

Occupational Interstitial Lung Diseases

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Objective: Evidence-based diagnostic and treatment guidelines for occupationally related interstitial lung diseases (ILDs) have been developed and are summarized herein. **Methods:** Comprehensive literature reviews were conducted with article abstraction, critiquing, objective grading, and evidence table compilation. A multidisciplinary expert panel drafted evidence- and consensus-based guidance. External peer-review was incorporated. **Results:** Recommendations for diagnosis (n=12) and management (n=4) of ILD were developed. Spirometric testing, chest radiographs, and high-resolution computerized tomographic scans were recommended based upon evidence. In addition to a detailed clinical history, carbon monoxide diffusion capacity, sputum sampling, exposure assessment, 6-minute walk test, and bronchoalveolar lavage were also recommended. There was no recommendation regarding chest magnetic resonance imaging due to lack of evidence. **Conclusions:** Recommendations for diagnosis and management of ILD are supported by quality evidence. These guidelines may be useful to help guide providers who are tasked with diagnosing and/or treating patients with occupationally related ILD.

Interstitial lung diseases (ILDs) are a heterogeneous group of more than 100 diseases that result in inflammation and/or scarring of the lung parenchyma. ILDs are classified together because of their similar clinical, roentgenographic, physiologic,

and/or pathologic features.^{1–3} Although causes of most ILDs are unknown, those that are occupationally related may be preventable.^{4,5}

Both occupational and non-occupational ILDs have similar pathophysiology(ies), progressive fibrotic changes, structural abnormalities, and common physiologic sequelae. Although the end results are similar, these disorders are distinguishable by the processes that lead to the fibrosis (ie, exposures). The term “occupational ILD” describes those ILDs that are thought to be related to occupational exposure(s). According to the National Occupational Exposure Survey, millions of US workers are potentially exposed to substances known to cause occupational ILD.

Occupationally related ILDs fall into four (often clinically overlapping) categories:

1. Pneumoconiosis is defined as the non-neoplastic reaction of the lungs to inhaled mineral or organic dusts and the resultant alteration of pulmonary tissue structure.^{5,6} Hundreds of types of pneumoconioses have been identified, but only three are common and therefore reasonably feasible for guidelines: (1) asbestosis; (2) silicosis; and (3) coal workers’ pneumoconiosis.^{5,7} In these conditions, the radiologic findings result from the accumulation of inflammatory and fibrotic responses triggered by dust deposition.
2. Hypersensitivity pneumonitis (HP), also known as extrinsic allergic alveolitis, describes a large family of disorders of immune response to inhaled antigens or low-molecular-weight chemicals, often associated with granulomatous pathological changes.⁵ Associated exposure agents include animal proteins, plant proteins, bacteria, fungi, and diisocyanates. HPs tend to be highly specific to occupational or environmental settings. In agricultural workers, the most common HP is farmer’s lung, an immune response to spores of thermophilic actinomycete bacteria. Farmer’s lung is one of the most frequent forms of HP, but there are many others including bird fancier’s lung, extrinsic allergic alveolitis, hot tub lung, humidifier lung, and mushroom picker’s disease.⁸

3. Other granulomatous diseases are chronic immune and foreign-body responses to antigens in the lung (which may be dusts and therefore also considered pneumoconioses); for example, reactions to beryllium (beryllium disease) or rarely to cobalt in cemented tungsten carbide (hard metal disease).^{9–12} Tissue response is mediated by immune mechanisms and may not localize to an area of dust accumulation. These disorders are uncommon and problems may develop at different exposure levels in different people. The clinical presentations are variable and may include systemic manifestations affecting multiple organ systems.
4. Diffuse interstitial fibrosis is a response to severe lung injury including irritant inhalation injury (eg, diffuse alveolar injury related to nitrogen oxides). Diffuse interstitial fibrosis should be distinguished from more common idiopathic interstitial fibrosis either of the “usual interstitial pneumonia” or the “non-specific interstitial pneumonia” types. Advanced forms of all of the occupational interstitial lung diseases may have a similar clinical presentation to diffuse interstitial fibrosis.

