

Diagnosis and Management of Idiopathic Pulmonary Fibrosis: Implications for Respiratory Care

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- Introduction
- Disease Overview
 - Epidemiology
 - Risk Factors
 - Pathogenesis
 - Natural Course of Disease
- Diagnosis
 - History
 - Physical Examination
 - Imaging
 - Pulmonary Function Tests
 - Laboratory Tests
 - Lung-Tissue Sampling
 - Pathology
- Treatment
 - Medical Treatment
 - Surgical Treatment
- Implications for Respiratory Therapists
- Summary

Although poorly understood, idiopathic pulmonary fibrosis is the most common of the idiopathic interstitial lung diseases. Its etiology is unknown, but how this fibrotic process develops in the lung has been studied over the last 60 years. It is a relatively rare disease, afflicting those 50–70 years of age, slightly more common among men than women, without racial predilection. The most common complaint is progressive shortness of breath. Pulmonary function testing reveals a restrictive ventilatory defect with a diminished diffusion capacity. The lungs demonstrate fibrotic and cystic areas interspersed with normal lung on radiographic and pathologic examination. No definitive medical treatment is available, although most patients are given trials of corticosteroids, alone or in combination with cytotoxic agents. On average, patients survive 2–4 years after diagnosis. Lung transplantation has been the only therapy shown to improve survival of those with idiopathic pulmonary fibrosis. *Key words: interstitial, lung diseases, pulmonary fibrosis, pulmonary function testing, fibrosing alveolitis, lung biopsy, management.* [Respir Care 2006;51(4):382–391. © 2006 Daedalus Enterprises]

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IDIOPATHIC PULMONARY FIBROSIS

Table 1. Histologic and Clinical Classification of Idiopathic Interstitial Pneumonias*

Histologic Pattern	Clinical, Radiologic, Pathologic Diagnosis
Usual interstitial pneumonia	Idiopathic pulmonary fibrosis/cryptogenic fibrosing alveolitis
Nonspecific interstitial pneumonia	Nonspecific interstitial pneumonia
Organizing pneumonia	Cryptogenic organizing pneumonia
Diffuse alveolar damage	Acute interstitial pneumonia
Respiratory bronchiolitis	Respiratory bronchiolitis interstitial lung disease
Desquamative interstitial pneumonia	Desquamative interstitial pneumonia
Lymphoid interstitial pneumonia	Lymphoid interstitial pneumonia

*In this context, the term "pneumonia" is interchangeable with "pneumonitis." (Adapted from Reference 8.)

Introduction

Noble and Homer published an elegant historical review recently, which described the many key discoveries regarding the pathologic processes of idiopathic pulmonary fibrosis (IPF). In that review they described the initial report by Hamman and Rich, in 1944, of 4 patients who died of a fibrotic lung disease, later named the Hamman-Rich syndrome. This syndrome was diagnosed in patients who presented with pathology findings of diffuse proliferation of fibrous tissue in the interstitium and alveolar cell lining.¹ Most clinicians during that period referred to this disease as IPF.

In 1957, Rubin and Lubliner further elaborated that this fibrotic lung process may have variants, such as those associated with systemic diseases.² In the 1960s, researchers, including Sheridan, Gaensler, and Gross, reported an acute component of this typically chronic lung disease.³⁻⁵ Gracey et al elaborated on the histopathology findings with the addition of electron microscopy images.⁶ It was also during this period that Liebow and Carrington described 5 distinct histologic patterns of idiopathic fibrotic lung diseases, in an effort to better describe their pathologic processes: usual interstitial pneumonitis (UIP), bronchiolitis interstitial pneumonitis, desquamative interstitial pneumonitis, lymphocytic interstitial pneumonitis, and giant-cell interstitial pneumonitis. The pathology description of UIP is now understood to be synonymous with that of IPF.⁷ Since the 1970s, scientists have questioned the role of the inflammatory process, the alveolar macrophage, growth factors, and epithelial cells in their contributions to understanding the pathogenesis of IPF.¹ Terminology has changed in concordance with the discoveries of distinct histopathologic diseases. Though they belong under the same category of idiopathic interstitial pneumonias, each currently described entity has its own discrete clinical course, histologic features, response to therapy, and prognosis (Table 1).

