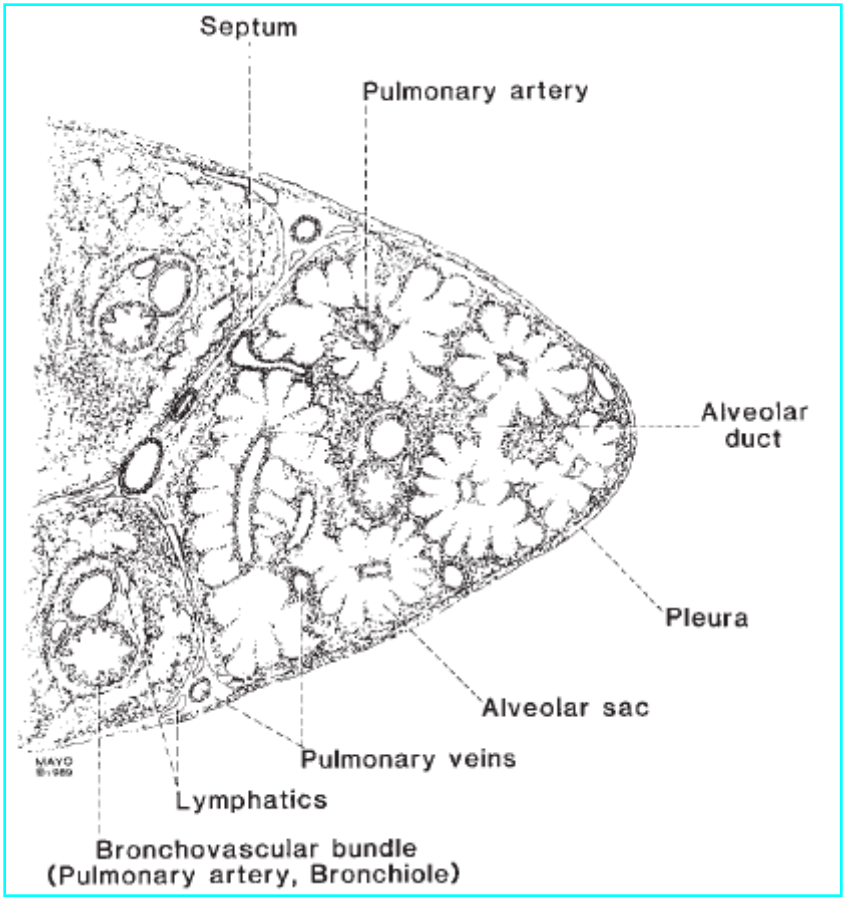
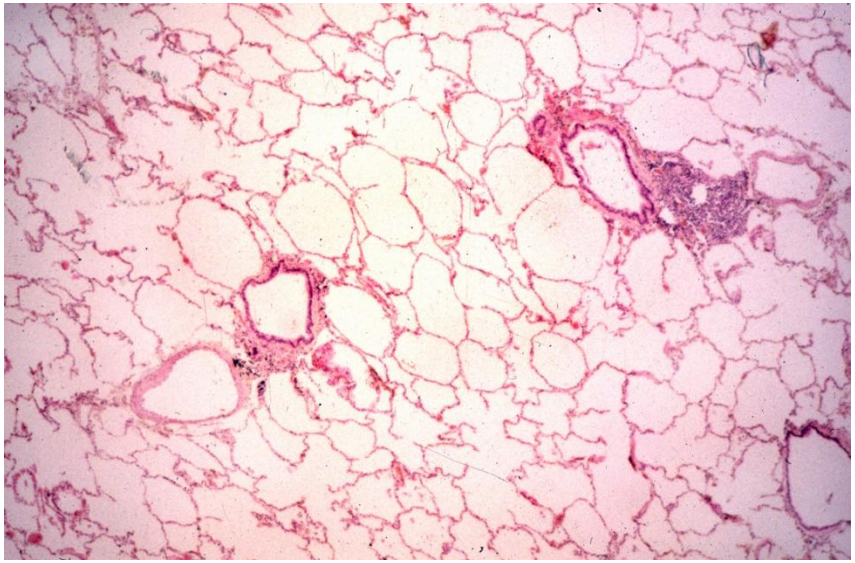
Comprehensive diagnosis of ILD: A multidimensional approach

2025. 07. 12

고려대학교 호흡기 내과 이은주

Interstitium





Interstitium

: space between the epithelial & endothelial basement membrane

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  - Blood testing
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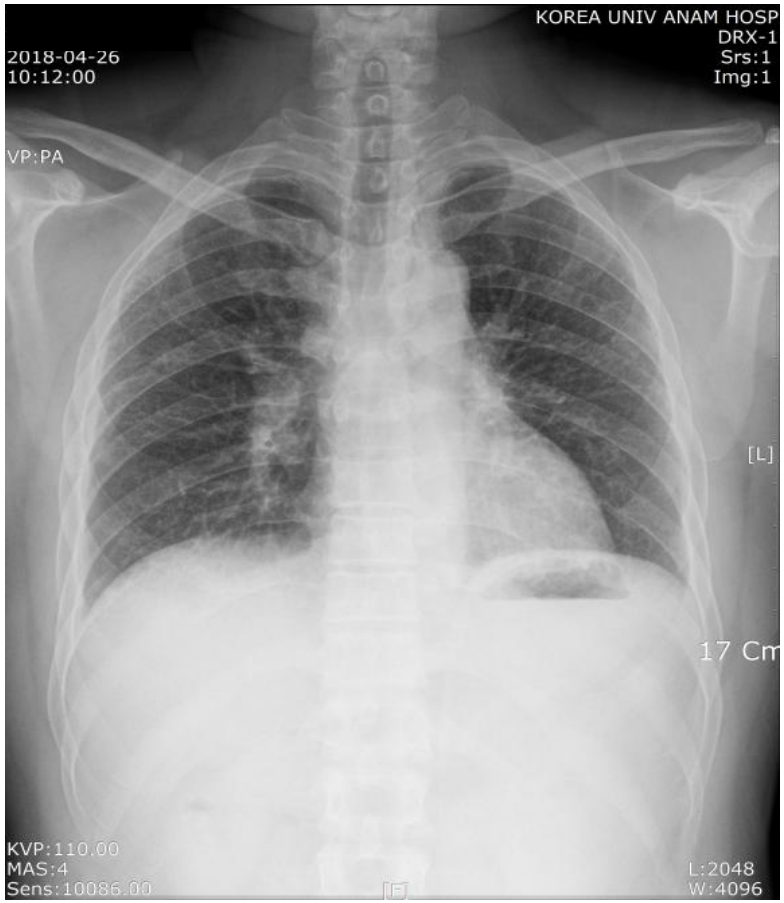
Case 1

- M/ 62

- CC: cough, sputum, dyspnea
- 한약방
- ex smoker : 10년 전 중단
- PHx : DM/HTN/TBc/hepatitis(-/+/-/-), 협심증(+)

