

ILD · Interstitial Lung Disease And Pulmonary Fibrosis

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THE STORY IN ONE SENTENCE

Interstitial lung disease is long-lasting swelling and scarring in the thin space between the air sacs, making it hard for oxygen to jump into the blood.

“ILD is lung scarring between air sacs. Always name which type. Use pirfenidone or nintedanib (anti-fibrotic drugs that slow scarring) for IPF. Use prednisone or other immune-calming drugs for inflammatory types like NSIP, hypersensitivity pneumonitis, or connective tissue ILD. Remove the trigger in drug-caused or exposure-related disease. High-resolution chest CT (HRCT) is the key test to see the pattern. Pulmonary function tests show stiff lungs (restrictive pattern). Check oxygen with walking (6-minute walk test) to catch hidden drops. Lung transplant is the only cure for end-stage fibrosis.”

Normal anatomy — the body's job

The lungs are built like a tree: the windpipe (trachea) branches into smaller tubes (bronchi) that end in clusters of tiny air sacs (alveoli). Between each air sac is a super-thin space called the interstitium, made of delicate tissue and tiny blood vessels (capillaries). This thin wall is the oxygen gate: oxygen from the air you breathe crosses this thin space into the blood, and carbon dioxide (the waste gas from your cells) crosses back out to be exhaled. Keep that picture in your head — a paper-thin gate between air and blood — because ILD is what happens when that gate gets thick and scarred.

BODY'S JOB

The interstitium's job is to stay thin so oxygen can jump quickly from the air sac into the blood. Think of it like a screen door: it needs to be strong enough to hold shape, but thin enough to let air pass. The blood vessels (capillaries) in the interstitium pick up oxygen and carry it to the heart, which pumps it to every cell in your body. At the same time, carbon dioxide (the waste gas from your cells) crosses back through the interstitium into the air sac to be breathed out. This swap happens millions of times a minute, silently, as long as the interstitium stays thin and healthy.

1. You breathe in. Air flows down the windpipe (trachea), through branching tubes (bronchi), and fills millions of tiny air sacs (alveoli).
2. Each air sac is wrapped in a net of tiny blood vessels (capillaries). Between the air sac and the blood vessel is the interstitium — a paper-thin space made of delicate tissue.
3. Oxygen in the air sac crosses through the thin interstitium and hops into the blood. At the same moment, carbon dioxide (the waste gas) crosses the other way, from blood into the air sac.
4. The oxygen-rich blood travels to the heart, which pumps it out to every organ and muscle. Carbon dioxide is breathed out.
5. This swap happens fast and smoothly because the interstitium is thin. If the interstitium gets thick or scarred, oxygen cannot cross easily, and your blood oxygen drops.

What breaks

The interstitium — the thin space between the air sacs and blood vessels — gets thick, swollen, and scarred. This makes it hard for oxygen to cross from the air you breathe into your blood. The scarring can be caused by your immune system attacking by mistake, breathing in mold or bird proteins over and over, certain drugs, or an unknown reason (idiopathic means no known cause). Once scarring starts, it can keep spreading, turning soft, stretchy lung tissue into stiff, thick scar tissue that does not work.

CLINICAL TERM

Interstitial lung disease (ILD) is a group of disorders in which the interstitium (the thin connective tissue and capillary network between alveoli) becomes inflamed and fibrotic (scarred). The specific type depends on the cause: with no known cause (idiopathic) pulmonary fibrosis (IPF) is progressive scarring with no known trigger, following a usual interstitial pneumonia (UIP) pattern on imaging; nonspecific interstitial pneumonia (NSIP) is inflammation and some scarring, often linked to autoimmune disease; hypersensitivity pneumonitis (HP) is an immune reaction to inhaled antigens like mold (often from hot tubs or humidifiers) or bird proteins (from pet birds or feather bedding); connective tissue disease-associated ILD (CTD-ILD) happens in people with rheumatoid arthritis, systemic sclerosis (scleroderma), polymyositis, dermatomyositis, or mixed connective tissue disease; sarcoidosis is noncaseating granulomas (tiny clumps of immune cells) in the lungs and often other organs like lymph nodes, eyes, or skin; drug-induced ILD is caused by medications like amiodarone (heart rhythm drug), methotrexate (rheumatoid arthritis or cancer drug), bleomycin (chemotherapy), or nitrofurantoin (urinary antibiotic). No matter the cause, the final common path is that the thin interstitium thickens and scars, blocking oxygen diffusion (the movement of oxygen from air to blood) and making the lungs stiff (restrictive physiology on pulmonary function tests). This break does not stay local. The downstream signals you will see are progressive shortness of breath (dyspnea), dry cough with no mucus, low oxygen saturation (hypoxemia, often worse with activity), fine crackles (Velcro crackles in the lungs (rales)) at the lung bases on exam, and digital clubbing (curved, bulging fingernails). Read all these findings backward — they all point to one upstream break: the scarred interstitium.

How the body compensates

The body tries hard to keep oxygen delivery steady even as the lungs scar. You breathe faster and take shallower breaths to move air through stiff lungs. Your heart pumps harder to send blood through scarred lung tissue. Over months, low oxygen triggers nail clubbing and can raise pressure in the lung blood vessels (pulmonary high blood pressure (hypertension), which is high blood pressure in the arteries going to the lungs). Vital signs and oxygen saturation can look okay early on while the body is working hard to cope. The danger is missing the slow downhill slide until the patient suddenly cannot breathe during an infection or acute flare-up (exacerbation) (a sudden, severe worsening). The job is to see the crash point coming by watching trends (how things are changing over weeks to months) and catching worsening lung function before compensation fails.

