Hypersensitivity pneumonitis:
Update of Practice Guideline for ILD

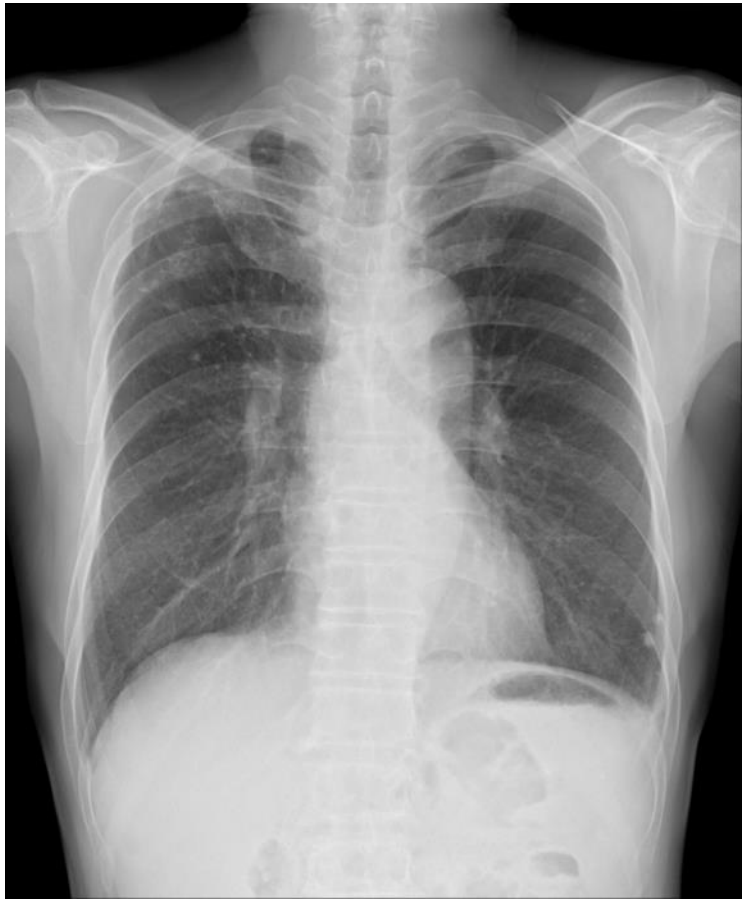
2021. 06. 05

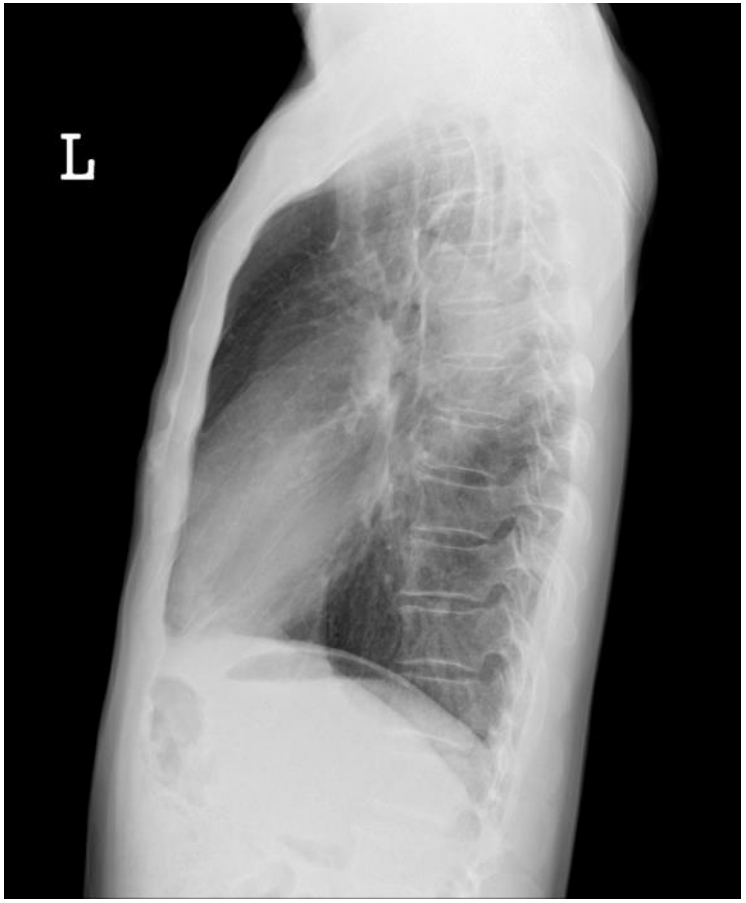
고려의대 안암 병원
이은주

Case 1

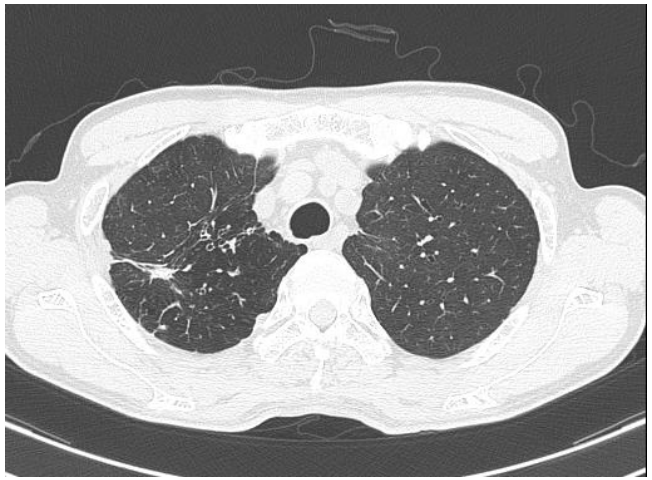
- M/ 66
- CC: Dyspnea, mMRC 2 (onset: 20 days ago)
- PI : gastric cancer로 본원 f/u 중인 분으로
  최근 20일 전부터 발생한
  호흡 곤란을 주소로 내원
- 애너멜 코팅 공장 (중국, 내원 2개월 전부터)
- smoker : 1* 40 PY
- 애완동물/가구(-/-)
  중국 거주, 2달 전에 최근 공장으로 이직

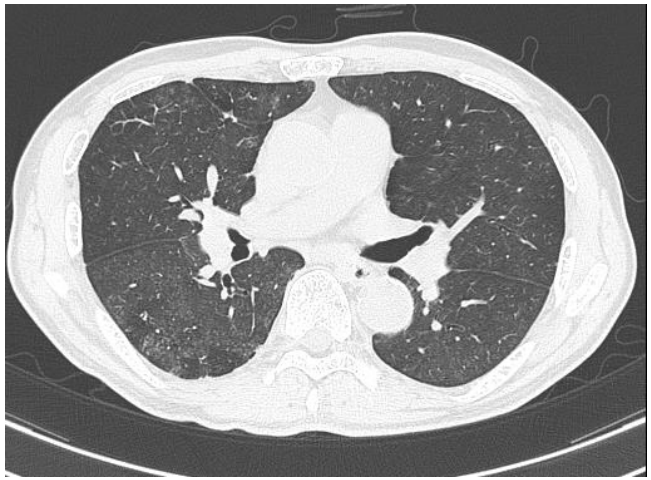
CXR (2014.2.9)

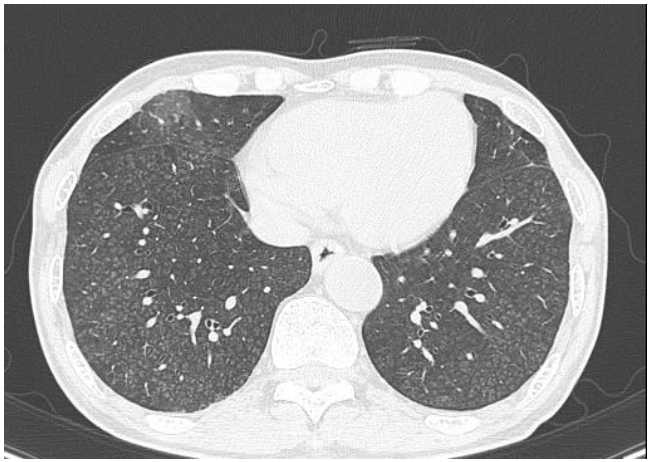


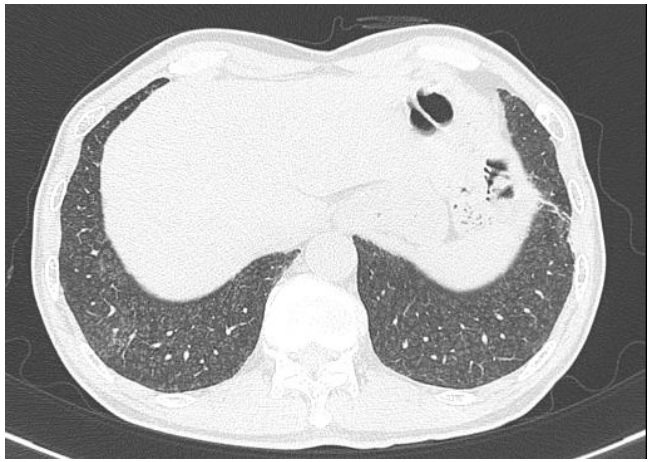


Chest CT (2014.1.28)









Bronchoscopy

- BAL Fluid (RML, lateral segment)

  : clear

  WBC: 390 (/μL)

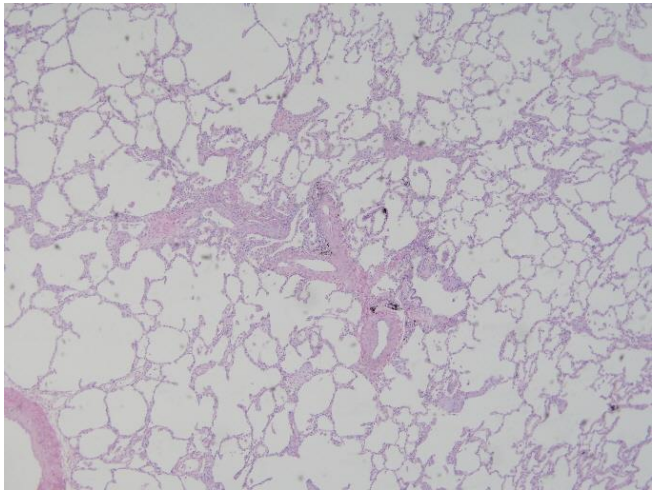
  (Neutro: 1%, Lympho: 82%, Eosino: 1%,

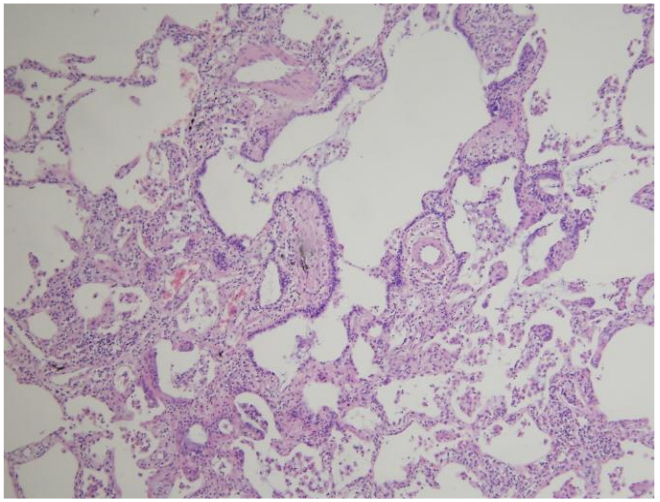
  Macrophage: 12%)