- ROS : C/S(+/+), dyspnea, mMRC 2
  arthralgia(-), dry mouth/eye(±/-), Raynaud phenomenon(-)
  skin rash(-), photosensitivity(-)
- P/Ex : whole lung inspiratory crackles(+)
- Lab : FANA: 1: 160 → ENA profile: negative
  ANCA, C3,C4, Anti-ds DNA, Ig A/M/G : negative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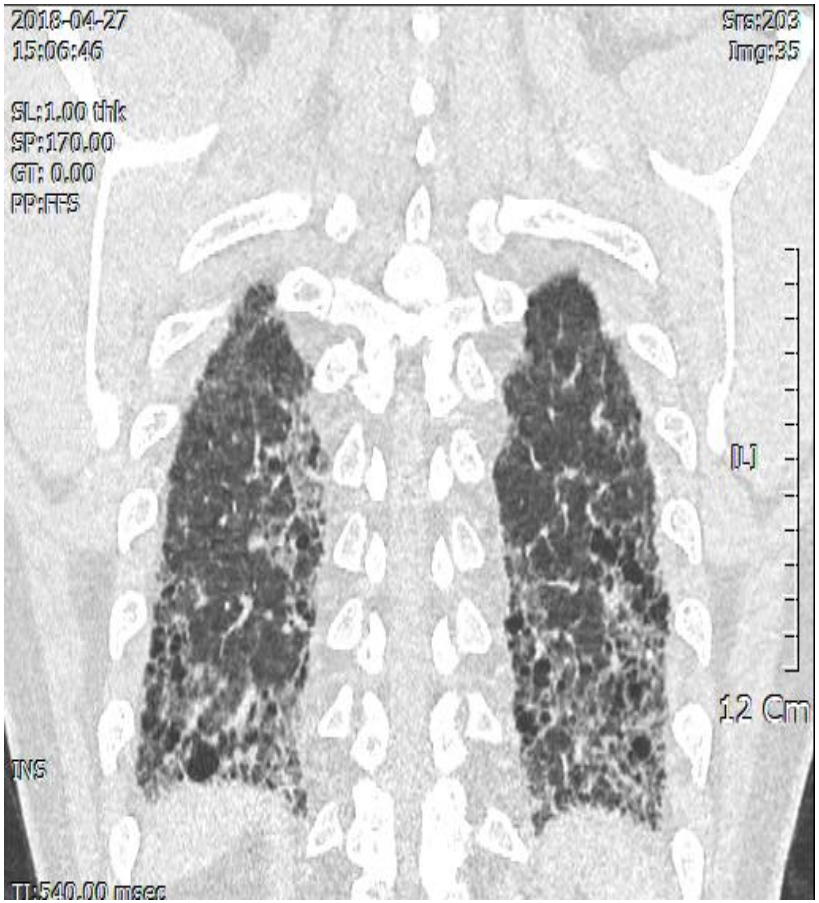
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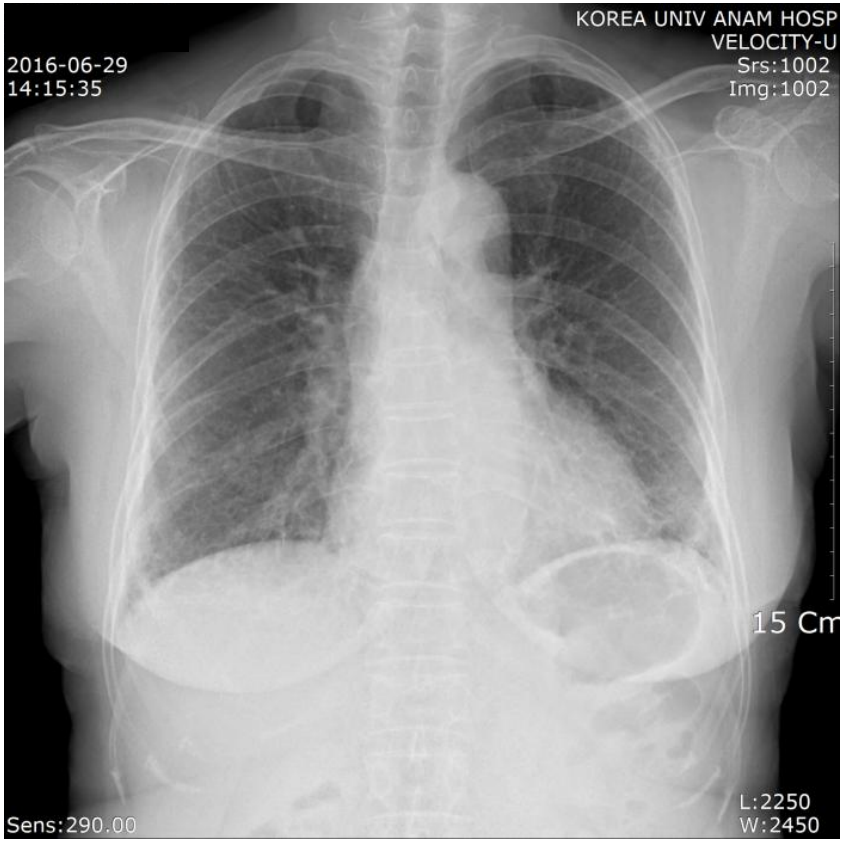
Case 2

- F/ 71
- CC: cough, sputum, dyspnea
- PI : 2006년 exertional dyspnea로 내원하여 VATS lung Bx 시행,
  UIP pattern 소견으로 IPF 진단 후 특별한 치료 없이 local f/u 중
  호흡기 증상 악화되어 내원
- 식당
- Never smoker
- PHx : DM/HTN/TBc/hepatitis(-/-/-/-)
- ROS : C/S(+/+), dyspnea, mMRC II
  arthralgia(-), dry mouth/eye(-/-),
  Raynaud phenomenon(-)
  skin rash(-), photosensitivity(-)
- Lab : FANA, ANCA, C3,C4, Anti-ds DNA, Ig A/M/G
  RF/anti CCP
  : All negative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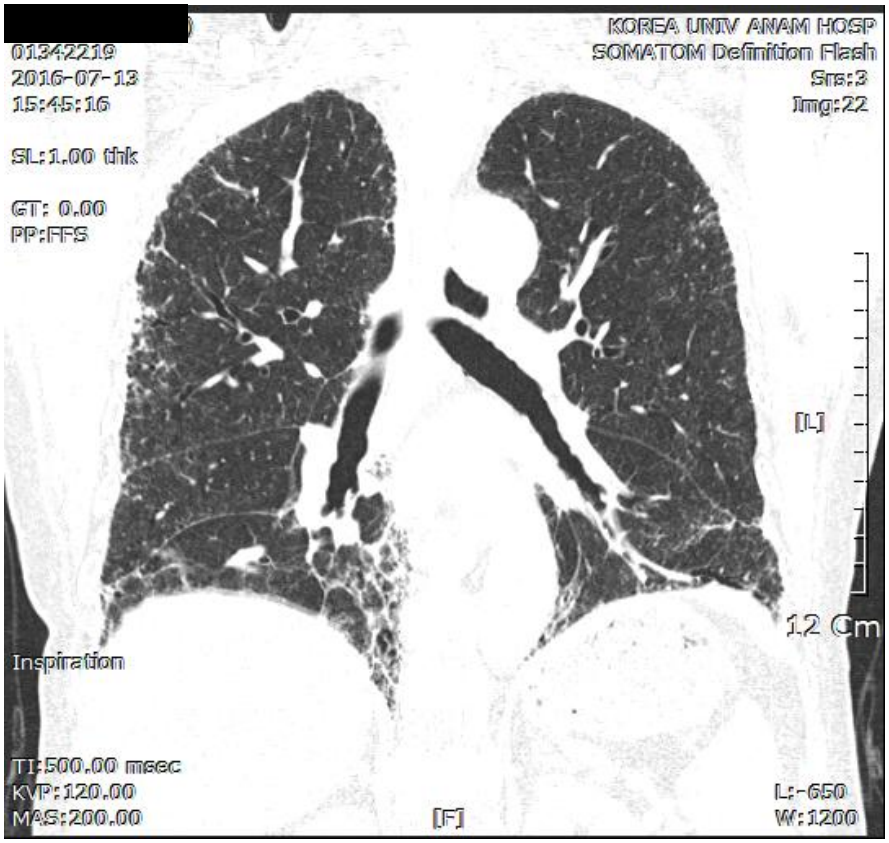
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- 2016.7월부터 Pirfenidone 투여하면서 stable 하게 지내던 중 2017년 겨울 arthralgia 발생하고, RF/ anti CCP (+) 로 conversion 되어 본원 류마티스 내과에서 RA 진단 됨