1. At first, you breathe faster (tachypnea, more than 20 breaths per minute) to pull in more oxygen and blow off carbon dioxide. Breathing faster feels normal to you, so you may not notice the change right away.

2. The lungs become stiff and lose stretch (reduced compliance), so you take smaller, shallower breaths. Deep breaths feel hard or uncomfortable.
3. Your heart rate goes up (tachycardia, more than 100 beats per minute at rest) to pump blood faster through the lungs, trying to pick up as much oxygen as possible from each breath.
4. Over weeks to months, low oxygen levels trigger changes in your fingertips: nails curve and bulge (digital clubbing). This is the body trying to grow more blood vessels to grab oxygen.
5. Blood vessels in the lungs tighten and scar (pulmonary vascular remodeling), raising pressure in the lung circulation (pulmonary high blood pressure (hypertension)). This makes the right side of the heart work harder, which can eventually lead to right heart failure (cor pulmonale, when the right side of the heart gets tired and weak).
6. During the compensated phase, oxygen saturation may be normal at rest (often above 90 percent) but drops fast with walking or activity (exertional desaturation, often dropping below 88 percent on a 6-minute walk test). This is a red flag that compensation is running out.
7. The crash point to watch for is an acute flare-up (exacerbation) (sudden worsening) in IPF, a lung infection (pneumonia), or heart failure tipping over. Once compensation fails, oxygen saturation plummets (often below 85 percent even with oxygen), breathing becomes extremely hard (respiratory distress), and the window to recover narrows fast. Mechanical ventilation (a breathing machine) may be needed, but outcomes are often poor in advanced fibrosis.
8. A patient who looks stable at one moment can be on a slow downhill slope. Always look at the trend: Is oxygen saturation lower than last month? Is walking distance shorter (measured by 6-minute walk test)? Is cough worse? Is the patient using more oxygen at home? A stable exam today does not mean stable disease.

Domino effect

1. The interstitium (the thin space between air sacs and blood vessels) gets swollen and scarred. — Depending on the type of ILD, the trigger is different: in IPF, the cause is unknown but the scarring is relentless; in hypersensitivity pneumonitis, repeated exposure to mold (often from hot tubs, humidifiers, or water-damaged buildings), bird proteins (from pet birds or feather pillows), or other antigens triggers an immune reaction; in connective tissue disease (like systemic sclerosis, rheumatoid arthritis, or polymyositis), the immune system attacks the lungs; in sarcoidosis, clumps of immune cells (noncaseating granulomas) form in the interstitium; in drug-induced ILD, medications like amiodarone, bleomycin, methotrexate, or nitrofurantoin damage lung tissue. No matter the cause, the result is the same: the thin interstitium thickens and scars, turning soft, stretchy lung tissue into stiff scar tissue that does not work.

2. Oxygen cannot cross easily from the air sac into the blood, so blood oxygen drops (hypoxemia). — Normally, oxygen hops across the paper-thin interstitium in a fraction of a second. When the interstitium is thick and scarred, oxygen has to travel through a thick wall, which takes longer and some oxygen never makes it across. Blood leaving the lungs has less oxygen than normal (often oxygen saturation below 88 percent with activity, sometimes below 90 percent at rest in advanced disease), and you feel short of breath (dyspnea), especially with activity like climbing stairs or walking fast.
3. The lungs become stiff and lose stretch (reduced lung compliance, restrictive pattern on pulmonary function tests). — Scar tissue is stiff and does not stretch like healthy lung tissue. As more interstitium scars, the lungs shrink and resist expansion. On pulmonary function tests (PFTs, breathing tests), total lung capacity (TLC, the total amount of air your lungs can hold) and forced vital capacity (FVC, the amount of air you can blow out after a deep breath) drop (restrictive pattern, usually TLC and FVC below 80 percent of predicted). You feel like you cannot take a deep breath, and breathing takes more effort.
4. You cough constantly, usually a dry cough with no mucus. — The scarred interstitium irritates nerve endings in the lungs (like the vagus nerve, which senses irritation and triggers coughing), triggering a cough reflex. The cough is the body trying to clear something that feels wrong, but there is no mucus or infection to clear — just the stiff, irritated tissue itself.
5. On exam, the doctor hears fine crackles (Velcro crackles in the lungs (rales)) at the bases (bottoms) of the lungs. — Scarred air sacs pop open during a deep breath, making a crackling sound like pulling apart Velcro. This classic finding is heard best at the bottom (bases) of the lungs, where scarring often starts, and is a hallmark of ILD on physical exam.
6. Over months to years, your fingernails curve and bulge (digital clubbing). — Long-lasting low oxygen (chronic low oxygen in the blood (hypoxemia)) triggers changes in the fingertips. The body grows extra tissue and blood vessels under the nail, making the nail curve and the fingertip bulge. Clubbing is a sign that oxygen has been low for a long time (usually months) and is seen in about 50 percent of people with IPF, less often in other ILD types.
7. Pressure in the lung blood vessels goes up (pulmonary high blood pressure (hypertension)), and the right side of the heart works harder and can eventually fail (cor pulmonale). — Scarring and low oxygen make blood vessels in the lungs tighten and narrow (pulmonary vasoconstriction). The right side of the heart (right ventricle) has to pump harder to push blood through these tight vessels. Over time, the right heart muscle gets tired, thick, and weak (right ventricular hypertrophy and failure), leading to right heart failure: legs and belly swell (peripheral swelling (edema) and fluid buildup in the belly (ascites)), liver gets congested (hepatomegaly), neck veins bulge (jugular venous distension), and breathing gets even worse.