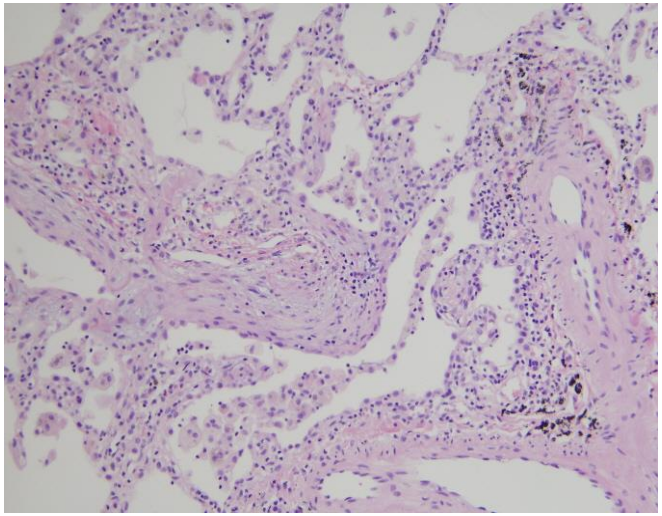
  CD4/CD 8 ratio : 0.07

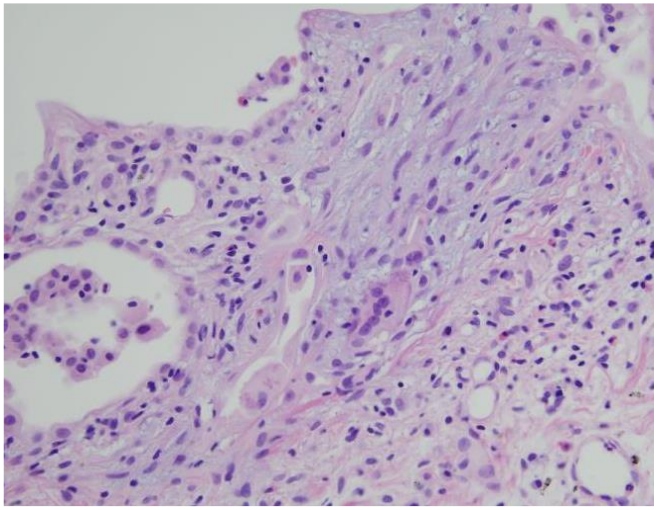
  G/S, AFB, Fungus, Virus: negative

VATS lung Bx(2014.02.12)





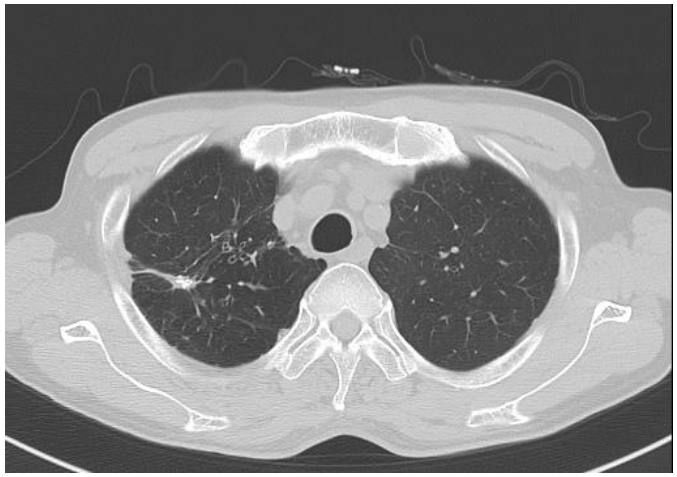


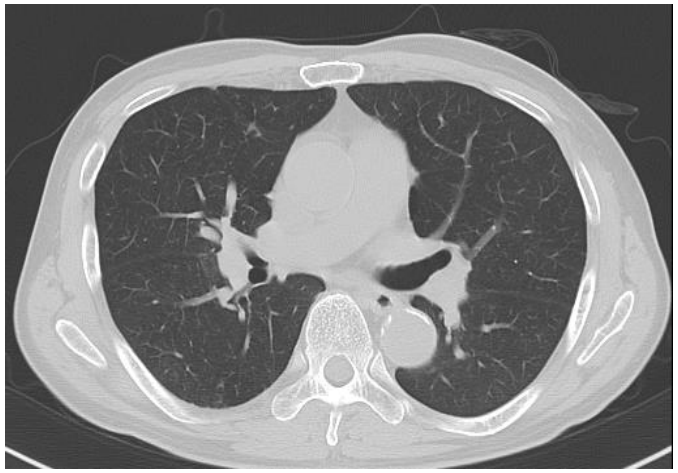


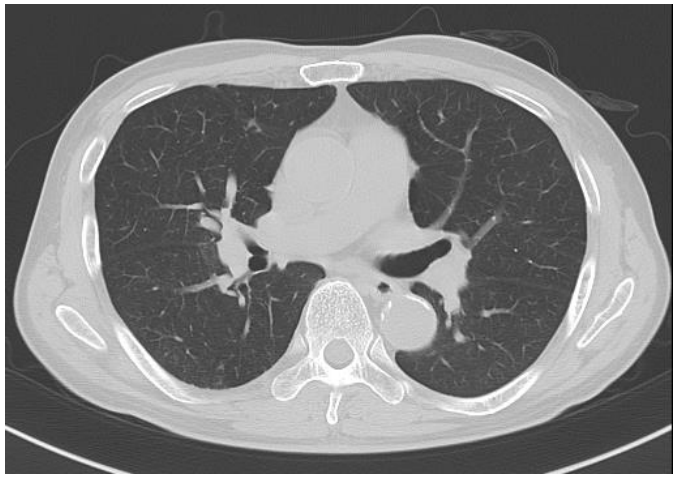
Progress

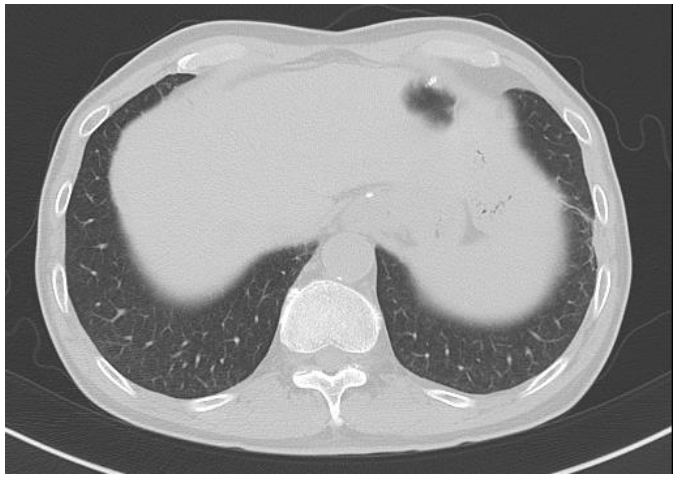
- Dx : HP, non-fibrotic
- Tx: 이직 고려
  solondo 0.5mg/kg start

F/U Chest CT (2014.5.13)









Case 2

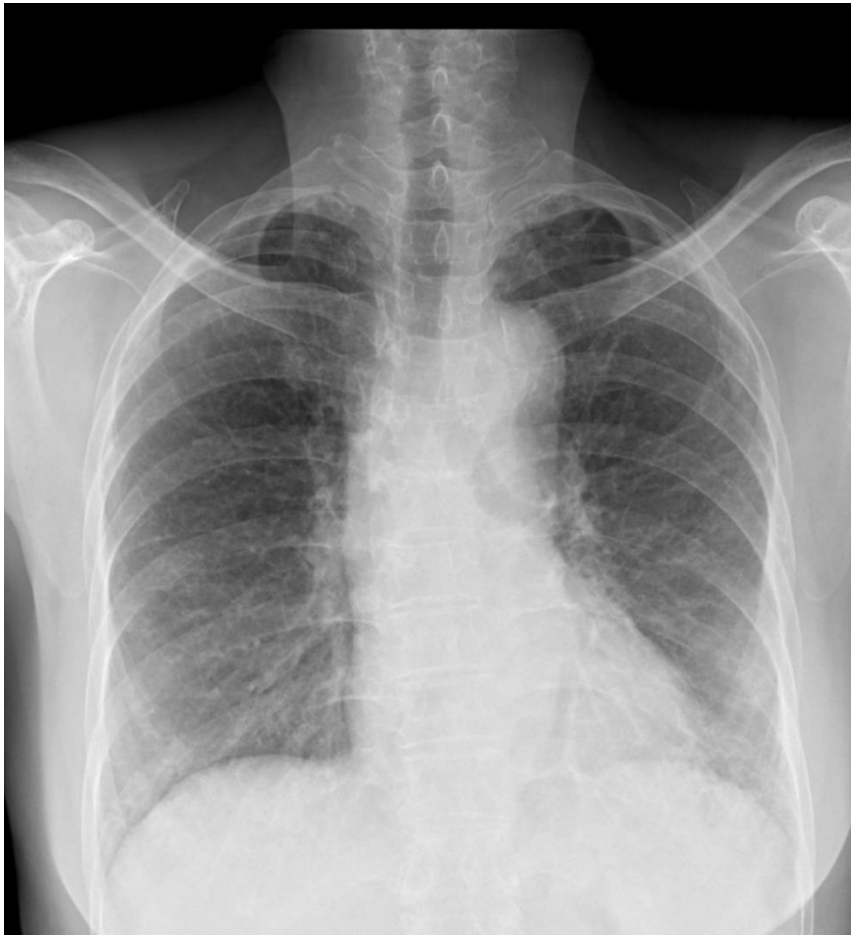
- F/ 64
- CC: Abnormal CXR
- PI : 한달 전 시행한 검진 CXR 이상으로 refer
- 주부
- Alcohol/ smoking (-/-)
- PHx : DM/HTN/TBc/hepatitis(-/+, 20년 전 진단/-/+, CHB carrier)
- 월곡동 햇볕 잘 드는 2층 양옥에서 10여년 넘게 거주
- 새로운 가구/ 애완 동물 /취미 생활 (-/-)

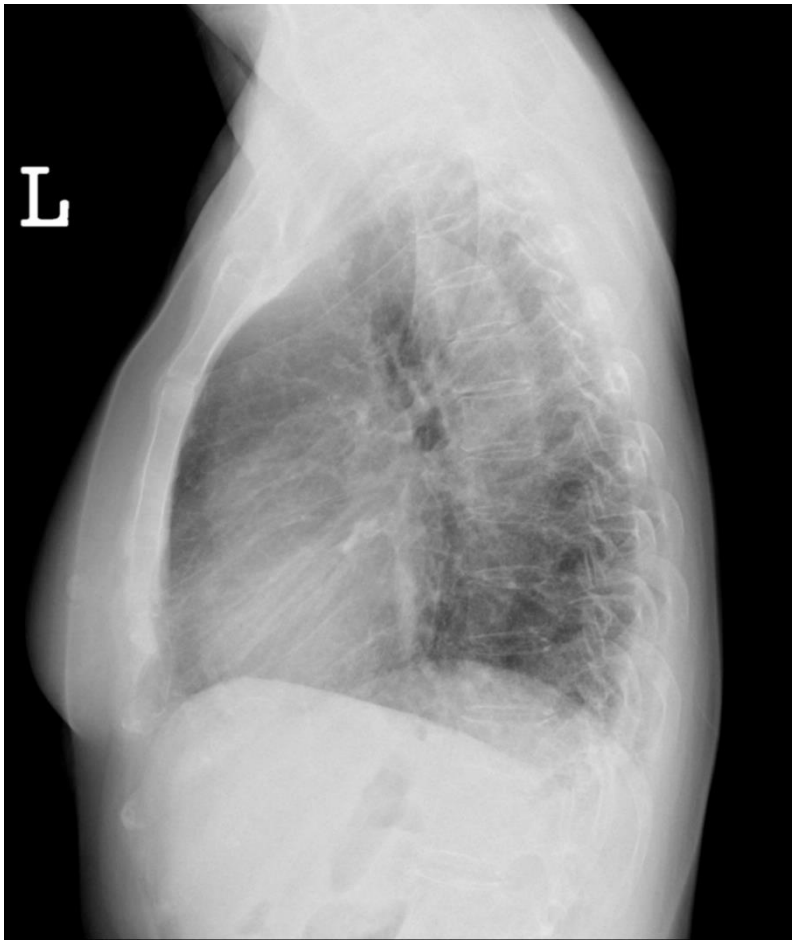
- ROS : C/S(-/-), dyspnea (-)
  rhinorrhea (+): clear
  arthralgia(-), dry mouth/eye(-/-),
  Raynaud phenomenon(-)
  peripheral cold feeling (+)
  skin rash(-), photosensitivity(-)

- P/Ex : V/S 130/90-110/min-24/min-36.8C
  coarse breathing sound with crackle on BLLF
  clubbing (-)

