (Table 1). For localized tumors, we use a different method, viz, aspiration needle biopsy under fluoroscopic control.\(^1\)

**REFERENCES**


**Table 1—Analysis of Histologic Findings in 298 Trephine Lung Biopsies Performed by Dr. S. Steel**

<table>
<thead>
<tr>
<th>Organizing Pneumonia</th>
<th>14</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tuberculosis</td>
<td>8</td>
</tr>
<tr>
<td>Sarcoïdosis</td>
<td>35</td>
</tr>
<tr>
<td>Polyarteritis Nodosa</td>
<td>3</td>
</tr>
<tr>
<td>Asbestosis</td>
<td>11</td>
</tr>
<tr>
<td>Fibrosing Alveolitis</td>
<td>55</td>
</tr>
<tr>
<td>Carcinoma</td>
<td>41</td>
</tr>
<tr>
<td>Others (eg allergic alveolitis; alveolar proteinosis)</td>
<td>82</td>
</tr>
<tr>
<td><strong>Total diagnostically significant</strong></td>
<td>249 (83.6%)</td>
</tr>
<tr>
<td><strong>Normal Lung</strong></td>
<td>27</td>
</tr>
<tr>
<td><strong>Total specimens obtained</strong></td>
<td>276 (93%)</td>
</tr>
<tr>
<td><strong>out of 298 procedures</strong></td>
<td></td>
</tr>
</tbody>
</table>

**A New Diagnostic System for Fibrosing Alveolitis (Interstitial Pneumonitis) Based on the Functional Anatomy of the Lung**

Robert C. Rosan, M.D.*

A diagnostic “profile” is established for the histologic diagnosis, based on completion of all entries in a

*From the Departments of Pathology and Pediatrics, Saint Louis University and Cardinal Glennon Memorial Hospital for Children, St. Louis.