8. In IPF, acute exacerbations (sudden, severe worsening) can happen, where breathing becomes extremely hard, oxygen drops fast, and the lungs look worse on CT scan with new ground-glass opacities (hazy patches that look like frosted glass). — We do not fully understand why, but in IPF the scarring can suddenly speed up (acute flare-up (exacerbation) of IPF, or AE-IPF), often triggered by a virus (like influenza or COVID-19), silent infection, aspiration (breathing in food or stomach acid), or for no clear reason. The already-damaged lungs cannot handle the extra hit, and the patient crashes. Mortality is high in acute exacerbations (about 50 percent die within a few months) even with ICU care, oxygen, and steroids.
9. Tracing back: All these findings — shortness of breath, dry cough, fine crackles, low oxygen (especially with walking), clubbing, stiff lungs on PFTs, pulmonary high blood pressure (hypertension) — point back to one upstream break: the scarred interstitium. Naming the type (IPF, NSIP, HP, CTD-ILD, sarcoidosis, drug-induced) guides treatment. — If it is IPF, anti-fibrotic drugs (pirfenidone or nintedanib) slow scarring (they do not reverse it, but they cut the rate of lung function decline by about 50 percent and buy time, often years). If it is inflammatory (NSIP, CTD-ILD, sarcoidosis, or hypersensitivity pneumonitis), immune-suppressing drugs like prednisone (a steroid), azathioprine, mycophenolate, or rituximab calm the immune attack and can stop or reverse some of the damage. If it is hypersensitivity pneumonitis or drug-induced ILD, removing the trigger (stop the drug, get rid of the mold source, remove pet birds or feather bedding) is the most important step and can stop progression if caught early. High-flow oxygen (often through a nasal cannula, sometimes 4 to 6 liters per minute or more) helps symptoms, keeps oxygen saturation above 88 percent, and prevents right heart failure. Pulmonary rehab (supervised exercise and breathing training) improves exercise tolerance and quality of life. Lung transplant is the only cure for end-stage fibrosis and is considered for people under 65 with advanced disease (FVC below 50 percent or oxygen needs above 4 liters) who are otherwise healthy. Picking the right treatment depends on knowing the type and cause, which is why high-resolution chest CT (HRCT, which shows the pattern of scarring — like honeycombing in IPF, ground-glass opacities in NSIP, or centrilobular nodules in hypersensitivity pneumonitis) and sometimes lung biopsy (usually video-assisted thoracoscopic surgery, or VATS) are needed to make the diagnosis. Multidisciplinary discussion (pulmonologist, radiologist, and pathologist together) is the gold standard for diagnosis.

Symptoms · what the patient feels, and why

- Shortness of breath that gets worse over weeks to months, especially during activity: Scarring (fibrosis) thickens the walls of the air sacs (alveoli) in the lungs, making it harder for oxygen to pass from the air into the bloodstream. When the body needs more oxygen during exercise, the damaged lungs can't keep up, so you feel breathless.

- Dry cough that doesn't go away and doesn't bring up mucus: Scarring and inflammation irritate the airways and the interstitium (the thin tissue between the air sacs). The body tries to clear the irritation by coughing, but because this isn't caused by mucus or infection, the cough stays dry.
- Crackling sounds (fine crackles or 'Velcro crackles in the lungs (rales)') heard through a stethoscope at the bottom of both lungs: When scarred air sacs pop open during a deep breath, they make a crackling sound—like pulling apart Velcro—that the doctor can hear with a stethoscope. This tells the doctor that the tiny air sacs are stiff and fibrotic.
- Feeling very tired all the time (fatigue): The scarred lungs can't pull in enough oxygen to meet the body's needs, so cells don't get the fuel they need to make energy. This leaves you feeling drained and worn out even after rest.
- Clubbing of the fingers—fingertips become round and the nails curve downward: Long-term low oxygen in the blood signals the body to grow extra tissue at the fingertips, making them bulge and the nails curve. Clubbing is a sign that the lungs have been struggling for a while.
- Unintended weight loss: Breathing with stiff, scarred lungs takes extra energy, and chronic inflammation can speed up the body's metabolism. Together, these burn more calories than you take in, leading to weight loss.
- Bluish color of the lips or fingernails (cyanosis): When the lungs can't get enough oxygen into the blood, the blood looks darker and gives a bluish tint to the skin, especially at the lips and fingernail beds where blood vessels are close to the surface.
- Fast, shallow breathing even at rest: Scarred lungs are stiff and can't expand well, so the body tries to pull in more oxygen by taking many quick, shallow breaths instead of slow, deep ones. This is a sign the lungs are severely damaged.

Focused exam

- Velcro crackles (fine, dry crackles) heard at the lung bases: When the interstitium — the thin tissue web that holds the air sacs together — becomes stiff and scarred, air moving through it makes short, high-pitched pops that sound like pulling apart Velcro. This sound is the main clue that the problem is in the interstitium, not the airways or blood vessels.
- Clubbing of fingernails and toenails: When the lungs cannot move enough oxygen into the blood for months or years, the body tries to fix it by sending extra blood to the fingertips. The tips swell and the nails curve downward like an upside-down spoon. Clubbing tells you the lung disease has been going on a long time and oxygen has been low for a long time.

