Cystic and Smoking-related Lung Disease

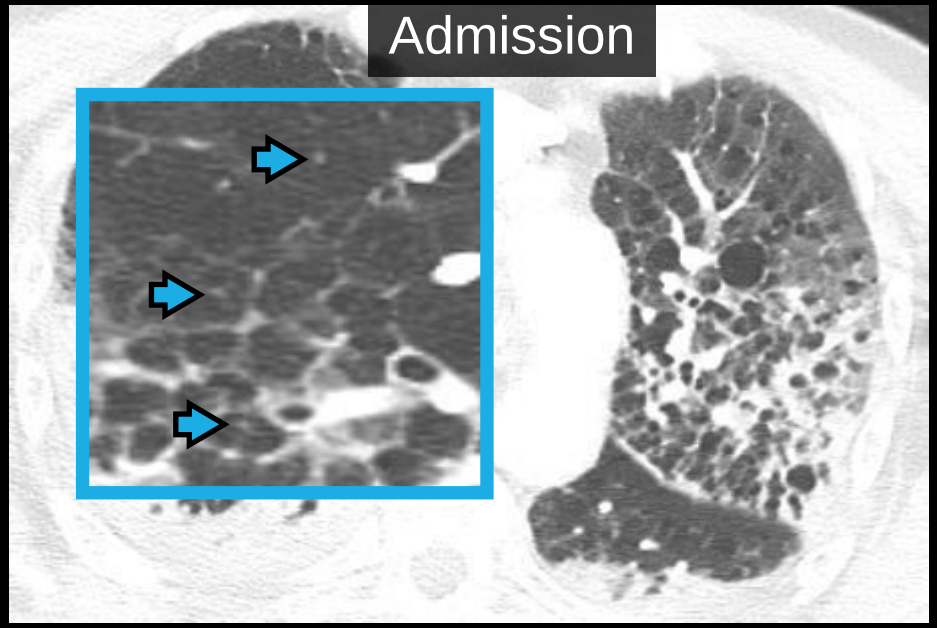
American College of Radiology™

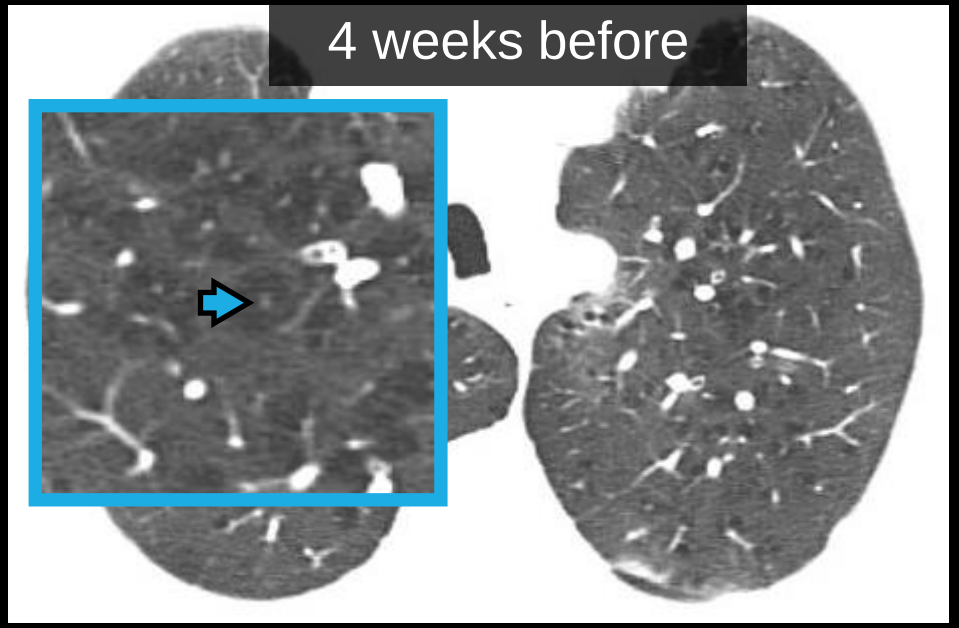
We Have No Relevant Disclosures

Objectives

- Recognize emphysema and lung cysts on HRCT and distinguish the two
- Describe HRCT findings of emphysema and cystic lung disease
- Show how integrating clinical and HRCT findings can obviate the need for surgical biopsy in some patients

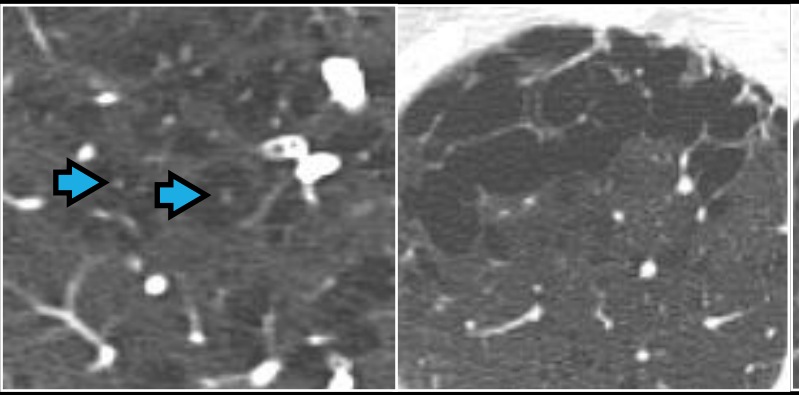
Patient w/ acute respiratory failure. Is this a cystic lung disease?





