Introduction
What is IPF?
Identifying and Diagnosing IPF
Multidisciplinary Care for IPF
Post-test and Evaluation

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The identification and management of patients with idiopathic pulmonary fibrosis (IPF) is replete with challenges. The symptoms of IPF are common to a variety of pulmonary conditions and easily missed by patients and clinicians. Suspicion of IPF often does not arise for at least several months after the onset of symptoms. Indeed, a key and common reason contributing to delayed diagnosis is the lack of expertise in IPF among community physicians. Primary care clinicians and pulmonary therapists may be unaware of the core signs, symptoms, and tests for IPF and its differential diagnosis. The early symptoms of IPF, dyspnea on exertion and dry cough, are often ignored by patients and primary care physicians and are attributed to aging or smoking. Because IPF most commonly occurs in men, older individuals (>50 years), and those with a history of smoking, clinicians may be focused on more common causes of pulmonary symptoms, especially in the community setting.

Studies of IPF also found that a multidisciplinary approach, including radiologists, pathologists, and pulmonologists, improved diagnostic agreement at both academic and community sites. A study from Europe found that a multidisciplinary approach, including radiologists, pathologists, and pulmonologists, improved diagnostic agreement at both academic and community sites.

The availability of new therapies shown to slow disease progression highlights the need for earlier diagnosis and intervention in IPF. It has been suggested that a “window of opportunity” may exist during which treatment can promote optimal outcomes. Furthermore, delays in diagnosis may limit treatment options, as well as increasing costs, reducing patient quality of life, and impacting survival. This CME/CE supplement.

Learning Objectives
At the conclusion of this program, participants should be better able to:

- Utilize the signs, symptoms, and epidemiology of IPF to better recognize patients in need of specialty care.
- Employ a multidisciplinary approach for IPF to enhance patient outcomes.
- Provide timely referral of patients with IPF to tertiary care to improve survival.
- Review clinical trial data supporting the efficacy and safety of pirfenidone and nintedanib.
- Select appropriate pharmacologic therapy for patients with IPF.
- Communicate with patients with IPF and provide effective disease-state education.

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- Dr. Chung has no relevant financial relationships to disclose.
- Dr. Cosgrove has been a consultant for: Boehringer Ingelheim, Genentech, and Global Blood Therapeutics. He also owns stock in Boehringer Ingelheim, Bristol Myer Squibb, and Genentech.
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**Introduction**

Idiopathic pulmonary fibrosis (IPF) is a rare but lethal lung disease with a prognosis worse than many cancers. The disease is characterized by insidious onset and a progressive decline in lung function due to fibrosis of the lung parenchyma. Although rare enough to be considered an orphan disease, IPF still accounts for 15,000 to 40,000 deaths per year in the United States—and the incidence and mortality of IPF are increasing.1-4

The prognosis of IPF is poor, with median survival estimates of 3.8 years or less from diagnosis.4 There is currently no cure for IPF, but two new drugs were recently approved by the FDA: nintedanib and pirfenidone. In clinical trials, these agents slowed the progression of disease in many patients, but they have not yet been shown to improve survival.5,6 The only intervention so far shown to extend survival in patients with IPF is lung transplantation.7 However, the availability of these new therapies highlights the need for earlier diagnosis and intervention in IPF. It has been proposed that a “window of opportunity” may exist during which treatment can promote optimal outcomes.8

Unfortunately, the gradual onset and nonspecific symptoms of IPF contribute to a high rate of missed or delayed diagnosis, leaving many patients untreated or inappropriately treated. Furthermore, delays in diagnosis may limit treatment options, increase costs, reduce patient quality of life, and decrease survival.9,10 In 2011 and 2015, updated guidelines for the management of IPF were published by an international coalition of societies, including the American Thoracic Society (ATS).7,11 These guidelines provide clinicians with evidence-based recommendations for the diagnosis and management of IPF. As valuable as the guidelines are, the limited evidence available means that IPF remains a clinical challenge for primary and specialty providers.

Persistent gaps in the care of patients with IPF include delayed or inaccurate diagnosis, delayed referral to specialty care, limited use of recommended multidisciplinary care, variable approaches to management, and poor patient-provider communication. This monograph attempts to address these gaps by reviewing the latest research into IPF and the key features of the disease to facilitate recognition of IPF in primary care, timely referral to specialists, and optimal management to maximize quality and quantity of life. Highlighted throughout the monograph are the experiences of real patients with IPF and their caregivers, as elicited through personal interviews. These individuals report their stories of delayed diagnosis, frustrations with the health care system, and preferences and hopes for therapy. Finally, data are included from an online clinical simulation to illustrate the real-world decisions and performance of both primary care and specialty clinicians in the diagnosis and management of this challenging disease. This online simulation program includes images from diagnostic studies and audio and video commentary from leading experts in IPF.

**What is IPF?**

IPF is the most common and lethal of the idiopathic interstitial pneumonias, a subgroup of the family of interstitial lung diseases (ILDs; Figure 1).12 ILDs involve inflammation of the interstitium, or the tissue and spaces around the alveoli of the lungs. IPF accounts for about 20% of all ILDs and is the most common and severe of the idiopathic interstitial pneumonias.12

IPF is clinically characterized by nonspecific symptoms, such as dyspnea on exertion and dry cough, and requires specific investigations (eg, high-resolution CT) for diagnosis. The disease is associated with aging (median age of onset 65-70 years) and is more common in men and patients with a history of smoking.7

Features of IPF that cloud understanding of the disease include its variable natural history, a high rate of complicating comorbidities, a paucity of accurate indicators of disease progression, and limited insight into its pathogenesis.13,14 Other factors contributing to suboptimal management include variation among providers in the application of guidelines recommendations and in the analysis of histologic and radiographic assays.14

**Pathophysiology**

The pathophysiology of IPF is poorly understood but likely involves multiple pathways and complex interactions between genetic, epigenetic, metabolic, and environmental factors.15 Indeed, the diversity of presentations, findings, and courses of disease in IPF suggest that fibrosis results from multiple pathogenic pathways, each of which may be influenced by endogenous and environmental factors.16 This multifactorial pathogenesis may explain the often poor results from clinical trials of agents that target individual mediators or pathways in IPF.15

The current model for the pathogenesis of IPF involves abnormal wound healing in response to persistent or recurrent injuries by environmental factors (eg, cigarette smoke, microaspirations, infection, dusts) on a background of genetic susceptibility.15,17 The result is an imbalance between profibrotic and antifibrotic...
Risk Factors for IPF
Although IPF is an idiopathic disease whose causes remain unknown, several potential risk factors have been identified, including cigarette smoking, environmental exposures, infection, gastroesophageal reflux, and genetic factors. The association between smoking and IPF is strong, especially among patients with a smoking history of >20 pack-years. Increased risk for IPF has also been described in association with exposure to certain dusts (eg, metal, wood, and agricultural dusts) and microbial agents (eg, Epstein-Barr virus, cytomegalovirus, and human herpesvirus-7 and -8). Investigation into these associations continues, and the role of exposures to dust or microbial agents in IPF remains putative. Gastroesophageal reflux is very common in patients with IPF and is often asymptomatic. An intriguing mechanistic association between microaspirations and IPF has been proposed, but no clear causative connection has yet been established. As noted, genetic factors likely play a role in susceptibility to IPF, and a small fraction of cases (<5%) involve familial forms of IPF (ie, affecting two or more family members). Several genetic factors have been investigated in sporadic IPF, but no genetic markers have yet been validated.