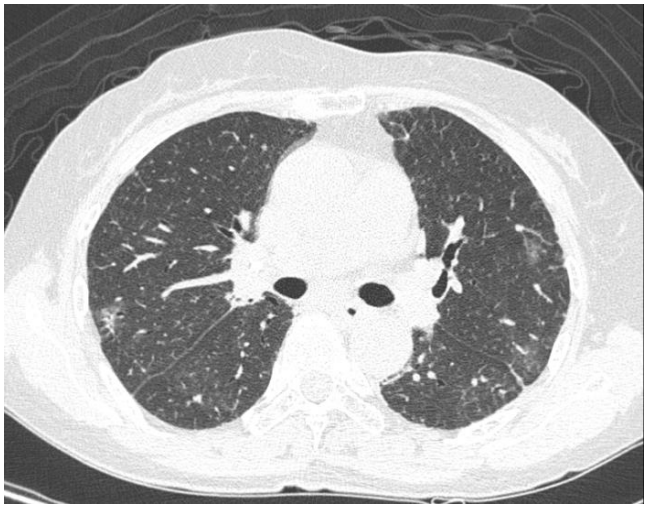
- Lab : Hb 12.5 g/dL – WBC 4400/μL - Plt 80k/μL
  ESR 66 mm/hr, CRP 1.4 mg/L
  LFT, BUN/Cr, e : WNL
  FANA, ANCA, C3,C4, Anti-ds DNA, Ig A/M/G : negative

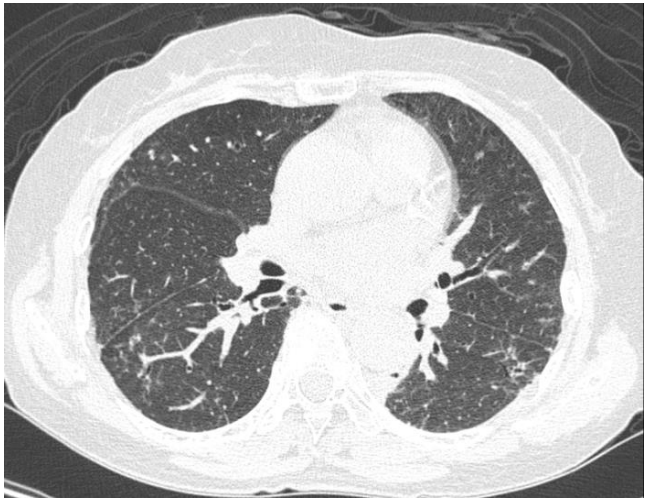
CXR (2010.1.21)

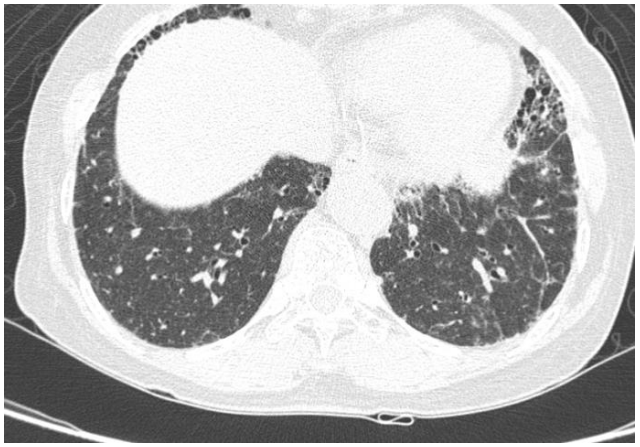


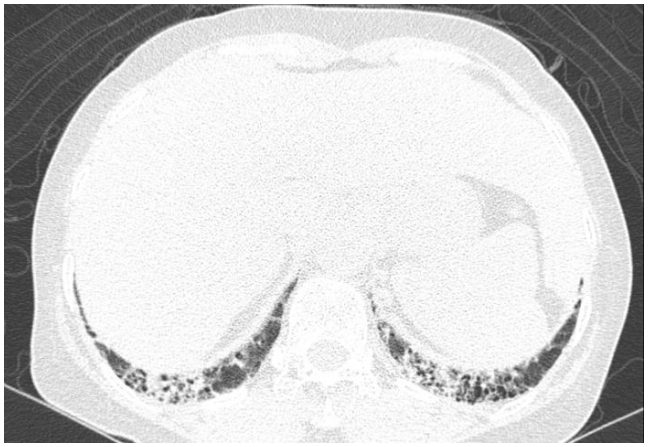


HR CT (2010. 02.04)

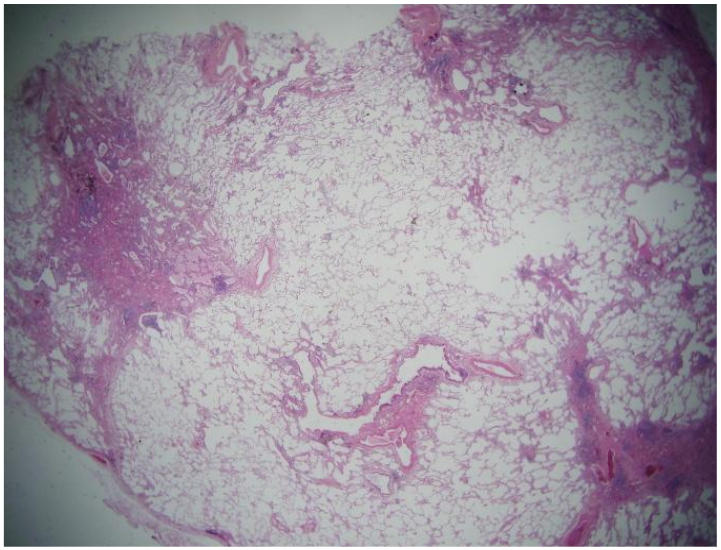


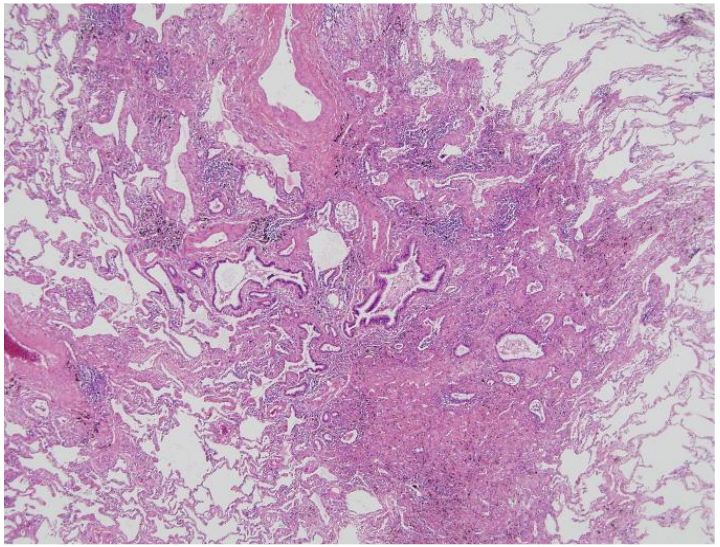


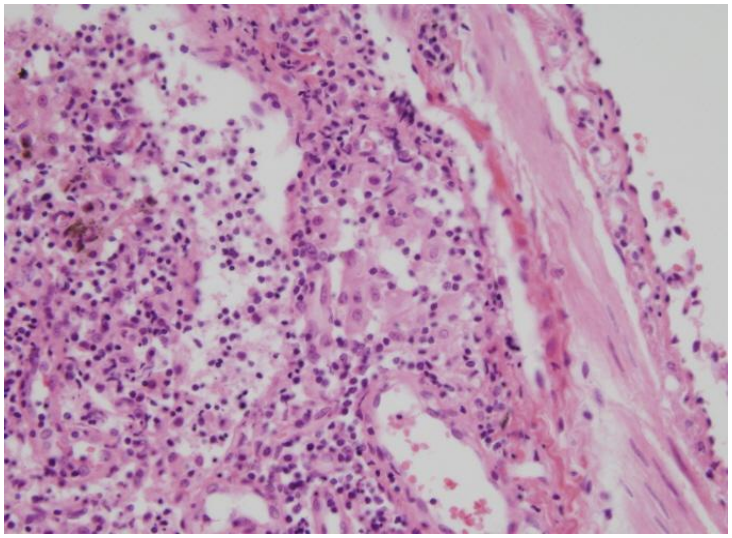


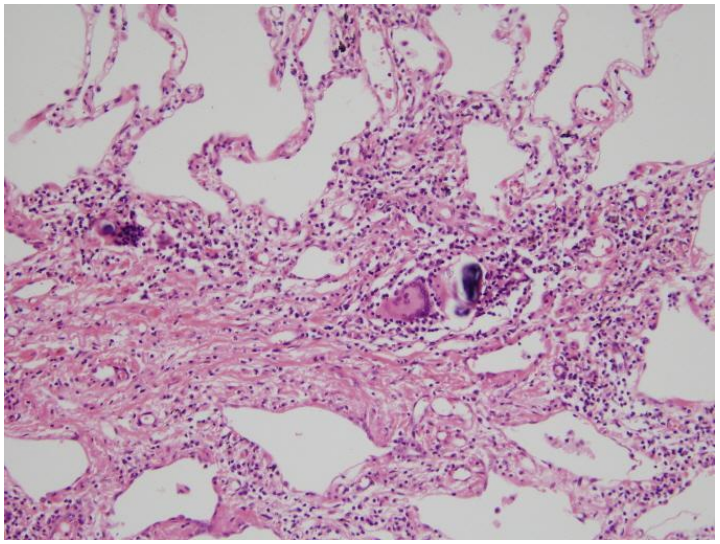


VATS lung Bx(2010.03.21)



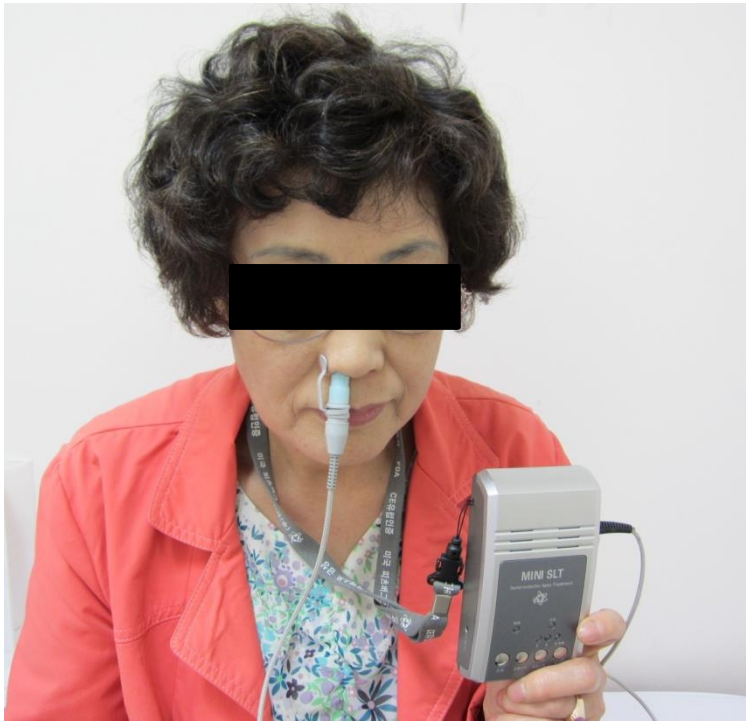






History

- 수개월 전부터 중국산 코에 넣는 레이저 기계 사용



Progress

- 중국산 기계 사용 하지 않도록 하고 외래 추적 관찰 키로 하던 중
  2010년 5월 이후 f/u loss 됨

- 2011년 4월 new onset cough/dyspnea 로 외래 다시 방문

  (이전에 사용하였던 중국산 레이저 기계는 지속적으로 사용하였다 함)

- 기계 사용을 중단(?) 하였으나
  호흡기 증상 악화 및 폐 기능 저하 진행

- 2017년 겨울 사망

Definition

- An inflammatory and/or fibrotic dz affecting the lung parenchyma & small airways

- Typically results from an immune-mediated rex provoked by an overt or occult inhaled Ag in susceptible individuals.

- Historically termed “extrinsic allergic alveolitis”

- First descriptions similar to HP appeared in 1713.
  (pt who worked with cereals)

  Farmer’s lung : 1932

  Mushroom worker : 1959

  Bird-breeder’s lung: 1960

Semin Roentgenol 2019; 54: 37-43

Am J Respir Crit Care Med 2020; 202: e36-e69

Clinical Manifestations-subtypes

- Acute, subacute, chronic
  : vaguely defined in the existing literature
  & not consistently associated with outcome.

- Fibrotic vs. Nonfibrotic HP
  : determined by the predominant presence or absence of
  radiologic and/or histopathological fibrosis
  more objective
  more consistently associated with the clinical course/outcome.