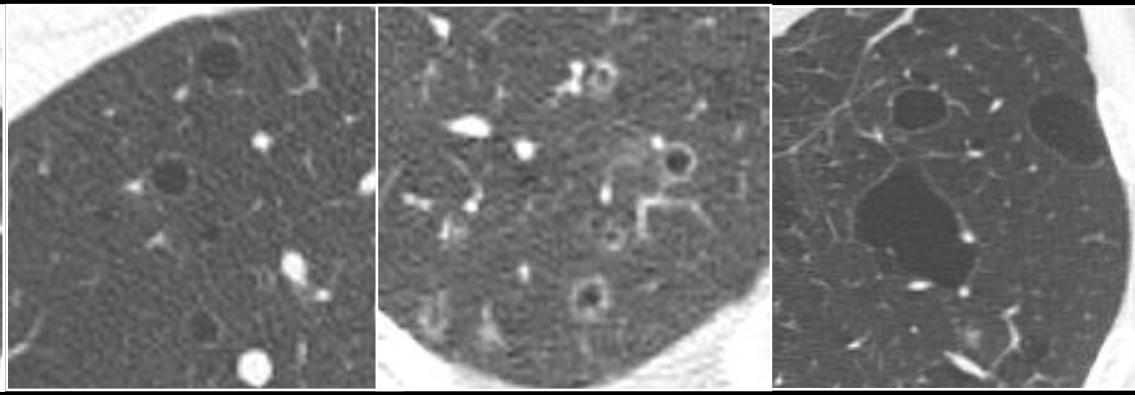
A - Yes
B - No
C – Can’t tell

Emphysema



- ✓ No walls
- ✓ Central dot (artery)
- ✓ Upper lobe predominant

Lung cysts



- ✓ Walls (thin, thick)
- ✓ No internal architecture
- ✓ Multiple patterns

Cyst

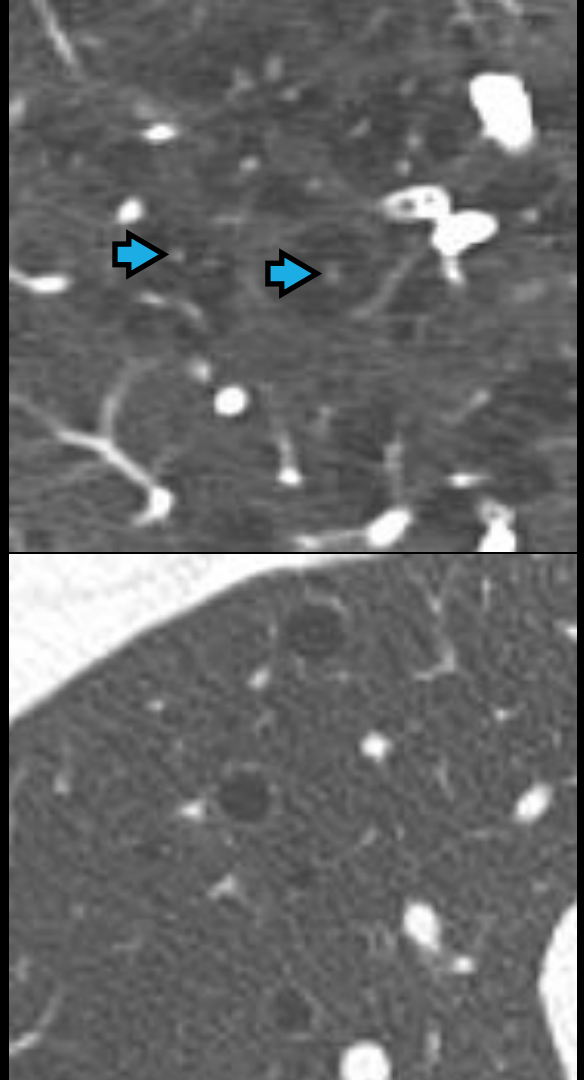
- Any circumscribed and well-defined air-containing structure in the lung parenchyma
- Thin and usually regular wall
- Radiology ≠ pathology
- Small number may be seen with aging (up to 5?)