- Oxygen saturation drops during six-minute walk test: When the interstitium (the tissue web between air sacs and blood vessels) is thick and scarred, oxygen cannot cross into the blood fast enough when muscles need more during walking. Oxygen saturation dropping below 88% during the walk shows the lungs cannot keep up with demand — a sign of severe interstitial lung disease.
- Restrictive pattern on pulmonary function test: low total lung capacity, low forced vital capacity, normal or high FEV₁/FVC ratio: Interstitial lung disease makes the entire lung stiff like a dried sponge, so it cannot stretch and fill with as much air as normal. Total lung capacity below 80% of predicted and forced vital capacity below 80% of predicted mean the lungs are small and stiff. The FEV₁/FVC ratio stays normal or goes up because the problem is not the airways — it is the tissue itself.
- High-resolution CT of the chest shows ground-glass opacities, reticular pattern, or honeycombing: CT can see the interstitium — the thin tissue web between air sacs — that is normally invisible. Ground-glass opacities mean the interstitium is swollen and inflamed. Reticular pattern means scarring organized into a lacy net. Honeycombing means end-stage scarring with clusters of tiny air pockets. Each pattern tells you which type of interstitial lung disease it is and which treatment will work.
- Progressive shortness of breath over weeks to months, worse with activity: Interstitial lung disease is not a sudden problem — it is chronic inflammation and scarring that slowly gets worse because more interstitium (the tissue web between air sacs) turns into scar tissue over time. Symptoms that worsen over weeks to months — not hours or days — point to interstitial lung disease, not asthma, pneumonia, or heart failure.

Diagnostics · every test answers a question

- High-resolution CT (HRCT) of the chest without contrast → What pattern of scarring is in the interstitium (the tissue web between air sacs), and does it match with no known cause (idiopathic) pulmonary fibrosis (usual interstitial pneumonia pattern with honeycombing and peripheral/basal scarring) or another type of interstitial lung disease?
- Pulmonary function tests: spirometry, lung volumes, and diffusing capacity for carbon monoxide (DLCO) → Are the lungs stiff and small (restrictive pattern), and can oxygen cross from air into blood (measured by diffusing capacity)?
- Six-minute walk test with continuous pulse oximetry → Does oxygen saturation drop when the patient walks, and how far can the patient walk before becoming too short of breath?
- Complete blood count (CBC), comprehensive metabolic panel (CMP), antinuclear antibody (ANA), rheumatoid factor (RF), anti-cyclic citrullinated peptide (anti-CCP), anti-Scl-70 (anti-topoisomerase), and anti-Jo-1 (anti-histidyl-tRNA synthetase) → Is there a connective tissue disease — like rheumatoid arthritis, scleroderma (systemic sclerosis), or polymyositis — causing the lung scarring?

- Surgical lung biopsy by video-assisted thoracoscopic surgery (VATS) if the HRCT pattern is unclear and the diagnosis will change treatment → What is the exact pattern of scarring and inflammation in the lung tissue when imaging alone cannot tell which type of interstitial lung disease it is?
- N-terminal pro-brain natriuretic peptide (NT-proBNP) and echocardiogram with estimated right ventricular systolic pressure (RVSP) → Is the scarred lung causing high pressure in the lung arteries (pulmonary high blood pressure (hypertension)) and straining the right side of the heart?
- Serum precipitins (antibodies to inhaled antigens such as bird proteins, mold, hay) if hypersensitivity pneumonitis is suspected → Is the lung scarring caused by an allergic reaction to something the patient breathes repeatedly at home or work (hypersensitivity pneumonitis)?
- Bronchoalveolar lavage (BAL) with cell count and differential if infection, eosinophilic pneumonia, or alveolar bleeding (hemorrhage) is in the differential → What kinds of cells are in the air sacs — immune cells, infection, blood — and does that point to a specific cause?

Treatment logic

- Identify the type of interstitial lung disease — with no known cause (idiopathic) pulmonary fibrosis (IPF) versus inflammatory ILD (NSIP, connective tissue disease-ILD, sarcoidosis, hypersensitivity pneumonitis) versus drug-induced — using high-resolution CT, clinical history, autoimmune labs, and sometimes lung biopsy → Knowing which type of scarring the patient has tells you whether to use antifibrotic drugs (for IPF, which is scarring without much inflammation), anti-inflammatory drugs like corticosteroids and immunosuppressants (for inflammatory ILDs where immune cells are attacking the interstitium), or simply stop the trigger (for drug-induced or hypersensitivity pneumonitis). The type is the map that chooses which medicine will work.
- For with no known cause (idiopathic) pulmonary fibrosis (IPF): start pirfenidone (an anti-inflammatory and antifibrotic drug) or nintedanib (a tyrosine kinase inhibitor that blocks scar-building signals) to slow the rate of lung stiffening and decline in lung function → These antifibrotic drugs tell fibroblasts (the cells that lay down scar tissue) to slow down. They cut the rate of lung-function decline by about half and reduce the risk of hospitalization and death. Patients still get worse over time, but much more slowly.

