Update On Interstitial Lung Disease ACOI 2022

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Conflict of Interest

Entry of patients into ASCEND Trial

Jansen Speaker's Bureau

Goals and Objectives

- To understand the epidemiology and anatomy of Interstitial Pneumonitis variants.
- To understand the initial diagnostics and basics of diagnosis.
- To provide an overview of the 8 types of Interstitial Pneumonitis.
- To understand treatment options of the Interstitial Pneumonitis variants.
- To introduce COVID-19 ILD

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Pulmonary Anatomy/Physiology

Interstitial Lung Version

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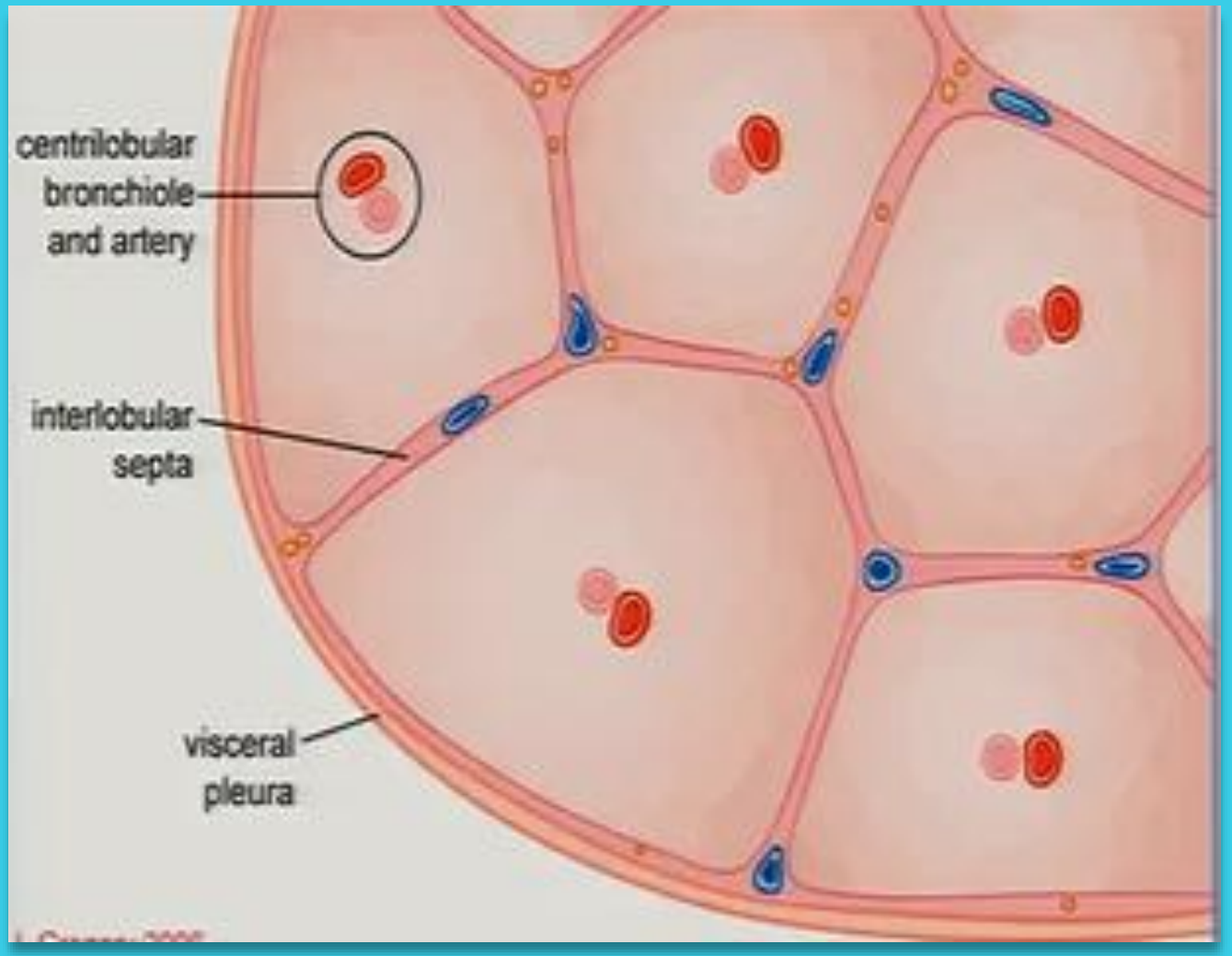
Secondary pulmonary lobule

- Functional unit where gas exchange occurs
- Can be visible on HRCT
- Irregular polyhedral shaped lobule approximately 1-2.5cm with 12-20 acini in one lobule with each acini about 0.5 to 1 cm and made of central and septal structures.



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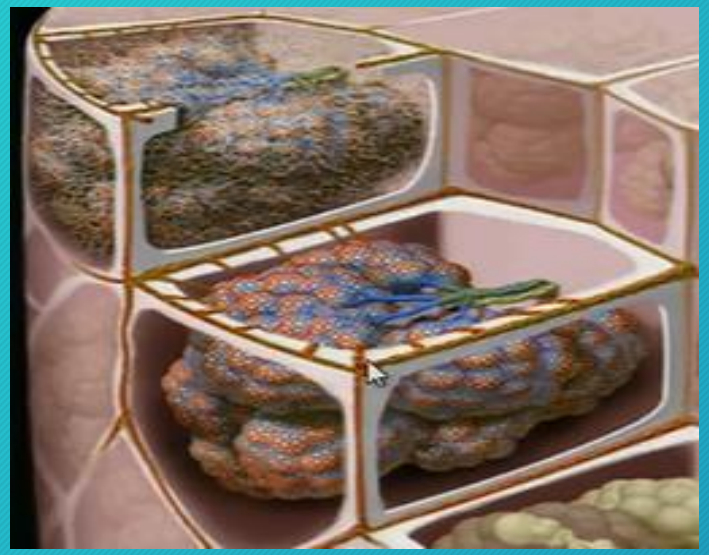
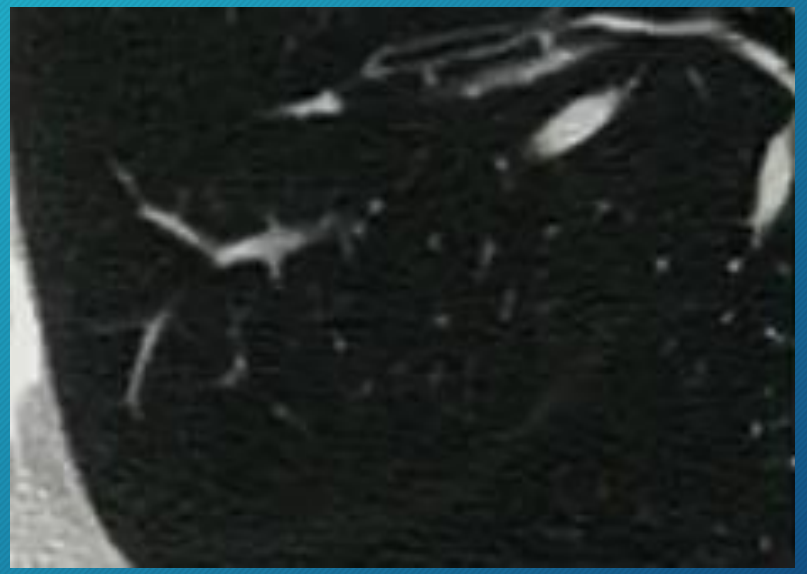
Pulmonary Anatomy/Radiologic Anatomy

Secondary Lobule Anatomy

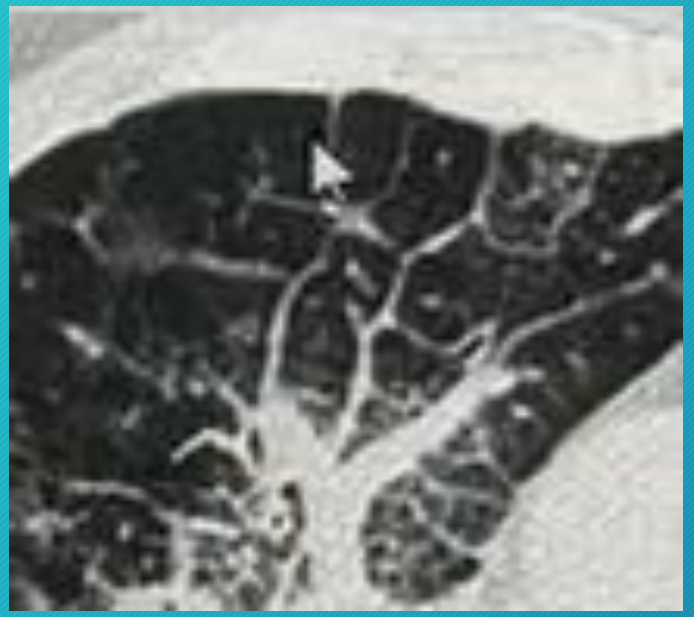


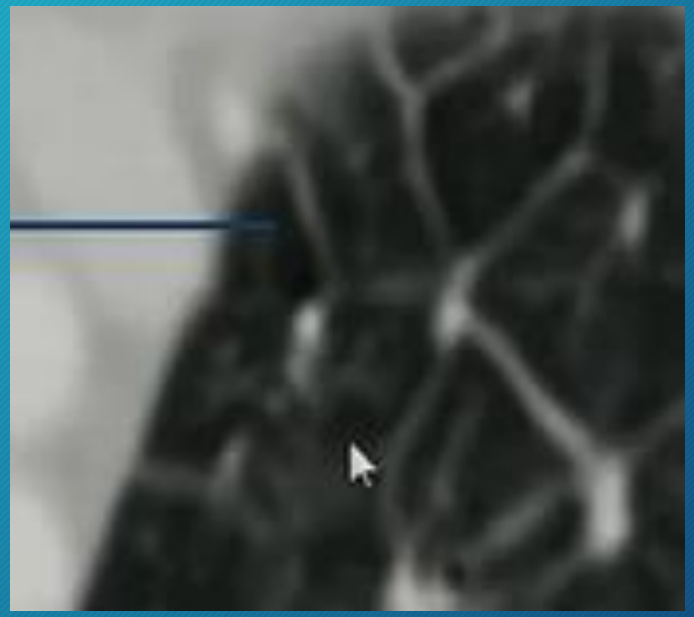
Normal HRCT : Lobules NOT visible



ILD: Radiologic Anatomic Descriptions

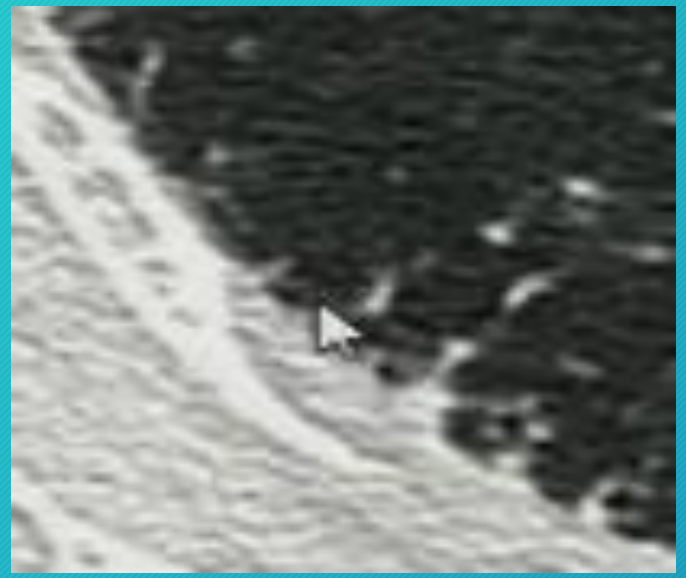
- Walls of secondary pulmonary lobule – thickened
- Septal lines to pleura and are perpendicular



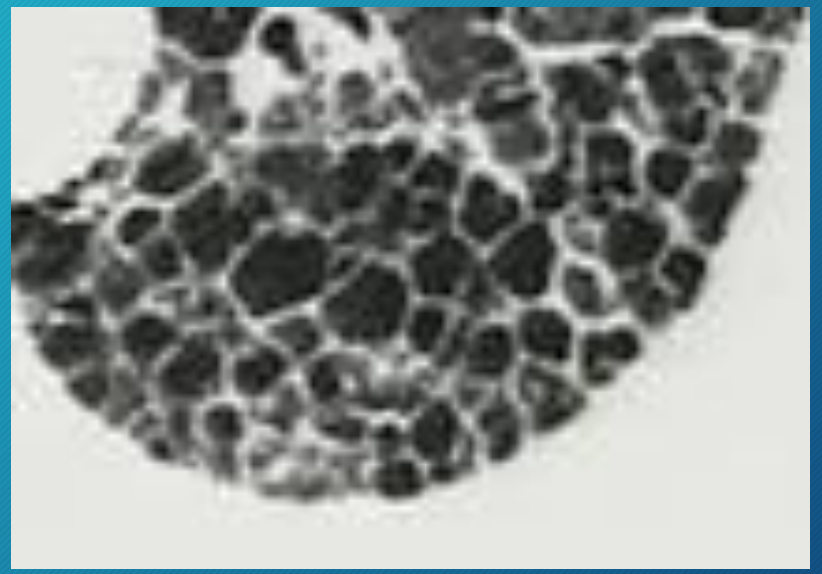


ILD: Radiologic Anatomy

Intralobular septal thickening: fine lines of intralobular septum



Honeycomb cysts: Small cystic spaces lined by bronchiolar epithelium, ~1cm in diameter, peripheral/subpleural.