Occupational ILDs have varied latency periods, usually measured in years, and present predominantly or exclusively with pulmonary manifestations. Extrapulmonary symptoms and signs rarely occur (eg, cases of beryllium disease, silica-associated autoimmune disease, or renal disease).^{5,13}

The prevalence of pneumoconioses in the United States has declined over the last decades, especially after institution of modern dust regulations and changes in industry practices; however, occupational ILDs continue to present a substantial risk to the US workforce. Silicosis continues to be the most common occupational lung disease worldwide with estimates of between 3600 and 7300 cases per year in the United States from 1987 to 1996.¹⁴ Silicosis currently causes approximately 150 deaths annually in the United States. Asbestosis continues to be seen as a legacy disease in older workers who were exposed prior to the institution of engineering controls and personal protective equipment designed to reduce exposure. On occasion, new cases of asbestosis are seen in younger workers such as those engaged in

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insulation removal without proper preventive measures including respiratory protection, engineering controls (eg, exhaust ventilation), and work practices (eg, wet processes).¹⁵ Coal workers' pneumoconiosis, which was declining in incidence for decades, has been rising in prevalence in recent years for reasons that are unclear.^{16,17} Other ILDs tend to be localized due to specific regional occupations and are not generally monitored closely. Some data on cases and trends of work-related lung disease are available in case studies and trends documented through the National Institute for Occupational Safety and Health's Work-Related Lung Disease Surveillance System (<http://www2a.cdc.gov/drds/WorldReportData/html/SourcesOfData.asp>).

GUIDELINE FOCUS/TARGET POPULATION

The American College of Occupational and Environmental Medicine's (ACOEM's) Occupational Interstitial Lung Disease Guideline is designed to provide health care providers with evidence-based guidance on the diagnosis and management of occupational ILD. This study summarizes findings from that Guideline (77 pages, 184 references).

Detailed methodology documents used for development of this guideline (including evidence selection, scoring, incorporation of cost considerations, and formulation of recommendations) have been previously published.^{18–20} Guidance and recommendations are developed with sufficient detail to facilitate assessment of compliance (Institute of Medicine) and auditing/monitoring (Appraisal of Guidelines for Research and Evaluation). The only Appraisal of Guidelines for Research and Evaluation¹⁸ and Institute of Medicine criterion not adhered to is incorporation of the views of the target population. Employees with occupational ILD were not involved in the panel or external review process. In accordance with the Institute of Medicine's Trustworthy Guidelines, this guideline underwent external peer review by individuals and professional societies familiar with this topic; detailed records are kept, including responses to external peer reviewers.²¹

The literature is routinely monitored and formally searched at least every 3 years for evidence that would change any of the recommendations. This guideline will be updated at least every 3 years or more frequently should evidence require it. These are recommendations for practitioners and decisions to adopt a particular course of action must be made by trained practitioners on the basis of available resources and the particular circumstances presented by the individual patient.

EVIDENCE REVIEW AND GRADING

All evidence related to ILD in searching four databases (PubMed, EBSCO, Cochrane Library, and Scopus) was included in this guideline. Comprehensive searches for evidence were performed for all databases through July 2015 to help ensure complete study capture. Reference lists of included articles were reviewed for inclusion. All included studies were abstracted and scored for quality. Guidance and recommendations were drafted based upon a table of evidence from abstracted data and objective scoring of epidemiological evidence of each study.

Recommendations are evidence-based on synthesis of the complete published body of literature on the topic of occupational ILD. Recommendations were graded from (A) to (C) in favor or against a specific diagnostic test or treatment, with (A) level recommendations having the highest quality body of literature. Quality evidence was developed into the evidence-based recommendations. Level (I) recommendations are based on insufficient published evidence and grounded in analogy to other similar treatments or diagnostic tests combined with panel consensus. In the context of these guidelines, "insufficient" indicates that the evidentiary base is too limited to support a formal and conclusive determination, not that the evidence does not support the recommendation. Recommendations and evidence tables were reviewed and amended by the multi-disciplinary Evidence-based Practice Occupational ILD Panel. Articles scoring moderate or high quality were included.²¹ Search strategies identified 955 article titles that were screened and all potentially appropriate study abstracts were reviewed and evaluated against specified inclusion and exclusion criteria. A total of 73 studies were included in these analyses. This guideline achieved 100% panel agreement on all recommendations.

RESULTS

Twelve recommendations were formulated for diagnostic testing (Table 1), of which six recommended in favor of the testing. There were four recommendations formulated for the management of occupational ILD (Table 2); all four were recommended.

