

Interstitial Lung Disease: The Journey to Diagnosis and Treatment

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INTERSTITIAL LUNG DISEASE
PROGRAM

MASSACHUSETTS GENERAL
HOSPITAL

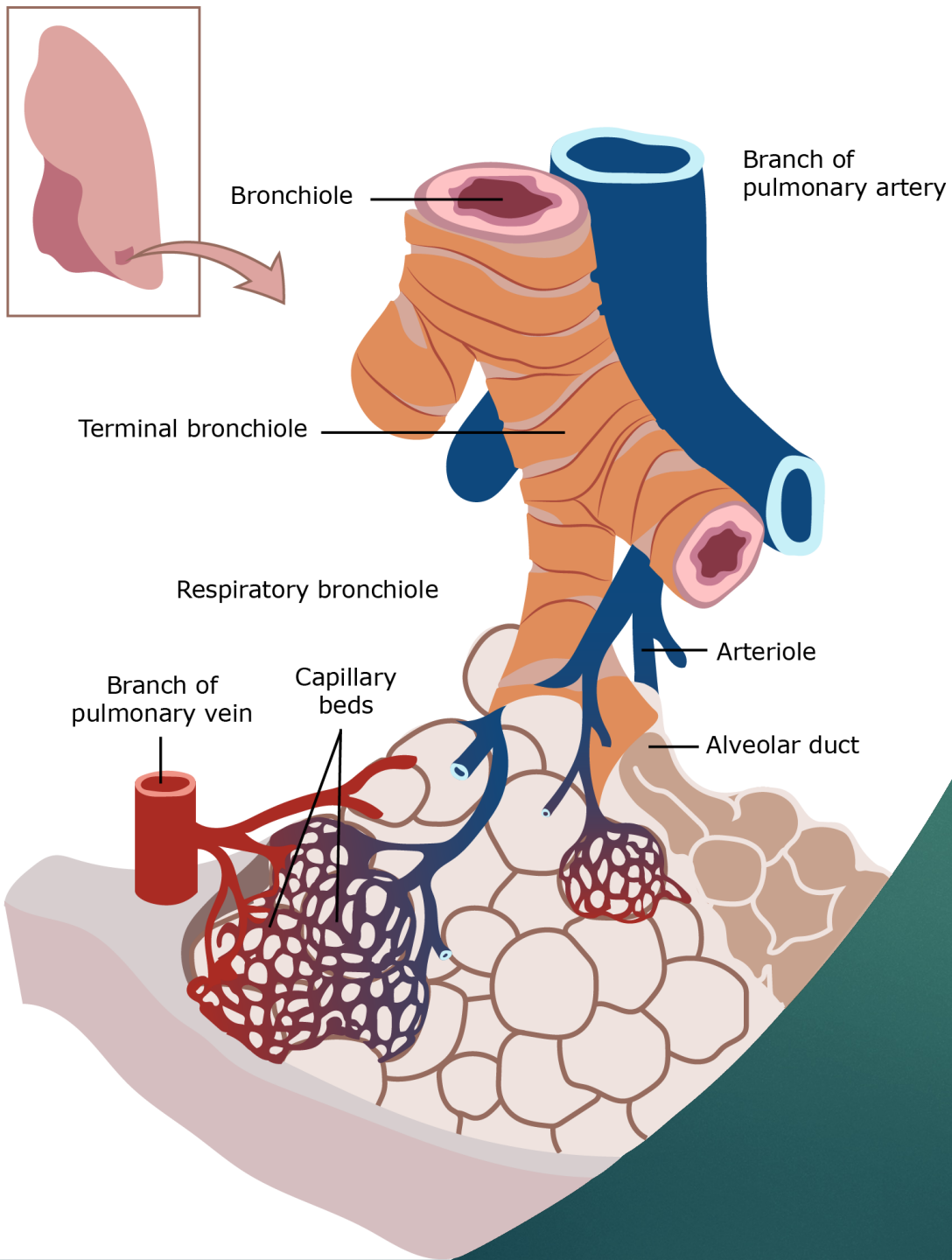
MARCH 10, 2021

Disclosures

- ▶ I have no relevant financial or nonfinancial relationships with products or services described, reviewed, evaluated, or compared in this presentation

What is it?

- ▶ Interstitial Lung Disease (ILD): an umbrella term used for a large group of lung diseases that cause scarring (fibrosis) of the lungs
- ▶ The scarring process makes the lungs stiff leading to shortness of breath, impaired exercise capacity, and impaired flow of oxygen from the air sacs to the blood
- ▶ In most cases, by the time the symptoms appear lung damage
- ▶ Lung damage from ILDs is often irreversible and may progress over time



What does “Interstitial” Mean?

The pulmonary interstitium is the tissue and space around the air sacs (alveoli) of the lungs

What is pulmonary fibrosis?

- ▶ **Pulmonary fibrosis** is a term used to describe scarring in the lung which can be due to many causes
- ▶ **Idiopathic Pulmonary Fibrosis** is a specific term used to describe a chronic, progressive, non-infectious process (pneumonia, or pneumonitis) in the lung of **unknown cause**
- ▶ “Fibrosis” ≠ “Idiopathic Pulmonary Fibrosis”

What should I do now?

- ▶ **DON'T** look it up on the internet until you have more information from an experienced pulmonologist
- ▶ **DO** search for tertiary care centers with an interstitial lung disease program near where you live
- ▶ **DO** search for an experienced group of pulmonologists, radiologists, surgeons, interventional pulmonologists, pathologists, and physical and respiratory therapists
- ▶ **DO** consider a hospital with an associated lung transplant program
- ▶ **DO** consider traveling for care

How can you prepare for your visit?

- ▶ Send all prior evaluation including doctor's clinic notes, consultant notes, breathing tests, blood work, imaging on a CD, and any pathology slides
- ▶ Assume everything may be relevant
- ▶ Write down questions

What Should I Expect at My Visit?