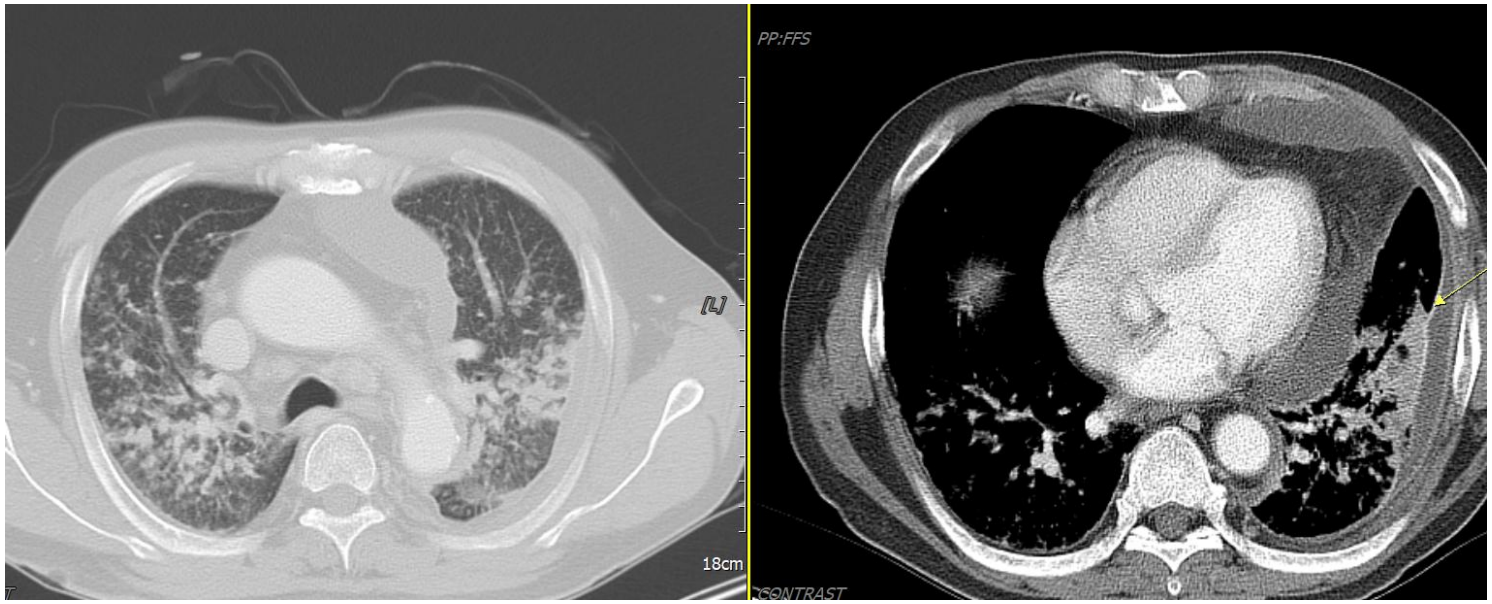
- Final Dx: RA-ILD (UIP pattern)

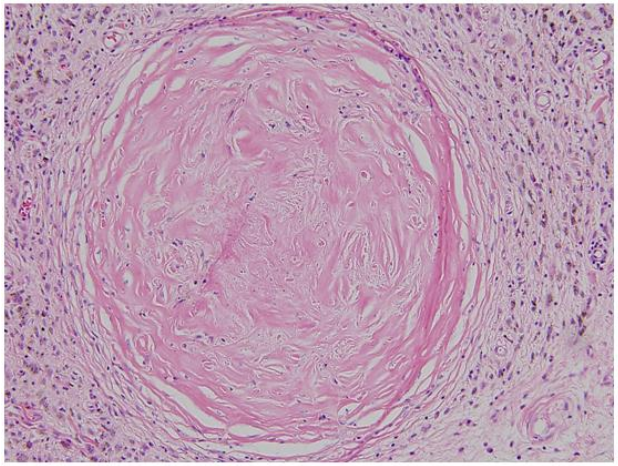
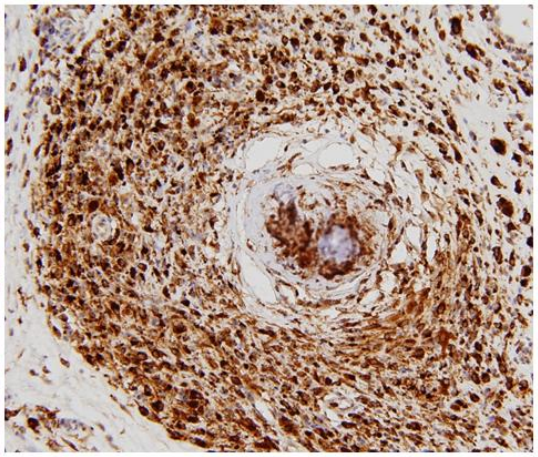
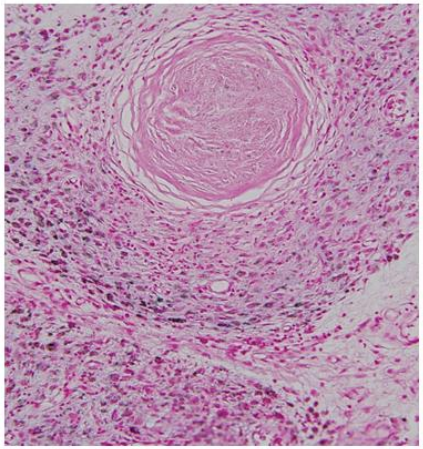
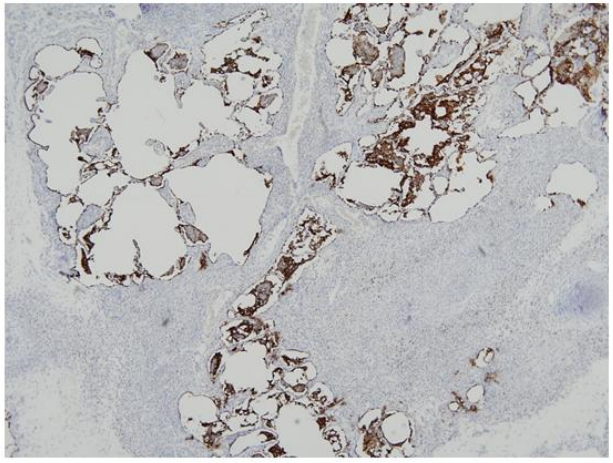
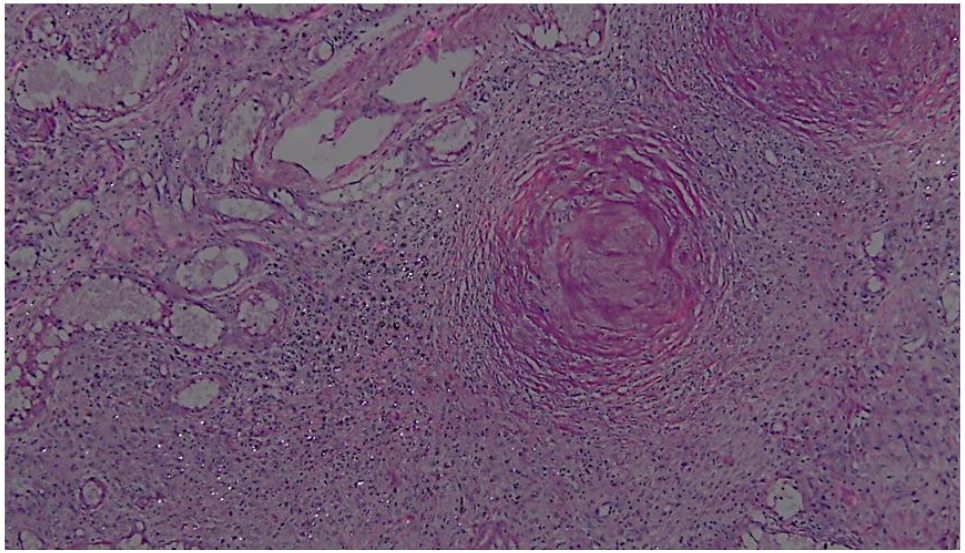
- Plan : pirfenidone 중단 후 추적 관찰

