Interstitial Lung Disease

ILD · Get the pattern, hunt the exposure, and decide fibrotic or inflammatory

IPF: ANTIFIBROTICS
not steroids

THE WORKUP *diagnosis is a multidisciplinary process, not a single test*

HISTORY IS THE HIGHEST YIELD

Occupational and environmental exposure — asbestos, silica, coal, **birds and feather bedding, mold, hot tubs**. **Drugs** — amiodarone, methotrexate, nitrofurantoin, bleomycin, **immune checkpoint inhibitors**. Smoking. **Connective tissue disease symptoms** — Raynaud, arthralgia, rash, dry eyes, reflux, proximal weakness.

HRCT IS CENTRAL

A **high-resolution CT with inspiratory and expiratory prone imaging**. The pattern often makes the diagnosis without biopsy. Look for **honeycombing, traction bronchiectasis, ground glass, mosaic attenuation and air trapping**, and note the **zonal distribution**.

SUPPORTING TESTS

PFTs with DLCO — typically restrictive with reduced transfer factor. **Serology**: ANA, ENA, rheumatoid factor, anti-CCP, myositis panel, ANCA. Consider **bronchoalveolar lavage** where infection or hypersensitivity pneumonitis is possible, and **biopsy only when it will change management**.

RECOGNIZE THE MAIN PATTERNS *they behave and are treated differently*

Pattern	HRCT features	Implication
UIP	**Subpleural, basal predominant honeycombing** with traction bronchiectasis, minimal ground glass	The pattern of **IPF**, but also seen in chronic hypersensitivity pneumonitis, rheumatoid and asbestosis. **Poorest prognosis.**
NSIP	**Ground glass with fine reticulation**, subpleural sparing, basal predominant	Strongly associated with **connective tissue disease**. Often **responds to immunosuppression**, unlike IPF.
Organizing pneumonia	**Patchy peripheral or peribronchial consolidation**, sometimes migratory, reversed halo sign	Cryptogenic or secondary to drugs, infection or connective tissue disease. **Usually steroid-responsive.**
Hypersensitivity pneumonitis	**Mosaic attenuation with air trapping**, upper or mid zone, centrilobular nodules; the "three-density sign"	**Antigen avoidance is the treatment** and the single most important intervention — identify and remove the exposure. May be fibrotic or non-fibrotic.

TREAT BY BEHAVIOR *the fibrotic / inflammatory split determines the drug*

1. **IPF is treated with antifibrotics** — **nintedanib** or **pirfenidone** — which slow the decline in FVC. They do not reverse fibrosis, and the goal is preserving trajectory.
2. **Do not give immunosuppression for IPF.** Combination prednisone, azathioprine and N-acetylcysteine caused **increased mortality and hospitalization** in trial data. This is one of the clearest "steroids are harmful here" lessons in respiratory medicine.
3. **Inflammatory ILD** — NSIP, organizing pneumonia, connective-tissue-disease-associated disease, non-fibrotic hypersensitivity pneumonitis — **does respond to corticosteroids**, usually with a steroid-sparing agent such as mycophenolate or azathioprine.
4. **Progressive pulmonary fibrosis (PPF)** is defined as **at least two of three criteria — worsening symptoms, radiological progression, and physiological progression — within the past year**, with no alternative explanation, in a patient with an ILD **other than IPF**. It is a **disease behavior, not a separate diagnosis**.
5. **Nintedanib is recommended for PPF** where standard management of the underlying fibrotic ILD has failed. Pirfenidone was not recommended in that guideline, though trial data support its use as a second-line option.

EVERYTHING ELSE THAT CHANGES OUTCOME *often more than the drug*

SUPPORTIVE CARE

Pulmonary rehabilitation — consistent symptom and functional benefit. **Ambulatory or long-term oxygen** for resting or exertional hypoxemia. **Vaccination**, smoking cessation, and treatment of **reflux** and **obstructive sleep apnea**. Screen for **pulmonary hypertension**, which worsens prognosis. Early **palliative input** for breathlessness and cough, which are frequently under-treated.

REFER AND WATCH FOR

Transplant referral early — refer at diagnosis in IPF rather than when they deteriorate, because the disease course is unpredictable. **Acute exacerbation of ILD** presents as rapidly worsening breathlessness with new ground glass on a background of fibrosis; **exclude infection, PE and heart failure first**, then treat with steroids, accepting the evidence is weak and mortality is high.

MONITORING & PROGNOSIS *what to measure, and what the numbers mean*

Measure	Why and how often
FVC	The main physiological endpoint. **Check every 3–6 months.** A **relative decline of ≥ 10% over a year** indicates progression and is one of the physiological criteria for PPF.
DLCO	Often falls before FVC. A **relative decline of ≥ 15%** is a marker of progression. Also flags emerging **pulmonary hypertension** when it falls out of proportion to lung volumes.
Exercise oximetry	**Desaturation on a walk test** frequently precedes resting hypoxemia and identifies who needs ambulatory oxygen. Resting saturations alone will miss it.
Symptoms and imaging	Worsening breathlessness or cough, and radiological progression on repeat HRCT, are the other two PPF domains. **Two of the three within a year defines progression.**

DRUG-INDUCED AND OCCUPATIONAL DISEASE *the reversible causes worth chasing hard*

DRUGS

Amiodarone — can appear years in, with a very long half-life so improvement is slow. **Methotrexate, nitrofurantoin** (classically long-term prophylaxis in older women), **bleomycin** (dose-related, worsened by high FiO_2), and **immune checkpoint inhibitors**, which cause pneumonitis needing prompt steroids and drug cessation. **Check every drug the patient has ever taken, not just current ones.**

OCCUPATIONAL & ENVIRONMENTAL

Asbestos — construction, shipbuilding, plumbing, and secondary exposure from washing work clothes; latency is decades. **Silica** in stonemasonry and the newer **engineered stone** epidemic. **Coal, beryllium, hard metals**. These carry **compensation and public health implications** — document the exposure carefully.

PEARLS & PITFALLS

- **Do not treat IPF with steroids and immunosuppression.** The combination increased mortality, and this remains a common and harmful reflex.
- **Take a real exposure history.** Birds, mold and hot tubs change the diagnosis to hypersensitivity pneumonitis, where removing the antigen is the treatment.
- **Review every drug chart** — amiodarone, methotrexate and nitrofurantoin all cause ILD.
- **PPF is a behavior, not a diagnosis.** Two of three domains progressing within a year makes any non-IPF fibrotic ILD eligible for antifibrotic therapy.
- **Screen for connective tissue disease properly.** NSIP is often the first manifestation, and it responds to immunosuppression when IPF would not.
- **Refer for transplant early**, not once they decompensate and the window has closed.

References: Idiopathic Pulmonary Fibrosis (an Update) and Progressive Pulmonary Fibrosis in Adults: an Official ATS/ERS/JRS/ALAT Clinical Practice Guideline (2022) · PANTHER-IPF · INBUILD and INPULSIS trials.

Educational aid; verify against local respiratory protocol and patient factors.