Suggests end-stage disease

Pulmonary Function Testing: ILD

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Interstitial Lung Disease/PFT Criteria

- PFT: Restrictive Defect
  - Decreased lung volumes (FVC, VC, TLC)
  - Normal expiratory flow rates (Ratio & FEV1)
  - Spirometry does **NOT** accurately diagnose restriction
  - Reduced TLC from single-breath technique should **NOT** be used
    - Body plethysmography
  - Widened A-a O2 gradient on ABG
  - Reduced DLCO to a greater extent than at the lung volume at which it is measured (often the first thing you see)

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PFT Issues – other

- **Mixed Obstruction/Restriction can occur obscuring picture**
- **Obesity:**
  - As BMI increases, ERV drops even with BMI 26-30
  - FRC reduces as the BMI > 40 (Stiffening)
  - DLCO tends to increase (but often remains in normal range)
  - VC, TLC, RV tend to decrease (but often remains in normal range)

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Diffuse Lung Disease

‘Idiopathic’ Interstitial Pneumonitis

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Diffuse Lung Disease Types: "Alphabet Soup"

- Usual (UIP) -> IPF
- Desquamative -> DIP (not really idiopathic as tobacco related)
- Respiratory Bronchiolitis -> RB-ILD (not really idiopathic as tobacco related)
- Diffuse Alveolar Damage -> AIP
- Nonspecific -> NSIP (overlap and similarities to UIP)
- Lymphoid -> LIP
- Cryptogenic organizing pneumonia (COP)
- Idiopathic Pleuroparenchymal Fibroelastosis

- Others: Hypersensitivity Pneumonitis -> HP: Acute / Chronic (not covered here)

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Important management strategy in ILD

Is it IPF or is it one of the rest?

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Diffuse Lung Disease

Idiopathic Pulmonary Fibrosis : IPF

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Diffuse Lung Disease - IPF

- Features of IPF:
  - breathlessness (>90%)
  - non-productive cough (>70%)
  - bibasilar crackles (>85%)
  - clubbing (>25%)
- Cause :unknown
  - Aging
  - Environmental ? (?dust, metals, irritants?)
  - Genetic ?common?
  - Risks: smoking, agricultural -> livestock, wood dust, metal dust, stone/sand.
  - GERD is increased in IPF especially awaiting transplant
  - Familial 0.5-3.7% familial especially where smoking is still a risk.

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Diffuse Lung Disease – IPF: Clinical

- Clinical:
  - Chronic progressive fibrosis
  - Age: older adults (usually > 55)
  - Prevalence: Male
  - More common in smokers either current or former
- Mortality high (30-70% at 5 years)
  - If someone has “IPF” for > 10 years you should question diagnosis.
- ~10% with IPF will develop lung cancer.
- ~10% of pts have an indolent course.

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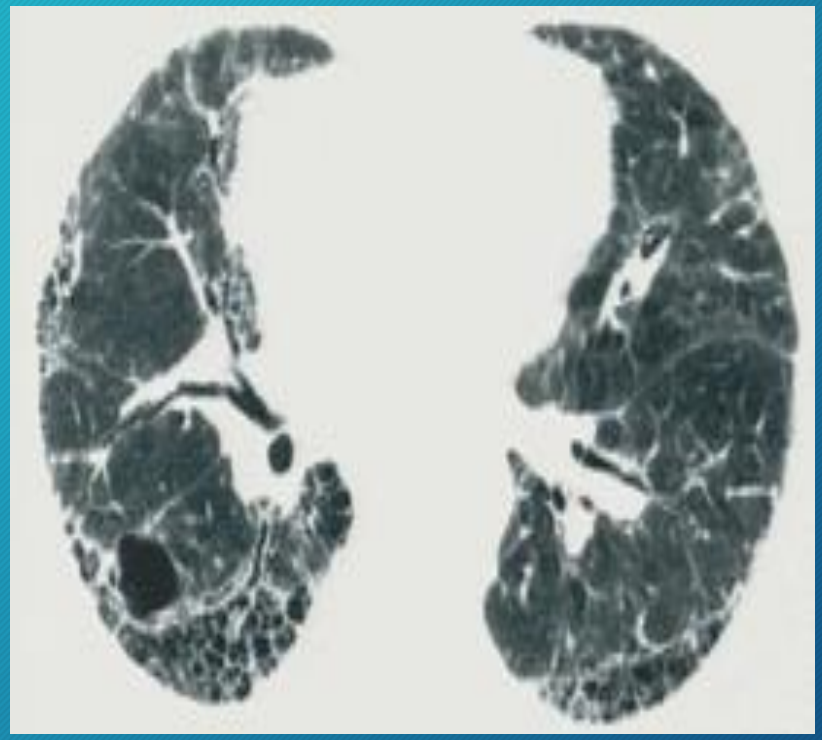
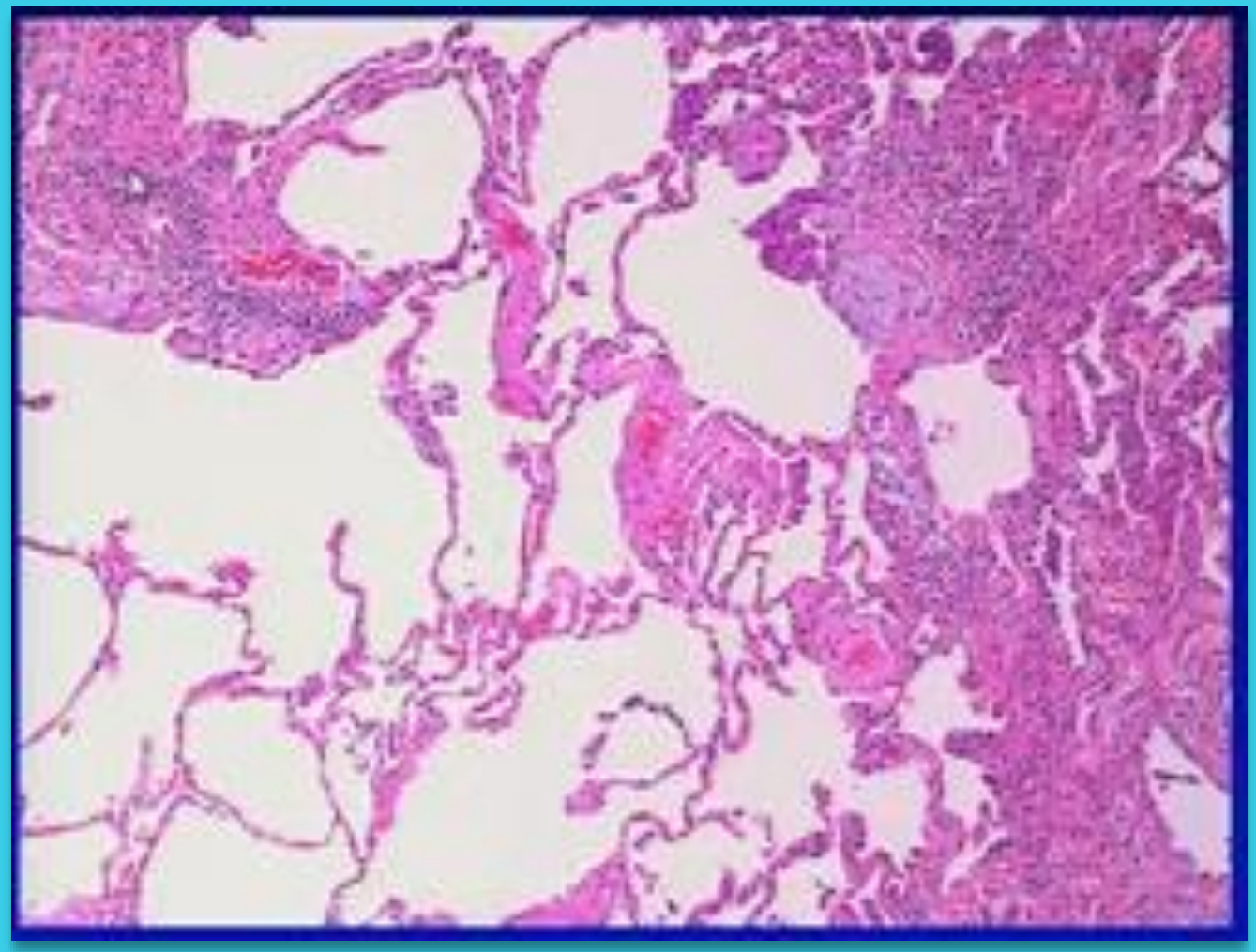
Diffuse Lung Disease – IPF Radiology: HRCT

- Predilection for subpleural regions (lower lobes)
- HRCT (4 key criteria)
  - Reticular opacities
  - Subpleural location
  - Honeycombing with +/- traction bronchiectasis
  - Few ground glass opacities



Diffuse Lung Disease IPF Histology

- Histologic features:
  - Heterogeneity
    geographically, temporally
  - Fibrosis
  - Inflammation
  - Cysts
  - Patchy normal lung.



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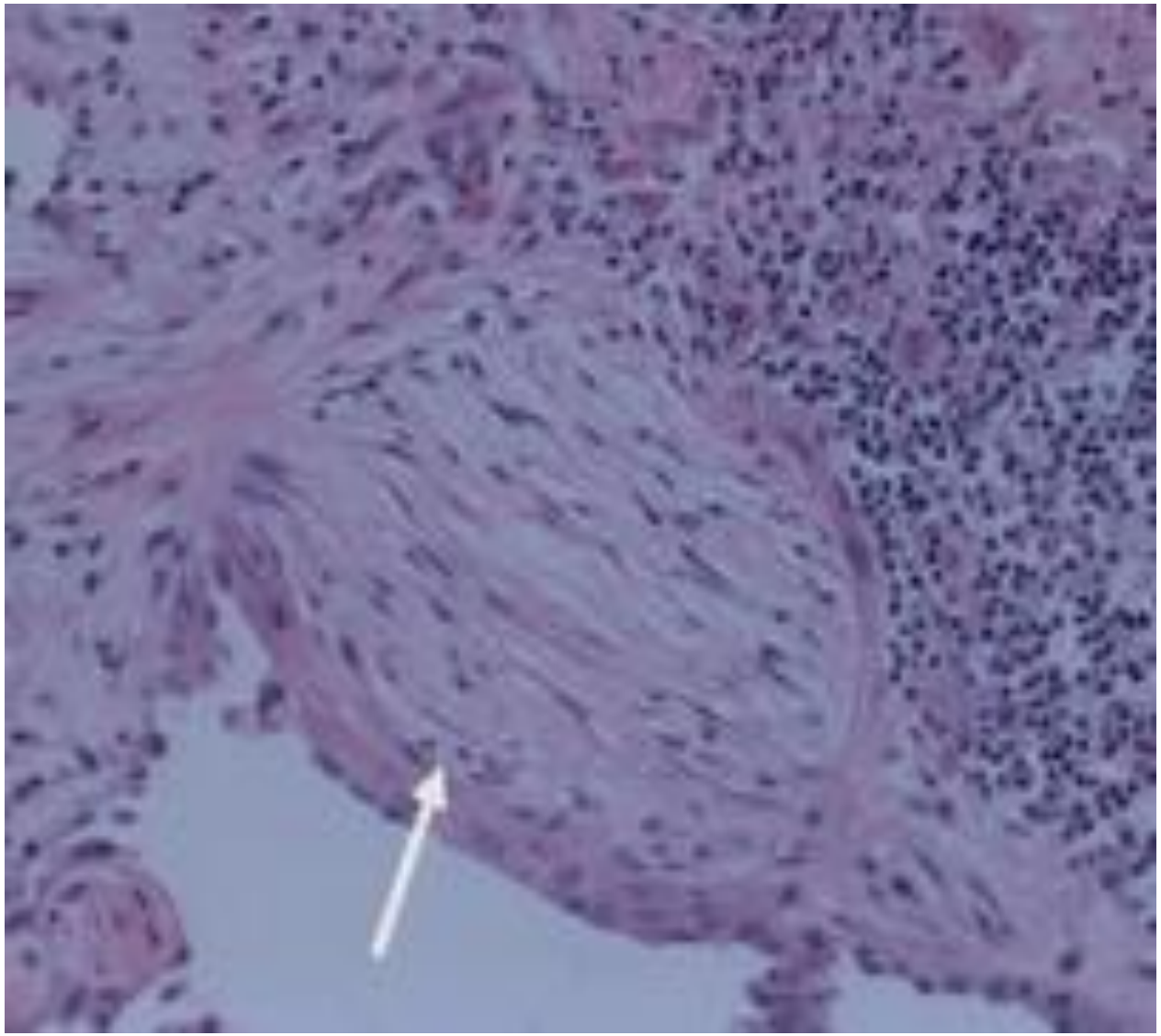
Diffuse Lung Disease IPF Histology

