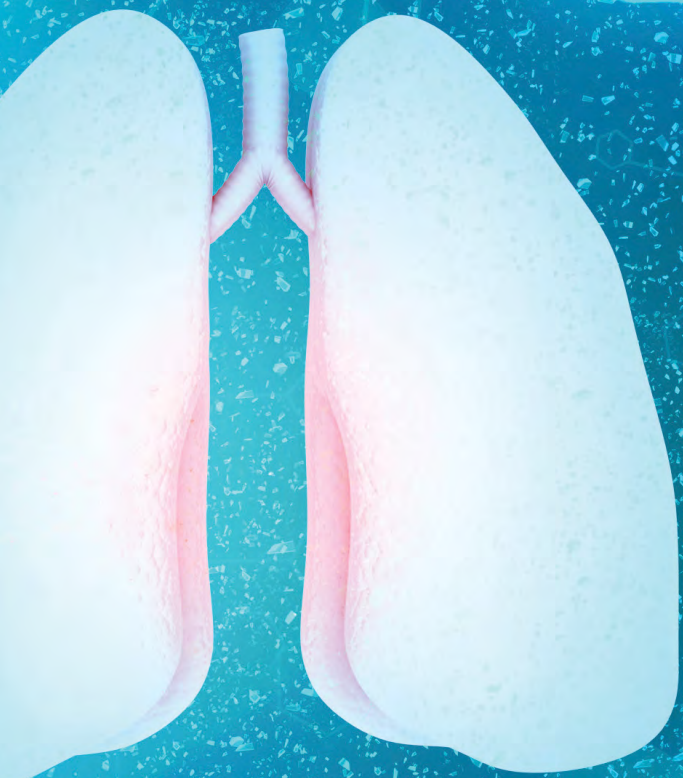
ILD Nursing and Allied Health Guide



Pulmonary Fibrosis Foundation™

Table of Contents

Dear Nurses and Allied Health Professionals

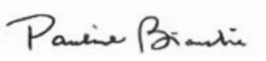
This is a guide that was developed by the Pulmonary Fibrosis Foundation in collaboration with several nurses and allied health professionals who are experts in the field of interstitial lung disease. We hope this is a valuable tool for all of you who care for patients affected by these challenging diseases.

As you know, the diagnosis and treatment of patients with interstitial lung disease is complex and our goal is to provide information identifying the disease, interpreting test results, managing comorbidities, disease management, and other supportive measures.

We recognize the important role that you play in the care, support, and education of these patients and are appreciative of all that you do.

We would especially like to recognize Jennifer Hayes, RN, BSN; Shanna Hoskinson, RN; Kathleen O. Lindell, PhD, RN; Wendi Mason, RN, MSN, ACNP; Tamra Perez, BSN, RN; Ashleigh Rodriguez, NP; and Anne Turner, BSN, RN, JD for the contributions they have made to this important resource.

Thank you,



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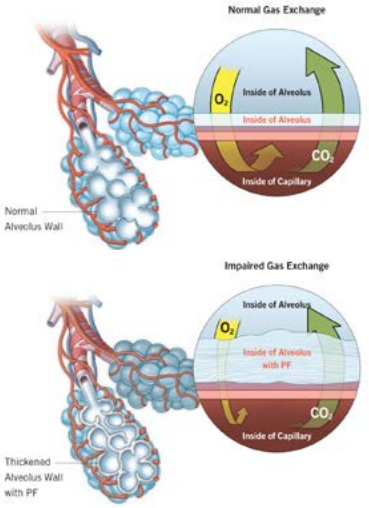
Introduction



The interstitial lung diseases (ILDs) are a family of over 200 related conditions characterized by inflammation, fibrosis (scarring), or other abnormalities in the alveolar walls (also known as the interstitium). These changes lead to thickening of the alveolar walls, making the lung stiff and making it difficult for oxygen to diffuse into the bloodstream. ILDs are not cancer and they are not infectious. In most cases, fibrosis is present. We use the general term "pulmonary fibrosis" (PF) to refer to any ILD in which fibrosis is present. Fibrosis can be identified on a high-resolution CT (HRCT) scan of the chest or on lung biopsy. As noted below, there are many different types of PF, but they may all share common features: exertional dyspnea, dry bothersome cough, crackles on lung exam, poor quality-of-life, supplemental oxygen requirement, and a progressive course and high mortality rate.

Patients living with PF are different than those with chronic obstructive pulmonary disease (COPD). They often require higher oxygen flow, experience more rapid progression, and have few therapies that improve their quality-of-life or survival. Nurses and allied health professionals play a central role in the care of patients with PF as detailed throughout this guide.

The incidence (new cases per year) and prevalence (number of cases right now) of ILD is not known. Based on available data, the prevalence of idiopathic pulmonary fibrosis (IPF), the most common idiopathic form of PF, has been reported to be 58.7 per 100,000 people for the US population. Additionally, the prevalence of IPF in US adults aged 60 and older has been reported to be approximately 200,000 and the prevalence of IPF in US adults aged 70 and older has been reported to be 429.3 per 100,000. Based on these prevalence estimates, up to 1 in 400 adults age 60 and older are living with IPF. Up to 1 in 200 adults age 70 and older are living with IPF. PF can affect anyone. Men, women, and children can all get PF. IPF is much more common in older adult males.

PART ONE:
Identifying the Disease

RECOGNITION OF ILD

Most patients with ILD will present with exertional dyspnea, chronic dry cough, or both. Physical examination will show crackles at both lung bases in most cases. ILD can then be identified by performing an HRCT scan of the chest. The initial work-up should also include pulmonary function testing (PFT) detailed below.

THE DIAGNOSTIC PROCESS

ILDs can be divided into two groups: (1) those in which a cause can be identified, and (2) those in which the cause is unknown, in which case we use the term "idiopathic interstitial pneumonia."

Identifying a cause always requires taking a careful history, performing a physical examination, sending serologies for connective tissue diseases, and obtaining a high-quality HRCT. In some cases, a lung biopsy is required. Here are some examples of ILDs of "known cause":

Connective Tissue Diseases: Autoimmune diseases such as rheumatoid arthritis, scleroderma, Sjögren's, and dermatomyositis/polymyositis can damage the lungs and cause connective tissue disease-associated interstitial lung disease (CTD-ILD). Sometimes, ILD is the first manifestation of a CTD. Patients should be carefully questioned about any symptoms that could indicate underlying disease, such as joint pain, stiffness, or swelling; skin thickening or tightening; rash; dry eyes; dry mouth; Raynaud's phenomenon; diffuse recurrent muscle pain or weakness; and severe heartburn with gastric regurgitation. Patients should also undergo autoimmune serology testing. In many cases, an ANA, RF and anti-CCP antibodies should be ordered. Additional serologies, such as Scl-70, anti-Ro (SS-A), anti-La (SS-B), and myositis antibodies should be ordered when indicated. If evidence is found of a possible undiagnosed CTD, a referral for evaluation by a rheumatologist should be considered.

Medications: A number of medications (such as amiodarone, nitrofurantoin, methotrexate, and certain chemotherapy agents) are known to have lung damage as a

possible effect. The ILD health professional must not only obtain a current medication list, but also review past medications (including cardiology, autoimmune, and cancer treatments). See Pneumotox **www.pneumotox.com/drug/index/** for additional information.

Environmental Factors (Hypersensitivity Pneumonitis): When gathering patient history, it is important to consider current and past environmental factors that can contribute to PF. Inhaled mold spores or bird proteins can trigger inflammation and fibrosis. A history of dampness, mold, or bird exposure in the home or workplace should immediately raise suspicion for hypersensitivity pneumonitis. When fibrosis is present, we often call this "chronic" hypersensitivity pneumonitis. An exposure history can be obtained by questionnaire. Involvement of an industrial hygienist or a home inspection for mold is indicated in some cases. Avoidance of the exposure is a critical part of the management of patients with hypersensitivity pneumonitis.

"Most patients with ILD will present with exertional dyspnea, chronic dry cough, or both."

Occupational (Pneumoconiosis): A wide variety of workplace exposures are potentially toxic to the lungs. "Black lung" in coal workers and asbestosis are two well-known examples of pneumoconioses. The rate of occupational diseases in the United States has declined due to improvements in occupational safety. However, occupational factors remain an important cause of ILD and obtaining a thorough occupational history is critical, including any time served in the armed forces, especially naval shipyards. Patients may not know if they are or were exposed to any potentially hazardous substances while on the job. They have a legal right to this information from both current and former employers. Material Safety Data Sheets (MSDS), available from their employer or online, can provide details about each substance, including whether it is linked to respiratory toxicity. Larger companies often employ an industrial hygienist, safety officer, or compliance manager who is responsible for maintaining safe working conditions and can help answer these questions. Patients can also contact their regional Occupational Safety and Health Administration (OSHA) office for help. OSHA is also an excellent resource for the provider who is trying to determine potential lung toxicity from an unfamiliar chemical or industrial process.

Radiation: Patients should be asked if they have ever received radiation therapy to the chest, which can cause PF.

IDIOPATHIC INTERSTITIAL PNEUMONIAS

The ILDs with no known cause make up a subgroup of ILDs called idiopathic interstitial pneumonias (IIPs). Idiopathic pulmonary fibrosis (IPF) is the most common disease in this group. Other IIPs include: idiopathic non-specific interstitial pneumonia (idiopathic NSIP), desquamative interstitial pneumonia (DIP), cryptogenic organizing pneumonia (COP), and unclassifiable ILD.