Case 3

- M/ 62

- CC: dyspnea, pleuritic chest pain
- PI : 3주 전부터 dyspnea 발생, 내원 10일 전부터 Lt pleuritic chest 발생하여 내원
- 벼루 공예 장인

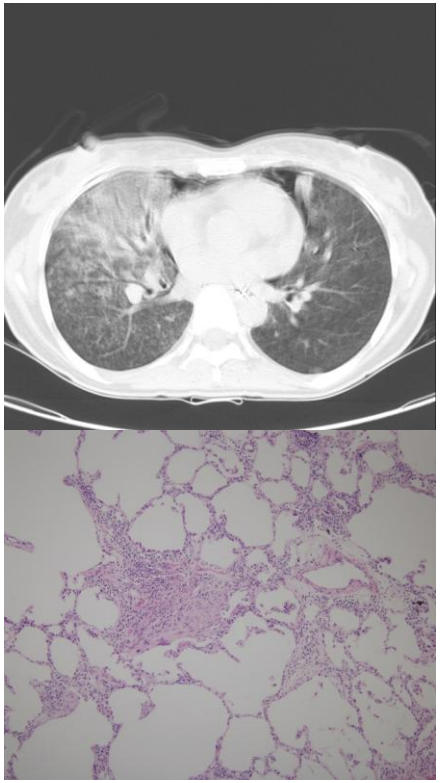


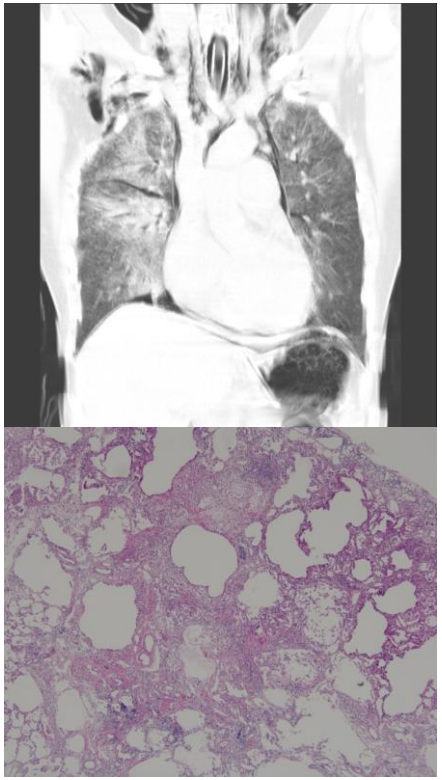







大韓民國

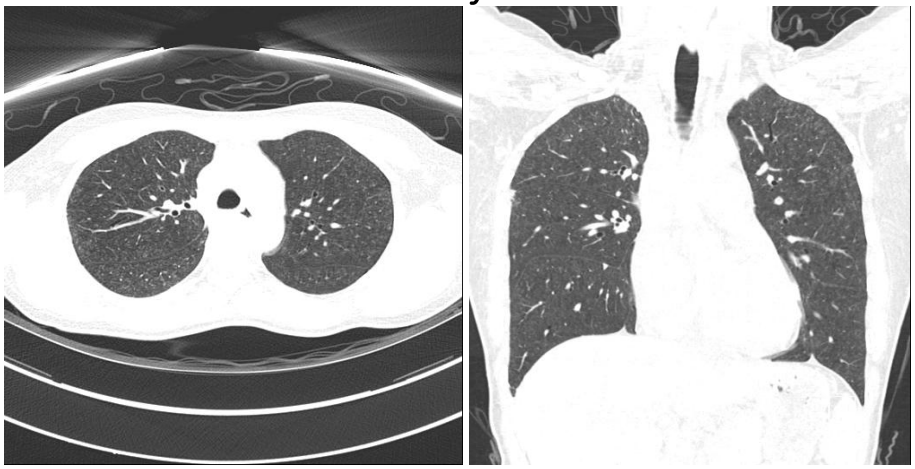
Case 4

- F/ 35, pregnant
- CC: Cough, dyspnea, mMRC 3 (onset: 3 weeks ago)





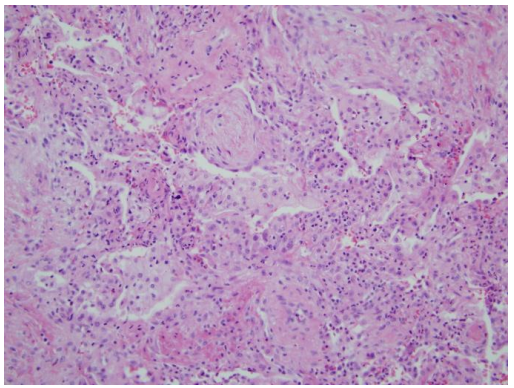
After 3 years



Am J Respir Crit Care Med 2014; 190: 706-708

Case 5

- M/ 57
- CC: Fever
- PI : 3년 전 Colon ca로 수술 후 f/u 중 recur 소견으로
  FOLFOX(oxali, 5-FU, LV)으로 항암제 시작
  4C, #1 oxaliplatin 투여 중 fever 발생하여 항암제 중단 후
  fever 호전되면 나머지 항암제 (5-FU, LV)을 투여하는 과정을
  8C 시행 후 F/U CT에서 이상 소견으로 의뢰



Med Princ Pract 2012; 21: 89-92

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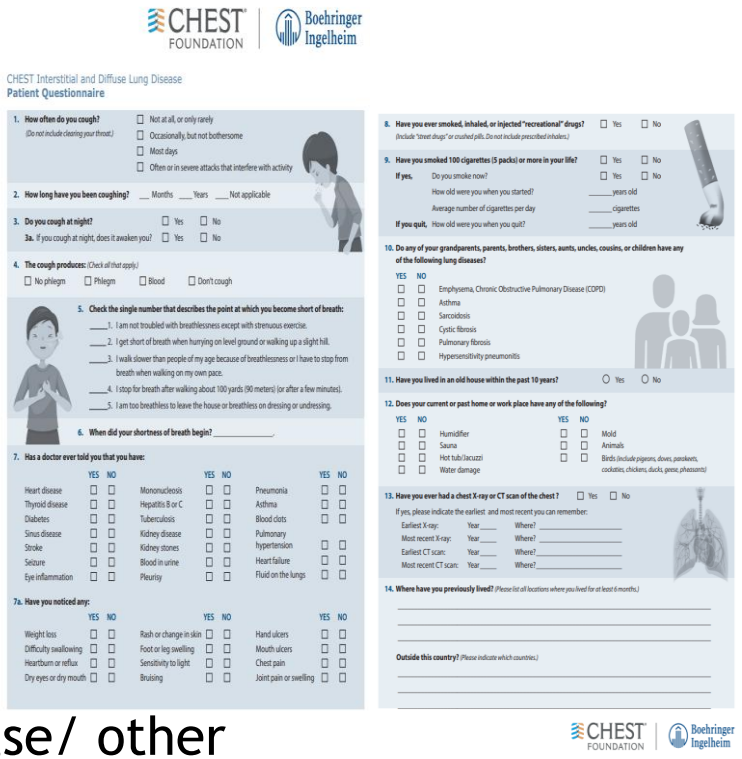
Clinical Evaluation