- Fibroblastic foci
- Inflamed fibrosis especially in honeycomb regions



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Diffuse Lung Disease – IPF Treatment History

- High dose prednisone was standard of care for >40 yrs despite NO firm evidence for benefit.
- Immunosuppressive (IS) agent azathioprine and cyclophosphamide also showed no firm evidence of efficacy.
  - 2012 PANTHER study was terminated due to higher mortality of AZA, prednisone and NAC vs placebo. NEJM 2012.

https://www.nejm.org/doi/full/10.1056/NEJMoa1113354

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Diffuse Lung Disease

Anti-fibrotic Agents

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Nintedanib (OFEV) - IPF

Tyrosine Kinase Receptor blocker - mediate elaboration of fibrogenic growth factors (eg, platelet-derived growth factor, vascular endothelial growth factor, fibroblast growth factor)

Appears to slow the rate of disease progression in IPF

www.nejm.org/doi/full/10.1056/NEJMoa1402584

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Nintedanib: Tomorrow & Inpulsis Trials

- TOMORROW I & II, INPULSIS I, II & III
- Annual rate of decline in FVC, time to exacerbation, change in baseline SGRO total score and mortality.
  - No difference however in key secondary endpoints.
- n=1231 (Nintedanib n=723, placebo n=508)
- Nintedanib has beneficial effect on **slowing** disease progression
- Diarrhea was most frequent side effect (61.5% vs 17.9%)

https://doi.org/10.1016/j.rmed.2016.02.001

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"Utility of Nintedanib for Severe Idiopathic Pulmonary Fibrosis"

- Nintedanib IPF: "real world"
- Criteria of INPULSIS trial
- Moderate n=34, Severe n=17
- Benefit reduced in patients in severe group
- EARLY treatment is important.

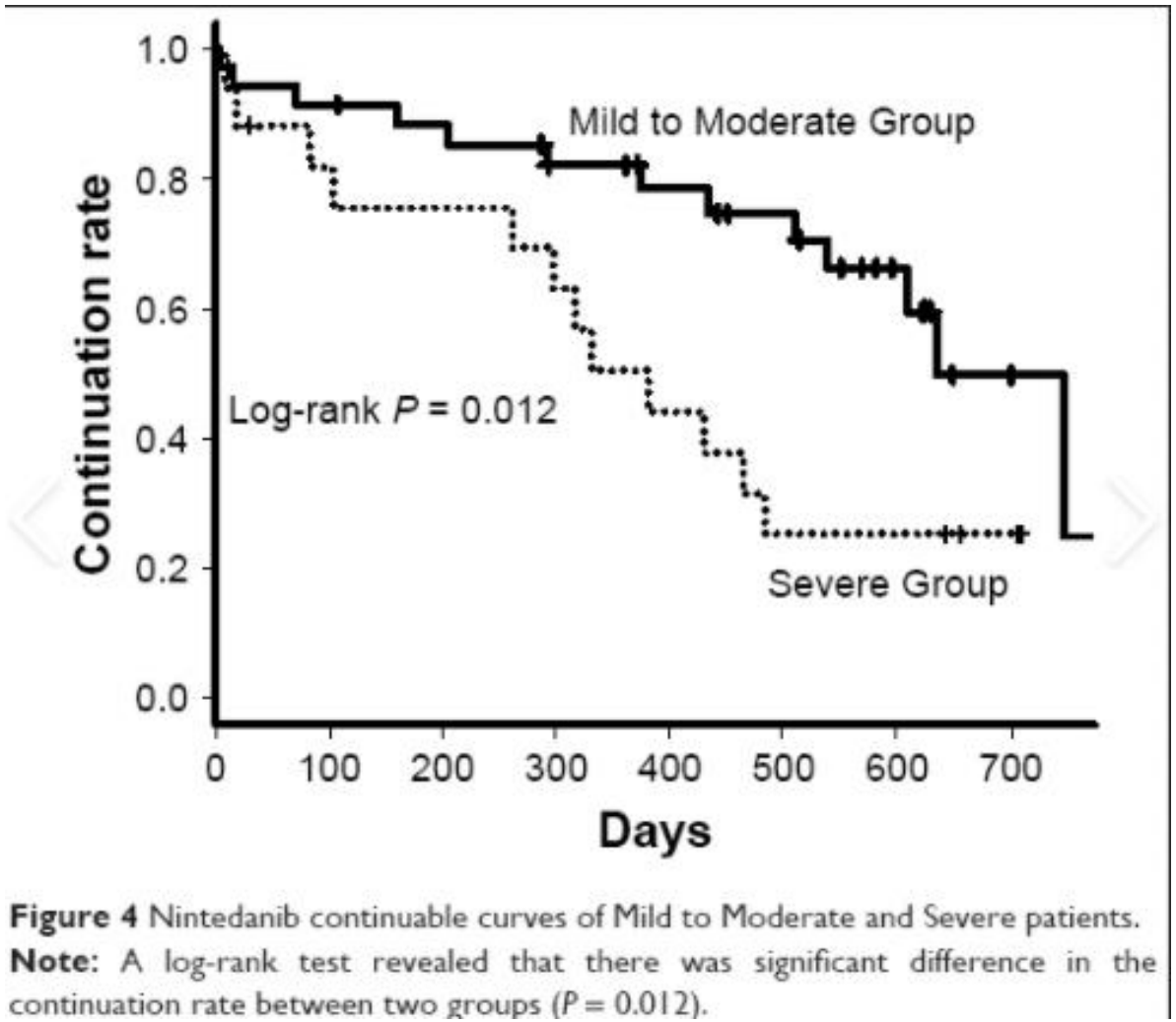

Figure 4 Nintedanib continuable curves of Mild to Moderate and Severe patients.
Note: A log-rank test revealed that there was significant difference in the continuation rate between two groups ($P = 0.012$).

https://doi.org/10.2147/DDDT.S179427

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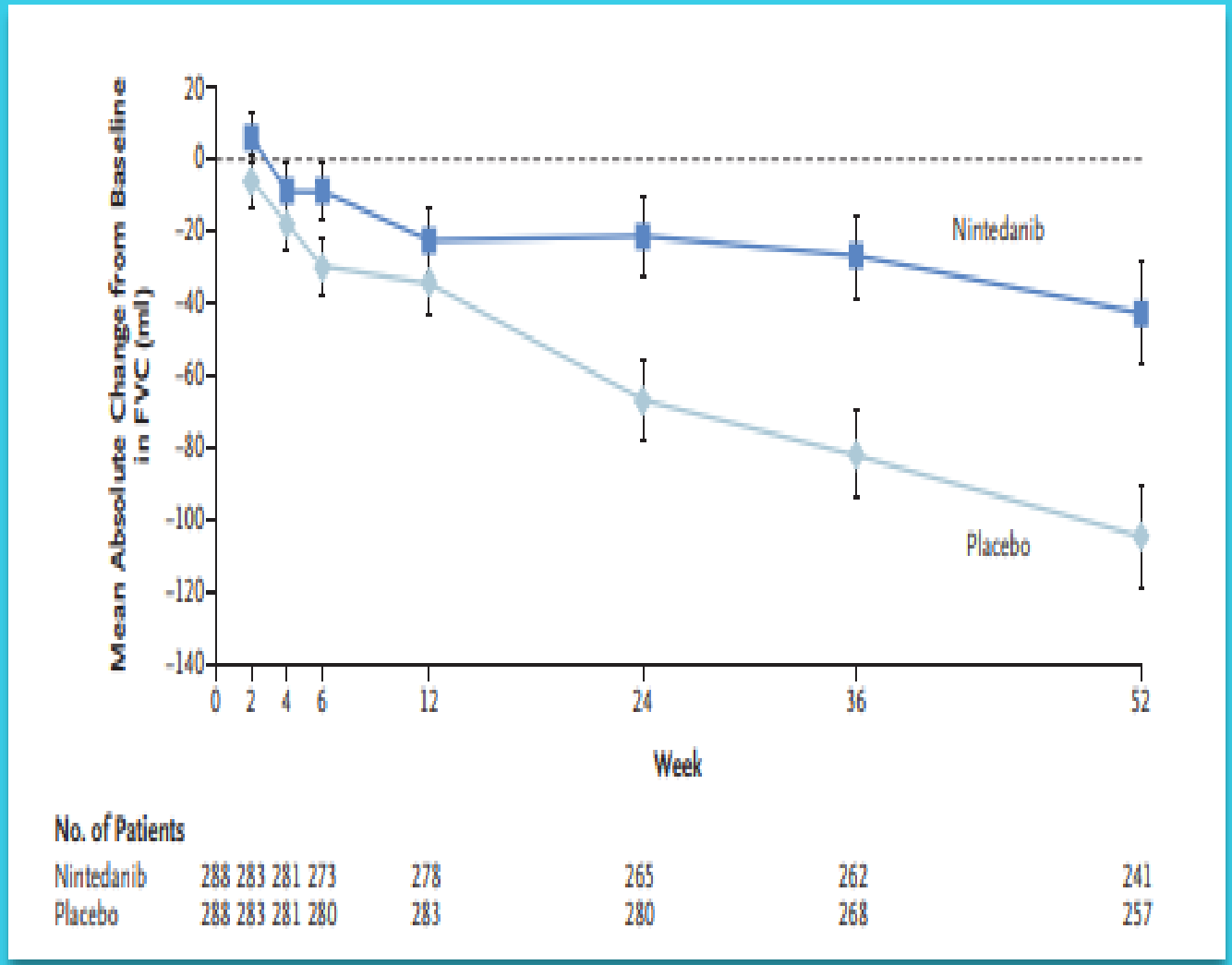
SENSCIS Trial: ILD From Systemic Sclerosis

- ILD from SS – double-blinded, placebo controlled, onset of SS non-Raynaud's symptoms within last 7 years.
- n=576, 51.9% diffuse cutaneous, 48.4% on Mycophenolate.
- 150mg Nintedanib PO BID, over 52 weeks
- Change in FVC 52.4ml vs 93.3ml with difference being 41.0ml, CI 2.9 to 79.0, p=0.04
- NO difference Modified Rodnan Skin Score and SGRO at week 52 showed NO difference.
- Diarrhea common AE: 75.7% vs 31.6%



https://www.nejm.org/doi/pdf/10.1056/NEJMoa1903076

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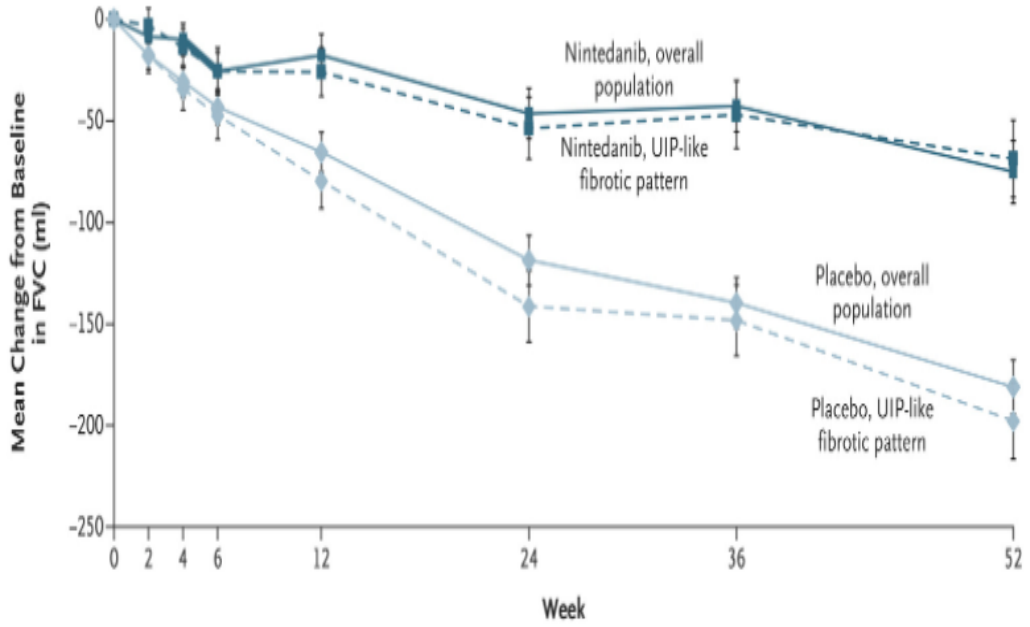
INBUILD Trial : “Not IPF”