The IIPs are diagnosed after a complete history, physical exam, blood work, and HRCT fail to identify a known cause of disease. In some cases, a confident diagnosis of an IIP can be made. A good example of this situation is IPF, which has characteristic features on an HRCT. But, in some cases, including some cases of IPF, a lung biopsy will be performed to make a specific diagnosis.

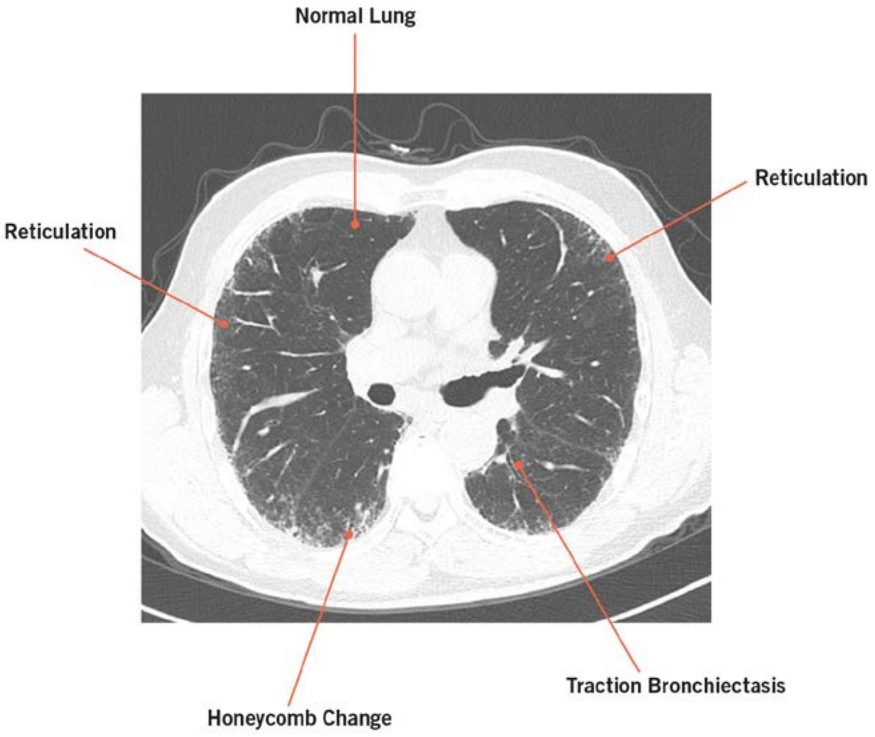
PART TWO:
Interpreting Test Results

HIGH-RESOLUTION COMPUTERIZED TOMOGRAPHY SCANS (HRCT)

Results of the HRCT chest scan without contrast should be interpreted by the radiologist, ideally with experience or expertise in reviewing ILD. The findings should then be reviewed by the pulmonologist or a healthcare provider with training in ILD to look for visual patterns of fibrosis and inflammation that can help point toward a specific diagnosis.

On CT imaging, air is typically black as noted by the air above the chest and throughout most of the lung in the normal patients. With abnormalities such as inflammation of fibrosis in the lung, varying degrees of white opacities are noted in the lung with structural changes such as honeycomb change or traction bronchiectasis.

On the next page, please see the diagram for a few examples of important findings on CT.



Reticulation

Irregular intersecting white lines. Reticulation indicates the presence of fibrosis. All forms of PF have reticulation.

Traction bronchiectasis: Dilated airways due to fibrosis.

Honeycombing

Thick-walled linear cysts, often occurring along the periphery of the lung. Due to fibrosis. Common in, but not specific for, IPF.

Ground-glass opacities/infiltrates

Hazy areas of the lung. Ground-glass is not specific for any one problem. Fluid (such as from heart failure), inflammation, infection, and other pathology can all show up as ground-glass. When "mosaic" ground-glass attenuation is present, it often indicates diseases that involve the small airways as seen in hypersensitivity pneumonitis, forms of bronchiolitis, and other conditions.

PULMONARY FUNCTION TESTS (PFTS)

Pulmonary function test (PFT) results can be useful for any trained healthcare provider. The presence of abnormal PFT findings can assist in making sure those that suggest ILD would then obtain an HRCT. See below for basic interpretation of PFTs.

Spirometry gives many results, but the most important for the diagnosis of ILD are forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), and the ratio of FEV1 to FVC (FEV1/FVC ratio). In ILD, the FVC can be normal in early disease and will decline as the disease progresses. This is one of the primary ways that we can track progression of PF, and it is often measured at every clinic visit. A normal FVC is often >80% of the predicted value, but each lab uses different thresholds.

The FEV1 often tracks with the FVC, and while it is extremely valuable in other diseases like asthma and chronic obstructive pulmonary disease, it is often not followed closely in PF. The FEV1/FVC ratio is typically normal (>70%) in PF.

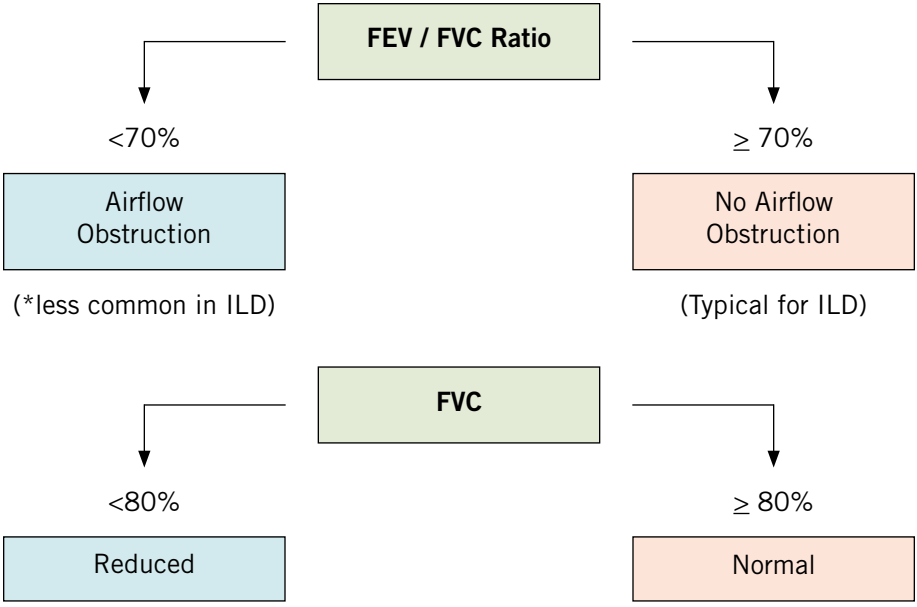
Lung volume measurement also gives many results, but the most important one is Total Lung Capacity (TLC), which is the volume of air the lungs can hold during the deepest possible breath in. Just like FVC, the TLC can be normal in early disease and will decline as the disease progresses. When TLC is reduced (<80% or so), we use the term "restrictive ventilatory defect." Some centers will follow TLC regularly and others will not.

Diffusing Capacity of the lung for Carbon Monoxide (DLCO) gives a measure of how quickly gas can move from inside the alveoli, through the (thickened) alveolar wall, and into the bloodstream. DLCO is reduced (<70-80%) in almost all cases of PF. A normal DLCO makes ILD unlikely. Like FVC, DLCO decreases as the disease progresses and is often measured at all or most clinic visits.

OXYGEN TESTING

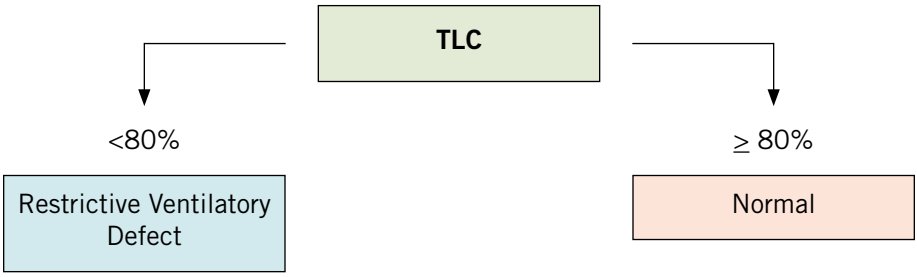
The need for supplemental oxygen is often tested at rest, during exertion, and when indicated, during sleep. Medicare has particular guidelines for determining the need for supplemental oxygen. If oxygen at rest or with exertion is not indicated, a nocturnal oximetry test or polysomnography can determine whether oxygen is needed during sleep.