The Hamman-Rich syndrome described 60 years ago has now been reclassified as acute interstitial pneumonitis

because of its rapidly progressive course, in contrast to the chronic course of IPF.^{9,10} Additionally, histology findings of acute interstitial pneumonitis are consistent with diffuse alveolar damage, whereas IPF has the characteristic pattern of UIP. In the United Kingdom, IPF is currently known as cryptogenic fibrosing alveolitis, because earlier studies proposed an alveolar inflammatory origin for the disease.

Despite many technological advances in the field of histopathology and important contributions by many researchers, there is still no clearly described mechanism for how this fibrotic process develops in the lungs.¹

Disease Overview

Epidemiology

IPF belongs under the broad category of interstitial lung disease (ILD). In the United States there are few published large-scale registries of ILD; reviews often cite problems with obtaining good epidemiology data on ILD and IPF for many reasons, including lack of a uniform definition to identify cases, lack of pathologic confirmation at the time of diagnosis, and differences in study designs and populations.¹⁰ One study from New Mexico found the prevalence of ILD to be approximately 60 per 100,000 female patients and 80 per 100,000 male patients. Over 40% of all ILD diagnoses were found to be IPF.¹¹ An estimated prevalence of 3–30/100,000 has been reported,¹²⁻¹⁴ with an estimated 15,000 new cases diagnosed every year in the United States.¹⁵ In the United Kingdom a prevalence of 15–18 per 100,000 is estimated, with an incidence of 5 per 100,000 per year.¹⁶ A recent study in Finland reported a prevalence of 16–18/100,000.¹⁷ These low numbers illustrate that IPF is a relatively rare entity, compared to other respiratory disorders such as asthma and chronic obstructive pulmonary disease.

IPF is typically seen in patients 50–70 years old, with two thirds of the patients being over 60 years old at the time of diagnosis.^{14,18} Though highly atypical, IPF should not be excluded in younger patients. The prevalence of IPF

was 2.7/100,000 between the ages of 35 and 44 years in one report.¹⁷ Slightly more males are affected than females, but no racial or ethnic predilection has been established.¹⁴

Risk Factors

Since no etiologic factors have been identified, risk factors for developing the disease have been difficult to discern. Studies on familial cases of pulmonary fibrosis support a genetic link; however, the expression of the disease among relatives may be affected by shared environmental exposures.¹⁸ One study estimated that 0.5–2.2% of cases have a genetic basis.¹⁹ Those with a genetic predisposition may present at a younger age.⁴ Some studies identify smoking as a potential risk factor,²⁰ while others have suggested that several viruses contribute to the development of IPF.²¹ Gastroesophageal reflux disease is also now being studied as a potential association. Patti et al, using ambulatory pH and esophageal manometry, found gastroesophageal reflux disease in two thirds of patients who had IPF, one third of whom did not complain of gastroesophageal reflux disease symptoms.²² It is recommended that patients with IPF be screened for reflux, even if they do not report reflux symptoms.

Pathogenesis

The pathogenesis of any disease process begins with etiologic or inciting factors, but no such factors have been identified for IPF, so no unifying pathogenic mechanism has been elucidated. However, many theories have been put forward. In the 1970s and 1980s the pathogenesis of IPF was blamed on inflammatory processes, based chiefly on the recovery of inflammatory cells in bronchoalveolar lavage fluid from IPF patients. Since then, other reports have spawned counter-arguments. A study using gallium scans and serum markers for inflammation did not show significant differences at initial presentation or follow-up.²³ Other factors found to contradict the primary inflammation theory include discoveries that (1) early-stage UIP was not found to be any more inflammatory than late-stage UIP, (2) inflammatory interstitial diseases such as hypersensitivity pneumonitis have not been found to commonly progress to end-stage fibrosis, (3) fibrosis has been induced in animal studies without involving an inflammatory response, and (4) anti-inflammatory medications such as corticosteroids generally do not improve the outcome of the disease.¹² The current thinking is that the airway inflammation is a result rather than a cause of the fibrosis,²⁴ though this theory remains highly controversial.