Am J Respir Crit Care Med 2020; 202: e36-e69

Classification-1

- A large prospective multicenter cohort study
- Cluster analysis (clinical Sx, Sn, PFT, CXR, CT, BAL, Blood)

Cluster	Richerson's classification			Total
	Acute	Subacute	Chronic	
1	21	7	13	41
2	7	18	102	127
Total	28	25	115	168

- Cluster 1 : more recurrent Sx (chill, body aches), normal X ray
  Cluster 2 : more clubbing, hypoxemia, restrictive PFT, fibrosis

- Subacute HP is difficult to define.

Int Arch Allergy Immunol 2009; 149: 161-166

Classification-2

	Clinical Behavior	Typical HRCT pattern	Histopathology pattern
Acute HP **:Sx duration < 6 m**	- Most reversible - Complete resolution possible - Sx related to exposures to the HP induced, which can resolved completely after further avoidance	Upper- & middle-lobe predominant GGO, poorly defined centrilobular nodules; mosaic attenuation, air trapping or, rarely, consolidation	Inflammatory (cellular) HP **lymphoplasmocytic/mononuclear (MΦ) infiltrates** **Airway-centric lymphocytic infiltrates/peribronchiolar** **Poorly/loosely formed granulomas** **Multinucleated giant cells** **NSIP cellular-like**
Chronic HP **:Sx duration > 6m**	- Potentially reversible to some extent - Risk of progression	Upper- & middle-lobe predominant fibrosis, peribronchovascular fibrosis, honeycombing, mosaic attenuation, and centrilobular nodules, relative sparing of the bases	Fibrotic HP **UIP-like** **NSIP fibrotic-like** **Airway-centered fibrosis, NOS** **Unclassifiable** **Histopathologic Sn of inflammatory HP can be present on the background of fibrosis**

Am J Respir Crit Care Med 2017;196:680-689

Clinical Manifestations-Sx, Sn, Px

- Dyspnea, cough, mid-inspiratory squeaks
  wt loss, flu-like Sx(chills, fever, malaise), chest tightness,
  wheezing
  acute vs. insidious
  may recurrent

- Poor Px
  : fibrotic HP (UIP like pattern), smoker, lower baseline VC,
  lack of BAL lymphocytosis,
  persistent exposure to the inciting Ag,
  inability to identify an inciting Ag

Am J Respir Crit Care Med 2020; 202: e36-e69

Clinical Manifestations-Epidemiology

- Prevalence of HP varies c regional disparities in climate, occupational exposures and environmental exposures.

  Highest among older individuals

  (> 65 yrs, mean Dx age (fifth or sixth decade))

- Incidence : 0.3-0.9 / 100,000

  4.9 – 54.6 / 100,000 bird breeders

  1.67-2.71/100,000 (USA, insurance based analysis)

Am J Respir Crit Care Med 2020; 202: e36-e69

Pathogenesis-Immunological dysregulation

- Humoral (Ag specific IgG)
  + Cellular (T helper cell type 1) immune responses.

  → lymphocytic inflammatory pattern
  + granulomatous inflammation

- Neutrophilic inflammation may play a role early in the dz course & during subsequent fibrosis.
- Th1 → Th2 contribute to pulmonary fibrosis.

- Genetic susceptibility
  : polymorphisms in MHC II, proteasome, transporter protein, MUC5B…

Am J Respir Crit Care Med 2020; 202: e36-e69

Pathogenesis-Inciting Ag

Table 2. Sources of Antigens Known to Cause HP

Matter	Typical Sources	HP "Disease"
Organic particulate matter		
I. Microbes		
Fungi/molds		
Aspergillus spp.	Contaminat	
Alternaria alternata, *Aureobasidium* spp.	Contaminat	
Botrytis cinerea	Upholstere	
Cephalosporium spp.	Contaminat	
Cladosporium spp.	Contaminat	
Cryptococcus spp.	food-proc	
Fusarium spp.	Organic wa	
Graphium spp.	Contaminat	
Mucor spp.	Moldy woo	
Penicillium spp.	*Aspergillus*	
Rhizopus spp.	Contaminat	
Trichoderma spp.	cooling s	
Phytase (enzyme from *Aspergillus* or *Trichoderma*)	Potted flow	
	Mold on gra	
	Contaminat	
	Contaminat	
	Peat	
Yeasts		
Candida spp.	Contaminat	
Geotrichum candidum	humidifier	
Saccharomyces cerevisiae	Moldy hay,	
Saccharomonospora viridis	Contaminat	
Saccharopolyspora rectivirgula	Contaminat	
Torulopsis glabrata	Human inte	
Trichosporon cutaneum	Milk mold	
	Baker's yea	
	Contaminat	
	Dried grass	
	Compost	
	Mushrooms	
Edible mushrooms		
Mushrooms (shiitake, bunashimeji, *Pleurotus*, *Pholiota*, *Lyophyllum*, *Agaricus*)	Mushrooms	
Bacteria		
Acinetobacter spp.	Contaminat	
Bacillus spp.	Contaminat	
Klebsiella spp.	Sewage tre	
Nontuberculous mycobacteria	Sawdust	
Phoma spp.	Moist wooc	
Pseudomonas spp.	Detergents	
Stenotrophomonas spp.	Biological c	
Staphylococcus spp.	Washing pc	
Streptomyces spp.	Contaminat	
Thermoactinomyces spp.	Moldy plant	
Endotoxin from pool-water sprays and fountains	Contaminat	
	Moldy show	
Acarus siro	Contaminated cheese	—
II. Proteins/enzymes		
Animal proteins		
Animal fur dust	Animal pelts	Furrier's lung
Avian droppings, serum, and feathers	Parakeets, canaries, budgerigars, pigeons, parrots, chicken, turkeys, geese, ducks, wild birds, pheasants	Bird fancier's disease, bird breeder's disease, pigeon breeder's lung, chicken breeder's lung
Avian feathers	Feather beds, pillows, duvets	Feather-duvet lung
Bats	Contact with bats	—
Carmine (from *Coccus cacti*)	Food and cosmetics	Carmine alveolitis, dyer's lung
Cow milk	Cow milk	Heiner syndrome
Fish feed	*Daphnia*, meat, mosquito larvae	Fish-feed alveolitis
Fish meal	Animal feed	Fish-meal alveolitis
Shell protein (oyster, sea snail, mussels)	Oyster-shell powder	Shellfish alveolitis, oyster-shell HP, mollusk-shell HP
Pig pancreas	Animal extracts	—
Pituitary proteins	Pituitary powder	Pituitary snuff-taker's lung
Rat and desert mouse (gerbil) urine, serum, pelts	Rats, gerbils	Alveolitis due to rat and mouse proteins
Silkworm proteins	Dust from	
Weevils (corn, wheat) (*Sitophilus* spp.)	Contamina	
Plant proteins		
Alginate	Seaweed	
Argan cake	Cosmetics phytoste	
Catechin	Green-tea	
Esparto dust	Esparto gr	
Grain flour (wheat, rye, oats, maize)	Flour dust	
Malt	Food-proc	
Legumes (soy)	Legumes (	
Paprika	Paprika du	
Pyrethrum	Plant-base	
Spinach	Spinach p	
Tiger nut	Horchata (	
Wood (cabreuva, cedar, mahogany, pine, ramin, umbrella pine)	Wood part	
Inorganic particulate matter		
I. Chemicals		
Acid anhydrides (pyromellitic and trimellitic anhydrides)	Polyuretha elastome car parts, shoes, imitation leather, rubber products, chipboards, elastic synthetic fibers, electrical insulations	
Acrylate compounds (methyl methacrylate)	Dental materials, lacquer, resin, glues	Methacrylate alveolitis
Copper sulfate	Copper-sulfate Bordeaux mixture	Vineyard sprayer's lung
Chloroethylene (trichlorethylene)	Degreasing agents, cleaning agents, extraction agents	Chemical alveolitis
Dimethyl phthalate and styrene	Industrial solvents, plasticizers	—
HFC-134a	Coolant fluid in laser hair-removal devices	Hair-remover lung
Isocyanates (toluene diisocyanate, methylene diphenyl diisocyanate, hexamethylene diisocyanate, MIC, NDI, polyisocyanate)	As in acid anhydrides	Isocyanate alveolitis
Tetrachlorophthalic and hexahydrophthalic acid	Hardener for epoxy resin	Acid anhydride alveolitis
Sodium diazobenzene sulfate	Laboratory reagent, chromatography	Chemical alveolitis
Triglycidyl isocyanurate	Polyester powder (powder paints)	Painter's lung
II. Pharmaceutical agents		
Penicillins, cephalosporins	Antibiotics	Drug-induced HP
Methotrexate	Immunosuppressive agents	
α-IFN	Immunomodulatory agents	
Lenalidomide	Hypolipidemics	
Pravastatin	Antidepressants	
Venlafaxine	Alkylating agents	
Temozolomide		
III. Metals		
Cobalt	Hard metals, alloys	Giant cell pneumonitis
Zinc (tungsten and alloys)	Zinc fumes	Zinc-fumes alveolitis
Zirconium	Zircon	Zirconium alveolitis
Beryllium	Batteries, computers, neons	Beryllium HP
TMI	Organometallic compound for semiconductors used in industry	—

Am J Respir Crit Care Med 2020; 202: e36-e69

Antigen Detection

- The use of a standardized questionnaire as an aide may be very useful. But it should be validated before using in routine clinical practice.

- Check the presence of serum specific IgG

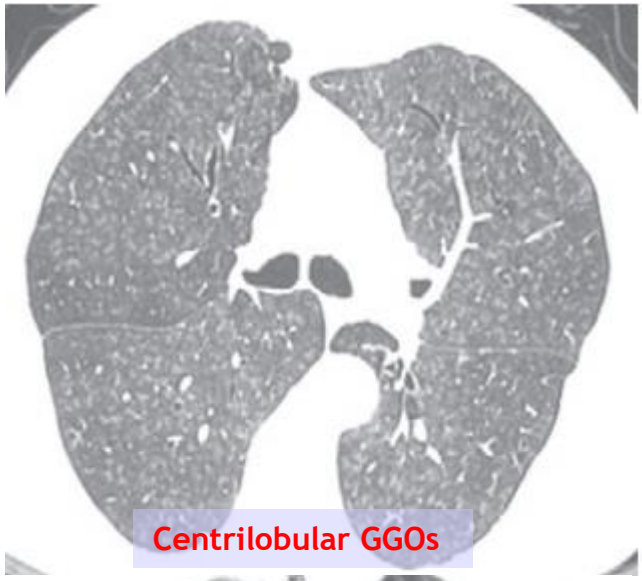
- Specific inhalation challenge
  : direct challenge with inhalation → to confirm an etiology
  not standardized/validated
  requires experienced personnel and laboratories

- Environmental sampling (ledge, fluid tank, carpet, wall board..)