- Symptoms
  - Dyspnea
  - Cough, hemoptysis, wheezing
  - Associated symptoms
- Medical history
  - medications/ comorbidity (CTD)
- Smoking history
  - ever vs. never / how much
- Exposure history
  - home / work / avocational/infectious
- Family history
  - pulmonary disease/ autoimmune disease/ other

Duration of ILD
Acute (days to weeks)
AIP, AEP, Nonfibrotic HP, COP
Subacute (weeks to months)
Sarcoidosis, drug induced ILD, COP, CTD-ILD, alveolar hemorrhage
Chronic (months to years)
IPF, sarcoidosis, fibrotic HP



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Physical examination

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Laboratory Testing – Blood testing

- Biochemical tests to evaluate hepatic & renal function
- Hematologic test to check for evidence of anemia, polycythemia, leukocytosis, or eosinophilia
- Urinalysis
- ±hepatitis serology, HIV
- Rheumatology lab: ANA, RF, CCP, anti-synthetase Ab(Jo -1),
  anti-dsDNA, anti-Sm, anti-RNP,
  Sjogren's Ab (SS-A/B)
  Scleroderma Ab(Scl -70, centromere)
  CPK, aldolase, anti-MDA-5, overlap Abs
- Pulmonary hemorrhage lab: Anti GBM Ab, ANCA, ANA,
  Antiphospholipid Ab
- Serologic test for HP Ab based on potential Ag

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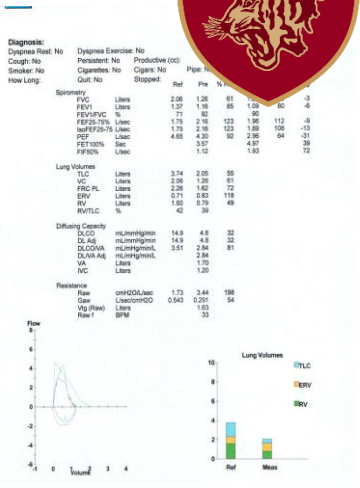
Laboratory Testing – PFT



- Assessment of the severity and pattern

- Restrictive defect
  : M/C, reductions in lung volumes ∝ dz progression
- Obstructive defect
  : Sarcoidosis, LAM/PLCH, HP, CPFE, constrictive bronchiolitis

- DL_{CO}
  : Reduction is common, but nonspecific
  not correlate well with dz Px, unless DL_{CO} <35%
  Longitudinal changes to assess dz progression or regression

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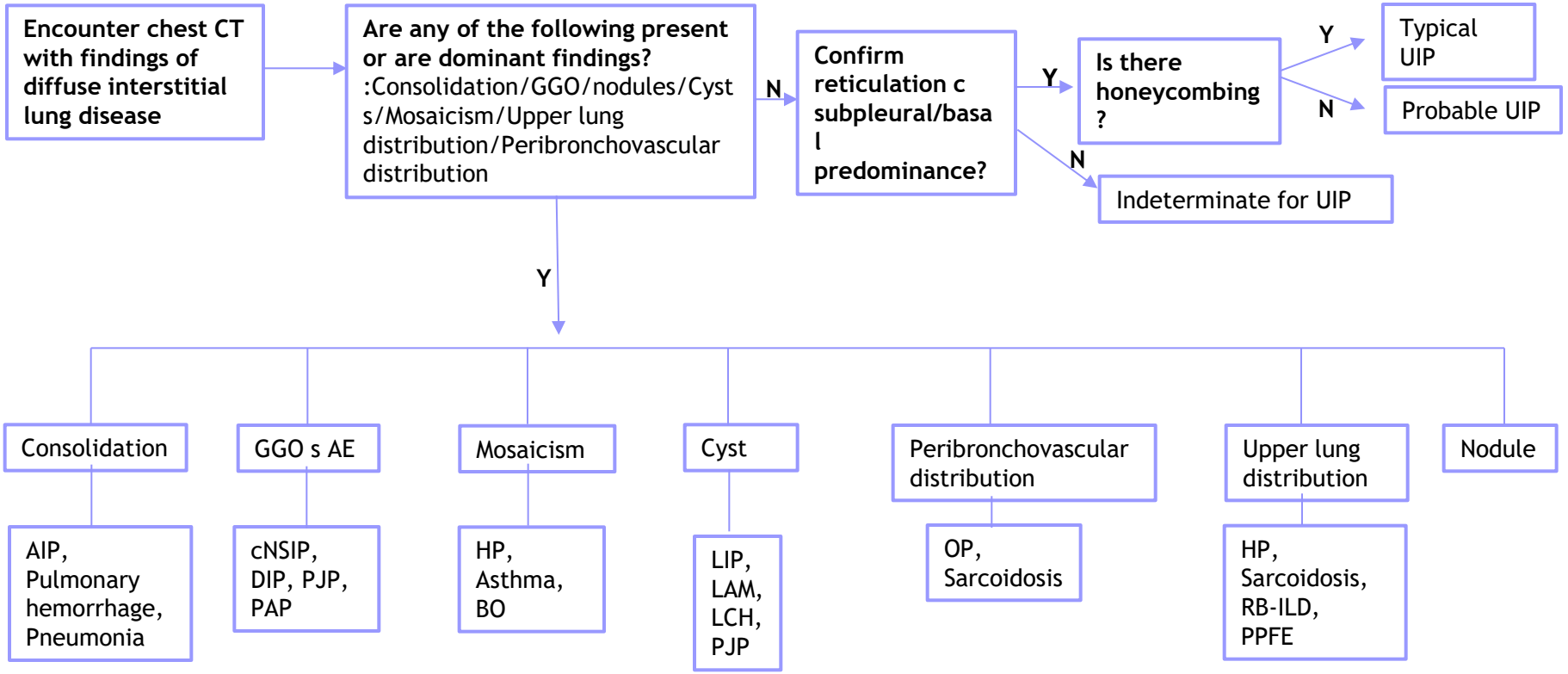
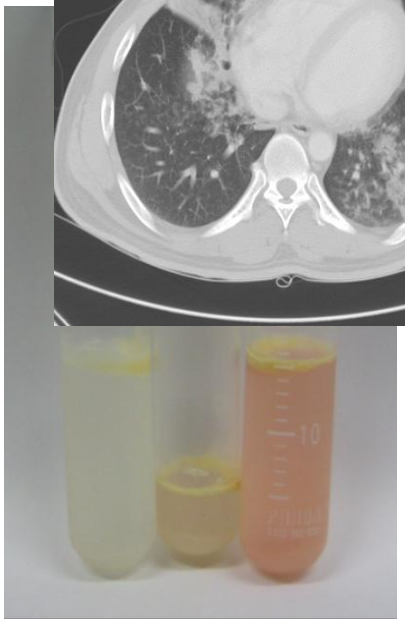
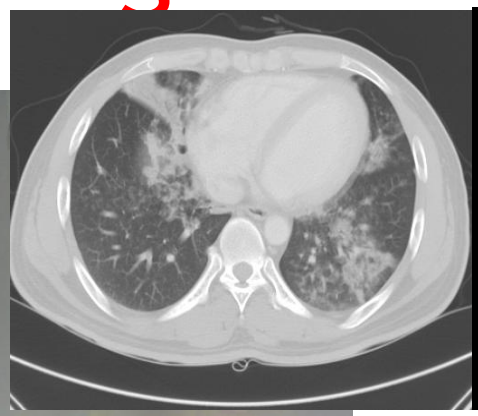
Laboratory Testing – Radiology assessment

