과민성 폐장염

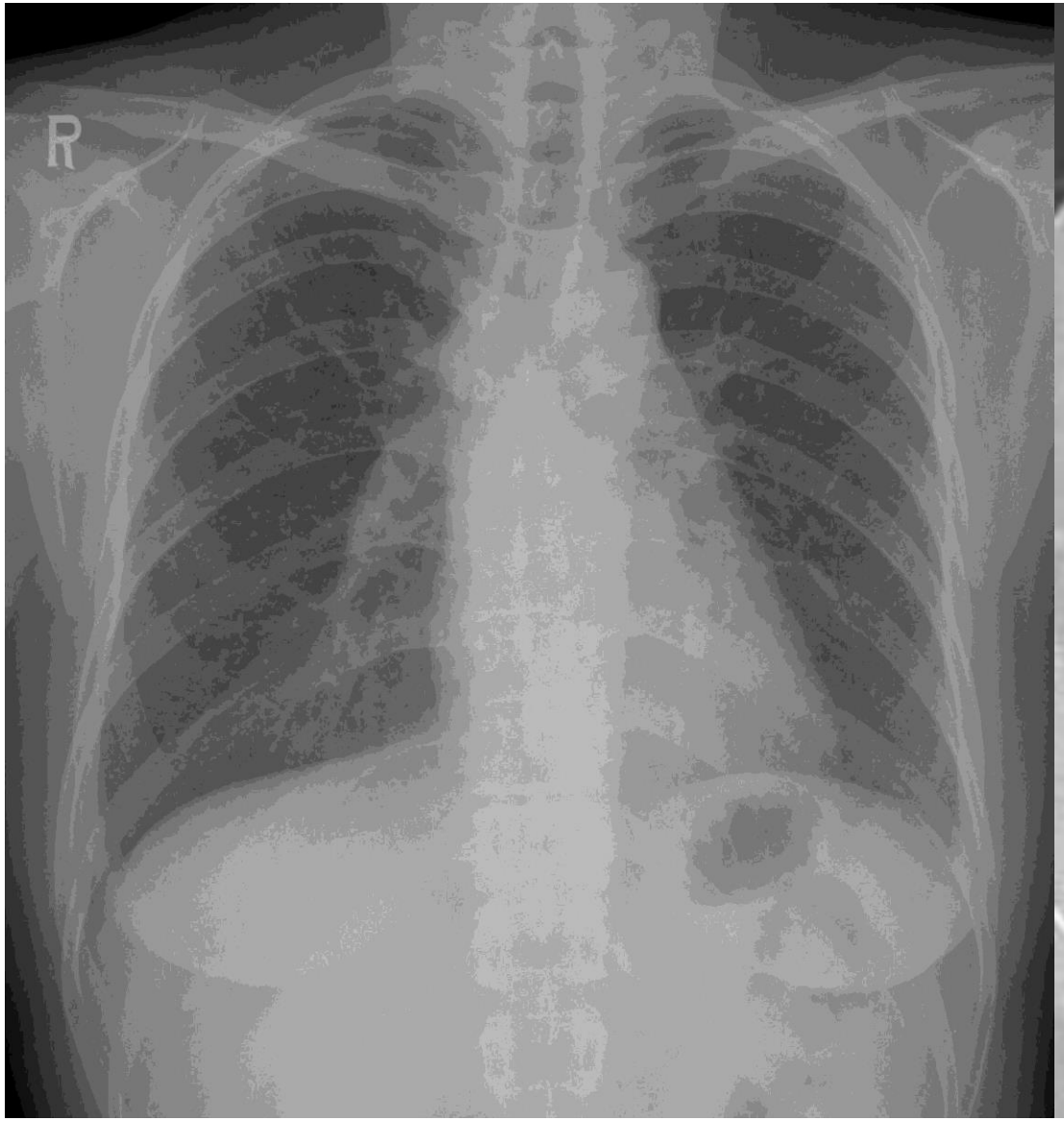
분당서울대학교병원 호흡기내과
박종선

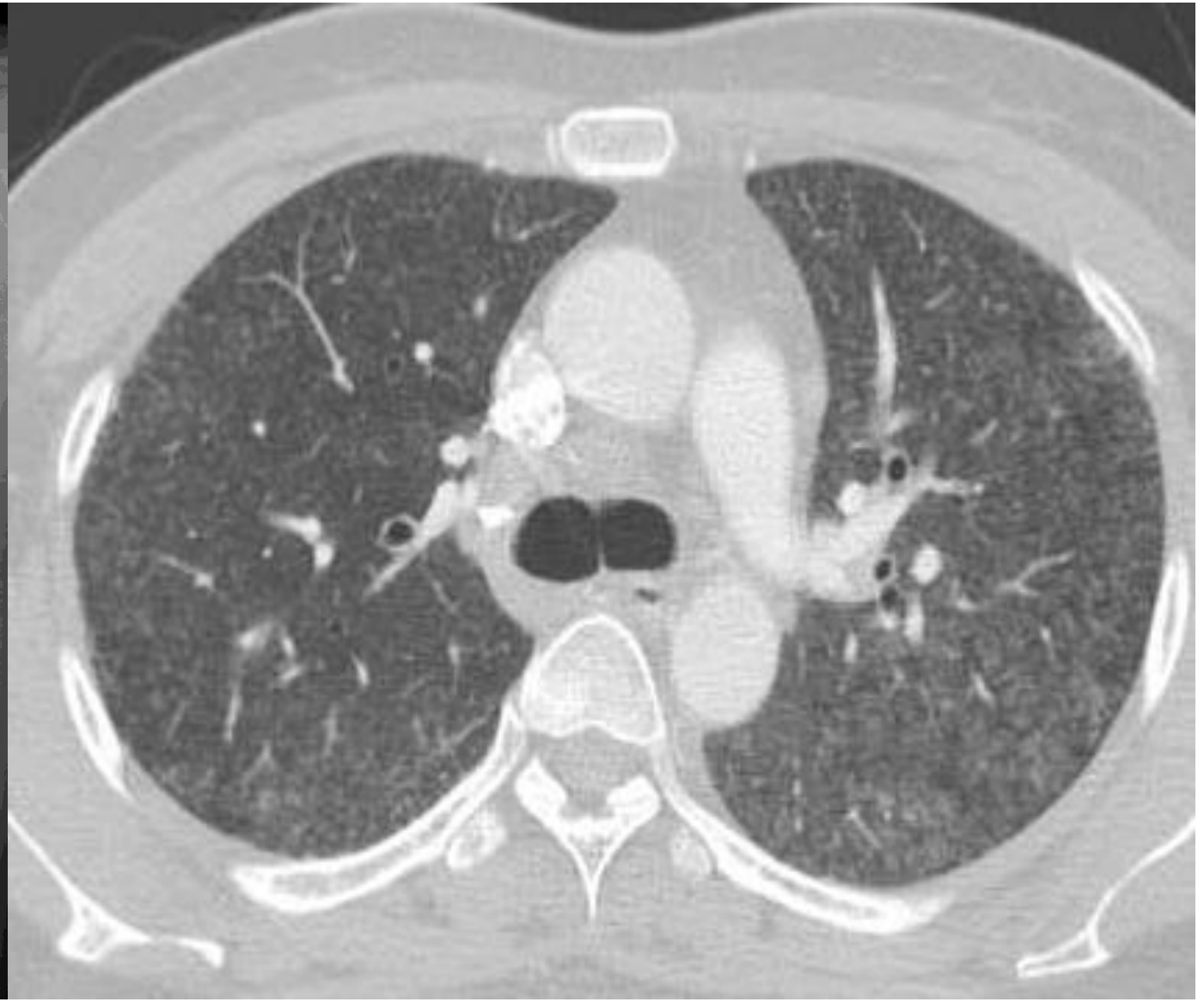
2021.9.4

F/42

- **C/C: 기침**

- 3주 전부터 거의 매일 실내 수영장에서 수영
- 1주 전부터는 수영이 끝난 후 미열과 기침이 발생
- 비흡연자


R



과민성 폐장염 (Hypersensitivity Pneumonitis, HP)

- Inflammatory and/or fibrotic disease affecting the lung parenchyma and small airways
- Immune-mediated reaction provoked by an overt or occult inhaled antigen in susceptible individuals.

Symptoms & signs

- Dyspnea, cough
- Midinspiratory squeaks
- Constitutional symptoms such as weight loss, flu-like symptoms (chills, low-grade fever, malaise)
- Chest tightness, wheezing
- Crackles or Cyanosis

Past classification: acute/subacute/chronic

급성 과민 폐렴 (<6mo)

- 단기간에 다량의 원인물질 폭로 후 발생.
- 대개 폭로 2-9시간 후에 호흡곤란, 기침, 근육통,오한, 발열, 두통, 쇠약감 등
- 발열, 빈호흡, 양측성 수포음과 심할 경우 청색증도 가능

만성 과민 폐렴 (>6Mo)

- 소량의 원인물질에 지속적으로 장기간 폭로 때 발생.
- 수개월에서 수년간 증상
- 발열은 없고 심한 호흡곤란, 기침, 체중감소, 식욕부진 등이 흔함.
- 기저부의 수포음과 빈호흡이 관찰.

→ Vaguely defined, not associated with clinical outcomes

Revised subtype of HP

- **Fibrotic HP** vs. **nonfibrotic HP**
- Determined by the predominant presence or absence of radiological and/or histopathological fibrosis
- More associated with the clinical course and other outcomes

Am J Respir Crit Care Med 2020: 202(3); e36–e69

Epidemiology

- Prevalence varies with regional disparities
- Incidence
  - 0.3 - 0.9 /100,000
  - Bird breeder's disease: 4.9/100,000
- 1-year prevalence: 1.67– 2.71/100,000 in U.S.
- Proportion of HP among all ILD cases: 2% - 47%

Am J Respir Crit Care Med 2020: 202(3); e36–e69

Ann Am Thorac Soc 2018;15(4):460-469

Natural History & Prognosis

- Nonfibrotic HP, avoid ongoing exposure → favorable prognosis
- Fibrotic HP, with a usual interstitial pneumonia (UIP)-like pattern
  → reduced survival

- Poor prognostic factors
  - Cigarette smoking
  - Lower baseline VC
  - Lack of BAL lymphocytosis
  - Persistent exposure to the inciting agent and/or inability to identify an inciting agent

- Inciting agent is not identified in 30–50% of cases

Am J Respir Crit Care Med 2020: 202(3); e36–e69

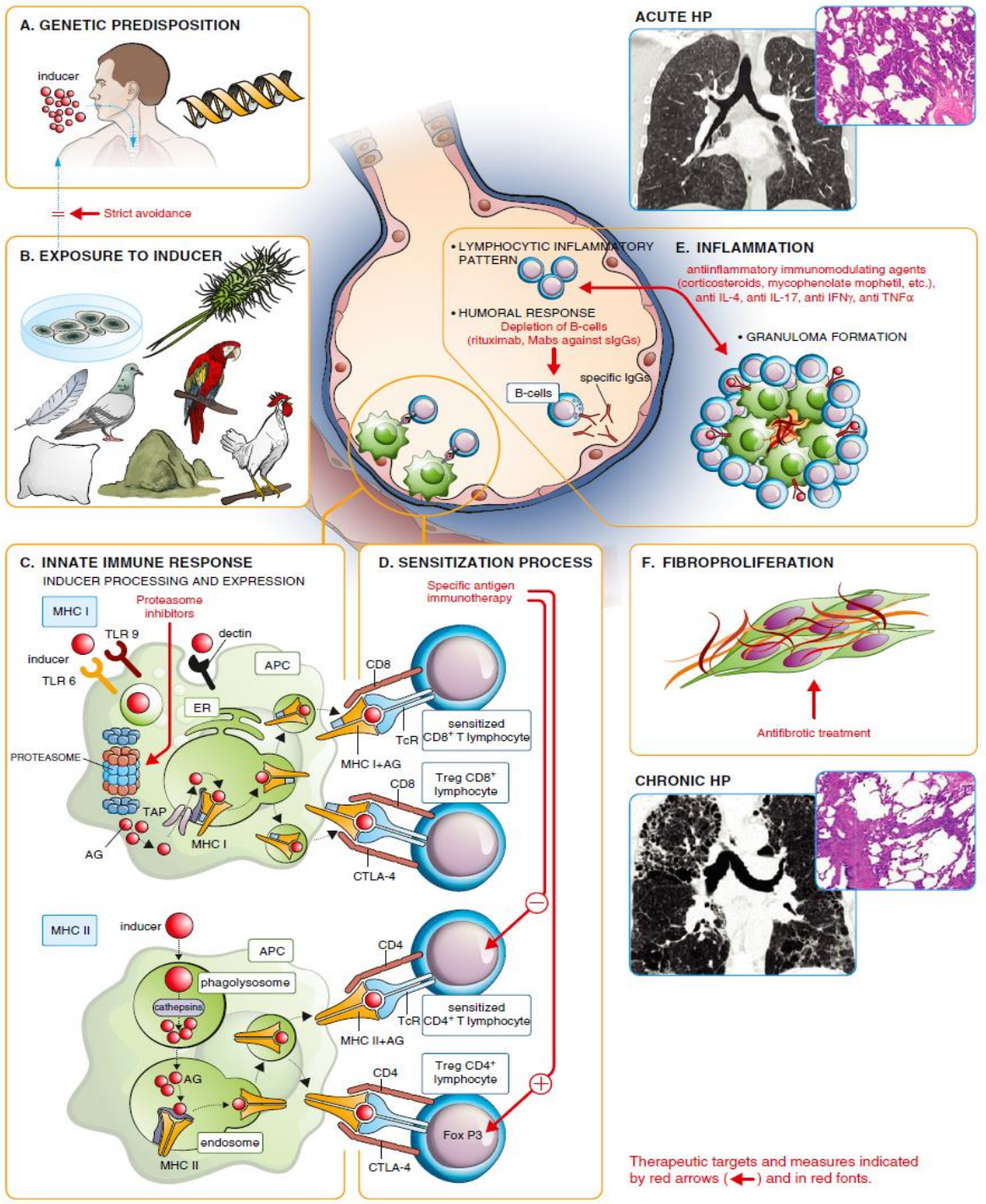
Pathogenesis

Immunological Dysregulation

- Humoral immune response
  - antigen-specific IgG antibody
- T-helper cell type 1 (Th1) cellular immune responses
- Lymphocytic inflammatory pattern and granulomatous inflammation

Genetic/Host Susceptibility

- Polymorphism in MHC II, proteasomes..
- MUC5B polymorphiam
- Telomere-related gene mutation..