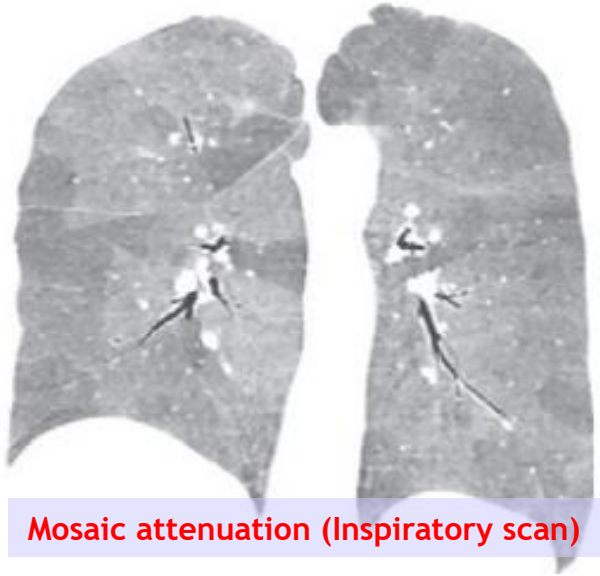
Respiratory Medicine 2016; 112: 97-105

Am J Respir Crit Care Med 2017;196:680-689

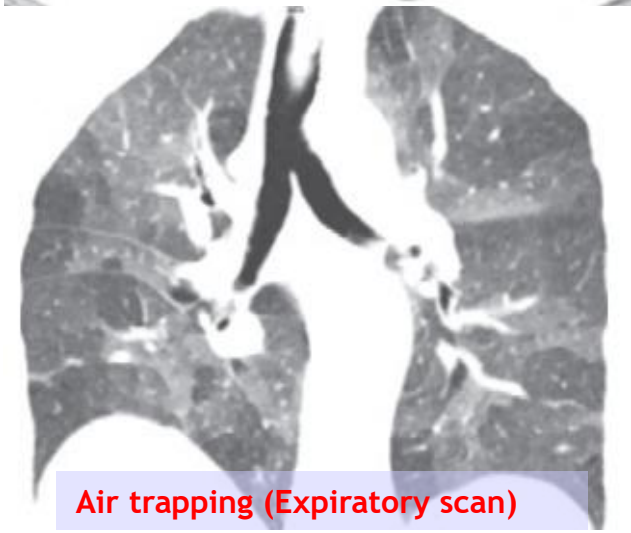
Radiologic Features-1 (Nonfibrotic)



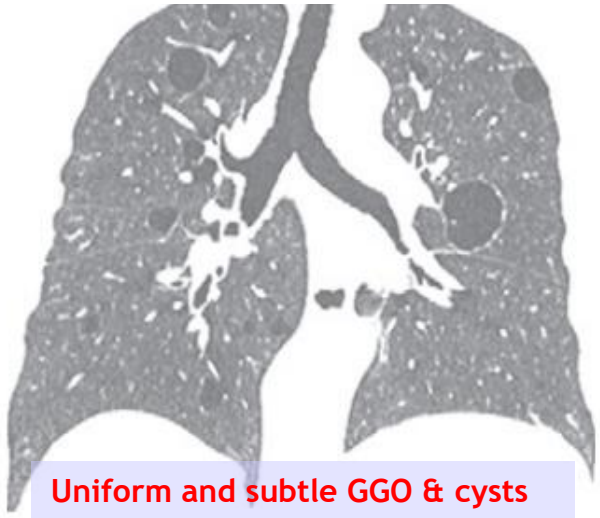
Centrilobular GGOs



Mosaic attenuation (Inspiratory scan)



Air trapping (Expiratory scan)



Uniform and subtle GGO & cysts

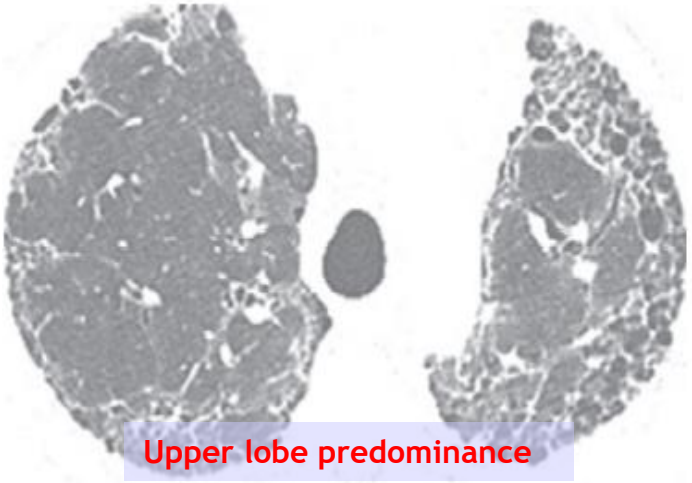
02: e36-e69

Radiologic Features-2 (Nonfibrotic)

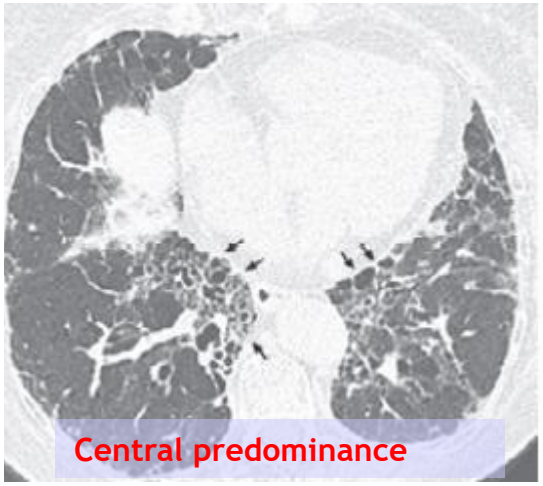
HR CT pattern	Typical HP	Compatible with HP	Indeterminate for HP
Description	Suggestive of a Dx of HP → Requires a) & b) both in a diffuse distribution a) at least 1 of parenchymal infiltration b) at least 1 of small airway dz	Nonspecific patterns that have been described in HP	N/A
Relevant radiological findings	a) Indicative of parenchymal infiltration : - GGOs - Mosaic attenuation b) Indicative of small airway dz: - ill-defined centrilobular nodules - air trapping Distribution : diffuse(craniocaudal, axial)	Parenchymal abnormalities: - Uniform & subtle GGOs - Airspace consolidation - Lung cyst Distribution: - diffuse - variant : lower lobe predominance peribronchovascular	N/A

Am J Respir Crit Care Med 2020; 202: e36-e69

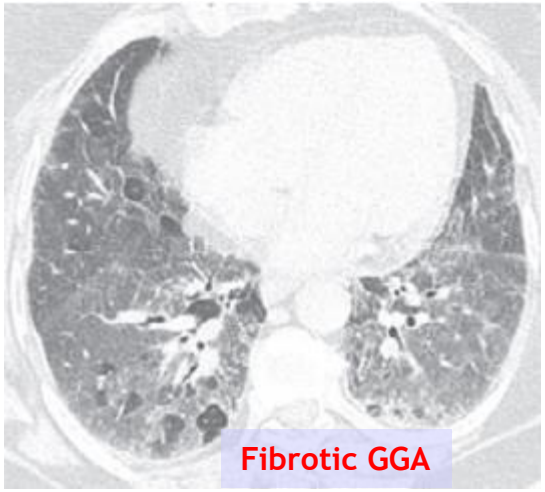
Radiologic Features-3 (Fibrotic)



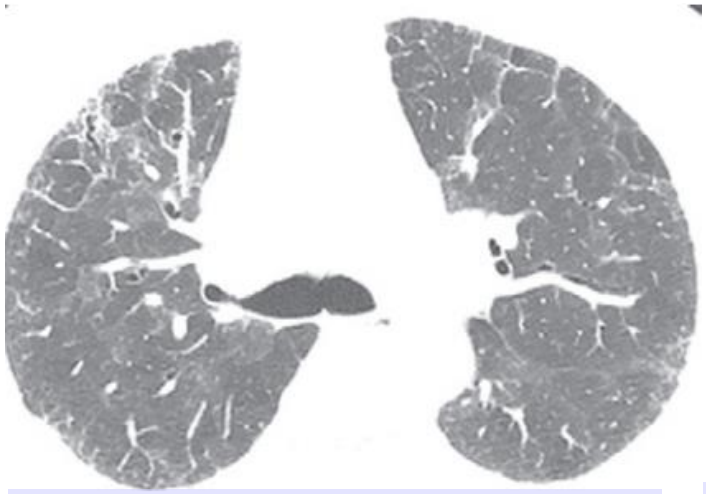
Upper lobe predominance



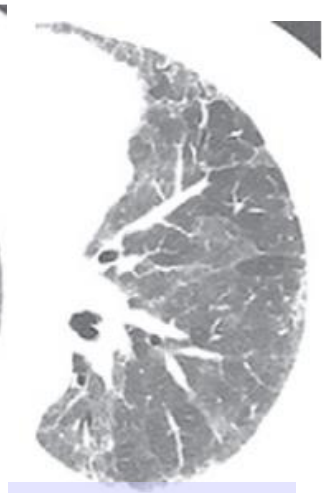
Central predominance



Fibrotic GGA



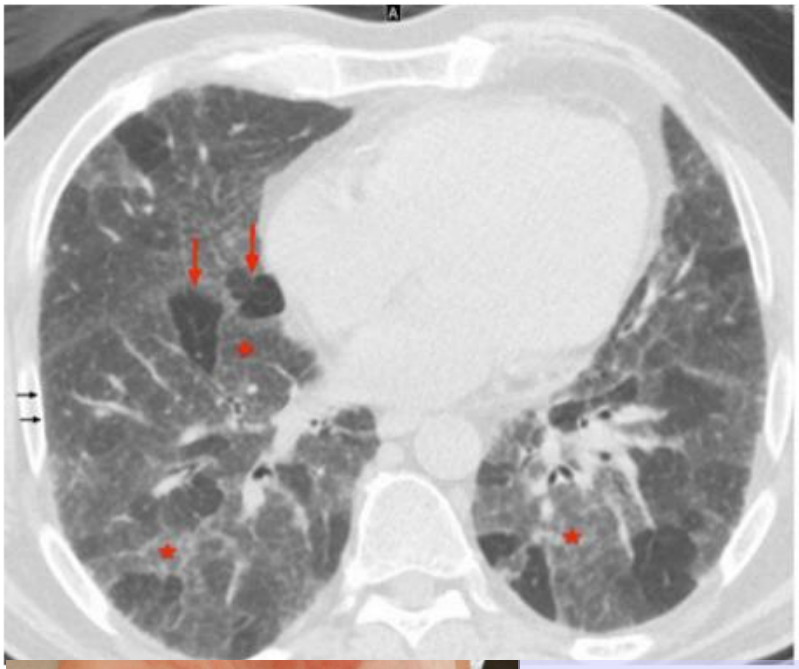
Coarse reticulation, minimal honeycombing in a random distribution

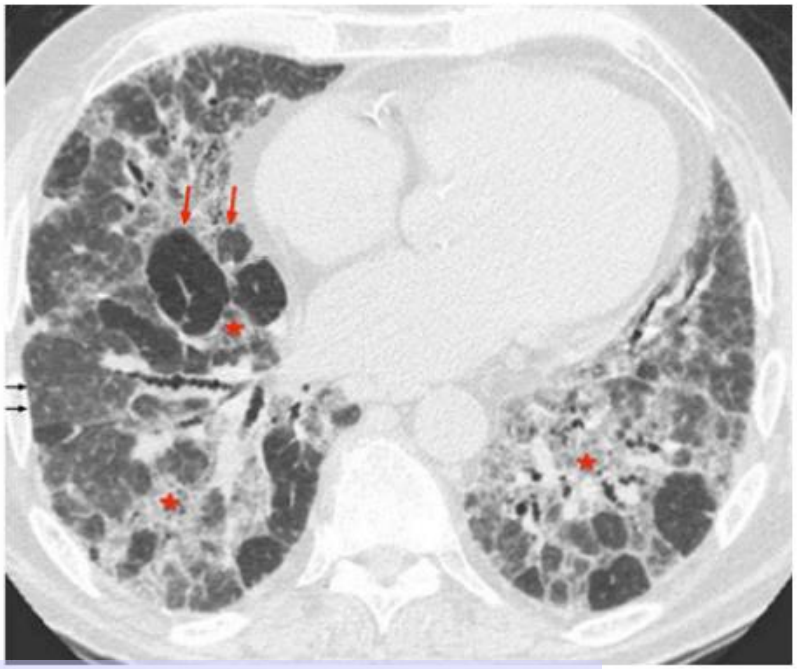


Small airway dz

Am J Respir Crit Care Med 2020; 202: e36-e69

Radiologic Features-4 (Fibrotic)





Three-density pattern

(inspiratory scan (Lt) expiratory scan (Rt))

(formerly called Headcheese Sn)

= Normal + GGOs(infiltration) + Lucent lung(obstruction)

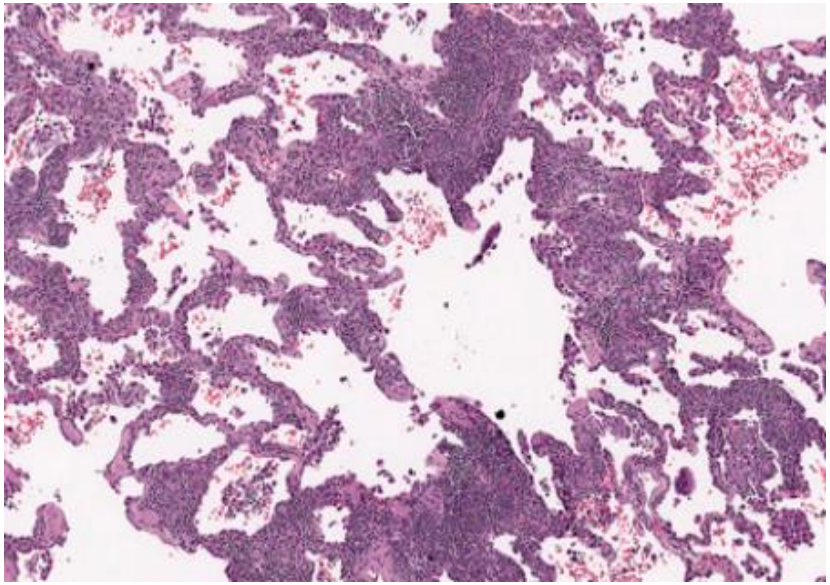
Am J Respir Crit Care Med 2020; 202: e36-e69