The Tragedy of Delayed Diagnosis
The identification of patients with IPF remains a major clinical challenge, especially in the primary care setting. The symptoms of IPF are common to a variety of conditions and are easily missed by patients and clinicians. Suspicion for IPF often does not arise for at least several months after the onset of symptoms. Because IPF most commonly occurs in men, older individuals (>50 years), and those with a history of smoking, clinicians may focus on more common causes of pulmonary symptoms in these patients, especially in the community setting. Indeed, the early symptoms of IPF, dyspnea on exertion and dry cough, are often ignored by patients and their physicians or attributed to aging or smoking history.

A central diagnostic challenge in IPF is its differentiation from a wide range of conditions (see Figure 1), some of which may be nearly indistinguishable from IPF without a thorough history, examination, and appropriate imaging. The results of a poor understanding of the diagnosis of IPF are evident in clinical studies. In one study, nearly half of patients initially diagnosed with IPF based on the 2011 ATS guidelines were found instead to have hypersensitivity pneumonitis (a clinically similar but pathophysiologically distinct ILD; see Figure 1). The importance of this distinction is highlighted by the differences in treatment approach; immunosuppressive therapy may be appropriate for hypersensitivity pneumonitis, but has been associated with increased risk for death in patients with IPF.
Identifying and Diagnosing IPF

Diagnostic Approach

As noted, the typical clinical presentation of IPF is nonspecific: progressive dyspnea on exertion and dry cough. Features that may increase suspicion for IPF include male gender, age >50 years, history of smoking (current or former), history of gastroesophageal reflux disease (GERD), and family history of IPF (or pulmonary disease of unknown etiology). In studies, the age range of patients with IPF is 55-80 years, and older age (ie, >70 years) is the most powerful clinical predictor of IPF in a patient with idiopathic ILD. Conversely, the probability of IPF in a patient younger than 50 years is extremely low.

Even a patient with most of these clinical features (except a family history of IPF) is likely to have a more common disorder, such as asthma, COPD, pneumonia, lung cancer, or heart disease. But recognizing this clinical pattern is the first step to correctly diagnosing IPF.

Physical Examination

On physical examination, patients with IPF demonstrate fine bibasilar crackles on auscultation. These fine inspiratory crackles, often called “Velcro crackles” because of their characteristic sound, are nearly constant in IPF and develop early in the course of the disease. To identify bibasilar crackles, auscultation must be performed over all lung fields, especially the lower fields; a cursory examination may miss this critical feature of IPF. Crackles on auscultation—which should never be considered normal—may result from a variety of diseases, including pneumonia, heart failure, IPF, or other pulmonary disease. Although Velcro crackles are not specific for IPF, their presence in an age-appropriate patient should prompt a thorough evaluation, including use of high resolution CT (HRCT). In fact, Velcro crackles in an older male patient likely signify IPF.

Other elements of the physical examination may also influence the likelihood of IPF. For example, finger clubbing is present in 25%-50% of patients with IPF. Such findings as weight loss or muscle wasting are not common in IPF and may suggest other diseases. Examination of the joints and skin may identify features consistent with alternative diagnoses, such as connective tissue disease. A cardiac examination is appropriate to identify features consistent with heart failure or other conditions.

Investigations

Studies that can help to rule out common causes of presenting symptoms and increase suspicion for IPF include pulmonary function tests (PFTs), oxygen saturation, and imaging. Findings on PFTs may suggest asthma or COPD but are not diagnostic for IPF. Typically, patients with IPF demonstrate a restrictive pattern on PFT. However, COPD may be comorbid with IPF in some patients (such as those with a history of smoking), and a PFT pattern that suggests COPD does not necessarily rule out IPF. When IPF is a possibility, DLCO should be included with the PFTs; DLCO is often reduced in patients with IPF due to impaired gas exchange. Finally, some PFT findings, including DLCO, have prognostic utility following a diagnosis of IPF.

Oxygen saturation is a standard test for patients who present with pulmonary or cardiac symptoms. However, because patients with IPF may have normal or near-normal oxygen saturation at rest, clinicians should consider a simple functional test of oxygen saturation. The six-minute walk test (6MWT) is a validated test that can easily be performed in the primary care setting by having patients walk as far as they can within six minutes (or until the onset of symptoms). The 6MWT can be performed in a hallway that has been measured and marked at regular intervals to determine the total distance walked within six minutes, or before the patient becomes symptomatic. A clinician walks with the patient to monitor oxygen saturation and symptoms. Metrics for the 6MWT include total distance walked, oxygen saturation on pulse oximetry, heart rate, and onset of symptoms such as dyspnea or chest pain. As noted by ATS guidelines, desaturation (ie, oxygen saturation <88%) on function indicates the need for supplemental oxygen and may inform prognosis in IPF.

Clinical Pearls

Recognizing the Key Clinical Features of IPF

- Symptoms: dry cough and dyspnea on exertion
- Age: >50 years; median age 65-70 years
- Gender: male predominance
- Smoking history: especially ≥20 pack-year history
- Bibasilar crackles: nearly constant in IPF; sound like Velcro being pulled apart
- Finger clubbing: occurs in 25%-50% of cases

Initial Investigations for Patients with Symptoms of IPF

- Spirometry/PFTs: restrictive pattern, reduced DLCO
- Pulse oximetry (with functional test): desaturation on activity
- Plain radiography: rule out common conditions (eg, pneumonia, heart failure)
- High-resolution CT: gold-standard imaging test for IPF*

*Often ordered in specialty care setting. PFTs=pulmonary function tests DLCO=diffusing capacity for carbon monoxide

6 globalacademycme.com/rheumatology • A Current Practice Snapshot of IPF Diagnosis and Management: Where We Are and Where We Need to Be
The Role of Imaging

The Right Test Can Be Diagnostic

Imaging is the most critical study in the diagnosis of IPF. Plain chest radiography is likely the first choice of many primary care clinicians, and may identify infiltrates (suggesting pneumonia), cardiomegaly (suggesting heart failure), or nodules or masses (suggesting lung cancer). In more advanced cases of IPF, plain radiography may identify evidence of reticular changes. However, plain radiography is neither sensitive nor specific for the diagnosis of IPF, and it often identifies no abnormalities in early stages of the disease.