Am J Respir Crit Care Med 2019: 200(3); 301–308

Sources of antigens

- Organic particulate matter
  - I. Microbes
  - II. Proteins/enzymes
- Inorganic particulate matter
  - I. Chemicals
  - II. Pharmaceutical agents
  - III. Metals

Am J Respir Crit Care Med 2020: 202(3); e36–e69

Matter	Typical Sources	HP "Disease"
Organic particulate matter		
I. Microbes		
Fungi/molds		
Aspergillus spp.		
Alternaria alternata, *Aureobasidium* spp.		
Botrytis cinerea		
Cephalosporium spp.		
Cladosporium spp.		
Cryptococcus spp.		
Fusarium spp.		
Graphium spp.		
Mucor spp.		
Penicillium spp.		
Rhizopus spp.		
Trichoderma spp.		
Phytase (enzyme from *Aspergillus* or *Trichoderma*)		
Yeasts		
Candida spp.		
Geotrichum candidum		
Saccharomyces cerevisiae		
Saccharomonospora viridis		
Saccharopolyspora rectivirgula		
Torulopsis glabrata		
Trichosporon cutaneum		
Edible mushrooms		
Mushrooms (shiitake, bunashimeji, *Pleurotus*, *Pholiota*, *Lyophyllum*, *Agaricus*)		
Bacteria		
Acinetobacter spp.		
Bacillus spp.		
Klebsiella spp.		
Nontuberculous mycobacteria		
Phoma spp.		
Pseudomonas spp.		
Stenotrophomonas spp.		
Staphylococcus spp.		
Streptomyces spp.		
Thermoactinomyces spp.		
Endotoxin from pool-water sprays and fountains		
Bacillus subtilis enzymes (subtilisin)		
Protozoa		
Amoebae		
Nematodes		
Nematodes	Contaminated humidifiers and air-conditioning systems	Humidifier lung
Mite		
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		
Rat and desert mouse (gerbil) ur serum, pelts		
Silkworm proteins		
Weevils (corn, wheat) (*Sitophilus*		
Plant proteins		
Alginate		
Argan cake		
Catechin		
Esparto dust		
Grain flour (wheat, rye, oats, ma		
Malt		
Legumes (soy)		
Paprika		
Pyrethrum		
Spinach		
Tiger nut		
Wood (cabreuva, cedar, mahoga pine, ramin, umbrella pine)		
Inorganic particulate matter		
I. Chemicals		
Acid anhydrides (pyromellitic and trimellitic anhydrides)	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	—

air-conditioning systems

Sources of antigens

Antigen	Source	Disease
Microorganisms		
Saccharopolyspora rectivirgula	Moldy hay and compost	Farmer's lung
Thermoactinomyces sacchari	Sugar cane residue (bagass)	Bagassosis
Bacillus subtlis proteins	Contaminated wood dust	Woodworker's lung
Penicillium casei	Cheese mold	Cheese washer's lung
Aspergillus clavatus	Contaminated barley	Malt worker's lung
Mycobacterium avium intracellulare	Hot tubs	Hot tub lung
Trichosporon cutaneum	Mold in Japanese homes	Japanese summer-type pneumonitis
Animal proteins		
Avian proteins	Bird droppings and feathers	Bird fancier's disease and pigeon breeder's disease
Rodent proteins	Rodent dander, urine, serum	Animal handler's lung and laboratory worker's lung
Animal fur dust	Animal pelts	Furrier's lung
Chemicals		
Isocyanates	Paint hardeners, polyurethan foams	Chemical walker's lung
Anhydrides	Plastic components	Chemical walker's lung
Pyrethrum	Insecticides	Insecticide user's lung

Korean Med Assoc 2009; 52(1): 49 - 58

Laboratory findings

- Bronchoalveolar lavage (BAL) fluid
  - Lymphocytosis: Lymphocytosis > 20%, often > 50%
  - Decreased CD4/CD8 ratio

- Serum antigen-specific IgG antibody
- Inhalation challenge

- 참고: Normal BAL fluid in nonsmokers
  - Macrophages >80%
  - Lymphocytes ≤ 15%
  - Neutrophils ≤ 3%
  - Eosinophils ≤ 0.5%
  - Mast cells ≤ 0.5%

Clinical practice guideline

AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis of Hypersensitivity Pneumonitis in Adults

An Official ATS/JRS/ALAT Clinical Practice Guideline

Ganesh Raghu, Martine Remy-Jardin, Christopher J. Ryerson, Jeffrey L. Myers, Michael Kreuter, Martina Vasakova, Elena Bargagli, Jonathan H. Chung, Bridget F. Collins, Elisabeth Bendstrup, Hassan A. Chami, Abigail T. Chua, Tamera J. Corte, Jean-Charles Dalphin†, Sonye K. Danoff, Javier Diaz-Mendoza, Abhijit Duggal, Ryoko Egashira, Thomas Ewing, Mridu Gulati, Yoshikazu Inoue, Alex R. Jenkins, Kerri A. Johannson, Takeshi Johkoh, Maximiliano Tamae-Kakazu, Masanori Kitaichi, Shandra L. Knight, Dirk Koschel, David J. Lederer, Yolanda Mageto, Lisa A. Maier, Carlos Matiz, Ferran Morell, Andrew G. Nicholson, Setu Patolia, Carlos A. Pereira, Elisabetta A. Renzoni, Margaret L. Salisbury, Moises Selman, Simon L. F. Walsh, Wim A. Wuyts, and Kevin C. Wilson; on behalf of the American Thoracic Society, Japanese Respiratory Society, and Asociación Latinoamericana de Tórax

This guideline is dedicated to the memory of Prof. Jean-Charles Dalphin† (June 2, 1956–October 17, 2019)

Am J Respir Crit Care Med 2020: 202(3); e36–e69

Subtype of HP

	Nonfibrotic HP	Fibrotic HP
HRCT findings	▪ Typical HP ▪ Compatible with HP ▪ Indeterminate for HP	▪ Typical HP ▪ Compatible with HP ▪ Indeterminate for HP
Histopathological findings	▪ Typical HP ▪ Probable HP ▪ Indeterminate HP	▪ Typical HP ▪ Probable HP ▪ Indeterminate HP

Am J Respir Crit Care Med 2020: 202(3); e36–e69

Radiologic findings; Nonfibrotic HP

HRCT Pattern	Typical HP	Compatible with HP	Indeterminate for HP
Description	The "typical HP" pattern is suggestive of a diagnosis of HP. It requires *a*) at least one HRCT abnormality indicative of parenchymal infiltration and *b*) at least one HRCT abnormality indicative of small airway disease, both in a diffuse distribution	"Compatible-with-HP" patterns are nonspecific patterns that have been described in HP	N/A
Relevant radiological findings	HRCT abnormalities indicative of parenchymal infiltration: • GGOs • Mosaic attenuation* HRCT abnormalities indicative of small airway disease: • Ill-defined, centrilobular nodules • Air trapping Distribution of parenchymal abnormalities: • Craniocaudal: diffuse (with or without some basal sparing) • Axial: diffuse	Parenchymal abnormalities: • Uniform and subtle GGOs • Airspace consolidation • Lung cysts Distribution of parenchymal abnormalities: • Craniocaudal: diffuse (variant: lower lobe predominance) • Axial: diffuse (variant: peribronchovascular)	N/A

Am J Respir Crit Care Med 2020: 202(3); e36–e69

Radiologic findings; Nonfibrotic HP

- Typical HP: at least one parenchymal infiltration and at least one small airway disease, both in a diffuse distribution in HRCT

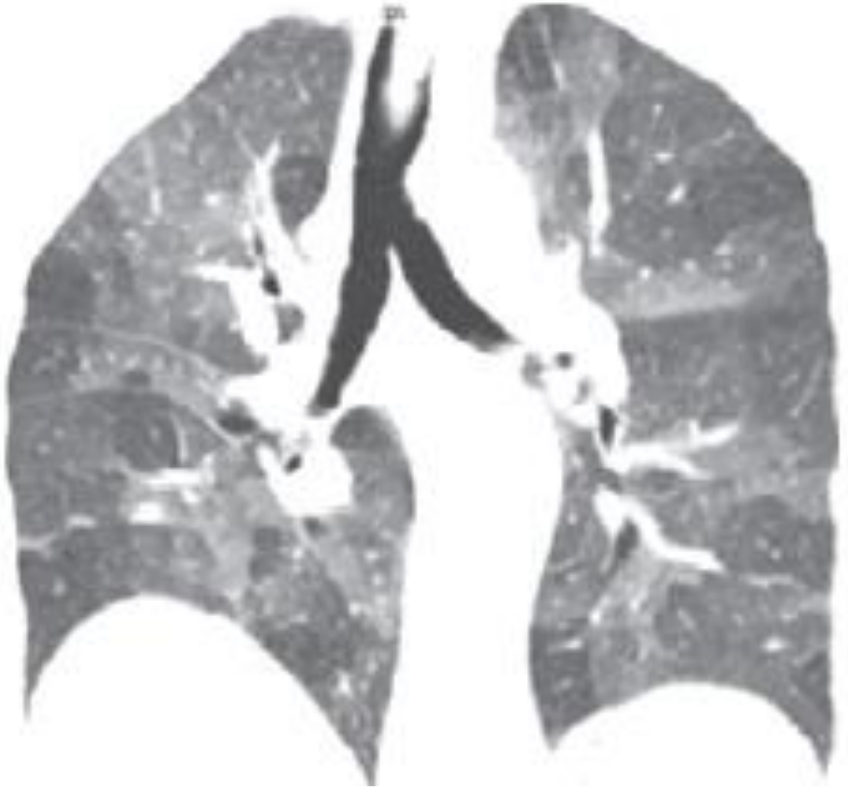
- Parenchymal infiltration (1)
  - GGOs
  - Mosaic attenuation
- Small airway disease (1)
  - Ill-defined, centrilobular nodules
  - Air trapping
- Distribution of parenchymal abnormalities
  - Craniocaudal: diffuse (with or without some basal sparing)
  - Axial: diffuse

Am J Respir Crit Care Med 2020: 202(3); e36–e69

Nonfibrotic typical HP

centrilobular nodules

mosaic attenuation (inspiratory scan)



air trapping (expiratory scan)

Am J Respir Crit Care Med 2020: 202(3); e36–e69

Radiologic findings; Fibrotic HP

HRCT Pattern	Typical HP	Compatible with HP	Indeterminate for HP
Description	The "typical HP" pattern is suggestive of a diagnosis of HP. It requires *a*) an HRCT pattern of lung fibrosis (as listed below) in one of the distributions and *b*) at least one abnormality that is indicative of small airway disease	"Compatible-with-HP" patterns exist when the HRCT pattern and/or distribution of lung fibrosis varies from that of the typical HP pattern; the variant fibrosis should be accompanied by signs of small airway disease	The "indeterminate-for-HP" pattern exists when the HRCT is neither suggestive nor compatible with a typical and probable HP pattern
Relevant radiological findings	HRCT abnormalities indicative of lung fibrosis are most commonly composed of irregular linear opacities/coarse reticulation with lung distortion; traction bronchiectasis and honeycombing may be present but do not predominate The distribution of fibrosis may be: • Random both axially and craniocaudally or • Mid lung zone–predominant or • Relatively spared in the lower lung zones HRCT abnormalities indicative of small airway disease: • Ill-defined, centrilobular nodules and/or GGOs • Mosaic attenuation, three-density pattern,* and/or air trapping (*often in a lobular distribution*)	Variant patterns of lung fibrosis: • UIP pattern: basal and subpleural distribution of honeycombing with/without traction bronchiectasis (*per 2018 diagnosis of IPF guidelines* [20]) • Extensive GGOs with superimposed subtle features of lung fibrosis Variant (predominant) distributions of lung fibrosis: • Axial: peribronchovascular, subpleural areas • Craniocaudal: upper lung zones HRCT abnormalities indicative of small airway disease: • Ill-defined centrilobular nodules, or • Three-density pattern* and/or air trapping	Lone patterns (i.e., not accompanied by other findings suggestive of HP) of: • UIP pattern (*as per 2018 IPF diagnosis guidelines* [20]) • Probable UIP pattern (*as per 2018 IPF diagnosis guidelines* [20]) • Indeterminate pattern for UIP (*as per 2018 IPF diagnosis guidelines* [20]) • Fibrotic NSIP pattern • Organizing pneumonia–like pattern • Truly indeterminate HRCT pattern