- ▶ Extended interview with the MD
- ▶ Pulmonary Function Testing
- ▶ Walk Testing
- ▶ Imaging
- ▶ Blood Work

The Interview

- ▶ What are the severity, duration, and pace of your symptoms?
- ▶ Do you have symptoms or signs of a systemic autoimmune disorder?
- ▶ Do you have involvement of other organs (heart, kidney, skin, joints, muscles) Is there evidence of it?
- ▶ Do you have a history of a relevant exposure, generally inhaled, known to result in the development of lung disease?
- ▶ Do you have pets, including birds?
- ▶ Were you exposed in your home or work environment? Is there water damage?
- ▶ Is the exposure significant? What about the intensity of the exposure?
- ▶ Is there a temporal association between the exposure and symptom onset?

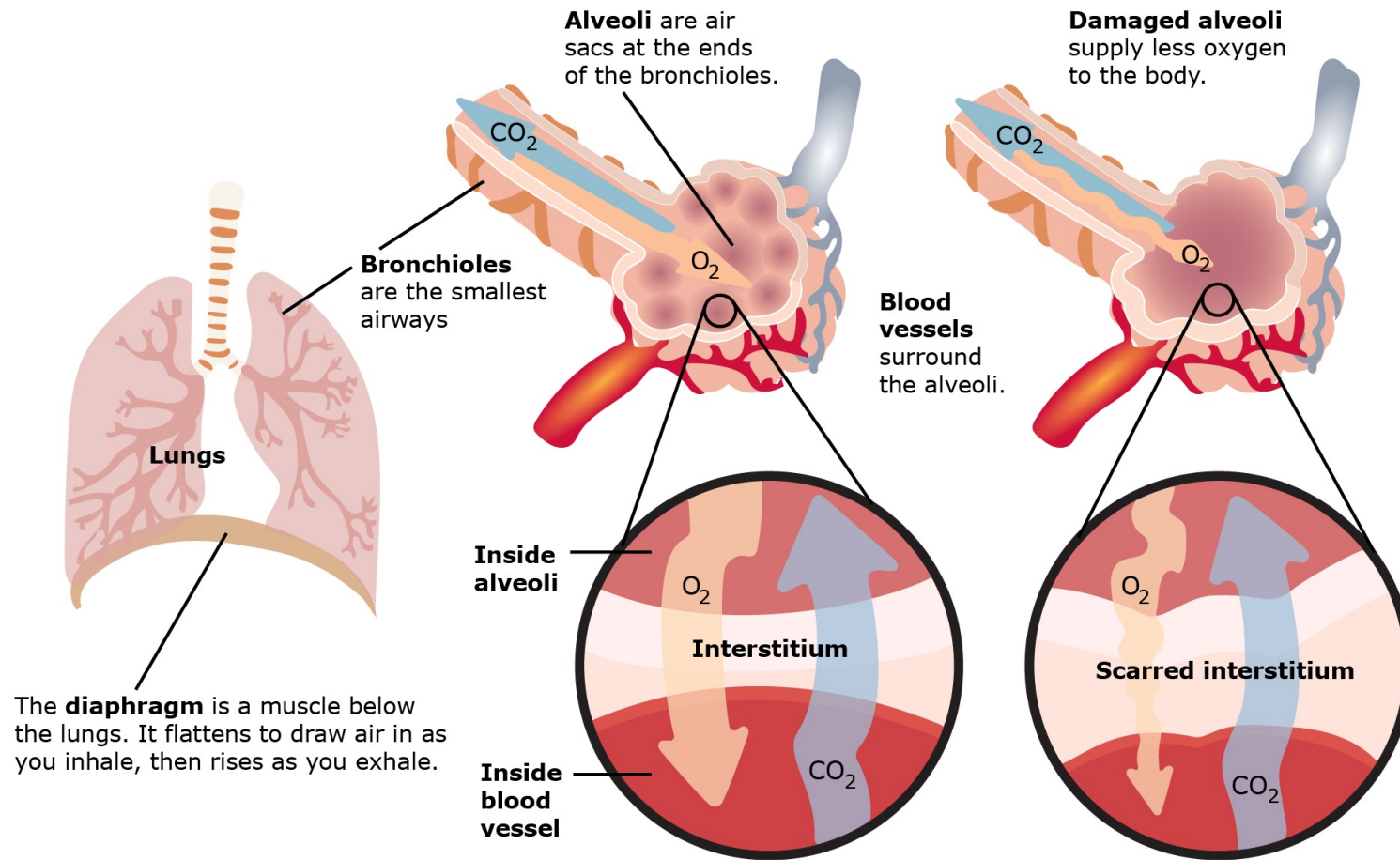
The Interview, continued

- ▶ Do you work in an occupation known to be at risk for the development of lung disease?
- ▶ What do you do specifically in your current job and previous jobs?
- ▶ What type of hobbies do you have?
- ▶ Does the patient use any medicines, herbs, vitamins, supplements, or recreational drugs that could account for the presence of lung disease?
 - Vaping/electronic cigarettes
- ▶ Is there a family history of lung fibrosis? Is there evidence of premature graying, cirrhosis, low platelets or other blood count abnormalities?

Functional Tests

- ▶ Pulmonary function testing
 - ▶ How much you breathe out in the first second (FEV1)
 - ▶ How much to breathe out in total (**FVC**)
 - ▶ How much you can breathe in (TLC)
 - ▶ How well is oxygen and carbon dioxide are transferred (diffused) between the lungs and the blood (**DLCO**)
- ▶ Walk test on room air
- ▶ 6 minute walk test

Why do oxygen levels go down?