SPIROMETRY



BOTH CAN BE SEEN IN ILD

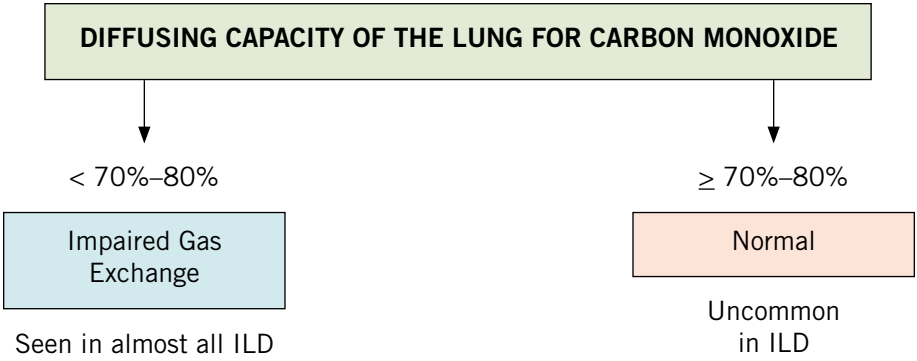
LUNG VOLUMES



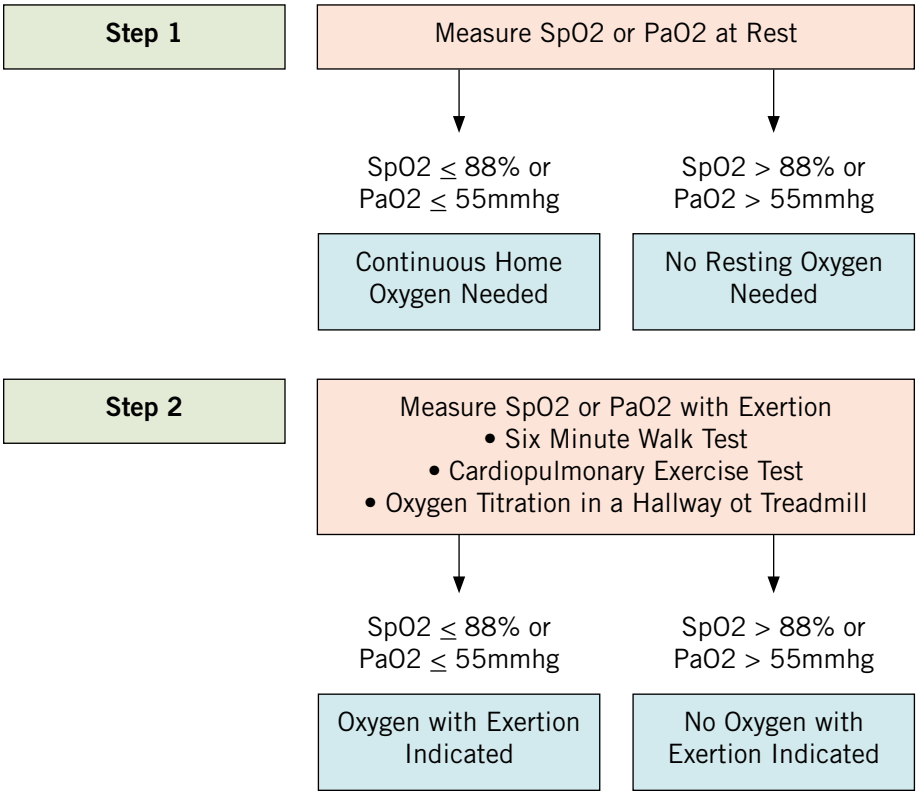
BOTH CAN BE SEEN IN ILD

*Can occur in RA-ILD, HP, Sarcoidosis, and combined COPD/ILD

DIFFUSING CAPACITY



OXYGEN TESTING



Please note that when the SpO2 is 89% or the PaO2 is 56-59, oxygen can also be prescribed if your patient has (1) dependent edema, (2) pulmonary hypertension or "cor pulmonale" determined by measurement of right heart catheterization, echocardiogram, or EKG (P waves greater than 3 mm in leads II, II, or aVF), or (3) a hematocrit > 56%.

It is important to determine and document how much oxygen (liter/minute flow and type of interface) is required to maintain saturations over 88% at rest and during ambulation when crafting the oxygen prescription.

Because of the higher cost of liquid oxygen systems, many home care companies no longer offer or encourage the use of concentrators and tanks for portability. However, if the ordering healthcare provider believes a specific modality of a system better accommodates the patient, it should be specified in the prescription.

6-MINUTE WALK TEST (6MWT)

The **6-minute walk test** (6MWT) is completed for a variety of reasons, including measurement of distance walked in six minutes, nadir (lowest) saturation, end-walk saturation, and heart rate recovery. These data–particularly any changes over time–can help inform prognosis. Use the European Respiratory Society (ERS)/American Thoracic Society (ATS) document "Field walking tests in chronic respiratory disease" for more information. **thoracic.org/statements/resources/copd/FWT-Tech-Std.pdf**

PART THREE:
Comorbidities

GASTROESOPHAGEAL REFLUX DISEASE (GERD)

Gastroesophageal reflux disease (GERD) occurs as a result of the weakening of the muscle tone of the lower esophageal sphincter (LES), a circular ring of muscle connecting the esophagus and stomach, leading to reflux of gastric contents into the esophagus. GERD has long been identified as a cause or trigger of pulmonary diseases such as asthma and chronic cough. An increasing body of evidence also suggests an association between the presence of GERD and IPF. IPF patients are also more likely to have a hiatal hernia, a risk factor for GERD. The role of GERD in the etiology, progression, and exacerbation of IPF remains uncertain.

PULMONARY FUNCTION TEST (PFT) REPORT

Spirometry is a test of your ability to breath out as hard and fast as you can. It is the primary test that tells us how healthy your lungs are. Each row below is a different measurement obtained during a Spirometry test. The first three rows are the most important ones. We will only focus on those three.

FVC stands for "Forced Vital Capacity." This is the amount of air that comes out when you take a deep breath and then blow out as hard as you can.

The FEV1 is the amount of air that came out immediately (in the first second) when you blow out as hard and fast as you can. This number is often reduced in PF.

This result is often called the "F.E.V.1.F.V.C. ratio." It is simply the FEV1 divided by the FVC and expressed as a percentage. A normal FEV1/FVC is greater than 70% — and most people with PF have an FEV1/FVC that is normal. A reduced FEV1/FVC suggests other kinds of lung diseases, such as asthma or COPD.

This test literally measures how much air is sitting in your lungs. We usually pay attention to the "TLC", since it is the best test of how much air your lungs can hold.

"TLC" stands for Total Lung Capacity. It is the amount of air that your lungs can hold when you take the deepest breath possible. A normal % Predicted value is greater than about 80%.

A diffusion capacity test measures how easily gases (like oxygen) can move from the inside of the air sacs into the bloodstream. The most important result in this section is the "DLCO", which is the primary diffusion test result.

Spirometry

FVC	Liters
FEV1	Liters
FEV1/FVC	%
FEF25–75%	L/sec
FEF25%	L/sec
FEF50%	L/sec
FEF75%	L/sec
PEF	L/sec
MVV	L/min
PIF	L/sec
FIF50%	L/sec
FET100%	Sec

Lung Volumes

VC	Liters
TLC	Liters
RV	Liters
RV/TLC	%
FRC PL	LIters
FRC N2	Liters
FRC He	LIters
Vtg	Liters

Diffusion

DLCO	mL/mmHg/min
DL Adj	mL/mmHg/min
VA	Liters
DLCO/VA	mLmHg/min/L
IVC	Liters

"Ref" stands for "Reference. Sometimes this column is also labeled "Predicted." These are the test results we expect if your lungs are healthy.

Ref	Pre Meas	Pre % Ref
3.45	1.64	48
2.74	1.40	51
79	86	
2.69	2.23	83
5.64	4.08	72
3.61	5.25	145
1.32	0.64	48
6.09	5.25	86
95		
4.17	2.46	59
3.73	2.23	60
	7.21	
3.45	1.64	48
5.37	2.55	47
2.01	0.91	45
38	36	
3.04		
3.04	1.11	37
3.04		
26.6	5.9	22
26.6	5.9	22
	2.32	
5.18	2.55	49
	1.63	

This is the actual result of each test. For example, for FVC, we expected this person to be able to blow out 3.45 Liters of air (Reference value), but he or she was only able to blow out 1.64 Liters of air. A low FVC is common in people with PF.

This column is often called "Percent Predicted." It is calculated as the Measured value divided by the Reference (predicted) value. A normal value in someone with healthy lungs might range from 80% to over 100%.

In this case, the FVC is 48% of the predicted value. Since 48% is lower than the normal range of 80% or more, the FVC in this case is abnormal. A low FVC is common in people living with PF. This is one of the most important test results that doctors pay attention to. As PF worsens, FVC tends to go lower and lower.

In this case the TLC is 47% of the normal value. Most people with PF have a low TLC.

The DLCO is 22% of the predicted value here. DLCO is almost always reduced in people with PF. And the DLCO is usually reduced to a much greater degree than the FVC or the TLC.