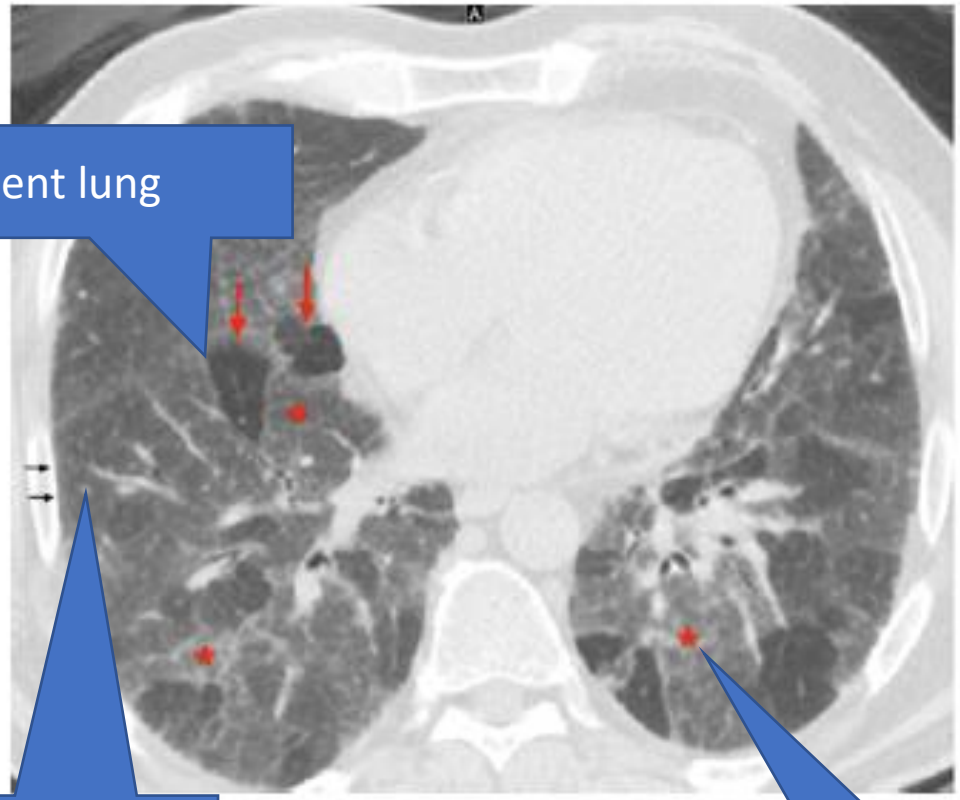
Radiologic findings; Fibrotic HP

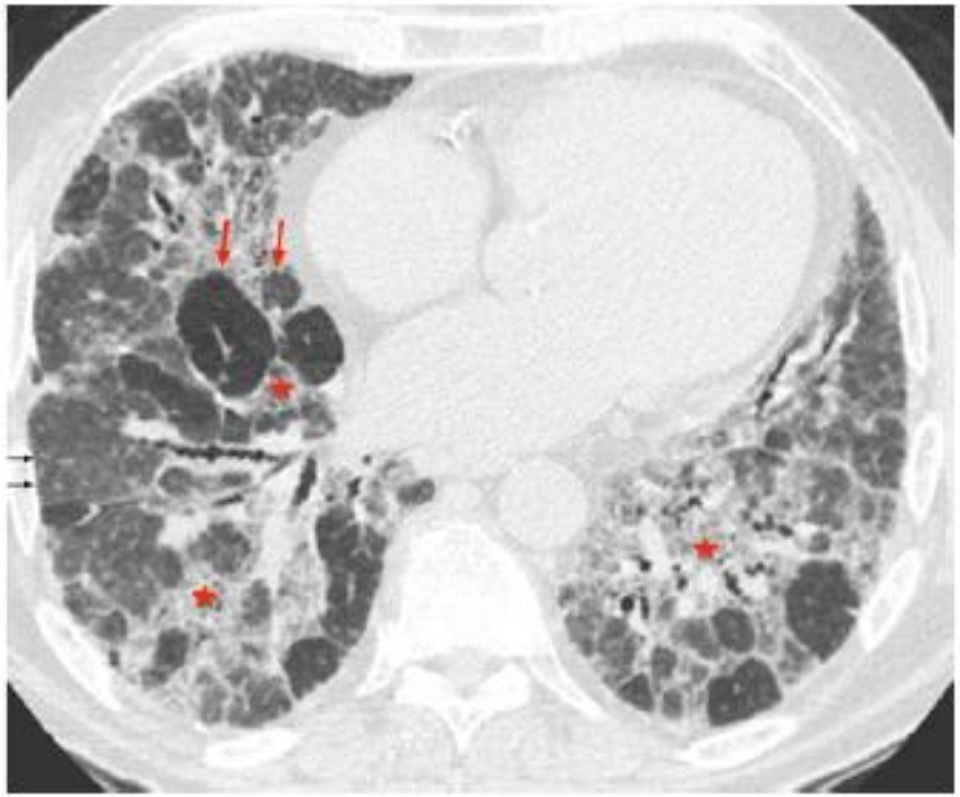
- Typical HP: an HRCT pattern of lung fibrosis in one of the distributions and at least one abnormality indicative of small airway disease

- Lung fibrosis (do not predominate):
  - Irregular linear opacities/coarse reticulation with lung distortion
  - Traction bronchiectasis and honeycombing
- Distribution of fibrosis:
  - Random both axially and craniocaudally or
  - Mid lung zone–predominant or
  - Relatively spared in the lower lung zones
- Small airway disease:
  - Ill-defined, centrilobular nodules and/or GGOs
  - Mosaic attenuation, three-density pattern*, and/or air trapping (often in a lobular distribution)

Am J Respir Crit Care Med 2020: 202(3); e36–e69

Three-density pattern





Lucent lung

Normal lung

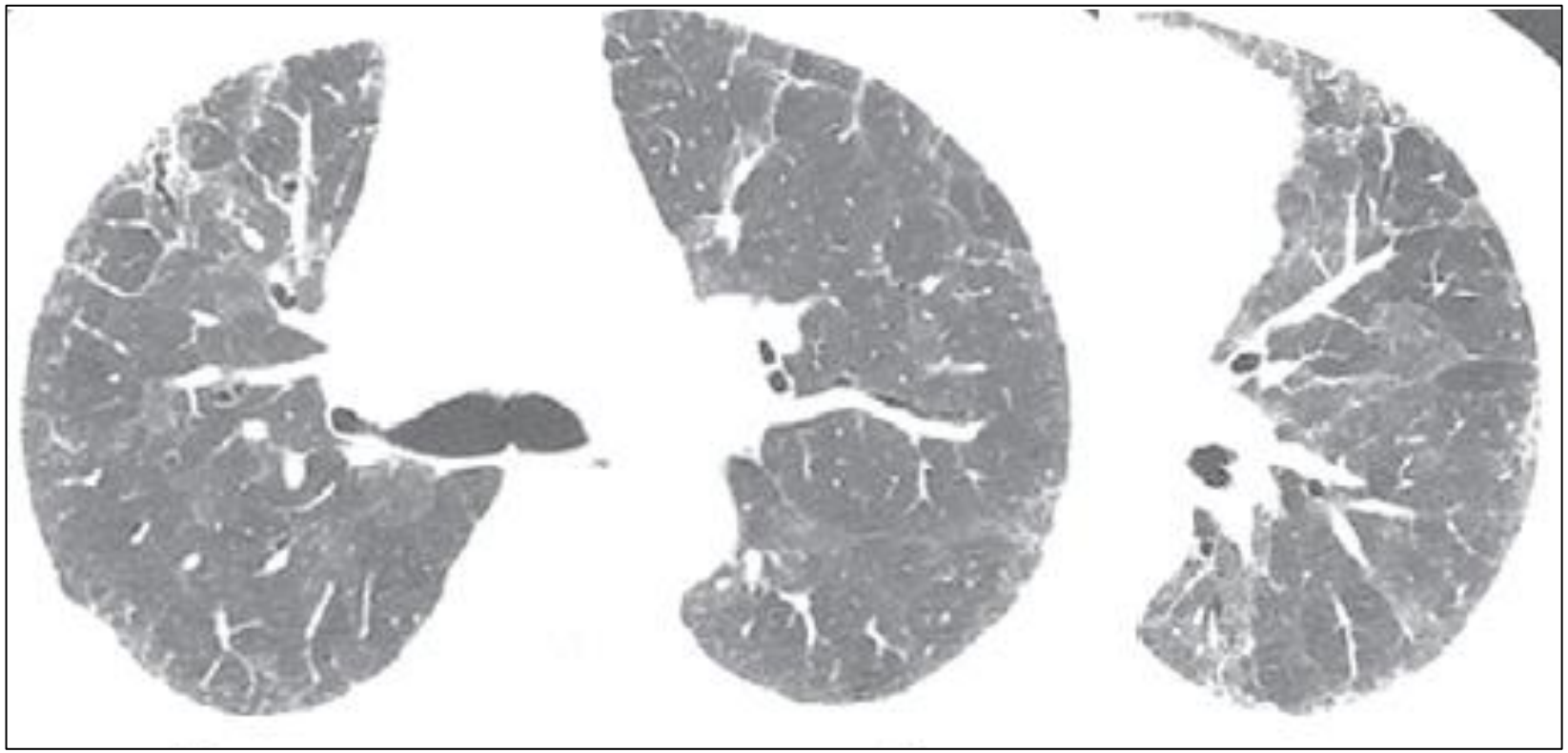
Ground-glass opacity

Inspiratory images

Expiratory images

Am J Respir Crit Care Med 2020: 202(3); e36–e69

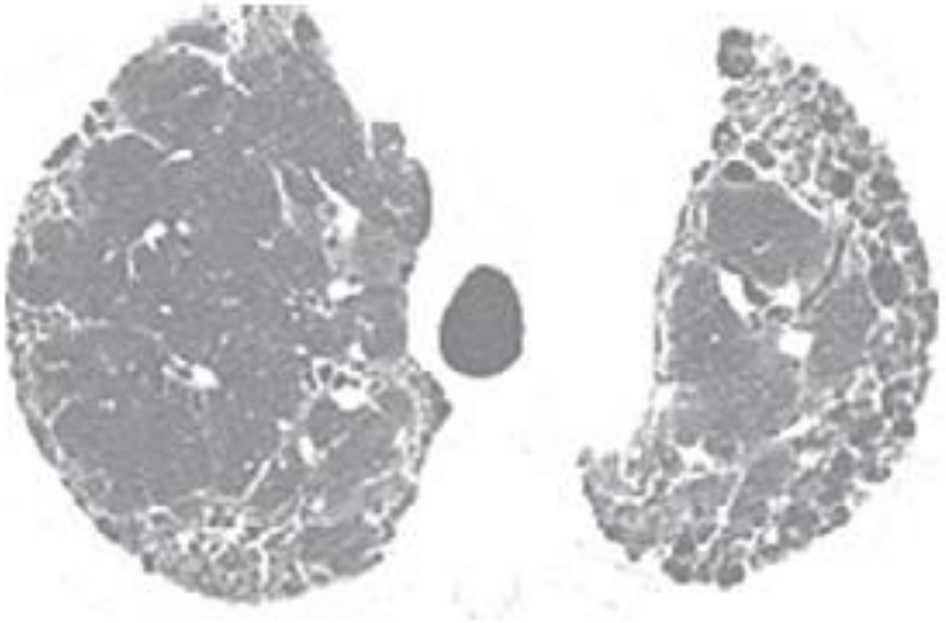
Fibrotic typical HP



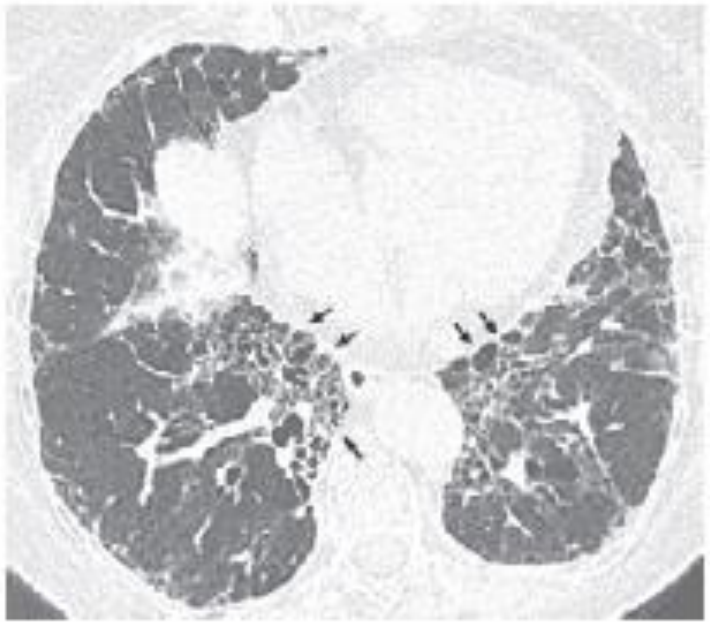
Coarse reticulation and minimal honeycombing in a random axial distribution with no zonal predominance in association with small airway disease.

