Alphabet Soup and Interstitial Lung Disease

Morning Report

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Overview

- Classification scheme
- Individual diseases within the alphabet soup
- Tables
- Quiz

Reminder

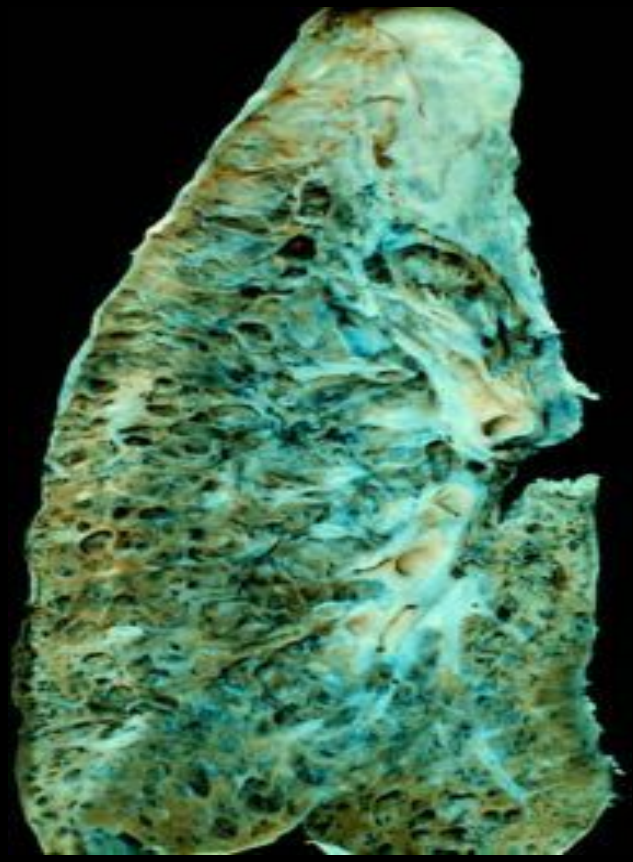
- Pathologic changes in interstitial lung disease involve cellular infiltration, scarring, and/or architectural disruption of the pulmonary parenchyma involving the interstitium, alveolar space, airways, and vascular and lymphatic structures as well as pleura.

Classification of ILDs
(In total, there are over 200!)

- Unknown cause (idiopathic)
- Systemic causes
  - Sarcoidosis
  - Rheumatologic/autoimmune
  - Lymphoproliverative/neoplastic

Idiopathic interstitial pneumonias

- IPF
- NSIP
- COP (BOOP)
- DIP/RB-ILD
- AIP
- LIP
- Eosinophilic pneumonia
- Pulmonary histiocytosis X
- LAM
- PAP
- Primary amyloidosis



Note: The histology of ALL of these except histiocytosis X is Inflammatory and fibrosing; histiocytosis X is granulomatous

Granulomatous lung disease

- T lymphocytes, macrophages, and epithelioid cells make up the granuloma
- Can progress to fibrosis
- Most common forms are sarcoidosis and hypersensitivity pneumonitis

Inflammation and fibrosis

- Injury to the epithelial surface causes an inflammatory response in the air spaces and alveolar walls
- In chronic disease, this spreads to adjacent interstitium and vasculature
- Progressive fibrosis leads to impairments in ventilation and oxygenation

IPF

- Most common idiopathic interstitial pneumonia with distinctly poor prognosis
- Older age group (>50y.o.)
- Patchy, basilar subpleural reticular opacities with traction bronchiectasis
- Temporal and spacial heterogeneity
- UIP*—alternating normal lung, interstitial inflammation, foci of proliferating fibroblasts, dense collagen fibrosis, and honeycombing; lymphocytoplasmic infiltrate in alveolar septa; type 2 pneumocyte hyperplasia

*can also be seen in CTDs, pneumoconioses, radiation, drug-induced lung disease, Chronic aspiration, sarcoidosis, and other conditions

DIP

- *Only* in cigarette smokers
- Occurs in 30's-40's
- Diffuse hazy opacities
- Intra-alveolar macrophage infiltrate with minimal interstitial fibrosis
- Good response to smoking cessation and glucocorticoids
- RB-ILD is a subset in which macrophages accumulate in peribronchial alveoli

AIP (Hamman-Rich Syndrome)

- Often in previously healthy patients with 7-14 day prodrome
- Most patients >40y.o.
- Diffuse, symmetric bilateral ground-glass opacities. May also be subpleural.
- Diffuse alveolar damage
- ARDS is a subset, but lung biopsy is required to confirm the diagnosis
- High requirement for mechanical ventilation and high mortality, but good recovery of lung function in survivors

NSIP

- Younger set of patients than IPF present with fevers and without clubbing
- Bilateral, subpleural ground-glass opacities and associated lower lobe volume loss. Honeycombing unusual
- Temporally and spacially homogenous
- Good response to steroids

COP/BOOP

- Presents in 40's-50's
- Bilateral patchy or diffuse alveolar and small nodular opacities with normal lung volumes and bronchial wall thickening and dilatation; often have recurrent and migratory opacities. Changes most common in periphery and lower lung zones
- Granulation tissue within small airways, alveolar ducts, airspaces, with chronic inflammation in the surrounding alveoli
- 2/3 respond to steroids

•"BOOP pattern" can be present with crypto, Wegener's lymphoma, hypersensitivity
•Pneumonitis, and eosinophilic pneumonia

LIP

- Rarest form, F > M
- Ground glass, reticular pattern with perivascular cysts
- BAL shows lymphocytosis
- Path pattern—cellular interstitial pneumonia with dense lymphoid infiltrate—associated with autoimmune and immunodeficiency disorders
- Ddx includes low-grade lymphoma