A theory that calls on “multiple-hits” places the lung in a state of chronic alveolar cell injury from an unspecified source. There is increased alveolar type I cell apoptosis.²⁴

Type I cells, when absent, lead to an unchecked proliferation of progenitor alveolar type II cells. These type II cells, which are the primary responders that regenerate the alveolar epithelium, abound, leading to the proliferation of stromal cells that give rise to fibrosis.^{24,25} This abnormal “wound healing” of the lung involves fibroblast migration, proliferation, and differentiation into myofibroblasts, with concurrent up-regulated response to fibrogenic cytokines and presumed decreased myofibroblast apoptosis.^{12,25,26} An imbalance of fibrogenic cytokines has been considered, as well as alteration of the fibroblast phenotype.²⁴ Cellular proliferation is normally halted once new cells attach to the basement membrane. However, if the basement membrane is lost or aberrant, as is thought to happen from the initial insult, the signal for halting cellular proliferation is lost.

A genetic basis has also been considered since the discovery of increased expression of 4 categories of genes responsible for signaling and forming the extra-cellular matrix of the lung.²⁵ An imbalance is thought to exist between matrix production and matrix degradation.²⁴

A recent paper on the comparison of histologic patterns of UIP and nonspecific interstitial pneumonitis suggests that UIP may start out as nonspecific interstitial pneumonitis.²⁷ A more cellular pattern evolves to an intermediate disease of mixed histology, which then progresses to end-stage fibrosis. Current consensus guidelines, however, keep UIP and nonspecific interstitial pneumonitis distinct, with recommendations to evaluate patients thoroughly for connective-tissue diseases whenever a nonspecific interstitial pneumonitis pattern is found.²⁷

Vascular remodeling has also been theorized to contribute to fibrogenesis. Pro-angiogenic chemokines from unchecked cellular activity increase blood-vessel production.²⁴ This process contributes to the hypoxia because of the increase in right-to-left shunting from anastomotic formations between the systemic and pulmonary microvasculature.²⁵

Important research to further elucidate IPF’s pathogenesis continues, in the hope of finding an effective therapeutic agent, of which there are currently none.

Natural Course of Disease

Symptoms are often subtle, such that patients wait 6 months or longer until they decide to seek medical attention. Average duration of symptoms before presentation is 24 months.¹² Martinez and colleagues studied patients with mild-to-moderate IPF and found that some patients had minimal deterioration of lung function or oxygenation, others had frequent hospitalizations for respiratory illness, and others experienced acute deterioration of their lung disease.²⁸ Patients who were younger (< 50 years old), female, had less abnormal pulmonary function test (PFT)

values, and who had shorter durations (of less severe symptoms) on presentation were found to have more favorable outcomes.^{10,29} A cellular bronchoalveolar lavage was also associated with better prognosis, though this association may reflect inclusion of idiopathic interstitial pneumonias other than IPF.

Whether the patient with IPF has a slow or rapid progression of the disease, overall prognosis is generally poor.²⁴ On the average, patients survive 2–4 years from the time of diagnosis.⁸ Decreased survival has been linked to older age, poor PFT values on presentation, recent deterioration of PFT values, and advanced fibrosis on pathology examination.³ The extent of fibrosis on high-resolution computed tomography (HRCT), and substantial desaturation during the 6-min-walk test are also associated with a poorer prognosis.²⁹ End-stage fibrosis is associated with the development of severe pulmonary hypertension with cor pulmonale, and possibly with subsequent left-ventricular dysfunction. The most frequent reason for death is progression of the disease;²⁹ 40% die of respiratory failure.³ Some individuals expire sooner, possibly because of an accelerated form of the disease, whereas others die of acute infection exacerbated by having diminished baseline reserve. The risk of infection is higher because of the subsequent bronchiectasis, poor mucociliary clearance, concurrent gastroesophageal reflux disease, and (often) therapeutic immunosuppression.¹⁴

Diagnosis

History

Obtaining a thorough history from the patient is essential to arriving at a diagnosis of IPF. The history is the first step in excluding other causes of ILD, and it is paramount to obtain a complete history of exposure to environmental, occupational, recreational, or medically related substances. Onset of symptoms is often described as insidious with a gradual progression.³⁰ Typically, the most common complaint is shortness of breath on exertion, which progresses slowly to often-disabling dyspnea at rest. Though approximately 5% of patients may be asymptomatic at the time of presentation,³¹ these patients may have substantially reduced their activities so as to avoid feeling short of breath. There is usually an irritating, nonproductive cough that is refractory to suppressants. Some patients may complain of constitutional symptoms such as low-grade fever, fatigue, malaise, and myalgias, though these are generally uncommon.^{4,5,29}