As a side note, plain radiography is also no longer recommended for routine lung cancer screening. Guidelines from multiple organizations, including the American Cancer Society and the US Preventive Services Task Force, currently recommend low-dose CT for annual screening of asymptomatic patients at high-risk for lung cancer, defined as patients aged 55-80 years with a ≥30 pack-year smoking history who currently smoke or who quit within the last 15 years.24,25 The guideline authors note low-dose CT offers greater sensitivity compared to plain radiography and reduced exposure to ionizing radiation compared to conventional CT.

However, neither low-dose nor conventional CT provides sufficient detail to definitely identify the hallmark radiographic feature of IPF: a pattern of findings called a usual interstitial pneumonia (UIP) pattern. In cases with clinical suspicion for IPF, the gold-standard imaging study is high-resolution CT (HRCT).7 HRCT provides sufficient detail to definitely identify the hallmark radiographic feature of IPF: a pattern of findings called a usual interstitial pneumonia (UIP) pattern. In cases with clinical suspicion for IPF, the gold-standard imaging study is high-resolution CT (HRCT).7 HRCT has 90%-100% positive-predictive value for a pathologic UIP pattern (i.e., a pattern confirmed by biopsy with histology).

According to current guidelines, this UIP pattern is a required criterion for a diagnosis of IPF. Features on HRCT that are consistent or inconsistent with UIP pattern on HRCT are illustrated in Table 1. In about two thirds of cases, a diagnosis of IPF can be made based on clinical history and a finding of UIP on HRCT.15

Although HRCT is considered the gold-standard test and is recommended by guidelines, the diagnostic features on HRCT are found in only about half of all patients with IPF, further increasing the difficulty of diagnosis.26 In fact, the typical honeycomb features of IPF on HRCT are a relatively late manifestation of the disease.20 In a patient with Velcro crackles or other potential signs of IPF who has does not have clear honeycombing on HRCT, a lung biopsy may be considered to support earlier diagnosis.23 When lung biopsies are not possible, either due to the patient’s condition or their resistance to an invasive procedure, the pulmonologist may order a surgical lung biopsy to help confirm the diagnosis.

### Table 1. HRCT Criteria for UIP Pattern

<table>
<thead>
<tr>
<th>UIP Pattern (all 4)</th>
<th>Possible UIP (all 3)</th>
<th>Inconsistent With UIP (any)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subpleural, basal predominance</td>
<td>Subpleural, basal predominance</td>
<td>Upper or mid-lung predominance</td>
</tr>
<tr>
<td>Reticular abnormality</td>
<td>Reticular abnormality</td>
<td>Peribronchovascular predominance</td>
</tr>
<tr>
<td>Honeycombing with or without traction bronchiectasis</td>
<td>Absence of features inconsistent with UIP pattern (third column)</td>
<td>Extensive ground glass abnormalities</td>
</tr>
<tr>
<td>Absence of features inconsistent with UIP pattern (third column)</td>
<td></td>
<td>Profuse micronodules</td>
</tr>
</tbody>
</table>

### CLINICAL PEARLS

- **ATS Required Diagnostic Criteria for IPF**
  - Exclusion of other known causes of ILD (e.g., environmental exposures, connective tissue disease, drug toxicity)
  - Presence of a UIP pattern on HRCT
  - Combinations of HRCT and surgical lung biopsy pattern

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### PATIENT EXPERIENCES

**Doing the Right Tests**

A 67-year-old man

“We circled everything for about two years. I saw a cardiologist, an ENT, an allergist—I was diagnosed with everything from sinus problems to allergies. I had multiple sessions of bronchitis and pneumonia. I went through two hernia operations because the coughing was so violent. The GP was trying to figure it out, but I was getting more and more sick.

“Then I saw an infectious disease doctor. He would ask questions, sit and think, scribble, ask more questions, circling around. After 45 minutes, he dragged me by the hand up a flight of stairs with an oximeter on my finger and nailed it.

He said, ‘I think you have pulmonary fibrosis.’ He called my insurance company to get me a high-res CT scan, and got me an appointment with a pulmonologist the next day. The pulmonologist wanted a lung biopsy. Within the next week and a half, a lung biopsy confirmed IPF.”

A 67-year-old man
test, patients are left with a diagnosis of suspected IPF, potentially preventing the initiation of disease-appropriate therapy.10

Further complicating diagnosis, a UIP pattern may also be found in other disorders.15 Even in specialty centers, a diagnosis of unclassifiable ILD is made in about 10% of patients who present with progressive pulmonary fibrosis.27 For these reasons, evaluation of suspected IPF by a multidisciplinary team is recommended by guidelines.

When Imaging May Not Be Enough: The Roles of Biopsy and Bronchial Alveolar Lavage

When a diagnosis of a UIP pattern is made with high confidence based on HRCT, a lung biopsy is not required, and the diagnosis of IPF is made by collaboration between the pulmonologist and radiologist. In some situations, such as when HRCT findings are inconclusive but suggest UIP, further testing may be required. This testing may include bronchoscopy, surgical lung biopsy, and/or bronchial alveolar lavage. In these cases, the care team, including the pulmonologist, radiologist, and/or pathologist, should review and discuss the necessary tests and findings.

Surgical lung biopsy is an invasive procedure with significant risk for mortality; depending on the study, mortality rates of 1%-6% (or even higher in non-elective cases) have been reported.28-30 Lung biopsy with histology can contribute to the diagnosis of conditions such as granulomatous disorders (eg, sarcoidosis) and can be used to confirm a diagnosis of IPF or differentiate uncertain diagnoses. However, as noted, HRCT findings have 90%-100% positive-predictive value for a pathologic UIP pattern, and surgical lung biopsy is not essential to confirm a UIP pattern identified on HRCT.

In fact, the appropriate role of surgical lung biopsy in the diagnosis of IPF remains debated. ATS guidelines suggest a role for surgical lung biopsy when HRCT findings for a UIP pattern are uncertain. However, small studies suggest that a possible UIP on HRCT may still have high specificity for IPF. For example, a retrospective study found that age >65 years and an HRCT finding of reticular abnormalities in the absence of honeycombing (the hallmark radiologic feature of IPF) had >95% likelihood of discriminating IPF from other interstitial pneumonias.21 In other words, older age and HRCT findings of possible UIP predicted a diagnosis of IPF in >95% of cases in this study, suggesting that surgical lung biopsy would be unnecessary in the vast majority of cases where HRCT findings were neither inconsistent nor definitive for UIP.