PLCH

- smoking-related
- Men 20-40y.o.
- PTX in ~25%, rarely hemoptysis and DI
- Ill-defined or stellate nodules, reticular or nodular opacities, and bizarre-shaped upper zone cysts, with preserved lung volumes and sparing of the costophrenic angles

LAM

- Premenopausal women with emphysema, PTX, hemoptysis, chylous pleural effusion, mostly caucasians
- Proliferation of atypical pulmonary interstitial smooth muscle and cyst formation, react with monoclonal Ab HMB45
- Accelerates in pregnancy, abates after oophrectomy
- Median survival 8-10 years

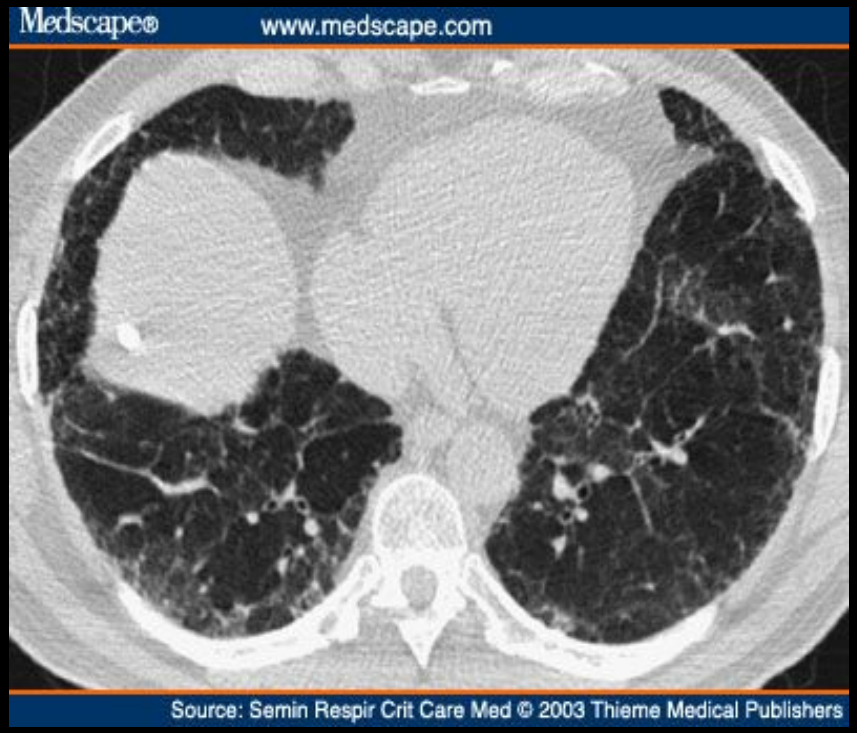
PAP

- Not actually and ILD, actually autoimmune with and IgG against GM-CSF
- Defect in macrophage processing of surfactant leads to accumulation of PAS-positive lipoproteinaceous material in the distal air spaces with little or no inflammation
- Presents in 30's-50's, M > F
- Labs show polycythemia, hypergammaglobunlinemia, increased LDH
- Ground-glass opacities and thickened intralobular strucutres and septa
- BAL can be therapeutic

	Age of onset	Alveolar	Interstitial	Mortality	Response to treatment
IPF	63	No	Yes	50% 2-3yr	Poor
DIP	42	Yes	Yes	27% 12yr	Moderate
AIP	49	Yes	Yes	62% 1-2mo	Poor
NSIP	49	Yes	Some	11% 17mo	Some forms
COP	57	Yes	Yes	0-10%	Excellent
LIP	45	Yes	Yes	10%	Good
PLCH	<40	No	Yes		Moderate
LAM	<40	Minimal	Yes		

	CT features	Distribution
IPF	Reticular, honeycombing	Lower peripheral
DIP	Ground glass, honeycombing	Mid to lower lung zones
AIP	ARDS	Diffuse
NSIP	Ground glass	Bilateral lower zone
COP	Nonsegmental infiltrate	Peripheral
LIP	Ground glass	Basilar
PLCH	Cystic, nodular	Mid-upper, CPA sparing
LAM	Cystic	Diffuse
PAP	Cystic	Diffuse