Physical Examination

Fine “Velcro-like” crackles or rales are audible on mid-to-end inspiration, initially heard at the bases, but eventu-



Fig. 1. Radiograph of a patient with idiopathic pulmonary fibrosis, showing increased bilateral symmetric interstitial markings, predominantly at the bases, with associated volume loss. There are no apparent pleural effusions or lymphadenopathy. The cardiac silhouette is within normal limits.

ally detectable with auscultation over the entire lung field. Digital clubbing, commonly of the fingers and occasionally of the toes,⁸ is present in about half of patients with IPF, and the clubbing sometimes precedes the pulmonary symptoms.³⁰ Findings consistent with pulmonary hypertension and subsequent right-heart failure, such as elevated jugular venous pressure, right-ventricular heave, accentuated second heart sound, and peripheral edema, may be seen in the later stages of the disease.⁸ Cyanosis may be present, though it is often an unreliable physical finding.³⁰ Equally important to obtaining a complete history, a thorough physical examination is required to elicit the findings above, but also to look for signs of other diseases (such as connective-tissue diseases) that must be excluded for the diagnosis of IPF.

Imaging

The chest radiograph may be normal in the early stage of the disease. Abnormalities on the plain radiograph, when found, are nonspecific and may include bilateral patchy peripheral reticular infiltrates, honeycombing at the bases, and volume loss (Fig. 1).³²

Chest HRCT has greatly improved IPF imaging and is currently the imaging modality of choice in evaluating this disease.^{26,33} The reported sensitivity of HRCT to diagnose IPF is in the range of 40–70%, with specificity of over 90%.^{34–37} In one study, IPF was correctly diagnosed with HRCT in 80% of patients with biopsy-proven disease.^{26,36,38} Patchy, irregular reticular opacities, usually in a subpleural distribution and predominantly in the basilar lung regions, are present on HRCT.³⁹ Honeycombing, traction bronchi-



Fig. 2. High-resolution computed tomogram of the chest, showing the nonuniform pattern of peripheral reticular interstitial markings and demonstrating temporal and spatial heterogeneity. A: Traction bronchiectasis. B: Honeycombing.

ectasis, bronchiolectasis, and lower-lobe volume-loss are also typical findings (Fig. 2). The combination of reticular and honeycomb changes is a strong independent predictor of mortality.⁴⁰ Patients in whom > 25% of the lungs demonstrate fibrotic changes have the worst prognosis and will probably progress despite therapy.⁴¹ The parenchymal changes are indistinguishable from those seen in other processes, including asbestosis and connective-tissue diseases. Additionally, findings of > 30% ground-glass attenuation, mosaic patterns, centrilobular nodules, pleural effusions, and lymphadenopathy are less consistent with IPF,⁴⁰ so it is important to look for diseases that have similar radiographic findings and also to search for alternative diagnoses when atypical features are observed.³² Classic findings on HRCT, combined with a characteristic clinical presentation, may be sufficient to diagnose IPF in some patients and obviate open-lung biopsy.⁸

Other imaging modalities, such as magnetic resonance imaging, positron emission tomography, gallium, indium, and technetium scans, currently do not have any proven value in the diagnosis and evaluation of IPF.²⁶

Pulmonary Function Tests

PFTs are obtained for diagnostic purposes as well as to follow progression of the disease and determine responses to therapy. The IPF patient may have normal or near-normal PFTs during the early phase of the disease. In a few unusual cases the PFT values may even be normal in the presence of histologic and radiologic evidence of IPF,^{9,42} so normal PFT values do not preclude the diagnosis of IPF.

As the fibrosis ensues, the lungs progressively become “stiff,” with consequent loss of compliance. The predom-

inant abnormality is a restrictive ventilatory defect, indicated by a reduced total lung capacity (TLC) and vital capacity (VC) on body plethysmography.⁹ With concurrent smoking history and a consequent obstructive ventilatory defect, lung volumes may be normal.³² In one report, lung volumes were higher in smokers with IPF than in those with IPF who had never smoked.^{32,43} The diffusing capacity for carbon monoxide (D_{LCO}), corrected for the hemoglobin level, is decreased, typically to a greater degree than at the lung volumes at which it is measured.⁴⁴ The decline in D_{LCO} may precede the lung-volume abnormalities.³² Hypoxia at rest or with exercise is present with or without a decreased alveolar-arterial oxygen difference. Some data suggest that the degree of fibrosis correlates with the amount of oxygen desaturation during exercise testing.⁴⁵

