Interstitial lung disease

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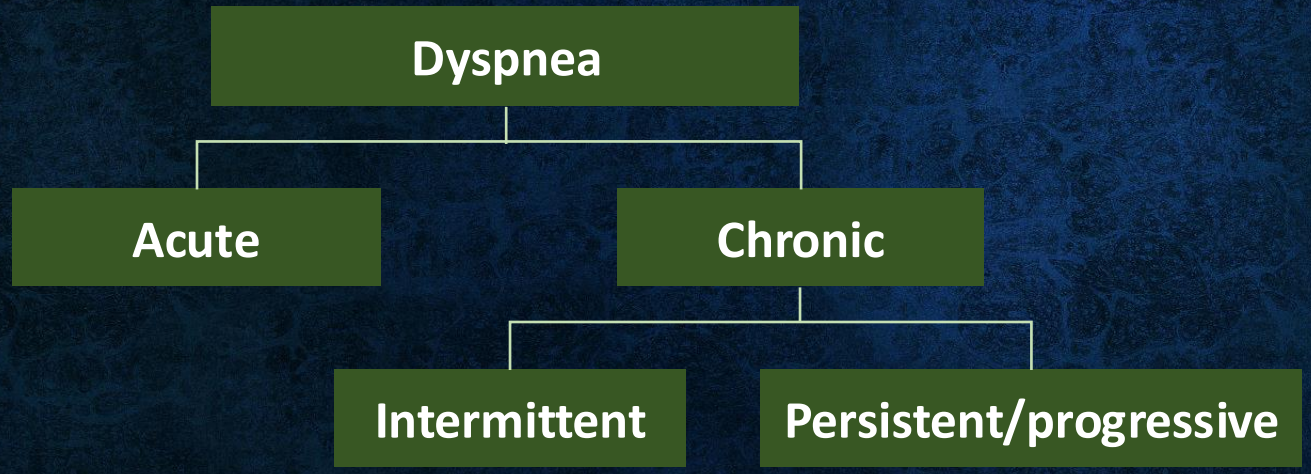
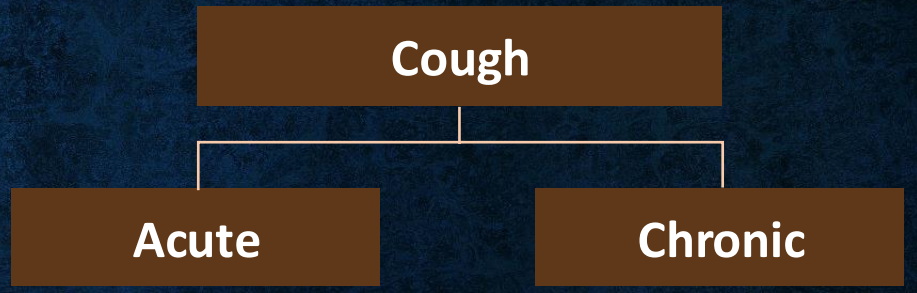
History taking

- Patient data and occupation
- Presenting symptom
- Underlying diseases and previous illness/treatment



- Review system
- Trigger
- Associated symptoms
- Risk factors



- Characters
- Trigger
- Review system
- Associated symptoms
- Risk factors

Dyspnea symptom

Modified Medical Research Council (mMRC) Dyspnea Scale

คำอธิบาย	คะแนน
ไม่มีความรู้สึกเหนื่อยเลย แม้ต้องออกกำลังอย่างหนัก	0
เหนื่อยเฉพาะเมื่อต้องเดินรีบ ๆ หรือ เดินขึ้นที่สูงเล็กน้อยเท่านั้น	1
เดินได้ช้ากว่าคนอายุใกล้เคียงกัน หรือ ต้องหยุดเดินเพื่อพักหายใจ	2
ต้องพักหายใจหลังเดินได้ 90 เมตร หรือ เดินราบได้เพียง 2-3 นาที	3
เหนื่อยเกินกว่าที่จะออกจากบ้าน หรือ เหนื่อยเมื่อต้องใส่เสื้อหรือถอดเสื้อ	4

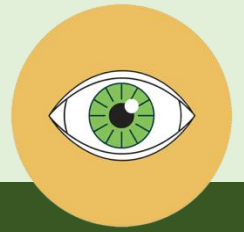
Modified Borg Scale

0	Nothing at all	ไม่รู้สึกเหนื่อยแม้แต่น้อย
0.5	Very, Very Slight (Just Noticable)	แค่เริ่มรู้สึกเหนื่อยเล็กน้อยเท่านั้น
1	Very Slight	เหนื่อยน้อยมาก
2	Slight	เหนื่อยเล็กน้อย
3	Moderate	เหนื่อยพอควร
4	Somewhat Severe	เหนื่อยค่อนข้างมาก
5	**Severe**	เหนื่อยมาก
6		
7	**Very Severe**	เหนื่อยสุดสุด
8		
9	**Very, Very Severe** (Almost Maximal)	เหนื่อยสาหัสสากรรจ์
10	**Maximal**	เหนื่อยที่สุดในชีวิต

Physical examination

- Respiratory system

- **Upright position**
- **Adequate (appropriate) exposure**
- **Anterior AND posterior**
- **On chest wall (NOT over clothing)**



Inspection

Palpation

Percussion

Auscultation

Physical examination

Sitting position

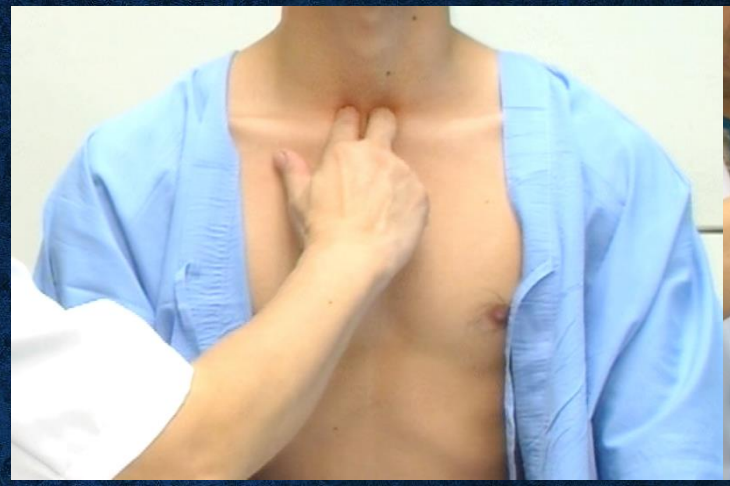
Adequate exposure

!

Directly on the chest

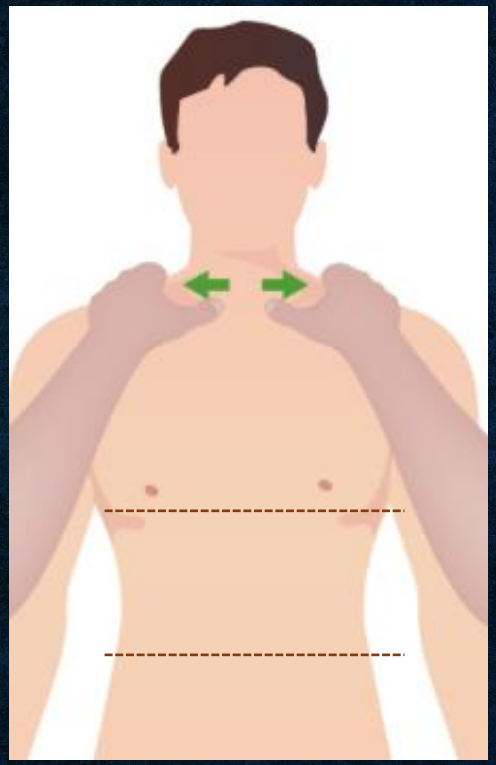
Compare both sides at the same level

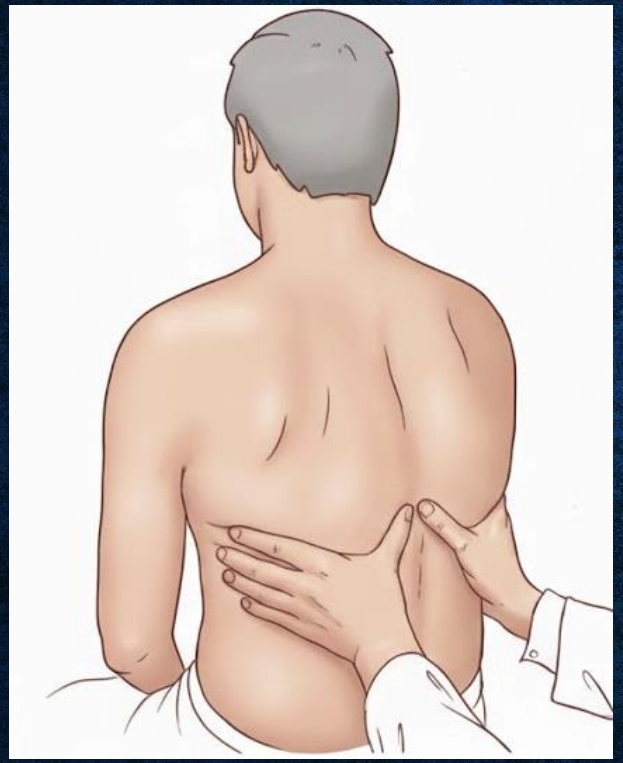
Physical examination



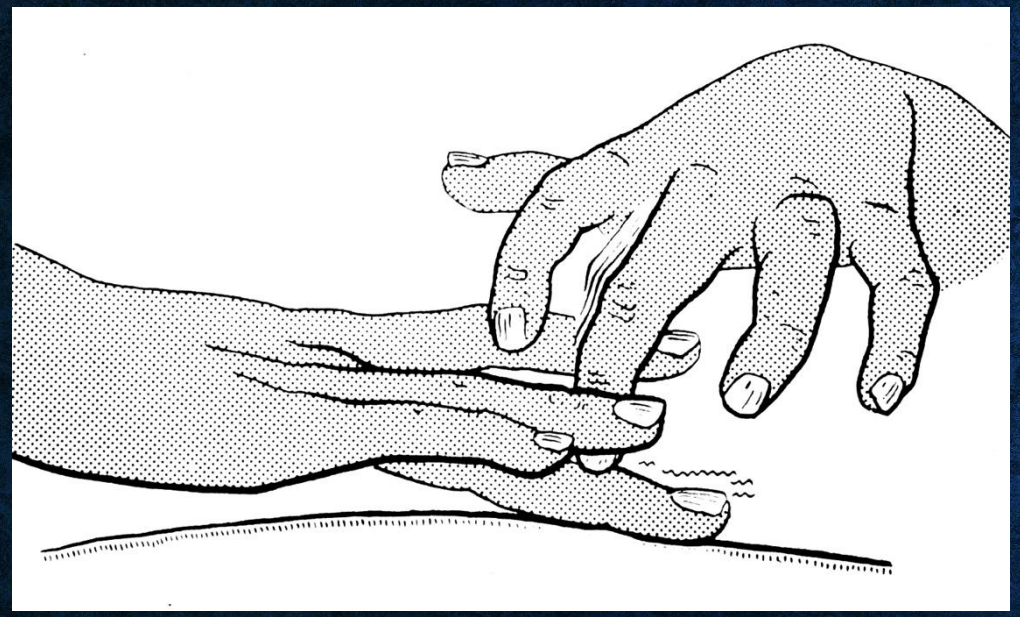
การตรวจร่างกายอย่างครอบคลุม (comprehensive physical examination) โดย รศ.พญ. จินตนา ศิรินาวิน และคณะ (version 1.3) พ.ศ. 2549.