SPIROMETRIC TESTING

Spirometry is an integral tool in the evaluation and assessment of the worker with suspected occupational ILD. Evidence ratings evaluate and isolate the specific contribution of the modality, taken alone, for clinical diagnosis and management, not

the need to obtain them as guidance in the evaluation. Spirometry was moderately recommended (evidence level B), for use in both the surveillance of workers and the clinical evaluation of potential ILD. Workers in occupations with exposures that are either known or thought to be associated with development of occupational ILD should have screening spirometric testing. This generally includes a baseline as well as periodic testing (that is most often annual) for ongoing exposures. Patients with a history of, and imaging consistent with, ILD should also have diagnostic spirometric testing. For those who have previously undergone spirometry, changes in test results should be evaluated over time. Interpretation of spirometric values over time calculates the magnitude of the loss (eg, in forced expiratory volumes), provides inferences on the variability of the earlier results, and suggests the duration of follow-up. When appropriate methods are used, longitudinal interpretation may facilitate early detection of important disease processes and provide objective correlation with changes in reported respiratory symptoms over time.^{22–24} ACOEM recommends that individuals with a decrement in forced expiratory volume in the first second (FEV₁) over time that is 15% more than that expected from aging alone should undergo further investigation.²⁵

Current American Thoracic Society/European Respiratory Society (ATS/ERS) recommendations categorize the severity of impairment based solely upon reductions in the FEV₁ as a percent of predicted as this measurement will decrease along with forced vital capacity (FVC) in moderate-to-severe restrictive impairment: mild = FEV₁ between the lower limit of normal and 70% of predicted; moderate = FEV₁ 60% to 69% of predicted; moderately severe = FEV₁ 50% to 59% of predicted; severe = FEV₁ 35% to 49% of predicted; and very severe = FEV₁ less than 35% of predicted.²⁶ Nevertheless, this approach may not entirely reflect the impact of the occupational ILD disease process on the individual's functional status.

Chest Radiographs

Chest imaging is an integral tool in the evaluation and assessment of the worker with suspected occupational ILD. Evidence ratings evaluate and isolate the specific contribution of the modality, taken alone, for clinical diagnosis and management, not the need to obtain them as guidance in the evaluation. Chest radiographs (posterior-anterior and lateral) are moderately recommended (evidence level B) for use in the diagnosis of asbestosis, silicosis, or coal workers' pneumoconiosis. They are

TABLE 1. Summary of Evidence-Based Recommendations for Diagnostic Testing of Occupational ILD

Test	Recommendation(s)
Spirometry	Spirometry for the diagnostic work up and monitoring of individuals at risk of occupationally related ILD and in surveillance programs in conjunction with other diagnostic testing—moderately recommended, evidence (B)*
Chest radiographs	Chest radiographs (posterior-anterior and lateral) for diagnosis of occupational ILD based on the following criteria: Diagnosis of silicosis, asbestosis, or coal workers' pneumoconiosis—moderately recommended, evidence (B)* Diagnosis for other occupational ILD, including but not limited to chronic beryllium disease, HP, and hard metal disease—recommended, insufficient evidence (I)*
HRCT	HRCT scans for the diagnosis of occupational ILD based on the following criteria: Diagnosis of asbestosis, coal workers' pneumoconiosis, or chronic beryllium disease—strongly recommended, evidence (A) Diagnosis of silicosis—moderately recommended, evidence (B)
DL _{CO}	DL _{CO} for use in diagnosing occupational lung disease—recommended, evidence (C)
Sputum	Sputum, both induced and spontaneous, as an aid for the diagnosis of occupational lung disease caused by asbestos—recommended, evidence (C)
BAL	BAL as an aid for the diagnosis of occupational lung disease caused by asbestos—recommended, evidence (C)

BAL, bronchoalveolar lavage; DL_{CO}, carbon monoxide diffusing capacity; HP, hypersensitivity pneumonitis; HRCT, high-resolution computed tomography; ILD, interstitial lung disease.

*Spirometry and chest radiographs are assumed to be performed on every case as part of the initial assessment.

recommended, but with insufficient evidence (I) for other occupational ILDs (chronic beryllium disease, HP, hard metal disease). Chest radiographs are a part of the usual evaluation of patients with respiratory symptoms. They are widely used for diagnosis and monitoring of ILDs. Chest radiographs show opacities, which represent the accumulation of these types of dust and the body's reaction to those exposure(s).^{27–31}

It is recommended that chest radiographs be performed by trained technicians according to the American College of Radiology/Society for Pediatric Radiology Practice Guidelines.³² Physicians who interpret chest radiographs for diagnosis and medical surveillance of occupational ILD should have appropriate training, experience, and skills.