Changes in the forced vital capacity and D_{LCO} should be monitored serially in patients undergoing medical treatment. The American Thoracic Society (ATS) and European Respiratory Society (ERS) international consensus statement outlines expected PFT values, which help determine clinical response to therapy.³² Typically, 2 or more measurements (as detailed below) documented on 2 consecutive visits over a 3–6 month period determine a stable, favorable, or failed response to therapy. A < 10% change in TLC or VC, a < 15% change in D_{LCO} , or no change in O_2 saturation or P_{aO_2} is considered stable. A \geq 10% increase in TLC or VC, a \geq 15% increase in D_{LCO} , or an improvement in O_2 saturation or P_{aO_2} is considered a favorable response to therapy. A \geq 10% decrease in TLC or VC, a \geq 15% decrease in D_{LCO} , or a worsening of O_2 saturation or rise in the alveolar-arterial oxygen difference at rest or exercise is considered a failed response to therapy.³² Forced vital capacity of 60–70% of predicted and D_{LCO} of 50–60% of predicted indicate a poor prognosis.⁴⁶

Laboratory Tests

No specific serum laboratory tests are available to diagnose IPF, but use of available tests can aid in differentiating IPF from other diseases and identifying complications and coexisting entities. Routine laboratory tests in the evaluation, including complete blood cell count, may support the presence of an infection. Erythrocyte sedimentation rate, rheumatoid factor, and anti-nuclear antibody are obtained to rule out an alternative diagnosis or coexistence of an autoimmune process.

Lung-Tissue Sampling

Bronchoscopy is rarely helpful in making a definitive diagnosis of IPF. Bronchoalveolar lavage fluid is typically obtained for Gram stain, culture, and differential cell counts in search of alternative diagnoses, including infection.⁸

Table 2. Diagnostic Criteria for Idiopathic Pulmonary Fibrosis in the Absence of a Surgically-Obtained Lung Biopsy

Major Criteria

- Exclusion of other known causes of ILD, such as certain drug toxicities, environmental exposures, and connective-tissue diseases
- Abnormal PFT values that evidence restriction (reduced VC, often with increased FEV₁/FVC) and impaired gas exchange (increased P_{(A-a)O₂}, decreased P_{aO₂} during rest or exercise, or decreased D_{LCO})
- Bibasilar reticular abnormalities with minimal ground-glass opacities on HRCT
- Transbronchial lung biopsy or BAL fluid with no features that support an alternative diagnosis

Minor Criteria

- Age > 50 years
- Insidious onset of otherwise unexplained dyspnea on exertion
- Duration of illness > 3 months
- Dry or “Velcro”-like bibasilar, inspiratory crackles

ILD = interstitial lung disease
 PFT = pulmonary function test
 VC = vital capacity
 FEV₁ = forced expiratory volume in the first second
 FVC = forced vital capacity
 P_{(A-a)O₂} = alveolar-arterial oxygen difference
 D_{LCO} = diffusing capacity of the lung for carbon monoxide
 HRCT = high-resolution computed tomography
 BAL = bronchoalveolar lavage
 (Adapted from Reference 8.)

Tissue samples from transbronchial biopsies are commonly inadequate and serve only to rule out other causes of interstitial lung disease.

Sampling lung tissue via thoracotomy or thoracoscopy is the accepted standard for making the diagnosis of IPF. Indications for surgical lung biopsy include an unclear diagnosis, age < 50 years old, constitutional symptoms, atypical features on chest imaging, and rapid progression of the disease.^{7,26} In selected cases, obtaining lung tissue via surgical lung biopsy may not be practical, and a clinical diagnosis may need to suffice. The ATS and ERS have created criteria for diagnosing IPF without a lung biopsy (Table 2). All of the major criteria and three of the 4 minor criteria greatly improve the likelihood of making a correct clinical diagnosis of IPF.⁸

Pathology

“Usual interstitial pneumonia,” the pathology description of IPF, originated from Liebow and colleagues in 1969, and was named “usual” because it was the most common pattern observed in the fibrotic lung diseases reviewed during that period.⁴⁷ We now know that the “UIP pattern” is not exclusive to IPF; it is also found in other diseases, including scleroderma, rheumatoid arthritis, polymyositis, dermatomyositis, and occupational lung diseases such as asbestosis. However, UIP has become synonymous with IPF and is the current term for the disease, though many clinicians still use IPF and UIP interchangeably.