Role of the Doctor's Office
Identify the oxygen needs of the patient
When indicated, the testing includes: • 6-minute walk test (6MWT) • High Altitude Simulation Test (HAST) • Overnight oximetry/sleep study • Arterial Blood Gas Test (ABG)
Provide the appropriate prescription and qualifying documents
Chart notes and testing results for the home care company
Work with the home care company • Submit Certificates of Medical Necessity (CMN) for insurance billing, primarily Medicare
Educate the patients on effective and safe use of oxygen

Role of the Home Care Company
Receive the prescription
Verify insurance coverage and bill insurance
Provide a basic oxygen system, including any equipment and disposable supplies, such as cannulas and humidifiers
Keep records of CMNs for Medicare
Provide 24-hour emergency service for equipment malfunctions or power outages
Provide education on proper and safe use of equipment
Play an important role in a patient's long term oxygen therapy Depending on where the patient lives and how much a patient travels, a local home care company or one of the national companies may be better suited to the patient's needs

Role of the Patient
Using supplemental oxygen is something the patient can control, though it can be a difficult transition
Having an SpO2 in the normal range will help prevent dyspnea in many patients
Using supplemental oxygen during activities will allow the patient to remain more active, thus improving quality of life
Avoiding low oxygen levels may help prevent pulmonary hypertension
Being more active and able to participate in rehabilitation may help patients maintain a healthy weight and improve their pre-transplant candidacy
Living longer by using supplemental oxygen is not proven in ILD, but it has been shown to prolong survival in chronic obstructive pulmonary disease (COPD)
Maintaining an SpO2 > 90% is encouraged by many clinicians. Some patients find it useful to purchase portable finger oximeters to monitor levels at home during different activities, if recommended by their healthcare provider.

GERD Diagnosis

Some patients with ILD will have symptoms of GERD, such as heartburn or regurgitation, while others will not have symptoms. This is referred to as "silent reflux." If clinically indicated, a diagnosis of GERD can be made using objective testing, such as ambulatory 24-hour pH monitoring, esophageal manometry, upper endoscopy, or barium swallow esophagram. However, the indication for these invasive tests without heartburn remains uncertain.

GERD Treatment

Most clinicians will treat GERD when symptoms, such as heartburn, are present. While current ATS/ERS/JRS/ALAT IPF Guidelines conditionally recommend antacid treatment to treat IPF, the treatment of asymptomatic GERD in IPF patients is controversial. While some non-randomized studies suggest that IPF patients treated with antacid therapy have better outcomes, others suggest that antacid therapy may increase the risk of infection. Anti-reflux surgery, the most common type being fundoplication, involves a laparoscopic procedure where the surgeon wraps the top part of the stomach around the esophagus in order to restrict the back-flow of stomach contents. A clinical trial of surgical fundoplication to treat GERD in IPF has been completed the results were suggestive of (but did not prove) a benefit.

GERD management can include lifestyle interventions including weight loss, elevating the head of the bed by six inches, avoidance of late evening meals, and elimination of food that can trigger reflux, such as chocolate, caffeine, alcohol, and spicy foods. Medical management of GERD includes antacids, such as H2 blockers and proton pump inhibitors (PPIs). Studies have shown that PPIs, most of which are now available over the counter, are more effective than H2 blockers, and there are no major differences in efficacy between the different PPIs. Both drugs suppress acid secretion by the stomach. Common side effects occurring in 1-2% of patients taking PPIs include nausea, constipation, diarrhea, headache, and skin rash. PPIs should be taken 30 minutes before eating.

PULMONARY HYPERTENSION

Pulmonary hypertension (PH) is defined as an elevation in the mean pulmonary arterial pressure greater than 25 mm Hg. PH is considered severe if cardiac index is < 2 L/min/m^2 or if mPAP is ≥ 45 mm Hg. The World Health Organization (WHO) classifies patients with PH into five groups based upon etiology. Patients diagnosed with ILD-associated PH are classified as WHO Group 3: "Pulmonary hypertension due to lung

diseases and/or hypoxia." PH is a recognized complication in patients with ILD.

Pulmonary Hypertension

PH has been reported to occur in 20-85% of patients with PF. In PF patients undergoing evaluation for lung transplantation, PH was associated with more severe fibrosis as measured by pulmonary function tests (PFTs) and resting oxygen saturation.

Due to overlapping primary symptoms of shortness of breath with progressive dyspnea on exertion and exercise limitation, it may be difficult to detect PH in patients with PF. Clues may include exertional dyspnea or fatigue whose severity seems out of proportion to the degree of lung disease as demonstrated by a severely decreased DLCO. Other symptoms may include chest pain or syncope with exertion. PH can also lead to right heart failure, which manifests as peripheral edema, elevated jugular venous pressure, and severe exertional limitation.

Although symptoms, an ECG (right ventricular hypertrophy), a chest CT scan (dilated main pulmonary artery, right ventricular dilation), and PFTs may hint at PH, an echocardiogram is the initial test of choice. Echocardiographic evidence of PH includes an estimated right ventricular (or pulmonary artery) systolic pressure greater than 40 mm Hg, reduced right ventricular ejection fraction, dilated right ventricle and/or atrium, and bowing of the interventricular septum.

Echocardiography, while useful, cannot diagnose PH. The gold standard for confirming the diagnosis is right heart catheterization. PH is defined as a mean pulmonary artery pressure (mPAP) > 25 mm Hg at rest, as measured by right heart catheterization. However, since there are no proven therapies for ILD-associated PH, right heart catheterization is only indicated in a minority of patients. Some indications might include evaluation for lung transplantation and suspicion that pulmonary hypertension may be the dominant condition, with mild ILD playing a small role in symptoms (such as in some cases of connective tissue disease).

Pulmonary Hypertension Treatment

The mainstay of therapy for PH in patients with ILD is supplemental oxygen therapy when indicated. Oxygen can dilate pulmonary arterioles and decrease pulmonary artery pressure in some patients.

The presence of PH has been associated with an increased risk of death in ILD. Nevertheless, since there are no proven therapies to treat PH in patients with ILD, pharmacological therapy is often not prescribed by clinicians. Medications approved for other forms of PH are not approved by the Food and Drug Administration (FDA) for patients with IPF-associated PH (WHO Group 3), due to lack of clinical trial evidence of efficacy and safety. Per 2011 American Thoracic Society (ATS) Guidelines, "Pulmonary hypertension should not be treated in the majority of patients with IPF, but treatment may be a reasonable choice in a minority in patients with moderate to severe pulmonary hypertension documented by right heart catheterization."

SLEEP APNEA

Sleep Apnea Diagnosis

Apnea means "not breathing." Obstructive sleep apnea (OSA) is the presence of recurrent episodes of upper airway obstruction (due to closure of the throat and upper airway) occurring at least five times per hour on average during sleep. OSA has been found to be common among those diagnosed with IPF. Traditionally, symptoms of sleep apnea include daytime sleepiness, snoring, gasping while sleeping, awakening and feeling that you can't breathe, falling asleep at inappropriate times (such as in a waiting room or during a conversation) or at unsafe times (such as driving a car), dry mouth, and headache upon awakening.

Risks and comorbidities associated with sleep apnea include obesity, GERD, and coronary artery disease. Physical examination findings may show a large neck circumference (men > 17 inches, women > 16 inches), a crowded airway (Mallampati III or IV), a deviated nasal septum, patulous soft palate, and scalloped tongue. Many IPF patients with OSA are not sleepy, may not be obese, and many do not have severe IPF. Some data suggest that OSA might even contribute to early lung injury and pulmonary hypertension. Polysomnography, a test used to diagnose OSA, should be considered in patients who have symptoms of OSA.

Sleep Apnea Treatment

If sleep apnea is diagnosed, patients can be treated with continuous positive airway pressure (CPAP) therapy or bilevel positive airway pressure (BiPAP) therapy if clinically indicated.

PART FOUR:
Disease Management

PROGRESSION OF PF

Early PF is often symptom-free, and patients frequently do not receive a diagnosis until they have moderate or severe disease. "Progression" means that fibrosis has built up over time. Progression occurs over different time periods that vary from person-to-person. Typical patterns of IPF progression include:

- *Intermittent Step-Wise Progression:* Most patients experience periods of stability alternating with periods of progression, as measured by increasing symptoms, decreasing FVC, decreasing DLCO, and increasing supplemental oxygen needs.
- *Rapid Progression:* Other patients will progress rapidly, experiencing a significant decline within 6 months to a year of diagnosis.
- *Acute Exacerbations:* Acute exacerbations are unpredictable, occur in about 10% of patients each year, and usually have a very poor outcome. While most are "idiopathic," some are due to infection, aspiration, or drug toxicity.

Patients with mild to moderate symptoms may believe they are stable. It is important to educate patients about the unpredictability of acute exacerbations and the inevitability of disease progression. This will enable them to engage in appropriate planning and make informed choices.

Although disease course cannot be predicted, there is a staging system available for IPF called the GAP score. The GAP score is based on age, sex, and physiology (FVC and DLCO) with scores ranging from 0 to 9 which correspond to three Stages: Stage I (score 0-3), Stage II (4-5), and Stage III (scores 6-8). One-year mortality rates are 6%, 16%, and 39%, respectively (see Table 1). It is important to be familiar with this tool because patients can easily find "GAP Calculators" on the internet and compute the score for themselves. There are limits to how the information should be used.

