CENTER FOR INTERSTITIAL LUNG DISEASE & PULMONARY HYPERTENSION
AT LAKELAND REGIONAL HEALTH

Interstitial Lung Disease

Recognition, evaluation and longitudinal management

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Learning objectives

INTERSTITIAL LUNG DISEASE

- Recognize the major clinical and HRCT patterns of ILD
- Use a structured evaluation that includes exposures and expanded autoimmune testing
- Distinguish potentially reversible inflammation from established fibrosis
- Choose therapy according to disease mechanism and progression
- Monitor for progression, treatment toxicity and pulmonary hypertension

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Why the terminology sounds confusing

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The vocabulary mixes patterns with diagnoses

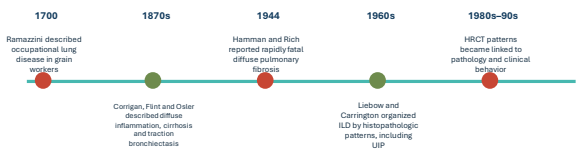
PATTERN	DIAGNOSIS
UIP	**IPF, RA-ILD, chronic HP**
What the lung looks like on HRCT or pathology	The disease causing that pattern after clinical context, exposures and serology are considered

The same UIP pattern can result from different diseases. The same disease can also produce more than one pattern.

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How the ILD vocabulary developed

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Modern imaging arrived after much of the pathology-based terminology was already established. That history explains some of today's overlap and confusion.

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Why ILD remains difficult

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More than 200 diseases can injure the interstitium

– Symptoms and spirometry overlap with common cardiopulmonary disease
– One radiographic pattern can reflect several different causes
– Inflammation and fibrosis often coexist in the same patient
– Diagnosis may evolve as exposures, serologies or systemic features emerge

The practical question

What is driving the lung injury now, and what can still be changed?

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A disciplined diagnostic sequence

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1 Clinical context	Time course, medications, exposures, autoimmune clues
2 HRCT pattern	Distribution, fibrosis, airways disease and expiratory imaging
3 Targeted testing	Expanded serologies, PFTs, echocardiography, selective bronchoscopy or biopsy
4 Multidisciplinary synthesis	Integrate discordant evidence and revise the diagnosis as new data appear

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Case 1: IPF with a CPFE phenotype

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74-year-old man

– Fibrosis first identified incidentally around 2019 after myocardial infarction
– Former smoker who quit around age 40
– Worked in phosphate mines operating heavy equipment
– Benign excisional cervical lymph-node biopsy during an early malignancy evaluation
– Lost to pulmonary follow-up, then returned after serial CTs showed progression and honeycombing

Diagnostic context

– ANA 1:80
– Extended myositis and scleroderma panels negative
– No connective-tissue disease phenotype
– No bird, mold or familial pulmonary-fibrosis history

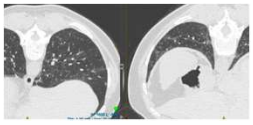
Working diagnosis: idiopathic UIP-pattern fibrosis with mild emphysema

No surgical biopsy required when the clinical context and definite UIP pattern align

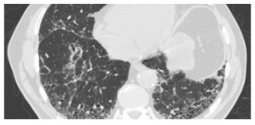
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Case 1: serial course

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Earlier fibrosis



Progression to a definite UIP pattern

Physiologic course

FVC: 4.03 L (04/2024) 3.81 L 3.66 L 3.60 L 3.28 L (05/2026)
TLC: 5.59 L 5.34 L 5.35 L 5.57 L 5.94 L
DLCO: 14.9 14.34 13.44 13.87 12.33

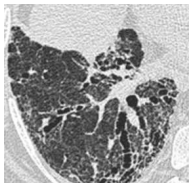
Treatment

Nintedanib stopped for intolerance
Pirfenidone continued
Nerandomilast added and tolerated
HRCT stable from 03/2024 through 04/2026

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UIP describes a pattern, not an etiology

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UIP pattern

– Subpleural and basal predominance
– Reticulation with traction bronchiectasis
– Honeycombing increases confidence
– Limited ground-glass opacity relative to fibrosis
– Common in IPF, but also occurs in rheumatoid arthritis, chronic HP and other fibrotic ILDs