- For inflammatory ILDs (NSIP, connective tissue disease-ILD, sarcoidosis, chronic hypersensitivity pneumonitis): use corticosteroids (prednisone starting at 0.5–1 mg/kg/day, tapered over months) plus a steroid-sparing immunosuppressant such as mycophenolate mofetil, azathioprine, or rituximab (a monoclonal antibody that wipes out B cells) to calm the immune attack on the interstitium → Immunosuppressants calm T cells, B cells, and macrophages (immune cells) that are inflaming and damaging the interstitium (the tissue web between air sacs). Less inflammation means less new scarring, better oxygen crossing into blood, and lung function that can stabilize or even improve.
- Give supplemental oxygen (by nasal cannula or portable concentrator) when oxygen saturation drops below 88% at rest or with activity → Extra oxygen in the air the patient breathes pushes more oxygen across the stiff, scarred interstitium (tissue web between air sacs) into the blood, so the body and brain get what they need. It reduces shortness of breath, lets patients move more, and improves survival in patients with chronic low oxygen (< 88% at rest or with activity).
- Prescribe pulmonary rehabilitation — a 6- to 12-week program of breathing exercises, walking training, strength training, and disease education — supervised by a respiratory therapist or physical therapist → Rehab trains the muscles and breathing patterns so the patient uses less oxygen during daily tasks and feels less short of breath with the lungs they have. Patients walk farther, feel less tired, and report better quality of life.
- Treat gastroesophageal reflux aggressively with proton-pump inhibitors (omeprazole 20–40 mg daily or pantoprazole 40 mg daily), elevate the head of the bed by 6–8 inches, and avoid eating within 3 hours of bedtime → Stopping reflux prevents stomach acid from silently spilling into the lower airways (microaspiration) and triggering more inflammation and scarring in the interstitium. Some studies suggest treating reflux slows disease progression in IPF, though the evidence is mixed.
- Refer for lung transplant evaluation early — when forced vital capacity drops below 80% of predicted, DLCO drops below 40% of predicted, the patient needs supplemental oxygen, or hospitalizations for breathing trouble are happening — even if the patient is still stable on treatment → Early referral finds patients who might get new lungs before they become too weak, too sick, or too oxygen-dependent for surgery. Lung transplant is the only treatment that can replace scarred lungs and restore normal oxygen levels. Five-year survival after transplant for ILD is about 50–60%, much better than waiting until the disease is end-stage.

Medications

Pirfenidone · Anti-fibrotic agent

Pirfenidone slows down the scarring (fibrosis) in the lungs by blocking several chemical signals that tell scar-making cells (fibroblasts) to keep laying down thick, stiff tissue. It also dials down

inflammation. Think of it like putting the brakes on a runaway scarring process that stiffens the lung's air sacs.

1. Pirfenidone enters the bloodstream and reaches the lungs.
2. It blocks TGF-beta (transforming growth factor beta, a chemical messenger that tells fibroblasts to make more scar tissue) and other pro-fibrotic signals.
3. It reduces the activity of fibroblasts so they produce less collagen (the thick rope-like protein that makes up scars).
4. It also lowers levels of inflammatory chemicals like TNF-alpha (tumor tissue death (necrosis) factor alpha), which otherwise fuel more scarring.
5. Over time, the rate of new scarring slows, helping preserve more working lung tissue.

SAFETY WATCH

Nausea and upset stomach (common; taking it with food helps). · Skin rash and sensitivity to sunlight (photosensitivity) — wear sunscreen and protective clothing outdoors. · Loss of appetite and weight loss. · Dizziness and tiredness. · Liver enzyme elevation — your doctor will check blood tests (liver function) regularly. · Avoid in severe liver disease or severe kidney disease.

Nintedanib · Tyrosine kinase inhibitor (anti-fibrotic agent)

Nintedanib blocks several growth-factor receptors (docking stations on cells) that normally tell fibroblasts to multiply and make scar tissue. By jamming these receptors — especially for PDGF (platelet-derived growth factor), FGF (fibroblast growth factor), and VEGF (vascular endothelial growth factor) — it slows the lung's scarring process.

1. Nintedanib enters the bloodstream and reaches the lungs.
2. It binds to and blocks tyrosine kinase enzymes inside growth-factor receptors (PDGFR, FGFR, VEGFR).
3. With these receptors blocked, fibroblasts receive fewer signals to multiply and lay down collagen.
4. New blood-vessel growth (which can feed fibrosis) is also slowed by blocking VEGFR.
5. Over time, the rate of new scarring slows, helping preserve lung function.

SAFETY WATCH

Diarrhea (very common; may need anti-diarrheal medication or dose adjustment). · Nausea and upset stomach. · Loss of appetite and weight loss. · Liver enzyme elevation — your doctor will monitor liver function tests regularly. · Increased risk of bleeding (nintedanib can interfere with clotting) — tell your doctor if you take blood thinners or notice unusual bruising. · High blood pressure — monitor blood pressure regularly. · Avoid in moderate-to-severe liver disease; use cautiously in kidney disease.

Prednisone (or other corticosteroids) · Corticosteroid (immune suppressor and anti-inflammatory)

Prednisone is a man-made version of cortisol (the body's natural stress hormone). It powerfully turns down the immune system's attack and inflammation. In inflammatory ILDs (like hypersensitivity pneumonitis, nonspecific interstitial pneumonia NSIP, organizing pneumonia, or ILD linked to autoimmune disease), prednisone tells immune cells to stop releasing inflammatory chemicals and to quiet down, which reduces lung damage and scarring.