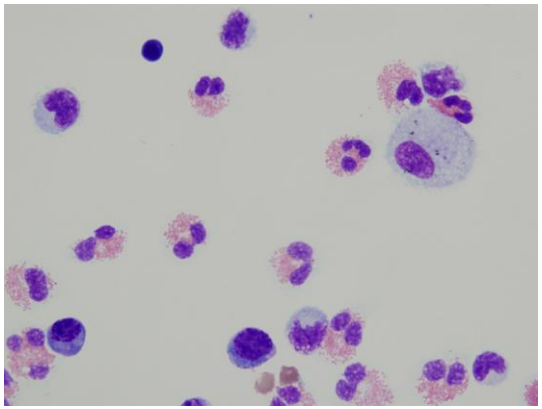


Clinical Imaging 2022; 88: 45-52

Laboratory Testing – Bronchoscopy 1







- Acute: acute EP, DAH, malignancy, infection
- Subacute/chronic
  : sarcoidosis, HP, PLCH, infection
- No established role in the assessment of progression/response to Tx

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Laboratory Testing – Bronchoscopy 2

I. Normal Adults (Nonsmokers)	BAL Differential Cell Counts
Alveolar macrophages	>85%
Lymphocytes (CD4+/CD8+ = 0.9–2.5)	10–15%
Neutrophils	≤3%
Eosinophils	≤1%
Squamous epithelial*/ciliated columnar epithelial cells†	≤5%

Lymphocytic cellular pattern	Eosinophilic cellular pattern	Neutrophilic cellular pattern
>15% lymphocytes	>1% eosinophils	>3% neutrophils
Sarcoidosis	Eosinophilic pneumonias	Collagen vascular diseases
Nonspecific interstitial pneumonia (NSIP)	Drug-induced pneumonitis	Idiopathic pulmonary fibrosis
Hypersensitivity pneumonitis	Bone marrow transplant	Aspiration pneumonia
Drug-induced pneumonitis	Asthma, bronchitis	Infection: bacterial, fungal
Collagen vascular diseases	Churg-Strauss syndrome	Bronchitis
Radiation pneumonitis	Allergic bronchopulmonary aspergillosis	Asbestosis
Cryptogenic organizing pneumonia (COP)	Bacterial, fungal, helminthic, *Pneumocystis* infection	Acute respiratory distress syndrome (ARDS)
Lymphoproliferative disorders	Hodgkin's disease	Diffuse alveolar damage (DAD)

Am J Respir Crit Care Med 2012; 185: 1004-1014

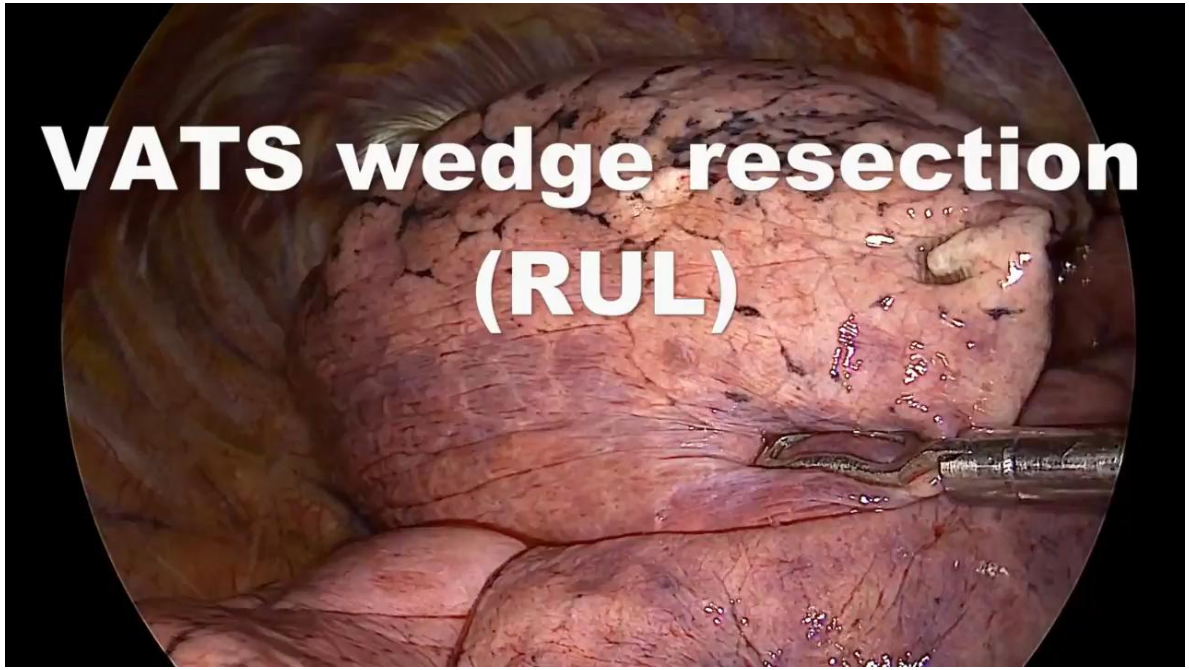
Laboratory Testing – Bronchoscopy 3

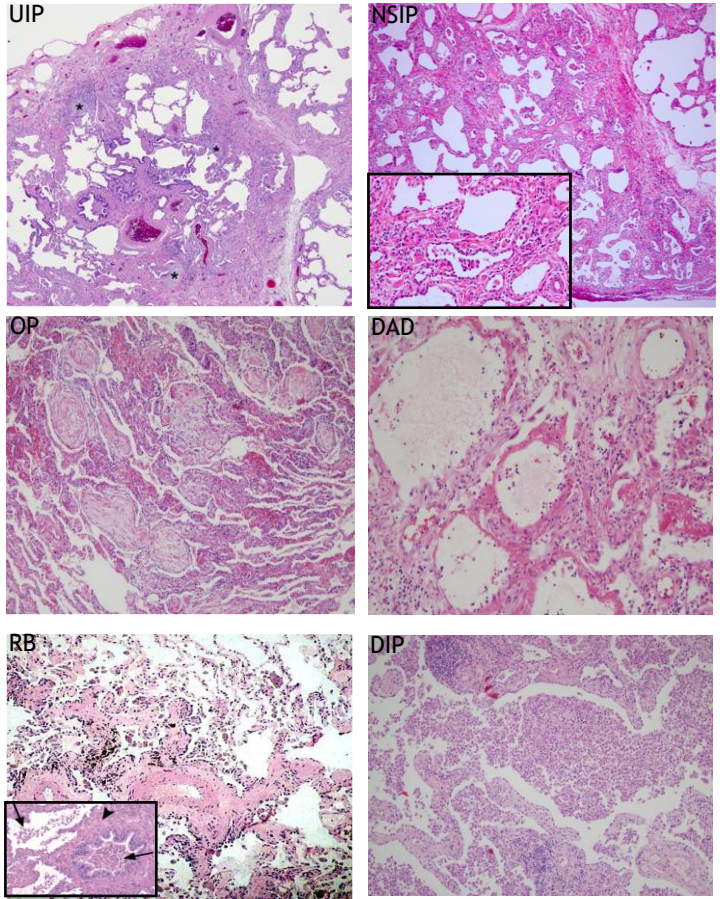
Condition	Bronchoalveolar lavage (BAL) finding
Acute interstitial pneumonia(AIP)	Neut ↑↑
Idiopathic pulmonary fibrosis(IPF)	AM ↑ Neut ↑
Desquamative interstitial pneumonia(DIP) / Respiratory bronchiolitis-ILD	AM (heavily pigmented) ↑↑
Organizing pneumonia	AM ↑, lymph ↑, Neut ↑
Eosinophilic pneumonia	Eosino > 25%
Sarcoidosis	Lymph ↑↑, CD4:CD8 ratio> 3.5
Hypersensitivity pneumonitis	Lymph ↑↑
Diffuse alveolar hemorrhage	Hemosiderin-laden macrophages, red blood cells
Diffuse-induced pneumonitis	Variable Lymph/ Neut
Pulmonary infections	Neut (suppurative, bacterial) ↑↑, Lymph (viral) ↑↑, Eosino (parasitic) ↑↑
Lymphangitic car, avelolar cell car, pul. lymphoma	Malignant cells
Pulmonary alveolar proteinosis	Cloudy BAL fluid c milky to light brown appearance, PAS+ amorphous debris
Lipoid pneumonia	Oily layer on surface of BAL fluid, lipid-laden macrophages
Pulmonary Langerhans' cell histiocytosis	Increased CD1+ Langerhans' cells > 5%
Asbestosis-related pulmonary dz	Dust particles, ferruginous bodies