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Case 2: Sjögren-associated fibrotic NSIP

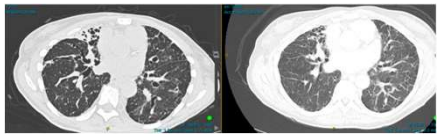
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Autoimmune phenotype

– Dry eyes and mouth, dysphagia and joint symptoms
– ANA 1:1280 with positive SSA
– Never smoker with no convincing causative exposure

– Fibrotic NSIP with traction bronchiectasis and focal honeycombing
– Anterior and upper-lobe fibrosis has progressed on serial imaging

ILD can precede or dominate the systemic autoimmune phenotype



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ILD may precede systemic autoimmune disease

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The lung can be the first involved organ

– Patients may lack arthritis, rash, weakness or established connective tissue disease at presentation
– A severely reduced DLCO or an abnormal HRCT may precede overt rheumatologic manifestations by years
– Repeat the history, examination and selected serologies when the phenotype changes
– Avoid dismissing a coherent autoimmune phenotype because classification criteria are not yet met

Clinical implication

A negative symptom review today does not permanently exclude autoimmune ILD.

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Standard autoimmune workup

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Our baseline panel

– Comprehensive ANA panel
– Comprehensive scleroderma panel
– Extended myositis panel, not a limited MyoMarker panel
– Rheumatoid factor and CCP
– ANCA
– IgG4

Add CK, aldolase and immunoglobulins when the history or phenotype supports them. Interpret every result in clinical context.

Expanded testing has changed management in patients whose earlier "negative rheumatologic workup" was incomplete.

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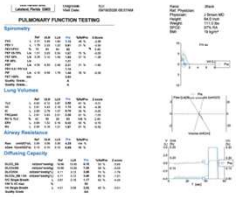
Case 2: treatment-resistant progression

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Physiologic decline

FVC 1.62 L → 1.12 L
TLC 3.45 L → 2.98 L
DLCO 7.18 → 6.18

– Antifibrotics: pirfenidone and nerandomilast
– Rituximab for the autoimmune component
– Tyvaso (inhaled treprostinil) for PH, with potential additional antifibrotic benefit
– Fibrosis and lung function worsened despite these interventions



Progression despite combined therapy
Now undergoing lung-transplant evaluation

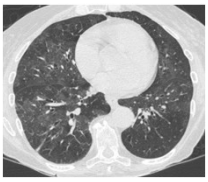
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Case 3: biopsy-proven mold-related HP

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Never-smoking oncology nurse

– Cough and progressive dyspnea began in summer 2024
– Initially diagnosed and treated as COPD despite being a never-smoker
– Progressive symptoms despite treatment prompted reevaluation
– Stopped working in February 2025 because of respiratory limitation
– VATS biopsy in August 2025 supported hypersensitivity pneumonitis
– No birds, farming, hot-tub or other typical exposure history
– A 100-year-old home had new attic insulation and unexplained floor discoloration



The hidden exposure

Professional ductwork sampling found heavy Cladosporium, Aspergillus and Penicillium

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Case 3: recovery after treatment and exposure remediation

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Pulmonary function recovery

FVC 1.52 L → 3.34 L
TLC 4.68 L → 6.51 L
DLCO 5.42 → 11.43

Initially treated with corticosteroids, then transitioned to mycophenolate

Exposure evidence

– Aspergillus fumigatus IgG 16.4
– Other HP serologies largely negative
– BAL lymphocyte count unavailable
– Biopsy and exposure investigation completed the clinical picture

After remediation and exposure avoidance, HRCT became nearly normal. She came off oxygen and treatment and returned to work.

A negative HP panel would not have found the cause

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Exposure assessment requires specificity

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Ask about dose, duration and setting

– Birds, feather products and contaminated humidifiers
– Mold, water damage, hot tubs and occupational bioaerosols
– Wood, metal, stone and agricultural dusts
– Aerosolized fragrances, cleaning products and hobby exposures
– Home, workplace, vehicle and intermittent high-dose exposures

"Any exposures?"