Fleischner 2024

Cyst

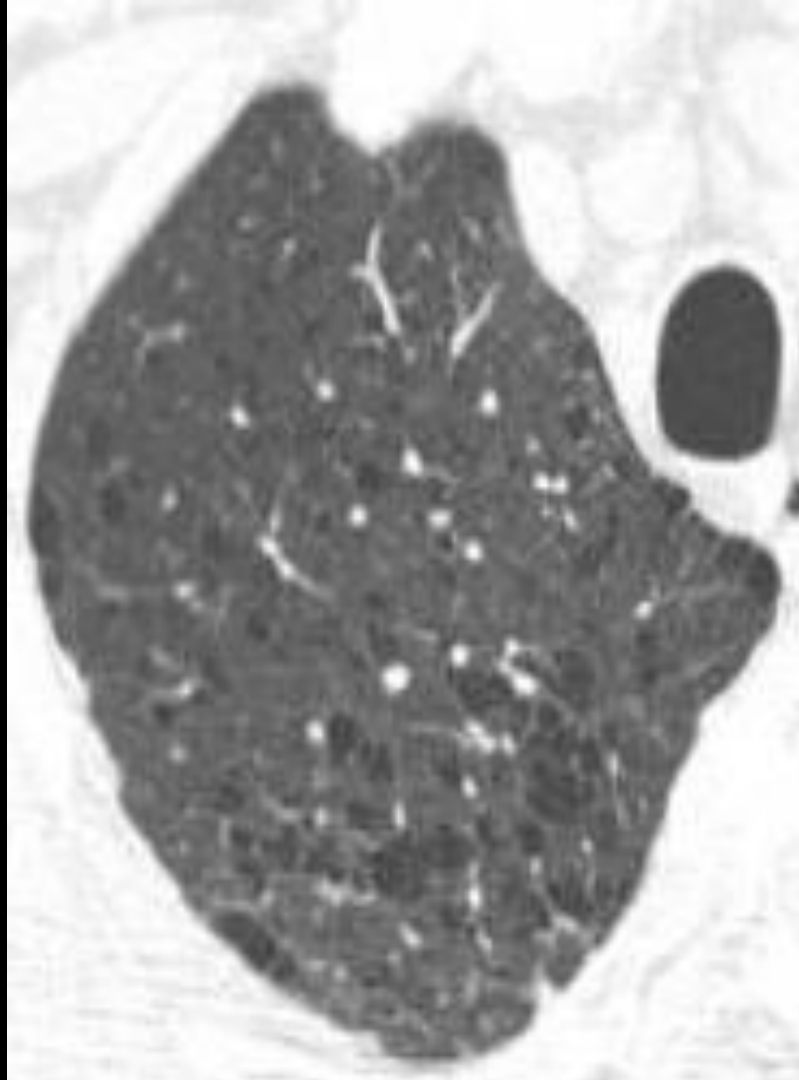
- Different from emphysema which lacks walls and has internal artery
- Small number may be seen with aging (up to 5?)

Araki et al



Emphysema

- Irreversible enlarged airspaces distal to and originating from the terminal bronchioles
- Accompanied by destruction of alveolar walls
- Absence of fibrosis no longer a criterion = they can co-exist



Fleischner 2024

Approach to Lung Cysts

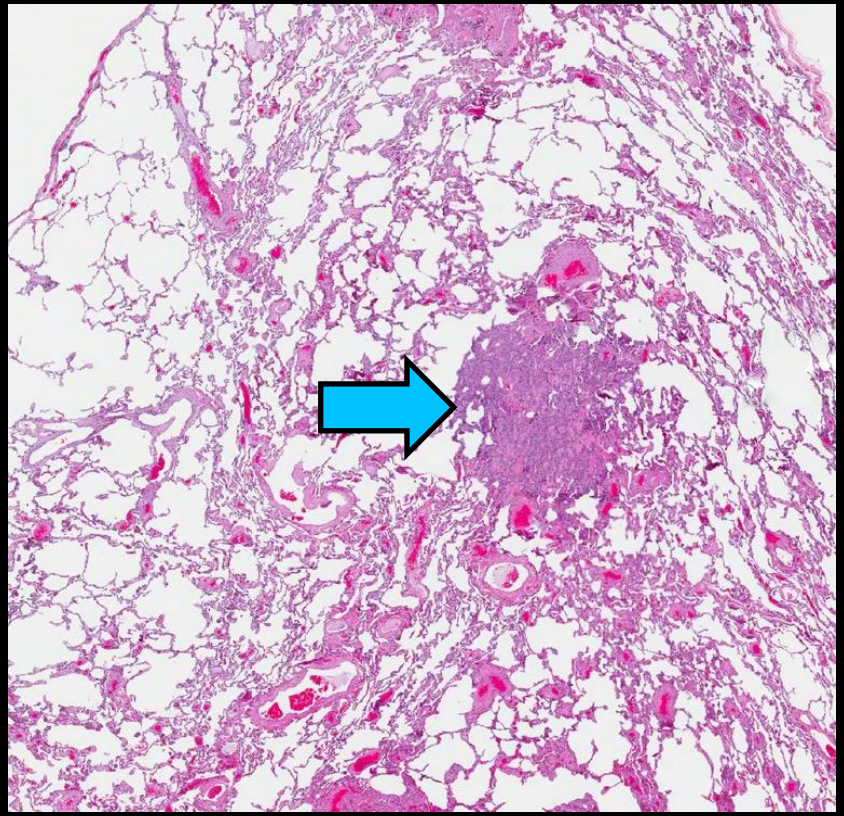
- Commonalities
  - Mechanism: presumed small airway obstruction
  - Spontaneous pneumothorax

Cystic Lung Disease

- Pulmonary Langerhans cell histiocytosis
- Lymphangioleiomyomatosis
- Lymphoid interstitial pneumonia
- Amyloidosis
- Light-chain deposition disease
- Birt-Hogg-Dubé syndrome
- Cystic metastases

Pulmonary Langerhans Cell Histiocytosis (PLCH)