High-Resolution Computed Tomography Scans

High-resolution computed tomography (HRCT) scans are strongly recommended (evidence level A) for diagnosis of asbestosis, coal workers' pneumoconiosis, or chronic beryllium disease. An HRCT scan is moderately recommended (evidence B) for diagnosis of silicosis. These recommendations are particularly for specific indications.

HRCT scans should be performed by trained technicians and according to

American College of Radiology guidelines.³² Readers of HRCT scans for occupational lung disease should have appropriate training and experience. These scans may be performed in both supine and prone positions and should be done at maximal inspiration.³³ There is also evidence to support scanning the entire thorax in patients with asbestosis, particularly to evaluate the presence of apical disease.³⁴ HRCT scanning is recommended when the findings make occupational ILD reasonably likely and when the chest radiograph alone is insufficient. Although useful in diagnosis of occupational ILD, an HRCT scan is not an essential part of the evaluation if chest radiographs document an occupational ILD that is consistent with the workers' exposure. If there are atypical features, subtle abnormalities on routine radiography, and/or competing causes for the findings, then an HRCT scan may be especially helpful in confirming or excluding a diagnosis of occupational ILD.

Carbon Monoxide Diffusing Capacity

Measurement of carbon monoxide diffusing capacity (DL_{CO}) is recommended (evidence level C) for use in diagnosing ILD. DL_{CO} should be performed according to the 2005 ATS/ERS statement.³⁵ It is

recommended that at least two DL_{CO} tests be performed and the average reported, and it is further recommended that the measurements from these two tests agree within 10%.³⁵ Smoking status must be obtained as cigarette smoking may cause measurable baseline levels of carbon monoxide causing an increased back-pressure and elevated carboxyhemoglobin measurements.³⁵

Sputum Samples and Bronchoalveolar Lavage

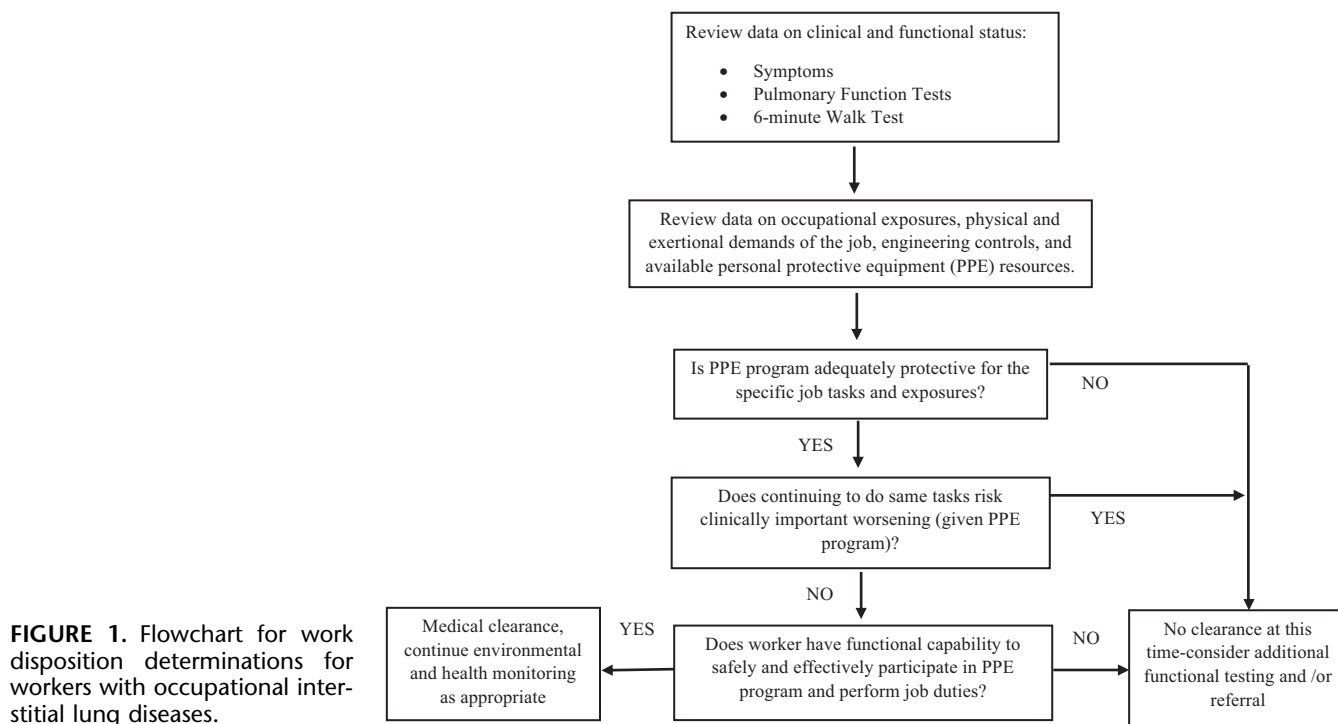
Sampling of sputum, both induced and spontaneous, is recommended (evidence level C) for diagnosing asbestos-related ILD. Sputum is less reliable than bronchoalveolar lavage (BAL) sampling because of the difficulty in obtaining quality specimens³⁶; however, sputum sampling has the advantages of being non-invasive and less expensive when compared with BAL.