Case #1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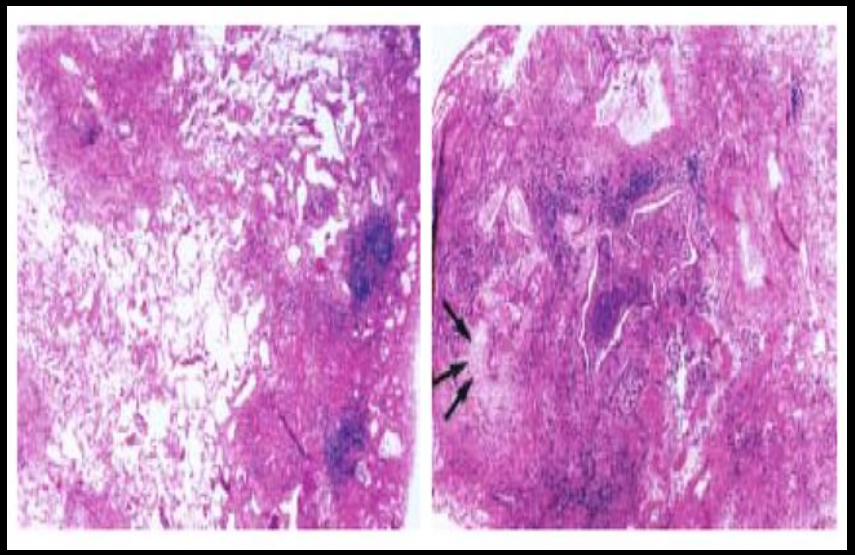
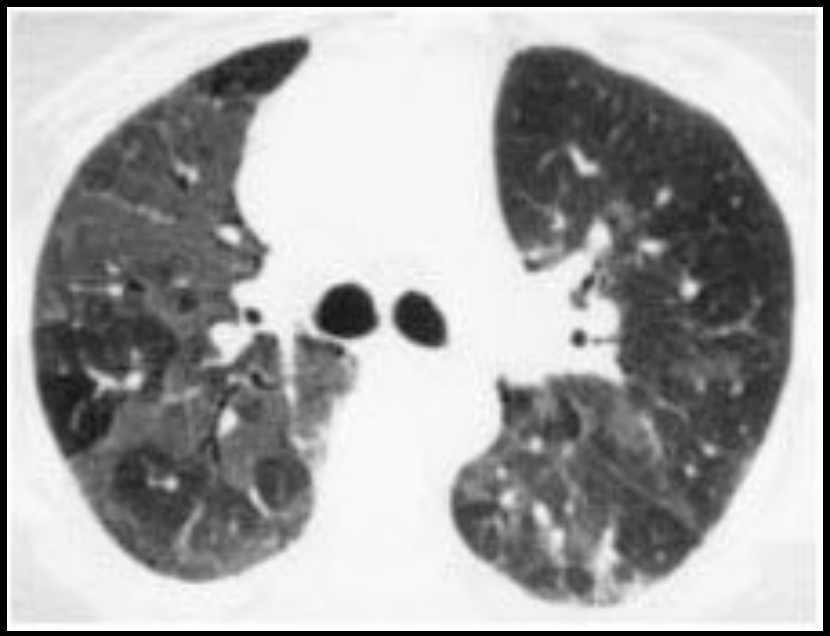
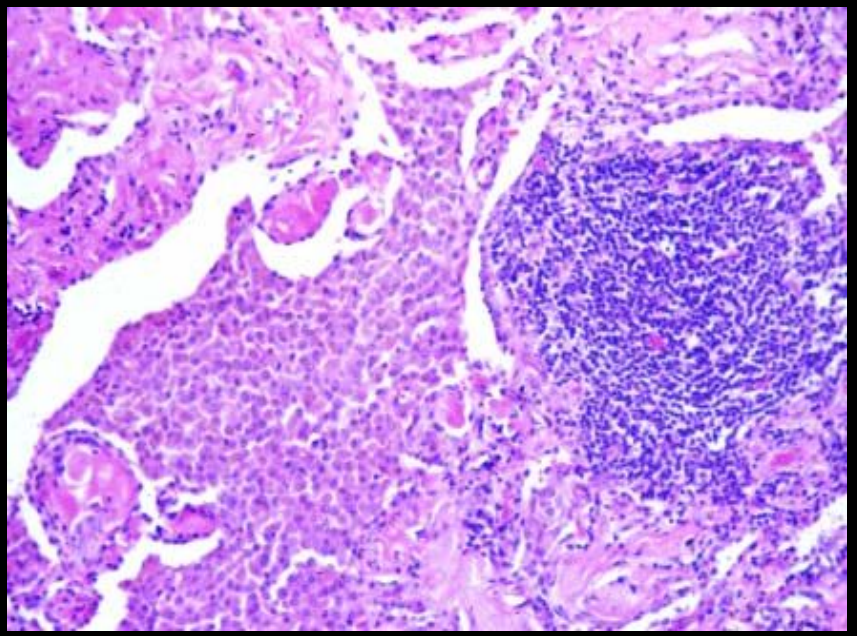


Answer: IPF

- CT scan: heterogeneous pattern with subpleural disease concentrated posteriorly, traction bronchiectasis/honeycombing, no nodules, little ground glass
- Path: heterogeneous paraseptal collagen deposition and fibroblast foci

