

Idiopathic Pulmonary Fibrosis: A Guide for Providers





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What is Idiopathic Pulmonary Fibrosis?

Idiopathic pulmonary fibrosis (IPF) is a disease of aging. The incidence of IPF increases with age; more than 150 people per 100,000 people aged 70 or older have IPF. Most IPF patients are diagnosed in their 60s. In fact, IPF is an extremely rare diagnosis among people younger than 55 years. Risk factors for IPF include cigarette smoking and certain genetic variants or mutations.

IPF is a progressive, incurable form of interstitial lung disease. Quite simply, IPF is the diagnosis when other potential causes of pulmonary fibrosis—like connective tissue disease and long-term, repeated exposure to aerosolized, organic antigens—are ruled out (i.e., after extensive evaluation, the cause remains unknown or idiopathic) and a certain pattern of lung injury, called UIP or usual interstitial pneumonia, is identified either on high-resolution chest computed tomography (HRCT) or in surgical lung biopsy specimens.

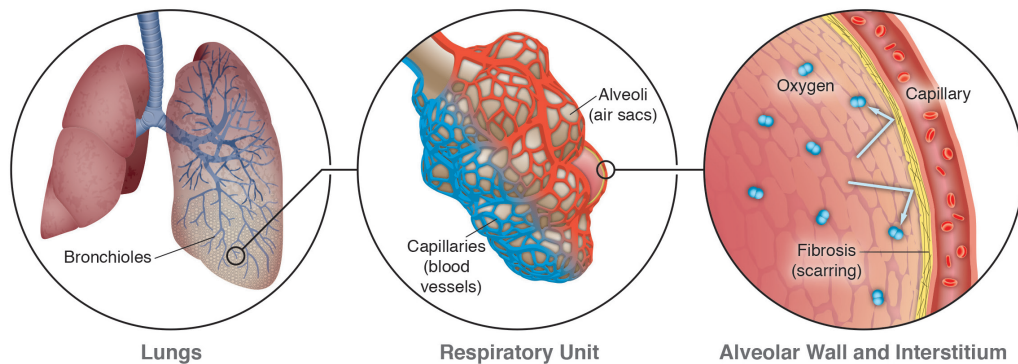
IPF typically presents with the insidious onset of exertional dyspnea. Patients commonly report first noticing difficulty breathing while walking up inclines. Dry, hacking cough, prompted by a “tickle” in the throat, is a common symptom of IPF. Fatigue is another bothersome symptom present in many patients with IPF. IPF does not cause joint inflammation, skin rash, Raynaud’s phenomenon, dry eyes/mouth or chest pain.

On physical examination, the hallmark finding is Velcro® crackles at the lung bases. If you don’t listen at the extreme postero-lateral aspects of the lungs, with the stethoscope directly against the skin, you might miss them. Finger clubbing is also present in some patients.

Pulmonary physiology most commonly reveals restriction and reduced diffusing capacity of the lung for carbon monoxide. Patients with combined IPF and emphysema may have normal spirometry or an obstructive ventilatory defect.

IPF is typically a life-shortening condition. Studies have shown that the median survival among cohorts of patients with IPF is 3-5 years from the time of diagnosis. This means that, in those studies, by 3-5 years after diagnosis, 50% of IPF patients had died, and 50% were alive. Prediction indexes, like the GAP index, use gender, age, and pulmonary physiology results to refine mortality predictions for individual patients.

As of 2017, IPF is incurable, but this does not mean nothing can or should be done. In 2014, the U.S. FDA approved two anti-fibrotic medications for the treatment of IPF. These approvals were the end result of a groundswell of research over the last two decades. This research led to an improved understanding of the pathogenesis of IPF. IPF is believed to result from repeated insult or injury to the lung (probably over many years) that, in the susceptible individual, may lead to the development of fibrosis. The injury is thought to trigger the so-called pro-fibrotic cascade of molecular effects that ultimately lead to the formation of fibroblast foci and the deposition of extra-cellular matrix and collagen (fibrosis). The fibrosis occurs within the interstitium (i.e., within alveolar walls), creating stiff lungs and impaired ability of oxygen to diffuse from airspace into capillaries (see image below). There are a number of drugs in development; most target various aspects of the pro-fibrotic cascade.