Radiologic Features-5 (Fibrotic)

HR CT pattern	Typical HP	Compatible with HP	Indeterminate for HP
Description	Suggestive of a Dx of HP → Requires a) & b) a) lung fibrosis in one of distributions b) at least 1 of small airway dz	Pattern/distribution of lung variant fibrosis + small airway dz	Neither Typical nor compatible
Relevant radiological findings	a) Lung fibrosis -irregular linear opacities/coarse reticulation c lung distortion traction bronchiectasis, honeycombing Distribution - random, mid lung zone predominant or relatively spared in lower lung zone Indicative of small airway dz: - ill-defined centrilobular nodules/GGO - mosaic attenuation, 3-density pattern, air trapping	Variant pattern of fibrosis: - UIP pattern - Extensive GGOs c superimposed subtle fibrosis Variant distributions of fibrosis - peribronchovascular, subpleural area, upper lung zone Indicative of small airway dz: - ill-defined centrilobular nodules/GGO *or* 3-density pattern, air trapping	Lone patterns : -UIP -fNSIP -OP -Truly indeterminate

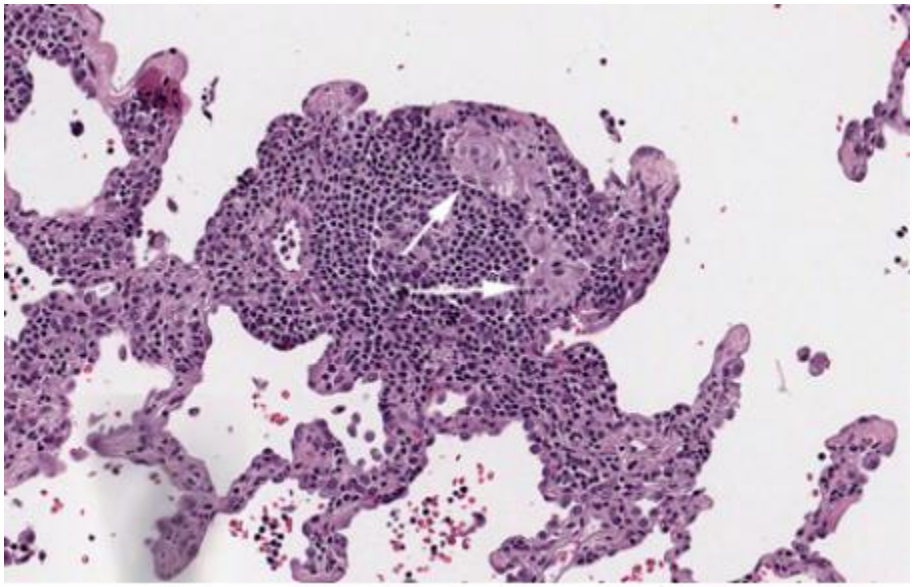
Am J Respir Crit Care Med 2020; 202: e36-e69

Histopathologic Features-1



Cellular bronchiolitis

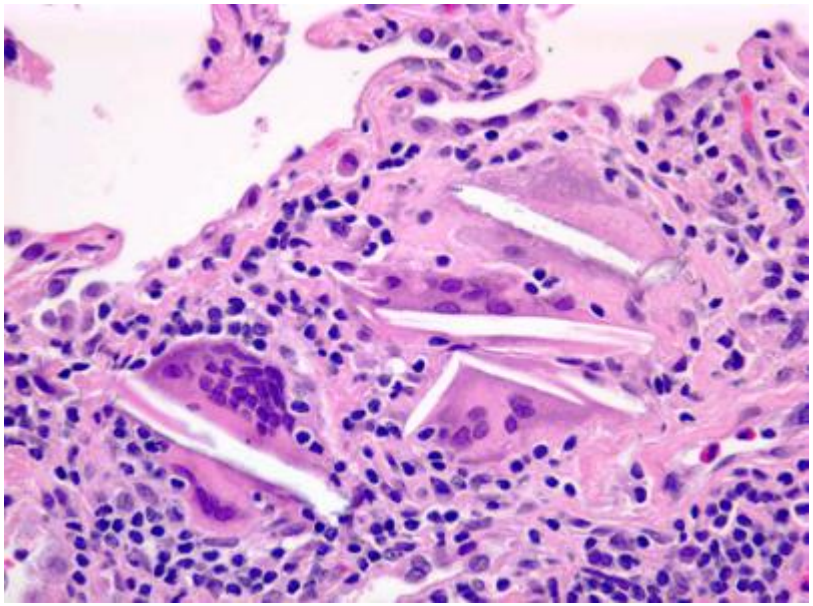
: peribronchiolar interstitium is expanded by lymphocytes without lymphoid aggregates or follicles



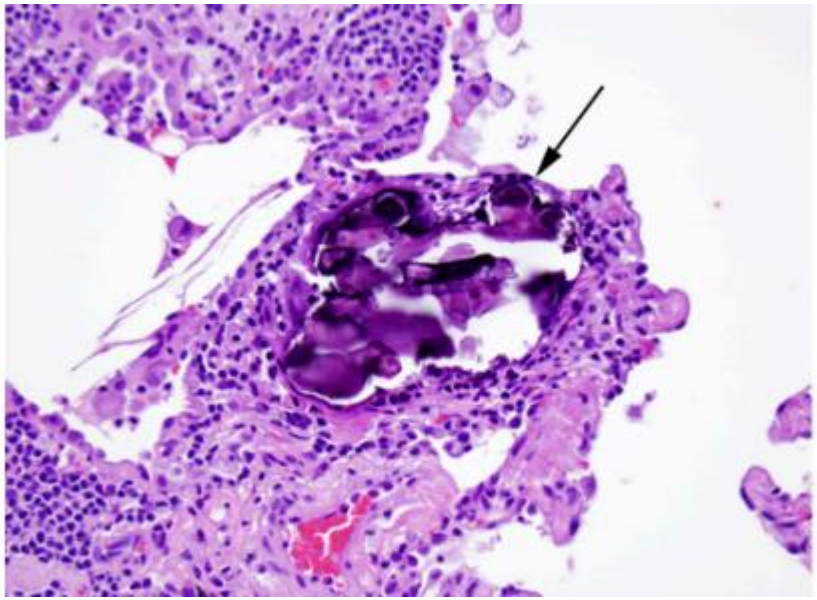
Poorly formed nonnecrotizing granuloma

Am J Respir Crit Care Med 2020; 202: e36-e69

Histopathologic Features-2



Giant cells + cytoplasmic cholesterol-like clefts



Cytoplasmic Schumann body

Am J Respir Crit Care Med 2020; 202: e36-e69

Histopathologic Features-3 (Nonfibrotic)

HP	Probable HP	Indeterminate for HP
One Bx site showing 1) +2) +3) 1) cellular interstitial pneumonia - bronchiolocentric - cellular NSIP-like pattern - lymphocyte-predominant 2) cellular bronchiolitis -lymphocyte predominant -± OP pattern -± foamy macrophage 3) poorly formed nonnecrotizing granulomas - loose clusters of epithelioid cells/ multinucleated giant cell ±intracytoplasmic inclusions - situated in peribronchiolar interstitium, terminal air space, OP *And* Absence of suggesting an alternative Dx	One Bx site showing 1) +2) 1) cellular interstitial pneumonia - bronchiolocentric - cellular NSIP-like pattern - lymphocyte-predominant 2) cellular bronchiolitis -lymphocyte predominant -± OP pattern -± foamy macrophage *And* Absence of suggesting an alternative Dx	One Bx site showing one of the following - 1) or 2) from 1st column - Cellular NSIP - OP - peribronchiolar metaplasia s other features to suggest fibrotic HP *And* Absence of suggesting an alternative Dx

Am J Respir Crit Care Med 2020; 202: e36-e69

Histopathologic Features-4 (Fibrotic)

HP	Probable HP	Indeterminate for HP
One Bx site showing 1) or 2) +3) 1) Chronic fibrosing interstitial pneumonia - architectural distortion, fibroblast foci ± subpleural honeycombing - fibrotic NSIP-like pattern 2) Airway-centered fibrosis -± peribronchiolar metaplasia -± Bridging fibrosis 3) poorly formed nonnecrotizing granulomas ± cellular interstitial pneumonia, ± cellular bronchiolitis ± OP *And* Absence of suggesting an alternative Dx	One Bx site showing 1) +2) 1) Chronic fibrosing interstitial pneumonia - architectural distortion, fibroblast foci ± subpleural honeycombing - fibrotic NSIP-like pattern 2) Airway-centered fibrosi -± peribronchiolar metaplasia -± Bridging fibrosis ± cellular interstitial pneumonia, ± cellular bronchiolitis ± OP *And* Absence of suggesting an alternative Dx	One Bx site showing either one of the following - 1) from 1st column ± cellular interstitial pneumonia, ± cellular bronchiolitis ± OP *And* Absence of suggesting an alternative Dx

Am J Respir Crit Care Med 2020; 202: e36-e69

Diagnostic Criteria-1

- Fibrotic HP should be considered in the DDx for all pts c a fibrotic ILD.

- Previous proposals have limitations such as
  incorporation bias(serum IgG, BAL studies),
  incomplete consideration of all informative features,
  absence of appropriate control groups,
  inadequate validation(questionnaires).

- No individual feature is sufficient in isolation, nor are any mandatory for Dx.

Am J Respir Crit Care Med 2020; 202: e36-e69

Diagnostic Criteria-2

- M/important 3 primary domains
  1) exposure identification

     (Hx c/s questionnaire, serum IgG c/s specific inhalation challenge)
  2) Imaging pattern
  3) BAL lymphocytosis/histopathological findings

- Diagnoses as definite (≥ 90% confidence)
  high-confidence (80-89%)
  moderate-confidence (70-79%)
  low-confidence (51%-69%)

- The Primary goal is to make a confident Dx using the least invasive approach.

Am J Respir Crit Care Med 2020; 202: e36-e69

Diagnostic Interventions

	Nonfibrotic	Fibrotic
Using Questionnaire	No recommendation/suggestion for or against. Recommends the development & validation	
Serum IgG testing	Suggestion, very low confidence	
BAL lymphocytosis	Recommendation, very low confidence	Suggestion, Very low confidence
TB forceps lung Bx	Suggestion, Very low confidence	No recommendation/suggestion for or against
TB lung cryoBx	No recommendation/suggestion for or against	Suggestion, Very low confidence
SLB	Suggestion only when all other diagnostic testing has not yield a Dx, Very low confidence	