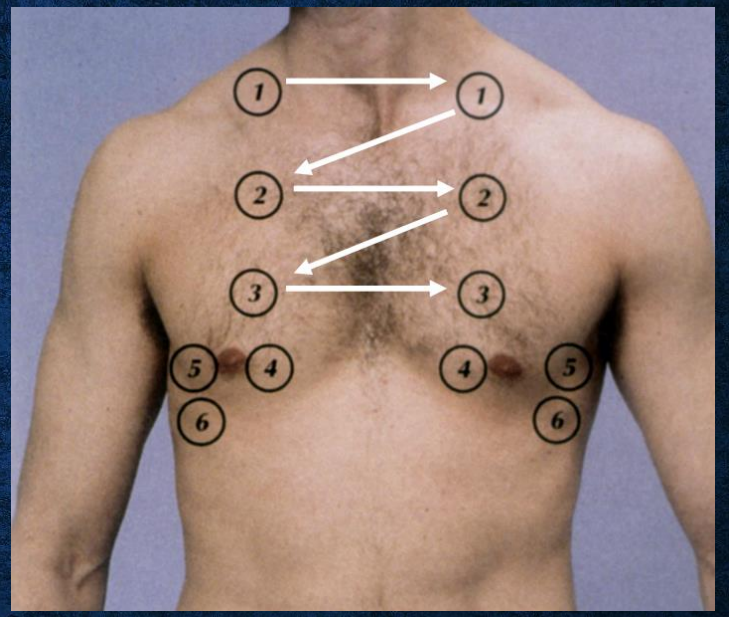
Chest expansion

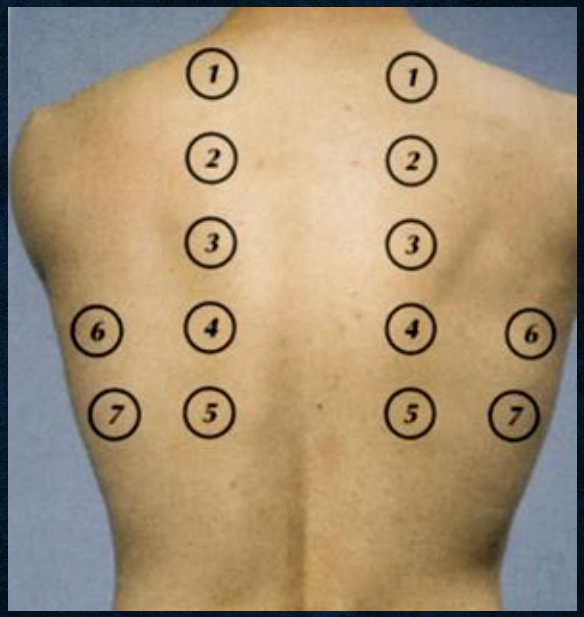




Percussion





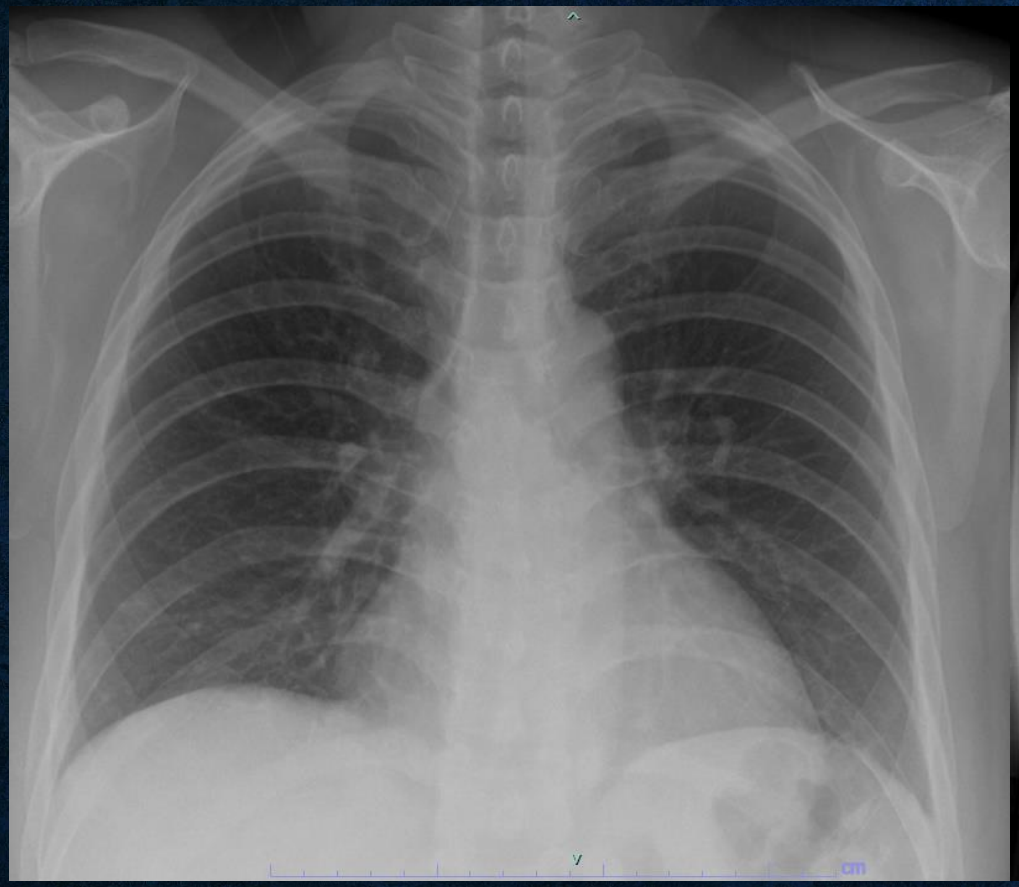


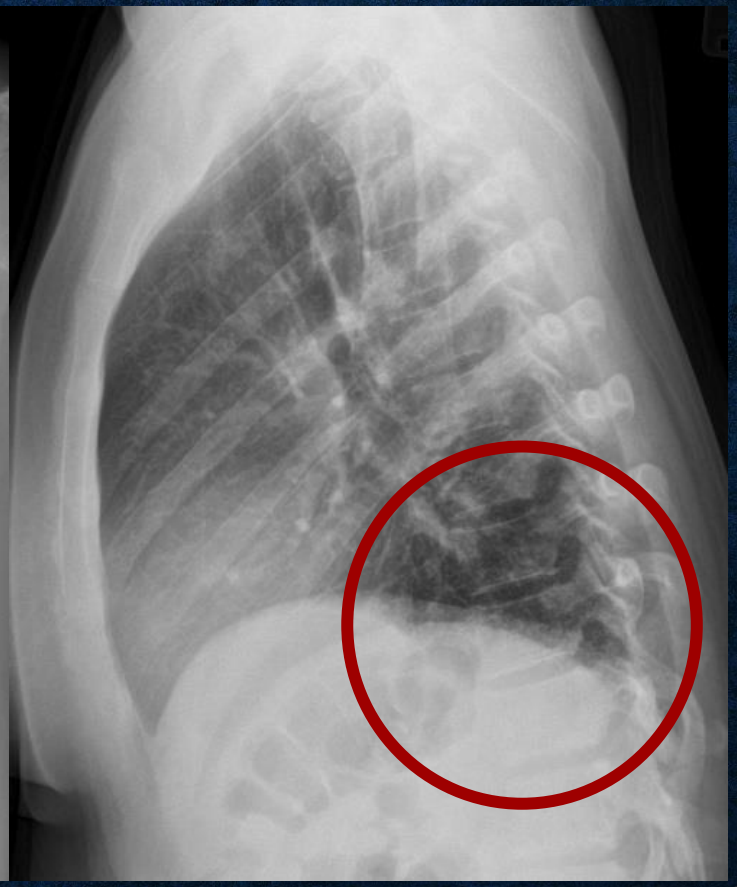
ซ้าย-ขวา/ซ้าย-ขวา หรือ
ซ้าย-ขวา/ขวา-ซ้าย ก็ได้

Physical examination

Finding	Consolidation	Collapse (Patent Airway)	Collapse (airway obstruction)	Effusion	Pneumothorax
Mediastinal shift	None	Toward	Toward	Away	Away
Vocal fremitus	Increase	Decrease	Decrease	Decrease	Decrease
Percussion	Dull	Dull	Dull	Dull	Hyperresonance
Breath sound	Bronchial	Decrease or bronchial	Absent	Decrease and bronchial above fluid level	Decrease or absent
Voice sound	Increase	Increase	Decrease	Decrease and egophony above fluid level	Decrease
Added sound	Crackle or none	None or crackle	None	Pleural rub or crackle	Succussion splash