- Nintedanib in lung fibrosis **other than IPF**
- 153 sites in 15 countries, n=663 (excluded AZA, CYC, Myco, Tacro, Ritux, CYSP)
- “Progressive fibrotic phenotype other than IPF:
  - affecting > 10% of lung volume on HRCT
  - Decline FVC of 5% to < 10% of predicted
  - Worsening symptoms, increased fibrosis
  - FVC at least 45% of predicted, DLCO of 30% to < 80% predicted
- Result: adjusted rate of decline difference FVC 107.0 ml per year



No. of Patients								
Overall population								
Nintedanib	332	326	320	322	314	298	285	265
Placebo	331	325	326	325	320	311	296	274
Patients with UIP-like fibrotic pattern								
Nintedanib	206	203	200	199	193	180	171	160
Placebo	206	202	202	201	197	190	176	162

https://www.nejm.org/doi/full/10.1056/NEJMoa1908681

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Pirfenidone (Esbriet)- IPF

Antifibrotic agent that inhibits TGF-b-stimulated collagen synthesis, decreases the extracellular matrix

Block fibroblast proliferation

https://www.nejm.org/doi/full/10.1056/NEJMoa1402582

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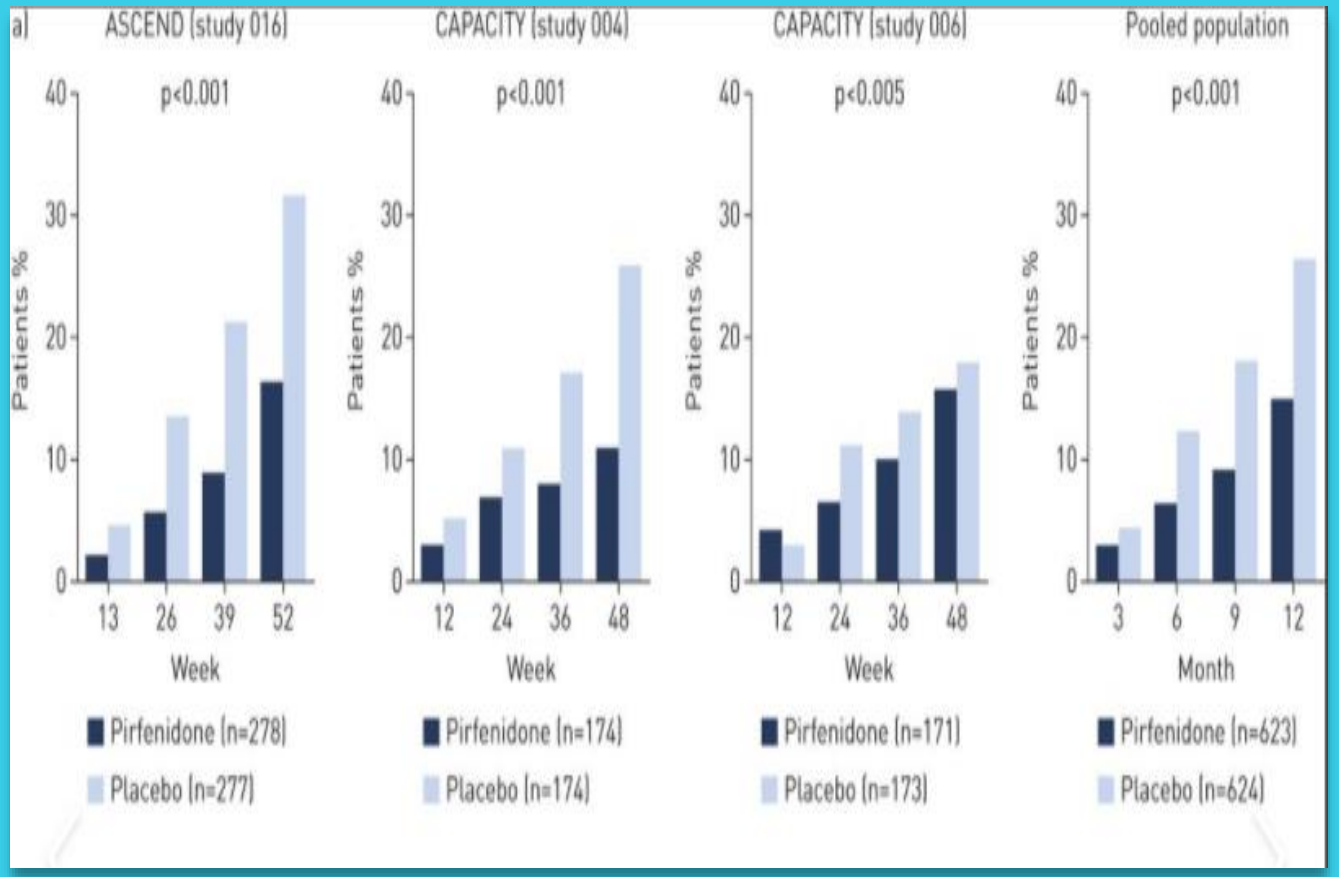
Pirfenidone : analysis of pooled data three multinational phase 3 trials

- Pirfenidone 2403mg per day vs placebo
- Pooled analysis at 1 year (ASCEND, Capacity 4 & 6)
- N=1247
- Pirfenidone reduced patients with > 10% decline in FVC by 43.8%
- Increased proportion with no decline by 59.3%
- Benefit of progression-free survival, 6MWD and dyspnea
- GI and skin-related AE most common.

https://erj.ersjournals.com/content/47/1/243



General Treatment Diffuse Lung Disease - IPF

- Supportive care for patients with IPF
  - Education
  - Pulmonary rehabilitation
  - Vaccinations:
    - *Streptococcus pneumoniae*, *I*nfluenza & COVID-19
- Virtually all patients will eventually require O2.
- Oxygen therapy GOC: maintenance of normal activity
  - possibly to prevent or delay the onset of secondary pulmonary hypertension (Group III Disease)

General Treatment Diffuse Lung Disease - IPF

- Patient's reported experience with IPF suggest that improved education and communication about the diagnosis and management are needed
- Discussion of end-of-life issues and advanced directives.
- Introduction of principles of palliative care for patients with IPF

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General Treatment Diffuse Lung Disease - Bronchodilators

- 1 in 10 with IPF have evidence of reversible airflow limitation
- Bronchodilators produced a mean intra-test increase in FVC with use of 0.04 L (2.71 vs. 2.75 L, $p < 0.001$) in this group.
- Reversible airflow limitation (increase in FEV_1 or FVC of ≥12% or ≥200 mL) occurred in 9.1% of patients.

Respiratory Medicine August 2015 Volume 109, Issue 8, Pages 1058–1062

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Diffuse Lung Disease - IPF

- Lung Transplant and IPF:
  - Associated diseases – GERD, PH, CAD & malignancy
- Limited life expectancy (2-4y) transplant is only treatment that prolongs survival
  - median IPF survival post transplant
    2014 : 4.5 y (ISHLT & OPTN) -> better now?
- Percentage of patients on list for IPF is higher, the average death rate on the list is 14-67%
- Number of BLT increasing vs SLT

Lung Transplantation in IPF: systematic review: BMC Pulm Med 2014 Aug 16;14:139. doi: 10.1186/1471-2466-14-139.

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Diffuse Lung Disease

The Other Ones

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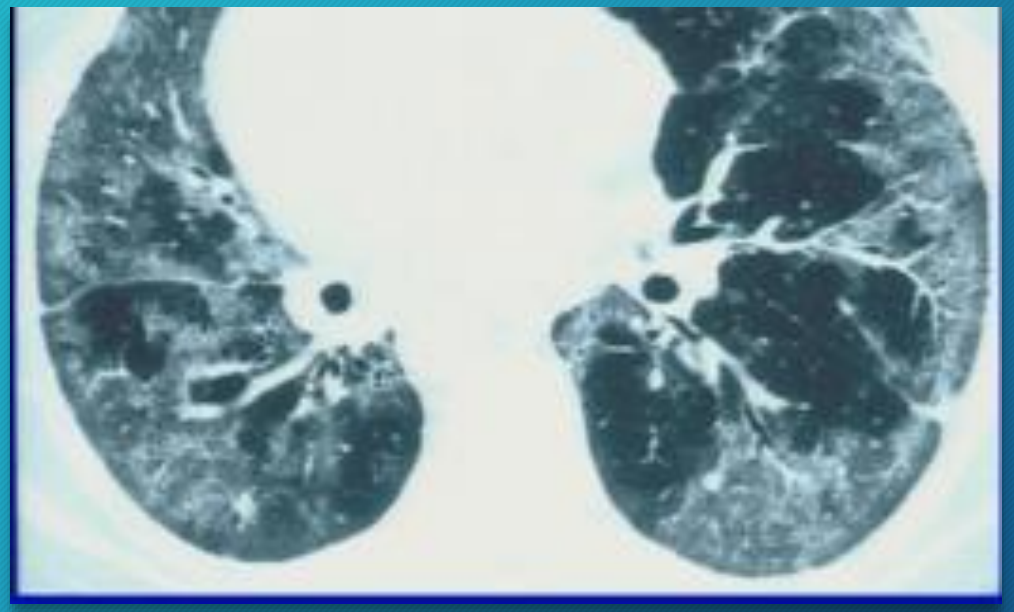
Diffuse Lung Disease - DIP

- Ground Glass opacities on HRCT
  - No honeycombing
- Histologic: intra-alveolar macrophages, temporally homogeneous appearance
  - Preserved lung architecture.
- Incidence: **> 90 % in smokers**
- Key is tobacco cessation
- Steroid responsive



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Diffuse Lung Disease - RBILD

Respiratory Bronchiolitis Interstitial Lung Disease

>90% in smokers

? variant of DIP

Severe fibrosis is rare

Excellent prognosis: if stop smoking

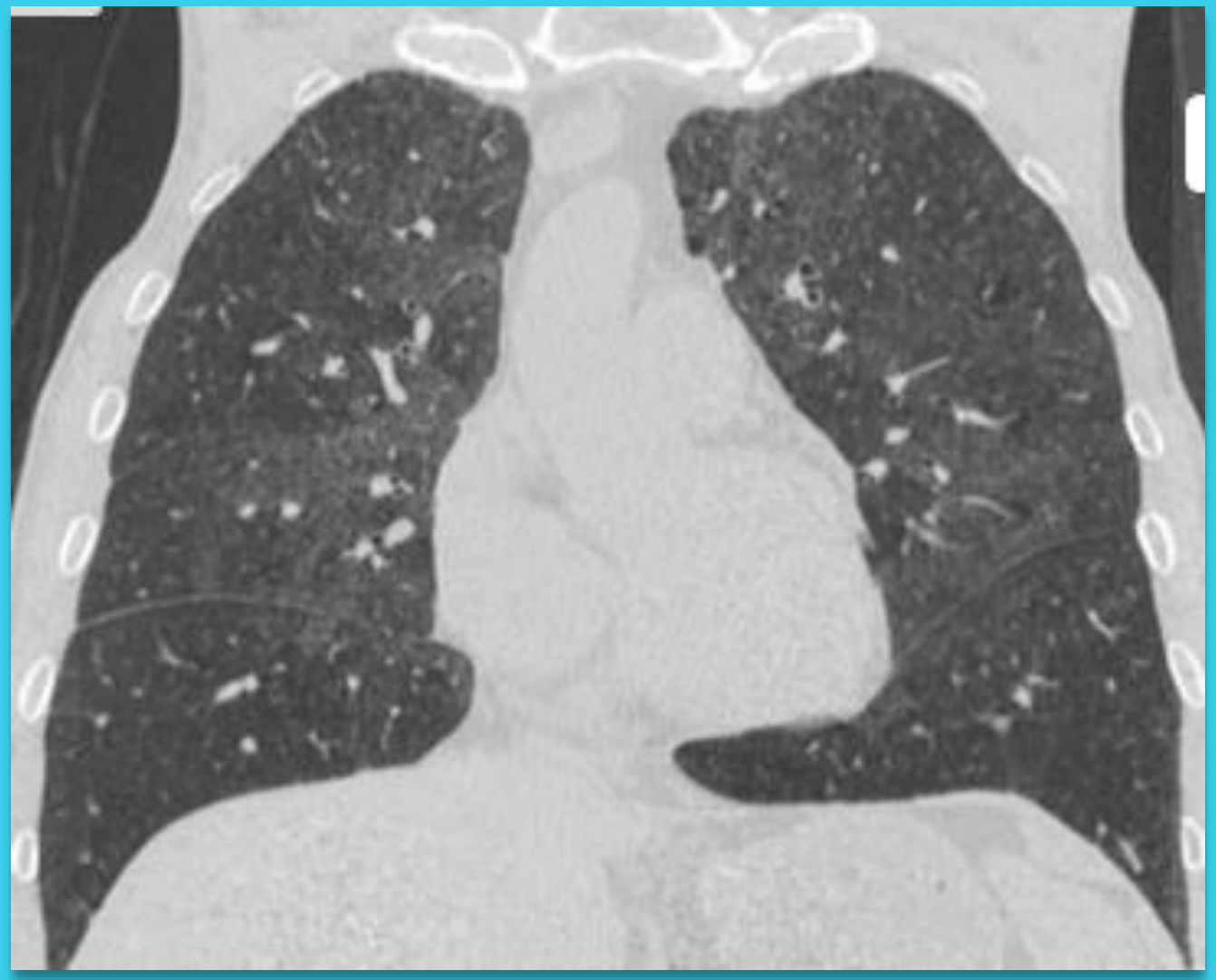
Pigmented macrophages within respiratory bronchioles

Bronchiolocentric, marker of cigarette smoking.