Am J Respir Crit Care Med 2012; 185: 1004-1014

Laboratory Testing – Lung Biopsy

- TBLB/C, VATS Bx, thoracotomy





Laboratory Testing – Lung Biopsy (TBLC)

- Observational, retrospective cohort study
  2011.3 -2017. 9, Single center(Italy), 699 ILD pt
  Deeply sedated, Intubated c a rigid tracheoscope
  under fluoroscopic guidance + Fogarty balloon for bleeding
  → 3.3 Bx/pt, 4.57mm (shortest axis)
  Diagnostic yield: 87.8(pathological) ~90.1% (MDD)
  ↑ different sites(than 1 site)
  ↓ FVC <50%, DLCO <35%
  Cx: PNX(19.2%, 134)→ chest tube (70%, 94)
  bleeding(12.4%, 87) (mild 29/moderate 53/severe 5)
  death (0.4%, 3)

BMC Pulmonary Medicine 2019; 19: 16

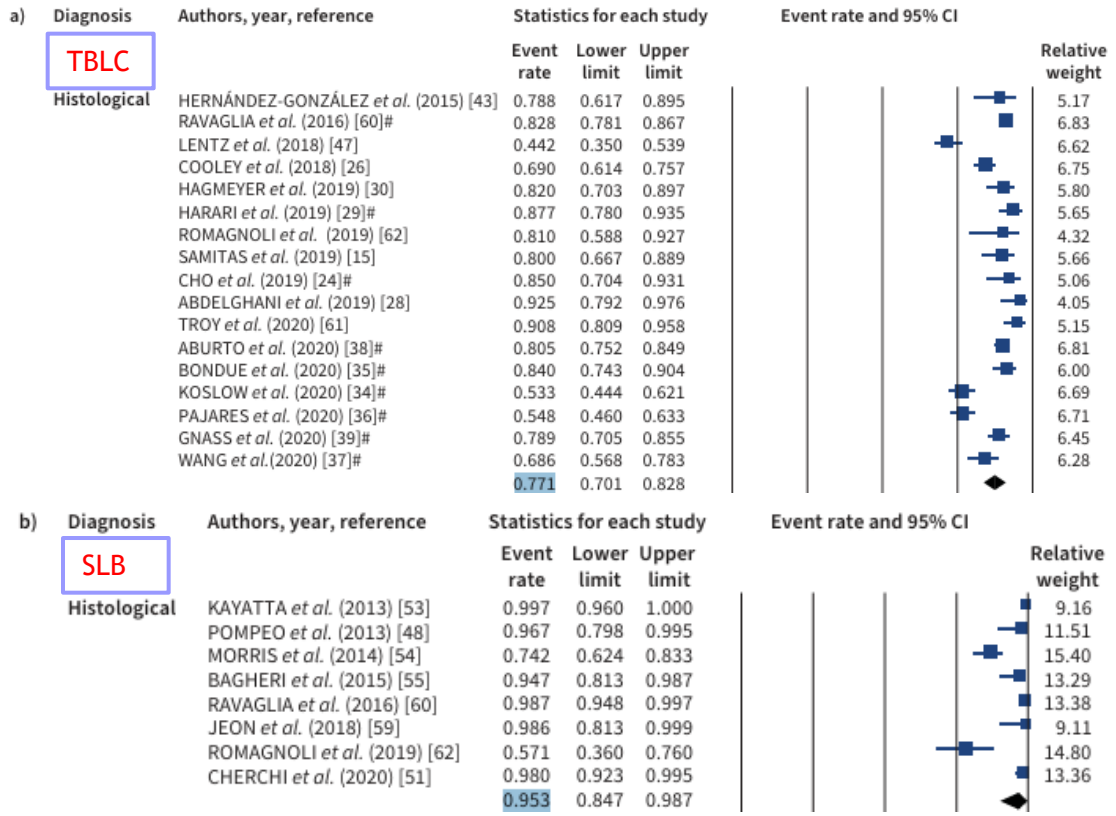
Laboratory Testing – Lung Biopsy (TBLC)

- CHEST Guideline and Expert Panel Report
  - TBC can be used to provide Bx for MDD Dx (weak, very low quality)
    Diagnostic yield: 80% for TBC vs 95% for SLB
  - At least 2 different sites (weak, low quality)
  - Bx with the tip of the cryoprobe located 1cm from the pleura
    (consensus-based statement)
  - Use of fluoroscopy (consensus-based statement)
  - Bronchial blocker either through an endobronchial tube
    or rigid bronchoscope(consensus-based statement)
  - Small cryoprobe(1.9mm) rather than a large cryoprobe(2.4mm)
    (consensus-based statement)

Chest 2020 ; 157: 1030-1042

Laboratory Testing – Lung Biopsy (TBLC)

- 2010.10~2020.10, 43 Studies(n=4550), TBLC(n=2824), SLB(n=1814)



TBLC
- Bleeding
  - mild (29.9%)
  - moderate (9.1%)
  - severe (1.6%)
- PNX 9.2%
  (chest drainage 5.6%)

SLB
- recurrent/persistent
  PNX 5.5%
- pneumonia/empyema 2.1%

30-day mortality
TLBC 0.6% vs SLB 1.7%

Eur Respir Rev 2022 ; 31: 210280

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Diagnostic Process

Perform Hx & P/Ex, including assessment of:

- Sx onset (acute/subacute/chronic)
- Occupational & Environmental exposure Hx including smoking hx
- Hx of CTD
- Family Hx
- Medication Hx
- Hx of RTx/Cancer
- Signs of systemic inflammation & other extrapulmonary dz

Imaging: CXR, CT, compare results with any prior imaging to assess evolution or progression

PFT: compare results with any prior PFT to assess evolution or progression

Lab test:

- CBC, basic metabolic panel, LFT, U/A
  ANA, RF, CCP,
  appropriate other serologies (ANCA, CPK, Aldolase, myositis/antisynthetase Ab Panel,
  ds DNA, SSA/SSB,
  anti SLC 70/anti centromere)

UpToDate, May 2025

Are there any likely environmental or iatrogenic etiologies?
(drug toxicities (bleomycin, immune checkpoint inhibitors..), RTx,
Inhaled organics (hay, grains, humidifiers, indoor pool, feathers, molds),
Inhaled inorganics(silica, asbestos, beryllium, coal)

Y

- **Remove identified cause**
- **Temporary systemic glucocorticoid Tx may be appropriate, depending on Dz severity & etiology**

- **Is there clinical recovery?**

Y

No further Diagnostic steps are necessary

N

Does the patient have suspected extrapulmonary dz?
(CTD, vasculitis, extrapulmonary sarcoidosis)