Blood work

- ▶ Auto-immune disease panel
 - ▶ Rheumatoid Arthritis
 - ▶ Scleroderma
 - ▶ Mixed connective tissue disease
 - ▶ Vasculitis
 - ▶ Myositis
 - ▶ Celiac Disease
- ▶ Environmental Exposure Panel

Imaging - HRCT

- ▶ High resolution CT scan with thin slices through the chest
- ▶ Optimal quality CT scans have **thin sections** (<2mm)
- ▶ Images should be obtained at full inspiration to total lung capacity
- ▶ Inadequate inspiration increases lung attenuation, potentially leading to misinterpretation of key findings
- ▶ **Prone CT imaging** is useful when the abnormality on the CT is near your back when lying supine
- ▶ Prone CT may also facilitate the diagnosis of **honeycombing** (we will get to this term)
- ▶ **Expiratory imaging** is useful to identify air trapping, a feature that may suggest an alternative diagnosis such as chronic hypersensitivity pneumonitis or ILD due to connective tissue disease

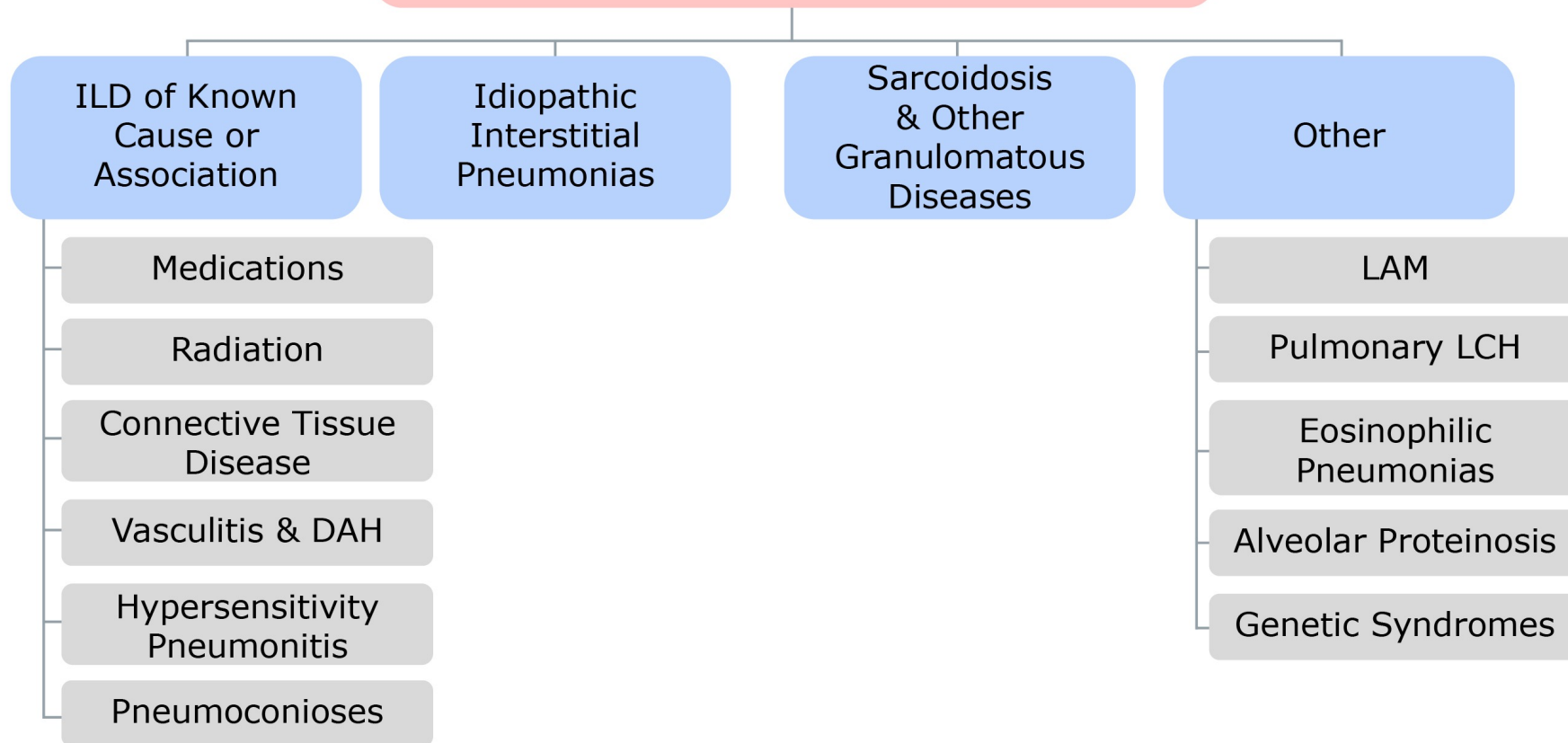
CT terminology

- ▶ **Interstitial thickening** is pathological thickening of the pulmonary interstitium
- ▶ **Ground-glass opacification/opacity (GGO)** is a descriptive term a haziness where you can still see bronchial and vascular markings
- ▶ **Reticular** - characterized by a fine network or netlike structure.
- ▶ **Subpleural reticulation** is a type of reticular interstitial pattern in a peripheral subpleural distribution
- ▶ **Bronchiolectasis** is a descriptive term which is given to dilatation of bronchioles, which are of smaller caliber than bronchi. It can arise in a number of pathologies

What clues does a CT give my doctor about my disease?

- ▶ What region of the lung is primarily affected (upper lung zones, lower lung zones or basal, diffuse)?
- ▶ Specifically, is it basilar predominant and along the edge of the lung (subpleural)?
- ▶ Is there evidence of early scarring (bronchiolectasis or bronchiectasis)?
- ▶ Is there evidence of late scarring (honeycombing)?
- ▶ Are there nodules? Where are they located?
- ▶ Is there air trapping when I exhale?

Interstitial Lung Diseases



Adapted from: ATS/ERS Guidelines for IIP. *AJRCCM*. 2002;165:277-304.

Alternative Idiopathic interstitial pneumonias

- ▶ Cryptogenic organizing pneumonia
- ▶ Acute interstitial pneumonia
- ▶ Nonspecific interstitial pneumonia
- ▶ Lymphoid interstitial pneumonia
- ▶ Desquamative interstitial pneumonia
- ▶ Respiratory bronchiolitis interstitial lung disease

What is UIP?