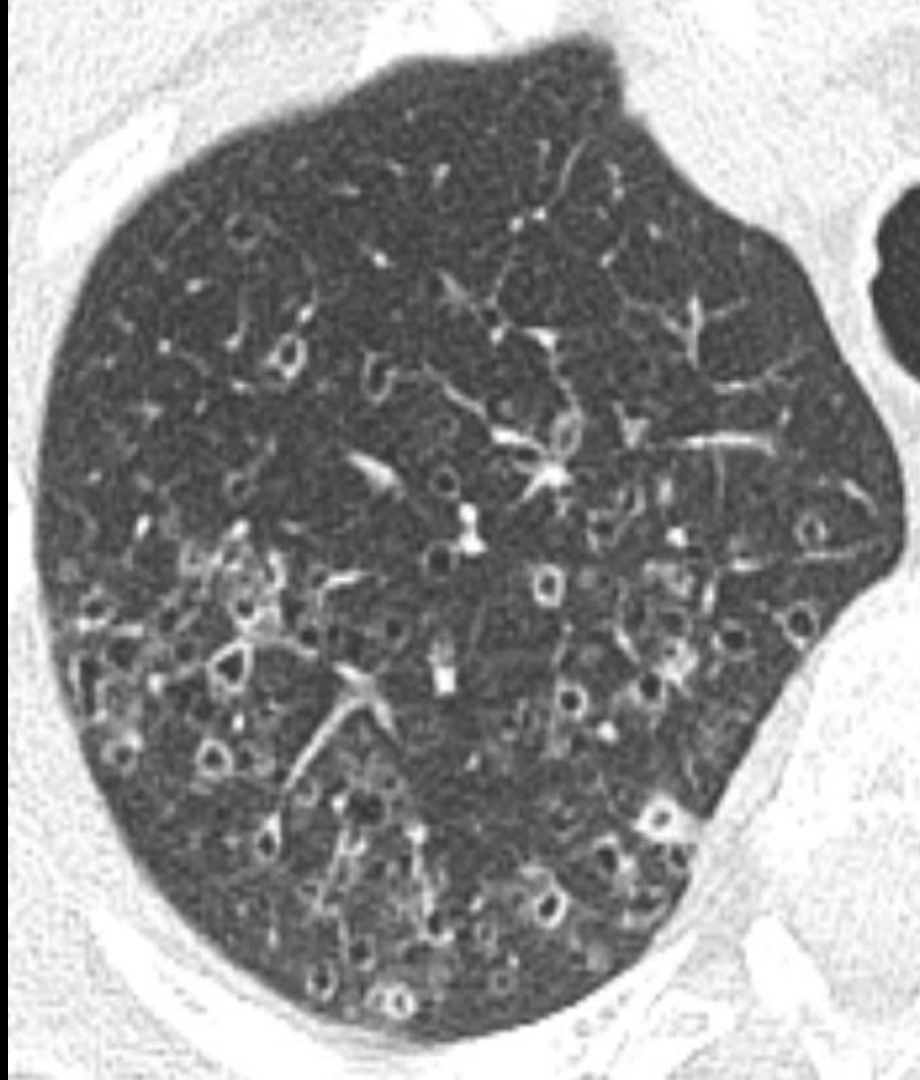
- Spectrum of histiocytoses
- Peribronchiolar infiltration of CD1a+ Langerhans and inflammatory cells in the lungs
- Nearly always associated with cigarette smoking in adults



Courtesy of Teri J. Franks, M.D. (Joint Pathology Center)

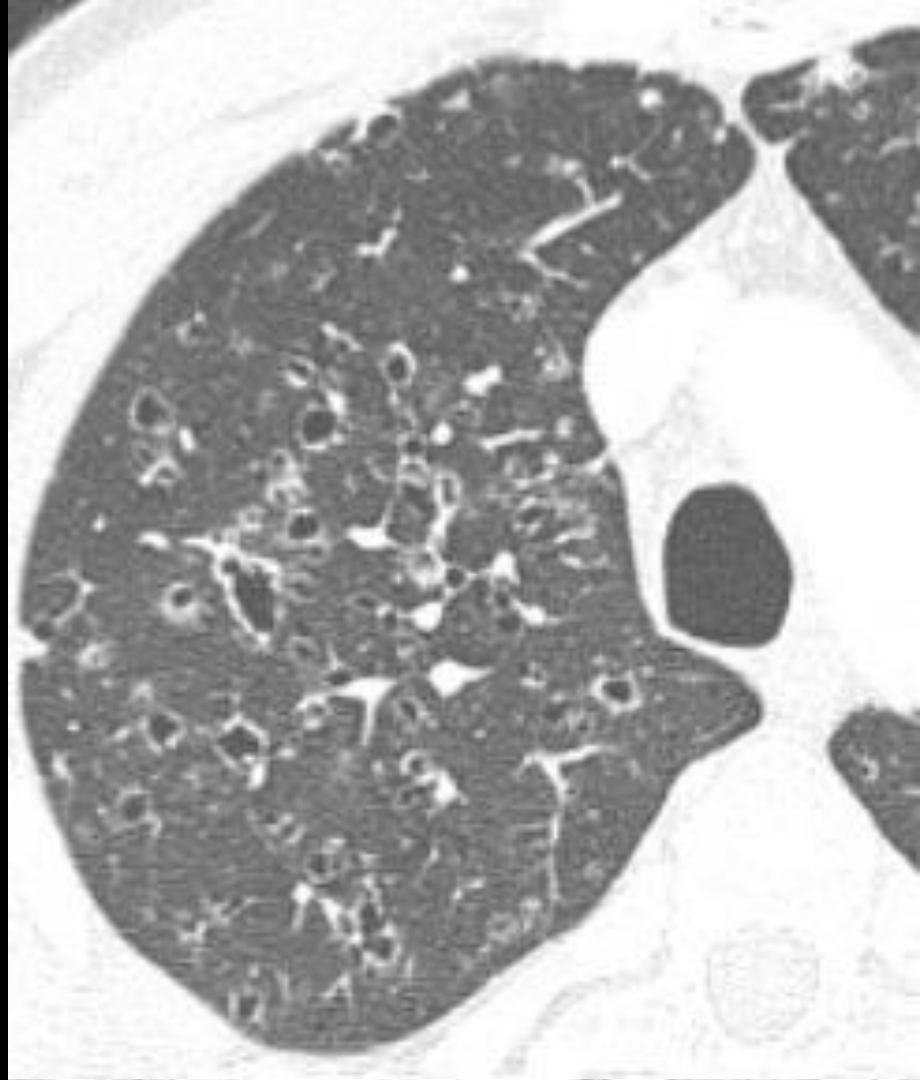
PLCH

- Solid nodules and/or cysts
- Upper and mid lung predominant
- Characteristic sparing of costophrenic sulci and anterior tips of lungs