A more recent study goes even further. In this retrospective study of 241 individuals enrolled in an IPF treatment trial, investigators found that 94% of patients with possible UIP on HRCT had histologic evidence of UIP on biopsy – but 95% of patients with HRCT findings inconsistent with UIP still had histologic evidence of UIP on biopsy.31 Because patients in this study were already diagnosed with IPF and enrolled in an IPF clinical trial, the findings cannot be generalized to the broader population of patients with IPF or ILD. Nevertheless, the findings do suggest that, in patients with clinical features consistent with IPF (ie, male, history of smoking, older age) and lacking alternative etiologies, IPF remains a likely diagnosis, regardless of HRCT findings.32

Bronchial alveolar lavage (BAL) also can contribute to the diagnosis of ILD when radiographic findings are not definitive. According to ATS guidelines for IPF, it is unclear whether BAL contributes significantly to the specificity of diagnosis.7 The ATS has also published guidelines for the use of BAL in the diagnosis of ILD.33 These guidelines note that BAL may be useful in the evaluation of patients with possible ILD when confidence in a UIP pattern on HRCT is lacking. Findings that may aid in the differential diagnosis include a predominantly inflammatory pattern, such as increased lymphocytes, eosinophils, or neutrophils, on BAL. For example, prominent lymphocytosis (>40%) may suggest hypersensitivity pneumonitis. However, a normal cell profile on BAL does not exclude microscopic abnormalities, and BAL alone is insufficient to diagnose most forms of ILD.7,33
Differential Diagnosis
As outlined by ATS guidelines, the diagnosis of IPF requires the exclusion of other forms of ILD (see Figures 1 and 2). This differential diagnosis relies on serologic blood tests, a detailed patient medical history, and identification of any relevant environmental exposures.

The Role of Primary Care: Timely Referral
Even for specialists, IPF can be challenging to diagnose and manage. The role of the primary care clinician is not necessarily to confirm a diagnosis of IPF but rather to recognize features that suggest an atypical or serious pulmonary disease and refer the patient to a specialist.

Too often, the challenges of recognizing the features of IPF in primary care result in delayed referral and diagnosis. In one cohort study, the median delay between onset of dyspnea and initial evaluation in tertiary care was 2.2 years – an especially long time considering that the median survival of patients with IPF is 3.8 years. A longer referral delay in this study was associated with increased risk of death, independent of disease severity. Findings such as these highlight the need for timely recognition of features that suggest an ILD (or IPF specifically) and immediate referral to a specialist.

The need for specialty care in IPF is highlighted by studies that demonstrate diagnostic inconsistencies among physicians. For example, a retrospective study found a lack of agreement between community and academic physicians in the diagnosis of parenchymal lung diseases, including IPF. In this study, the likelihood of reaching a diagnosis of IPF differed between community and academic settings. The study also found that a multidisciplinary approach, including radiologists, pathologists, and pulmonologists, improved diagnostic agreement at both academic and community sites. These data highlight the benefits of referral and multidisciplinary collaboration.

PATIENT EXPERIENCES
The Importance of Specialty Care
A 67-year-old man
“If I had to give advice to someone having symptoms that might be IPF, I’d tell them to get to a pulmonologist. And if you’re not convinced of the answer, see a second doctor. I think waiting can let you be robbed of some of your life. I don’t have time to ignore that flower; I don’t have time to waste. Stop and pull the precious parts of life out—a kid, a cat, a really good book—savor it. That’s what they need a correct diagnosis for.”

Figure 3. The multidisciplinary team
The challenges of diagnosis and early referral indicate the need for the evaluation of possible IPF by an experienced multidisciplinary team.
A Current Practice Snapshot of Idiopathic Pulmonary Fibrosis Diagnosis and Management: Where We Are and Where We Need to Be

This infographic was developed using a mix of data from scientific sources and two currently available CME/CE simulation activities designed to educate clinicians and also identify trends in IPF diagnosis and management. A “Clinical Practice Snapshot” was created from the simulation data to enable a comparison of current practice against the IPF evidence base and IPF guidelines (both presented in this supplement). Primary care physicians and pulmonologists participated in each simulation, providing an additional layer of data for analysis.

1 Delayed Diagnosis Is the Tragedy of IPF

IPF is the most common and severe of the idiopathic interstitial pneumonias. Identification of patients with IPF remains a major clinical challenge, especially in the primary care setting. The symptoms of IPF are common to a variety of conditions and are easily missed by patients and clinicians, and suspicion for IPF does not arise for several months.

- Onset of symptoms
- Initial evaluation in tertiary care
- Death?

2 Recognizing a Progressive Clinical Pattern Is the First Step to Correctly Diagnosing IPF

Causes of IPF remain unknown, but several potential risk factors have been identified. Typical clinical presentation is nonspecific: progressive dyspnea on exertion and dry cough.

### Risk Factors & Symptoms

- Smoking history, especially ≥20 pack-years
- Bibasilar crackles (sound like Velcro being pulled apart)
- Dyspnea on exertion
- Male predominance
- Finger clubbing: occurs in 25%-50%
- Age: >50 years; median age 65-70 years
- Environmental exposures
- Dry cough
- Infection
- Gastro-esophageal reflux disease (GERD)
- Genetic factors
- Male predominance
- Finger clubbing: occurs in 25%-50%
- Age: >50 years; median age 65-70 years

3 Specific Investigations Are Important to Increase Suspicion for IPF

- Pulse oximetry (with functional test): desaturation on activity
- 6-minute walk test
- Spirometry/pulmonary function tests: restrictive pattern, reduced diffusing capacity of the lungs for carbon monoxide
- Plain radiography: rule out common conditions (eg, pneumonia, heart failure)
- High-resolution CT (HRCT): gold-standard imaging test for IPF (often ordered in specialty care setting)

4 HRCT Is Underutilized in Diagnosing IPF

In cases with clinical suspicion for IPF, the gold-standard imaging study is HRCT.

- Where we are:
  - In the simulation case, HRCT was chosen at diagnosis by:
    - 13% of PCPs (n=227)
    - 53% of Pulmonologists (n=40)
- Where we need to be:
  - Suspected IPF
    - Identifiable causes for ILD?
      - Yes
      - High Resolution CT
        - UIP
        - Possible UIP
        - Inconsistent with UIP
          - Surgical Lung Biopsy
            - MDD
              - IPF
              - IPF/Not IPF
              - Not IPF

Clinicians are much more likely to order HRCT later in the diagnostic process – a reasonable and appropriate choice, but one that lengthens the time to confirmed diagnosis and delays the start of treatment.

UIP: usual interstitial pneumonia; MDD: multidisciplinary discussion; ILD: interstitial lung disease.
**5 It Is Important for PCPs to Have a Low Threshold for Referral**

PCPs should be ready to recognize features that suggest an atypical or serious pulmonary disease and refer the patient to a specialist, preferably one with experience in IPF.

**Where we are:**
33%

**Where we need to be:**
Any of the symptoms and test results discussed in sections 2 and 3 suggest a referral may be appropriate.

In the simulation case, 33% PCPs (n=38) did not choose to refer a patient after findings on a HRCT scan.

**6 Multidisciplinary Care Is Essential in the Management of IPF**

The challenges of diagnosis and early referral indicate the need for the evaluation of possible IPF by an experienced multidisciplinary team.

**7 Several Conditions Are Frequently Comorbid with IPF**

Comorbidities with IPF may affect patient function, outcomes, and quality of life. Comorbidities should be managed to improve patient function and quality of life and minimize impact on pulmonary function.

- GERD
- Chronic obstructive pulmonary disease
- Pulmonary hypertension
- Lung cancer
- Obstructive sleep apnea
- Venous thromboembolism

**8 Several Nonpharmacologic Therapies Are Recommended**

Nonpharmacologic therapies include supplemental oxygen, pulmonary rehabilitation, and lung transplantation.