Chest X-ray





Infiltrates

- Interstitial / alveolar process
- Distribution

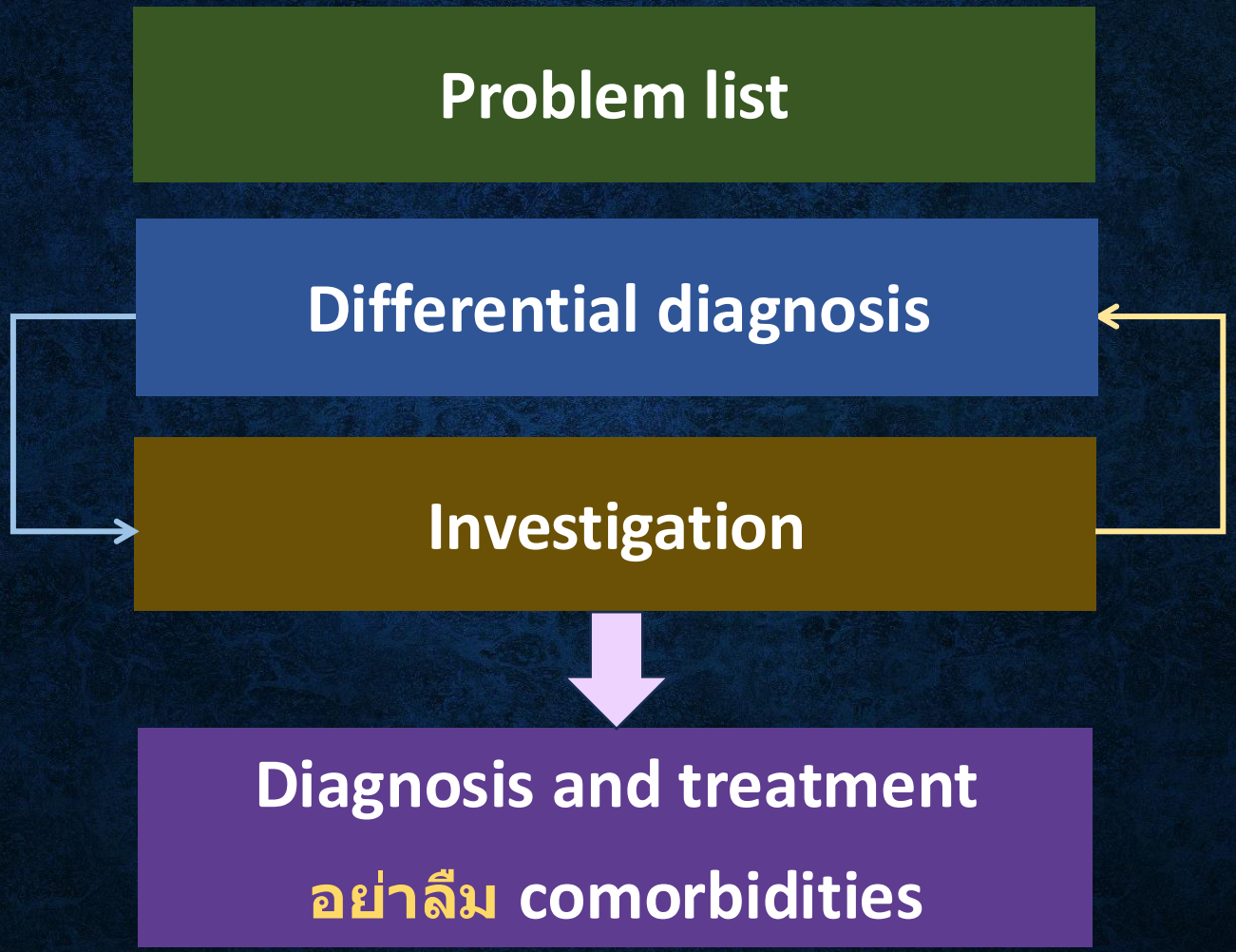
Lung volume

Associated finding

- Sign of pulmonary hypertension
- Pleural effusion
- Mediastinal lymph node
- Esophagus
- Subcutaneous emphysema

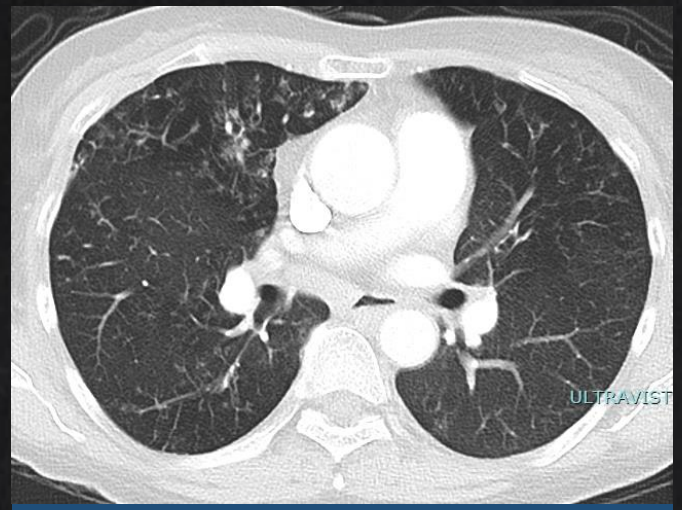
Ask for previous film?

Diagnostic approach

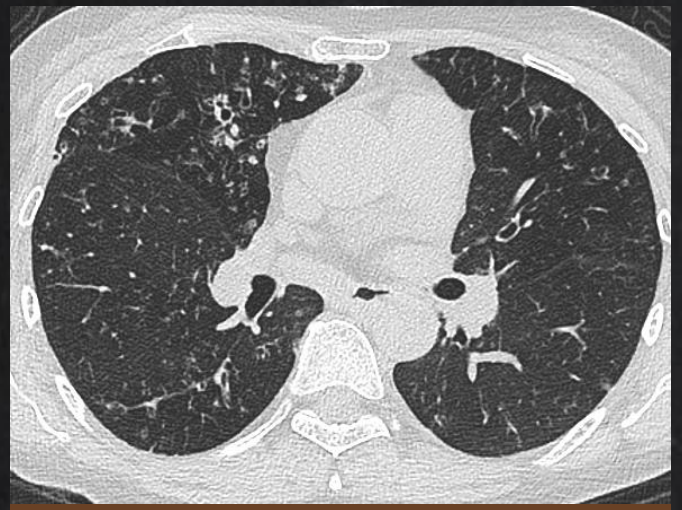


Essential tips in HRCT

CT chest (5 mm slice)



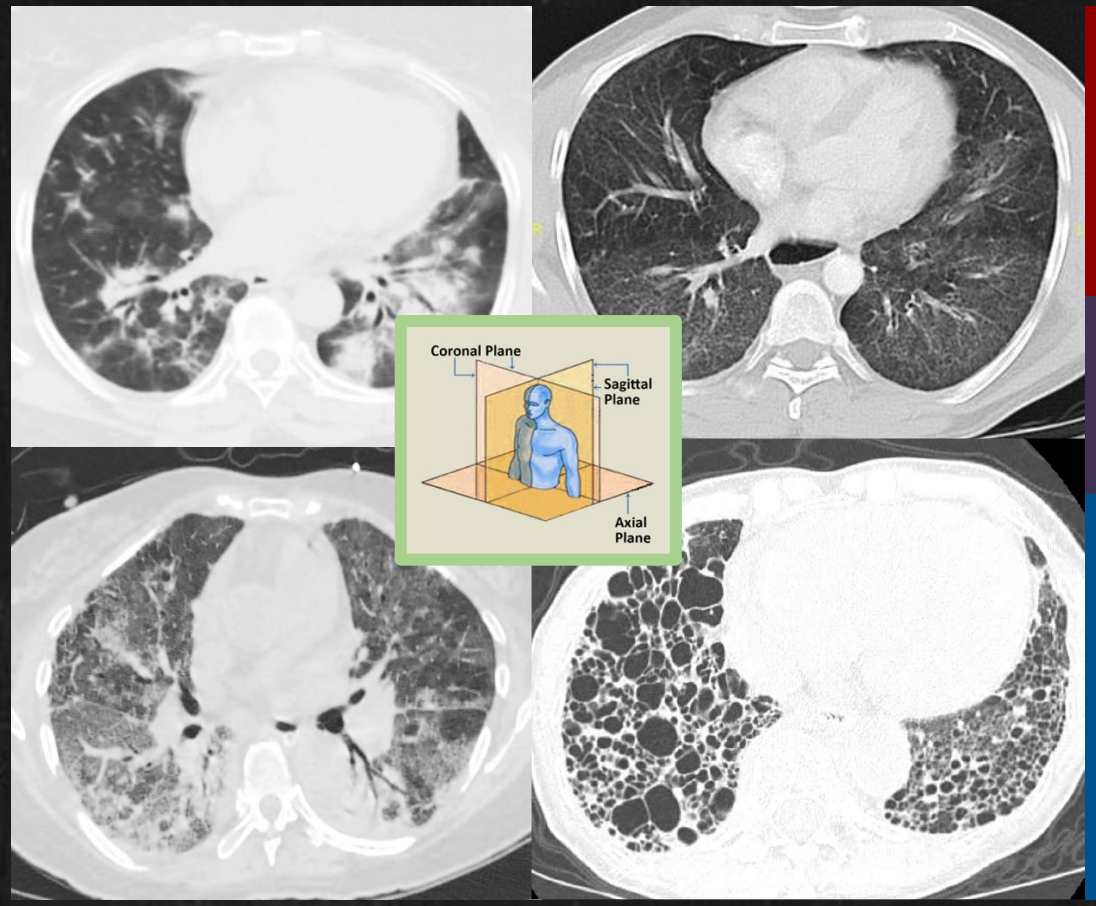
Thin slice CT chest (1.25 mm)



HRCT

- Thin collimation → 1-1.5 mm.
- Indication :
  - Interstitial lung disease
  - Bronchiolitis, bronchiectasis
- Non contrast

Essential tips in HRCT



Abnormalities

- Interstitial/alveolar process
- Other findings
- Distribution

Lung volume

- Decreased/architectural distortion
- Increased/airtrapping

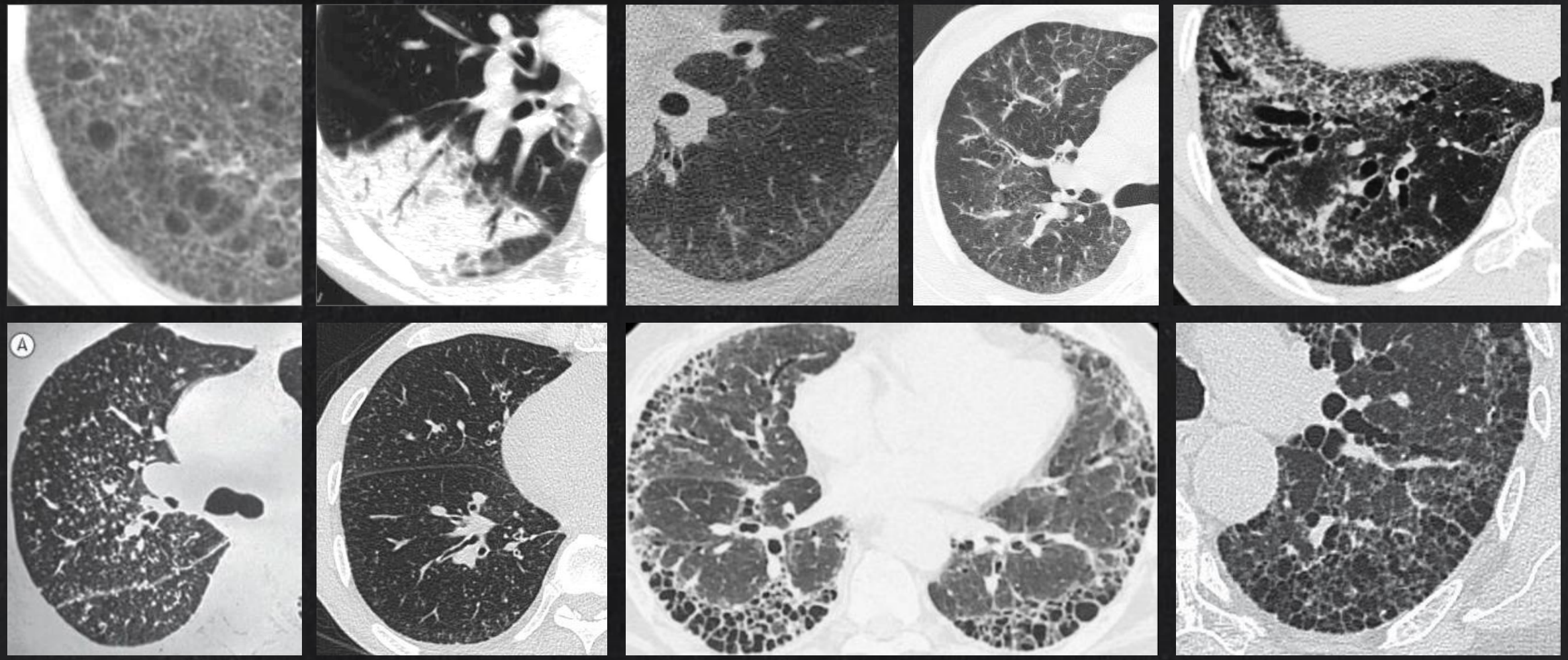
Associated finding

- Sign of pulmonary hypertension
- Pleural effusion
- Mediastinal lymph node
- Esophagus
- Subcutaneous emphysema