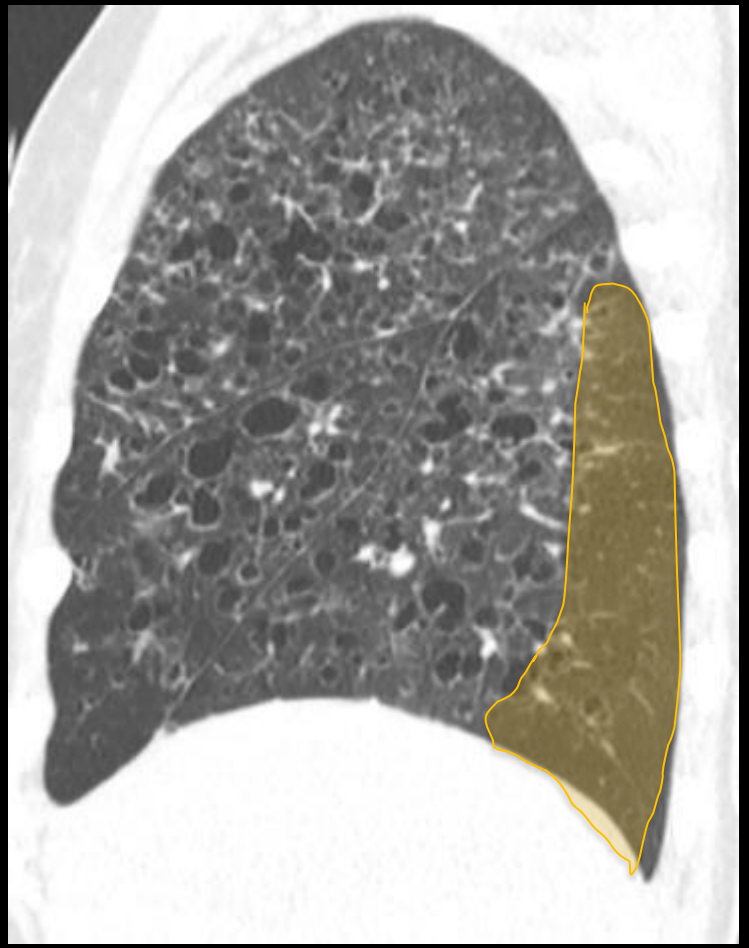


PLCH

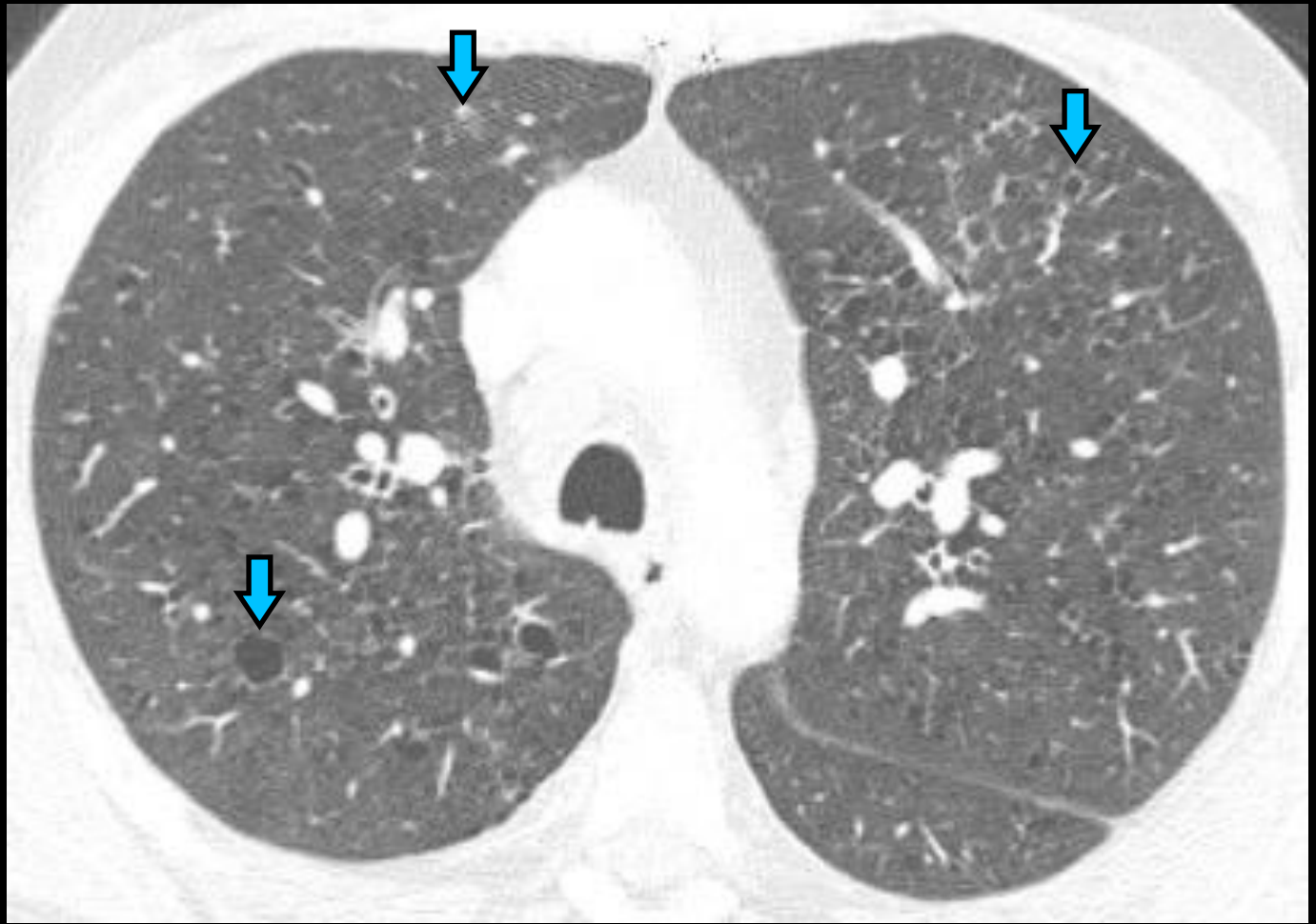
- Nodules:
  - Irregular, “dirty”
  - 1-10 mm
  - +/- cavitation
- Cysts
  - Irregular, “bizarre”
  - Variable sizes
- Same distribution



