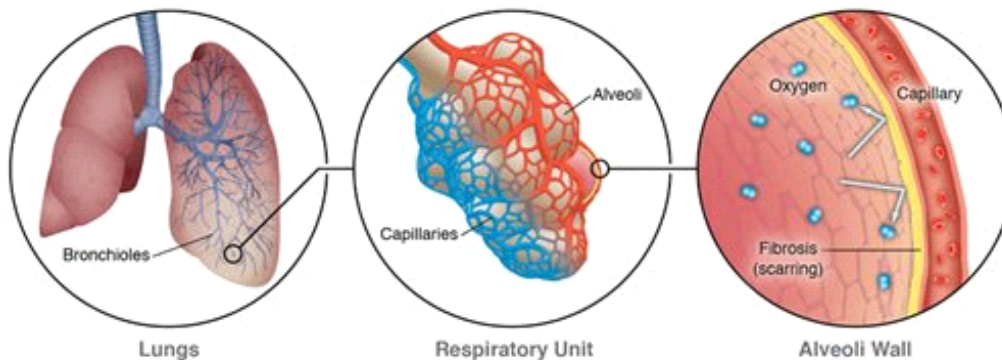


## Interstitial Lung Disease

Interstitial lung disease (ILD) is a broad category of lung diseases that includes more than 130 disorders which are characterized by scarring (i.e. “fibrosis”) and/or inflammation of the lungs. ILD accounts for 15 percent of the cases seen by pulmonologists (lung specialists).

Let’s take a look inside the lungs to see what is happening with interstitial lung disease.

In interstitial lung disease, inflammation and/or scarring (fibrosis) occurs in the interstitium of the lung. The interstitium of the lung refers to the microscopic area within the walls of the alveoli (air sacs) between the membrane of the air sac and the membrane of the surrounding blood vessels. Like the leaves on a tree, the alveoli arise from the tiniest bronchioles (airways). There are hundreds of millions of alveoli in a lung: more than a couple would fit on the period at the end of this sentence. Each alveolus (individual air sac) is surrounded by a network of tiny blood vessels (capillaries) — like mesh encircling the alveolus. The air sac and blood vessels together are called a respiratory unit. This is where the exchange of oxygen and carbon dioxide takes place. Normally, oxygen passes easily from inside the air sac, through its membrane, across the interstitium and through the membrane of the blood vessel in which red blood cells are lined up and ready to be loaded with oxygen like empty train cars waiting to be filled with cargo. In interstitial lung disease, inflammation, scarring or fibrosis thickens the interstitium, making the lung thick and restricted from filling to their normal capacity and preventing oxygen from passing freely into the bloodstream.



### Some Common Forms of ILD are:

- Idiopathic (unknown) pulmonary fibrosis
- Connective tissue or autoimmune disease-related ILD
- Hypersensitivity pneumonitis
- Chronic eosinophilic pneumonia
- Pulmonary Langerhans cell histiocytosis
- Familial pulmonary fibrosis
- Drug-induced lung disease
- Sarcoidosis
- Lymphangiomyomatosis (LAM)
- Cryptogenic organizing pneumonia
- Smoking-related ILD

## What are Common Symptoms of ILD?

The most common symptoms of ILD are shortness of breath, also known as dyspnea, as well as cough and fatigue. Many people describe dyspnea as a feeling of breathlessness. Most frequently, shortness of breath appears insidiously, not abruptly. Usually, shortness of breath is first noticed during exertion or with strenuous activity. For example, early on, a person with ILD may notice shortness of breath only when running or hurrying to catch a bus. Later in the course of ILD, he or she may notice shortness of breath when casually walking across the street or walking from room to room indoors.

Cough due to ILD is typically a dry and hacking cough. Fatigue or low energy is very common in people with ILD. People with systemic autoimmune or connective tissue disease may have muscle or joint aches, rash and other non-respiratory symptoms.

## What are the Causes of ILD?

The causes of interstitial lung disease (ILD) fall into four general categories. The first is autoimmune or connective tissue disease. Some autoimmune diseases that can cause ILD are:

- Scleroderma (systemic sclerosis)
- Rheumatoid arthritis
- Polymyositis/Dermatomyositis
- Large, medium or small vessel vasculitis
- Inflammatory bowel disease.

The second category of cause of ILD is exposure to an agent that damages the lungs. For example, ILD can be caused by workplace exposure to inorganic dust — asbestos, silica or hard metal dust. Mold, bacteria or bird proteins are examples of organic dusts that can cause ILD. Smoking can cause ILD. Medications used to treat another condition, such as chemotherapy drugs, gastroesophageal reflux drugs, amiodarone or nitrofurantoin, are examples of drugs that have been linked to ILD.

The third category is related to genetics. Multiple members of one family may develop ILD, and some of these cases have been tracked to a single set of genes. Some inherited diseases are known to cause ILD. Examples include Hermansky-Pudlak syndrome and Tuberous Sclerosis Complex.