Case #2

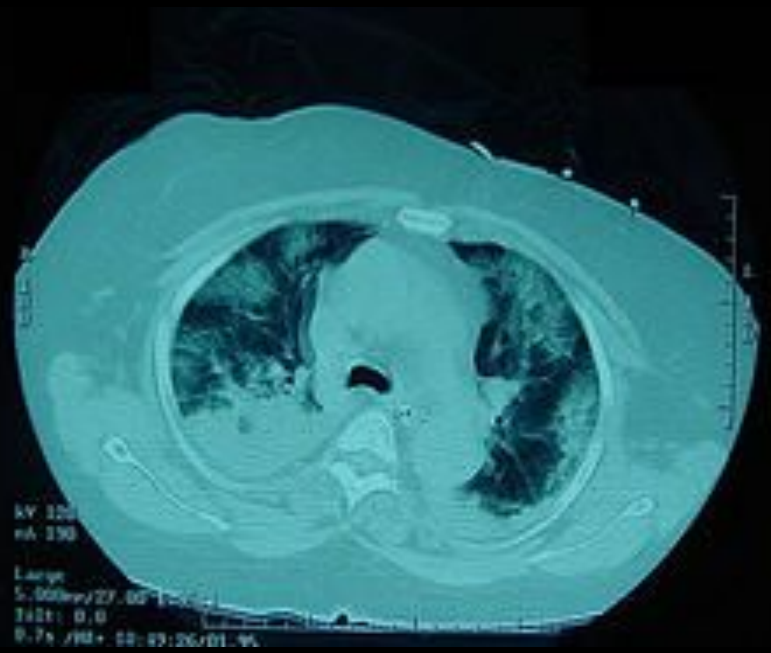


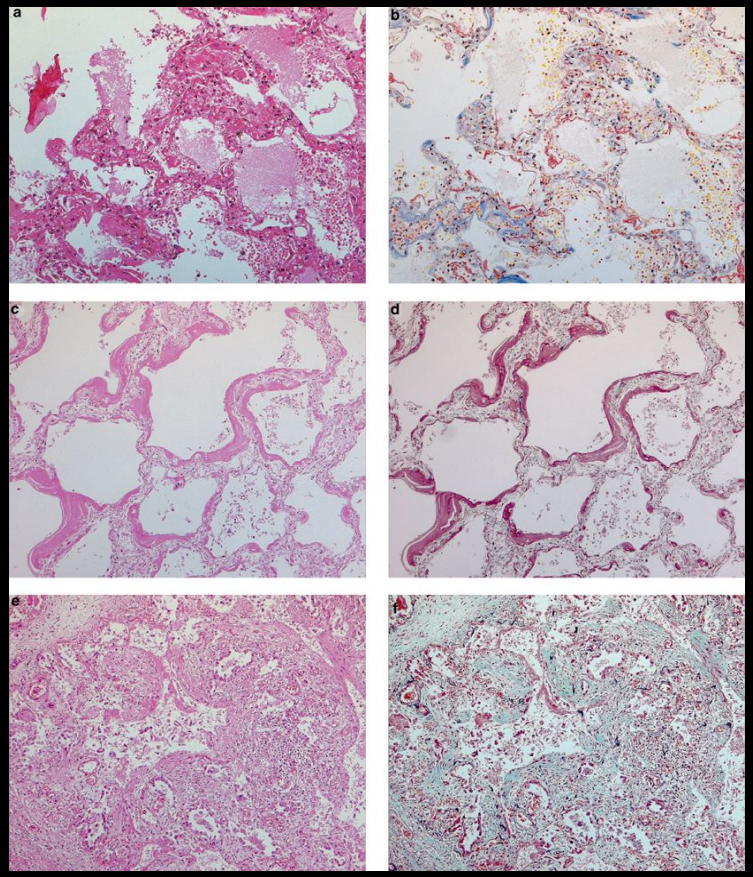


Answer: DIP

- CT: Mosaic ground-glass opacity with vascular definition in the areas of ground-glass opacity and lobular sparing
- Path: large numbers of slightly-eosinophilic staining macrophages with interstitial lymphoid aggregates

Case #3

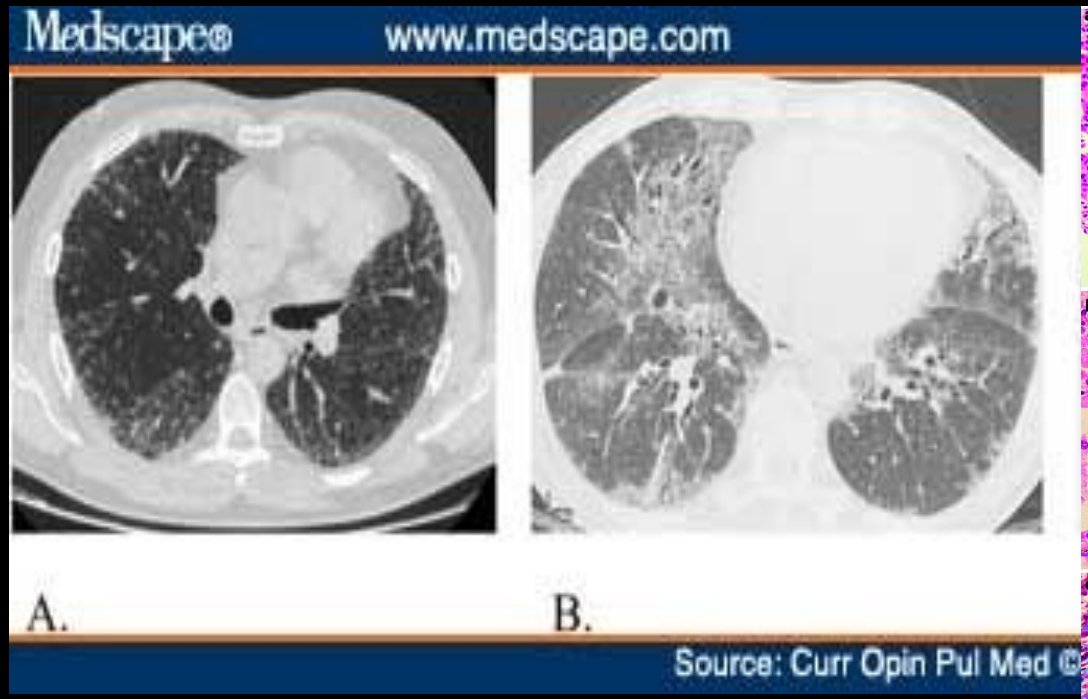


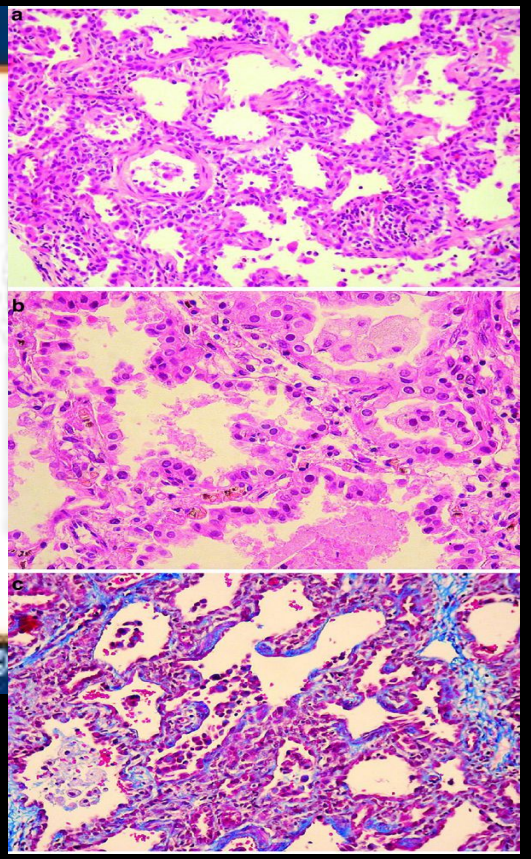


Answer: AIP

- CT: Bilateral alveolar and interstital infiltrates
- Path: Early exudative phase showing vascular congestion, with interstitial and airspace edema and inflammatory cell infiltrates (top left) and fibrinous exudates (top right), organizing phase diffuse alveolar damage (bottom two)