Making the Diagnosis of IPF

The first thing to consider when making a clinical summary diagnosis of IPF is whether you are, in fact, dealing with idiopathic disease. Pulmonary fibrosis has many potential causes, each of which must be ruled out before a diagnosis of IPF is made.

Distinguishing IPF Mimics

The three conditions that most commonly mimic IPF are idiopathic fibrotic nonspecific interstitial pneumonia (iNSIP), pulmonary fibrosis from subtly evident connective tissue disease, and exposure-related pulmonary fibrosis (most commonly fibrotic hypersensitivity pneumonitis).

Determining whether the cause is idiopathic (i.e., truly unknown) is really somewhat of a judgment call once a detailed and comprehensive history and physical examination is performed. A comprehensive history includes asking about other medical conditions and exposure to medications that have pulmonary fibrosis as a potential toxicity. If you are not certain about whether a medication has the potential for pulmonary toxicity, check the website pneumotox.com. A comprehensive history also includes a thorough (essentially life-long) occupational and environmental exposure history. Ask about specifics of job duties and the buildings or areas where those duties occurred; ask about the home environments they have resided in. In most cases, you are in search of chronic, repeated exposure to toxic fumes, dusts, gases, vapors or aerosolized organic antigens (molds, bacteria and bird antigens are the main culprits). Intake questionnaires can help in completing this enormous task.

Unfortunately, there are no rules about how much exposure is enough to cause pulmonary fibrosis or how much exposure will allow the diagnostician high confidence that the disease is not idiopathic; this is where the judgment comes in. A multi-disciplinary conference, in which cases of pulmonary fibrosis are carefully reviewed by a team of physicians, allows open discussion of diagnostic possibilities and promotes confidence in whatever clinical summary diagnosis is rendered.

Another issue to consider when making a clinical summary diagnosis of IPF is whether a surgical lung biopsy is needed. There is also some judgment that goes into this decision. First consider the most straightforward case: a 65 year-old male,

former 25 pack-year smoker, with no significant medical history whatsoever, presents with six months of exertional dyspnea, a dry cough, fatigue and a HRCT scan with a pattern of usual interstitial pneumonia. There is no suggestion of autoimmunity in a comprehensive systems review or on careful physical examination, and he has no known exposures linked with pulmonary fibrosis. There is very, very high confidence in a diagnosis of IPF, and a surgical lung biopsy is not needed.

Confidence in the diagnosis of IPF decreases – and alternative diagnoses are considered – when the HRCT scan reveals a pattern of possible UIP, or there is a potentially significant exposure, or there is serum autoantibody positivity, or there is some other feature that argues against an IPF diagnosis (e.g., the patient is a 45 year-old woman: young women are more likely than patients of other demographics to have autoimmune disease). The decision around whether a surgical lung biopsy should be performed revolves around the practitioner's and patient's need for more diagnostic certainty: does the practitioner need the information to make an informed decision about therapy? Does the patient need to know to have peace of mind? How would information from a surgical lung biopsy change management? Is the patient well enough to undergo the surgery? How much weight should be given to the risk of surgery-related acute exacerbation? All of these questions (and others) are important to consider before a patient is sent to surgical lung biopsy.

HRCT

Emerging data suggest that many patients with HRCT scans showing the pattern of possible UIP will indeed have UIP-pattern lung injury in surgical lung biopsy specimens. The likelihood of this increases with age: one study suggested that a possible UIP pattern on HRCT correctly identifies UIP pattern on biopsy 92% of the time among patients 60 years old, 96% of the time among patients 65 years old, and 100% of the time among patients 70 years old. This is only one study, but the data are compelling.