Key is tobacco cessation.

Diffuse Lung Disease – RBILD Radiology

- Poorly defined centrilobular nodules
- If advanced, develop fibrosis affecting the subpleural regions / lower lung zones (can mimic IPF)
- Patchy areas of hypoattenuation (~40%)



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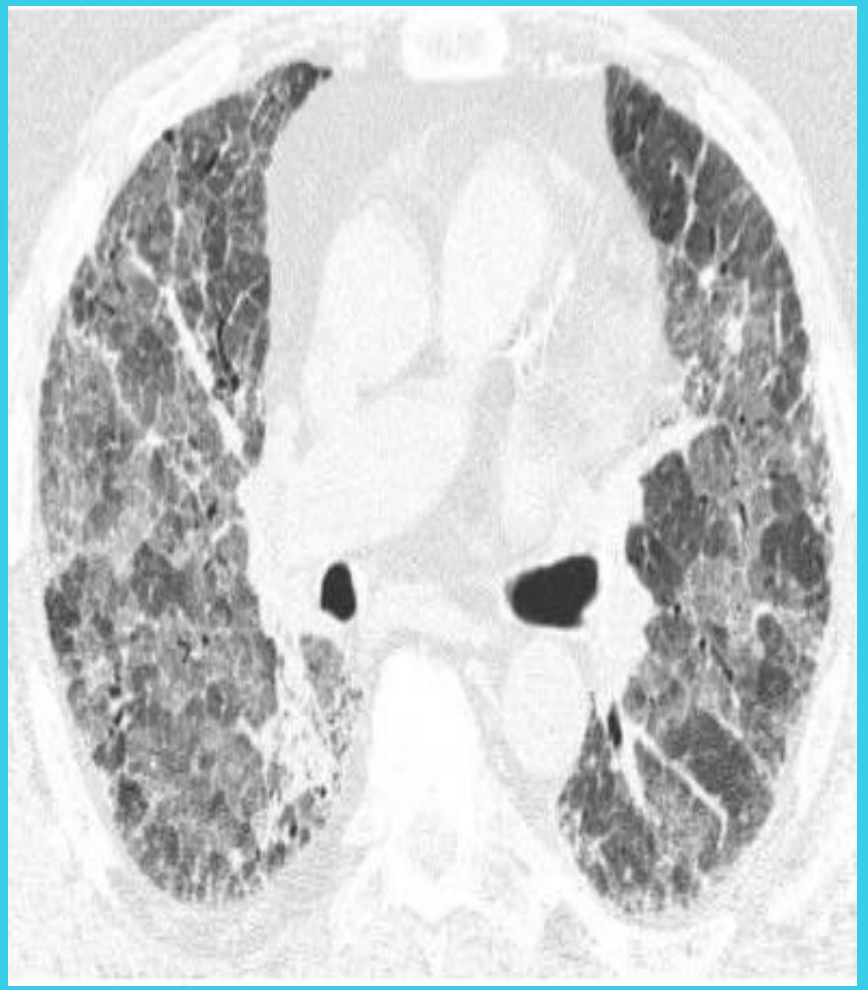
Acute Interstitial Pneumonia (AIP)

- Idiopathic/Acute diffuse lung injury described by Hamman & Rich in 1935. (rapid progression) Similar in presentation to ARDS - subset of idiopathic ARDS?
- Male = Female, not associated with tobacco smoking, most > 40 y with mean age 50-55y. Etiology is not clear? onset over 1-2 weeks. Mortality up to 70% at 3 months.
- HRCT – consolidation (early) changes into Ground Glass Opacity (late) cyst formation and honeycombing. Bilateral and symmetrical, traction bronchiectasis ~ 80%, architectural distortion of lung, slight predilection to dependent portion of the lung.



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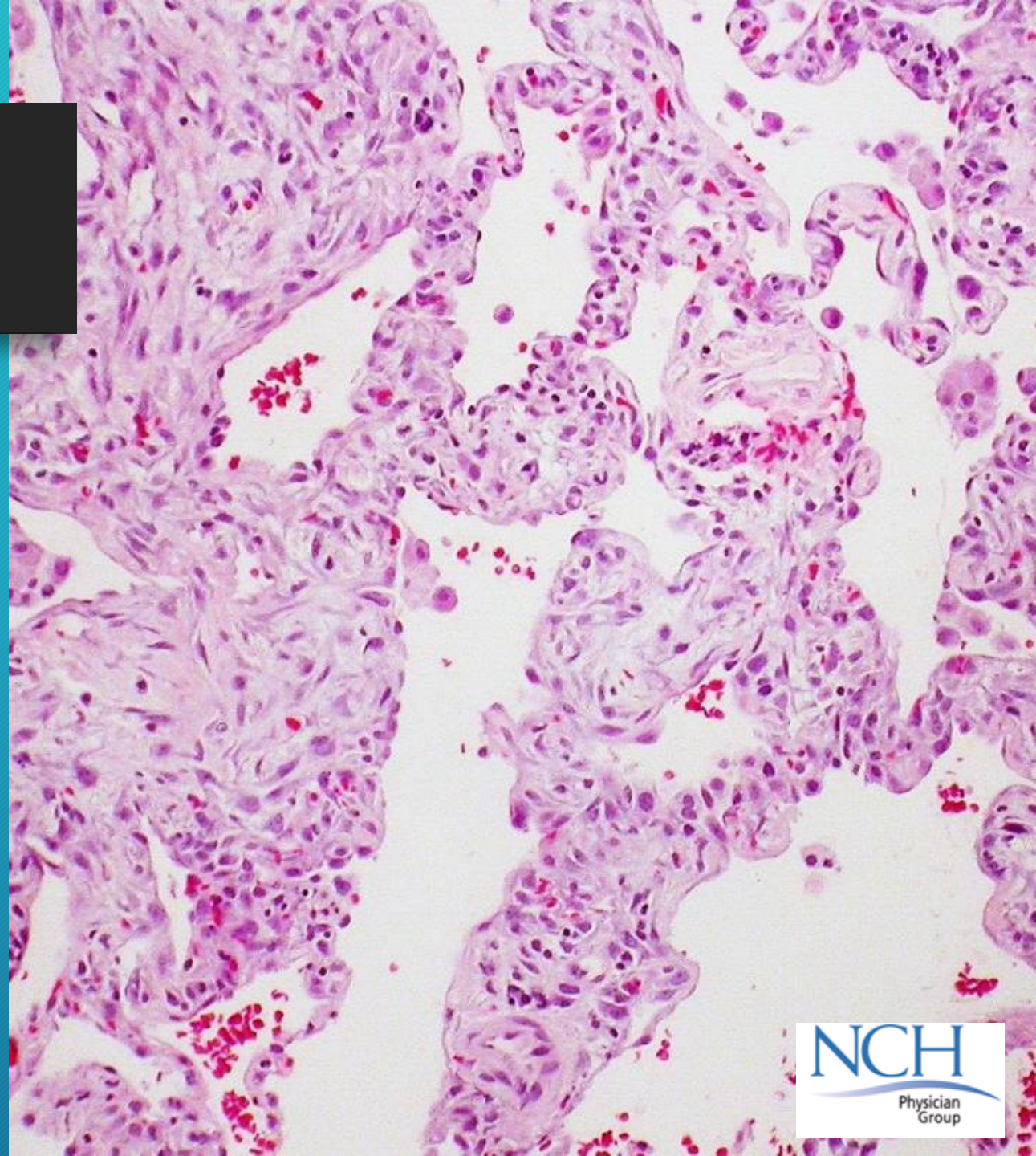
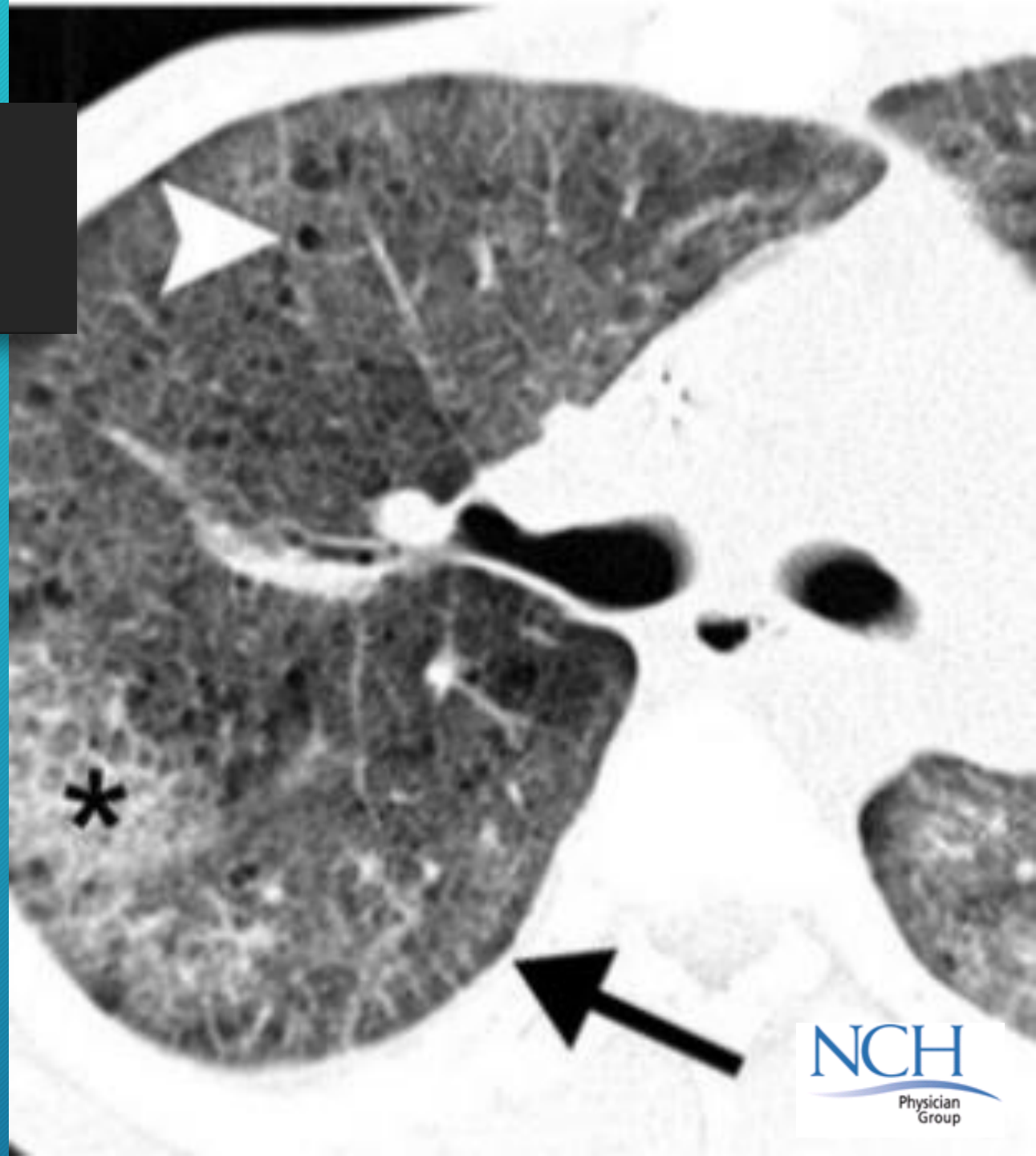
Acute Interstitial Pneumonia (AIP)

- Necrosis of alveolar lining cells, extravasation of fibrin.
- Histology: Diffuse hyaline. “DAD”: diffuse and homogeneous fibrosis.
  - 10-20% of diffuse lung disease.
- Fibroproliferative organizing phase: dense collagen deposits.
- Late – scarring with diffuse honeycombing, reactive alveolar cells “hobnail” appearance, squamous metaplasia.
- Possible late steroid response?