The histopathology shows a loss of the alveolar structure, with subsequent formation of areas made of collagen

and fibroblastic foci. These foci are made of fibroblasts and myofibroblasts that form in the air spaces and interstitium.²⁵ Temporal heterogeneity is observed, characterized by a pattern of normal lung alternating with areas of inflamed or fibrotic lung interspersed with areas of honeycombing (Figs. 3, 4, and 5).²⁴ Honeycombed areas are composed of mucin-filled cystic airspaces lined by bronchiolar epithelium. Patients suffering from an accelerated phase (or “exacerbation”) of IPF may exhibit a UIP pattern along with signs of infection, alveolar damage, or capillary inflammation.⁸ Flaherty and colleagues suggested that a multi-disciplinary approach, involving a pulmonologist, radiologist, and a pathologist, is vital to arriving at the correct diagnosis of IPF.⁴⁷

Treatment

Medical Treatment

Although no form of medical therapy has yet been discovered that prolongs survival, the general approach to treatment is to attempt to suppress progression with corticosteroids, alone or in combination with cytotoxic agents such as azathioprine or cyclophosphamide. Three decades ago it was considered standard therapy that, once corticosteroids were started, they “should be continued for the life of the patient.”³⁰ We now know that corticosteroids have no proven survival benefit.²⁶ Although well-tolerated by most, addition of azathioprine to corticosteroids also has little or no benefit in the treatment of IPF.⁴⁸ Nevertheless, based on small trials, a combination of prednisone and azathioprine is proposed as standard therapy in the IPF

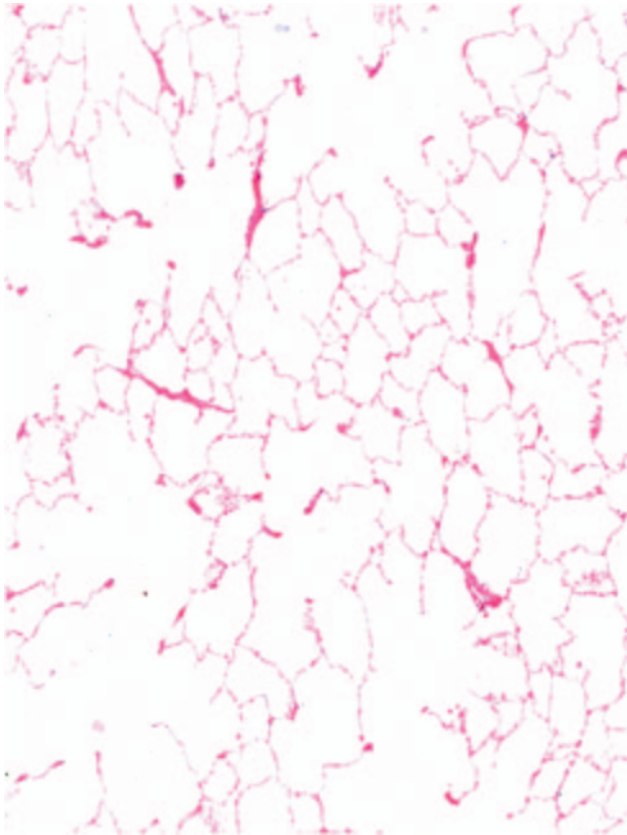


Fig. 3. Normal lung architecture.