While patients may want to know their stage and their "risk", you should communicate to your patient that even if they are "Stage III" with a 39% risk of death in 1-year, that means that 61% of people live longer than 1 year – and there is no way to know if your

Predictor Gender	Points	Predictor Age (y)	Points	Predictor Physiology	Points
				FVC, % predicted	
Female	0	≤60	0	>75	0
Male	1	61-65	1	50-75	1
		>65	2	<50	2
				DLCO, % predicted	
				>55	0
				36-55	1
				≤35	2
				Cannot perform	3
				Total Possible Points	**8**

patient is in the 39% group or the 61% group. There are several limitations that patients should understand. Also remember that the GAP score only applies to IPF. Also, the GAP stage was developed before anti-fibrotic therapy was available in the United States, and therefore your patients may have a better "average" outcome than that predicted by the GAP score. In addition, other forms of PF may have a better prognosis.

http://annals.org/data/JournalsAIM

Stage	Mortality	% Risk
I (Points 0-3)	1-y	5.6
	2-y	10.9
	3-y	16.3
II (Points 4-5)	1-y	16.2
	2-y	29.9
	3-y	42.1
III (Points 6-8)	1-y	39.2
	2-y	62.1
	3-y	76.8

SUPPLEMENTAL OXYGEN

Home Oxygen Delivery Systems

It is vital to maintain appropriate oxygen levels as oxygen plays an important role in the energy metabolism of living organisms. Air is approximately 21% oxygen, 78% nitrogen, and about 1% argon and other trace gases.

One of the most common symptoms ILD patients experience is dyspnea on exertion. Because of the nature of the disease, it is not unusual for a patient to have resting oxygen saturations within normal limits and then desaturate with activity. The increase in cardiac output during exertion means there is less time for oxygen to diffuse from the alveoli through the alveolocapillary membrane and into the bloodstream. As the disease progresses, desaturation becomes more severe and occurs with lesser degrees of exertion.

Types of Oxygen Systems

Basic oxygen delivery systems include an in-home stationary unit and a portable system that allows the patient to leave the home.

> **"One of the most common symptoms ILD patients experience is dyspnea on exertion."**

STATIONARY SYSTEMS

Stationary Concentrator

Oxygen concentrators work by extracting and separating oxygen from other gases and moisture in room air. Oxygen then accumulates in a reservoir, which provides a continuous stream of highly concentrated oxygen (> 94%). Stationary concentrators have the ability to produce enough oxygen to meet most needs up to 10 LPM. The unit stays in the room in which it is placed and patients use different lengths of oxygen tubing to move around. A hidden cost is the electricity required to power the concentrator, which is not reimbursable. The concentrator is a reliable and relatively inexpensive option, although noisy. A humidifier should also be used once a patient requires more than 4-5 LPM to prevent bloody noses, congestion, and irritation, as the oxygen flow tends to dry out nose membranes.

Stationary Liquid System

When oxygen is cooled to a very low temperature (approximately 300 degrees below zero Fahrenheit), it becomes a liquid. To remain in liquid form, oxygen must be held in insulated canisters. Large amounts of oxygen can be stored in a container at low pressure in liquid form. Stationary liquid systems provide not only a large storage capacity, but also allow for filling and refilling smaller units. As the liquid oxygen leaves the container, it warms up to room temperature and becomes a gas. Conventional liquid oxygen systems are quiet, have no major moving parts, and require no power source to operate. Depending on the patient's consumption rate and liter flow, the canister needs to be refilled approximately every two weeks.

PORTABLE SYSTEMS

Compressed Gas Tanks

Tanks in a variety of sizes are inexpensive and readily available. Using them with a backpack allows for hands-free activities. However, tanks can be heavy. Some patients use a wheeled cart to be mobile, especially if larger tanks are required. No power source is needed, and the patient does not need to refill as they are delivered full. They can be used with conserving devices so that patients who tolerate pulse dose delivery (where a breath generates the oxygen to be delivered) can go longer on one tank. Patients are required to store cylinders safely and learn how to change the conserving devices. It follows that the higher the liter flow, the faster the tank will be depleted, so a variety of sizes based on a patient's liter flow and activity level may allow greatest flexibility.

Liquid Portable Units

This portable system is used in conjunction with the stationary unit and requires the patient to refill as needed. The portable unit is lighter than an oxygen E-cylinder tank, lasts longer, and is worn over the shoulder with a strap. While lighter, it's prone to leaks if not kept upright. It requires dexterity to refill, and has a danger of cold burning during refilling. Patients have complained of evaporation and less tank life in humid weather.

Portable Oxygen Concentrators

Portable oxygen concentrators (POCs) are simply smaller versions of the stationary unit. A portable concentrator runs on battery, allowing for increased portability. A

patient carries additional batteries to allow for greater time away from an outlet. POCs can be plugged in to recharge and come with car adapters to allow for use during driving trips. POCs are the accepted mode of oxygen delivery on airplanes. Battery life depends on the patient's liter flow and oxygen consumption. The higher the liter flow, the faster a battery is depleted. The main limitation, especially for ILD patients, is the limited liter flow. Many of the small units provide a maximum of 2 LPM, while ILD patients require a higher level of liter flow than many of the POCs provide. In many cases, POCs cannot deliver sufficient oxygen flows for ILD patients with severe exertional desaturation. Another issue is that patients who need more than 3 LPM on the 6-minute walk test in order to maintain SpO2 > 88% use continuous flow and cannot tolerate the pulse dose delivery system.

Portable oxygen systems give patients greater freedom to participate in activities outside the home to maintain quality of life. The right system for each patient depends on his or her activity level, goals, and ability to utilize one system over another.

Cannula Options

With all systems, the general rule is the higher the patient's required liter flow and use of continuous flow instead of pulse dose flow, the more limited the patient's options. Some strategies for patients on a higher flow are to change from a regular nasal cannula to either a pendant or mustache oxymizer cannula.

These cannulas are simple conserving devices that accumulate oxygen usually wasted during exhalation and store it in a 20 milliliter reservoir. The patient then receives a bolus of oxygen at the beginning of inhalation. It is important to note that humidifiers cannot be used along with the conserving cannula.

OXYGEN SAFETY

Oxygen itself is not flammable, but because it is an accelerant, patients should take precautions to prevent injury. Compressed tanks should be kept 8-10 feet away from any flame or spark, such as candles, stoves, fireplaces, electric razors, and people who smoke. Petroleum-based products should be avoided; patients should use aloe or cocoa butter products for dry nose instead. Unused cylinders should be secured to avoid falling and becoming projectiles. Home concentrators should be well-ventilated, and patients should be cautioned to avoid tripping on their oxygen tubing.

Using supplemental oxygen can be a major adjustment for a patient. Many are embarrassed to be seen in public wearing a cannula. Patients who were previously active may perceive oxygen use as a signal to cease their activities. The health care team must educate patients about the need for supplemental oxygen to aid in facilitating continued activities that give them joy.

ANTIFIBROTIC THERAPIES

Two antifibrotic drug therapies, pirfenidone and nintedanib, are available to help slow disease progression in IPF. One antifibrotic therapy, nintedanib, is available to help slow the disease progression in systemic sclerosis-associated ILD (Ssc-ILD). With long term follow up of patients on antifibrotic therapies, the decrease in disease progression is associated with improved survival. For full prescribing information, see FDA.gov.

Pirfenidone (Esbriet®, Pirfenex®, Pirespa®): Pirfenidone is an antifibrotic and anti-inflammatory drug approved to treat IPF in the US, Europe, Canada, and Asia. In clinical trials, pirfenidone has been shown to slow progression of mild-to-moderate IPF.

Dosing

267 mg capsules or tablets; uptitrate to 3 capsules orally 3 times daily with meals over 14 days. MUST be taken with full meals. Once on a stable dose, an 801mg tablet (equivalent to 3 capsules) is available.

Adverse Reactions

The most common adverse reactions (≥10%) are nausea, rash, abdominal pain, upper respiratory tract infection, diarrhea, fatigue, headache, dyspepsia, dizziness, vomiting, anorexia, gastro-esophageal reflux disease, sinusitis, insomnia, weight decreased, and arthralgia.

Warnings & Precautions

Elevated liver enzymes: ALT, AST, and bilirubin elevations have occurred. Monitor ALT, AST, and bilirubin before and during treatment. Temporary dosage reductions or discontinuations may be required.

Photosensitivity and rash: Photosensitivity and rash have been noted. Avoid exposure to sunlight and sunlamps. Wear sunscreen and protective clothing daily. Temporary dosage reductions or discontinuations may be required.

Gastrointestinal disorders: Nausea, vomiting, diarrhea, dyspepsia, gastroesophageal reflux disease, and abdominal pain have occurred.

Elevated liver enzymes and drug-induced liver injury: In the post-marketing period, non-serious and serious cases of drug-induced liver injury, including severe liver injury with fatal outcome, have been reported. Inform patients about the need for periodic monitoring. Monitor ALT, AST, and bilirubin prior to the initiation of therapy in all patients, then monthly for the first six months and every three months thereafter, and as clinically indicated. Measure liver function tests promptly in patients who report symptoms that may indicate liver injury, including fatigue, anorexia, right upper abdominal discomfort, dark urine, or jaundice. Temporary dosage reductions or discontinuations may be required.

Drug Interactions

Moderate (e.g., ciprofloxacin) and strong inhibitors of CYP1A2 (e.g., fluvoxamine) increase systemic exposure of pirfenidone and may alter the adverse reaction profile of pirfenidone. Discontinue fluvoxamine prior to administration of pirfenidone or reduce to 267 mg three times a day. Consider dosage reduction with use of ciprofloxacin.

The full prescribing information is available at: **https://www.gene.com/download/pdf/esbriet_prescribing.pdf**

Nintedanib (OFEV®): Nintedanib is an anti-fibrotic drug that is approved in the United States to treat IPF, scleroderma-associated ILD (SSc-ILD), and chronic interstitial ung diseases (ILDs) in which fibrosis continues to progress. In clinical trials, nintedanib has been shown to slow the decline of lung function in SSc-ILD, progressive fibrosing ILD, and mild-to-moderate IPF.