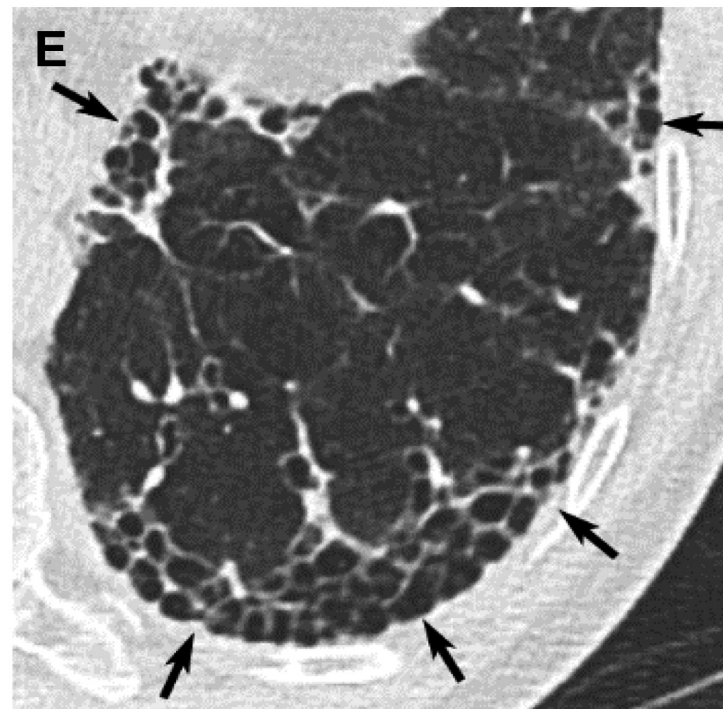
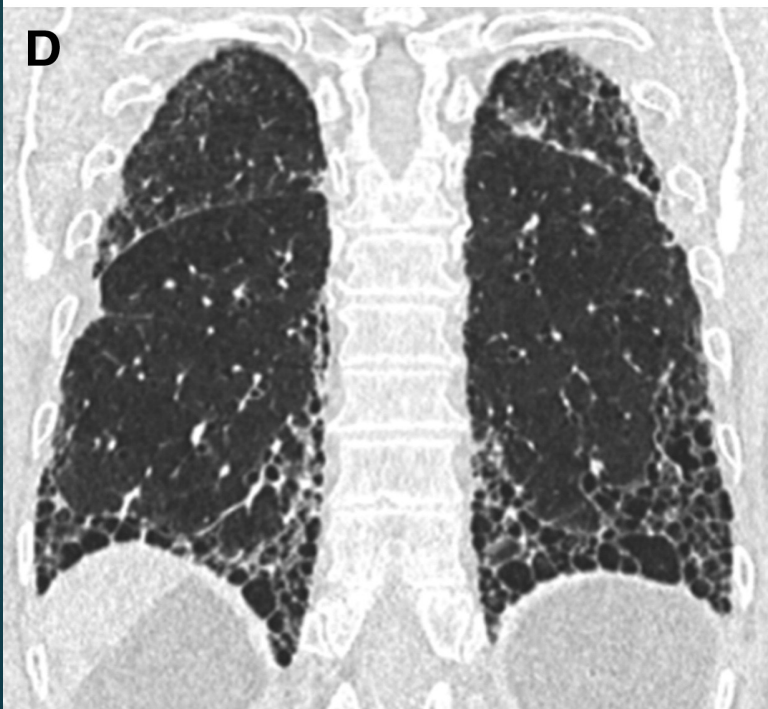
- ▶ Usual Interstitial Pneumonia
- ▶ A histopathologic and radiologic pattern of interstitial lung disease, which is the hallmark pattern for idiopathic pulmonary fibrosis (IPF)
- ▶ This pattern can also be seen in other diseases associated with pulmonary fibrosis (e.g. rheumatoid arthritis)

The Current Classification by CT scan

Diagnostic categories of UIP on CT

CT distribution	Typical UIP CT pattern	Probable UIP CT pattern	CT pattern Indeterminate for UIP	CT features most consistent with non-IPF diagnosis
CT features	Basal (occasionally diffuse) and subpleural predominant. Distribution is often heterogeneous.	Basal and subpleural predominant. Distribution is often heterogeneous.	Variable or diffuse	Upper or mid lung predominant fibrosis Peribronchovascular predominance with subpleural sparing
	Honeycombing. Reticular pattern with peripheral traction bronchiectasis/ bronchiolectasis* Absence of features to suggest an alternative diagnosis	Reticular pattern with peripheral traction bronchiectasis/ bronchiolectasis* Honeycombing is absent	Evidence of fibrosis with some inconspicuous features suggestive of non-UIP pattern*	Any of the following: Predominant consolidation Extensive pure ground glass opacity (without acute exacerbation) Extensive mosaic attenuation with extensive sharply defined lobular air trapping on expiration Diffuse nodules or cysts

*** Reticular pattern is superimposed on ground glass opacity, and in these cases is usually fibrotic. Pure ground glass opacity however would be against the diagnosis of UIP/IPF and would suggest acute exacerbation, hypersensitivity pneumonitis or other conditions**



Am J Respir Crit Care Med, 2018
<https://www.atsjournals.org/doi/abs/10.1164/rccm.201807-1255ST>

Should I have a bronchoscopy?

- ▶ If your CT pattern is typical for UIP, then the answer is no, probably not
- ▶ If your CT pattern is probable UIP, indeterminate, or suggestive of an alternative diagnosis, then the answer is maybe
- ▶ Bronchoscopy is more likely to be performed if infection, eosinophilic pneumonia, or sarcoidosis is suspected
- ▶ Bronchoscopy includes a bronchoalveolar lavage (BAL) and biopsies

When do we consider a biopsy?

- ▶ Probable UIP
- ▶ Indeterminate for UIP
- ▶ Alternative diagnosis
- ▶ Health and functional status of the patient (PFT, oxygenation, comorbidities)
- ▶ Biopsy for molecular studies not yet ready for prime time

Biopsy is not recommended when.....

- ▶ Your HRCT scan is typical for UIP
- ▶ You have significant impairment in lung function or oxygenation
- ▶ You have other significant co-morbidities making a surgical procedure high risk

What type of biopsy should I have?