PLCH: Typical

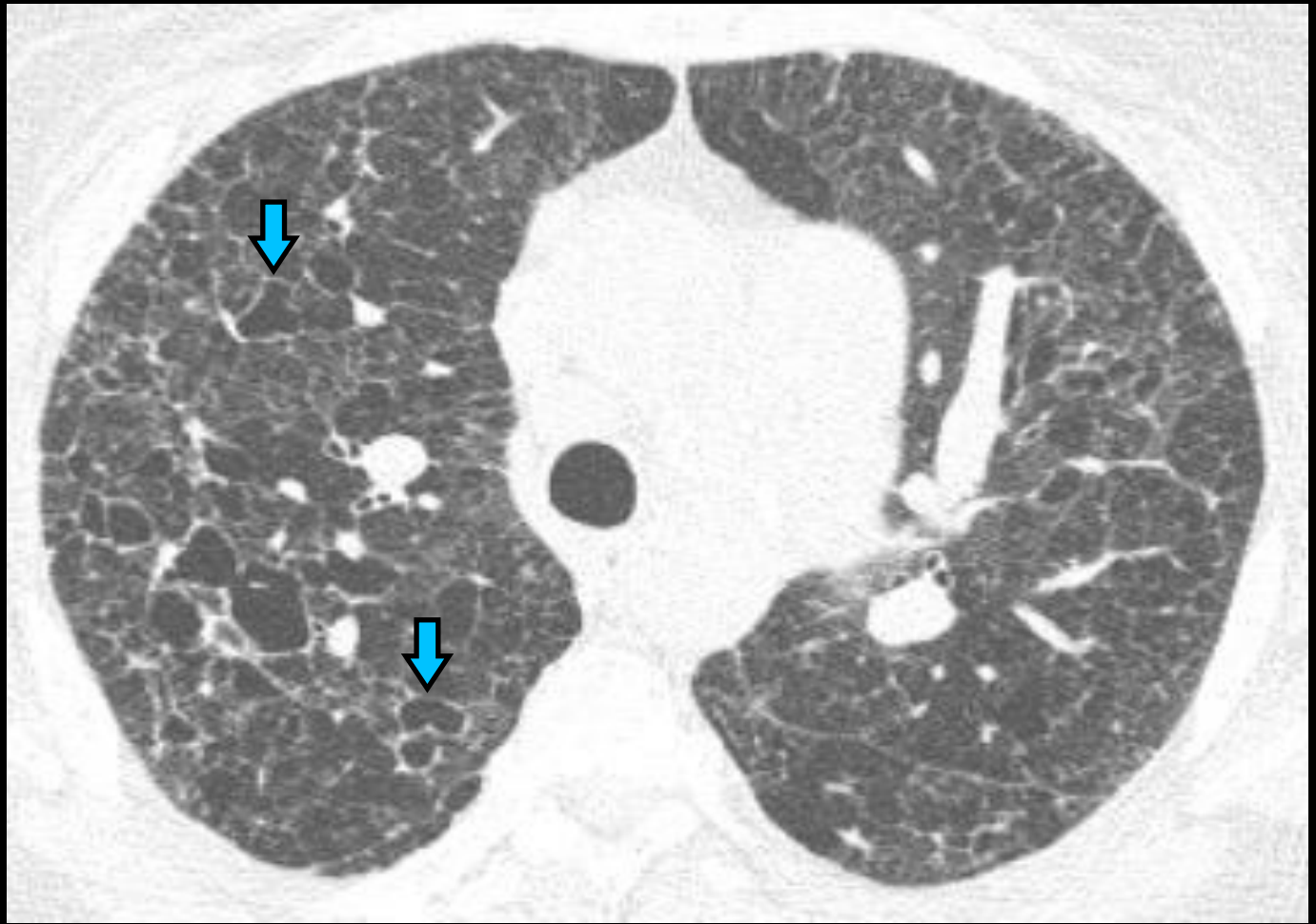


PLCH: Mild

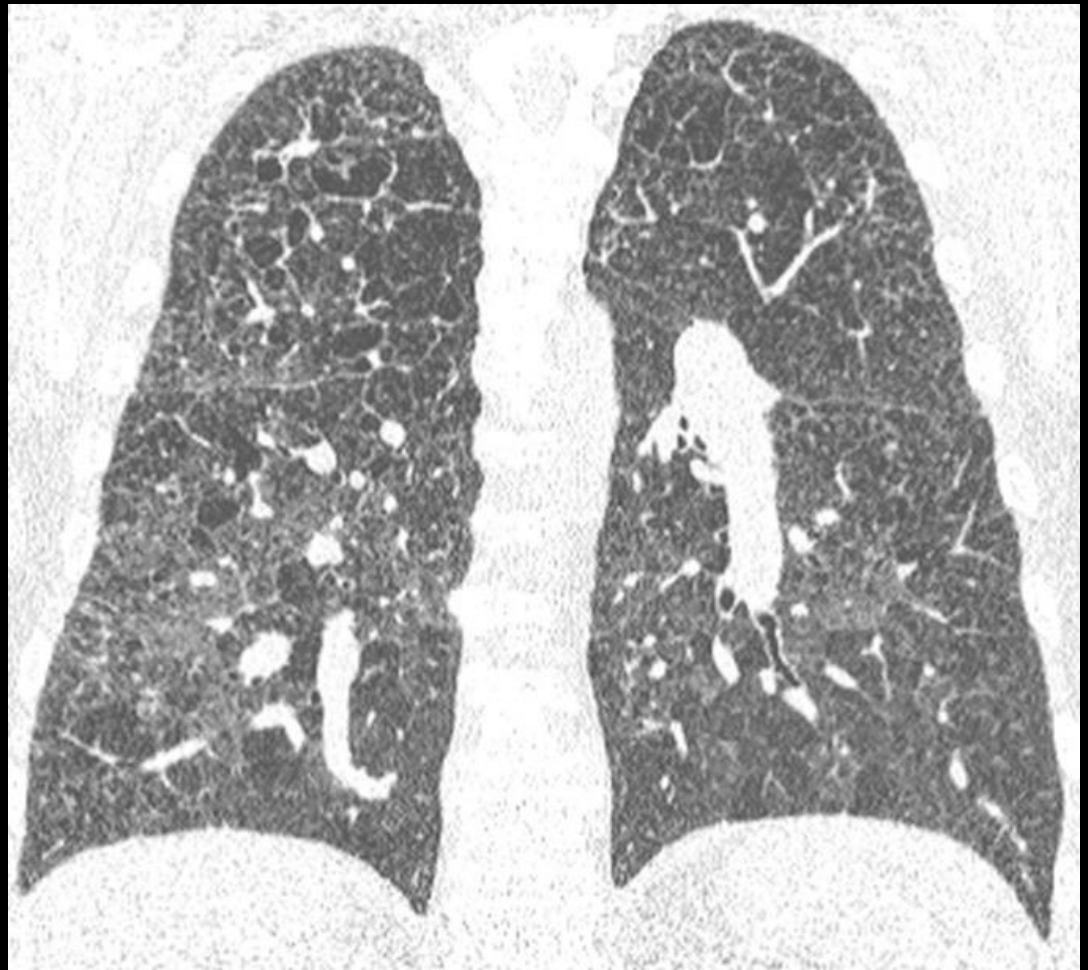


PLCH: Mild

PLCH: Advanced



PLCH: Advanced



PLCH: Severe: Often confused with emphysema