**Where we are:**
PCPs’ first choice was to manage comorbidities
n=23

**Where we need to be:**
When other options fail:

1st Choice
Supplemental oxygen

2nd Choice
Pulmonary rehabilitation

3rd Choice
Lung transplantation

**9 There Are Pharmacological Agents Specifically Recommended for IPF**

In the last decade, the treatment of IPF has undergone a radical evolution. Agents once thought to be effective have proven to be ineffective or even harmful. The emergence of two FDA-approved and guideline-recommended therapies is a major advance in the treatment of IPF.

**Where we are:**
The majority of PCPs chose therapies that the ATS recommends against using as appropriate initial therapy:

- PCPs, n=18
  - 61%
- Pulmonologists, n=40
  - 12%

**Where we need to be:**

The majority of pulmonologists (88%, n=40) appropriately started with one or the other of the approved drugs for IPF.

**10 Effective Patient-Provider Communication Is Necessary**

Effective patient-provider communication contributes to greater patient understanding of disease states and the patient’s role in management.

- Provide empathy and maintain a balance between truth and hope
- Provide education that helps patients self-manage their disease
- Encourage shared decision-making
- Explain use of supplemental oxygen
- Refer patients and caregivers to support groups and resources, such as Pulmonary Fibrosis Foundation

**Additional Information:**


**QR Code:**

Please scan the QR code on the left or go to: http://www.globalacademycme.com/index.php?id=15230 for an in-depth, interactive version of this infographic.
Multidisciplinary Care for IPF

The challenges described above indicate the need for the evaluation of possible ILD by an experienced multidisciplinary team. The importance of multidisciplinary care is supported by guidelines and illustrated by studies of diagnostic accuracy. For example, a study from Europe found high accuracy for the diagnosis of IPF at expert centers (approaching 90%), but the level of agreement within the expert teams was only fair to moderate. ATS guidelines specifically recommend collaborative evaluation and management by a multidisciplinary team, including a pulmonologist, a radiologist, and, possibly, a pathologist.

PATIENT EXPERIENCES
Diagnostic Delays and the Need for a Multidisciplinary Team

A 78-year-old man
“I had a CT scan [in] 2011, but I felt I had the beginnings of IPF 4 or 5 years prior when I started running and was suddenly wheezing. My primary care doctor of 30 years told me I had bronchitis/athletic asthma and so I started taking inhalers. I went through a series of misdiagnoses for five years. I was a competitive swimmer doing 10ks and martial arts, and I finally went in to a pulmonologist because my times for swimming were dropping. I had shortness of breath and weight loss—I dropped 50 pounds the year preceding my diagnosis—but the shortness of breath only bothered me because of my swimming times decreasing. I saw four different pulmonologists in four years trying to confirm my IPF diagnosis.”

Ideally, the care team should have experience with diagnosing and managing ILD. For example, radiologists without experience with ILD may not recognize the features of a UIP pattern on HRCT. Indeed, the distinctions between honeycombing (a hallmark feature of the UIP pattern) and traction bronchiectasis or concurrent emphysema and fibrosis can be challenging, even for experienced observers. When primary care clinicians recognize features that suggest a possible ILD, they should consider referring the patient to an ILD center, even before an HRCT is performed.

Common Comorbidities
Several conditions are frequently comorbid with IPF and may affect patient function, outcomes, and quality of life. A recent retrospective study of 272 patients with IPF found that 12% had no comorbidities, 58% had 1-3 comorbidities, and 30% had 4-7 comorbidities. The most common comorbidities were cardiovascular, pulmonary, and oncologic. Predictably, median survival differed significantly by the number of comorbidities, ranging from 66 months among patients with no comorbidities to 48 months among those with 1-3 comorbidities and 35 months among those with 4-7 comorbidities (P=0.004).

Common comorbidities include GERD, COPD, obstructive sleep apnea, and pulmonary hypertension. GERD is highly prevalent in IPF, occurring in as many as 90% of patients, and may be associated with worsening or exacerbation of IPF. In more than 50% of patients with IPF, GERD may be clinically silent. Obstructive sleep apnea is similarly prevalent, occurring in up to 88% of cases. Pulmonary hypertension is also common, with estimates ranging from one third to more than three quarters of patients with IPF, depending on the study and setting. Finally, patients with IPF have increased risk for lung cancer and venous thromboembolism.

All comorbidities should be managed to improve patient function and quality of life and minimize impact on pulmonary function. For example, some studies suggest that the treatment of GERD (even in asymptomatic patients) may improve outcomes in some patients with IPF. However, other studies have not supported this association. Current ATS guidelines recommend treating GERD in most patients, even when reflux is asymptomatic. Some common comorbidities, such as COPD, may complicate the diagnosis and treatment of IPF; these patients should be managed by a specialist with experience in IPF.

Because IPF is a progressive and fatal disease, some clinicians and patients may choose to ignore comorbid conditions. This choice may reflect a sense of fatalism about IPF or a well-meaning urge to minimize medical interventions. But such therapeutic nihilism sends the wrong signal to patients, suggesting that there is nothing medicine can offer them. It also ignores the potential to improve patient function and quality of life and could contribute to worsening of pulmonary function and progression of disease.

Table 2. Features associated with increased risk of mortality in IPF

<table>
<thead>
<tr>
<th>Baseline factors</th>
<th>Longitudinal factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Level of dyspnea</td>
<td>• Increase in level of dyspnea</td>
</tr>
<tr>
<td>• DLCO &lt;40% predicted</td>
<td>• Decrease in FVC by ≥10% over time</td>
</tr>
<tr>
<td>• Desaturation ≤88% during 6MWT</td>
<td>• Decrease in DLCO ≥15% absolute value</td>
</tr>
<tr>
<td>• Extent of honeycombing on HRCT</td>
<td>• Worsening of fibrosis on HRCT</td>
</tr>
<tr>
<td>• Pulmonary hypertension</td>
<td></td>
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</table>

FVC=forced vital capacity, DLCO=diffusing capacity for CO, 6MWT=six-minute walk test, HRCT=high-resolution CT
Prognosis Factors

Although IPF is known to be a fatal disease, determining prognosis for an individual patient remains challenging. Several possible natural histories of IPF have been described, ranging from relatively stable disease to rapid progression and death. Most patients experience a gradual worsening of lung function over the course of years. Some patients remain stable for long periods of time, while others experience a rapid progression of disease. A minority of patients (~5%-10%) experience unpredictable acute exacerbations, sometimes related to secondary causes (e.g., pneumonia).7

Validated biomarkers have not been established, and current prognostic models do not reliably predict disease course. Factors associated with increased risk of mortality in clinical studies are listed in Table 2. An interesting recent study from Japan found that history of smoking had a paradoxical influence on survival.45 In this retrospective study, 32 patients with IPF who never smoked had significantly shorter median survival compared to 66 patients with IPF who smoked (18.5 vs 26.3 months; P<0.0001). Never-smokers also had significantly more acute exacerbations (50% vs 18.2%; P<0.0001). These findings suggest that different pathogenetic mechanisms may play a role in patients with and without a history of smoking, and that IPF in never-smokers may be a more aggressive form of disease. However, prospective studies are required to confirm these preliminary findings.