HRCT findings

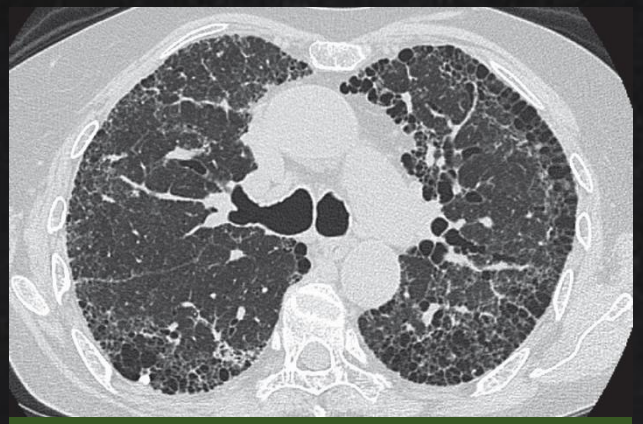
HRCT findings	
Nodules	Micronodules
Reticular lines	Reticulation
Ground-glass opacity	High attenuation
Consolidation	
Mosaic pattern	
Honeycombing	Low attenuation
Traction bronchiectasis	
Cysts	

HRCT findings

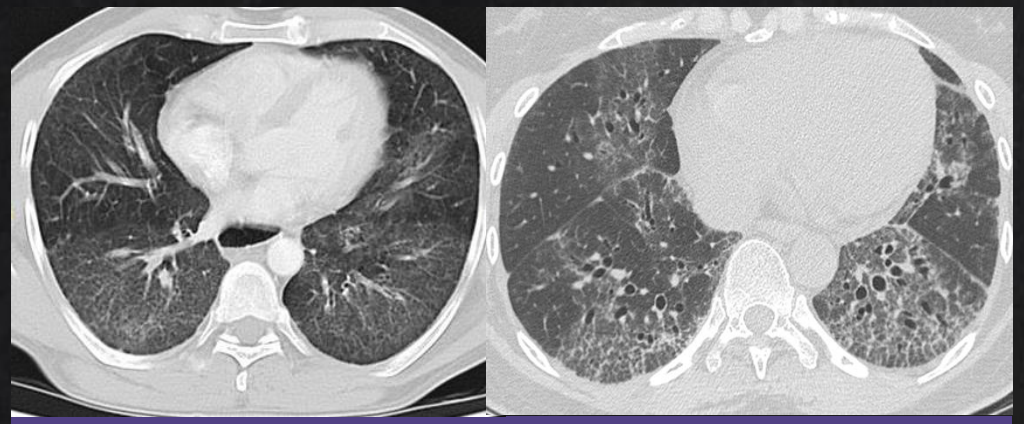


HRCT patterns	UIP	NSIP	OP
GGO	+/-	**+++**	+
Consolidation	-	-	**+++**
Reticulation	++	++/+++	Perilobular pattern with linear opacities
Traction bronchiectasis	**+++**	+	-
Honeycombing	**+++**	+/-	-
Cystic lesion	-	+ (bronchiolectasis)	-
Nodule	-	-	+/- Small, ill-defined peribronchial nodules
Distribution and associated findings	• Subpleural area • Basal lungs	• Subpleural area • Basal lungs • +/- Immediate subpleural sparing (20-50%)	• Focal or multi-focal • Subpleural or peribronchial distribution • Reverse halo (20%)

Common HRCT pattern in IP



UIP

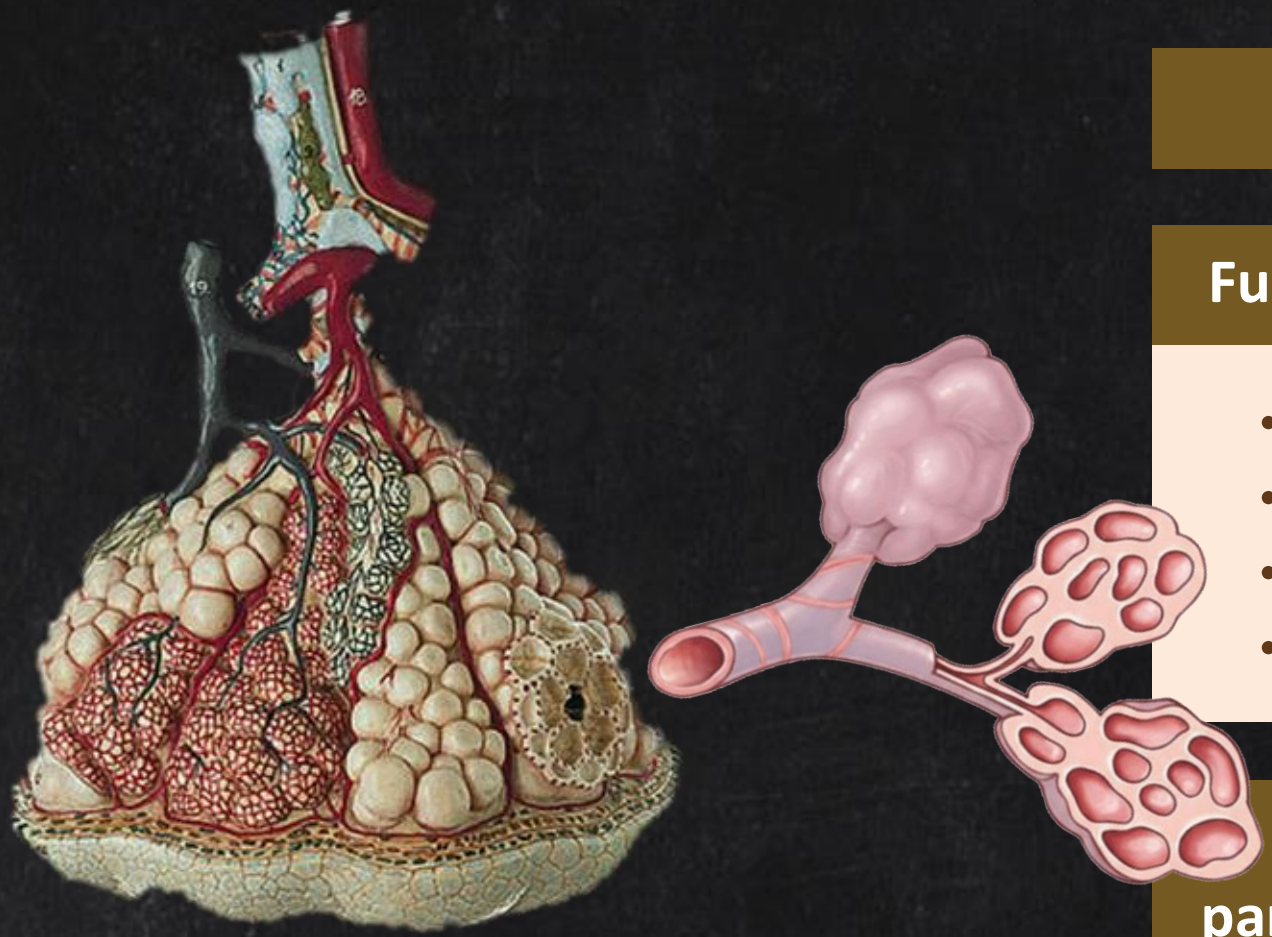


NSIP

OP

IP, interstitial pneumonia
UIP, usual interstitial pneumonia
NSIP, non-specific interstitial pneumonia
OP, orgainizing pneumonia

Interstitial lung disease



Pulmonary parenchyma

Functional gas-exchanging tissue

- Alveoli
- Alveolar ducts
- Respiratory bronchioles
- Interstitium

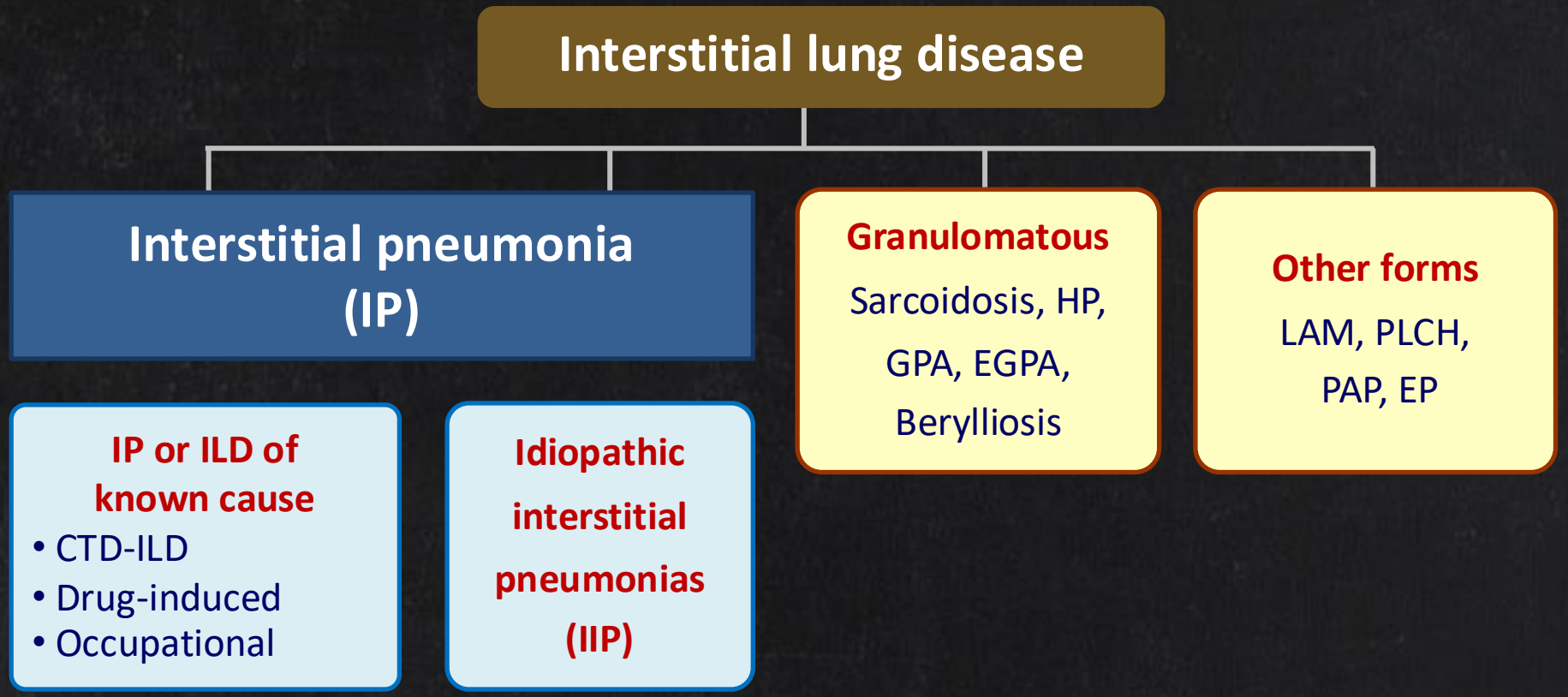
Diffuse parenchymal lung disease (DPLD)

