INTRODUCTION

Non-neoplastic (medical) lung disease can be considered in two disparate arenas:

1. Acute lung disease, in which a frozen section may be requested and a diagnosis is expected by the clinician on the next day; and
2. Chronic lung disease, in which the final diagnosis can be contemplated and researched.

This section will not reiterate the literature on the statistical frequencies of various types of medical lung disease; rather, it will provide a practical approach for the pathologist who sees fewer than one medical lung biopsy per day.

The following tables point out some basic tenets of terminology and then craft an outline of the big picture for medical lung disease.

A Specific Lung Disease

- Usual interstitial pneumonitis (UIP)
- Desquamative interstitial pneumonitis (DIP)
- Lymphocytic interstitial pneumonitis (LIP)
- Bronchiolitis obliterans (BO)
- Eosinophilic granuloma (EG)
- Diffuse alveolar damage (DAD)
- Pulmonary capillaritis

A Lung Disease or a Pattern

- Bronchiolitis with patchy organizing pneumonia (BPOP)
- Nonspecific interstitial pneumonitis (NSIP)
- Cellular interstitial pneumonitis
- Chronic eosinophilic pneumonia (CEP)
- Hemorrhage

A Lung Pattern

- DIP-like
- Lymphocytic interstitial infiltrate
- Granulomatous pneumonitis
- Diffuse interstitial fibrosis

A Clinical Evaluation, Not a Pathological Diagnosis

- Acute lung injury
- Rheumatoid lung disease
- Drug-induced lung disease
- Churg-Strauss syndrome

From: Current Clinical Pathology: Lung Pathology: A Consultative Atlas
By S. Houser, U. J. Balis, and E. J. Mark © Humana Press, Totowa, NJ
A Common Observation

- Atypical pneumocytes
- Pigmented histiocytes
- Focal fibrosis

Medical Lung Disease: The Big Picture

- Acute
  - Floridly fibrotic (DAD, prognosis poor)
  - Fluid and cells (infection, hemorrhage, edema, fibrin, prognosis good)
- Chronic
  - Linear (interstitial, UIP, prognosis poor)
  - Nodular (bronchiolar and alveolar, BPOP, prognosis good)

General Guidelines in Diagnosis of Diffuse Lung Disease

- Have an idea of how ill the patient is
- Have an idea of the pace of the disease
- Appreciate problems in sampling (diffuse vs localized on X-ray)
- Use all tissue
- Do not overdiagnose (do no harm)

Pathological Findings in Open Lung Biopsy of Acute Respiratory Distress Syndrome

- DAD (90%)
- Hemorrhage (capillaritis)
- Infectious pneumonia
- Acute fibrinous pneumonia
- Acute eosinophilic pneumonia
- Edema (interstitial or alveolar)
- Emboli (blood clot, fat, talc, tumor)
- Bronchioloalveolar carcinoma
- Intra-alveolar fibrosis
- Acute transplant rejection

Lung Biopsy for Acute Disease or in the Immunosuppressed Patient: Technical Considerations

- Culture and smears
- Frozen section (DAD vs infection)
- Stains for organisms ordered at onset
- Direct immunofluorescence for unexplained hemorrhage
- Electron microscopy rarely crucial

Lung Biopsy for Chronic Disease: Technical Considerations

- Frozen tissue for immunopathology (collagen vascular disease, lymphoid proliferation)
- Fix quickly in one piece before lung deflates, then section
- Stains for elastic tissue and collagen ordered at outset
- Polarization microscopy
- Electron microscopy never crucial
**Final Clinical and Pathological Correlation**

- Acute or chronic
- Diffuse or localized
- Mild or life threatening

**BIOPSY TYPES AND ARTIFACTS**

The first step in evaluating a lung biopsy for medical lung disease is to determine the adequacy of the specimen. One way to accomplish this is to record the number of alveoli on a transbronchial biopsy or the number of lobules on an open biopsy. A bronchoscopic biopsy should have a minimum of 20 alveoli and optimally 100 alveoli. The interstitium is that space lying between epithelial basement membrane and vascular basement membrane. There is a continuity of the interstitium around bronchovascular bundles, alveolar walls, interlobular septa, and pleura. Interstitial pneumonitides generally have the least specific histological findings of the various categories of lung disease, and consequently they are the most difficult to diagnose on a transbronchial biopsy. A needle or bronchoscopic biopsy may be followed by open biopsy if a specific diagnosis is necessary. However, a specific diagnosis is not always necessary. It may be sufficient, for instance, to exclude sarcoidosis on a transbronchial biopsy and assume the diagnosis of usual interstitial pneumonitis with a nonspecific diagnosis of interstitial fibrosis histologically.

An open biopsy should have a minimum of three lobules, which means at least 2 cm in length and 1 cm in depth. A long but superficial biopsy, which samples only a few millimeters of subpleural lung, is unsatisfactory. Video-assisted thoracoscopy now supplants thoracotomy in most patients who require open lung biopsies. Thoracoscopic biopsies are intermediate in size between those obtained by a transbronchial technique and by an open thoracotomy. They are usually multiple (commonly three specimens), the larger number compensating for the smaller size of these specimens. About one half of each thoracoscopic biopsy will be compressed. Furthermore, these biopsies sample only the immediate subpleural zone and emphasize processes that can be seen rather than felt.

Artifacts lead to the overdiagnosis of a disease state and never contribute to a diagnosis of normal, which is psychologically the most difficult diagnosis to make. Most artifacts are produced either by irregular sampling or by the handling and squeezing of tissue during the surgical procedure. Each biopsy technique has artifacts peculiar to it. Diagnosis of interstitial lung disease is most prone to artifact, alveolar filling disease less so, and infectious disease and neoplasia least so.

**Artifacts of Open Lung Biopsy**

- Sampling of hard nodule
- Tip of lobe
- Left to deflate
- Crushed by clamp
- Operative hemorrhage
- Too small specimen
Diagnostic Considerations of Seemingly Normal Lung Biopsy

- Sampling problem—90%
- Respiratory bronchiolitis
- Constrictive bronchiolitis
- Cellular interstitial pneumonitis
- Interstitial edema
- Diffuse alveolar septal amyloid
- Pulmonary hypertension
- Fat emboli
- Veno-occlusive disease
- Cystic lymphangiectasis
- Capillary hemangiomatosis