BAL is recommended (evidence level C) as an aid to the diagnosis of ILD caused by asbestos. BAL should be performed according to the ATS/ERS guidelines on performance of BAL for ILD.³⁷ BAL is a high-cost procedure with a moderate risk of adverse events. This must be considered when deciding if BAL is a necessary step in the diagnosis

TABLE 2. Summary of Recommendations for Management of Occupational ILD

Recommended
Pharmacological treatment of occupational interstitial lung disease follow established guidelines for treatment of ILD (I)
Exposure assessment should be completed for workers diagnosed with occupational interstitial lung disease (I)
Six-minute walk test in individuals with ILD as a means to monitor response to treatment or progression of the disease (C)
Process of decision-making as to whether a worker who has been diagnosed with occupational ILD might return to a specific job/exposure should follow the flowchart (Fig. 1) below (I)

ILD, interstitial lung disease.



of occupational ILD. It is particularly indicated when a definitive diagnosis is required and/or to help address potentially competing causes of ILD.

MANAGEMENT OF OCCUPATIONAL ILD

This guideline also addresses management of occupational ILD after diagnosis. Apart from hypersensitivity pneumonitis and the granulomatous occupational ILDs, the literature reviewed did not support a recommendation for specific drug therapy directed at controlling the underlying fibrotic process. The panel recommended, with insufficient evidence (I), that supportive pharmacological treatment of inorganic pneumoconioses follow established guidelines for treatment of non-occupationally related ILDs.

In addition, it is recommended with insufficient evidence (I) that an exposure assessment be completed for workers diagnosed with occupational ILD. It is further recommended to educate all parties that complete avoidance of further exposure to the identified agent is preferred; however, due to economic constraints of job change or loss, complete removal is not always feasible. In these cases, reduction of exposure to the lowest feasible level with frequent monitoring to assure early recognition of disease acceleration or cardiopulmonary complications is recommended. The coordinated use of the following five

strategies is recommended for the management of workers diagnosed with occupational ILD:

1. General management of restrictive lung disease due to interstitial fibrosis.
2. Specific management of the underlying disease.
3. Specific management of comorbidities.
4. Prevention of further loss of lung function and major complications.
5. Evaluation of work capacity and fitness for duty.

It is recommended to use the 6-minute walk test (evidence level C) to monitor response to treatment or progression of ILDs. This test should be conducted in accordance with the ATS recommendations for conducting the 6-minute walk test.³⁸

The general management of ILD includes supplemental oxygen if desaturation is documented. Systemic glucocorticosteroids may be effective when used judiciously in hypersensitivity pneumonitis and beryllium disease. Glucocorticosteroids have occasionally reported modest effects in other ILDs such as silicosis, asbestosis, and coal worker's pneumoconiosis.^{39,40} Bronchodilators and inhaled corticosteroids may have a role in the presence of an accompanying airways effect, as in HP, cobalt-induced asthma, or dust-related airway diseases.

DISCUSSION

This is the first occupational ILD-related guideline published that is based on literature review, literature grading, and expert panel consensus. It is a robust resource for both the front-line practicing physician, the occupational medicine specialist, and pulmonary/allergy specialists who diagnose and manage occupationally related ILDs. The strengths of this guideline include the following: (1) comprehensive literature search; (2) a large database of studies from which to base recommendations; (3) the methodological literature abstraction and grading; (4) the expert medical panel; and (5) expert external review processes. The main weaknesses stem from a general lack of high-quality diagnostic and treatment studies that are specific to occupationally related ILDs. Further rigorous studies are needed in occupational settings for both diagnosis and management of occupationally related ILD.

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