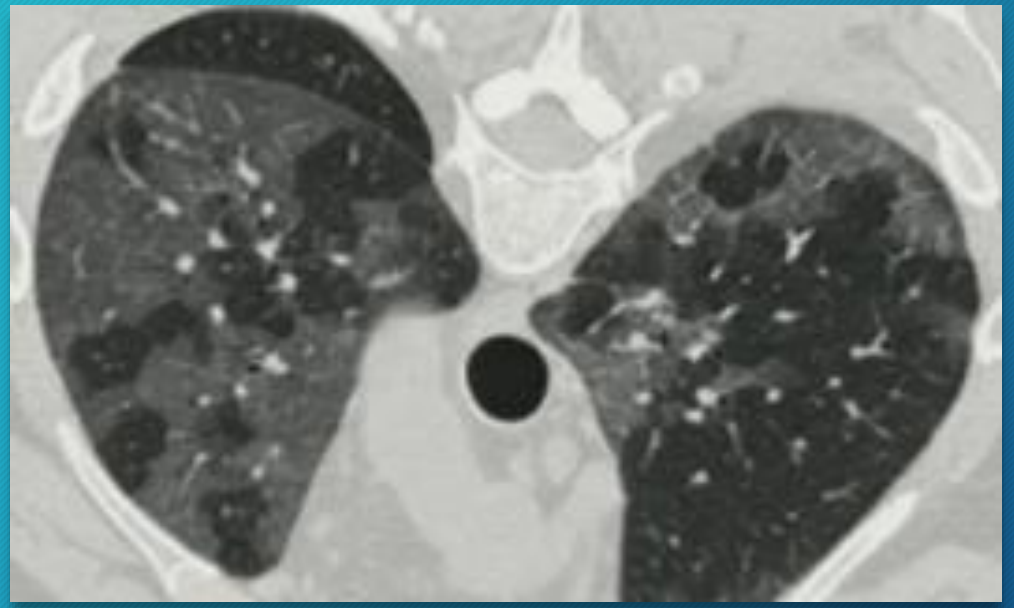
Lymphocytic Interstitial Pneumonia (LIP)

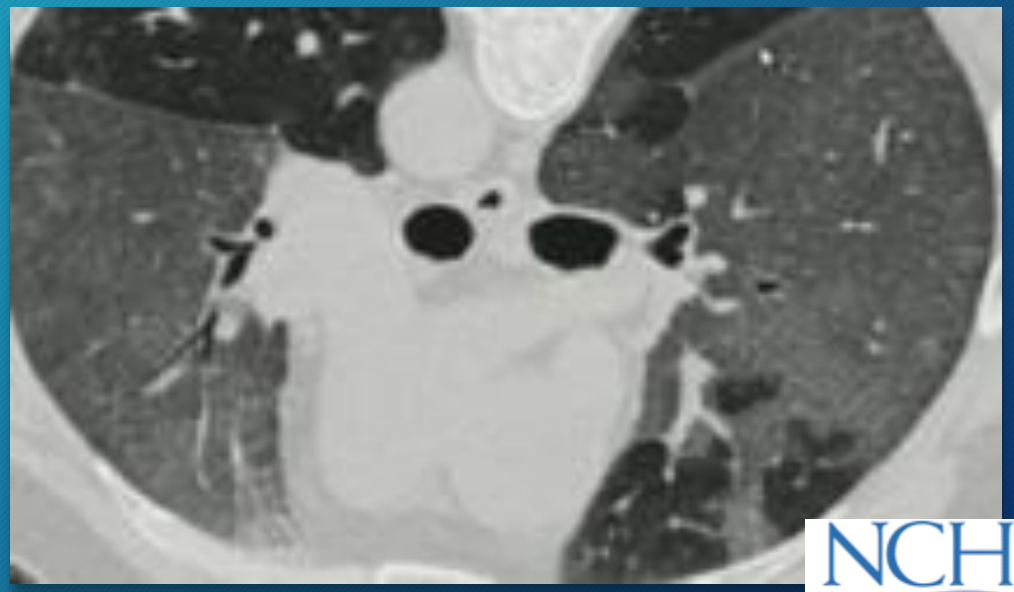
- **Lymphocytic Interstitial Pneumonia (LIP) unclear etiology, associated HIV (post PCJ) or Autoimmune etiology (SLE, RA, Hashimoto) or Immunologic (CVID).**
- **? Virally mediated: dense lymphocytes.**
- Diffuse hyperplasia of bronchial-associated lymphoid tissue
- Clinical: Coughing, dyspnea and crackles
- Diagnosis with HRCT Cysts/Reticular Changes/GGO
- Biopsy – expansion of lymphocytic (T&B cells) and immune cells usually infiltrative along bronchi & vascular bundles.



Diffuse Lung Disease - NSIP

- Ground glass opacities on HRCT
- Histology is temporally uniform
- Honeycombing is **NO**T a dominant feature
- No fibroblastic foci (a difference from IPF)
  - UIP: +++ honeycombing, +/- GGO.
  - NSIP: +/- honeycombing, +++ GGO.





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Diffuse Lung Disease - NSIP

- Woman > men, < 50 y/o, predominate cough and dyspnea
- HRCT bilateral GGO, irregular, traction bronchiectasis, lower lung zones with sub-pleural scarring
- Two forms are Cellular NSIP and Fibrotic NSIP
  - Histology is temporally homogeneous as opposed to heterogenicity of UIP.
- NSIP has few prospective studies on Rx
  - ? prednisone / azothioprine ? / Mycophenolate?
- Short term prognosis is better than UIP
  - course if subacute (weeks) may be steroid responsive (esp cellular NSIP), the longer you go with it the higher the mortality, can progress over years though, most survive ~ 10+ y.

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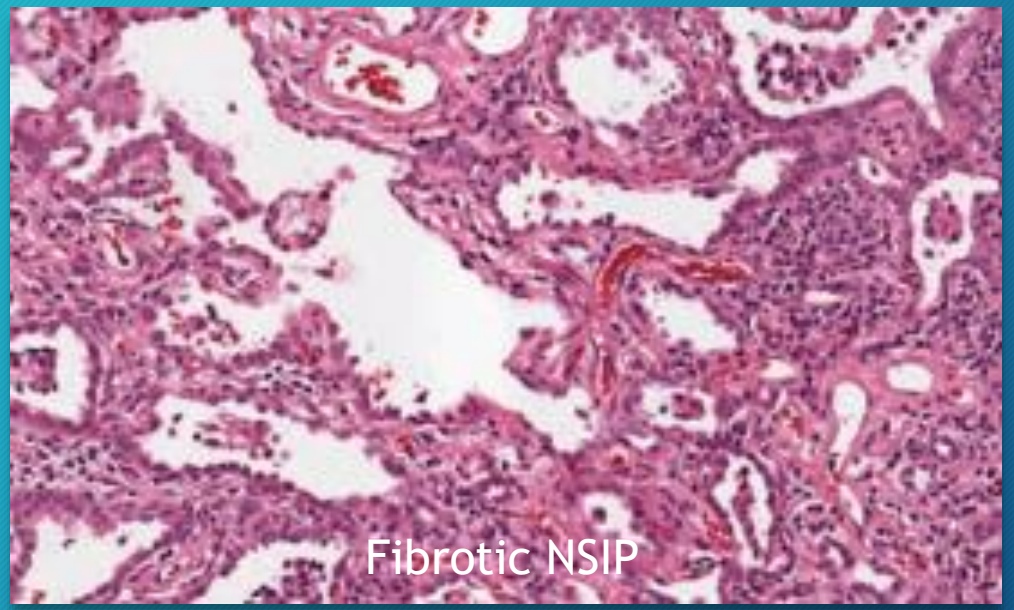
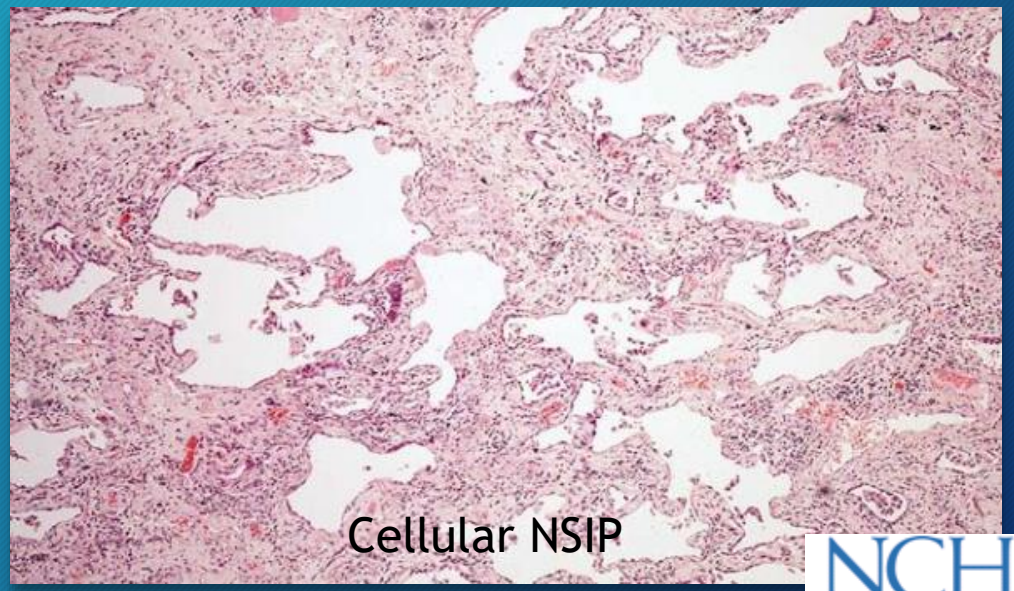
NSIP BAL & Biopsy

- NSIP vs IPF -> BAL total and differential cell counts do not differ
  - BAL neutrophilia and/or eosinophilia poor outcome
  - BAL lymphocytosis correlates to a cellular biopsy and less honeycombing ? More likely NSIP? (ATS position statement)
- Biopsy
  - Cellular – mild/mod chronic interstitial inflammation, Type II pneumocyte hyperplasia, lung architecture preserved.
  - Fibrotic Dense/loose interstitial fibrosis (uniform), mild/moderate chronic interstitial inflammation, lung architecture preserved (enlarged airspaces)





S. Veeraraghavan, P.I. Latsi, A.U. Wells, P. Pantelidis, A.G. Nicholson, T.V. Colby, P.L. Has lam, E.A. Renzoni, R.M. du Bois

European Respiratory Journal 2003 22: 239-244; **DOI:** 10.1183/09031936.03.00105202