Am J Respir Crit Care Med 2020: 202(3); e36–e69

Fibrotic compatible-with-HP pattern



Upper-lung-zone predominance



Central predominance
(peribronchovascular)

Fibrotic ground-glass attenuation

Am J Respir Crit Care Med 2020: 202(3); e36–e69

Hist s: Nonfibrotic HP

Nonfibrotic HP (cellular HP)
Typical histopathological features of nonfibrotic HP; at least one biopsy site showing all three of the following features:

1. Cellular interstitial pneumonia
   - Bronchiolocentric (airway-centered)
   - Cellular NSIP-like pattern
   - Lymphocyte-predominant
2. Cellular bronchiolitis
   - Lymphocyte-predominant (lymphs > plasma cells) with no more than focal peribronchiolar lymphoid aggregates with germinal centers
   - ±Organizing pneumonia pattern with Masson bodies
   - ±Foamy macrophages in terminal air spaces
3. Poorly formed nonnecrotizing granulomas†
   - Loose clusters of epithelioid cells and/or multinucleated giant cells ± intracytoplasmic inclusions
   - Situated in peribronchiolar interstitium, terminal air spaces, and/or organizing pneumonia (Masson bodies)

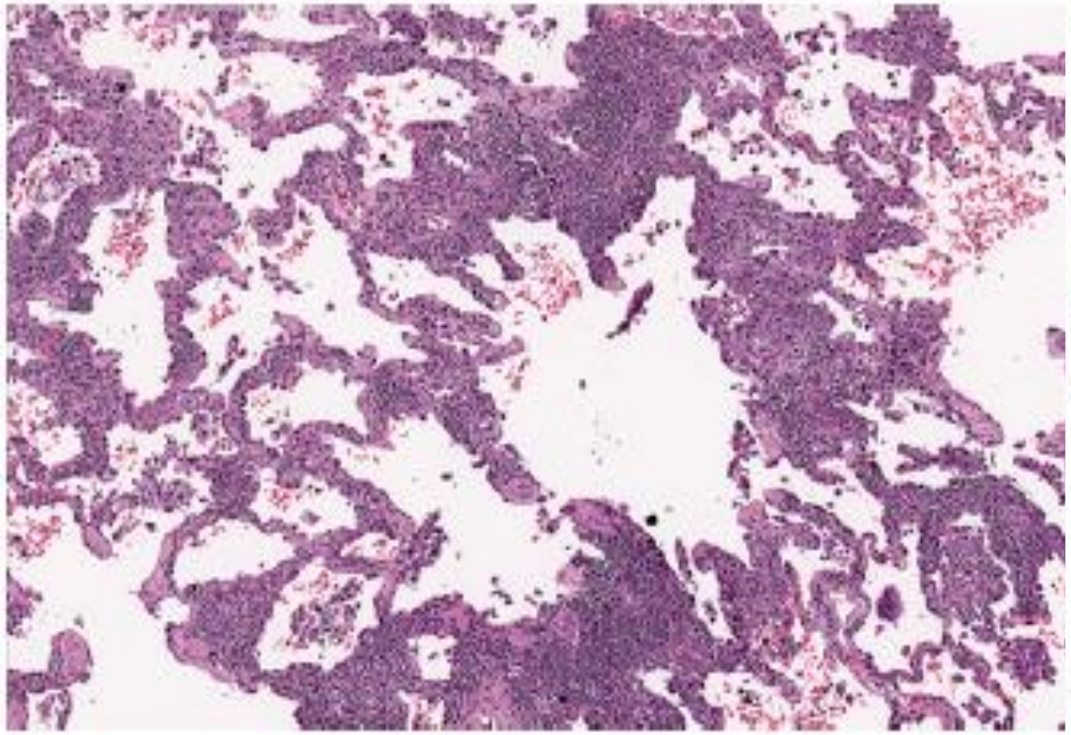
and

Absence of features in any biopsy site to suggest an alternative diagnosis
- Plasma cells > lymphs
- Extensive lymphoid hyperplasia
- Extensive well-formed sarcoidal granulomas and/or necrotizing granulomas
- Aspirated particulates

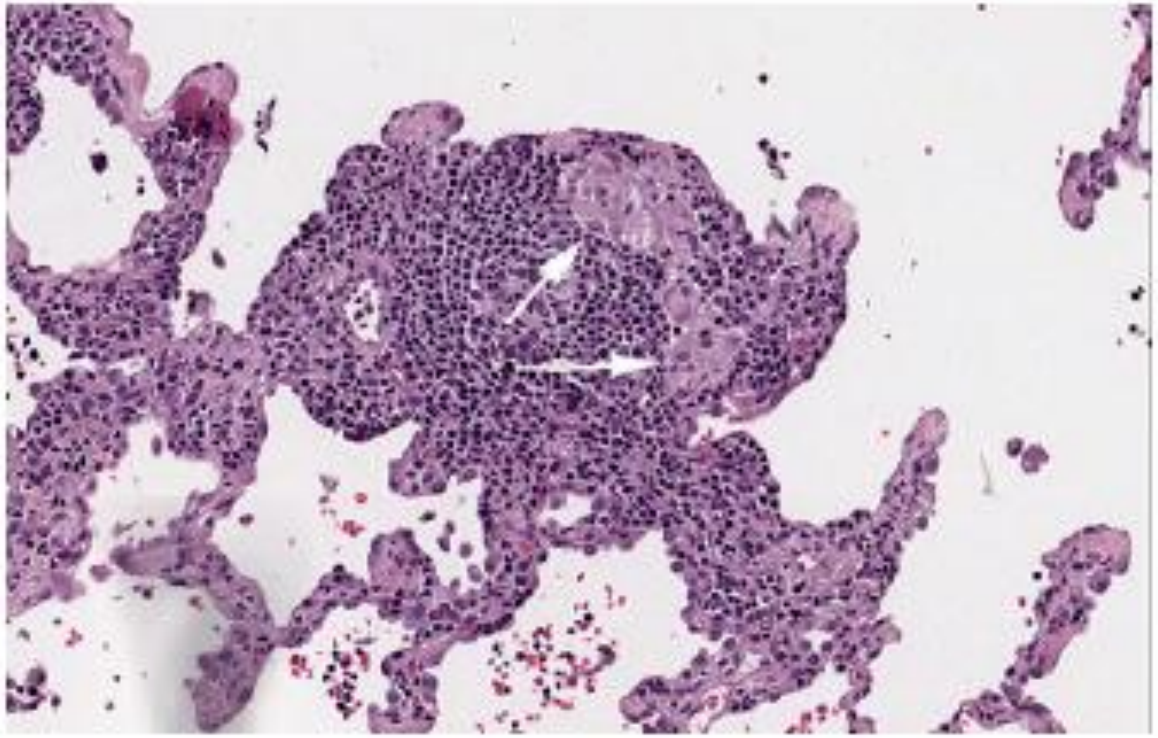
HP	e HP	Indeterminate for HP
Nonfibr Typical 1. Ce 2. Ce 3. Po *and* Abser	atures (*1* and *2* from st one biopsy site: pneumonia c (airway-centered) e pattern dominant tis dominant a cells) with no more onchiolar lymphoid germinal centers eumonia pattern with hages in terminal air in any biopsy site to tive diagnosis ymphs oid hyperplasia rmed sarcoidal /or necrotizing ulates	At least one biopsy site showing one of the following: • *1* or *2* from the first column • Selected IIP patterns ○ Cellular NSIP pattern ○ Organizing pneumonia pattern ○ Peribronchiolar metaplasia *without* other features to suggest fibrotic HP *and* Absence of features in any biopsy site to suggest an alternative diagnosis • Plasma cells > lymphs • Extensive lymphoid hyperplasia • Extensive well-formed sarcoidal granulomas and/or necrotizing granulomas • Aspirated particulates