1. Prednisone enters the bloodstream and travels to immune cells.
2. It crosses into the cell and binds to glucocorticoid receptors inside.
3. The drug-receptor pair moves into the nucleus and changes gene activity, turning OFF genes that make inflammatory chemicals (cytokines like IL-1, IL-6, TNF-alpha) and turning ON genes that calm inflammation.
4. Fewer immune cells arrive in the lungs, and the ones already there release less inflammatory chemicals.
5. Inflammation in the lung tissue drops, which can prevent new scarring and sometimes allow existing inflammation to clear.

SAFETY WATCH

High blood sugar (can trigger or worsen diabetes) — monitor blood sugar if you are at risk. · Weight gain, increased appetite, and fluid retention (puffiness). · Mood changes: irritability, anxiety, trouble sleeping, or (rarely) severe mood swings. · Weakened bones (osteoporosis) with long-term use — your doctor may prescribe calcium, vitamin D, and a bone-protecting drug (bisphosphonate). · Increased risk of infections (especially fungal, bacterial, and viral) — watch for fever, cough, sores. · Stomach irritation or ulcers — take with food; your doctor may add a stomach-protecting drug. · High blood pressure and higher cholesterol. · Cataracts and glaucoma with long-term use. · Never stop prednisone suddenly after weeks of use — it must be tapered slowly to let your adrenal glands wake up again.

Mycophenolate mofetil · Immunosuppressant (antimetabolite)

Mycophenolate blocks a key enzyme (IMPDH, inosine monophosphate dehydrogenase) that lymphocytes (a type of white blood cell) need to multiply. By stopping lymphocytes from dividing, it turns down the immune attack in inflammatory ILDs (like NSIP, connective-tissue ILD, or sarcoidosis) and is often used as a steroid-sparing agent to lower the prednisone dose.

1. Mycophenolate is absorbed and converted to mycophenolic acid (the active form).
2. It enters lymphocytes and blocks IMPDH, an enzyme needed to make guanosine (a building block of DNA).
3. Without enough guanosine, lymphocytes cannot copy their DNA and divide.
4. Fewer immune cells are produced, so the inflammatory assault on lung tissue slows.
5. Over time, lung inflammation drops and the need for high-dose steroids may decrease.

SAFETY WATCH

Stomach upset, nausea, diarrhea, and abdominal cramps (common; taking it with food may help). · Increased risk of infections (bacterial, viral, fungal) — watch for fever, cough, sores, or unusual symptoms. · Low white blood cell count (leukopenia) — your doctor will check blood counts regularly. · Anemia (low red blood cells) and low platelet count. · Avoid live vaccines while on this drug. · Risk of certain cancers (lymphoma, skin cancer) with long-term use — practice sun safety and have regular skin checks. · Avoid during pregnancy and while breastfeeding (it can cause birth defects); use reliable contraception.

Azathioprine · Immunosuppressant (antimetabolite)

Azathioprine is converted in the body into chemicals that interfere with DNA and RNA production in dividing cells, especially lymphocytes (immune cells). By slowing lymphocyte multiplication, it turns down the immune attack in inflammatory ILDs. It is sometimes used as an alternative or add-on to mycophenolate, though newer evidence favors mycophenolate in many ILDs.

1. Azathioprine is absorbed and converted to 6-mercaptopurine and then to active metabolites.
2. These metabolites get mistakenly incorporated into DNA and RNA in place of normal building blocks.
3. The faulty DNA disrupts cell division, so lymphocytes cannot multiply normally.
4. Fewer immune cells are produced, reducing the inflammatory attack on the lungs.

SAFETY WATCH

Nausea and upset stomach (common early on; often improves with time). · Bone marrow suppression — low white blood cells, red blood cells, or platelets — your doctor will check blood counts regularly. · Increased risk of infections. · Liver enzyme elevation — liver function tests will be monitored. · Increased risk of certain cancers (lymphoma, skin cancer) with long-term use. · Drug interaction with allopurinol (a gout medicine) — the combination can cause dangerous bone marrow toxicity; dose must be reduced if used together. · Avoid live vaccines. · Avoid during pregnancy (risk of birth defects); use reliable contraception.

Rituximab · Monoclonal antibody (B-cell depleting agent)

Rituximab is a laboratory-made antibody that targets CD20, a protein on the surface of B cells (a type of white blood cell that makes antibodies). By binding to CD20, rituximab marks B cells for destruction. This is used in ILDs driven by autoimmune disease (especially connective-tissue ILD like rheumatoid arthritis-ILD or systemic sclerosis-ILD) where B cells fuel the immune attack.

1. Rituximab is given by IV infusion into the bloodstream.
2. It binds to CD20 on the surface of B cells.
3. The body's immune system recognizes the antibody-coated B cells as targets and destroys them (through complement activation and antibody-dependent cell killing).
4. B cell numbers drop sharply, which lowers autoantibody production and reduces the immune attack on lung tissue.
5. Over weeks to months, inflammation in the lungs decreases.

SAFETY WATCH

Infusion reactions during or shortly after the IV — fever, chills, rash, low blood pressure, shortness of breath (pre-medications like acetaminophen and antihistamines are given to reduce this risk). · Increased risk of infections, including serious viral infections (like hepatitis B reactivation, which can be fatal — you will be screened for hepatitis B before starting). · Progressive multifocal leukoencephalopathy (PML), a rare but deadly brain infection caused by JC virus. · Low immunoglobulin levels over time, making you more vulnerable to infections. · Low white blood cell and platelet counts. · Avoid live vaccines; check with your doctor about timing of other vaccines. · Rarely, severe skin reactions.