Case #4

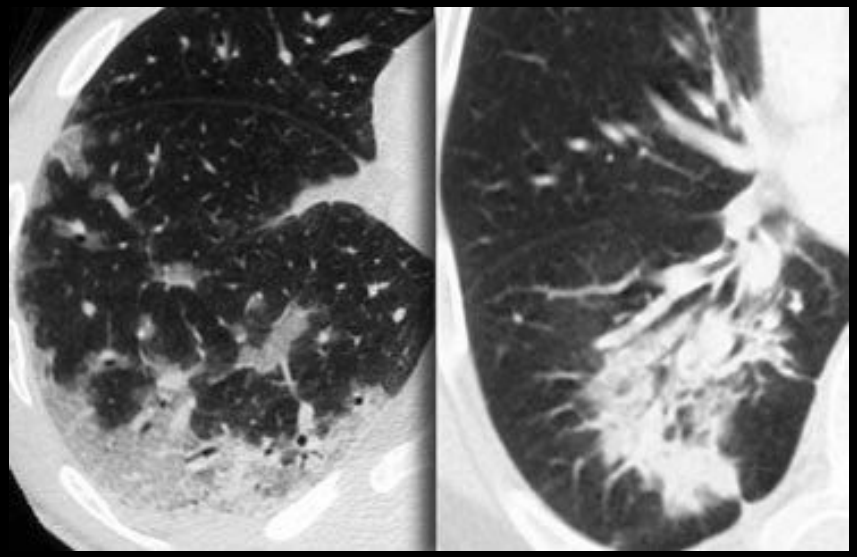


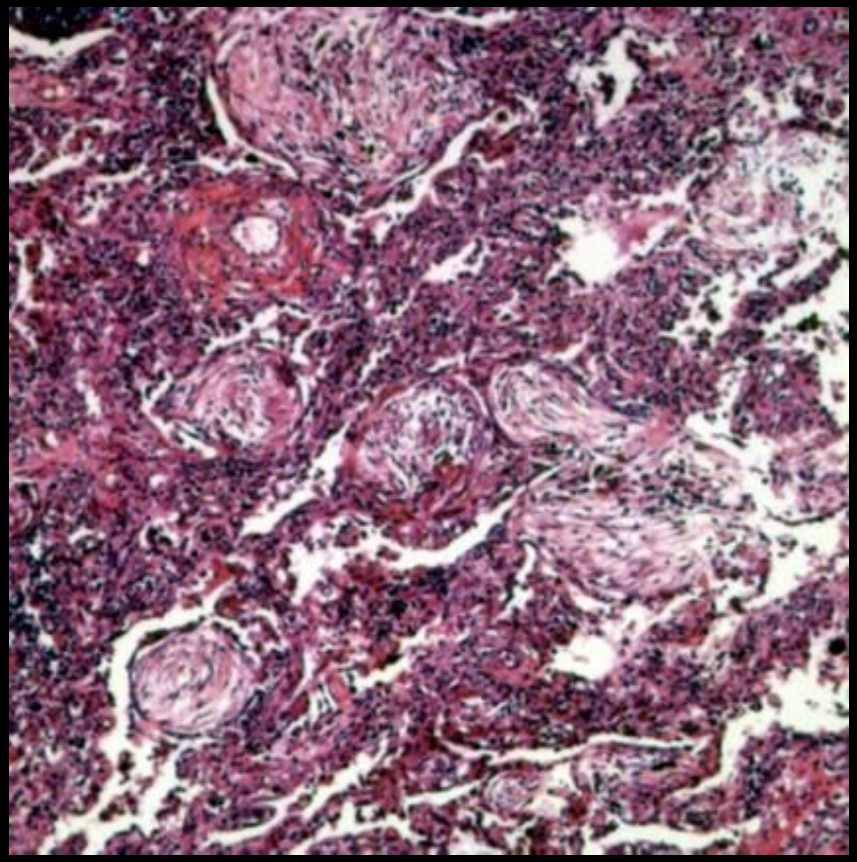


Answer: NSIP

- A: Fibrotic variant with reticular subpleural lines with uniform distribution, bronchiolectasis, and areas of ground glass attenuation
- B: Cellular variant with ground glass opacities and traction bronchiectasis
- Path: homogeneous expansion of interstitium by inflammatory cells, myofibroblasts, and Type II pneumocytes hyperplasia