A broad yes-or-no question misses the exposure pattern that matters.

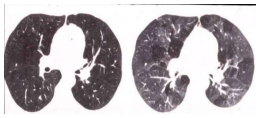
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HRCT technique changes the interpretation

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Minimum useful protocol

– Thin sections with high-resolution reconstruction
– Full inspiratory acquisition
– Prone imaging when dependent opacity may mimic disease
– Expiratory imaging to reveal air trapping
– Direct comparison with prior studies, not isolated report text



Inspiratory and expiratory imaging can expose small-airways physiology hidden on routine CT.

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PFTs answer a different question than CT

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Physiology

– FVC tracks restriction but may remain preserved in CPFE
– TLC confirms restriction and can clarify discordant spirometry
– DLCO can reveal early vascular or parenchymal disease
– Trends in absolute liters matter more than isolated percent-predicted values

Imaging

– HRCT defines distribution and pattern
– Fibrosis can progress despite a stable FVC
– Expiratory imaging detects air trapping
– Discordance should trigger reassessment rather than forced categorization

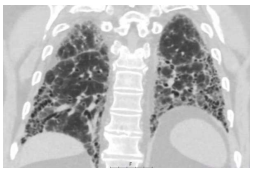
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Application case: combined pulmonary fibrosis and emphysema

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49-year-old man

– Rapidly progressive respiratory failure
– Oxygen requirement increased to 20 L/min
– Transitioned to hospice and died three weeks later



Why the physiology can mislead

– Emphysema and fibrosis exert opposing effects on lung volumes
– Spirometry and volumes can appear pseudonormal
– DLCO is often severely reduced
– Pulmonary hypertension is common and carries major prognostic weight

A reassuring FVC does not reflect the severity of CPFE

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Bronchoscopy and biopsy are selective tools

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Bronchoalveolar lavage

– Useful when infection, eosinophilic disease, alveolar hemorrhage or selected HP questions remain open
– Cell counts rarely establish an ILD diagnosis alone

Tissue sampling

– Consider when the expected result could change management
– Balance diagnostic yield against age, physiology, oxygen need and procedural risk
– A biopsy that names a pattern without changing treatment may add little

Every invasive test needs a management question

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Multidisciplinary discussion

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Pulmonology | **Thoracic radiology** | **Pathology / rheumatology**

The goal is a working diagnosis with an explicit confidence level, competing explanations and a plan for reassessment.

Consensus should clarify uncertainty, not conceal it.

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Management follows the active mechanism

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Inflammatory activity

– Ground-glass or organizing pneumonia pattern
– Autoimmune features or active systemic disease
– Potential response to immune suppression

Progressive fibrosis

– Increasing fibrosis on serial HRCT
– Declining FVC or DLCO
– Worsening symptoms despite appropriate therapy

Many patients need both pathways addressed

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Antifibrotic therapy

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When fibrosis is progressive or the diagnosis is IPF

– Start an antifibrotic when the expected benefit outweighs tolerability concerns
– In our practice, we favor nerandomilast when appropriate and accessible
– Nintedanib and pirfenidone remain important alternatives
– Monitor adverse effects, weight and liver chemistry
– Treatment slows progression. It does not reverse established fibrosis

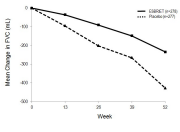
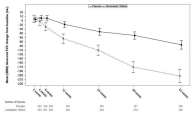
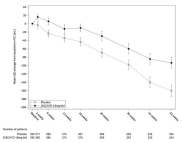
Clinical goal

Preserve lung function and time

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FVC preservation with three antifibrotics

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Pirfenidone (Esbriet)	Nintedanib (Ofev)	Nerandomilast (Jascayd)
ASCEND / label Study 1	INPULSIS-1 / label Study 2	FIBRONEER-IPF, 18 mg twice daily
		
193 mL less decline	**125 mL/year preserved**	**64 mL less decline**
52-week mean change −235 vs −428 mL	Annual FVC decline −115 vs −240 mL	Adjusted 52-week change −106 vs −170 mL

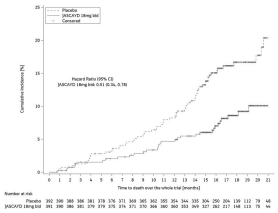
Separate placebo-controlled trials, NOT a head-to-head comparison. Different axes and analyses.
78% of FIBRONEER-IPF participants received background nintedanib or pirfenidone.