The fourth category is called “idiopathic,” meaning the cause is unknown. Some examples of idiopathic ILD include:

- Idiopathic pulmonary fibrosis
- Idiopathic nonspecific interstitial pneumonia
- Acute interstitial pneumonia
- Sarcoidosis
- Lymphangioleiomyomatosis (LAM).

## How is ILD Diagnosed?

When the diagnosis of ILD is suspected, your doctor considers the following:

- **Your medical history** – This includes: a review of all the person’s symptoms, a listing of current and former medications and a review of any environmental and occupational exposures to dust, gases, chemicals, pets (in particular birds) and humidifiers.
- **A complete physical examination** - Findings of crackling sounds in the lungs and changes in the skin, joints and fingernails can help direct further evaluation.
- **A chest X-ray and high resolution computed tomography (CT) scan** - Results are often abnormal with ILD. Chest x-rays and routine CT scans of the chest are not adequate for evaluating or diagnosing ILD.

- **Pulmonary function tests** - These breathing test results help determine the severity of ILD.
- **Arterial blood gas** - This test measures the amount of oxygen and carbon dioxide in your blood. The results may be normal or show a reduced oxygen level.
- **Exercise testing** - This test may show a decrease in your oxygen level during activity. Testing may include a six minute walk, oxygen titration and exercise tolerance test.
- **Laboratory data** – Blood work may be done to test for autoimmune disease and other disorders that can cause ILD.
- **Bronchoscopy with bronchoalveolar lavage** – A bronchoscopy may be done to check for inflammatory cells in your lungs or to sample small pieces of the lung to look for evidence of a specific ILD. Bronchoscopy involves inserting a tube through the nose into your trachea (windpipe) to see the airways. In bronchoalveolar lavage a small amount of sterile saline is placed in one area of your lung and then withdrawn. This fluid contains cells that will be analyzed under the microscope. Small biopsy tools may be used through the bronchoscope if indicated.
- **Surgical lung biopsy** – In many cases of ILD, a surgical lung biopsy is needed to get enough lung tissue to make a specific diagnosis. This may be performed with the use of a thoracoscope. This allows the surgeon to biopsy multiple areas of one lung through a few very small incisions.

## What is the Treatment for ILD?

Treatment for ILD is based upon the specific ILD diagnosis and the severity of disease. Sometimes, an approach of watchful waiting without drug therapy is appropriate. Many forms of ILD can be treated successfully with medications. Some medications are only appropriate for certain forms of ILD and not others.

Regardless of the cause of ILD, the goals of treatment are:

- To decrease inflammation and prevent the formation and/or progression of lung scarring
- To remove the source of the problem, when possible
- To minimize and manage potential complications of ILD
- To improve or prevent deterioration in a person's quality of life.

## What are Some of the Medications?

**Oral Corticosteroids** - Prednisone or some other form of corticosteroid is used in many forms of ILD. Corticosteroids can have significant side effects.

- Corticosteroids can have significant side effects. Some of the side effects include:
  - Increased appetite, weight gain, high blood pressure, salt and fluid retention, tendency to bruise easily, depression, psychosis or hyper excitability and difficulty sleeping. There also is a tendency to develop diabetes, peptic ulcer, infections, cataracts and osteoporosis (weakening of the bones).
  - Talk with your health care provider about preventing and watching for these side effects.

**Immune Suppressing or Steroid Sparing Medications** - These medications are sometimes prescribed along with or in place of corticosteroids. Each has its own side effect profile and requirements for monitoring. Some of the most commonly prescribed immunosuppressive drugs used in patients with ILD include the following:

- Mycophenolate mofetil (CellCept®) or mycophenolic acid (Myfortic®)
- Azathioprine (Imuran®)
- Cyclophosphamide (Cytoxan®)
- Rituximab (Rituxan®)

**Anti-Fibrotic Medication** - Two medications have been approved by the U.S. Food and Drug Administration for the treatment of people with idiopathic pulmonary fibrosis (IPF). Nintedanib (Ofev®) has also been approved for people with scleroderma-related ILD or other types of progressive pulmonary fibrosis.

- Pirfenidone (Esbriet®) Pirfenidone is an oral medication taken three times daily. The specific mechanism is unknown, but available data suggest it inhibits transforming growth factor beta, and it seems to have both anti-fibrotic and anti-inflammatory properties. Pirfenidone slows the progression of disease for some people with IPF.
  - Some side effects include: Nausea, loss of appetite, stomach upset and photosensitivity (a tendency to easily develop sunburn; this may be severe).
- Nintedanib (Ofev®) Nintedanib is an oral medication taken twice daily. It is a triple kinase inhibitor that blocks several pathways that lead to the development of scars. Like pirfenidone, nintedanib slows the progression of disease for some people with IPF, scleroderma-related ILD or other types of progressive pulmonary fibrosis.
  - Some side effects include: Diarrhea and, less often, nausea and vomiting.