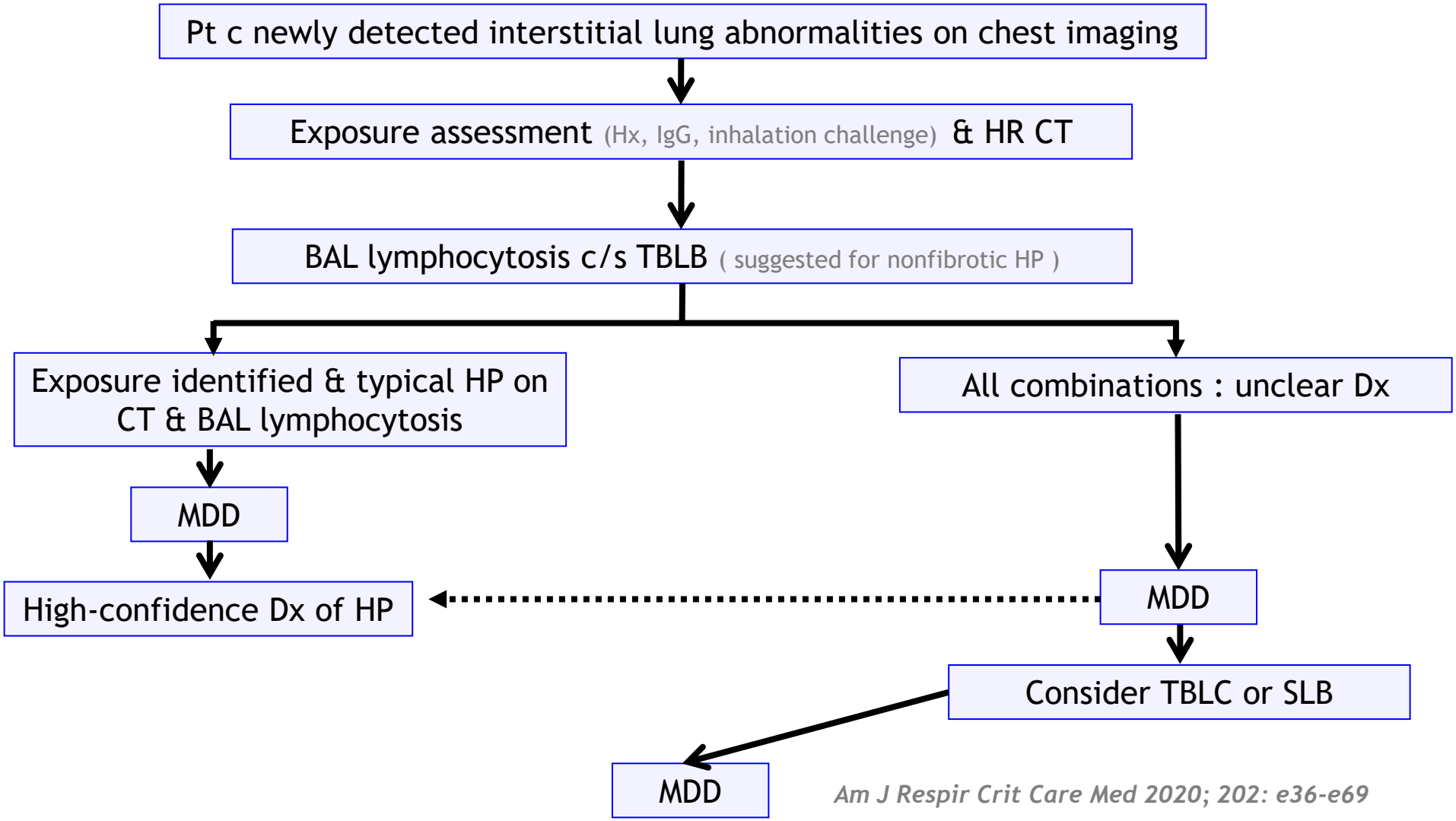
Distinguishing HP from other ILD

: Sensitivity 83%, specificity 68%

Lack of standardization

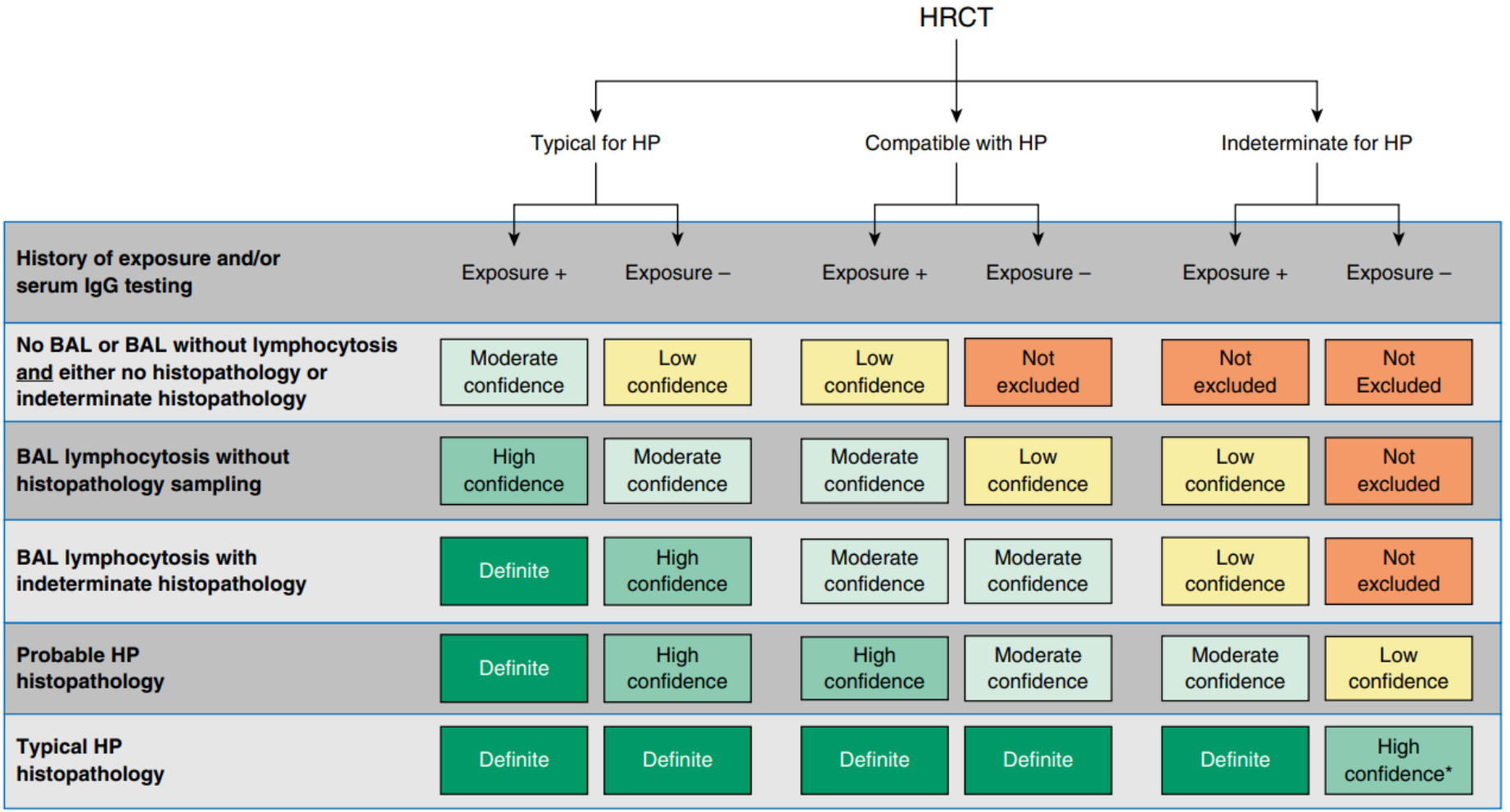
Am J Respir Crit Care Med 2020; 202: e36-e69

Algorithm for Diagnostic evaluation



Am J Respir Crit Care Med 2020; 202: e36-e69

Algorithm for Diagnostic evaluation

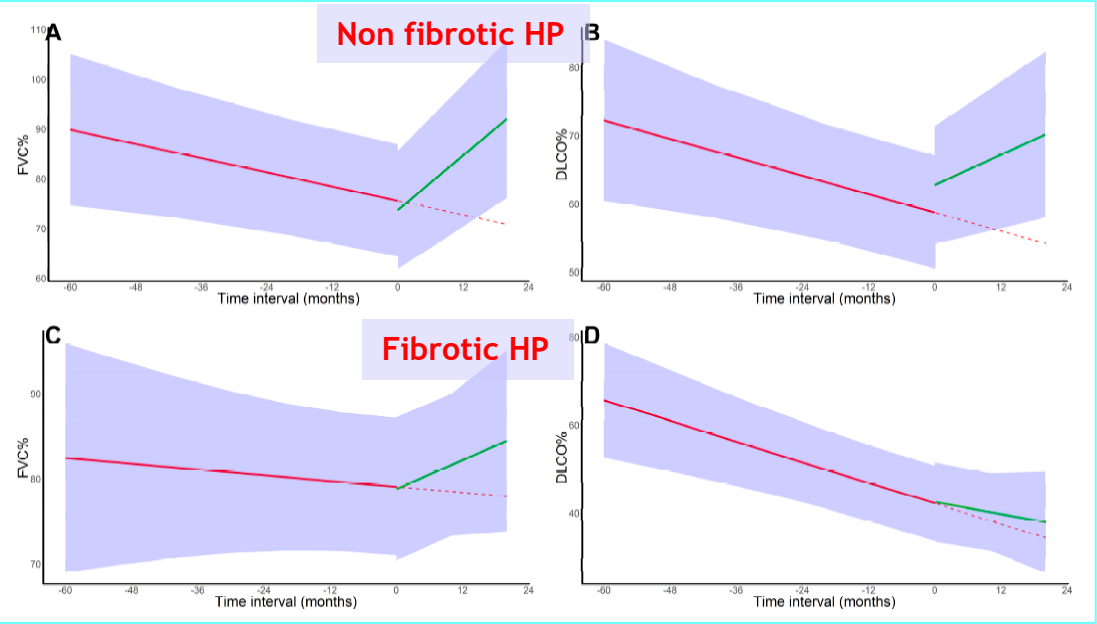


History of exposure and/or serum IgG testing	Typical for HP: Exposure +	Typical for HP: Exposure –	Compatible with HP: Exposure +	Compatible with HP: Exposure –	Indeterminate for HP: Exposure +	Indeterminate for HP: Exposure –
No BAL or BAL without lymphocytosis and either no histopathology or indeterminate histopathology	Moderate confidence	Low confidence	Low confidence	Not excluded	Not excluded	Not Excluded
BAL lymphocytosis without histopathology sampling	High confidence	Moderate confidence	Moderate confidence	Low confidence	Low confidence	Not excluded
BAL lymphocytosis with indeterminate histopathology	Definite	High confidence	Moderate confidence	Moderate confidence	Low confidence	Not excluded
Probable HP histopathology	Definite	High confidence	High confidence	Moderate confidence	Moderate confidence	Low confidence
Typical HP histopathology	Definite	Definite	Definite	Definite	Definite	High confidence*

Am J Respir Crit Care Med 2020; 202: e36-e69

Treatment-1

- Exposure avoidance



2005.1-2016.12

A single center cohort study (Belgium)

Non-fibrotic (n=93) vs. fibrotic (n=109)

Red line : before terminating exposure

Green line : after terminating exposure

Fibrosis: extensive fibrosis,
traction bronchiectasis,
honeycoming

J Clin Med 2019; 8: 14

Treatment-2

- Steroid
  : varying doses & duration
  (0.5 mg/kg for a few days
  → slow tapering over several months to a year of longer)

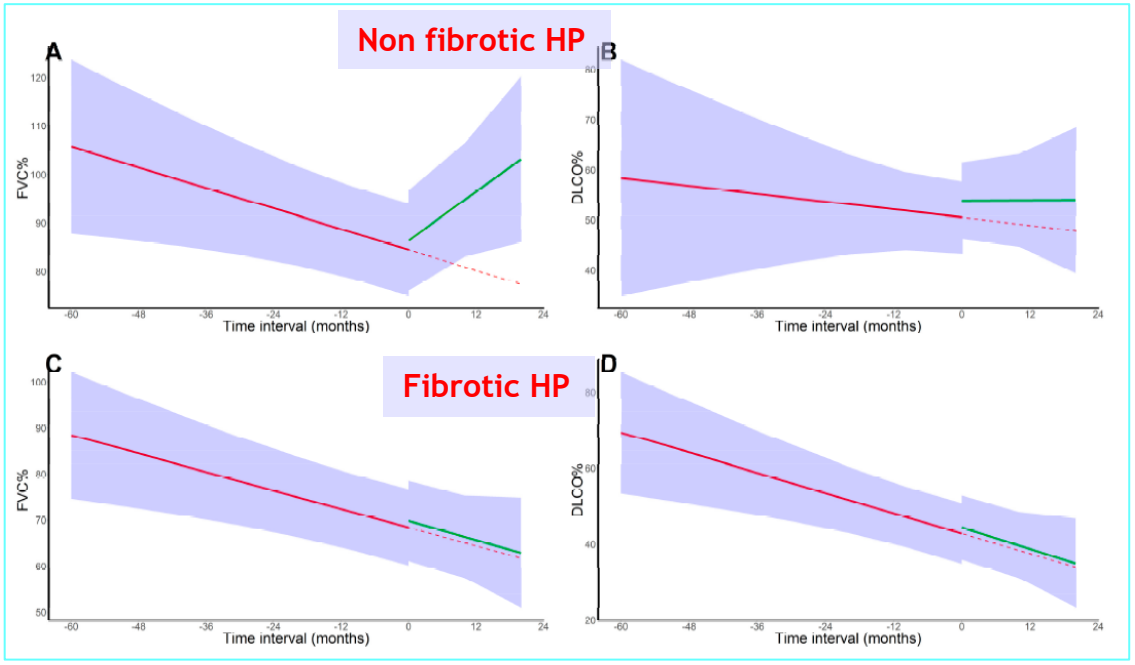
- 1 RCT
  acute farmer's lung
  steroid (n=20) vs placebo (n=16) for 8 wk
  → steroid improved lung function more rapid
  but no influence on the lung term result (5 yrs)