Non-pharmacologic Therapies

Several non-pharmacologic therapies are recommended for many patients with IPF. These modalities include supplemental oxygen, pulmonary rehabilitation, and lung transplantation.

Oxygen Therapy

Oxygen therapy can improve the ability of patients with IPF to function. It is not clear whether supplemental oxygen affects survival in IPF, but it can improve patient function and quality of life. The ATS guidelines recommend long-term oxygen therapy for patients with IPF who demonstrate clinically significant resting hypoxemia, which they define as an oxygen saturation <88%. Supplemental oxygen may also help patients who do not have resting hypoxemia to become more active. This is an important consideration, because patients with IPF are likely to decondition as their disease progresses.

Despite the significant benefits of oxygen, patients may resist its use. Patients may cite the inconvenience of the required devices and the stigma of using oxygen in public. Cost may also be an issue for some patients. Finally, newly diagnosed patients may benefit from guidance on how to work with a supplier to obtain devices appropriate for their lifestyle and clinical needs. When prescribing oxygen therapy, clinicians should explain to patients what it is, why it will help them, and how to select the right oxygen system. By addressing issues such as convenience, stigma, and cost, clinicians can help patients overcome barriers to the appropriate use of oxygen.

PATIENT EXPERIENCES

The Importance of Fitness

A 63-year-old woman:

“I would advise others to stay as healthy as possible. Get into a regimen of working out with oxygen, supervised if you can, to try to ward off advancement. It’s so individualized, you never know—it may never progress, or it may progress fast. Stay positive. A cure is coming. Stay healthy enough so that, when a cure comes, you can get it.”

PATIENT EXPERIENCES

Oxygen Therapy

A 71-year-old woman:

“The big thing is oxygen. That has become the biggest factor in having this illness. I’m 24/7 on oxygen, probably within six months of it having been prescribed....I got a small carry-around at first, but [the supplier’s] idea of portable is not at all what I needed portable to be. Thank God I had some money so I could purchase things on my own, so I could have some sort of life. That has been trial and error and a frustration, because [my doctor] knows about using oxygen but she doesn’t understand the day to day and how it changes one’s life.”

Pulmonary Rehabilitation

Pulmonary rehabilitation programs for IPF may include aerobic conditioning, strength and flexibility training, nutritional guidance, education, and psychosocial support. In controlled trials, pulmonary rehabilitation improved exercise capacity, lung function, symptoms, and quality of life in patients with IPF. These improvements may be greatest in patients with the lowest levels of baseline function. Accordingly, the 2011 ATS guidelines recommend pulmonary rehabilitation for most patients with IPF. These programs may last several weeks or a few months and can be repeated periodically—for example, yearly—to help patients maintain function.
Lung Transplantation
Many patients with IPF will not be candidates for lung transplantation. However, appropriate patients may have reduced risk for mortality following transplantation. In clinical studies, lung transplantation is associated with five-year survival rates of about 50%.[46] Outcomes such as these suggest a tradeoff between risk for death due to IPF and the multiple risks of lung transplantation, which include acute rejection, infection, and cancer, among others. Nevertheless, for some patients with IPF, lung transplantation may increase both the quantity and quality of life.

The ATS guidelines encourage clinicians to discuss lung transplantation soon after the diagnosis of IPF is confirmed. In general, younger, healthier patients may be considered for the procedure. Patients found to be potential candidates should be referred as soon as possible for evaluation.

Pharmacologic Treatment
In the last decade, the treatment of IPF has undergone a radical evolution. Agents once thought to be effective have proven to be ineffective or even harmful. The emergence of two FDA-approved and guideline-recommended therapies is a major advance in the treatment of IPF.

Nintedanib or pirfenidone should be the only initially prescribed pharmacological therapy for IPF.

An understanding of different AE profiles of these therapies is necessary to determine the appropriate therapy for the patient.
52 weeks, the primary end point (annual rate of decline in FVC) in INPULSIS-1 was -114.7 mL with nintedanib vs -239.9 mL with placebo (95% CI, 77.7 to 172.8; P<0.001); and in INPULSIS-2, -113.6 mL versus -207.3 mL (95% CI, 44.8 to 142.7; P<0.001). In INPULSIS-1, there was no significant difference between groups in the time to first acute exacerbation (P=0.67), but in INPULSIS-2, there was a significant benefit with nintedanib compared to placebo (hazard ratio 0.38; 95% CI, 0.19 to 0.77; P=0.005).

In conclusion, these clinical trials demonstrated reduced rate of decline in pulmonary function, consistent with a slowing of disease progression. Nintedanib was approved by the FDA for the treatment of IPF and is recommended by the updated 2015 ATS treatment guidelines.11

**Pirfenidone**

Pirfenidone is an oral antifibrotic agent that has demonstrated efficacy for IPF in clinical trials. In a major international, 52-week clinical trial, 555 subjects with IPF were randomized to pirfenidone (2403 mg per day) or placebo.5 Enrolled subjects had FVC 50%-90%, FEV1/FVC ≥0.80, and HRCT- and/or biopsy-confirmed diagnosis of IPF. At study end, the pirfenidone group had a relative reduction of 47.9% in the proportion of patients with no decline in FVC (P<0.001) with pirfenidone vs placebo. Subjects in the pirfenidone group also had reduced decline in 6MWT distance (P=0.04), suggesting greater preservation of functional capacity. Finally, pirfenidone improve progression-free survival compared to placebo (P<0.001).

On the strength of these clinical trials, pirfenidone was approved for the treatment of IPF and is recommended by the updated 2015 ATS treatment guidelines.11

**SELECTING AND MANAGING PHARMACOLOGIC THERAPY**

The emergence of two FDA-approved and guideline-recommended therapies is a major advance in the treatment of IPF. These agents provide options for patients today and hope for future advances in therapy. Ongoing studies may determine if these medications can also improve survival in this lethal disease. But patients must be treated if they are to receive these benefits.

Unfortunately, evidence suggests that a substantial proportion of patients with IPF receive no pharmacologic therapy at all.51,52 For example, studies have found that many patients with IPF are managed with corticosteroids, despite a strong recommendation against corticosteroid monotherapy in the ATS guidelines; in one study, for example, 49% of patients were treated with oral corticosteroids.52 A prospective study from Germany found that one third of subjects with IPF were treated with pirfenidone, reflecting its recent approval in Europe prior to the study.51 However, none of the subjects were treated with nintedanib (not approved in Europe at the time), nearly a quarter received corticosteroids, one third received acetylcysteine, and 17.9% received no treatment at all.51 Other surveys have reported similar wide variations in the treatment of patients with IPF, including inconsistent use of pirfenidone as monotherapy and in combination with other agents.52

The variation in treatment patterns described by these studies is disheartening. The data reveal frequent use of inappropriate therapies and uncertainties regarding the use of approved therapies. An important response to these data is to ensure that appropriate patients are treated with an approved therapy. Current data indicate that many patients in clinical trials experienced reduced progression of disease when treated with the proportion of patients with no decline in FVC (P<0.001) with pirfenidone vs placebo. Subjects in the pirfenidone group also had reduced decline in 6MWT distance (P=0.04), suggesting greater preservation of functional capacity. Finally, pirfenidone improve progression-free survival compared to placebo (P<0.001).