- ▶ Surgical lung biopsy
- ▶ Tertiary care center by surgeons familiar with the diagnosis of interstitial lung disease
- ▶ Typically involves a biopsy from three different areas or lobes
- ▶ The proportion of biopsies yielding a specific diagnosis is high (88%)
- ▶ 1/3 were IPF
- ▶ Rest were potentially treatable etiologies
- ▶ Overall mortality 3.5%; some of the deaths were probably disease related, because procedure-related mortality was 1.7%

Transbronchial Biopsy

- ▶ Review of 7 studies showed that 75% of biopsies yielded an adequate sample
- ▶ A specific diagnosis was obtained from these samples in 50%
- ▶ 64% of patients will remain undiagnosed
- ▶ No current recommendation for or against transbronchial biopsy as an alternative to surgical biopsy

What is cryobiopsy?

- ▶ A probe is deployed through the bronchoscope and placed near the chest wall. The probe is cooled for a few seconds, freezing and causing the lung tissue around it to stick to the probe
- ▶ The scope and probe are removed, and bleeding is controlled using a balloon occlusion catheter
- ▶ Cryobiopsy obtains larger tissue samples compared to forceps transbronchial biopsy
- ▶ Review of 13 studies indicates cryobiopsy provides adequate sample in the majority of biopsies, leading to specific diagnosis in 80%; 20% remain undiagnosed
- ▶ No recommendation for or against this type of biopsy