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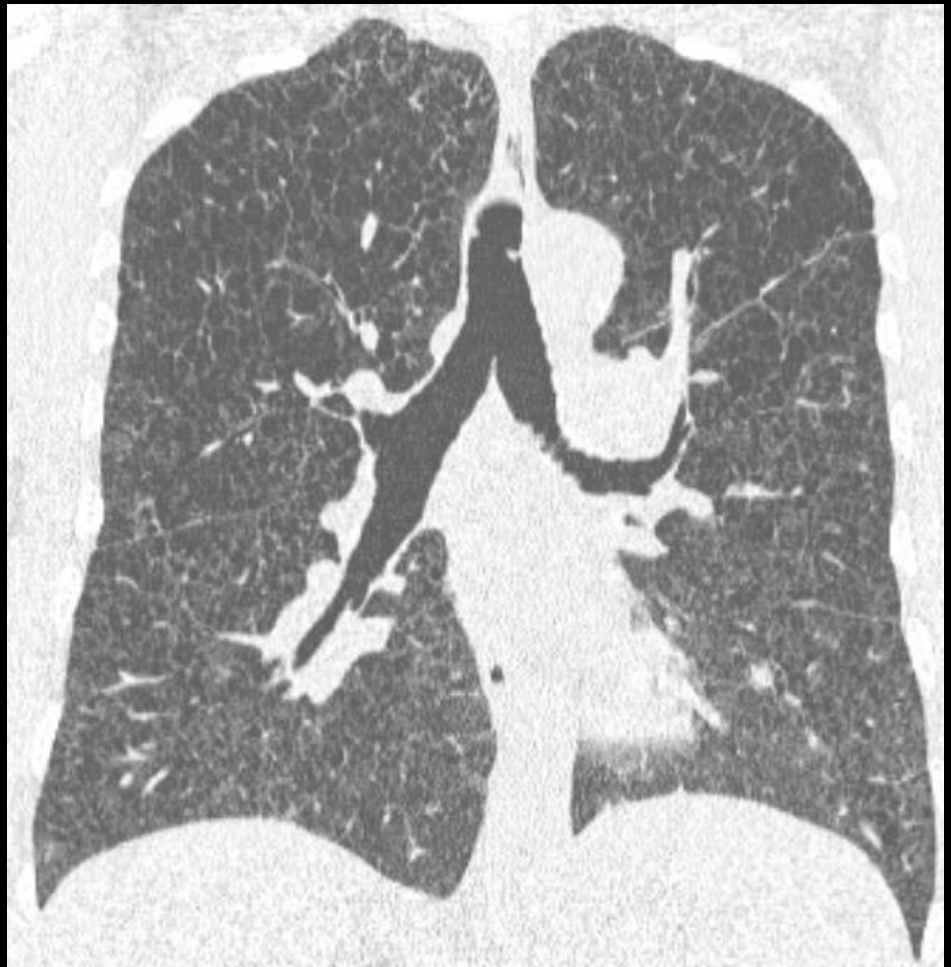
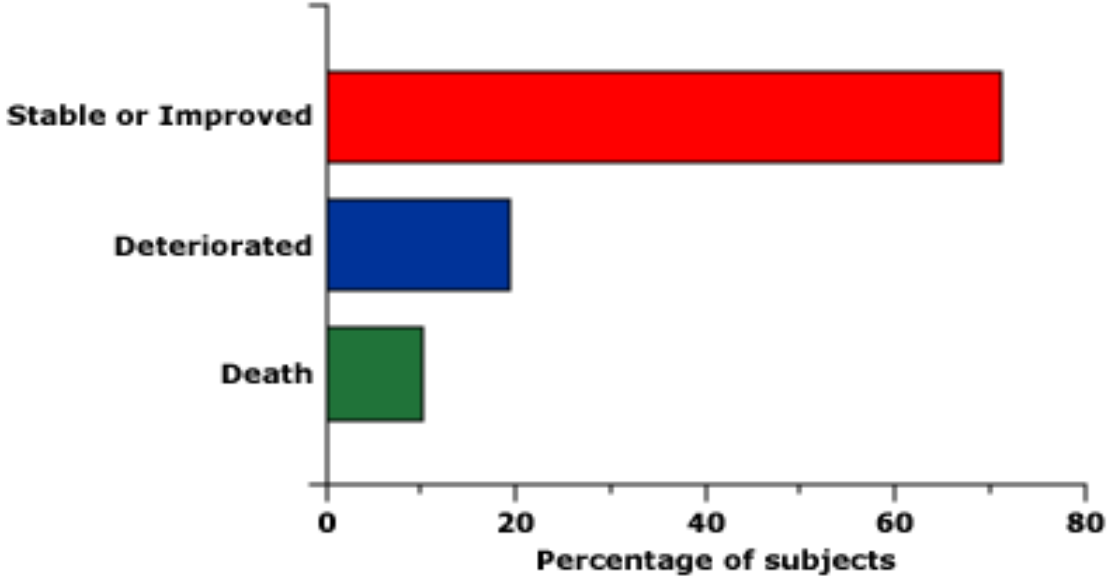


PLCH