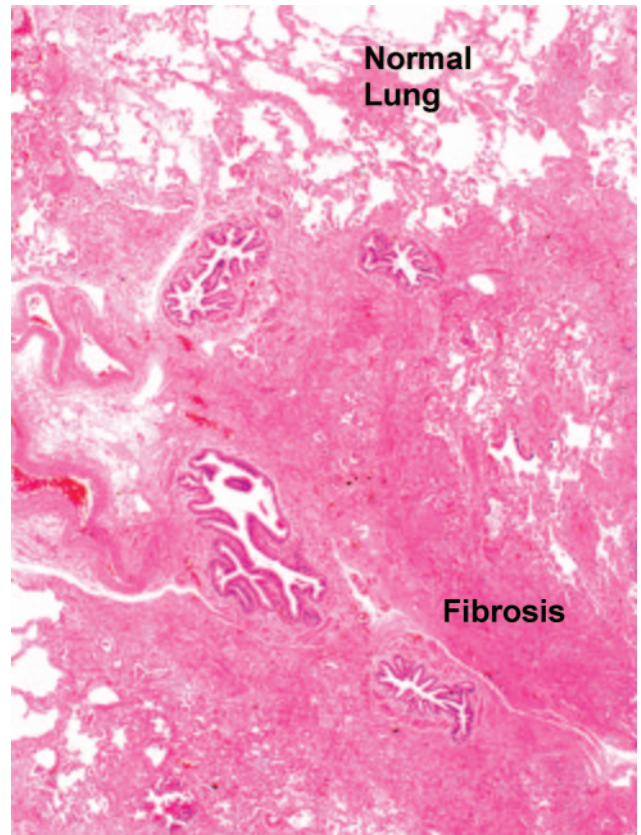


Fig. 4. Fibrotic lung interspersed with areas of normal lung.

consensus statement from the ATS and ERS,³² which recommended a starting dose of prednisone (or its equivalent) of 0.5 mg/kg (ideal body weight) per day for 4 weeks, with a gradual taper down to 0.125 mg/kg (ideal body weight) per day. Azathioprine is started at 2–3 mg/kg (ideal body weight) per day. Doses are typically initiated with 25–50 mg/d and increased gradually, by 25-mg increments every 7–14 days until a maximum dose of 150 mg/d is reached. It is important to monitor for the many adverse effects of prednisone and the mainly hematologic and hepatocellular effects of azathioprine during the therapy. Since objective improvement may not be observed until after 3 months of treatment, it is recommended that this combination therapy, if well tolerated, be continued for at least 6 months. If the patient's clinical condition is worse after 6 months, the medications should be discontinued or changed. The decision to continue long-term medical therapy should be made on an individual basis, based on evidence of sustained improvement or stabilization.³² Similar to prednisone and azathioprine, studies with cyclophosphamide in combination with corticosteroids also have not demonstrated any significant survival benefit⁴⁸; in fact, substantial toxic effects have been reported.⁴⁹ The ATS/ERS guidelines recommend starting cyclophosphamide at 25–50 mg/d and

increasing gradually by 25-mg increments every 7–14 days until a maximum dose of 150 mg/d is reached.³²

The refractory nature of IPF to anti-inflammatory and cytotoxic agents led to recent studies on the role of regulating fibroblast function and collagen synthesis.²⁴ In a multinational study, interferon-gamma-1b did not show a significant effect on the primary end point of survival, but it did demonstrate a potentially greater benefit for those with less severe disease.⁴⁸ The INSPIRE trial, started in December 2003, is currently ongoing to further discern the benefits of interferon-gamma-1b.⁴⁹

Neither colchicine nor penicillamine has been found to be any more effective than corticosteroids alone in the treatment of IPF.^{48,49} Pirfenidone is under investigation, and though in prior studies this drug has been reported to stabilize the disease,^{48,49} a mortality impact has yet to be observed.²⁶

A study of N-acetylcysteine, though not powered to detect an effect on survival, did find a more favorable rate of decline of forced vital capacity and D_{LCO} in those who received the drug versus those on placebo.⁵⁰

Other agents being studied include CD36 synthetic peptide, captopril, decorin (anti-transforming growth factor), bosentan, niacin, and taurine.²⁶