A simple, straightforward way to think about IPF is the following: IPF = idiopathic clinical circumstance + UIP on HRCT or surgical lung biopsy. On HRCT, UIP is characterized by the following criteria:

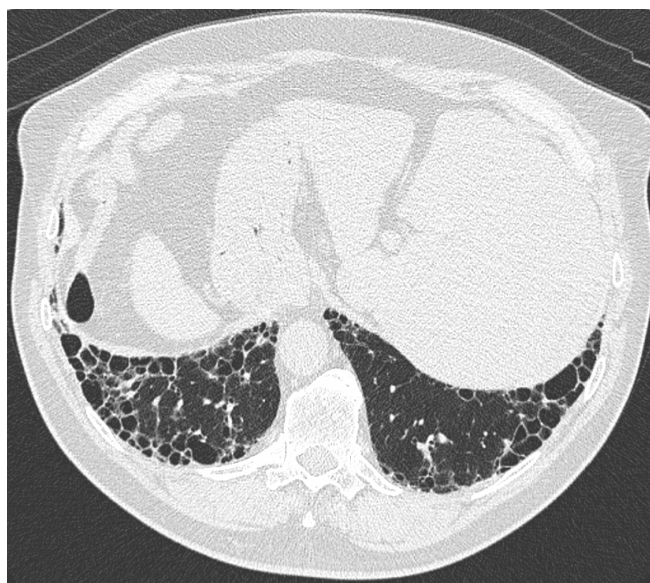
1. Subpleural, basal predominance.
2. Reticular opacities.

3. Honeycombing with or without traction bronchiectasis.
4. Absence of extensive ground glass opacities, micronodules, discrete cysts away from areas of honeycombing, or consolidation.

The positive predictive value of UIP on HRCT for UIP on surgical lung biopsy is incredibly high. Thus, if UIP is found on HRCT, a surgical lung biopsy is not needed to confirm the presence of UIP in the lung.

In surgical lung biopsy specimens, UIP is characterized by the following criteria:

1. Marked fibrosis/architectural distortion in a predominantly subpleural/paraseptal distribution.
2. Patchy involvement of the lung parenchyma. Thus, there are areas of normal lung in the specimen.
3. Presence of fibroblastic foci.
4. Absence of hyaline membranes, organizing pneumonia, granulomas, marked interstitial inflammatory cell infiltrate away from honeycombing, predominant airway-centered changes, or other features to suggest an alternate diagnosis.



Slice through the extreme bases of the lungs from a HRCT with the patient prone. The scan showed a UIP-pattern. The predominant finding is bilateral honeycombing. Note how the honeycomb cysts are situated in rows in the immediate subpleural regions.

Treatment of IPF

The first thing to realize is that there are treatments: there are pharmacologic and non-pharmacologic therapies for IPF.

Pharmacologic Therapy

Antifibrotics. In 2014, the U.S. Food and Drug Administration (FDA) approved two medications for the treatment of IPF. Their approval created incredible hope in the IPF community and spurred enthusiasm for identifying other agents that might have beneficial effects on the course of IPF.

The two approved drugs, nintedanib and pirfenidone, were each shown in large, confirmatory trials to modestly slow progression of the disease over 52 weeks: subjects randomized to receive placebo lost about 200cc of lung capacity, and subjects randomized to receive drug (either nintedanib or pirfenidone) lost about 100cc of lung capacity.

Unfortunately, neither drug improved quality of life, and each was associated with potential, usually manageable side-effects. Whether to go on one of these drugs is a discussion every provider should have with their IPF patients. The second thing to realize is that medications are only one facet of therapy for IPF.

Non-pharmacologic Therapy

Besides oral drugs, there are other things to consider when treating patients with IPF; these include the need for supplemental oxygen and assessments for comorbid conditions, along with a few others enumerated in the paragraphs below.

- 1. Supplemental oxygen:** it is our practice to assess IPF patients' oxygen needs at every clinic visit and to prescribe supplemental oxygen to treat low blood oxygen levels during sleep or while a patient is awake, whether at rest or while exerting. Even if a patient does not have a resting or exertion-induced peripheral oxygen saturation < 90%, it is our practice to perform a nocturnal oximetry study to determine what peripheral oxygen saturations are during sleep.
- 2. Pulmonary rehabilitation:** it is our practice to refer patients with IPF to pulmonary rehabilitation and to encourage a home exercise program.