Dosing

150 mg capsules; one capsule orally every 12 hours taken with food

Adverse Reactions

Most common adverse reactions (≥5%) are: diarrhea, nausea, abdominal pain, vomiting, liver enzyme elevation, decreased appetite, headache, weight decreased, and hypertension.

Warnings & Precautions

Hepatic impairment: nintedanib is not recommended for use in patients with moderate or severe hepatic impairment. In patients with mild hepatic impairment (Child Pugh A), the recommended dosage is 100 mg twice daily approximately 12 hours apart taken with food. Consider treatment interruption, or discontinuation for management of adverse reactions in these patients.

Elevated liver enzymes and drug-induced liver injury: ALT, AST, and bilirubin elevations have occurred with nintedanib, including cases of drug-induced liver injury. In the post-marketing period, non-serious and serious cases of drug-induced liver injury, including severe liver injury with fatal outcome, have been reported. The majority of hepatic events occur within the first three months of treatment. Liver enzyme and bilirubin increases were reversible with dose modification or interruption in the majority of cases. Monitor ALT, AST, and bilirubin prior to initiation of treatment, at regular intervals during the first three months of treatment, and periodically thereafter or as clinically indicated. Temporary dosage reductions or discontinuations may be required.

Gastrointestinal disorders: Diarrhea, nausea, and vomiting have occurred. Treat patients at first signs with adequate hydration and antidiarrheal medicine (e.g., loperamide) or anti-emetics. Discontinue nintedanib if severe diarrhea, nausea, or vomiting persists despite symptomatic treatment.

Embryo-Fetal toxicity: Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception.

Arterial thromboembolic events have been reported. Use caution when treating patients at higher cardiovascular risk including known coronary artery disease.

Bleeding events have been reported. Use nintedanib in patients with known bleeding risk only if anticipated benefit outweighs the potential risk. nintedanib should also be used with caution (if at all) in patients on anticoagulants or dual anti-platelet therapy.

Gastrointestinal perforation has been reported. Use nintedanib with caution when treating patients with recent abdominal surgery, previous history of diverticular disease or receiving concomitant corticosteroids or NSAIDs. Discontinue nintedanib in patients who develop gastrointestinal perforation. Only use nintedanib in patients with known risk of gastrointestinal perforation if the anticipated benefit outweighs the potential risk.

Drug Interactions

Co-administration of P-glycoprotein and CYP3A4 inhibitors may increase nintedanib exposure. Monitor patients closely for tolerability of nintedanib.

The full prescribing information is available at:
https://docs.boehringer-ingelheim.com/Prescribing%20Information/PIs/Ofev/ofev.pdf

PULMONARY REHABILITATION

Exercise is an important component in the treatment and management of ILD. The health benefits of exercise are well-documented and can improve the patient's quality of life. Benefits include improved dyspnea and quality of life, more efficient use of oxygen, weight loss, and creating an overall sense of well-being. Exercise does not improve lung function, but neither does it harm the lungs. A person with ILD experiences a loss of control with their lung condition, and exercise becomes a form of self-management.

Pulmonary rehabilitation (PR) is specifically designed for people with lung diseases such as chronic obstructive pulmonary disease (COPD) and ILD. PR programs provide a safe, secure environment for exercising, as well as classes on controlling and improving symptoms and overall health in people with pulmonary disease.

As there are differences in the lung mechanics and disease progression between a person with COPD and a person with ILD, modifications are necessary. The person with ILD will have oxygen desaturation during exertional activities, and oxygen supplementation is usually required. This desaturation can be severe; the person with ILD should be monitored closely with pulse oximetry and may require increased oxygen flow rates during exercise. Continuous oxygen delivery should be available to those with ILD, as opposed to oxygen conserving devices (pulse dose delivery), to maintain pulse oximetry values > 90% saturation.

A person with connective tissue-related PF, such as rheumatoid arthritis, may benefit from a PR program that includes a physical therapy component to minimize joint pain and damage. For patients who are candidates for lung transplantation ongoing PR is an important part of the preparation for surgery and aftercare.

PR programs are usually 8-12 weeks, with 2-3 sessions per week. A multidisciplinary team that includes an exercise physiologist provides an initial assessment, develops goals, and prepares an individualized exercise program with progress reports throughout participation. It is imperative that any comorbidities, such as hypertension or diabetes, are stable before undergoing PR. Communication between the patient's provider and the program team is essential.

After completing the initial program, individuals are expected to continue the exercise regimen on their own. Studies show that the benefit gained from PR will be lost if the individual does not continue to exercise. Many PR programs offer a maintenance, or "graduate," program for a small fee to encourage people to continue to exercise. For many, it provides a means to stay connected to people with the same lung condition and serves as a support system.

PR was initially established for people with moderate to severe COPD per the Global Initiative for Chronic Obstructive Lung Disease (GOLD) diagnosis guidelines, and this can pose challenges for obtaining insurance coverage for ILD patients. A policy statement issued by the American Thoracic Society (ATS) and updated in June 2016 includes additional local determination coverage guidelines for reimbursement.

> "Patients appropriate for PR must have a diagnosis of a chronic, stable respiratory disorder with disabling symptoms that impair the patient's function. PFTs need to show FVC, FEV1, and/or DLCO of < 65% predicted on PFT within 1 year of PR. There must be the expectation of measurable improvement in a reasonable and predictable amount of time, and the patient must be able, motivated, and willing to participate."

"Benefits include improved dyspnea and quality of life, more efficient use of oxygen, weight loss, and creating an overall sense of well-being."

Local Medicare determination policies vary regionally; however, national policies determine final coverage. Currently, no national policy for PR coverage exists for persons diagnosed with ILD.

Patients with ILD may visit PR facilities prior to starting a program. There are several factors involved in selecting a PR facility, including location and program schedule. If the facility is close to home, attendance is higher. While overall functional improvement in ILD patients remains less than those with COPD, studies of a modified PR program have shown statistical improvement in quality of life for a lung condition that has few treatment options.

Prednisone Therapy

Prednisone is a pharmacological therapy that reduces inflammation. Some clinicians use prednisone to treat patients who have lung inflammation as part of their PF. However, long-term use in patients with IPF may be harmful.

Selected side effects of prednisone:

- Increased appetite and weight gain
- Susceptibility to infection
- Fluid retention
- Mood changes
- Insomnia
- Osteoporosis, fractures, and avascular necrosis of the hip
- Increased blood sugars and diabetes
- Hypertension
- Fragile skin and bruising

Dose adjustments are typically on a case-by-case basis and should always be tapered down and not stopped abruptly.

NON-STEROID IMMUNOSUPPRESSIVE THERAPY

Immunosuppressive therapy can be effective in decreasing immune response and inflammation in patients. However, patients must be informed that there is a Black Box warning on some of these medication and pregnancy is contraindicated. Patients of childbearing age should use two forms of birth control to prevent pregnancy. These drugs are FDA-approved, but have not been FDA-approved to treat ILD.

Common Medications:

- Mycophenolate (CellCept®)
- Azathioprine (Imuran®)

- Cyclophosphamide (Cytoxan®)
- Infliximab (Remicade®)
- Rituximab (Rituxan®)
- Methotrexate

Possible Side Effects (vary by medication):
- Increased risk for infection (and tuberculosis for infliximab)
- GI symptoms (nausea, vomiting, diarrhea)
- Pancreatitis (azathioprine)
- Liver problems (azathioprine)
- Hematuria and bladder cancer (cyclophosphamide)
- Various cytopenias

Lab Monitoring & Prophylaxis
While taking these medications, it is important to monitor blood work. Most patients taking a non-steroid immunosuppressant will require periodic monitoring of CBC, LFTs, and basic metabolic panel.

Other prophylactic considerations while using immunosuppressive medications include:
- Age-appropriate vaccination (best performed prior to immunosuppression). Remember not to give live vaccines to immunosuppressed patients.
- Prophylaxis for *Pneumocystis jiroveci* (PCP; now abbreviated PJP) with sulfamethoxazole-trimethoprim, a sulfa antibiotic. For sulfa allergic patients, dapsone can be used if a G6PD level is normal. Another alternative is atovaquone.
- Osteoporosis treatment and prevention while on prednisone.

PALLIATIVE CARE

Palliative care (PC) is an approach that improves quality of life for patients facing life-threatening illness and their families by preventing and relieving suffering. This is achieved through early identification, assessment, and treatment of pain and other physical, psychosocial, and spiritual problems. The focus is on managing symptoms and addressing advance care planning to improve quality of life.

PC should be offered upon diagnosis of a serious illness. Several professional organizations have developed consensus guidelines for implementation of PC. The National Consensus Project for Quality Palliative Care evolved from the work of five palliative care organizations: the American Academy of Hospice and Palliative Medicine;

Center to Advance Palliative Care; Hospice and Palliative Nurses Association; Last Acts Partnership; and National Hospice and Palliative Care Organization. The mission of the National Consensus Project for Quality Palliative Care was to create guidelines that improved the quality of palliative care in the United States.

"Palliative care involves management of symptoms, which is relevant even in patients with mild to moderate disease."