Am J Respir Crit Care Med 2020: 202(3); e36–e69

Nonfibrotic HP



cellular bronchiolitis



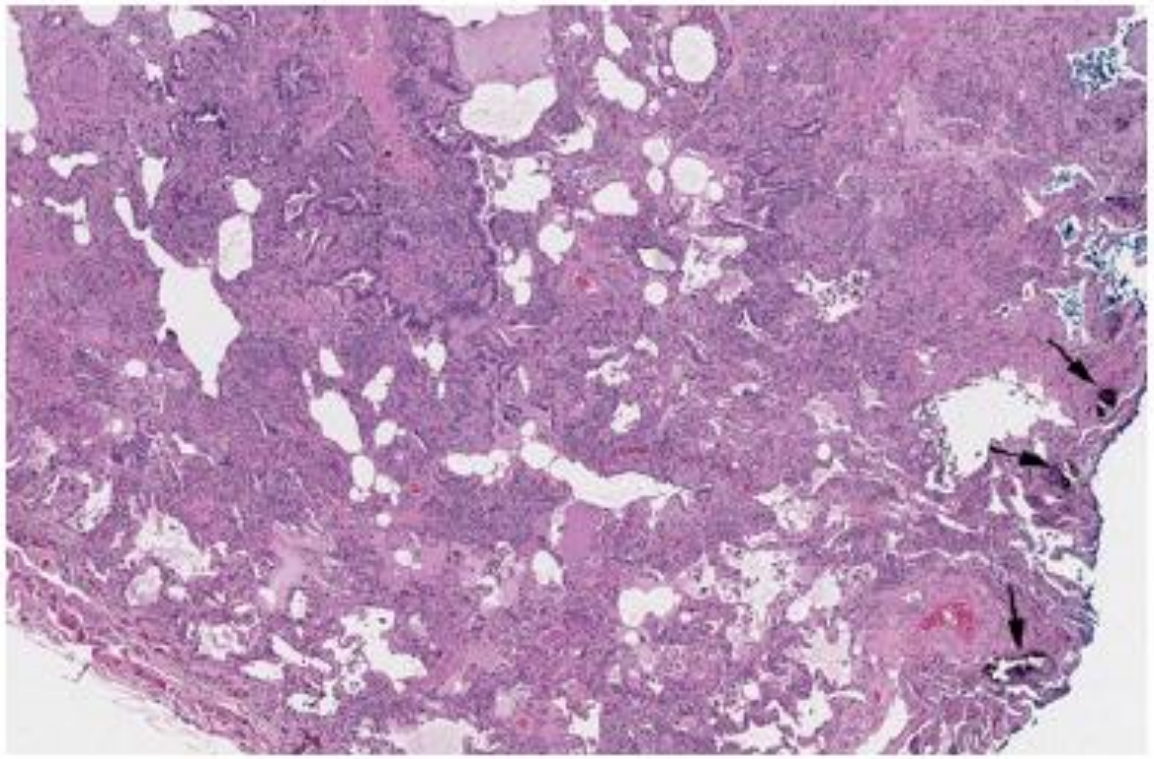
poorly formed nonnecrotizing granuloma

Histopathologic findings: Fibrotic HP

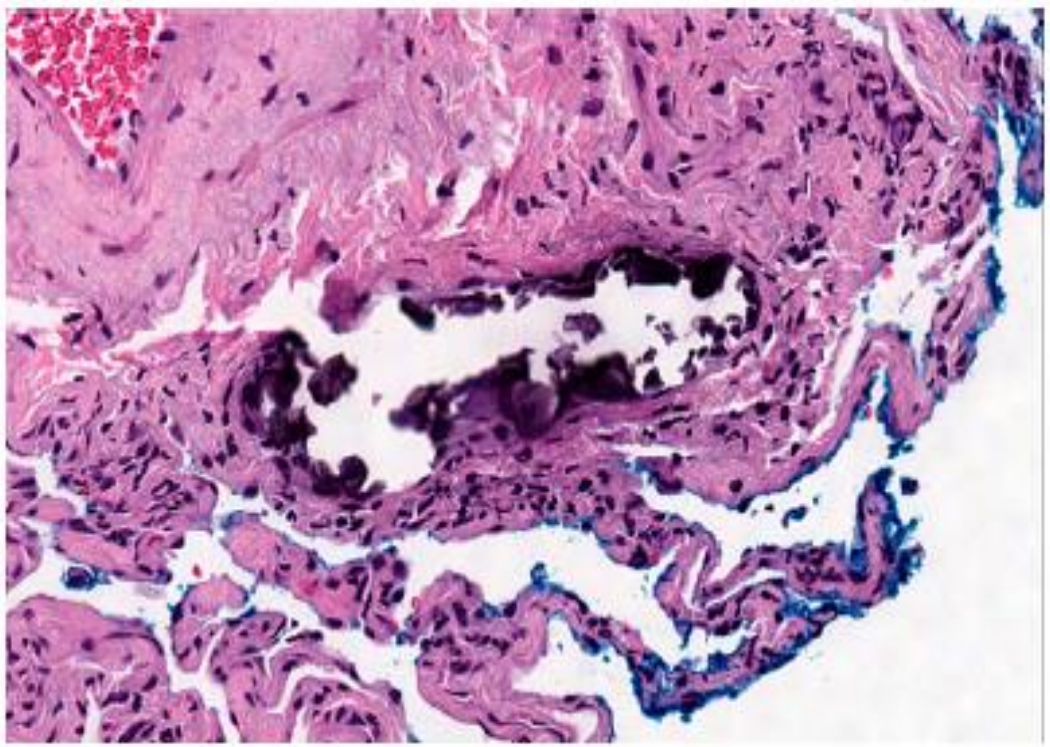
HP	Probable HP	Indeterminate for HP
Fibrotic HP‡ Typical histopathological features of fibrotic HP; *1* or *2 and 3* in at least one biopsy site: 1. Chronic fibrosing interstitial pneumonia • Architectural distortion, fibroblast foci ± subpleural honeycombing • Fibrotic NSIP-like§ pattern 2. Airway-centered fibrosis • ±Peribronchiolar metaplasia • ±Bridging fibrosis‖ 3. Poorly formed nonnecrotizing granulomas† ±Cellular interstitial pneumonia ±Cellular bronchiolitis ±Organizing pneumonia pattern *and* Absence of features in any biopsy site to suggest an alternative diagnosis • Plasma cells > lymphs • Extensive lymphoid hyperplasia • Extensive well-formed sarcoidal granulomas and/or necrotizing granulomas • Aspirated particulates	Both of the following features (*1* or *2* from first column) in at least one biopsy site: 1. Chronic fibrosing interstitial pneumonia • Architectural distortion, fibroblast foci ± subpleural honeycombing • Fibrotic NSIP-like pattern 2. Airway-centered fibrosis • ±Peribronchiolar metaplasia • ±Bridging fibrosis‖ ±Cellular interstitial pneumonia ±Organizing pneumonia pattern ±Cellular bronchiolitis *and* Absence of features in any biopsy site to suggest an alternative diagnosis • Plasma cells > lymphs • Extensive lymphoid hyperplasia • Extensive well-formed sarcoidal granulomas and/or necrotizing granulomas • Aspirated particulates	Either one of the following features in at least one biopsy site: 1. Chronic fibrosing interstitial pneumonia • Architectural distortion, fibroblast foci ± honeycombing • Fibrotic NSIP-like pattern ±Cellular interstitial pneumonia ±Cellular bronchiolitis ±Organizing pneumonia pattern *and* Absence of features in any biopsy site to suggest an alternative diagnosis • Plasma cells > lymphs • Extensive lymphoid hyperplasia • Extensive well-formed sarcoidal granulomas and/or necrotizing granulomas • Aspirated particulates

Am J Respir Crit Care Med 2020: 202(3); e36–e69

Fibrotic HP



expansion of the peribronchiolar interstitium

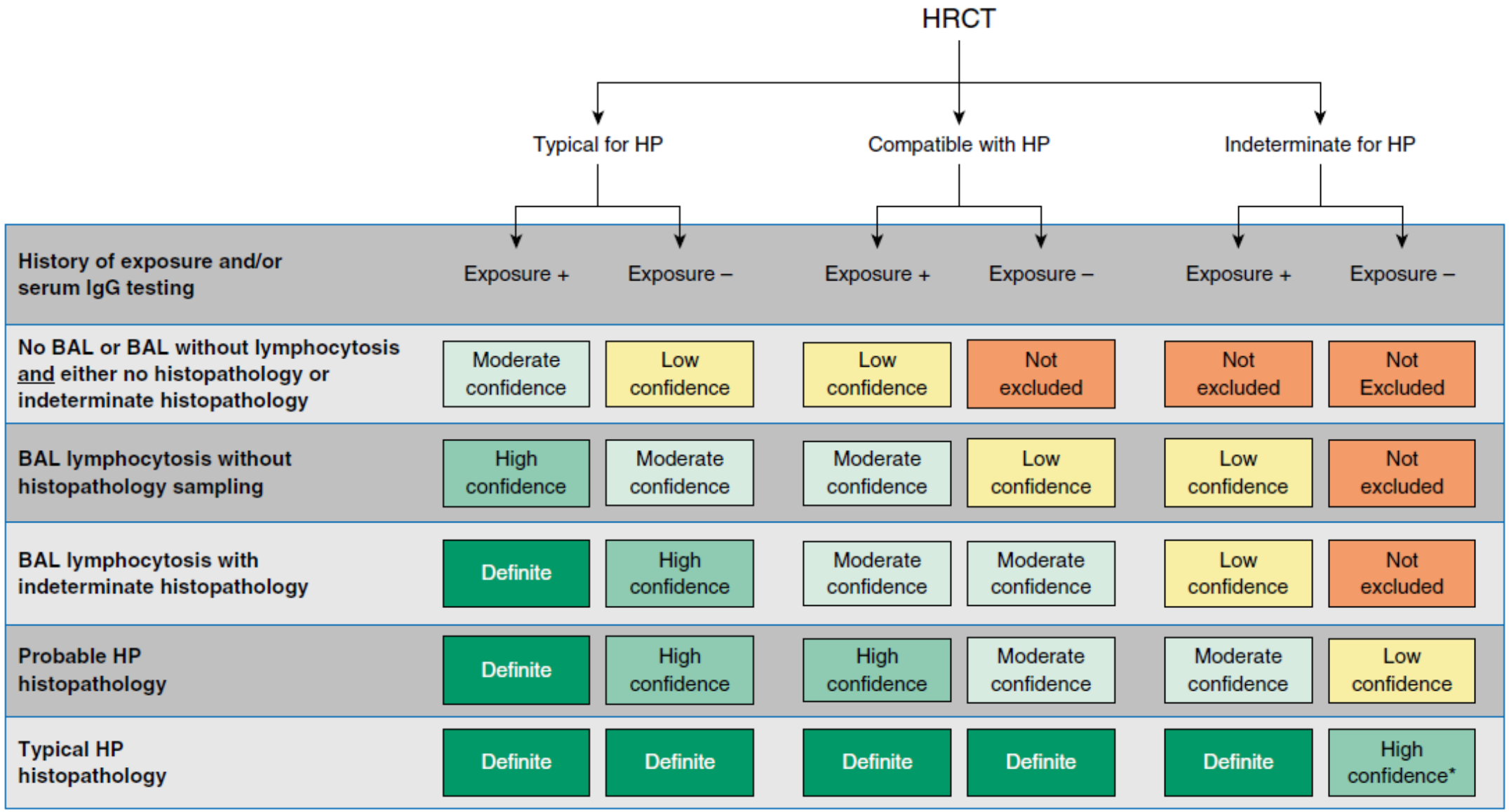


Schaumann bodies

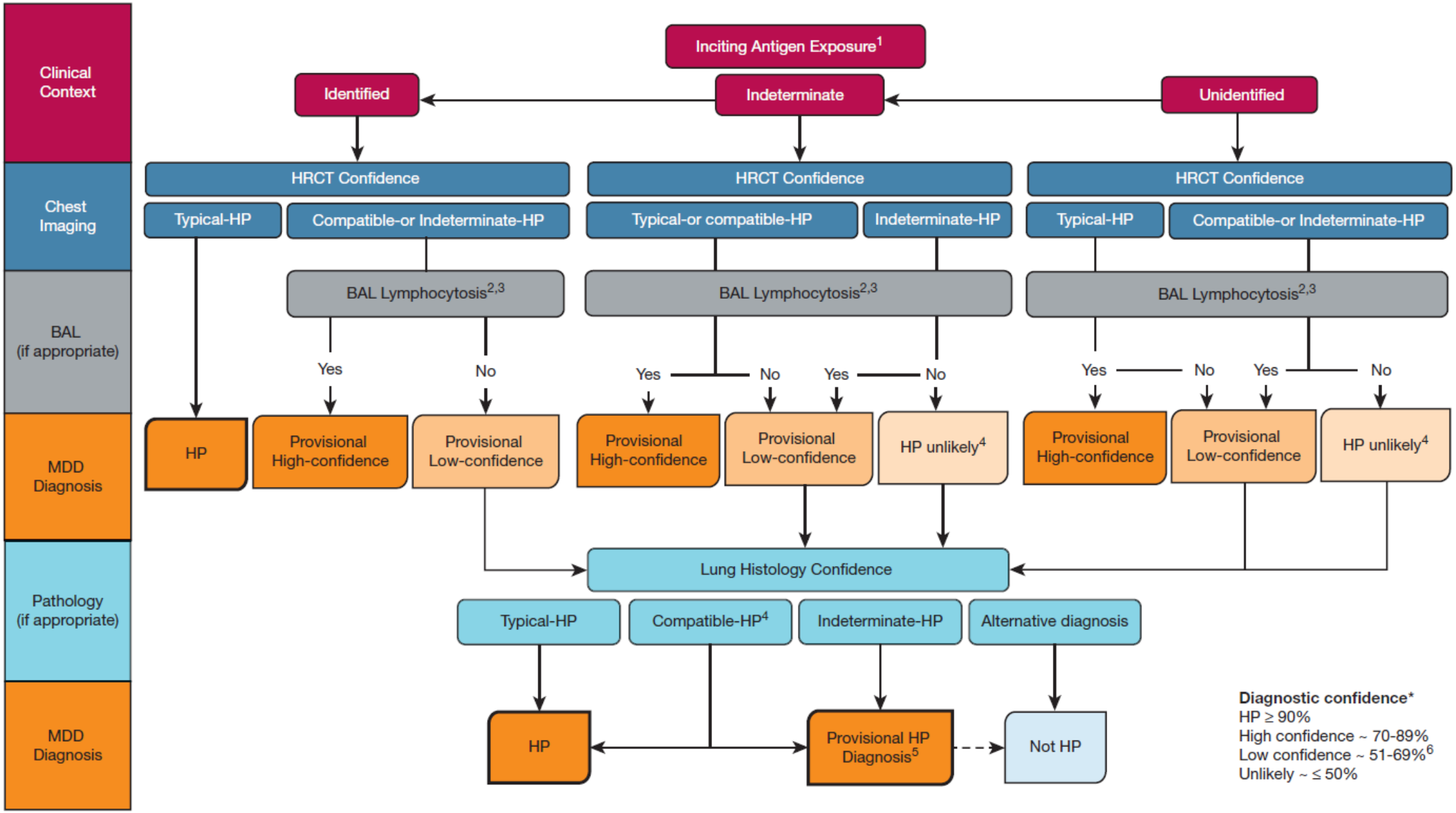
Diagnosis

- Exposure identification
  - Absence of an identifiable exposure in up to 50% of fibrotic HP
- Chest HRCT scan pattern
- Bronchoscopic/histopathological findings

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



Am J Respir Crit Care Med 2020: 202(3); e36–e69



CHEST 2021; 160(2):e97-e156

Treatment

- Antigen avoidance

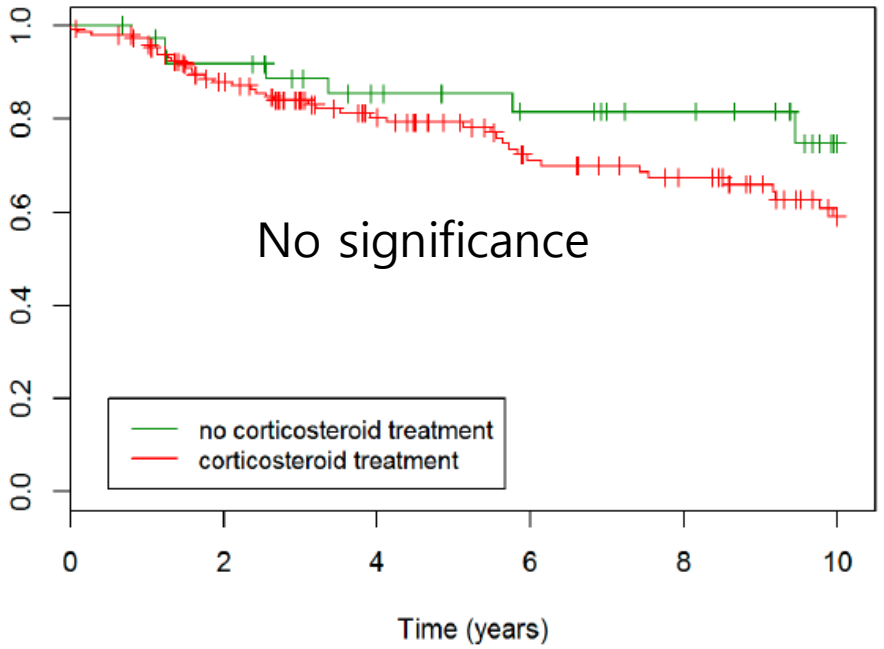
- Glucocorticoids
  - prednisone 0.5 mg/kg per day (up to 30 mg per day)
  - Acute: 1~2 weeks, tapered over the next 2~4 weeks
  - Chronic: 4~8 weeks, tapered to 10mg/day by 3months
- Immunosuppressants
  - Azathioprine (AZA)
  - Mycophenolate mofetil (MMF)
- Rituximab
- Antifibrotic agents
  - Nintedanib
  - Pirfenidone
- Lung transplantation