In conclusion, these clinical trials demonstrated reduced rate of decline in pulmonary function, consistent with a slowing of disease progression. Nintedanib was approved for the treatment of IPF and is recommended by the updated 2015 ATS treatment guidelines.11

**CLINICAL PEARLS**

- **Pharmacologic Interventions for IPF**
  - FDA-approved and recommended:
    - Nintedanib
    - Pirfenidone
  - NOT effective and NOT recommended:
    - Ambrisentan, macitentan, bosentan
    - Imatinib
    - N-acetylcysteine monotherapy
    - Prednisone monotherapy
    - Triple therapy (prednisone, azathioprine, N-acetylcysteine)
    - Warfarin

---

**PATIENT EXPERIENCES**

**The Need for Patient-level Education**

A 74-year-old man:

“When they told me I had IPF, it went 30,000 feet over my head. I didn’t have a clue what they were talking about. I saw three physicians that did not really explain what this was about. Or, they did say the usual: ‘Scarring of the lung, only remedy is lung transplant.’ So what? I was in LaLa land! They really didn’t explain in a way that connected with the patient. I found out from the Internet that it is a terminal disease. Instead of showing me pictures of lung terminology—tell me, what does it mean? ‘I expected, I guess, my pulmonologist to sit me down and explain things...’ What I would expect to hear, with 20/20 hindsight: ‘You have IPF. It’s a scarring of the tissue, it cannot be corrected, it deteriorates, it’s terminal. This is what we can do: we can help you with this and that.’ So, educate me.”

---

**Communication Gaps**

A 71-year-old woman:

“I could not walk very far and had shortness of breath. Shortly after, I was diagnosed with pneumonia. The doctor had me do a couple of X-rays...All they said to me was, ‘It isn’t a tumor, but your lungs show signs of cracked glass.’ End of explanation. ‘Based on what I know now, there were a number of tests they should’ve given me...’ I didn’t have a pulmonary lung function test. No discussion of any treatment at all. No medication. No diagnosis. Nothing. No one thought it was...”
with one of the approved therapies, and this hope should be offered to patients in clinical practice.

At this time, we have little evidence to guide selection between the two approved therapies for individual patients. No head-to-head studies have been performed comparing these two agents, and current evidence does not suggest any differences between the agents with regard to efficacy.\(^5\)\(^3\)\(^4\) Therefore, the key issues to consider when selecting between these agents include side effect profiles, risk for drug-drug interactions, and frequency of administration.

**Side Effects and Interactions**

Both drugs were fairly well tolerated in clinical trials. However, some patients may experience side effects that they cannot tolerate. For example, pirfenidone in trials was associated with risk for skin rash and gastrointestinal events, such as nausea and reflux. Therefore, the agent should be taken with food, and patients should be counseled to avoid exposure to sunlight and sunlamps.\(^5\)\(^5\) In clinical studies, dose adjustments were also shown to improve treatment continuation in patients experiencing adverse events.\(^5\)\(^5\) For patients with GERD, pirfenidone may increase risk for reflux, and the presence of symptomatic GERD might be a reason to consider the alternative agent. Pirfenidone is metabolized primarily by the CYP1A2 enzyme, and administration of CYP1A2 inhibitors or inducers may affect pirfenidone serum drug levels. Strong inhibitors of CYP1A2, such as fluvoxamine, should be discontinued before initiating pirfenidone. Dose adjustments may be required when pirfenidone is coadministered with less-potent inhibitors of this enzyme.\(^5\)\(^6\)

The most common side effects of nintedanib in trials were gastrointestinal, particularly diarrhea, which was reported by 62% of patients in studies.\(^6\)\(^5\)\(^7\) In most cases, the diarrhea was mild and did not require dose adjustment or discontinuation. However, nintedanib might not be the best option for patients with diarrhea at baseline. Because nintedanib is predominantly metabolized by the P-gp enzyme, coadministration of P-gp inhibitors or inducers may alter serum levels of the drug.\(^5\)\(^8\)

Finally, the agents differ with regard to administration. Pirfenidone is administered as three capsules three times per day. Nintedanib is administered as one capsule every 12 hours. Both agents should be taken with food.

The selection of specific therapy for IPF should be made using a shared-decision making (SDM) model. In SDM, clinicians share information with patients and then find agreement on goals and treatment approach. Patients’ preferences and beliefs regarding the disease and its treatment should be elicited using open-ended questions. The final choice of treatment should be left to the well-informed patient.

**Communicating With the Patient**

Effective patient-provider communication contributes to greater patient understanding of disease states and the patient’s role in management. However, surveys suggest that patients would prefer improved communication with their clinicians.\(^5\)\(^9\) Patients with IPF have reported a lack of support as they attempt to understand the diagnosis and disease process.\(^6\)\(^0\) Patients have also cited a lack of informational educational resources regarding IPF and its management at the time of diagnosis.\(^6\)\(^1\)\(^6\)\(^2\)

Effective education of patients diagnosed with IPF is essential to promote their ability to engage in self-management. But often patients are left with insufficient information, and many turn to the Internet for more. As clinicians know, this can be problematic for everyone involved.

The impact of this lack of communication may be exacerbated by the fact that most patients with IPF see multiple clinicians before being diagnosed; 40% of patients have consulted three or more physicians, and may have received conflicting information along the way.\(^5\)\(^9\)
Methods for the improvement of patient-provider communication have been proposed and explored in the literature. Basic principles include fostering mutual respect, harmonizing clinical goals, providing a supportive environment, and providing the right information with transparency and full disclosure. Additional approaches include patient-centered techniques such as maintaining eye contact, avoiding interruptions, encouraging patient participation, and soliciting the patient’s beliefs, values, and preferences. Providing information at a level the patient can understand is critical. Avoiding jargon can help patients better understand the medical aspects of the disease. Many patients may seek information from other sources, especially the internet. Information-seeking should not be discouraged, but many sources may leave patients with more questions than answers.

Finally, clinicians should counsel all their patients with IPF about the valuable support groups that are available. These organizations, such as the Pulmonary Fibrosis Foundation, provide an understanding community where patients and clinicians can share their stories and learn about others’ experiences.

**Telling Patients They Have IPF**

Once a diagnosis of IPF is confirmed, it is time for the conversation that many clinicians dread: telling the patient that he or she has a progressive and fatal disease. This discussion must be conducted with empathy and should maintain a delicate balance between truth and hope. Current evidence suggests that people diagnosed with IPF will live 2 to 5 years from the time of diagnosis. Some of the variation in this range may relate to the fact that a delayed diagnosis is common in IPF; as noted earlier, the average time from onset of symptoms to referral for specialty care is about 2 years.