Supplemental oxygen · Supportive therapy (not a drug)

Supplemental oxygen is breathed in through a nasal tube (cannula) or mask to raise the amount of oxygen in your blood when your scarred or inflamed lungs cannot pull in enough on

their own. It does not treat the disease itself, but it keeps your organs (especially your heart and brain) fed with the oxygen they need, prevents strain on the heart, and helps you feel less short of breath and more able to move.

1. Oxygen from a tank or concentrator flows through tubing into your nose or mouth.
2. The higher concentration of oxygen in each breath increases the oxygen level (partial pressure) in the air sacs.
3. More oxygen dissolves into the blood and binds to hemoglobin in red blood cells.
4. Oxygen-rich blood circulates to the heart, brain, muscles, and other organs, keeping them working.
5. The heart does not have to pump as hard to deliver oxygen, which prevents right heart strain (cor pulmonale).

SAFETY WATCH

Oxygen is generally very safe, but high-flow oxygen over long periods can (rarely) suppress the breathing drive in people who rely on low oxygen to trigger breathing (mostly in advanced COPD, not typical in ILD). · Dry nose and throat — use a humidifier bottle on the oxygen system. · Skin irritation from the nasal cannula tubing — adjust fit and use skin-protective pads if needed. · Fire hazard — oxygen makes things burn faster; never smoke or use open flames (candles, stoves) near oxygen equipment. · Tripping hazard from tubing — arrange tubing carefully at home.

Pulmonary rehabilitation · Supportive therapy (not a drug)

Pulmonary rehabilitation is a supervised exercise and education program that trains your breathing muscles, builds stamina in your legs and arms, and teaches you breathing techniques and energy-saving strategies. It does not change the lung disease itself, but it helps you use the lung function you have more efficiently, reduces shortness of breath during activity, and improves your quality of life and ability to do daily tasks.

1. You attend sessions (usually 2–3 times a week for 6–12 weeks) with a respiratory therapist and exercise specialist.
2. You do aerobic exercise (walking, cycling) at a level that challenges but does not overwhelm you.
3. You do strength training (weights, resistance bands) to build muscle.
4. You practice breathing exercises (pursed-lip breathing, diaphragmatic breathing) to control shortness of breath.
5. Over time, your muscles use oxygen more efficiently, your heart pumps more effectively, and you feel less breathless doing the same activities.

SAFETY WATCH

Rare risk of muscle soreness or minor injury — the therapist will tailor exercises to your ability and monitor you closely. · If you have severe heart disease or very advanced lung disease, your doctor will assess whether rehab is safe or needs special modifications. · Use supplemental oxygen during exercise if prescribed. · Tell the rehab team immediately if you feel chest pain, dizziness, or extreme shortness of breath during exercise.

Vaccinations (influenza, pneumococcal, COVID-19, RSV) · Preventive therapy (not a drug for the disease itself)

Vaccines train your immune system to recognize and fight specific viruses and bacteria before you get infected. In ILD, your lungs are already damaged and cannot handle the extra injury from infections like flu, pneumonia, COVID-19, or RSV (respiratory syncytial virus). Vaccines significantly lower your risk of these infections and of severe illness if you do catch them.

1. The vaccine is given (usually by injection, sometimes by nasal spray).
2. Immune cells encounter the vaccine antigen (a piece of the virus or bacteria).
3. B cells produce antibodies that stick to and neutralize the real germ if you are exposed later.
4. T cells learn to kill infected cells.
5. Memory cells remain in your body for months to years, ready to respond quickly if the real infection shows up.

SAFETY WATCH

Mild arm soreness, redness, or swelling at the injection site (common and harmless). · Low-grade fever, fatigue, or body aches for a day or two after the vaccine (a sign your immune system is responding). · Allergic reactions are very rare but possible — stay for 15 minutes after the shot so staff can help if needed. · Live vaccines (like nasal flu vaccine, shingles vaccine Zostavax) should be AVOIDED if you are on strong immunosuppressants (prednisone >20 mg/day, mycophenolate, rituximab, etc.) — ask your doctor which vaccines are safe for you. · Inactivated vaccines (flu shot, pneumococcal, COVID-19 mRNA, recombinant shingles vaccine Shingrix, RSV) are safe even on immunosuppressants.

Proton pump inhibitor (e.g. omeprazole, esomeprazole) for gastroesophageal reflux disease (GERD) · Proton pump inhibitor (acid suppressor)

Proton pump inhibitors (PPIs) block the proton pumps in the stomach lining that produce stomach acid. By lowering acid production, PPIs reduce acid reflux (when stomach contents wash back up into the throat and can be breathed into the lungs — called aspiration). In ILD,

repeated micro-aspiration of acid can worsen lung inflammation and fibrosis. Treating reflux may slow disease progression, especially in IPF.

1. The PPI is absorbed and enters the bloodstream.
2. It travels to the parietal cells and is activated in the acidic environment of the stomach.
3. It binds to and permanently blocks the proton pump enzyme.
4. The stomach produces much less acid.
5. With less acid, there is less acidic reflux and less chance of lung injury from aspiration.
6. The blocked pumps are slowly replaced over days, so the drug is taken daily for ongoing effect.

SAFETY WATCH

Generally well tolerated with few side effects. · Headache, nausea, diarrhea, or abdominal pain (uncommon). · Long-term use (years) has been linked to low magnesium, low calcium (increased fracture risk), low vitamin B12, and increased risk of certain infections (C. difficile diarrhea, pneumonia) — your doctor may monitor labs if you are on a PPI long-term. · Rarely, kidney disease (interstitial nephritis) or low blood levels of magnesium, calcium, or B12. · PPIs can interact with clopidogrel (Plavix), reducing its effectiveness — talk to your doctor if you take both.