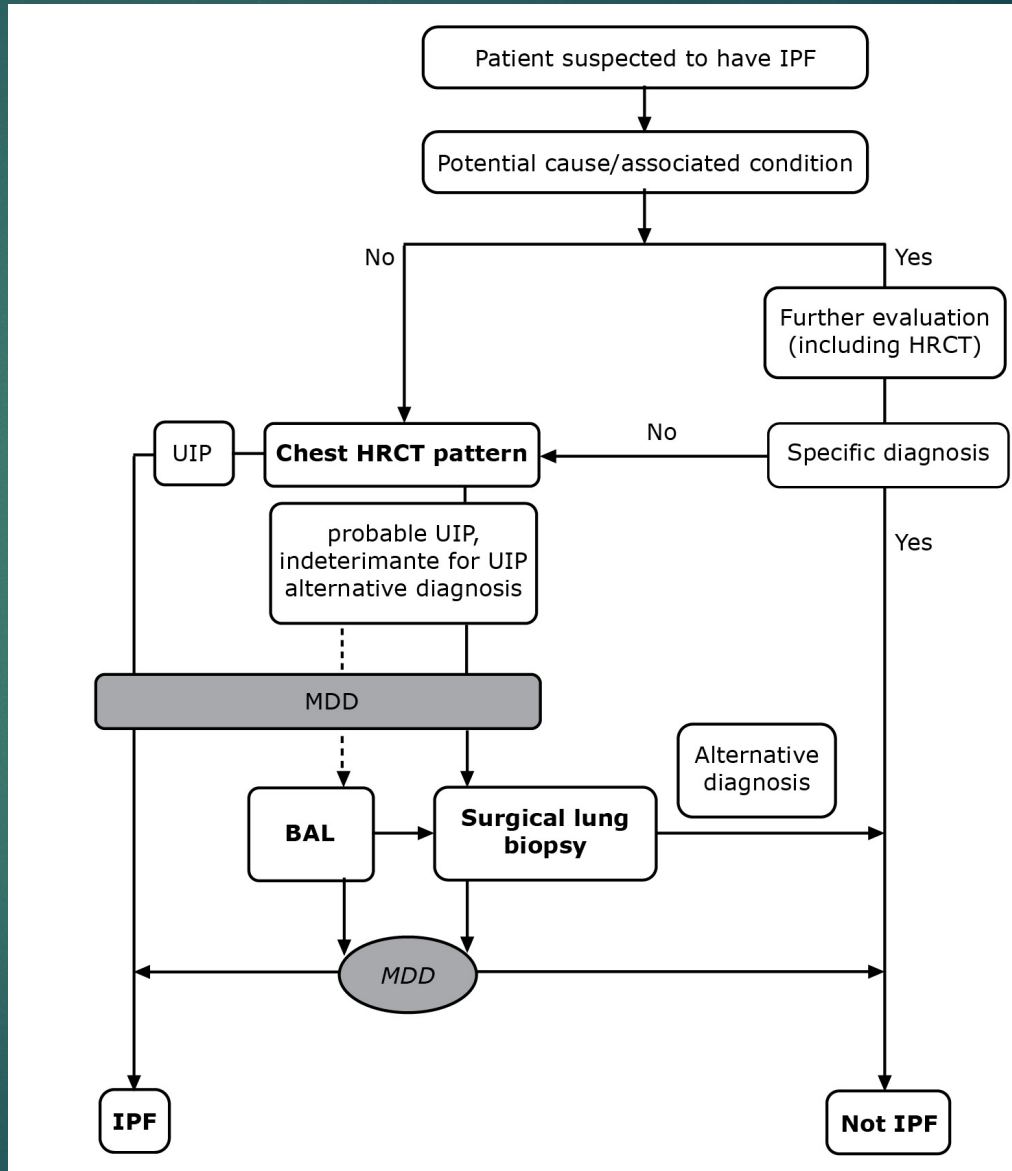
Complications

- ▶ Pneumothorax or collapsed lung
- ▶ Bleeding
- ▶ General anesthesia

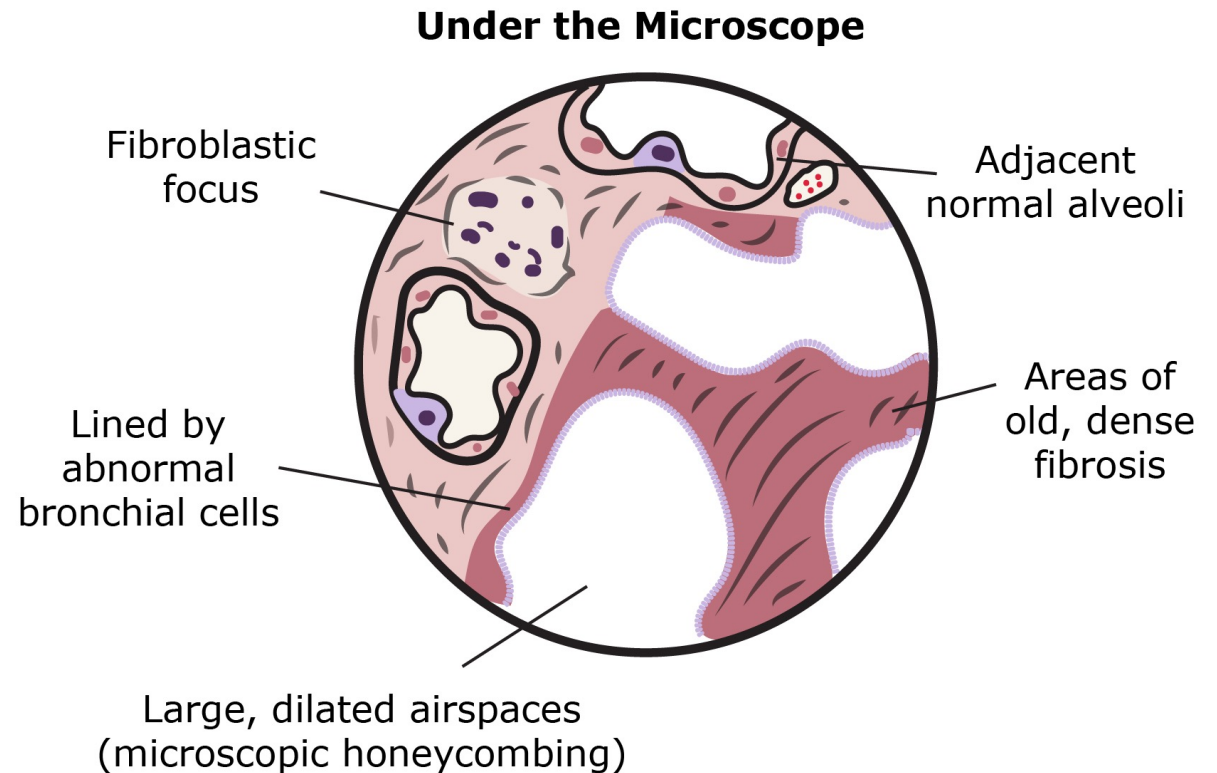
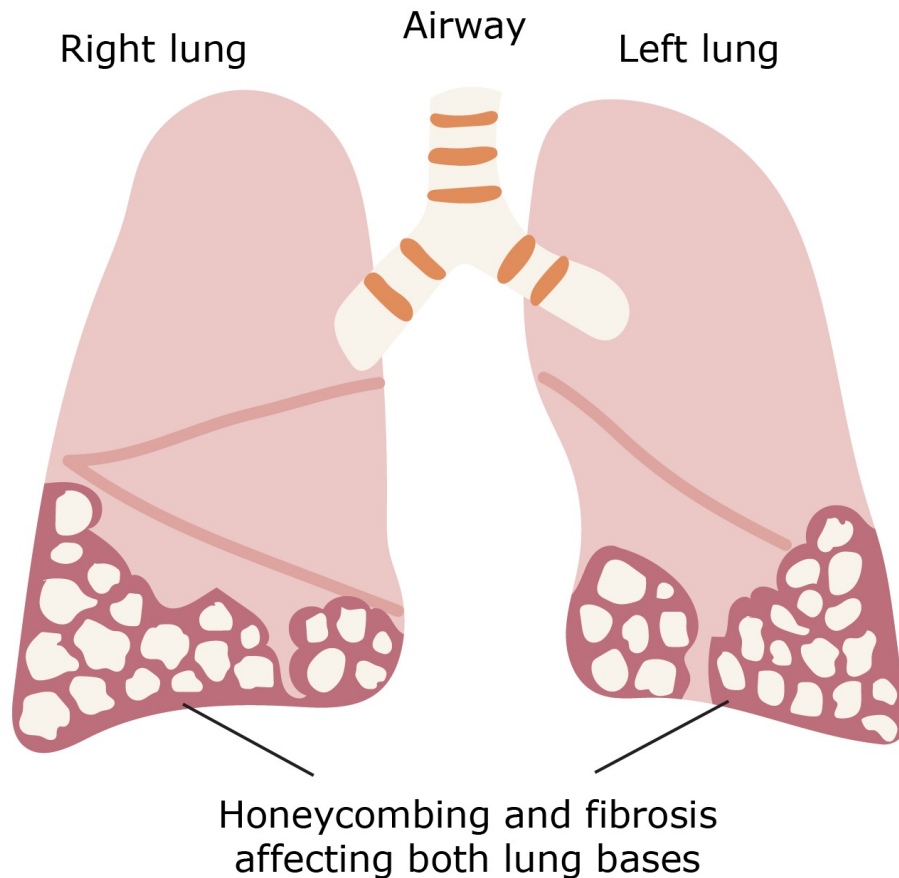
Multidisciplinary Discussion (MDD)

- ▶ A collaboration of multiple specialists with the ability to interpret and communicate complex clinical data patterns, and to synthesize uncertain or sometimes conflicting information
- ▶ The clinician interprets the history and physical exam to develop a clinical context
- ▶ The thoracic radiologist interprets the pattern present on high resolution computerized tomographic (CT) scanning of the chest
- ▶ The pathologist interprets the histopathologic pattern seen on lung biopsy
- ▶ All of this information must be shared using common terminology, in order for clinical decision-making to occur
- ▶ Since “classic” clinical stories and patterns are uncommon, some degree of clinical uncertainty is often present; **acknowledgement of this limitation and a clear plan to address it are essential**

Suggested Approach for the Evaluation of IPF and ILD



Pulmonary Fibrosis or Usual Interstitial Pneumonitis (UIP)



Why take the risk of biopsy?