Because of the potential side effects of the above medications, your doctor will carefully monitor you while on therapy. This will include routine bloodwork. The decision to treat people with ILD involves a careful weighing of the potential risks and benefits of therapy. The potential benefits from the treatment usually outweigh the risks from the medication side effects.

## What are Some Other Therapies?

**Oxygen Therapy** - Oxygen is required for some people with ILD because of low level of oxygen in the blood. Some may need oxygen therapy all of the time while others may need it only during sleep or exercise. Improving the level of oxygen in the blood through the use of supplemental oxygen can help relieve strain on the heart and lungs and improve symptoms of shortness of breath and fatigue. There often is a stigma associated with oxygen. Many people are embarrassed and are concerned with how it will look and worry about how it will change their lifestyle. There are different options for oxygen systems, and people are still able to get out their homes and even travel. Most people find once they are on oxygen, they are able to be more active, as they are not as short of breath. National Jewish Health can discuss what oxygen system will best fit your lifestyle.

**Pulmonary Rehabilitation** - This is a program that is recommended for all patients with IPF to help you achieve your highest level of functioning. This program includes education, exercise conditioning, breathing techniques and energy saving techniques, respiratory therapy evaluation, nutritional counseling and psychosocial support.

The specific goals of pulmonary rehabilitation are to improve quality of life by: decreasing respiratory symptoms and complications, encouraging self management and control over daily functioning, improving physical conditioning and exercise performance, improving emotional well-being and reducing hospitalizations.

## Lung Transplant: Is it Right for You?

Response to therapy varies widely. Some types of ILD may respond quickly, and others may not respond at all. Treatment is considered successful if symptoms, physiologic findings and X-ray findings are stabilized. Even with treatment, many types of ILD progress naturally with a worsening of symptoms, X-ray findings and physiologic findings. Sometimes worsening is due to a complication of the disease or therapy. This may include conditions such as pulmonary hypertension or right heart failure. Some therapies may result in infection, muscle weakness and osteoporosis.

ILD may progress despite therapy. If this happens, lung transplantation may be an option for you. Lung transplant surgery replaces one or two diseased lungs with healthy lungs from a non-living donor. With improved surgical techniques and post-transplant care, this may offer you improved quality of life and longer survival. ILD doesn't recur in transplanted lungs.

Lung transplantation is only performed at specialty medical centers. Your health care team may determine that

lung transplant is the best option for you and that you are healthy enough for surgery. After an extensive evaluation, appropriate candidates are placed on a waiting list. A position on the waiting list is determined by disease severity. Wait times vary from transplant center to transplant center.

For transplant centers nearest to you, visit the Organ Procurement and Transplantation Network website.

## Clinical Trials

There are areas of active investigation into new treatment options for people with idiopathic pulmonary fibrosis. To find out more information you can go to our website or to <http://www.clinicaltrials.gov> for general information on all ongoing clinical trials in the US.

## An Action Plan for ILD

Sometimes it is hard to know what to do when your symptoms change or worsen. Do you call your doctor? Go to the emergency room? Your health care provider can tell you what you can do when this happens. This is an **Action Plan**. Knowing when your symptoms are getting worse can help you and your health care provider decide what you should do in your home, at your health care provider's office or in the emergency room.

A change or increase in the symptoms you usually have may be the only early warning sign. When your symptoms are getting worse, you may notice one or more of the following:

- An increase in shortness of breath or coughing
- A general feeling of ill health
- Feeling of lack of energy or fatigue
- Fever

Symptoms do not go away when they are ignored. Therefore, call your health care provider if you have new or worsening symptoms lasting longer than a day.

Talk with your caregiver and family members about symptoms and your Action Plan.

## What is the Prognosis with ILD?

The progression and prognosis of ILD vary from disease to disease and from person to person. It is important to determine the specific form of ILD in each person. What happens over time and what treatments might be useful depend on the diagnosis.

Because there is so much variability in disease behavior, in available therapeutic options and in responses to therapy, and because it is never possible to fully account for a person's unique characteristics, there is no way to make a blanket statement about prognosis in people with ILD. All people with ILD should be followed closely by a health care provider. This allows for timely assessments of disease status and discussions of prognosis and other aspects of their case.

## What is the Role of National Jewish Health?

As a center specializing in the care of people with ILD, our health care providers have vast experience in treating people with these rare and complex conditions. In conjunction with your local provider, doctors at National Jewish Health develop and implement a detailed plan of diagnosis and care based on the latest information available regarding ILD.

There is a tremendous amount of interest in understanding the mechanisms of inflammation and scarring in ILD, and extensive research in this area is being conducted at National Jewish Health. The National Institutes of Health has designated and funded National Jewish as a Specialized Center of Research for ILD. Together with our basic scientists, the doctors and staff at National Jewish Health work to broaden our understanding of the causes of ILD and develop new treatment approaches.



Visit our website for more information about support groups, clinical trials and lifestyle information.

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