Am J Respir Crit Care Med 2017;196:680-689

Am Rev Respr Dis 1992; 145: 305

Treatment-3

- Steroid



2005.1-2016.12

A single center cohort study (Belgium)

Non-fibrotic (n=93) vs. fibrotic (n=109)

Red line : before steroid

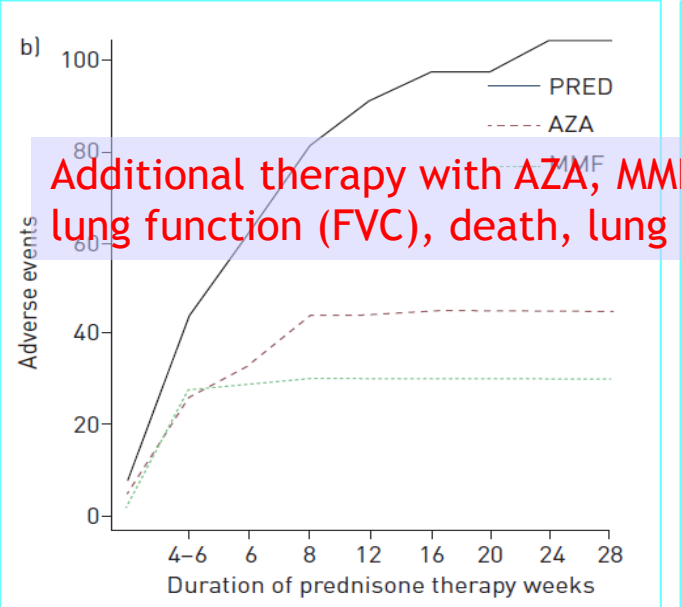
Green line : after steroid

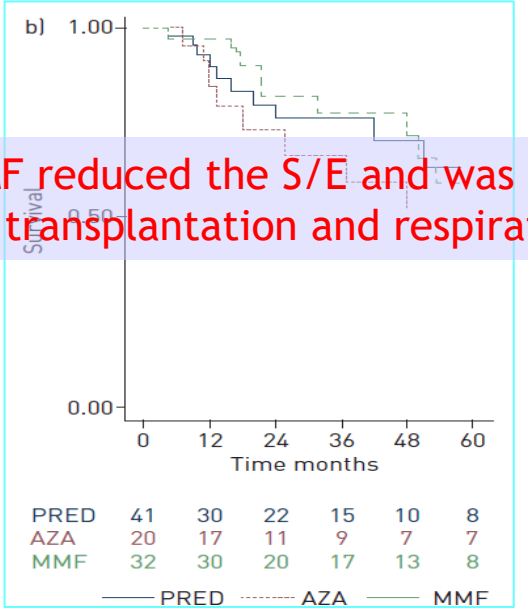
J Clin Med 2019; 8: 14

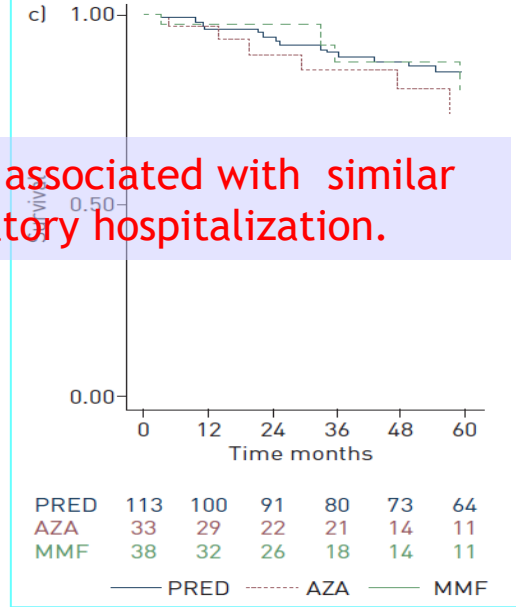
Treatment-4

- Immune-modulating agents

  steroid only vs. steroid + azathioprine/mycophenolate mofetil







Additional therapy with AZA, MMF reduced the S/E and was associated with similar lung function (FVC), death, lung transplantation and respiratory hospitalization.

2006-2015, Chicago (131 HP 중 93명 치료받음)

Pred only (n=41), 40mg/d x 11 wk

Pred + AZA(n=20), 40mg/d+ 125mg/d x 8 wk

Pred + MMF(n=32), 20mg/d + 2000mg/d 9 wk

External validation(4 center,184 HP)

Pred only (n=113)

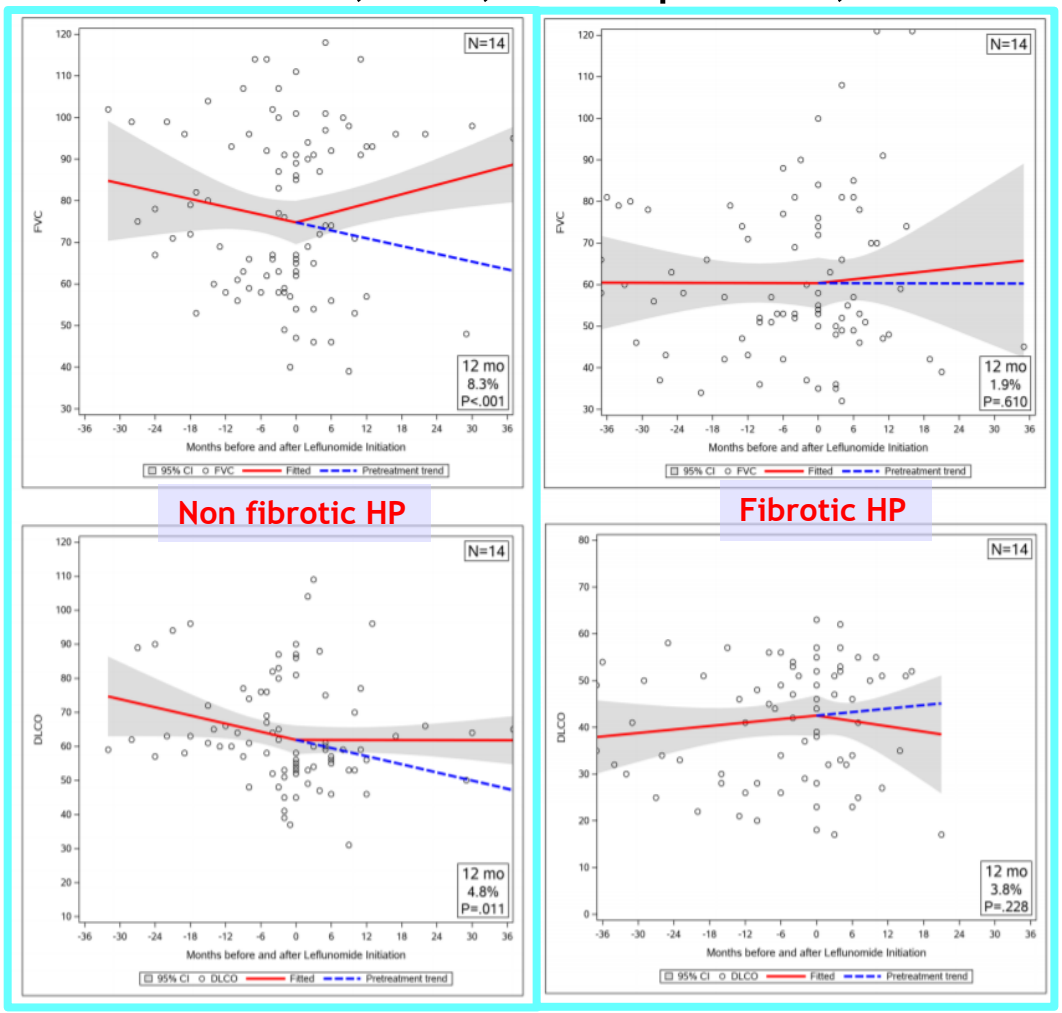
Pred+AZA (n=33)

Pred+MMF (n=38)

ERJ Open Res 2017; 3: 00016-2017

Treatment-5

- Leflunomide, USA, retrospective, 1 center



28 cHP

Nonfibrotic (n=14, fibrosis≤20%)

Fibrotic (n=14, fibrosis > 20%)

Steroid ± AZA/MMF/cyclophosphamide

➔ adding Leflunomide

Median duration: 293 days

S/Ex: GI Sx(D, N, LFT), skin rash, neuropathy

➔ Discontinuation(40%)

BMC Pulmonary Medicine 2020; 20: 199

Treatment-6

Agent	Study design	Population	Aims	Primary outcome	Main result
Nintedanib (INBUILD)	Phase III, RCT	Progressive fibrosing ILD (cHP, 26%)	Efficacy & safety	Annual rate of FVC decline	Nintedanib was effective in reducing in the annual rate of FVC decline
Pirfenidone (RELIEF)	Phase II, RCT	Progressive fibrotic ILD (cHP, 45%)	Efficacy & safety	ΔFVC % from baseline to week 48	Pirfenidone might attenuate dz progression as measured by decline in FVC

N Engl J Med 2019; 381: 1718-27

Lancet Respir Med 2021; 9: 476-86

Treatment-7

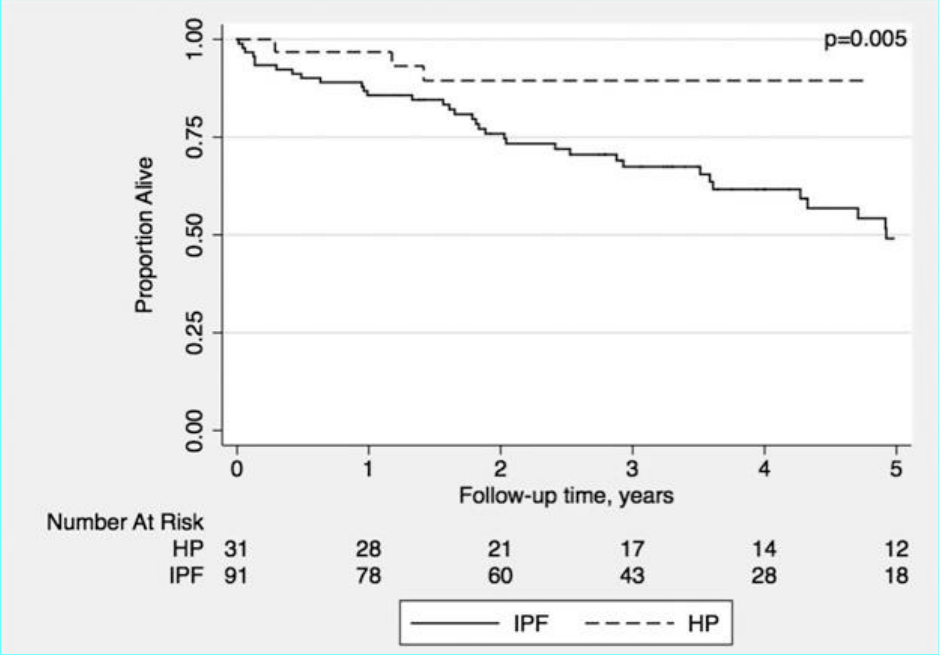
- Lung transplantation

  2000.1~2013. 7, Retrospective cohort study, UCSF (USA)

  31 HP vs. 91 IPF (among 183 lung transplantation for ILD)

  excellent survival after LT relative to IPF

  2 (among 31) developed recurrent HP in their allografts.



Chest 2015;147:1558-1565

Summary

- HP must be considered in the DDx for pt c newly identified ILD.
- HP was categorized into 2 subtypes : nonfibrotic vs. fibrotic.

- Need for a thorough Hx & a validated questionnaire, serum IgG testing.
- For nonfibrotic HP, recommendation for BAL lymphocyte and suggestion for TBLB and SLB.
  For fibrotic HP, suggestion for BAL lymphocyte, TB cryoBx and SLB.

- Diagnostic criteria and algorithm were made.
- More consensus/evidence is necessary for Tx of HP.