Biopsy can open up avenues for treatment that would not otherwise be pursued or covered by insurance

Lung
pathology

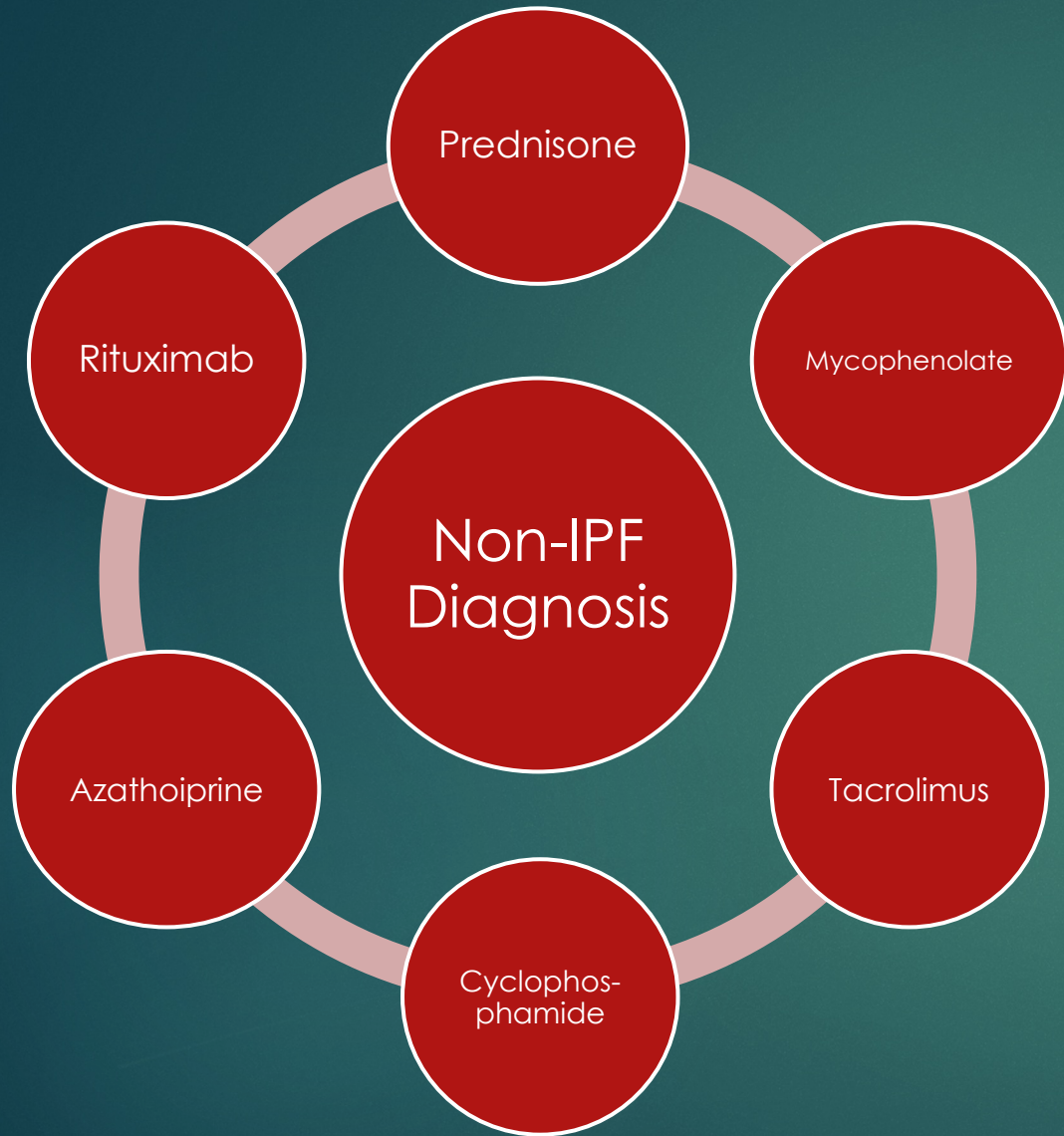
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graph TD; A[Lung pathology] --> B[Anti-inflammatories]; A --> C[Anti-fibrotics];
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A flowchart with a red box at the top containing the text 'Lung pathology'. Two white arrows point downwards from this box to two separate red boxes at the bottom. The left box contains the text 'Anti-inflammatories' and the right box contains the text 'Anti-fibrotics'.