3. **Vaccinations:** it is our practice to recommend that all IPF patients receive an influenza vaccine every year, the 13- and 23-valent pneumococcal vaccines every 5-7 years, and a pertussis booster if not previously received.
4. **Assessments for comorbid conditions:** coronary artery disease, obstructive sleep apnea, gastroesophageal reflux disease (GERD), pulmonary hypertension and mood disturbance/anxiety are not uncommon in patients with IPF. We believe practitioners should routinely ask patients whether they have any symptoms attributable to these conditions and have a low threshold to screen for their presence. Given the potential link between GERD and IPF, we believe it is not unreasonable to suggest that patients with IPF elevate the head of their bed 6-8 inches, allowing gravity to help prevent any reflux that might otherwise occur.



Forming a Partnership

When diagnosed with IPF, patients want to know that they have a partner in their provider. The fact that IPF is an incurable disease often leaves patients and their caregivers feeling helpless and hopeless. Therefore, a provider's role is to help the patient and caregiver maximize their quality of life while living with IPF. Key elements in forging this partnership include honest communication, shared decision-making and education.

Talking with Patients About IPF

As in patients with other life-threatening conditions, patients with IPF want to know the truth about their disease. A duty of providers who care for patients with IPF is to talk truthfully about the seriousness of IPF while being careful not to take away hope.

Communicating with IPF patients (and their caregivers who should be included in the discussion) takes time and some intuition. Some patients want all the detail, others do not. We should not force information on them and not deliver it until they are ready to hear it. Striking the right balance—delivering the right amount of information at the right times—is important. Although IPF is an incurable condition (currently), patients need to know that there are things providers can do for them. Seeing IPF patients in clinic every three months gives providers the opportunity to do several things, including:

- Monitor patients' need for supplemental oxygen (during sleep and exercise)
- Assess patients' activity levels and encourage participation in pulmonary rehabilitation and a daily home exercise program
- Vaccinate against influenza, pneumococcus and pertussis
- Evaluate and treat acute respiratory infections if they arise
- Assess emotional/mental health
- Assess patients' and caregivers' support networks and inform them about local or online support groups
- Determine whether lung transplant is an option and refer if appropriate
- Discuss sensitive topics like end-of-life wishes
- Monitor patients' shortness of breath, cough and fatigue; determine their cause (do not just assume they are due entirely to IPF); and evaluate and intervene as appropriate



Patients want a partner in their battle against IPF. A provider who informs and educates is a partner that patients and their caregivers can rely on to share in making the best decisions for patients. Using language that reflects a partnership can be incredibly powerful.

Providers should discourage patients from randomly searching for information on the internet. Encourage patients to access online information from trusted and reliable sources including websites from National Jewish Health, the American Thoracic Society, or the Pulmonary Fibrosis Foundation.

Helping patients with IPF and their caregivers focus on living one day at a time, reflecting on the things they can do and not what they can't, and reassuring them that they will always have the support they need are essential to helping patients live as well as possible despite IPF.

Stages of IPF

While there is no formal staging system for IPF, the role of oxygen in the disease trajectory and its impact on a patient's and their caregiver's quality of life can be represented in four stages. This four stage model can help patient's better understand how to live a full life with IPF, and we believe they can also help caregivers better appreciate what patients are currently experiencing and what may lie ahead.

Stage 1 – Recently diagnosed

Stage 2 – Needing oxygen with activity, but not at rest

Stage 3 – Needing oxygen 24 hours a day, with activity, at rest and during sleep

Stage 4 – Advanced oxygen needs

For more information on the stages of IPF, and how providers, patients and caregivers might use the detailed information contained in each, please access the patient education booklet entitled Understanding IPF at nationaljewish.org/IPF.

Educational Resources and Shared Decision-Making Tools

Please visit nationaljewish.org/IPF for downloadable tools, practice aids and IPF patient education materials. To order an IPF patient education toolkit, please contact the Office of Professional Education at proed@njhealth.org.

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National Jewish Health
1400 Jackson Street
Denver, Colorado 80206

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