Terms and definition

Interstitial lung disease (ILD)	• A group of pulmonary disorders • Typically involving the parenchyma • May affect small airways
Interstitial pneumonia (IP)	• Pattern-based subset of ILD • A group of diseases that are either interstitial or alveolar filling disorders, with some affecting both compartments

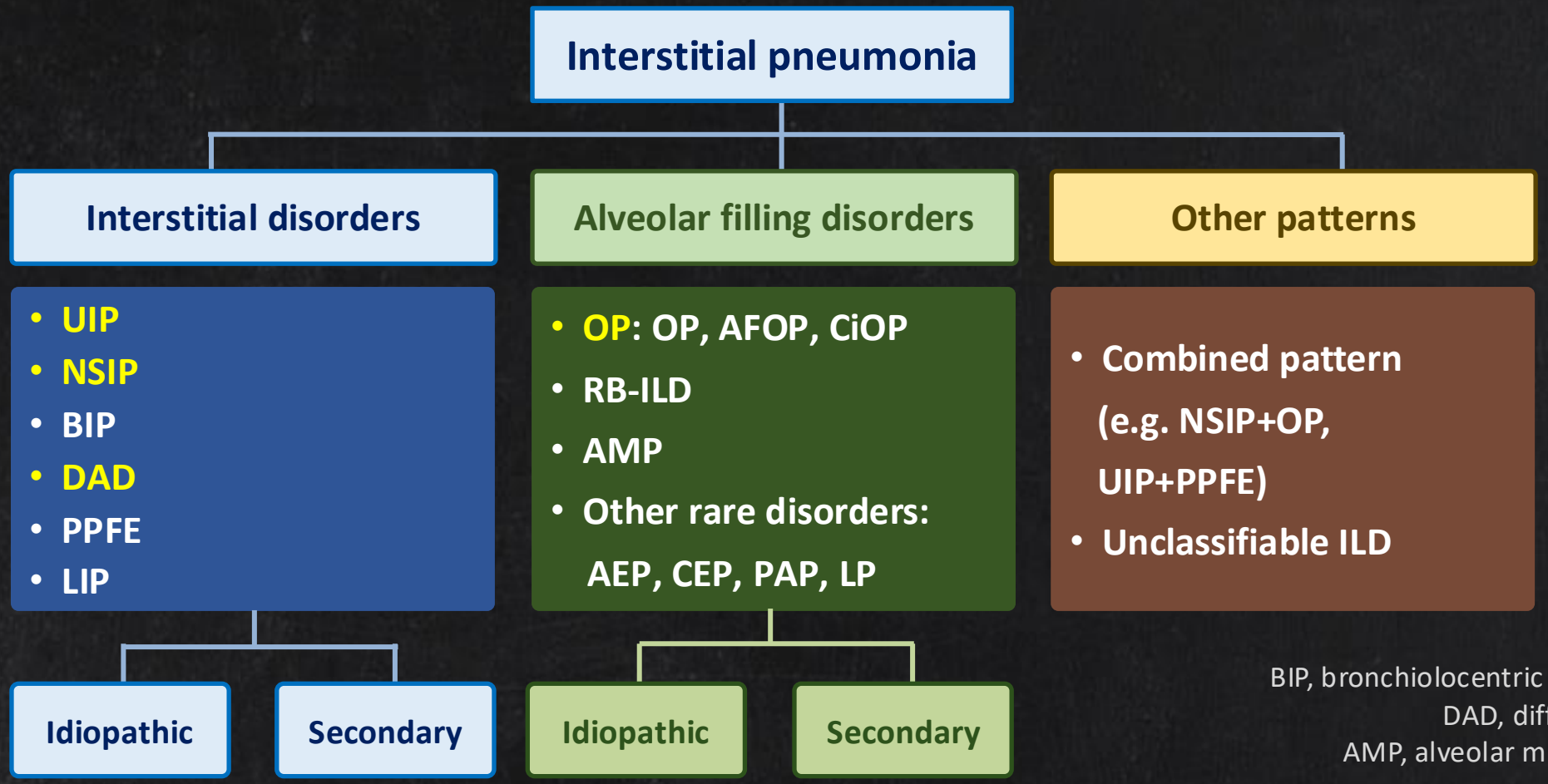
Bankier AA, et al. Fleischner Society: 4th Edition. Radiology 2024;310:e232558.
Ryerson CJ, et al. A consensus statement from the Fleischner Society. Am J Respir Crit Care Med 2025;211:1756-74.

ILD classification



ATS/ERS Classification of the IIPs. AJRCCM 2002;165:277-304.
ATS/ERS Statement. AJRCCM 2013;188:733-48.

Interstitial pneumonia classification



BIP, bronchiolocentric interstitial pneumonia
DAD, diffuse alveolar damange
AMP, alveolar macrophage pneumonia
LP, lipoid pneumonia
EP, eosinophilic pneumonia
LIP, lymphocytic interstitial pneumonia

Ryerson CJ, et al. Eur Respir J. 2025 Aug 7:2500158.

Interstitial pneumonia

HRCT patterns or histopathology → Disease

Identify causes and associated disease

Suspicious of ILD
- Symptom and sign
- Chest X-ray
- Initial investigation

HRCT

Multidisciplinary discussion (MDD)

Diagnosis

Yes

Diagnosis

PFTs
- **Severity assessment**
- **(Diagnosis)**
- **Monitoring**

No

Bronchoscopy can make diagnosis

Yes

Bronchoscopy

Yes

Diagnosis

No

MDD

No

Diagnosis

Yes

Diagnosis

No

SLB or TBCB

A 48-year-old female

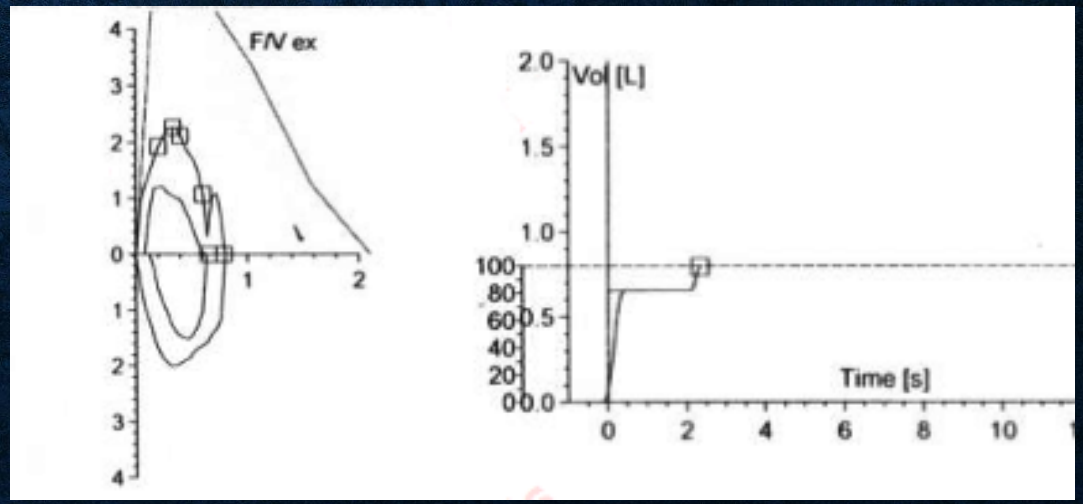
Feb 2016	Value	% predicted
FEV1/FVC, %	82	95.3
FVC, L	2.39	**75.7**
TLC		**71.6**
DLCO		**39**
DLCO/VA		**50**
6MWD, m	498	
SpO_2 (pre), %	98	
SpO_2 (post), %	96	