Case #5

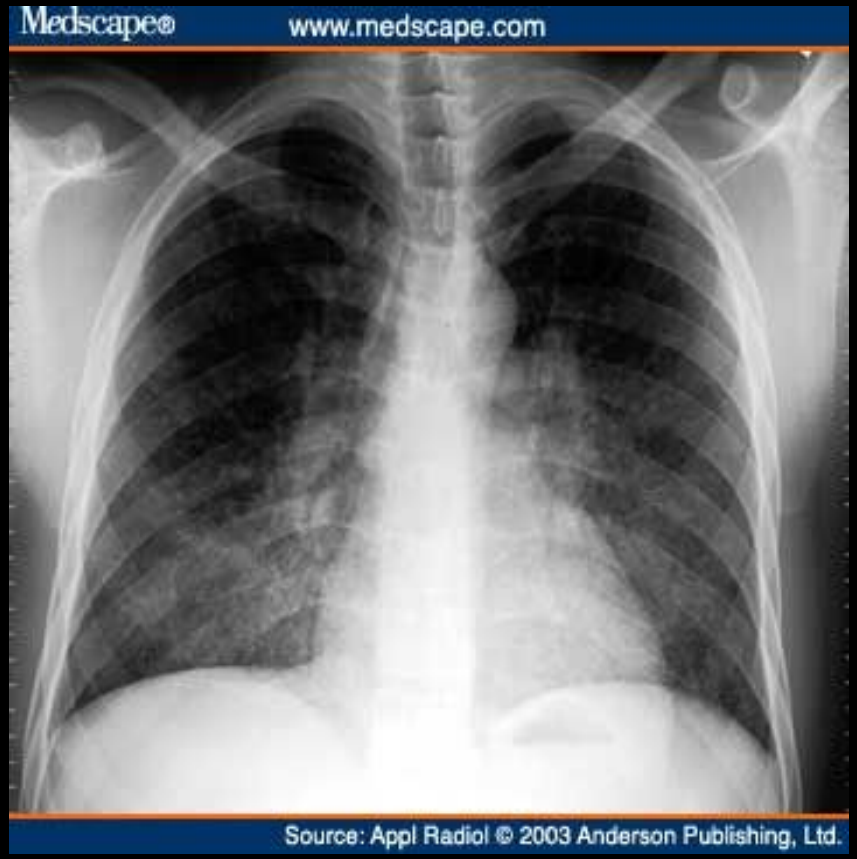




Answer: COP

- CT: patchy non-segmental consolidations in a subpleural and peripheral distribution
- Path: diffuse fibrous organization of the airways with obliteration of normal lung architecture

Case #6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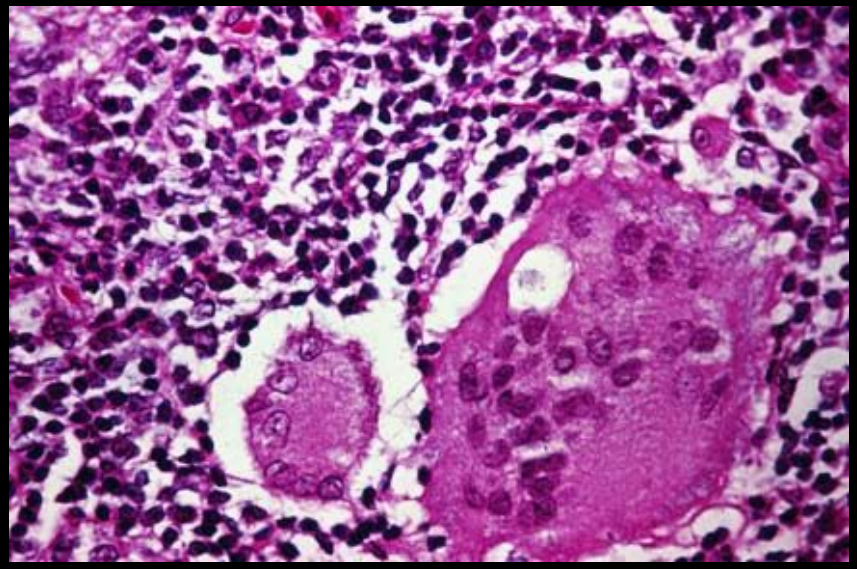
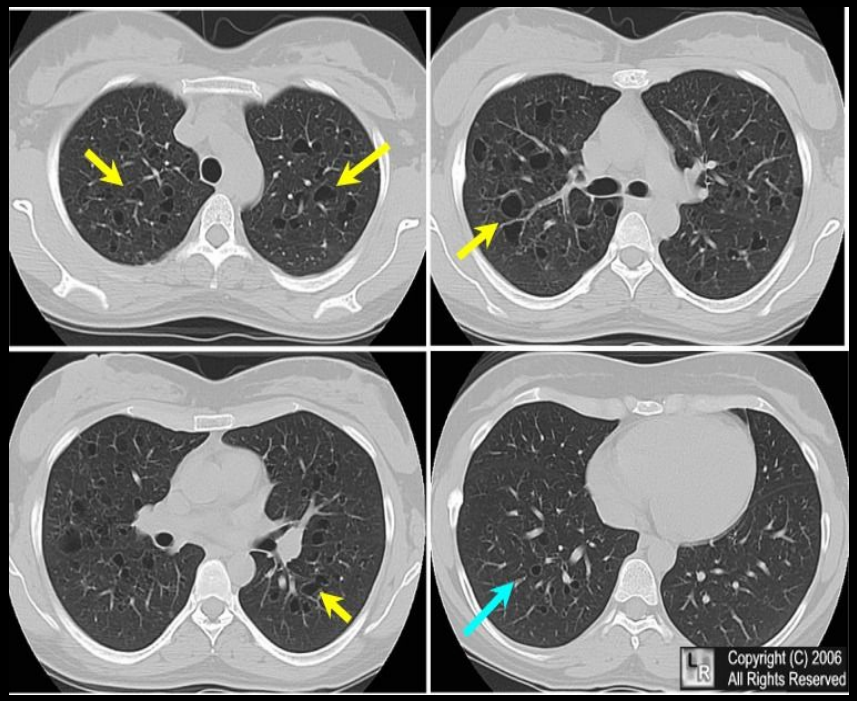
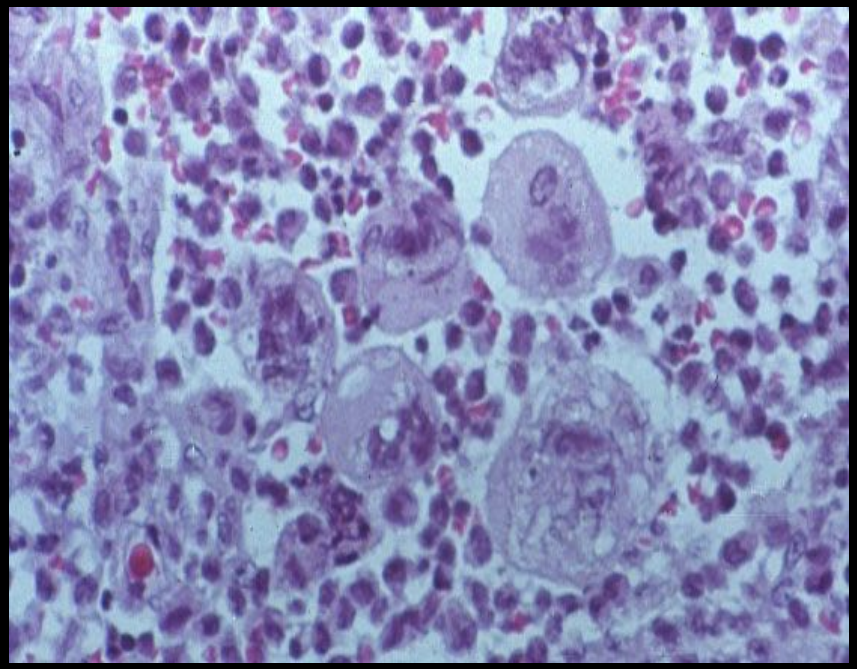