Corticosteroids

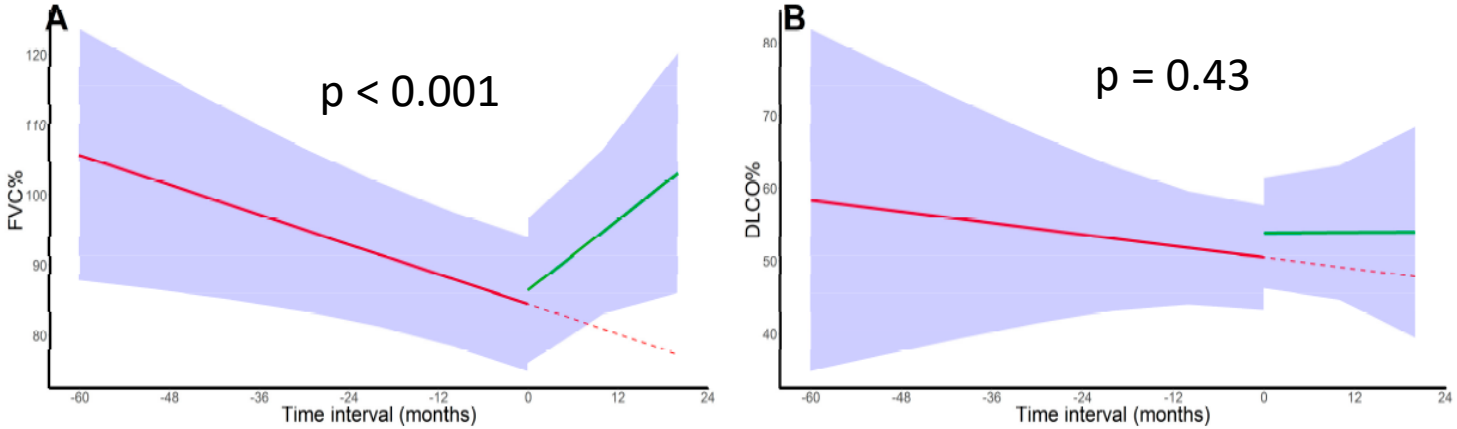
N=202

93 nonfibrotic HP, 109 fibrotic HP

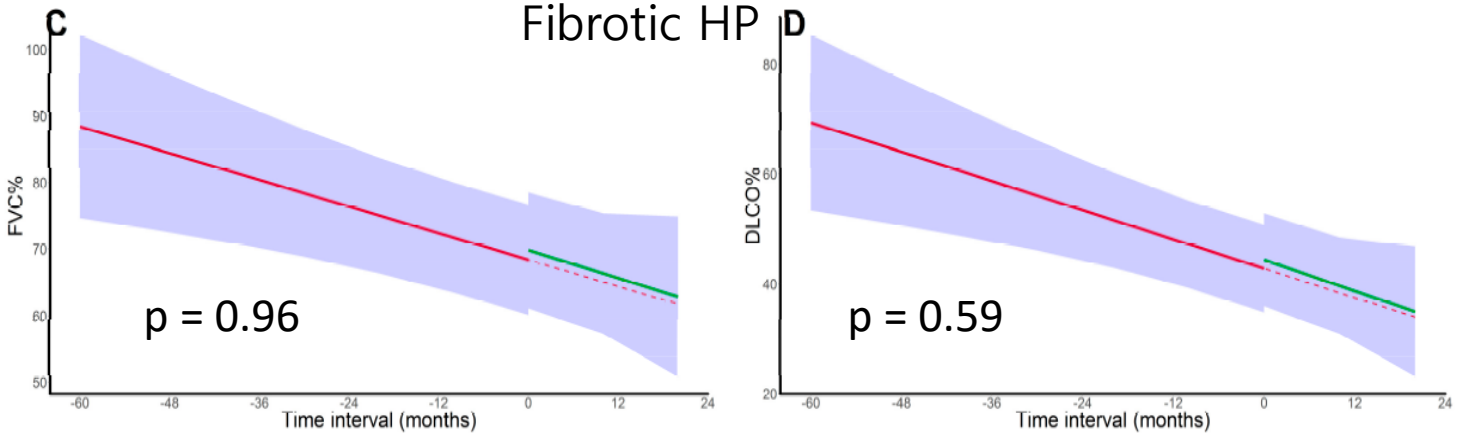
80% had corticosteroid Tx



Nonfibrotic HP



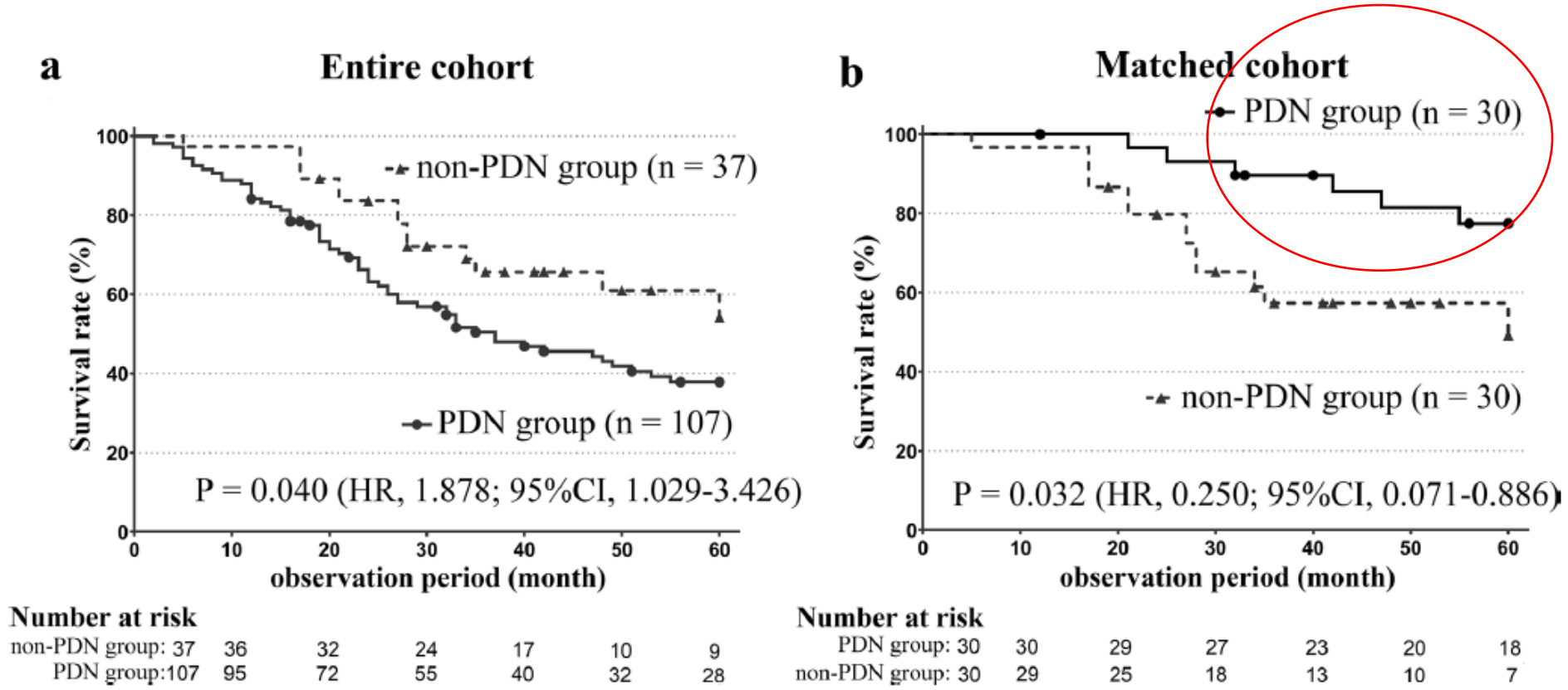
Fibrotic HP



J Clin Med 2019: 8;14

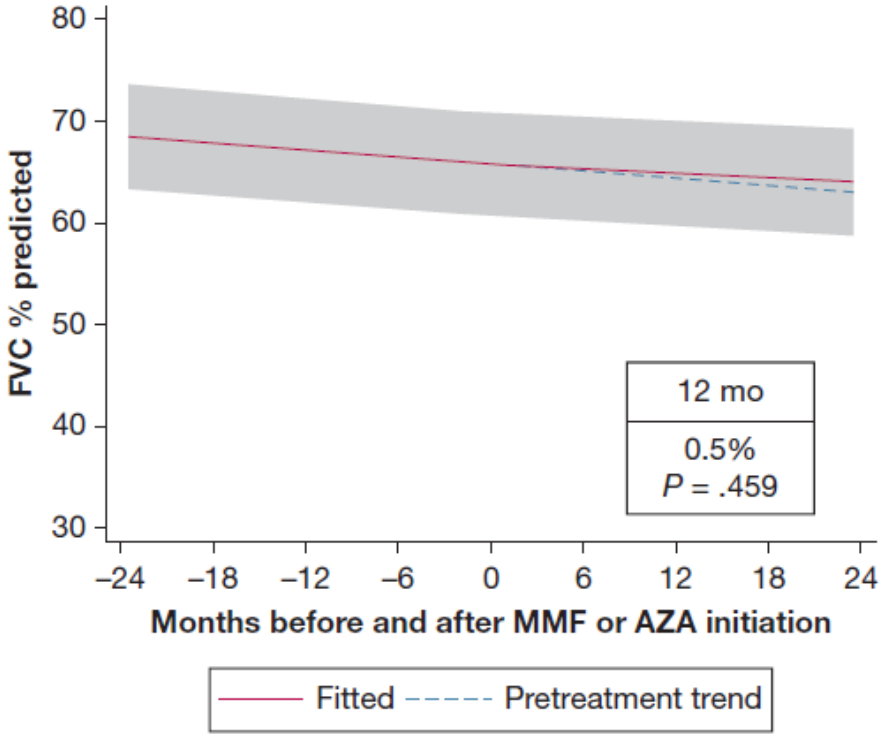
Corticosteroids in fibrotic HP

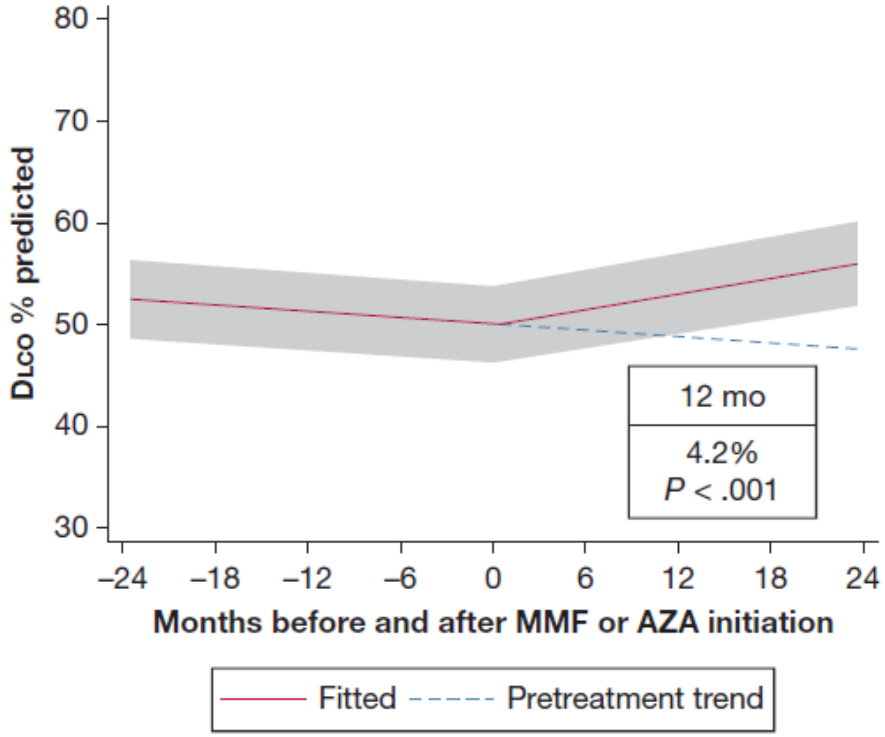
N=144, fibrotic HP w/o extensive fibrosis, Japan



BMC Pulm Med 2021: 21:243

Immunosuppressants: MMF or AZA





- Retrospective data, 4 center
- No effect on FVC, but improvement in DLCO of 4.2% (P < 0.001) after 1 year treatment.