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Jascayd: survival signal and its limits

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PPF: FIBRONEER-ILD



All-cause mortality

HR 0.51
95% CI 0.34–0.78

18 mg twice daily vs placebo
Follow-up up to 114 weeks

Important caveat

No prespecified multiplicity control for mortality. The key secondary composite did not reach statistical significance.

IPF trial: mortality HR 0.66 (95% CI 0.41–1.08), not statistically significant.
Encouraging PPF signal; not definitive proof of a survival benefit across fibrotic ILD.

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Immune suppression

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Match the agent to phenotype, comorbidity and urgency

– Mycophenolate or Myfortic often anchors CTD-ILD and IPAF treatment
– Azathioprine offers an alternative when appropriate
– Rituximab, tocilizumab, abatacept, IVIG or tacrolimus may fit selected autoimmune phenotypes
– Screen for infection risk and monitor CBC, CMP and immunoglobulins according to therapy
– Reassess whether inflammation remains active before escalating treatment

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Supportive care changes outcomes

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– Pulmonary rehabilitation for conditioning, symptom control and confidence
– Oxygen titration at rest, during exertion and during sleep
– Vaccination and prompt treatment of respiratory infection
– Reflux and aspiration assessment when clinically indicated
– Nutrition, sleep, cough and palliative symptom support
– Early transplant referral before the therapeutic window narrows

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Longitudinal monitoring

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Our center's usual monitoring approach

– PFTs every 6 months
– HRCT at least annually
– Earlier HRCT after treatment changes or suspected progression
– At least annual echocardiography for PH screening
– Symptoms, oxygen requirement and functional capacity at every visit

Monitoring has two jobs

Detect progression early

Recognize complications that change prognosis or treatment

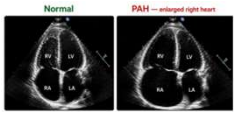
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Pulmonary hypertension screening in ILD

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Do not reduce the echo to RVSP

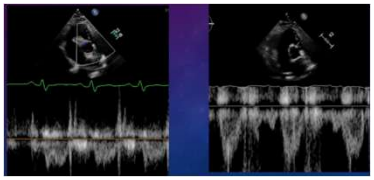
– Review RVOT flow for midsystolic notching
– Compare right atrial and left atrial size
– Look for septal flattening and LV compression
– Assess RV basal-to-apical geometry and systolic function
– Integrate the echo with symptoms, oxygen needs, DLCO, walk testing and biomarkers
– Proceed to right-heart catheterization when the result will change management



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RVOT Doppler can reveal pressure overload

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Midsystolic notching

– Suggests increased pulmonary vascular load
– Can add confidence when TR velocity or RVSP is limited
– Requires attention to acquisition quality and the full echo phenotype

Referral decisions should reflect the whole right-heart study.

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When progression appears disproportionate

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- Recheck the exposure and medication history
- Confirm adherence and treatment tolerance
- Compare serial HRCT images directly
- Review infection, aspiration, edema and anemia
- Screen for pulmonary hypertension
- Revisit the diagnosis in multidisciplinary conference
- Escalate transplant evaluation when trajectory or reserve is concerning

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Case takeaways

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Case 1: IPF / UIP	A UIP pattern needs clinical context to establish IPF
Case 2: Sjögren fibrotic NSIP	Progression despite combined therapy prompts transplant evaluation
Case 3: exposure-related HP	Treatment and exposure remediation can produce substantial recovery
Application case: CPFE	DLCO, oxygen need and PH risk may outpace spirometry

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Clinical takeaways

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- Start with pattern, context and disease behavior
- Use a standardized exposure and autoimmune evaluation
- Remember that ILD can precede systemic autoimmune manifestations
- Treat inflammation and progressive fibrosis according to the active phenotype
- Monitor with PFTs, serial HRCT and deliberate PH screening
- Refer early when the physiology, trajectory or right heart becomes concerning

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