It is important to bear in mind that each patient’s experience of IPF may differ from that of others. For example, mortality statistics are based on broad populations of patients, which may combine older and younger patients, or patients who are untreated and those who have been treated aggressively. It is worth the effort to explain this to patients at the level of their understanding.

Furthermore, new therapies continue to be developed that can affect the course of the disease. The first therapies indicated for use in IPF were approved by the FDA as recently as 2014.

**Summary**

In summary, IPF is a rare but fatal disease. Challenges in managing IPF include making a timely diagnosis, early referral to specialty care, discussing the disease with patients, and choosing appropriate treatment. The key take-home lessons for primary care are to recognize features of the disease, perform a thorough evaluation (including PFTs, oximetry, and imaging), and refer all patients with features that suggest an atypical lung disease to a specialist, preferably one with experience in ILD.

In the specialty setting, the crucial test is HRCT; a typical UIP pattern on HRCT has 90%-100% positive-predictive value for a UIP pattern and obviates the need for biopsy in most cases. Following the identification of a UIP pattern, a diagnosis of IPF must be confirmed by differentiating from other ILD, as the treatment of IPF differs substantially from the management of other ILD. Both nonpharmacologic (oxygen, rehabilitation, lung transplantation) and approved pharmacologic therapies (nintedanib, pirfenidone) should be considered and tailored to individual patients’ needs.
References


1. Idiopathic pulmonary fibrosis is associated with all of the following features, EXCEPT:
   A. Older age
   B. Female gender
   C. History of smoking
   D. Progressive dyspnea on exertion

2. All of the following findings on physical examination are consistent with idiopathic pulmonary fibrosis, EXCEPT:
   A. Muscle wasting
   B. Finger clubbing
   C. Bibasilar crackles
   D. Normal joint examination

3. All of the following investigations should be considered for a patient presenting with features consistent with idiopathic pulmonary fibrosis, EXCEPT:
   A. Low-dose CT
   B. Cardiac workup
   C. 6-minute walk test
   D. Pulmonary function tests

4. In a patient with suspected idiopathic pulmonary fibrosis based on history, presentation, and clinical findings, which of the following tests should be performed?
   A. Conventional CT
   B. High-resolution CT
   C. Surgical lung biopsy
   D. Plain chest radiography

5. All of the following conditions are commonly comorbid in patients with idiopathic pulmonary fibrosis, EXCEPT:
   A. Asthma
   B. Obstructive sleep apnea
   C. Gastroesophageal reflux disease
   D. Chronic obstructive pulmonary disease

6. In the INPULSIS-1 and INPULSIS-2 studies, nintedanib was associated with which of the following outcomes compared to placebo?
   A. Significantly longer survival
   B. No significant differences in outcomes
   C. Significantly reduced rate of decline in FVC
   D. Significantly longer time to acute exacerbation

7. In a large-scale trial in patients with idiopathic pulmonary fibrosis, pirfenidone was associated with all of the following outcomes compared to placebo, EXCEPT:
   A. Increased proportion of subjects with no decline in FVC
   B. Reduced proportion of subjects with decline in FVC of ≥10%
   C. Significantly reduced decline in 6-minute walk test distance
   D. No significant differences between groups in progression-free survival

8. In clinical trials, the common side effects of nintedanib included skin rash and reflux, and the side effects of pirfenidone included diarrhea. True or false?
   A. True
   B. False

9. When helping a patient with idiopathic pulmonary fibrosis select between the approved pharmacologic therapies, all of the following should be considered, EXCEPT:
   A. Frequency of administration
   B. Relative efficacy of each agent
   C. Potential drug-drug interactions
   D. Side effect profiles of each agent

10. When counseling a patient with idiopathic pulmonary fibrosis, all of the following should be emphasized, EXCEPT:
    A. Appropriate use of oxygen therapy
    B. Evaluation for lung transplantation
    C. Benefits of pulmonary rehabilitation
    D. Estimates of life expectancy from clinical studies
A Current Practice Snapshot of IPF Diagnosis and Management: Where We Are and Where We Need to Be Evaluation Form

Original Release Date: December 1, 2016 • Most Recent Review Date: December 31, 2017 • Estimated Time to Complete Activity: 1.5 hours

To assist us in evaluating the effectiveness of this activity and to make recommendations for future educational offerings, please take a few moments to complete this evaluation form. Your response will help ensure that future programs are informative and meet the educational needs of all participants. CME/CE credit letters and long-term credit retention information will only be issued upon completion of the post-test and evaluation online at: http://tinyurl.com/XXXXXX.

Please indicate your profession/background:
- MD/DO
- MSN/BSN/RN
- PA
- APN/NP
- PharmD/RPh
- Resident/Fellow Researcher
- Administrator
- Student
- Other; specify ________________________________

LEARNING OBJECTIVES: Having completed this activity, you are better able to:

- Utilize the signs, symptoms, and epidemiology of IPF to better recognize patients in need of specialty care.
- Employ a multidisciplinary care team approach for IPF to enhance patient outcomes.
- Provide timely referral of patients with IPF to tertiary care to improve survival.
- Review clinical trial data supporting the efficacy and safety of pirfenidone and nintedanib.
- Select appropriate pharmacologic therapy for patients with IPF.
- Communicate with IPF patients and provide effective disease-state education.

<table>
<thead>
<tr>
<th>If you do not feel confident that you can achieve the above objectives to some extent, please describe why not.</th>
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<tbody>
<tr>
<td>Based on the content of this activity, what will you do differently in the care of your patients/regarding your professional responsibilities? (check one)</td>
</tr>
</tbody>
</table>
- Implement a change in my practice/workplace.
- Seek additional information on this topic.
- Do nothing differently as the content was not convincing.
- Do nothing differently. System barriers prevent me from changing my practice/workplace.

OVERALL EVALUATION

| The information presented increased my awareness/understanding of the subject. |
| The information presented will influence how I practice/do my job. |
| The information presented will help me improve patient care/my job performance. |
| The program was educationally sound and scientifically balanced. |
| Overall, the program met my expectations. |
| I would recommend this program to my colleagues. |

<table>
<thead>
<tr>
<th>OVERALL EVALUATION</th>
<th>Strongly Agree</th>
<th>Agree</th>
<th>Somewhat Agree</th>
<th>Disagree</th>
<th>Strongly Disagree</th>
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Author demonstrated current knowledge of the topic.
Author was organized in the written materials.
Author was organized in the written materials.
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What topics do you want to hear more about, and what issue(s) regarding your practice/professional responsibilities will they address?

Please provide additional comments pertaining to this activity and any suggestions for improvement.

The Postgraduate Institute for Medicine thanks you for your participation in this CME/CE activity. All information provided improves the scope and purpose of our programs and your patient care.

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