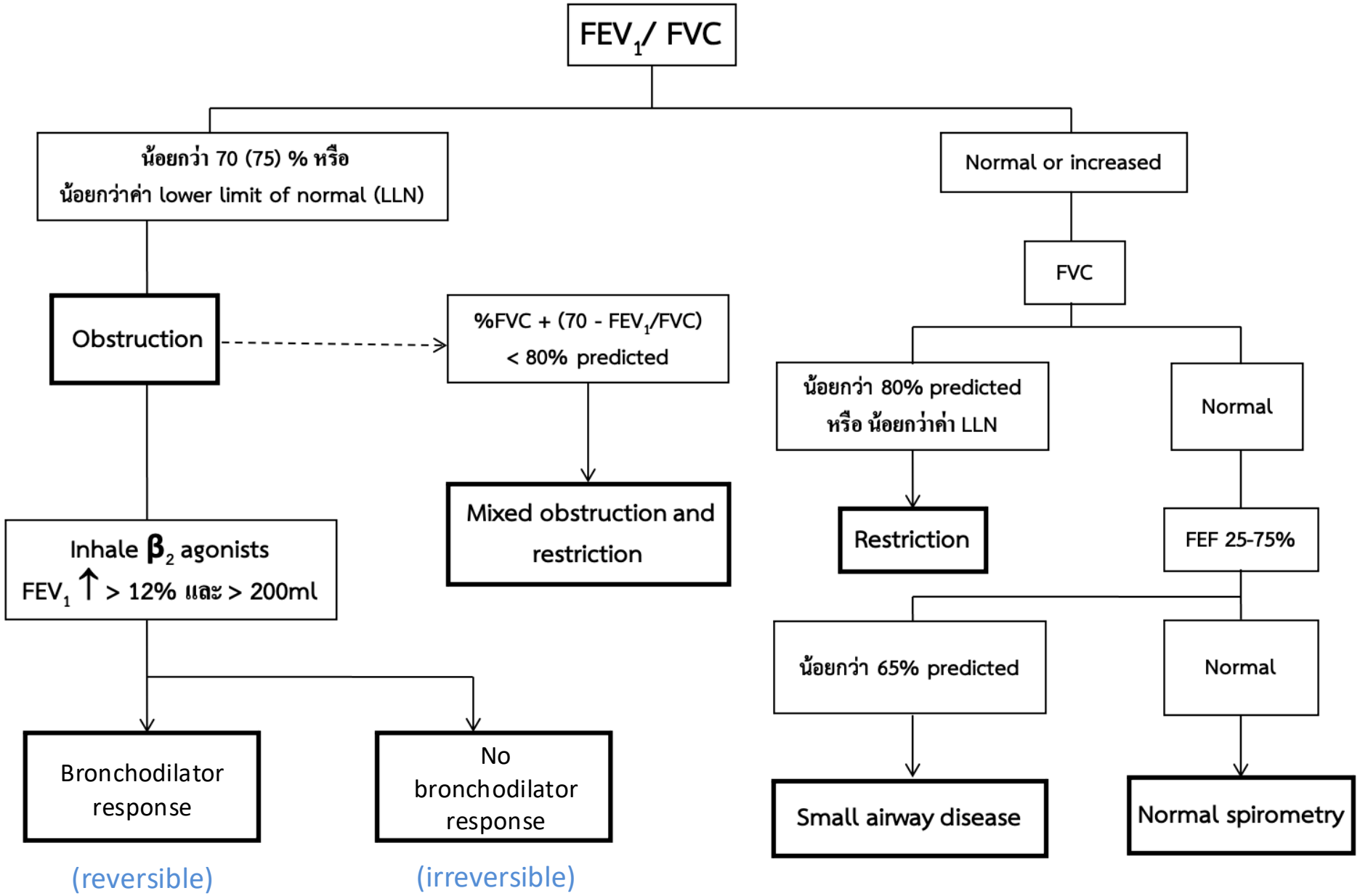
Spirometry interpretation

Quality

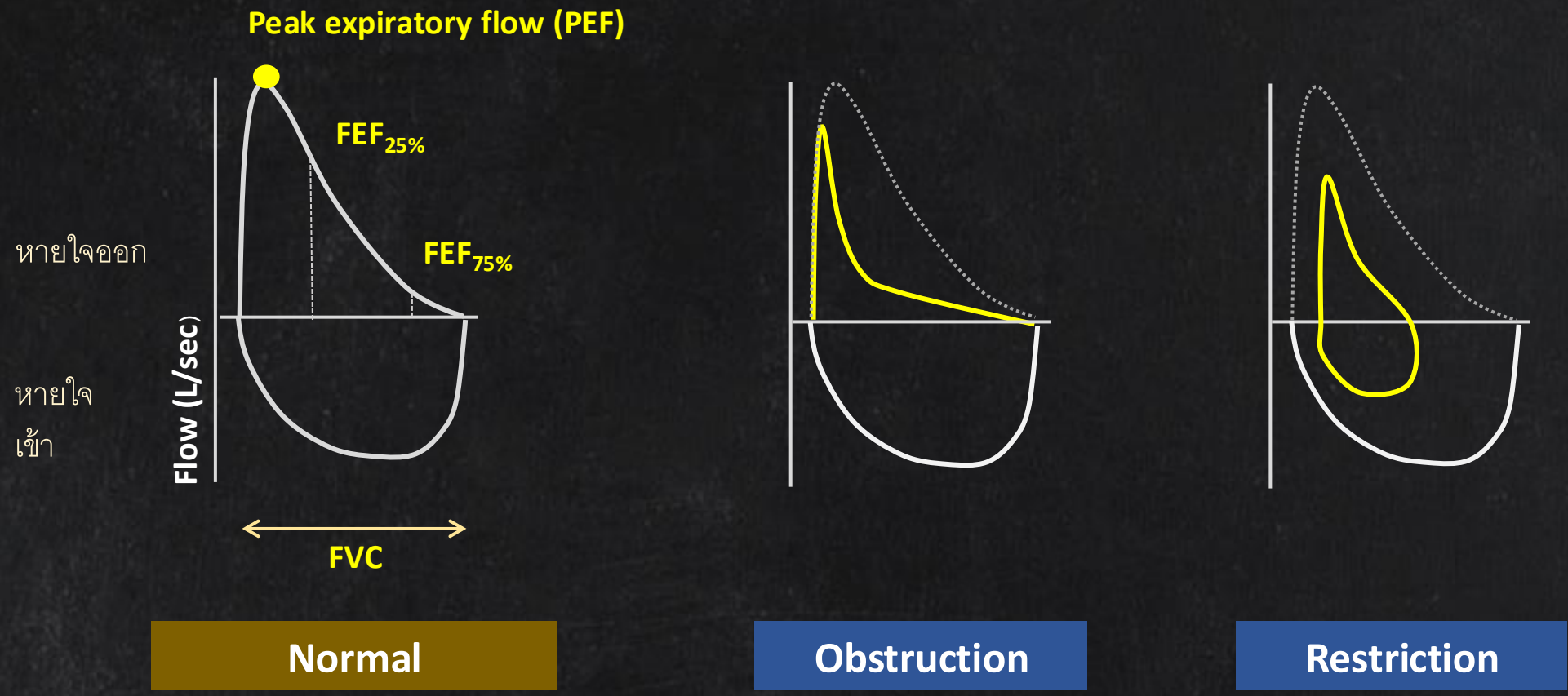
Acceptability and repeatability
- Volume-time curve
- Flow-volume loop

Interpretation
- Obstruction
- Restriction
- Mixed

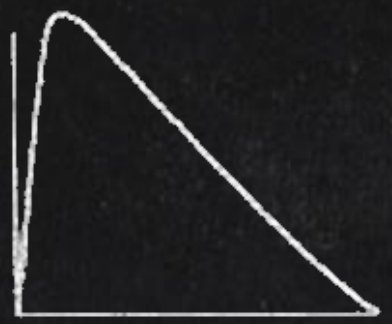



FEV1/ FVC
น้อยกว่า 70 (75) % หรือ
น้อยกว่าค่า lower limit of normal (LLN)
Normal or increased
Obstruction
%FVC + (70 - FEV1/FVC)
< 80% predicted
FVC
น้อยกว่า 80% predicted
หรือ น้อยกว่าค่า LLN
Normal
Mixed obstruction and
restriction
Restriction
FEF 25-75%
Inhale β2 agonists
FEV1 ↑ > 12% และ > 200ml
น้อยกว่า 65% predicted
Normal
Bronchodilator
response
No
bronchodilator
response
Small airway disease
Normal spirometry
(reversible)
(irreversible)