Answer: LIP

- CXR: diffuse, fine nodular changes particularly in the lower lobes
- Path: Lymphocytes and plasma cells within interstitial tissue

Case #7

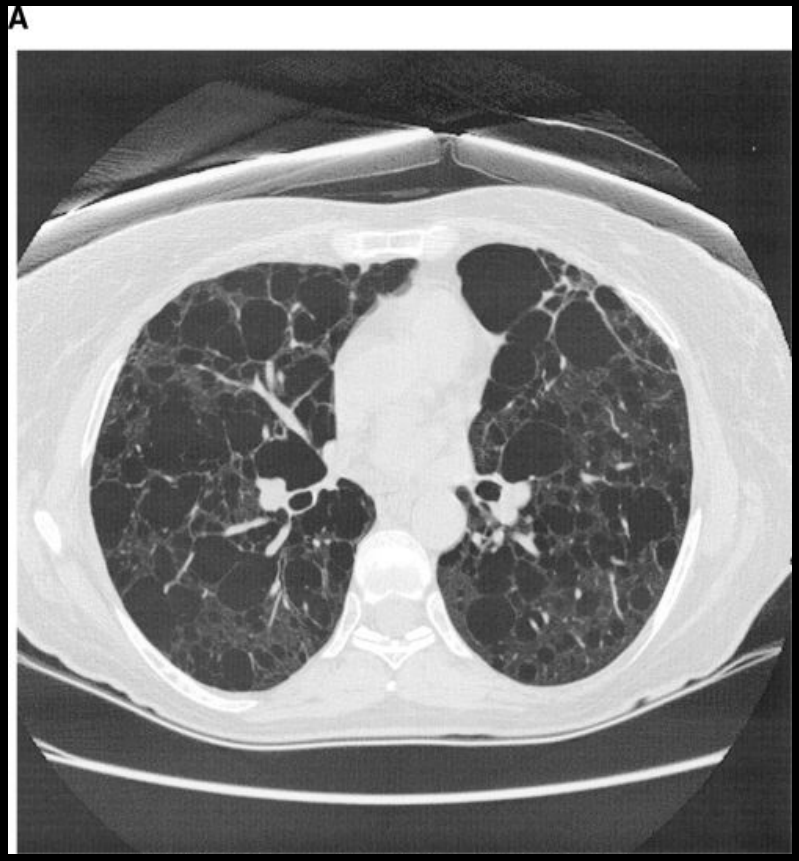


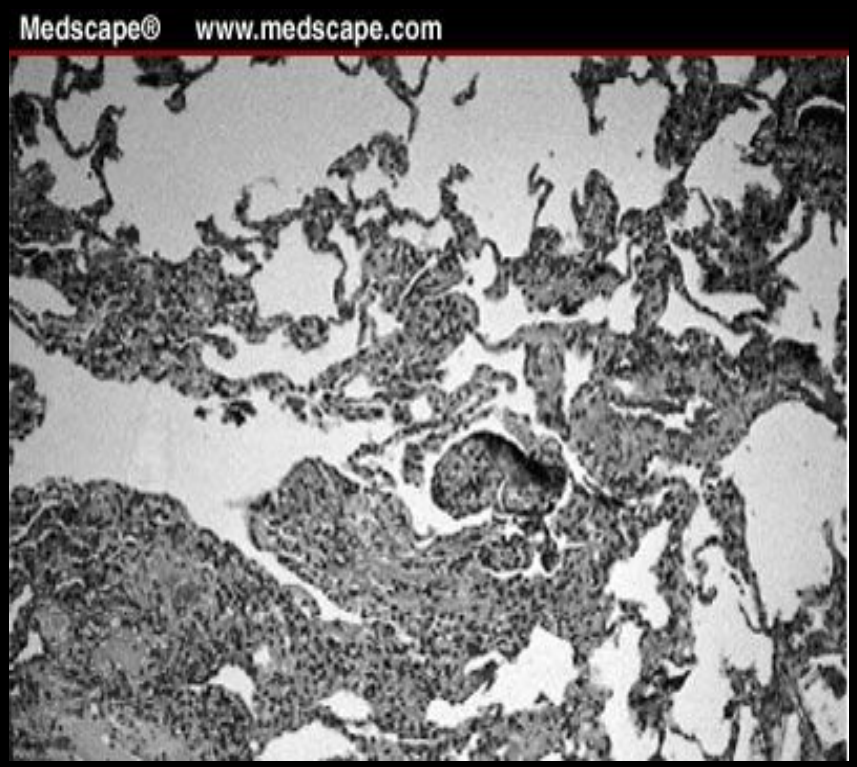


Answer: PLCH

- CT: multiple small, irregularly-shaped, cysts of varying sizes with thin walls scattered throughout the lungs (yellow arrows) relatively sparing the bases
- Path: eosinophilic granuloma

Case #8

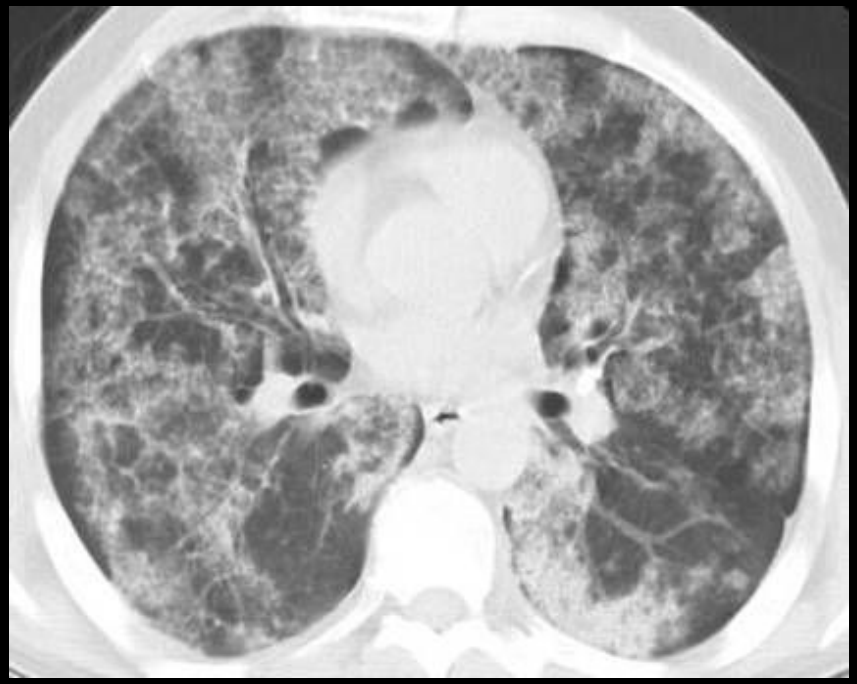


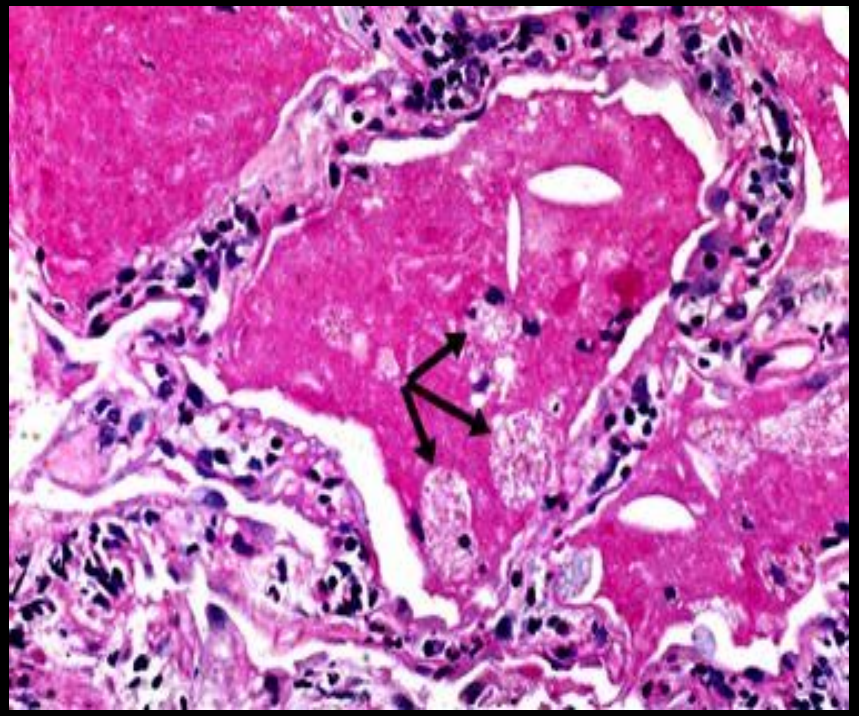


Answer: LAM

- CT: Diffuse parenchymal cysts
- Path: nodular proliferation of smooth muscle (LAM) cells replacing the lung parenchyma and jutting into air spaces

Case #9





Answer: PAP

- CT: patchy ground glass opacities and septal thickening in a geographic distribution
- Path: intra-alveolar accumulation of surfactant components and cellular debris, with minimal interstitial inflammation or fibrosis

Sources

- MKSAP 14, ILD section, p. 18-32
- Gross, T and Gary Hunninghake. “Idiopathic Pulmonary Fibrosis.” NEJM Vol. 345, No. 7, p. 517-526
- Harrisons’s Chapters 237 and 243
- Multiple “google images” searches