N-acetylcysteine (NAC) · Antioxidant and mucolytic (use is now limited)

N-acetylcysteine is an antioxidant that can neutralize harmful oxygen radicals (reactive molecules that damage cells) and may replenish glutathione (the body's own antioxidant). It was once thought to slow fibrosis in IPF by reducing oxidative stress, but large trials (PANTHER-IPF) showed NO benefit in IPF and possible harm when combined with prednisone and azathioprine. It is now NOT recommended for routine use in IPF. It may still be used in some other ILDs on a case-by-case basis, and it is used as a mucolytic (mucus thinner) in some lung diseases, though evidence in ILD is weak.

1. NAC is absorbed (by mouth or inhaled) and enters the bloodstream and lungs.
2. It donates sulfur groups that help rebuild glutathione, a key antioxidant.
3. Glutathione neutralizes reactive oxygen species, potentially reducing cell damage.
4. In mucus, NAC breaks chemical bonds that make mucus thick and sticky, making it easier to cough up.

SAFETY WATCH

Nausea and upset stomach (common, especially at high doses). · Bad taste and odor (like rotten eggs). · Rash or itching (rare). · Bronchospasm (wheezing, tightness) if inhaled, especially in people with asthma. · In the PANTHER-IPF trial, the combination of NAC + prednisone + azathioprine was harmful (increased hospitalizations and deaths) — NAC should NOT be used with that combination.

Red flags

- Oxygen level (SpO₂) below 88% at rest or dropping below 88% during walking—means the lungs can't keep blood oxygen high enough and the patient may need oxygen therapy or hospital care right away.
- Sudden, severe shortness of breath or chest pain—could signal a collapsed lung (pneumothorax), blood clot in the lung (pulmonary a traveling clot lodging in a vessel (embolism)), or heart failure from lung disease, all of which need emergency care.
- Confusion, sleepiness, or trouble staying awake—may mean carbon dioxide is building up in the blood because the lungs can't clear it, a dangerous sign that breathing is failing.
- Rapid worsening over days to weeks (acute flare-up (exacerbation) of IPF)—scarring suddenly speeds up, oxygen drops fast, and the person may need the ICU and a ventilator; this can be life-threatening.
- Swelling of the ankles and belly, along with a raised neck vein—suggests the right side of the heart is failing because high pressure in the scarred lungs is making the heart work too hard (cor pulmonale).

Nursing priorities

1. Check oxygen saturation with pulse oximeter at rest and after walking 30 feet; give supplemental oxygen by nasal cannula to keep SpO₂ above 88 percent. — Scarred lung tissue cannot exchange oxygen well, and low oxygen (hypoxemia, which means not enough oxygen in the blood) damages the heart and brain; keeping SpO₂ above 88 percent protects organs while doctors work on the underlying disease.
2. Listen to lung sounds in all fields and report new or louder Velcro-like crackles at the lung bases. — Velcro crackles (fine crackling sounds like pulling apart Velcro) mean stiff, scarred air sacs (alveoli, which are tiny lung balloons where oxygen moves into blood); worsening crackles signal disease progression needing treatment adjustment.

3. Monitor respiratory rate, work of breathing, and use of neck or belly muscles to breathe every 4 hours. — Using accessory muscles (extra breathing muscles in the neck and abdomen) or breathing faster than 20 times per minute at rest means the lungs are failing to move enough air, signaling respiratory failure that may need ICU care or mechanical ventilation (breathing machine).
4. Teach energy-saving techniques like sitting while dressing, using a shower chair, and pacing activities with rest breaks. — Scarred lungs cannot increase oxygen delivery during activity, so muscles run out of oxygen quickly, causing extreme tiredness (fatigue); conserving energy prevents dangerous oxygen drops and improves quality of life.
5. Weigh the patient daily at the same time and watch for sudden weight gain or new swollen ankles. — ILD causes pulmonary high blood pressure (hypertension) (high pressure in lung blood vessels from scarring), which weakens the right side of the heart and causes fluid buildup; catching right heart failure early allows doctors to add diuretics and adjust treatment.
6. Give pirfenidone or nintedanib with food at the same times every day and teach the patient to report nausea, diarrhea, or skin sensitivity to sunlight. — These anti-fibrotic drugs (medicines that slow lung scarring) work best with steady blood levels; nausea and diarrhea are common side effects that cause patients to stop the medicine, losing the benefit of slowed disease.
7. Screen for depression and social isolation; connect the patient with pulmonary rehabilitation programs and ILD support groups. — Chronic breathlessness traps patients at home and causes fear, loneliness, and depression; pulmonary rehab (exercise and breathing training) improves exercise tolerance and mood even when lungs stay scarred.
8. Teach infection prevention: hand washing, avoiding crowds during flu season, and getting pneumonia and yearly flu vaccines. — Scarred lungs cannot clear mucus and bacteria well, so any respiratory infection (cold, flu, pneumonia) can trigger acute worsening (exacerbation, which means sudden flare-up) that causes permanent lung damage or death.

Sources

- ATS/ERS/JRS/ALAT Clinical Practice Guideline: Idiopathic Pulmonary Fibrosis (2018)
- American Thoracic Society (ATS)
- Fleischner Society
- CHEST

Last reviewed: 2026-07-07