CHEST 2017; 151(3):6 19-625

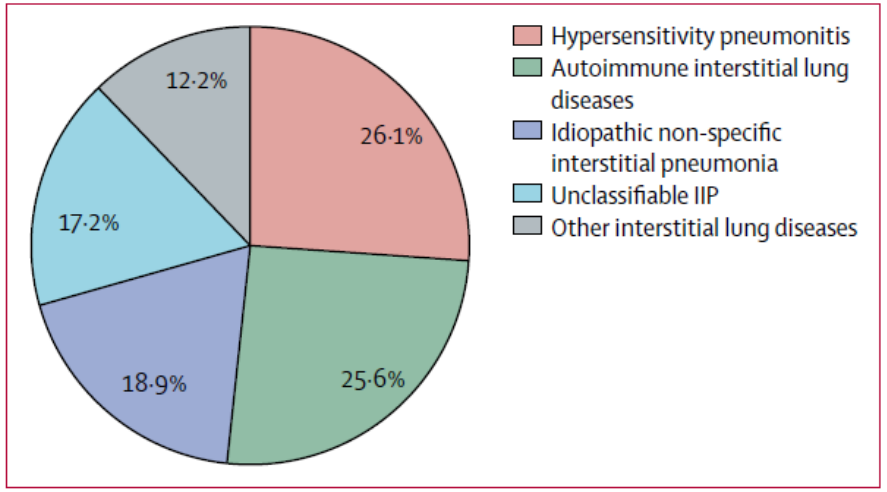
Antifibrotics: nintedanib, pirfenidone

Agent	Registration No.	Study design	Population	Aims	Primary end point	State
Nintedanib	NCT02999178 (INBUILD)	Phase III, randomized, double blind, placebo-controlled	Fibrosing ILDs	Efficacy and safety	Annual rate of FVC decline	Completed, published results
Pirfenidone	NCT02496182	Phase II/III, placebo-controlled, open-label, proof of concept	cHP	Efficacy and safety	FVC over 52 weeks	Completed, published results
Pirfenidone	EudraCT 2014–000861-32 DRKS00009822 (RELIEF)	Phase II, randomized, double blind, placebo-controlled	cHP	Efficacy and safety	Absolute change in % FVC from baseline to week 48	Completed
Pirfenidone	NCT02958917	Phase II, randomized, double blind, placebo-controlled	cHP	Efficacy and Safety	Mean change in % FVC from baseline to week 52	Ongoing

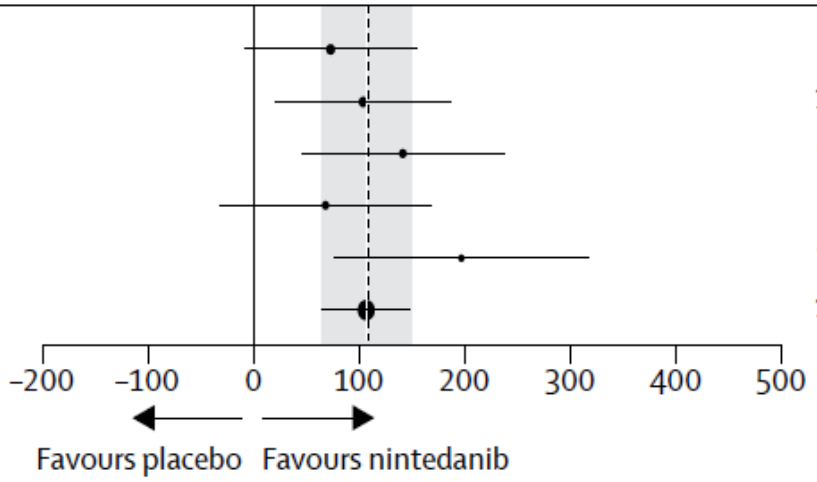
Tuberc Respir Dis 2020;83:122-131

Antifibrotics: nintedanib

- INBUILD study
  - 26% of chronic HP
  - Reduced the annual rate of FVC decline



	n analysed		Difference (95% CI)	Treatment by subgroup by time interaction
	Nintedanib	Placebo		
Hypersensitivity pneumonitis	84	89	73·1 (–8·6 to 154·8)	p=0·41
Autoimmune interstitial lung diseases	82	88	104·0 (21·1 to 186·9)	
iNSIP	64	61	141·6 (46·0 to 237·2)	
Unclassifiable IIP	64	50	68·3 (–31·4 to 168·1)	
Other interstitial lung diseases	38	43	197·1 (77·6 to 316·7)	
All patients	332	331	**107·0 (65·4 to 148·5)**	



N Eng J Med 2019;381:1718

Lancet Respir Med 2020;8: 453–60

Antifibrotics: pirfenidone

- Open-label Study With Pirfenidone
  - 22 chronic HP
  - Immunosuppressant + pirfenidone
  - Not associated with improvement of FVC, DLCO
  - But improved quality of life

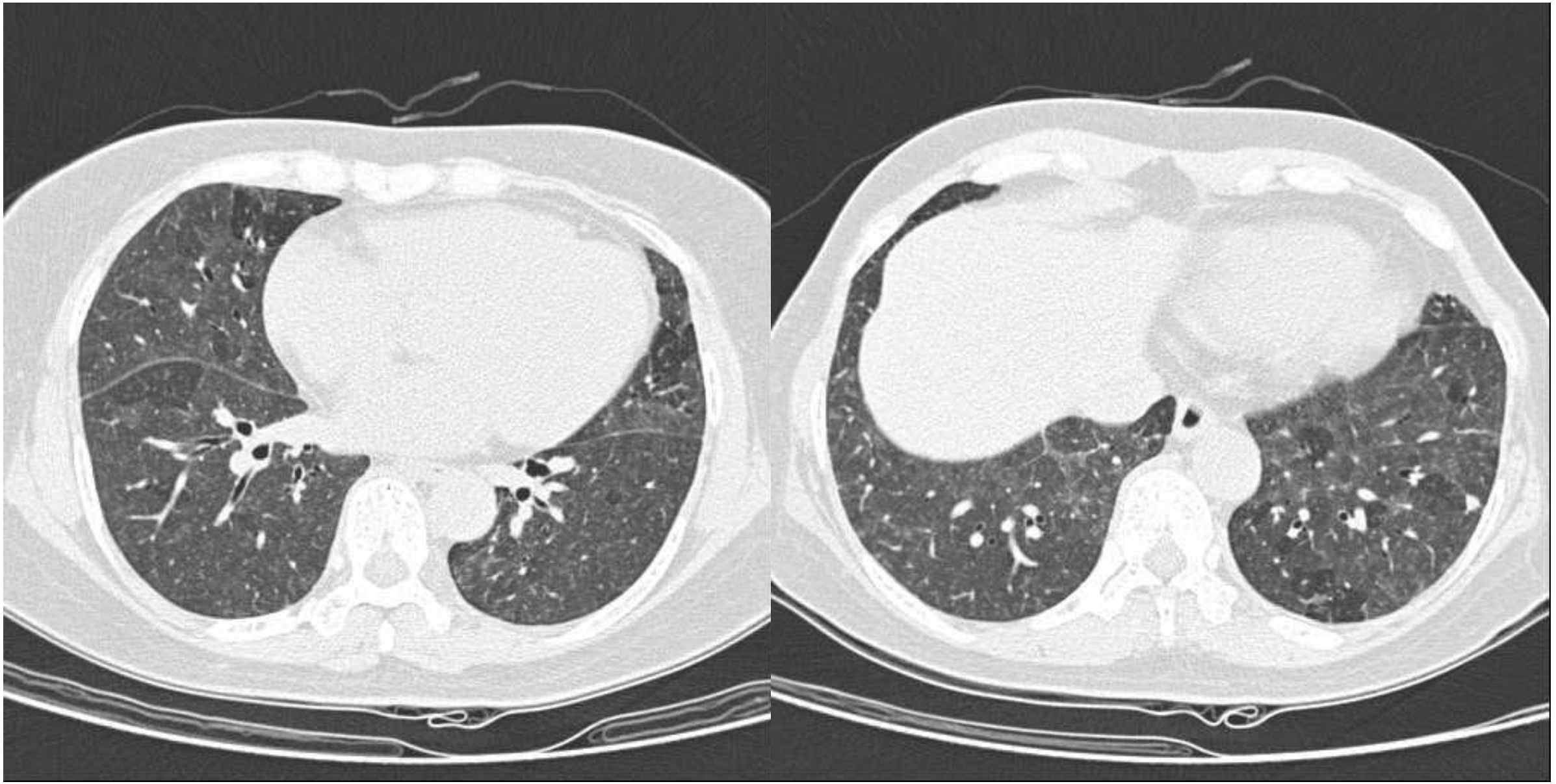
- RELIEF study
  - 45% of chronic HP
  - Decreased change of FVC% predicted

Arch Bronconeumol 2020; 56(3):163-169

Lancet Respir Med 2021;9: 476

F/58, cough, sputum for 3 months

- 2012
- 충북 제천, 농사-고추 따기 등
- 비료 포대 접는 일
- 가축 (-)
- 비흡연자
- 25년 된 조립식 주택, 베란다- 곰팡이 약간



F/58, cough, sputum for 3 months

2012 VATS lung biopsy

Lung, right upper lobe, wedge resection :

Cellular interstitial pneumonia

with 1) lymphoplasmacytic inflammation

2) peribronchial and subpleural distribution

3) a few foreign-body type giant cells and granulomas formation

4) type II pneumocyte hyperplasia

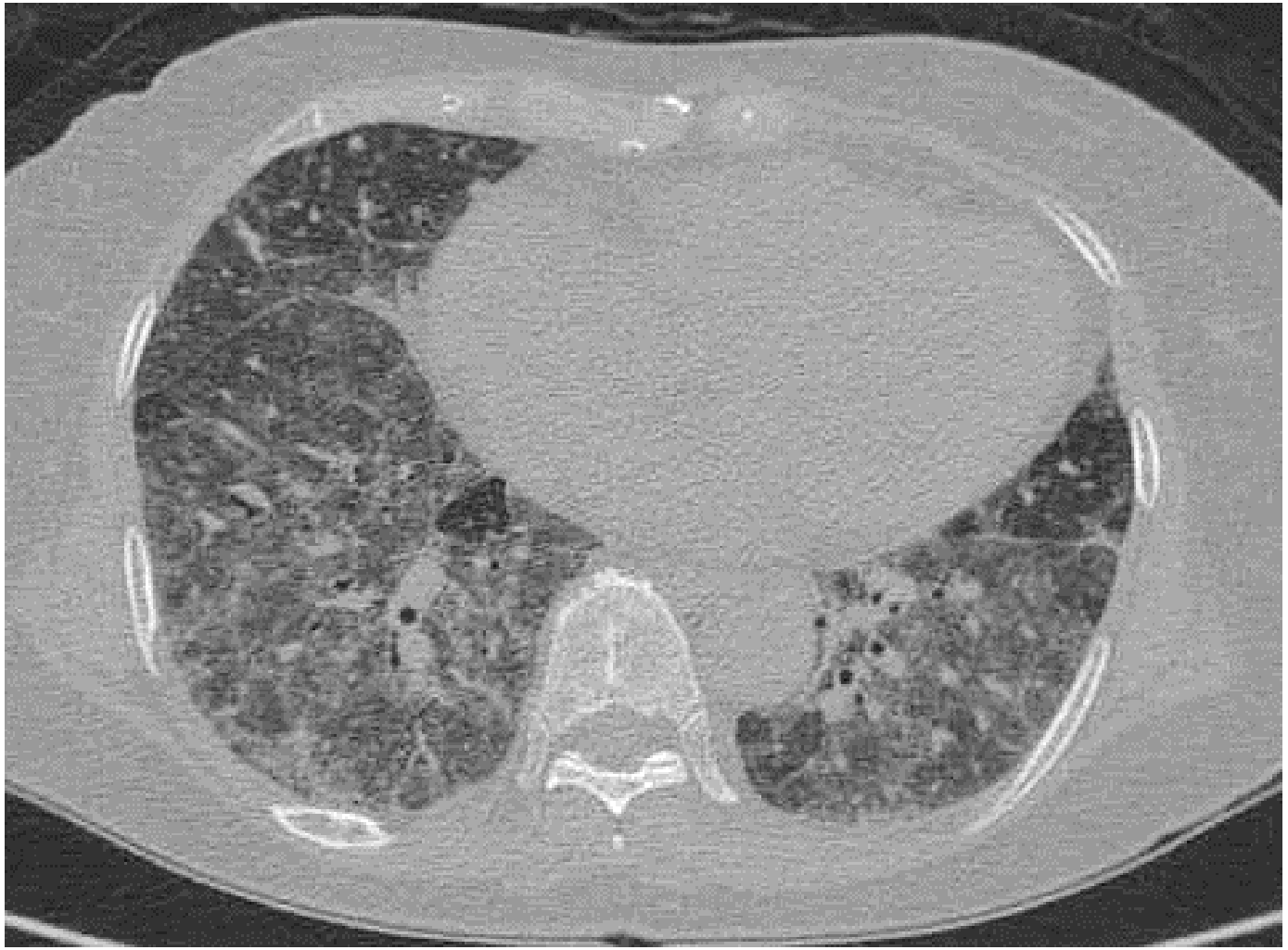
Consistent with hypersensitivity pneumonia