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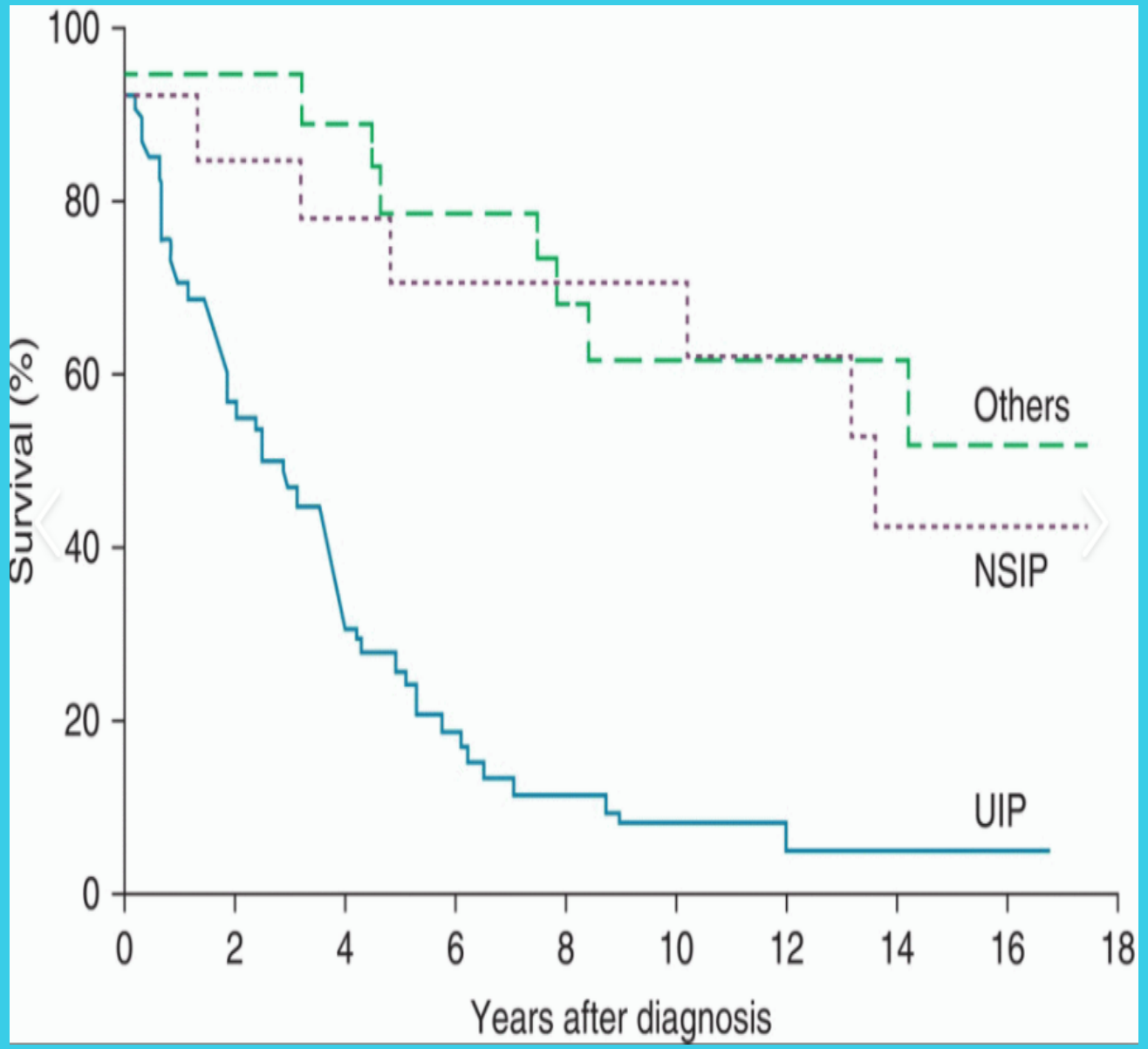
NSIP Course & Treatment

- “Steroid-responsive IPF” in literature may represent NSIP, DIP, RBILD.
- Progressive disease – course of treatment with steroids possible azathioprine, cyclophosphamide and possible mycophenolate.
- Refractory NSIP remains uncertain, lung transplantation is of importance in the current management of progressive refractory disease.



Diffuse Lung Disease – COP (aka “BOOP”)

- **Steroid responsive**: 2/3rds complete response / normalize
  - ~10% not respond.
- Etiology: ? - toxic fumes, XRT, Chemo, Rx, exogenous agents
- Clinical: subacute (2-12wks), cough, dyspnea, fever, antecedent Resp Tract Infect (>30%), **mimics CAP** [lobar consol], not very common, See: rales 68%, rare wheezing, no clubbing,
- Restrictive defect on PFT in 72%, reduced DLCO in 86%, but airway obstruction only in 20%,

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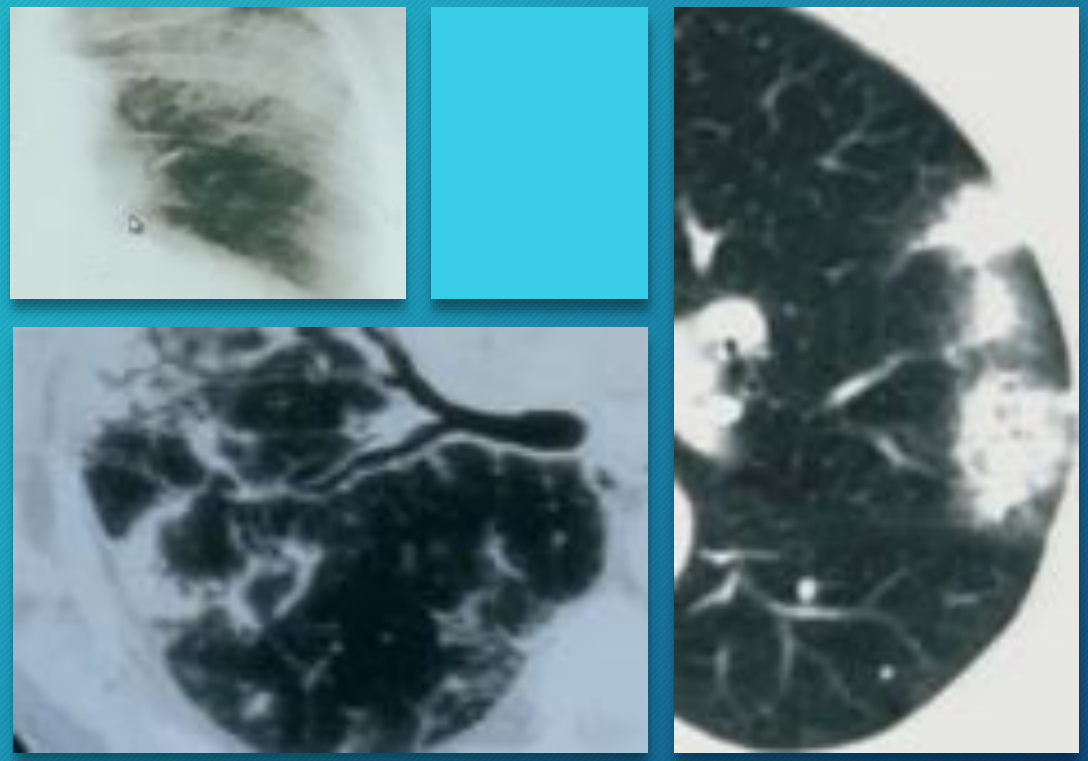
Diffuse Lung Disease – COP Radiology

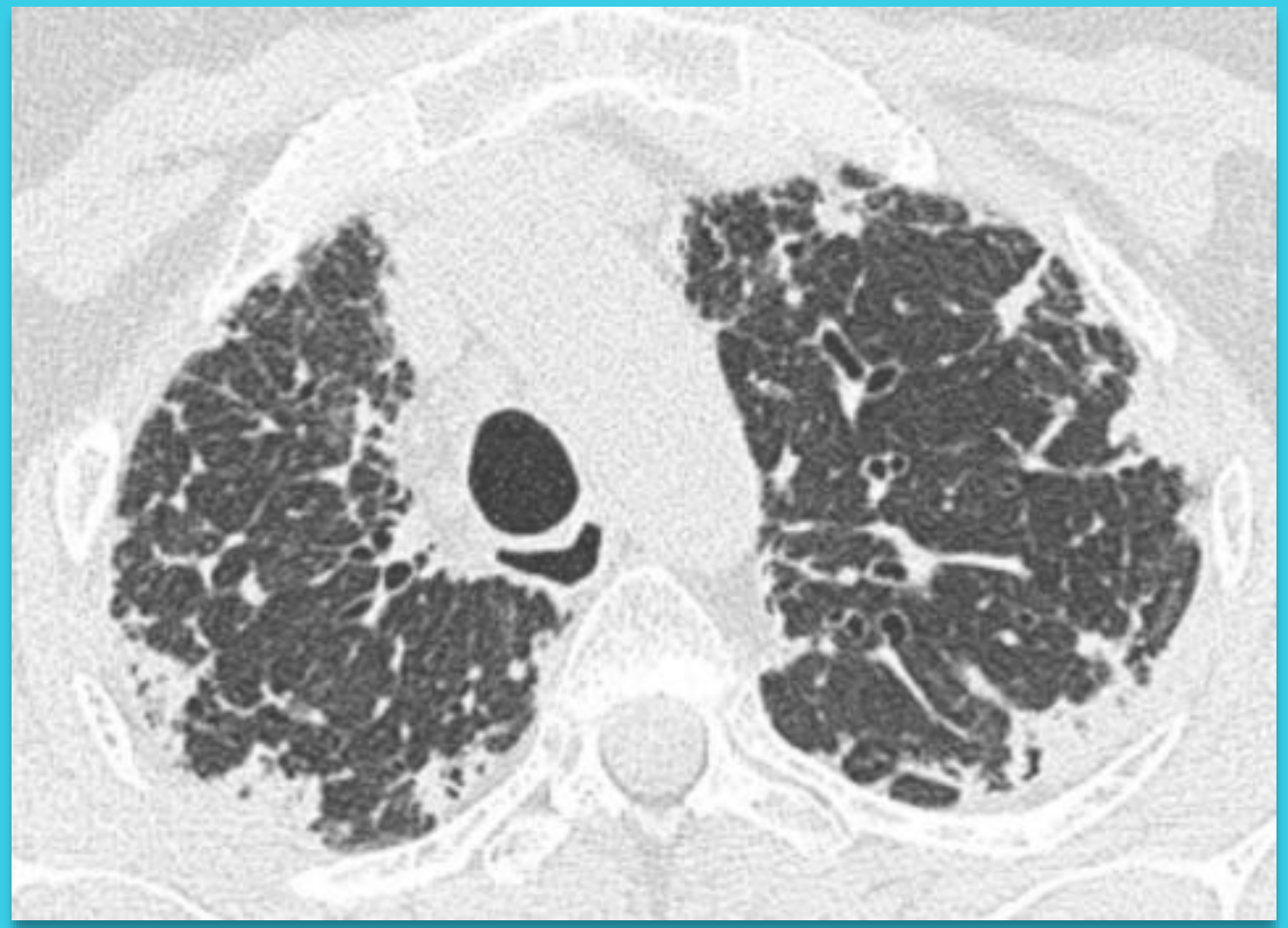
- Opacities segmental/lobar that WAX and WANE
- Reticulonodular 10-30%
  - **Normal CXR** or mild hyperinflation in <10%.
- Honeycombing **NOT** seen.
- HRCT: dense consolidation 79%, GGO 60% and nodules 30%.



Variable Presentation

Idiopathic Pleuroparenchymal Fibroelastosis

- Rare upper lobe fibrosis of the pleura and subpleural lung parenchyma.
- Etiology: unknown: possible relation to infection, autoimmune and genetic links.
- Age: 50s, M=F, usually non-smokers.
- Progressive (60%)
- Possible treatment : corticosteroids



Diffuse Lung Disease
Idiopathic Interstitial Pneumonias

- Diffuse Lung Disease (Idiopathic Interstital Pneumonias) are diseases mostly of unknown etiology that share similar clinical and often radiologic features and are distinguished many times by their histiopathologic features.
- There are 8 subtypes with varying degrees fo inflammation and fibrosis.
- The damage they cause lead to shortness of breath.
- Care of these patients is multi-disciplinary, that is where multiple disciplines come in.

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A new ‘epidemic’?

What is it exactly ?

COVID-19 ILD

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COVID-19/IPF share possible AT2 cytopathic features

- AI-guided analysis of > 1000 human lung trascriptomic datasets
  - July 2022
- Findings:
  - COVID-19 IL15-centric cytokine storm process
  - IPF-specific gene signatures were found
  - Produces Alveolar Type II (AT2) cytopathies and a monocyte-driven process
    - DNA damage
    - Damage-induced progenitor state
    - Secretory senescence phenotype (SASP)
- Known drivers of IPF and felt to be early triggers of the process
- Role of anti-fibrotics?