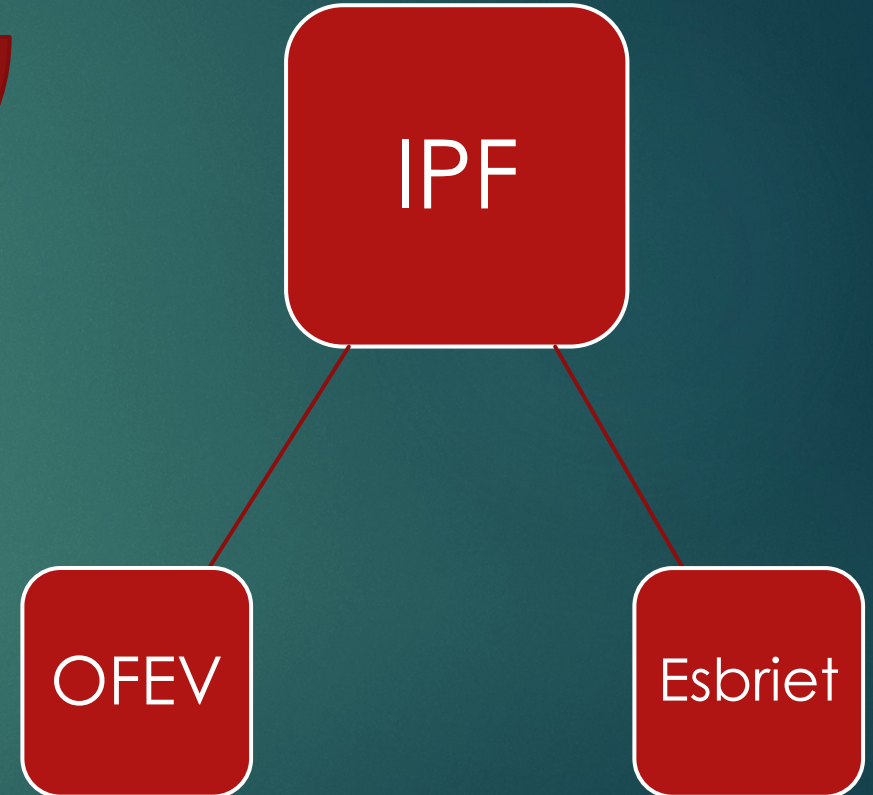
Anti-
inflammatories

Anti-fibrotics

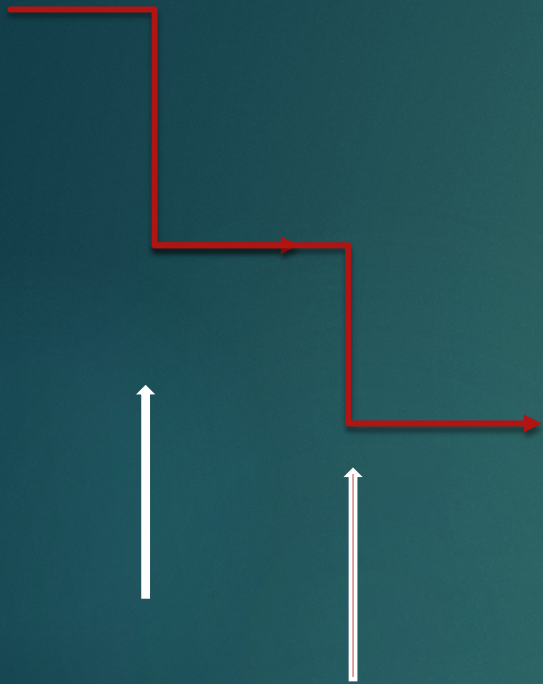
<u>IPF suspected*</u>		Histopathology pattern			
		UIP	Probable UIP	Indeterminate for UIP	Alternative diagnosis
HRCT pattern	UIP	IPF	IPF	IPF	Non-IPF dx
	Probable UIP	IPF	IPF	IPF (Likely)**	Non-IPF dx
	Indeterminate for UIP	IPF	IPF (Likely)**	Indeterminate for IPF***	Non-IPF dx
	Alternative diagnosis	IPF (Likely)** /non-IPF dx	Non-IPF dx	Non-IPF dx	Non-IPF dx



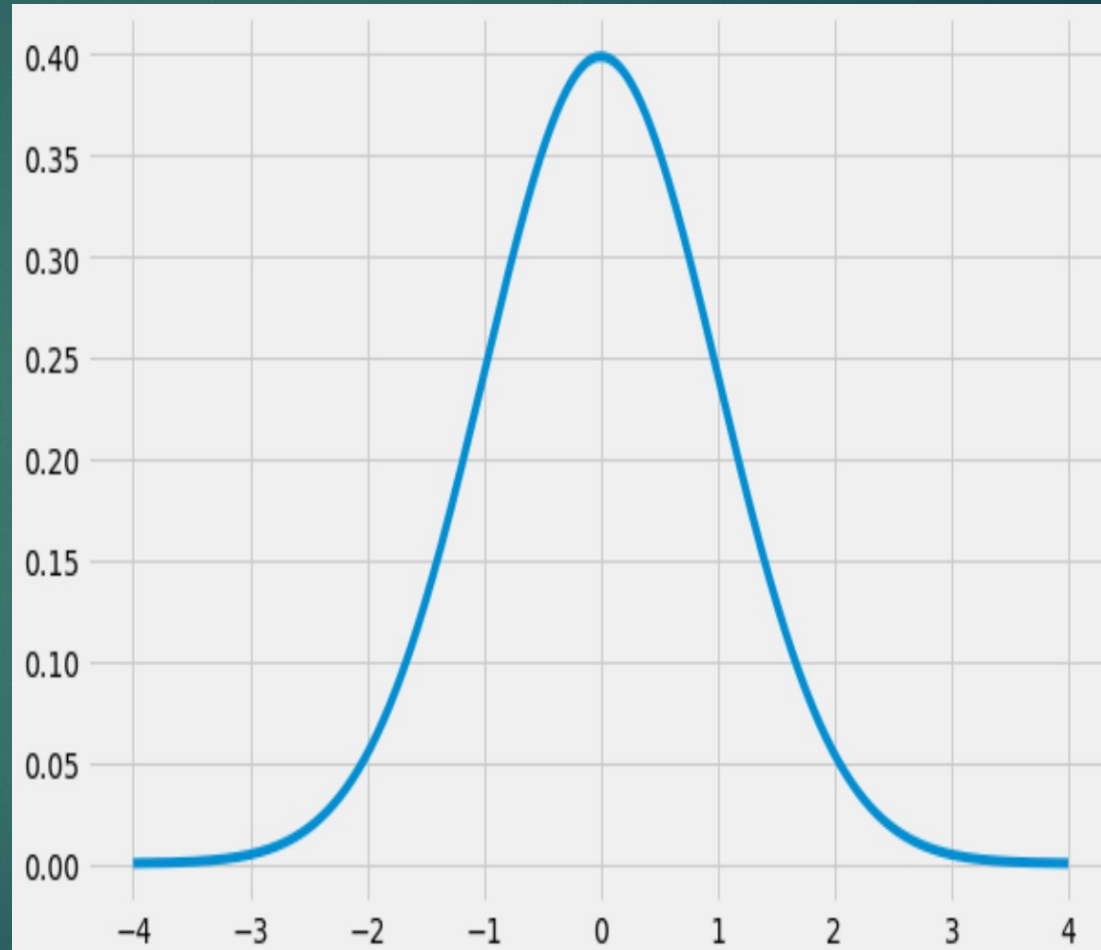
Fibrosing ILD



Prognosis



Acute Exacerbation



Familial pulmonary fibrosis

Extrapulmonary disease such as bone marrow failure or liver disease

At least 30% of patients who have sporadic or familial pulmonary fibrosis have genetic predisposing factors known to increase the risk of pulmonary fibrosis