Pd 20mg ~ taper off within 2 months → F/U loss

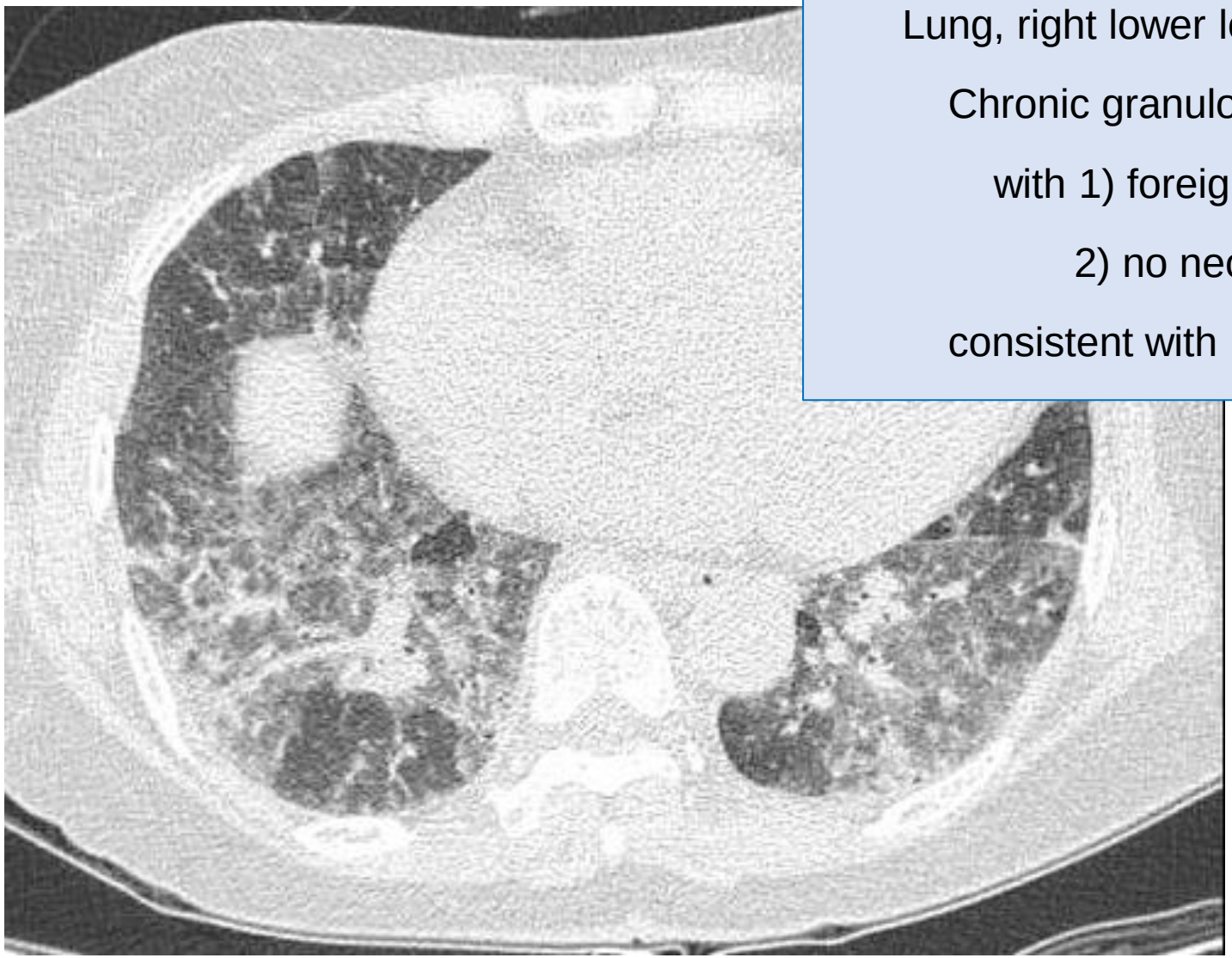
2016 dyspnea, lower leg pitting edema

Nephrotic syndrome, Kidney biopsy: MPGN

High dose steroid + MMF → F/U loss



2017 dyspnea, wheezing



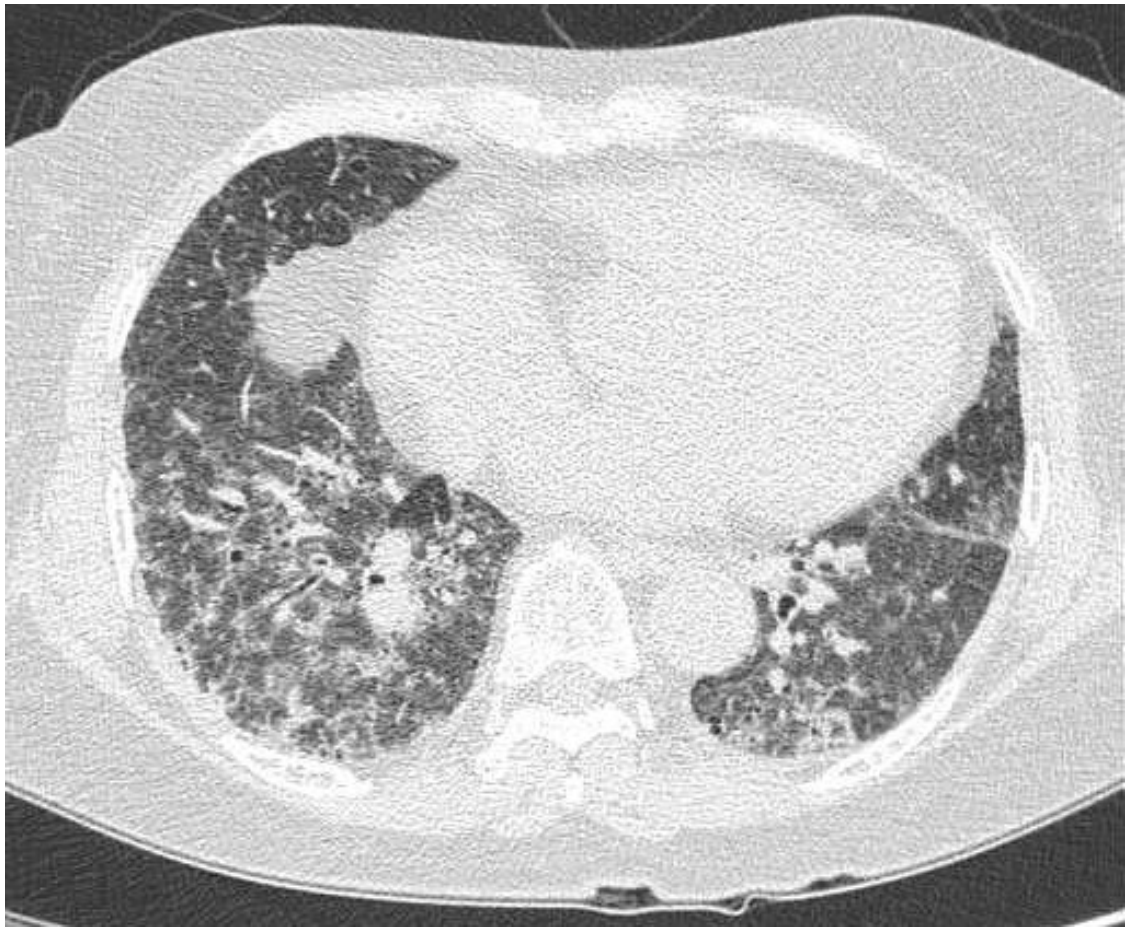
Lung, right lower lobe, transbronchial lung biopsy :

Chronic granulomatous inflammation

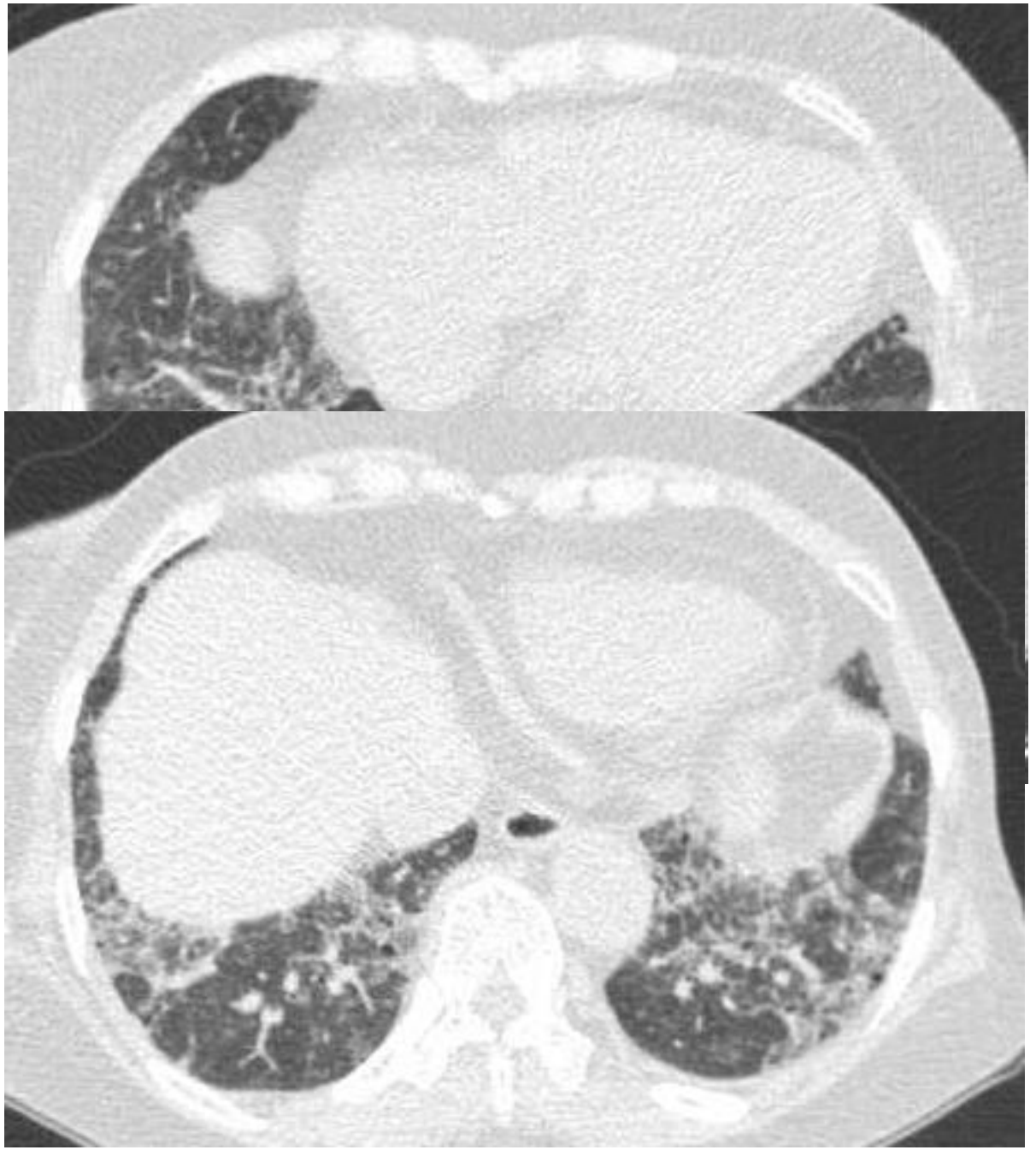
with 1) foreign body type multinucleated giant cells

2) no necrosis

consistent with Hypersensitivity pneumonitis



2019



Summary

- Careful history taking is important for the diagnosis of HP.
- Two subtypes of HP: Nonfibrotic vs fibrotic HP
- Diagnosis of HP can be made by multidisciplinary discussions
  - Radiologic findings
  - BAL lymphocytosis
  - Histopathologic findings
- Treatment of HP
  - Avoidance of antigen
  - Corticosteroids and/or immunosuppressants
  - Antifibrotics might be helpful in fibrotic HP.