Y

N

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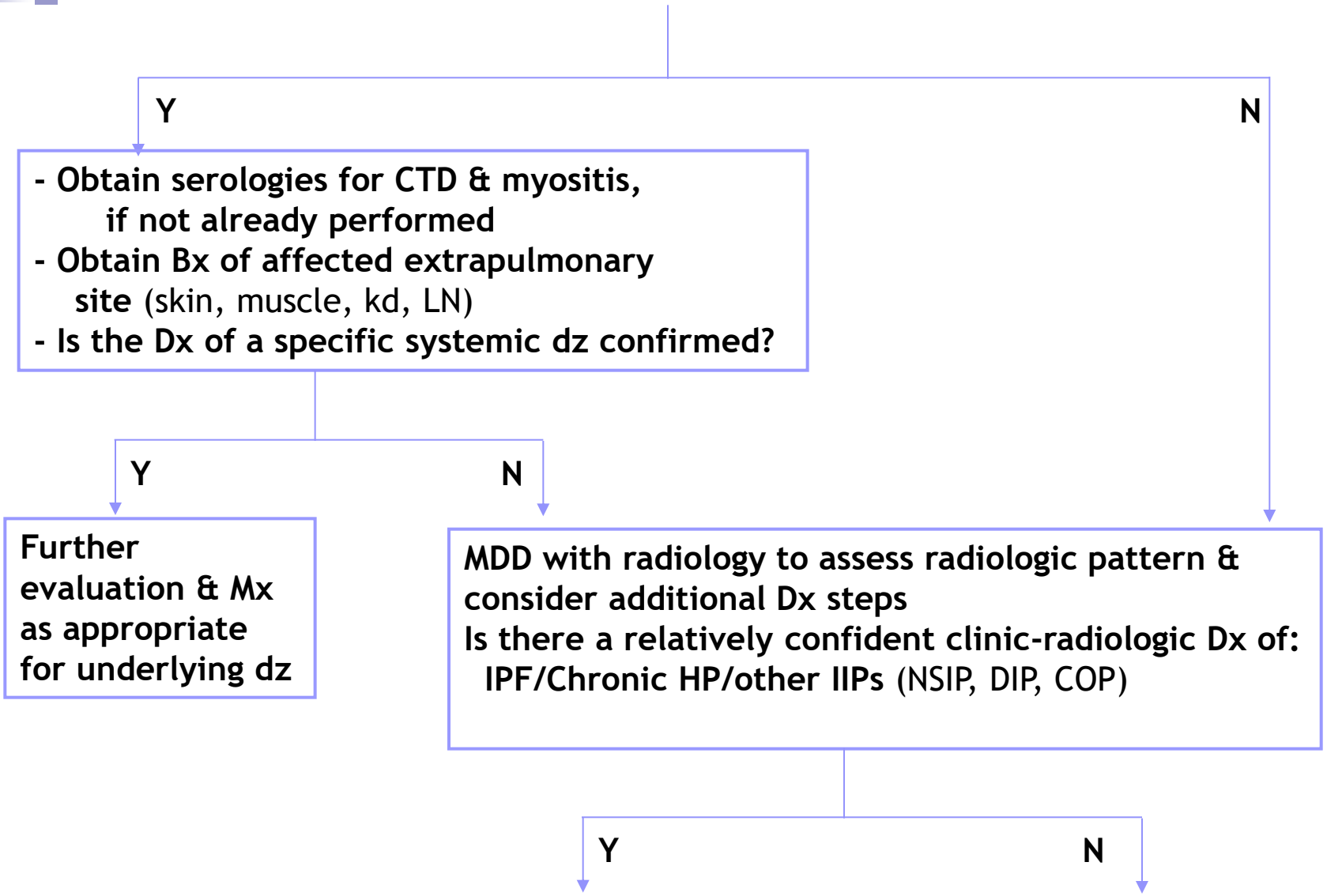
N



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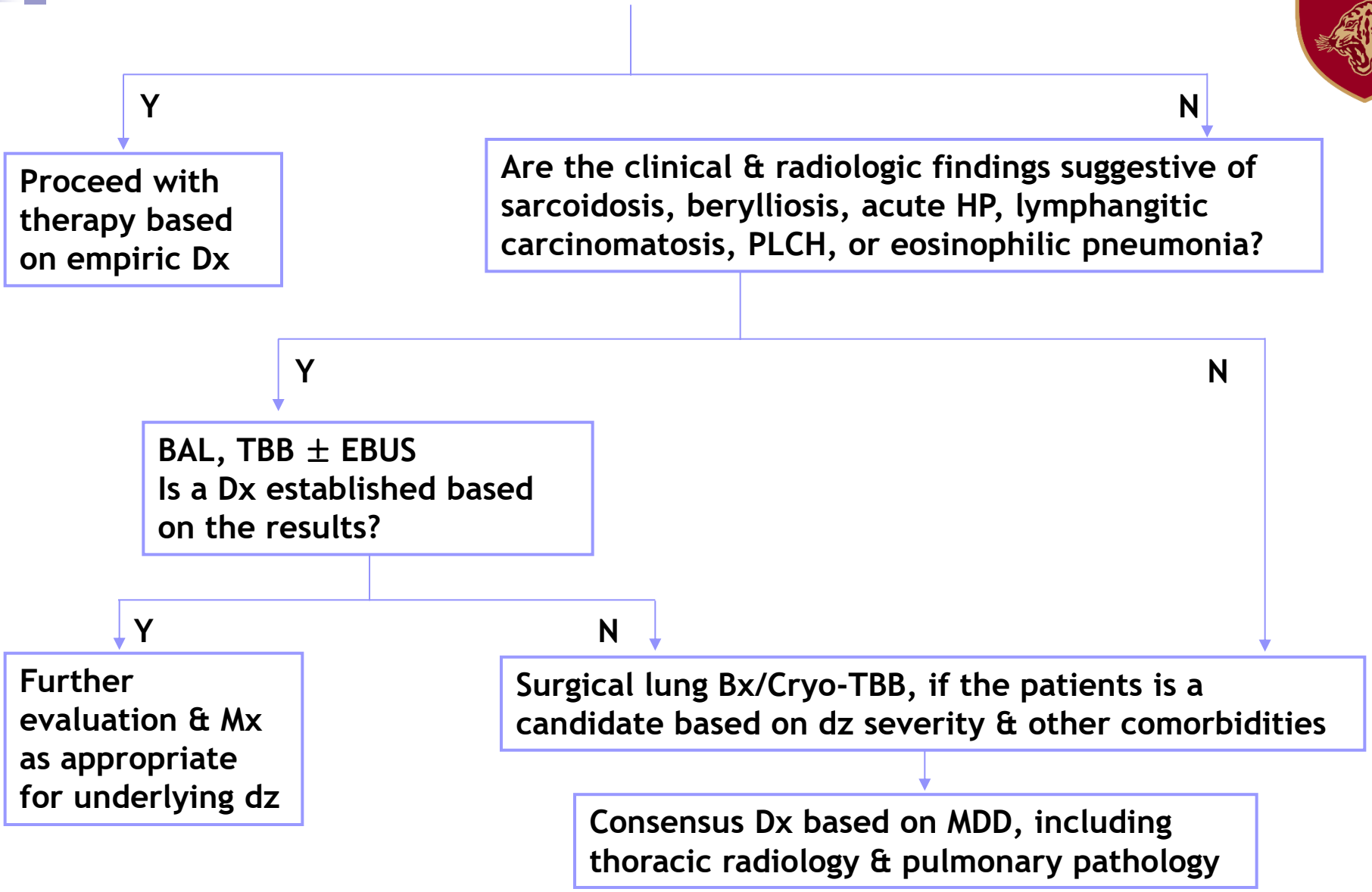

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Summary

- A history, physical examination, autoimmune serologies, and Chest CT are essential components of evaluation that should be performed in all pts presenting with a new ILD.
- BAL cellular analysis has a role in specific situations.
- The most important distinction in ILD classification is between IPF and non-IPF ILDs.

Summary

- All available data should be considered within a multidisciplinary discussion, which is considered the gold standard for ILD Dx and can provide additional information on the anticipated disease behavior and expected response to therapy.

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