PC involves management of symptoms, which is relevant even in patients with mild to moderate disease. Patients receive emotional and spiritual support to enable them to live better with the consequences of an incurable illness. It can be a means to assist patients and families through the process of reflection, discussion, and communication of treatment preferences for end-of-life (EOL) care. This process, known as advance care planning, is "a more deliberate, organized, and ongoing process of communication to help an individual identify, reflect upon, discuss, and articulate values, beliefs, goals, and priorities to guide personal care decisions up to and including EOL care." The mantra of "It is wise to hope for and expect the best, but it is also wise to prepare for the worst" is a way to introduce advance care planning to ILD patients and their caregivers.

An interdisciplinary team can deliver PC, known as specialty palliative care, or a member of the clinical care team can deliver PC, known as primary palliative care. PC practitioners are trained to conduct discussions regarding EOL planning and may be helpful in initiating and facilitating such discussions.

Often confused with hospice, PC has different goals. Because PC focuses on assisting patients and family caregivers to better manage symptoms associated with disease progression, primary and/or specialty palliative care should ideally occur soon after diagnosis. For ILD patients, this is particularly important as disease progression is difficult to predict.

Many ILD patients represent a group of individuals with a chronic respiratory disease who are without disease-reversing treatment options and, absent lung transplantation, face progressive decline and death. The goals of PC are to prevent and relieve suffering, support the best quality of life for patients and their families, and encourage discussions regarding EOL preferences. Studies report that even when patients and caregivers understood the terminal nature of the disease, they did not appreciate that symptoms could escalate rapidly, resulting in death. Because the disease course of ILD is unpredictable, early introduction of PC should be considered as a standard of care to maximize benefits and improve quality of life.

"The goals of palliative care are to prevent and relieve suffering, support the best quality of life for patients and their families, and encourage discussions regarding end-of-life preferences."

LUNG TRANSPLANTATION

Single (unilateral) or double (bilateral) lung transplantation is available to patients who meet very stringent criteria. It is reserved as a mechanism to save the life of the patient, not simply to improve quality of life. However, mortality with lung transplant is high, with median survival rates of 5-6 years overall, and only 3.5 to 4 years for adults over 65 years old. Therefore, it is important to understand the totality of the risks of the procedure and the complications that may result from the medications given following transplant.

"It is important to determine whether a patient would ever want a lung transplant."

There are many lung transplant centers in the United States. Outcomes and transplant volume for each center can be found on the Scientific Registry of Transplant Recipients website (**srtr.org**). Each center has its own criteria for transplant, based on the agreements of those who serve on the transplant team (e.g., thoracic surgeons,

pulmonologists, pharmacists, psychiatrists, and social workers). These criteria may change as patient outcomes change, insurance approvals are granted or denied, or team members change. Essentially, most lung transplant centers require patients to be relatively healthy, physiologically young, and without obvious reasons contraindicated for immunosuppression.

Prior to 2005, the United Network of Organ Sharing (UNOS) awarded donor lungs on a first-come, first-serve basis to patients waiting longest on the list. Now patients receive a score based largely on disease severity, measured by diagnosis type, oxygen requirements, distance walked during 6MWT, degree of pulmonary hypertension, and other factors. Donor lungs are then matched to the patient with the highest score.

It is important to determine whether a patient would ever want a lung transplant. If so, the patient should plan to meet the lung transplant team as soon as they are diagnosed. For many patients, it may take months or years to be placed on the waiting list. During this time, patients are often asked to improve their overall health (e.g., weight loss, participation in pulmonary rehabilitation, adherence to medications and oxygen, age-appropriate cancer screening, and management of coronary artery disease and other comorbidities) and to attend all healthcare visits and perform all requested tests and procedures.

CLINICAL TRIALS

Clinical research is important for understanding ILD, and for developing improved treatment and disease management. While scientists can create *in vitro* and/or animal models of ILD, clinical research is necessary to translate these discoveries as they apply to a human subject. People with ILD have many opportunities to take part in clinical research that provides essential knowledge about ILD. Many volunteers derive a sense of well-being from knowing that they are contributing to the eventual cure of this debilitating lung condition.

Current treatment of ILD consists of either treating the underlying cause if known, or slowing down disease progression, as in IPF. The development of new treatments for ILD target the steps that lead to scar formation, such as injury, proliferation, and abnormal tissue repair that results in fibrosis. Investigational agents target one or more of the fibrotic pathways with the intent to interrupt the formation of more fibrosis. Two approved drugs, pirfenidone and nintedanib, slow down the progression of IPF in some individuals. Improved survival and/or reversal of the fibrosis are the ultimate

goals of current and future investigational treatments.

"Current treatment of ILD consists of either treating the underlying cause if known, or slowing down disease progression, as in IPF."

Funding for clinical research in ILD may be through pharmaceutical, government, or foundation sponsors. Research may be investigator-initiated or developed by industry sponsors. Regardless of how it is funded or initiated, clinical research costs millions of dollars to conduct and requires multiple sites, ILD specialists, experienced study coordinators, and willing participants. For a listing of current clinical trials, visit **trials.pulmonaryfibrosis.org**.

The PFF has developed tools to make it easier for patients, caregivers, and healthcare providers to find and learn about clinical trials:

PFF CLINICAL TRIAL FINDER

The PFF Clinical Trial Finder is a searchable tool for people living with pulmonary fibrosis, their caregivers, and loved ones to learn about clinical research opportunities closest to them. This searchable platform filters the type of trial, patient characteristics, and proximity to home thereby accelerating the development of new treatment options for patients. If users are interested in learning more about any particular study, they should contact the listed site coordinator via email or phone.

The clinical trial finder obtains information directly from ClinicalTrials.gov, a service of the National Institutes of Health, which provides details on publicly and privately supported clinical trials. We strongly recommend that patients consult with their healthcare provider about the trials that may interest them and refer to our terms of service.

PF DRUG DEVELOPMENT PIPELINE

The PFF has launched a PF Drug Development Pipeline tool to educate the PF community about drug development in relevant areas of interstitial lung disease,

including IPF, HP, RA-ILD, SSc-ILD, Sarcoid-ILD, chronic cough and lung transplant.

The Pipeline tool allows viewers to filter by Study Phase, Disease Condition, Intervention Type, and Funder Type so that they can find information that is relevant to them. It includes interventional drugs that are in development or have been approved for the market in the United States. All drugs with active clinical trials will link to trial specific information in the PFF Clinical Trial Finder tool on the PFF website. Additional features of the Pipeline tool include a Drug Development Pipeline Glossary, a User Feedback Form, and links to pertinent news and announcements about drug development and corresponding trials.

You can access these tools at: **pulmonaryfibrosis.org/clinicaltrials.**

PART FIVE:
Advising and Supporting Patients With Pulmonary Fibrosis

MONITORING PULSE OXIMETRY AT HOME

Some, but not all, clinicians counsel their patients to monitor oxygen saturation at home. Pulse oximetry is an indirect, non-invasive measurement of a person's hemoglobin oxygen saturation and is commonly referred to as SpO2. Individuals with ILD requiring oxygen supplementation may wish to measure their oxygen saturation levels at home in order to adjust their oxygen flow rate according to activity level or to alert their physician if oxygen levels decrease acutely, if directed by their physician.

Pulse oximetry devices work by emitting red and infrared light through pulsating tissue that is received by a photodetector or sensor and converted to a numeric value. This value represents the percentage of oxygen bound to the hemoglobin molecule in red blood cells. Normal values are 97% to 100%. In order to maintain healthy cells, tissue, and organs, a SpO2 of > 90% is needed. The accuracy of pulse oximetry devices is +/- 2% as compared to arterial blood gas measurements, making their use practical for

home monitoring.

There are many pulse oximeter devices on the market that can be applied to the finger, toe, earlobe, or forehead. Choosing the right type of sensor depends on a number of physiological factors.

- *Raynaud's phenomenon, temperature changes, low blood pressure*: All can decrease perfusion to the skin and provide false SpO2 readings.
- *Tremors or other excessive movement*: These can interfere with the device sensor readings as the sensor requires pulsation.

Other things that may produce a false reading include nail polish, false fingernails, and nail bruising, as well as the size and placement of the sensor.

EDUCATING THE PATIENT AND FAMILY

- Include an explanation of the purpose of the SpO2 monitoring and equipment.
- Demonstrate how the pulse oximeter should be used for the most accurate readings.
- Provide instructions on adjusting oxygen flow rates based on the pulse oximeter readings per the physician's orders. People with PF will have varying oxygen needs depending on their levels of activity (e.g., 2 LPM at rest, 4 LPM with exercise).
- Provide direction on when to call a physician with low readings.
- Instruct the patient not to smoke.
- Inform the patient that pulse oximeters can be checked for proper functioning by bringing the device to clinic visits and testing against clinic equipment.

Encourage the patient to not "live" by his or her pulse oximeter. The purpose of home monitoring is to decrease anxiety by knowing that it is safe to continue usual activities. This form of self-management teaches patients to predict when they will need to increase oxygen flow rates without always having to measure their SpO2.

SMOKING CESSATION

The health risks of smoking tobacco are well established. According to the Centers for Disease Control and Prevention (CDC), smoking is the leading preventable cause of death in the United States. About 480,000 people each year die from the effects of smoking in this country alone. Smoking leads to the development of chronic obstructive lung disease (COPD), emphysema, and lung cancer. Smoking also causes a number of interstitial lung diseases.