BioMedicine, The Lancet Discovery Science. July 2022
https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(22)00366-8/fulltext

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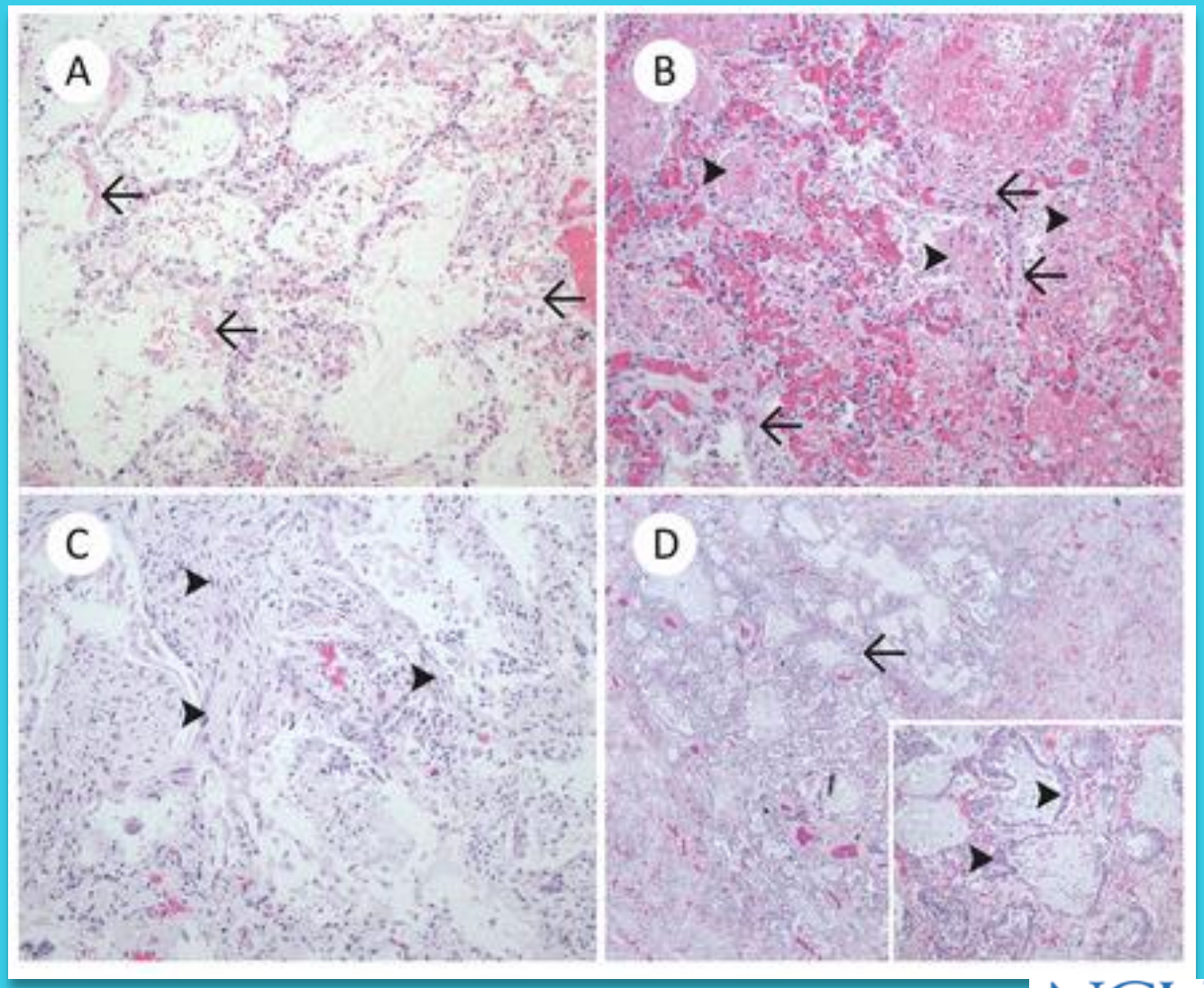
Post COVID-19 ILD

- Post COVID-19 Interstitial Lung Disease is NOT understood.
- NOT due to viral invasion
- Pathophysiology proposed
  - Excessive Cytokines
  - Abnormal repair processes
    - Epithelial, mesenchymal and alveolar macrophages after lung injury
- Role of Corticosteroids?



Used with Permission: BMJ Journal of Clinical Pathology, Fatal Pulmonary Fibrosis:
a post-COVID-19 autopsy case,
http://dx.doi.org/10.1136/jclinpath-2020-206879

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Persistent Post-COVID19 ILD

- Myall et. al: Single center prospective structured assessment protocol
- n=837 at 6 weeks post dc from hospital
  - 325/837 with symptoms
- n=35/387 with persistent functional deficits & ILD changes (4.8%)

Persistent Post-COVID-19 Inerstital Lung Disease.
An Observational Study of Corticosteroid Treatment. Myall et. Al
Annals of the American Thoracic Society. MyVolume 18, Issue 5
https://doi.org/10.1513/AnnalsATS.202008-1002OC

Table 4. Results after structured assessment of patients with interstitial lung disease after infection with SARS-CoV-2

Structured Assessment	Value
Resting Sp_{O_2}, %	95.5 ± 3
MRC dyspnea score, median (IQR)	
Before COVID-19	1.0 (0–3)
After COVID-19	3.00 (1–5)
6MWT distance, m	291.2 ± 153.2
6MWT, % predicted	54.9 ± 25.0
6MWT min Sp_{O_2}	90.0 ± 6
Lung function	
FEV_1, L	2.4 ± 0.7
FEV_1, %	86.0 ± 13.7
FVC, L	3.2 ± 1.0
FVC, %	91.9 ± 16.0
FEV_1/FVC, %, median (IQR)	77.8 (73.2–82.4)
T_{LCO}, SI	5.6 ± 2.2
T_{LCO}, %	60.6 ± 24.9
KCO, T_{LCO}/L	1.3 ± 0.3
KCO, %	88.0 ± 87.6–88.15

Definition of abbreviations: 6MWT = 6-minute walk test; COVID-19 = coronavirus disease; FEV_1 = forced expiratory volume in 1 second; FVC = forced vital capacity; IQR = interquartile range; KCO = transfer coefficient; MRC = Medical Research Council; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; SI = International System of Units; Sp_{O_2} = oxygen saturation as measured by pulse oximetry; T_{LCO} = transfer factor of the lung for carbon monoxide.

Data are presented as mean ± standard deviation unless otherwise stated.

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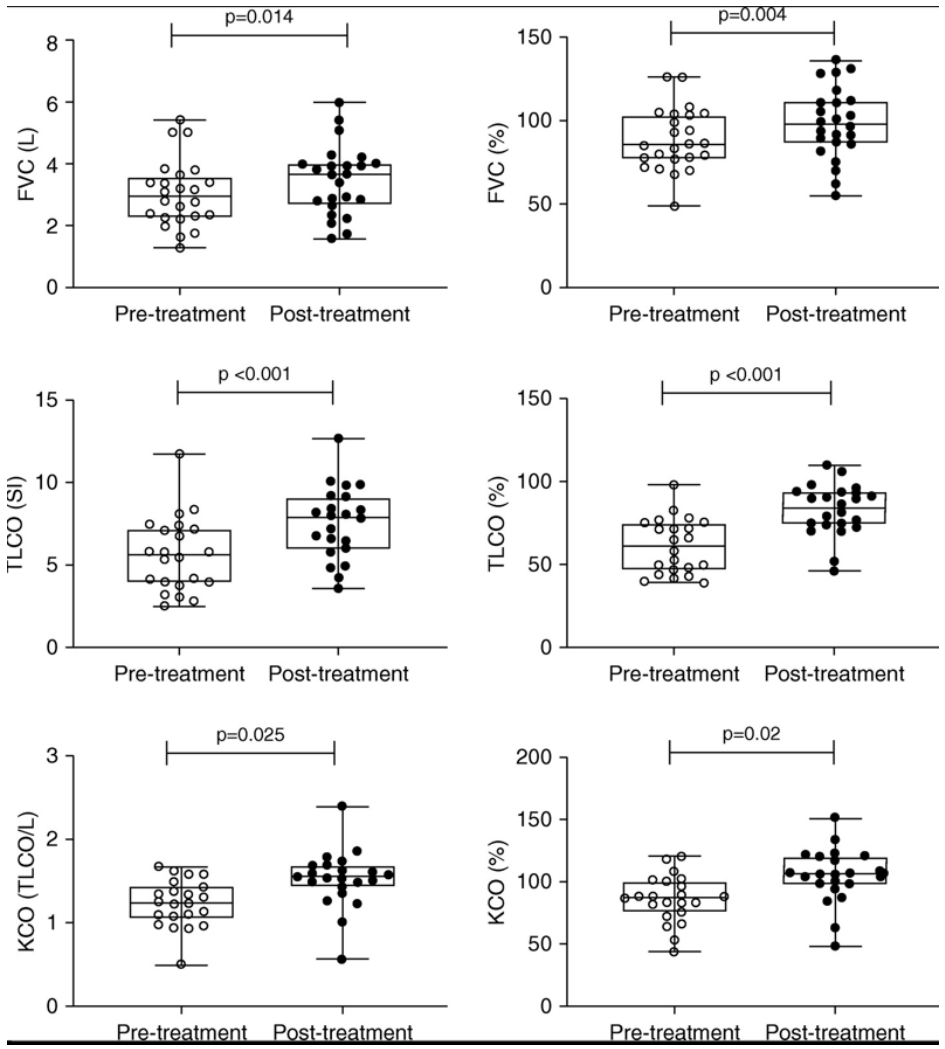
Persistent Post-COVID19 ILD

- Biochemical markers indicated improving systemic inflammation in all patients.
- In the ILD patients 30/35 received steroids
  - improvement of DLCO in 31.6%
  - Improvement in FVC in 9.6%



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Persistent Post-COVID19 ILD : Steroid Use

- <u>Pitfalls:</u>
- Short-term follow up 6 weeks
- Etiology of post-COVID-19 fibrotic changes is unclear.
  - Ventilator-induced injury, hyperoxia, superimposed bacterial injury?
- Study shows majority of patients required supplemental O2 and 46% were intubated.
- Restrictive lung physiology in absence of improving symptoms got steroids, others did not.
  - 21/59 (2.5%) had < 15% lung involvement and no restriction
  - 3/59 had fixed changes
- At NCH – abnormal HRCT post COVID-19 to CPEX -> ILD pattern
  - Un-published data

Study of Corticosteroid Persistent Post-COVID-19 Inerstital Lung Disease.
An Observational Treatment. Myall et. Al
Annals of the American Thoracic Society. MyVolume 18, Issue 5
https://doi.org/10.1513/AnnalsATS.202008-1002OC

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Current Clinical Trials Post COVID ILD

Treatment	NCT Number		Phase	Number Enrolled	Study Design
Nintedanib	NCT04338802	[34]	II	96	Single-center, randomized, placebo-controlled 150 mg POBID for 8 weeks
	NCT04541680	[35]	III	250	Single-center, randomized, placebo-controlled 150 mg POBID for 12 months
	NCT04619680	[36]	IV	120	Multicenter, randomized, placebo-controlled 150 mg POBID for 180 days
Pirfenidone	NCT04282902	[37]	III	294	Single-center, randomized, placebo-controlled 2 × 267 mg POTID for 4 weeks
	NCT04607928	[38]	II	148	Multicenter, randomized, placebo-controlled 2 × 267 mg POTID, 7 days after 4 × 267 mg TID for 24 weeks
Treamid	NCT04527354	[39]	II	60	Multicenter, randomized, placebo-controlled study 50 mg daily PO for 4 weeks
Collagen-Polyvinylpyrrolidone	NCT04517162	[41]	I	90	controlled 1.5 mL IM BID for 3 days, then 1.5 mL QD for 4 days
Prednisone	NCT04551781	[42]	–	450	Single-center, randomized, placebo-controlled 20 mg daily for 14 IM
Bovhyaluronidase azoximer	NCT04645368	[43]	–	160	Multicenter, randomized, placebo-controlled 3000 ME IM once in 5 days for 15 IM
BIO 300 (genistein)	NCT04482595	[44]	II	66	Single-center, randomized, placebo-controlled 1500 mg daily PO for 12 weeks
Tetrandrine	NCT04308317	[45]	IV	60	Single-center, randomized, compared to standard therapy 60 mg daily PO for a week
Fuzheng Huayu Tablet	NCT04279197	[46]	II	160	Single-center, randomized, placebo-controlled 1.6 g TID PO for 24 weeks
Anluohuaxian	NCT04334265	[47]	–	750	Multicenter, randomized, compared to standard therapy 6 g BIDPO for 3 months
Stromal Vascular Fraction	NCT04326036	[48]	I	10	Single-center, randomized, placebo-controlled IV for 6 months, No data for injection frequency
IN01Vaccine	NCT04537130	[49]	Ib	40	On first stage, IN01 is injected on days 1, 14, 28, 42, and 56, On support stage, vaccination is carried out every 2 months with the same dosage and regimen as during introduction, compared to the patients receiving standard therapy

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Specific Agents: Nintedanib/Pirfenidone & Steroids

Nintedanib & Pirfenidone

- Known antifibrotic medications
- Lung fibroblasts
- NO evidence **to date** that these agents affect severity of COVID symptoms.
- Side effects similar COVID
- Trial time-lines ongoing

Glucocorticoids

- Early data on possible prolonged use may be beneficial in reducing severity of subsequent post-COVID fibrosis.
- Slows fibrosis in animal (rat) models (caveolin-1, TNF-α, TGF-β1, PDGF)

Yu W., Guo F., Song X. Effects and Mechanisms of pirfenidone, prednisone and acetylcysteine on pulmonary fibrosis in rat idiopathic pulmonary fibrosis models. Pharm. Biol. 2017;55:450–455. doi: 10.1080/13880209.2016.1247879.

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Questions ?

Thank you !

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