Flow-volume loop

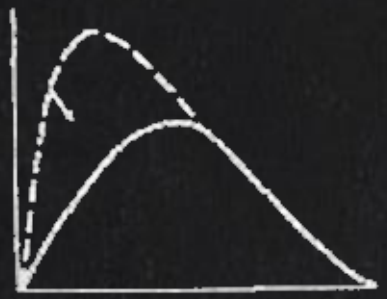


Flow-volume loop

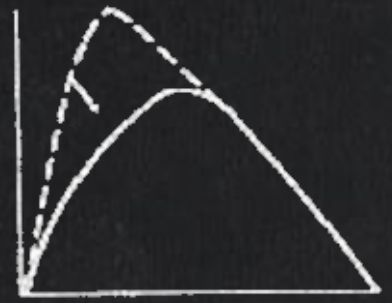


Normal

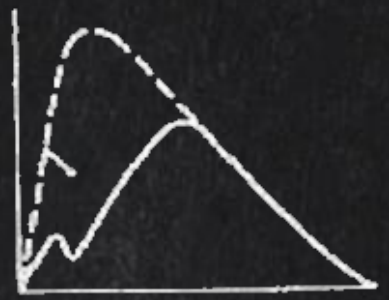
Normal variant



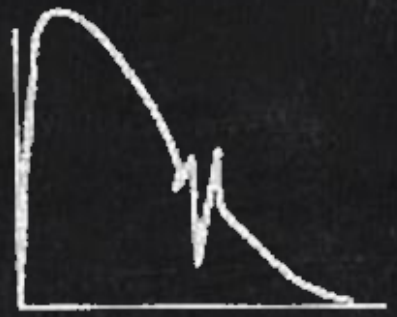
Poor effort



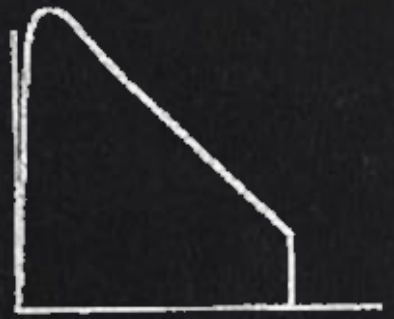
Poor effort



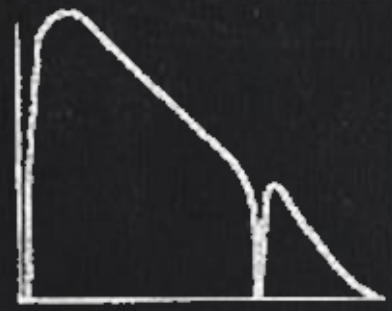
Hesitating start



Cough

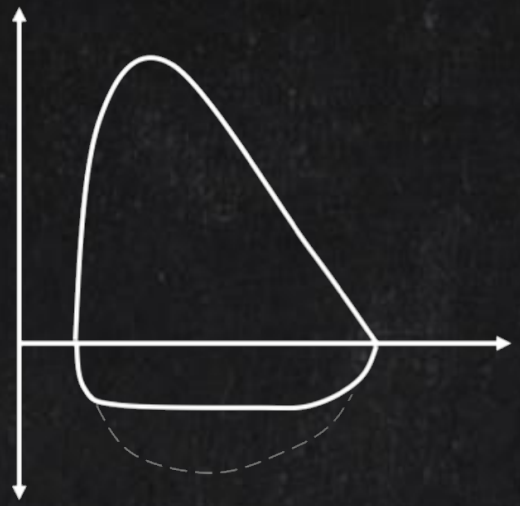


Quit too soon/ tongue occlude



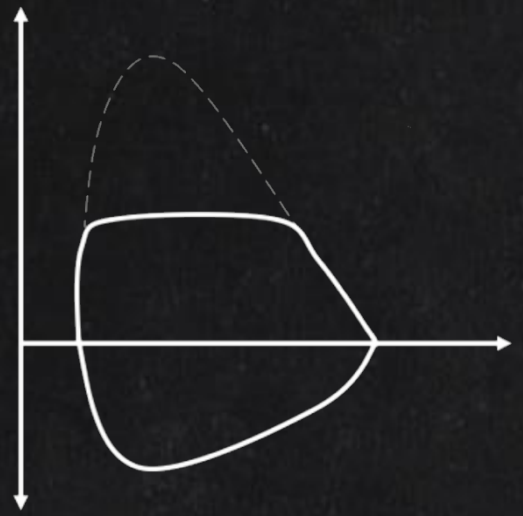
Stop exhale momentarily

Flow-volume loop: UAO



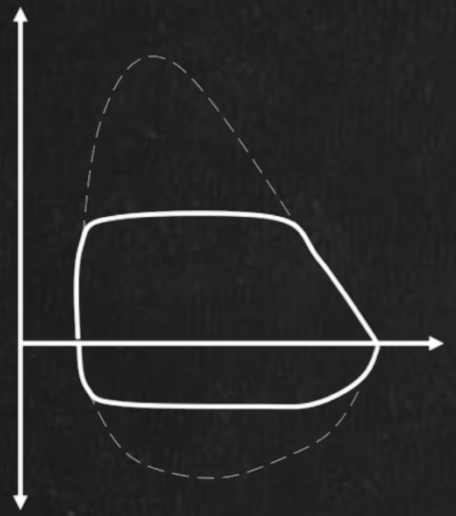
Variable extrathoracic

- Vocal cord paralysis
- Tracheomalacia



Variable intrathoracic

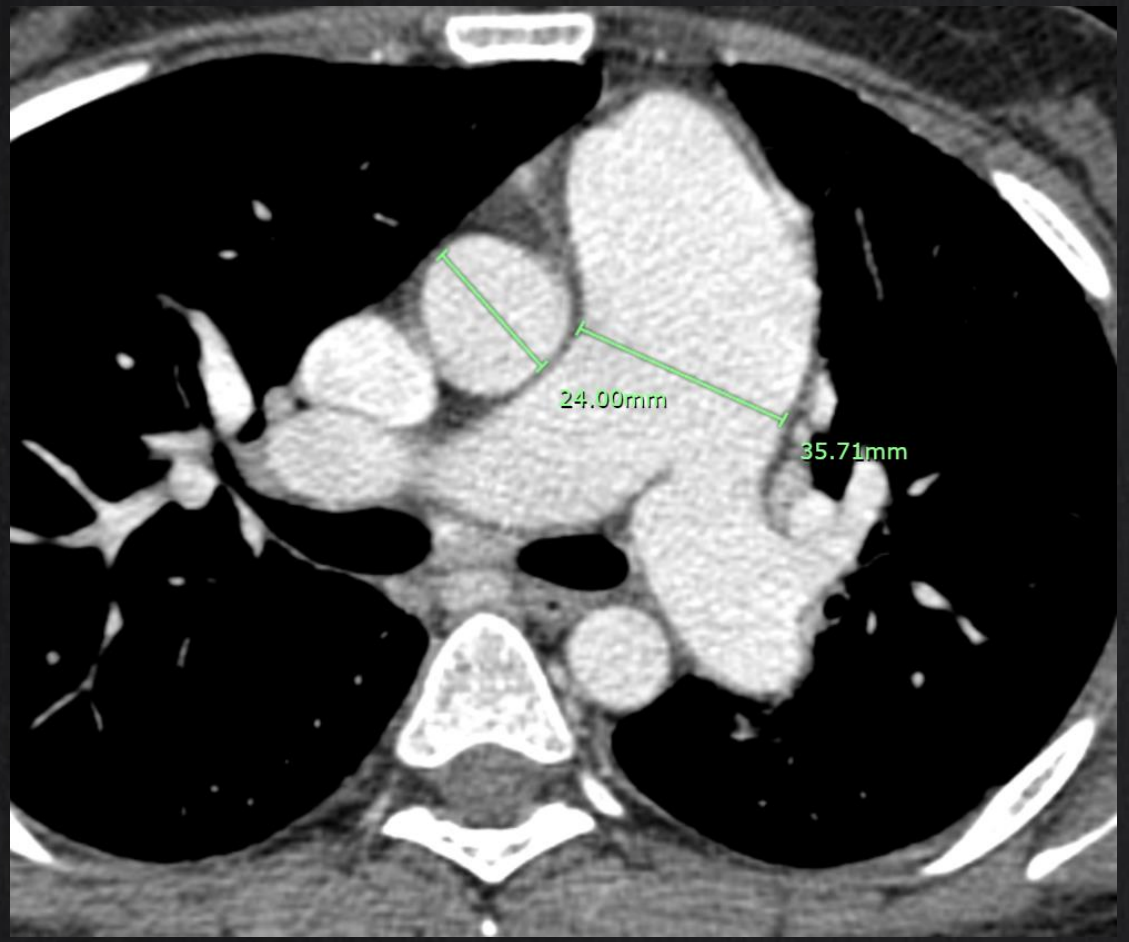
- Tracheomalacia
- Tumor of trachea or main bronchus
- Polychondritis



Fixed UAO

- Tracheal stenosis
- Tracheal tumor
- Goiter
- Vocal cord paralysis

Pulmonary hypertension



Pulmonary hypertension

Mean pulmonary arterial pressure (mPAP) > 20 mmHg

Definition	Hemodynamic characteristics		
	mPAP, mmHg	PAWP, mmHg	PVR, WU
PH	**> 20**		
Pre-capillary PH	> 20	**≤ 15**	> 2
IpcPH		**> 15**	
CpcPH		**> 15**	
Exercise PH	mPAP/CO slope between rest and exercise > 3 mmHg/L/min		

IpcPH, isolated post-capillary PH; **CpcPH**, Combined post- and pre-capillary PH

Humbert M, Kovacs G, Hoeper MM, et al. Eur Heart J. 2022 Aug 26:ehac237.

Pulmonary hypertension

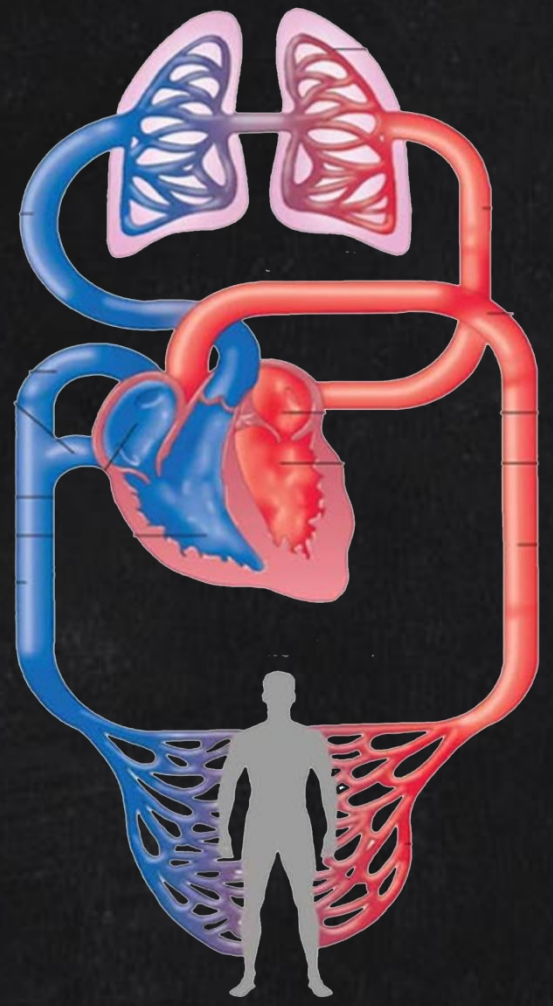
1	2	3	4	5
PAH	**Left heart disease**	**Lung diseases and/or hypoxia**	**Pulmonary artery obstructions**	**Unclear or multifactorial mechanisms**
• Idiopathic • Heritable • Drugs and toxins • Associated with - CTD - HIV - Portal hypertension - Congenital heart disease - Schistosomiasis • PVOD/PCH • Persistent PH of the newborn	• Heart failure - HFpEF - HFrEF • Valvular heart disease • Congenital/acquired cardiovascular conditions leading to post-capillary PH	• Obstructive lung disease or emphysema • Restrictive lung disease • Mixed restirctive/ obstructive lung disease • Hypoventilation syndrome • Hypoxia without lung disease (e.g. high altitude) • Developmental lung disorders	• CTEPH • Other pulmoanry artery obstructions	• Hematological disorders e.g. hemolytic anemia, chronic myeoloproli-ferative disorders • Systemic disorders e.g. sarcoidosis, PCLH, NF type 1 • Chronic renal failure with or without hemodialysis • Pulmonary tumor thrombotic microangiopathy • Fibrosing mediastinitis

Humbert M, Kovacs G, Hoeper MM, et al. Eur Heart J. 2022 Aug 26:ehac237.

Pulmonary hypertension

Precapillary pulmonary hypertension

1. PAH
3. Lung diseases and/or hypoxia
4. Pulmonary artery obstructions
5. Unclear or multifactorial mechanisms



Postcapillary pulmonary hypertension

2. Left heart disease
5. Unclear or multifactorial mechanisms

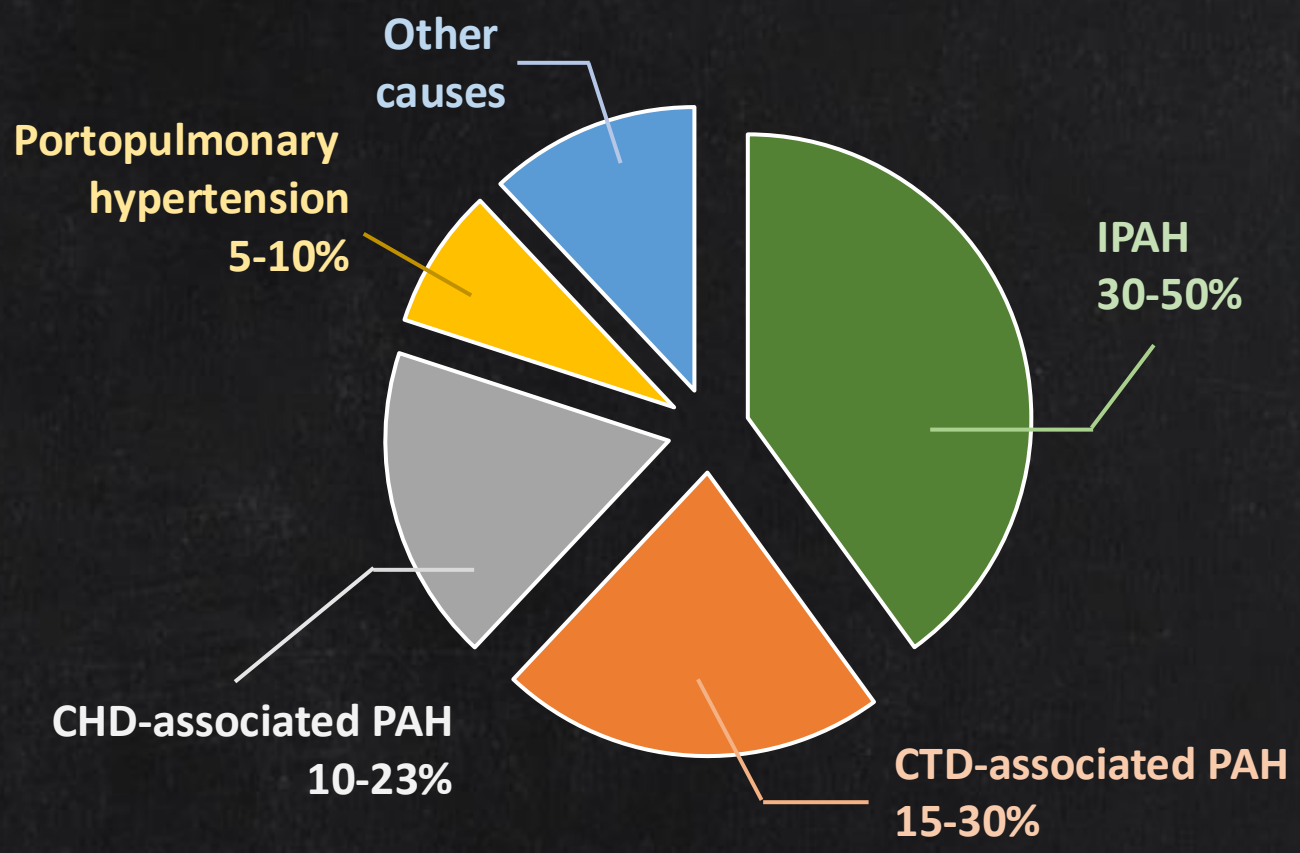
Humbert M, Kovacs G, Hoeper MM, et al. Eur Heart J. 2022 Aug 26:ehac237; Miller AC. Am J Hosp Med 2020;4(2):1-11.

Pulmonary arterial hypertension

PAH → pre-capillary PH in the absence of other causes of pre-capillary PH

Prevalence of 48-55 cases/million adults

- **Idiopathic (IPAH)**
- Heritable
- **Drugs and toxins**
- Associated with
  - **CTD**
  - HIV
  - Portal hypertension
  - **Congenital heart disease**
  - Schistosomiasis
- PVOD/PCH
- Persistent PH of the newborn



Lau EMT, et al. Nat Rev Cardiol 2017;14:603-14; Humbert M, et al. Eur Heart J. 2022 Aug 26:ehac237.