THE IMPORTANCE OF VACCINES

Influenza and pneumonia combined were the eighth leading cause of death in 2014. CDC recommendations vary year-to-year. Check the **CDC.gov** website for current recommendations on influenza and pneumococcal vaccinations.

For the ILD patient, any respiratory infection can become serious and life-threatening. As a result, quality care requires that the ILD nurse understand these vaccines and encourage patient compliance.

PULMONOLOGIST TESTING PROTOCOLS AND FOLLOW UP

Every doctor will have a different strategy to monitor ILDs. Usually, doctors use a combination of the following to determine if the disease is stable or changing:

Symptoms

One of the most important signs that something has changed in the lungs is a change in the amount of breathlessness experienced with exertion. A new or worsening cough can also be a sign that something in the lungs has changed. If a patient experiences one of these problems, the doctor will first try to determine whether symptoms are due to progression (new scar tissue in the lungs) or something else (an infection, a blood clot, a heart problem, etc.).

Pulmonary Function Tests (PFTs)

Doctors routinely order one or more of the following pulmonary function tests to monitor:

Spirometry

For most people with PF, monitoring the FVC can tell a doctor whether the disease is stable or progressing and whether the disease is mild, moderate, or severe. Normal is between 80 and 100% of the predicted value (which is based on age, gender, height, and ethnicity). As more scar tissue develops in the lungs, FVC will go down.

Lung volume measurement

Normal is between 80 and 100% of the predicted value for age, gender, height, and race and decreases as more scar tissue develops in the lungs. This test is not performed as frequently as spirometry as it is more costly and time consuming and provides similar information as spirometry.

Diffusing capacity (DLCO)

Scar tissue makes the transfer of oxygen less efficient. Just like FVC and TLC, DLCO is expressed as a percentage of the normal value and goes down as more scar tissue develops in the lungs. Do not be surprised by a DLCO that is much lower than the FVC or TLC— that is expected in people living with PF.

Walking Tests

Doctors will compare the walking distance and oxygen levels to results from previous visits to determine whether lung disease has progressed. Doctors often also use this test to determine whether or not a patient needs to use supplemental oxygen during exertion.

High-Resolution CT Scans

Comparing the change between two HRCT scans can tell a doctor if there is more scarring in the lungs. Some doctors perform multiple HRCT scans each year, some once per year, and some only when there is a change in symptoms, spirometry, or walking test results.

There are other tests doctors sometimes use to better understand disease and its impact on health, including arterial blood gas testing, cardiopulmonary exercise testing, and an echocardiogram. Some forms of PF may also affect the heart. To investigate this possibility, a doctor might order an echocardiogram (or ultrasound) of the heart or a cardiopulmonary exercise test.

Appendix

REQUIREMENTS FOR HOME OXYGEN THERAPY (CMS)

The Centers for Medicare and Medicaid Services (CMS) requires that all of the following criteria be met in order to qualify the patient for reimbursement for home oxygen therapy through Medicare:

(1) A Certificate of Medical Necessity (CMN), CMS-484—Oxygen form, must be completed each time oxygen is ordered.

(2) For Initial Certification, pulse oximetry or arterial blood gas testing must be performed either:
   a. "Closest to, but no earlier than, 2 days prior to a hospital discharge", or
   b. "Within 30 days of the date of Initial Certification while the patient is in a chronic stable state."

(3) Group I Initial Certification (lasts 12 months)
   a. One of the following criteria must be met:
      i. Oxygen saturation < 88% by either pulse oximetry or arterial blood gas analysis (at rest, during exercise, or during sleep), or;
      ii. Arterial partial pressure of oxygen < 56-59 mm Hg (at rest, during exercise, or during sleep), or;
      iii. A decrease in oxygen saturation of > 5% during sleep, or;
      iv. A decrease in arterial partial pressure of oxygen by >
      v. 10 mm Hg.
   b. If (a) or (b) is met only *during exercise*, there must be documentation of improvement in hypoxemia during exercise with oxygen.
   c. If any of these criteria are met only during sleep, both of the following must be true:
      i. Criterion must be met for at least 5 minutes, AND
      ii. Must be accompanied by "signs or symptoms" of hypoxemia (such as insomnia, nocturnal restlessness, P pulmonale on EKG, pulmonary hypertension, or hematocrit > 56%)

(4) For Group I Recertification, oxygen testing must occur prior to the 13th month of oxygen therapy and the patient must be seen in-person within 90 days prior to recertification.

(5) Group II Initial Certification (lasts 3 months)
   a. One of the following criteria must be met:
      i. Oxygen saturation of 89% by pulse oximetry or arterial

blood gas analysis at rest breathing room air while awake; during exertion; or during sleep, or;

ii. Arterial partial pressure of oxygen 56-59 mm Hg at rest breathing room air while awake; during exertion; or during sleep.

b. In all cases, there must be dependent edema, pulmonary hypertension, or a hematocrit > 56%

(6) For Group II Recertification, oxygen testing must occur between the 61st and 90th day following initial certification and the patient must be seen in-person within 90 days prior to recertification.

(7) Requirements for documentation in the medical record

a. Diagnosis, duration of condition, clinical course (worsening, stable, or improving), and prognosis
b. Results of pulse oximetry and/or arterial blood gas testing (printed results or written in the notes)
c. If portable oxygen is needed, notation that the patient is mobile within the home
d. Nature and extent of functional limitations
e. Type of delivery device and frequency of use
f. Must substantiate the information provided on the Certificate of Medical Necessity

FINDING ACCURATE DISEASE EDUCATION MATERIALS

Misinformation Online

The diagnosis of a rare and terminal disease brings many unique challenges for patients and their nurses. When a patient receives a diagnosis of ILD, many will immediately turn to the Internet for information. According to a study published in the *American Journal of Respiratory and Critical Care Medicine*, most online information directed toward patients is inaccurate and/or outdated.

Researchers found that when searching the internet for "idiopathic pulmonary fibrosis," 48% of the first 200 websites listed described IPF "treatments" that were either not indicated for IPF or were harmful. In addition, 54% of the sites were not updated, with 31% of these outdated sites describing medications that have now been found to be harmful for IPF patients. Although sites produced by government agencies, not-for-profit and advocacy organizations, and academic medical centers tend to be the most reliable, even these were sometimes found to contain inaccurate and outdated information.
Yet health care professionals as a whole spend little time educating the public on how to evaluate the validity of what they read online. It is therefore incumbent upon the ILD

health professional to not only provide patients with a list of reliable resources, but to also educate the patient on how to make decisions on the information they find online.

Promoting Reliable Resources

Patients should be advised to seek out professional, government, and non-profit sites first. Commercial sites can also provide excellent patient education materials, but should be approached with caution due to the risk for bias.

Remind patients to keep in mind that news stories may actually be disguised advertisements that were written by a seller, but appear to be from a journalist. Teach patients to always look at the "About Us" information on a website. If the site owner or author is not obvious and their affiliations aren't clear, the site should be approached with caution.

Understanding Research Studies

Patients need help understanding basics about research studies. Valid medical studies are published in peer-reviewed professional journals. This means that an editorial board of scientists who are independent from the researcher reviews the research for credibility before allowing it to be published. Studies that are self-published, e.g., "we conducted a study and 70% of our patients said that they felt better," should be viewed with a high degree of suspicion.

Anecdotal evidence refers to when an example is used to try to prove a general claim. For example, "My grandmother drank 3 BigWig shakes every day and she lived with IPF for 8 years, therefore BigWig shakes make you live longer." While this evidence can be helpful when looking for new areas to research, by itself it has no meaning. People selling "natural" or "alternative" therapies rely heavily on anecdotes because they lack any credible scientific evidence supporting their products.

There is a big difference between having an effect on the body and being able to treat or cure a disease. For example, just because "Substance A" was shown to "increase anti-fibrotic activity in the blood," it does not mean that "Substance A" will treat ILD. Our bodies' processes and the disease's processes are much more complicated than that.

To access PFF resources for clinical trials, including the PFF Clinical Trial Finder and PF Drug Development Pipeline, please visit the Clinical Trials Education Center at **pulmonaryfibrosis.org/clinicaltrials.**

Creating a Safe and Informative Space

ILD patients and families need to feel safe to ask questions about their Internet research. Patients and caregivers should never feel foolish for asking questions about what they see and hear online.

Some helpful Internet resources include:

ATS Fact Sheets
https://www.thoracic.org/patients/patient-resources/fact-sheets-az.php

NHLBI
https://www.nhlbi.nih.gov

NORD
https://rarediseases.org

Caregivers of Rare Diseases
https://www.rarecaregivers.org/

Caregiving Tools from AARP
https://www.aarp.org/caregiving/

Advanced Planning and End of Life Resources
www.caringinfo.org/i4a/pages/index.cfm?pageid=1

Social Security Disability
https://www.ssa.gov/benefits/disability/

Mental Health Resources
https://helpguide.org/

Hospice
https://hospicefoundation.org/

Palliative Care
https://getpalliativecare.org/

UNOS Transplant Living
https://unos.org/

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The Pulmonary Fibrosis Foundation mobilizes people and resources to provide access to high quality care and leads research for a cure so people with pulmonary fibrosis will live longer, healthier lives.