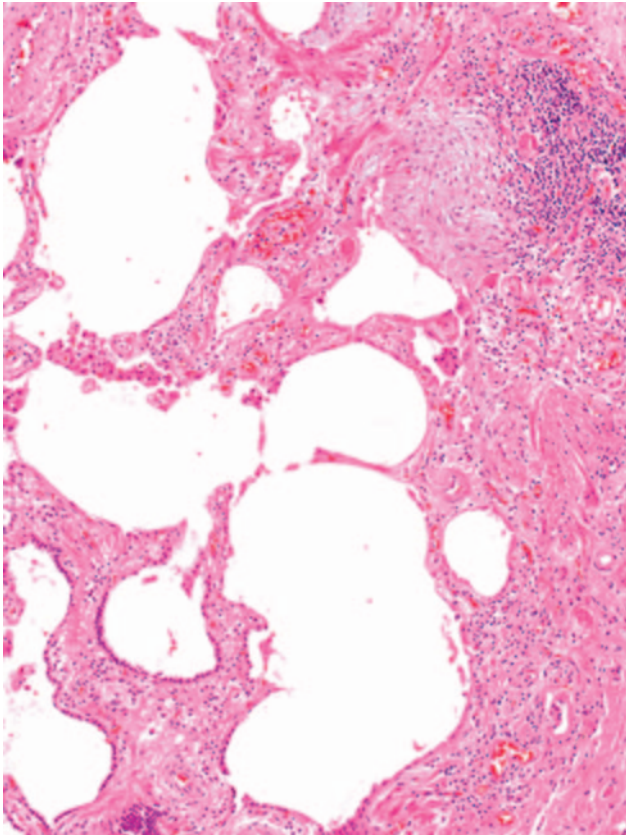


Fig. 5. A: Fibroblastic foci at the progressive edge of fibrotic lung tissue. B: Nonspecific chronic inflammation.

Surgical Treatment

Of all the interventions adequately studied, only lung transplantation has been proven to prolong the lives of patients with IPF. As mentioned before, survival after diagnosis averages 2–4 years. A recent report indicated that the median waiting time for a lung transplant has increased to almost 4 years in the United States. In that report it was observed that IPF patients have the worst deterioration, having greater than 30% mortality while awaiting transplantation.⁴⁶ Thus, regardless of symptomology or optimized medical therapy, the decision to refer the patient for lung transplantation should be made as early as possible, given the progressive nature of this incurable disease. At 1 year post-transplant, the survival rate is 65%, decreasing to 38% after 5 years.⁴⁶

Implications for Respiratory Therapists

Respiratory therapists will have many opportunities to care for patients with IPF, in the outpatient and inpatient settings. PFTs are obtained initially as part of the basic evaluation, and serially to follow the progression of the disease and monitor response to therapy. Exercise testing

has also had an increasingly important role in monitoring disease progression and prognosis. Supplemental oxygen is often needed, and occasionally high-flow oxygen systems are necessary to maintain these patients. A pulmonary rehabilitation program, though more commonly used by patients who have chronic obstructive pulmonary disease, may improve quality of life for the IPF patient.⁵¹

Once hospitalized, patients often require respiratory care with supplemental oxygen, as well as routine administration of bronchodilators for those with concurrent obstructive disease. Patients with severe fibrosis and little pulmonary reserve may experience progression of their disease or suffer an infection, which can lead to hospitalization and eventual admission to the intensive care unit. Mechanical ventilation is challenging in this population, as these patients are often difficult to ventilate *and* oxygenate.

If the patient recovers from the acute illness, he or she awaits lung transplantation. Transplant recipients who are without postoperative complications are liberated from the ventilator as soon as they recover from the anesthesia. Patients are encouraged to perform incentive spirometry during the first few days after the surgery. Promptly after discharge they are enrolled in a pulmonary rehabilitation program to further strengthen their respiratory muscles and improve overall conditioning. Transplant patients are then followed with serial PFTs to screen for potential graft complications.

Thus, there are a myriad of opportunities for the respiratory therapist to participate in caring for IPF patients, in both the clinic and hospital setting. The respiratory therapist, along with the pulmonologist, pathologist, and radiologist are important members of the multidisciplinary team who serve to optimize the diagnosis and management of patients with IPF.

Summary

Though IPF is a relatively rare disease, it is the most common of the idiopathic interstitial lung diseases. Theories about IPF's etiology are under debate. IPF mostly afflicts people 50–70 years of age, it is slightly more common among men than women, and it does not occur more or less frequently in different races. The most common complaint is progressive shortness of breath. Pulmonary function testing indicates a restrictive ventilatory defect and diminished D_{LCO} . The radiograph and pathology appearance of IPF is of fibrotic and cystic areas interspersed with normal lung. No current medical treatments improve survival, but most IPF patients are nevertheless given trials of corticosteroids, alone or in combination with cytotoxic agents. Lung transplantation is the only known therapy that improves survival. On average, patients survive 2–4 years after diagnosis.

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IDIOPATHIC PULMONARY FIBROSIS

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