Drug and toxins

Definite association	Possible association
• Aminorex • Benfluorex • Dasatinib • Dexfenfluramine • Fenfluramine • Methamphetamines • Toxic rapeseed oil	• Alkylating agents e.g. cyclophosphamide, mitomycin C) • Amphetamines • Bosutinib • Cocaine • Diazoxide • Direct-acting antiviral agents against hepatitis C virus (sofosbuvir) • Indirubin (Chinese herb Qing-Dai) • Interferon alpha and beta • Leflunomide • L-tryptophan • Phenyl propanolamine • Ponatinib • Selective proteasome inhibitors (carfilzomib) • Solvents (trichloroethylene) • St John's Wort

Humbert M, Kovacs G, Hoeper MM, et al. Eur Heart J. 2022 Aug 26:ehac237.

CTD-associated PAH

	Prevalence, %	Method
All CTD	2.8-32	
SSc	3.6-32 8.2 18	- RHC Echo
SLE	2.8-4.2	Echo
RA	21-27.5	Echo

- Female predominance (female:male ratio ~4:1)
- Prevalence varies
  - Type of CTD
  - Definition of PH
  - Method used (echocardiography, RHC)

Yang X, et al. Clin Rheumatol 2013;32:1519; Humbert M, Kovacs G, Hoeper MM, et al. Eur Heart J. 2022 Aug 26:ehac237.

Left heart disease

Feature	PH-LHD Unlikely	Intermediate probability	PH-LHD Likely
Age	<60 years	60–70 years	>70 years
Obesity, hypertension, dyslipidaemia, glucose intolerance/ diabetes	No factors	1–2 factors	>2 factors
Presence of known LHD	No	Yes	Yes
Previous cardiac intervention	No	No	Yes
Atrial fibrillation	No	Paroxysmal	Permanent/persistent
Structural LHD	No	No	Present
ECG	Normal or signs of RV strain	Mild LVH	LBBB or LVH
Echocardiography	No LA dilation E/e′ <13	No LA dilation Grade <2 mitral flow	LA dilation (LAVI >34 mL/ m^2) LVH Grade >2 mitral flow

Humbert M, Kovacs G, Hoeper MM, et al. Eur Heart J. 2022 Aug 26:ehac237.

Group 3 PH

2015 ESC/ERS Guidelines
3. Pulmonary hypertension due to lung diseases and/or hypoxia
3.1 Chronic obstructive pulmonary disease
3.2 Interstitial lung disease
3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern
3.4 Sleep-disordered breathing
3.5 Alveolar hypoventilation disorders
3.6 Chronic exposure to high altitude
3.7 Developmental lung diseases (Web Table III)

2022 ESC/ERS Guidelines
GROUP 3 PH associated with lung diseases and/or hypoxia
3.1 Obstructive lung disease or emphysema
3.2 Restrictive lung disease
3.3 Lung disease with mixed restrictive/obstructive pattern
3.4 Hypoventilation syndromes
3.5 Hypoxia without lung disease (e.g. high altitude)
3.6 Developmental lung disorders

Galie N, et al. Eur Respir J 2015;46:903-75; Humbert M, Kovacs G, Hoeper MM, et al. Eur Heart J. 2022 Aug 26:ehac237.

Group 3 PH

- **Mild** PH is common in **advanced** parenchymal and interstitial lung diseases

Diseases	mPAP (mmHg)	Prevalence
Advanced COPD	> 35-40	1-5%
IPF	≥ 25	8-15%
Severe IPF	≥ 25	30-50%
End-stage IPF	≥ 25	> 60%
OHS		?

Humbert M, Kovacs G, Hoeper MM, et al. Eur Heart J. 2022 Aug 26:ehac237.

Group 3 PH

Definition of

Severe PH group 3

2015 ESC/ERS Guidelines

- mPAP > 35 mmHg
- mPAP ≥ 25 mmHg with CI < 2.5 L/min/m^2

2022 ESC/ERS Guidelines

- PVR > 5 WU

Galie N, et al. Eur Respir J 2015;46:903-75; Humbert M, Kovacs G, Hoeper MM, et al. Eur Heart J. 2022 Aug 26:ehac237.

PH from ILD ?

- SSc-ILD → 31% of clinically significant SSc-ILD patients had PH
- Up to 25% of these patients have mPAP > 35 mmHg → **Out of proportion PH**

- Alternative or combined mechanisms
  - Intrinsic vascular disease
  - Other causes e.g.
    - PH group 2 e.g. myocardial fibrosis, impaired microcirculatory function, fibrosis of conducting system, microvascular and atherosclerotic coronoary vessel disease, hypertensive crisis
    - CTEPH

Hinchcliff M, et al. J Rheumatol 2011;38:2172-9.

Treatment

Specific treatment

- **Treat specific disease**
  - Corticosteroids
  - Immunosuppressants
  - Antifibrotics
- Lung transplantation

Other treatment

- Treat comorbid diseases
- Smoking cessation
- Improve nutrition
- Vaccination
- Long-term/ambulatory oxygen
- Pulmonary rehabilitation
- Psychosocial support
- Palliative care

First-line treatment in CTD-ILD

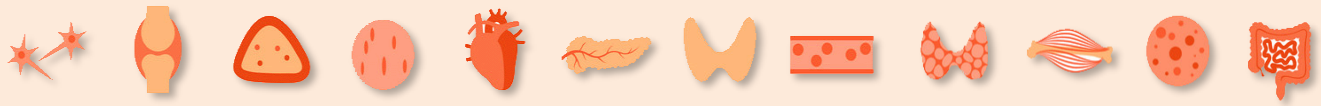
		SSc	IIM	MCTD	RA	Sjogren
First-line ILD Rx	**Preferred**	**MMF** Tocilizumab RTX	MMF AZA, RTX, CNI	MMF AZA, RTX	MMF AZA, RTX	MMF AZA, RTX
	Additional options	CYC Nintedanib AZA	JAKi CYC	Tocilizumab CYC	CYC	CYC
+ Glucocorticoids		**Strongly against****	Short-term	Short-term	Short-term	Short-term

- Treatments are listed in order based on a hierarchy established by head-to-head votes
- Which first-line therapy to use → depends on specific situations and patient factors

*Conditionally recommend or against
**Strongly recommend or against

Johnson SR, et al. ACR/CHEST guideline 2023. Arthritis Rheumatol 2024 Jul 8.

Factors to determine treatment

Diagnosis	• Classification criteria of specific CTD • Onset and disease behavior (chronic, subacute, RP-ILD)
ILD subtypes	• HRCT (+/- histopathologic) pattern
Disease severity and risk of progression	• Clinical, imaging, PFTs • Demographic data, serology (individual basis)
Extrapulmonary organs	
Patient factors	• Precaution/contraindication • Patient's preference and healthcare rights
Physicians	• Experience and hospital resources

Factors determine treatment

SSc-ILD

Clinical data	HRCT and/or histopathologic pattern	Extent of disease	Risk of progression
• Symptoms and O_2 sat • Extrapulmonary organ involvement	• NSIP • UIP • OP	• Limited • Extensive ↓ • HRCT extent > 20% • FVC < 70% predicted	• Low risk • High risk ↓ • Disease extent (severity) • High anti-Scl-70 • Early onset of ILD • Exertional desaturation • FVC decline ≥ 10% • DLCO decline ≥ 15%

Goh NS, et al. Am J Respir Crit Care Med 2008;177:1248-54.
Jung E, et al. Arch Rheumatol 2018;33:322-7.
Distler O, et al. Eur Respir J 2020;55: 1902026.
Goh NS, Arthritis Rheumatol 2017;69:1670-8.

Follow-up and monitoring

Clinical

- Dyspnea
- Cough
- Desaturation (resting/exertional)

PFT

- FVC decline ≥ (5)-10%
- DLCO decline ≥ (10)-15%
- 6MWT (Distance and O_2 saturation)

Imaging

- HRCT progression

Oxygen therapy

- Increase survival in COPD patients with severe chronic resting arterial hypoxemia

$PaO_2 \leq 55$ mmHg or $SaO_2 \leq 88\%$	PaO_2 55-60 mmHg or $SaO_2 > 88\%$
With or without hypercapnia	Pulmonary hypertension
Confirm twice over 3-week period	Polycythemia (Hct > 55%)

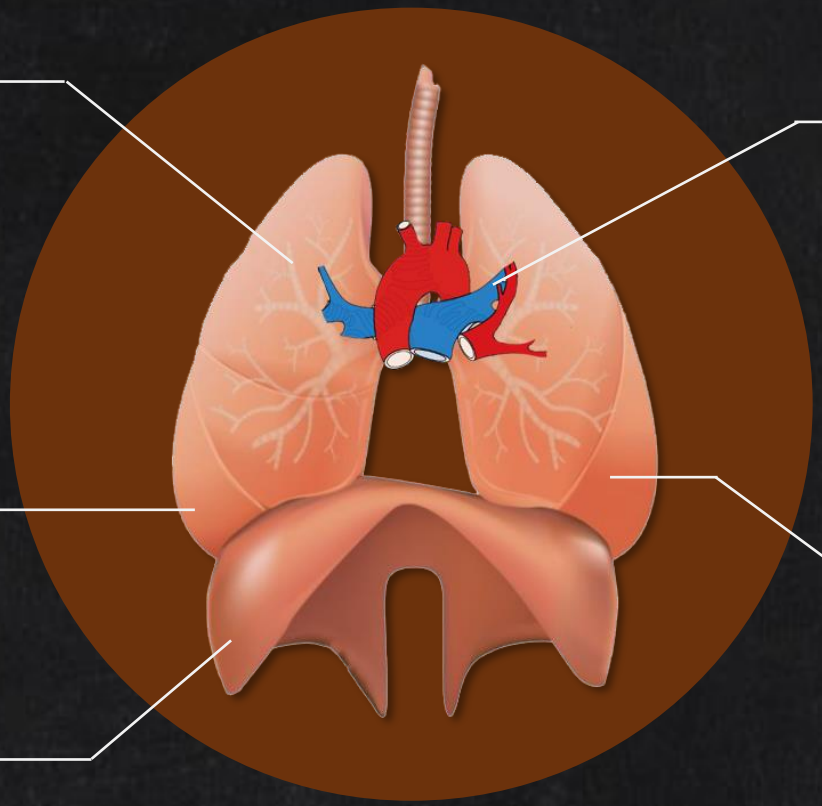
- > 15 hours per day
- Titrate to keep $SaO_2 \geq 90\%$

Progression of disease

- Bronchiectasis
- Bronchiolitis obliterans
- Follicular bronchiolitis
- Small airway disease
- Xerotrachea/xerobronchitis
- Upper airway involvement

- Pleural effusion
- Pneumothorax
- Pneumomediastinum

- Diaphragmatic paralysis
- Shrinking lung syndrome
- Muscle weakness



- Pulmonary arterial hypertension
- Pulmonary embolism
- CTEPH
- Pulmonary capillaritis

- Interstitial lung disease
- Infection
- Pulmonary edema
- Drug-induced pneumonitis
- Acute pneumonitis
- Diffuse alveolar hemorrhage
- Lung nodules
- Secondary amyloidosis
- Pulmonary lymphoma

Conclusion