Clinical course of pulmonary Langerhans cell histiocytosis

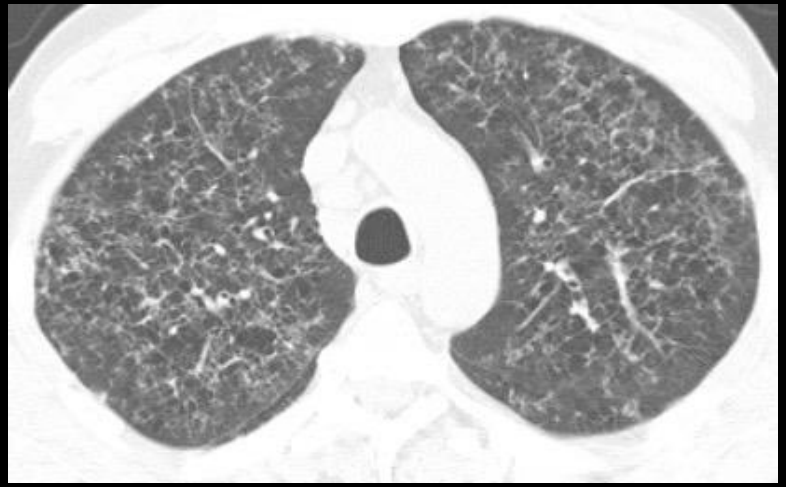


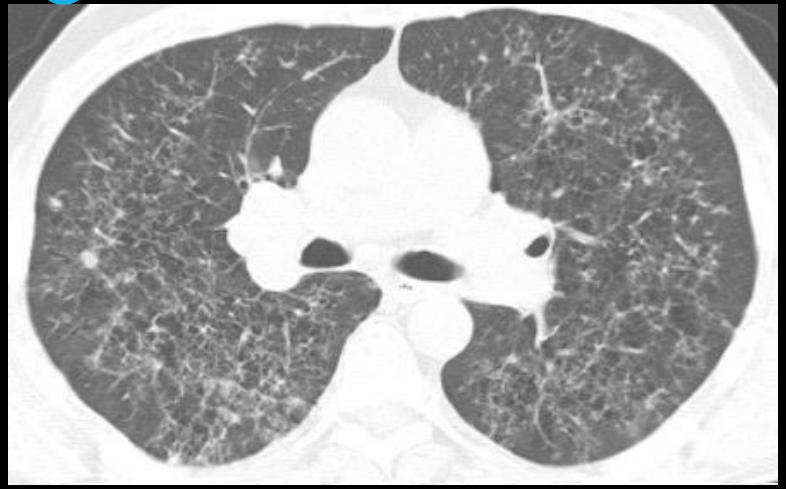
UpToDate® Accessed March 2022.

PLCH: Progressive

Presentation

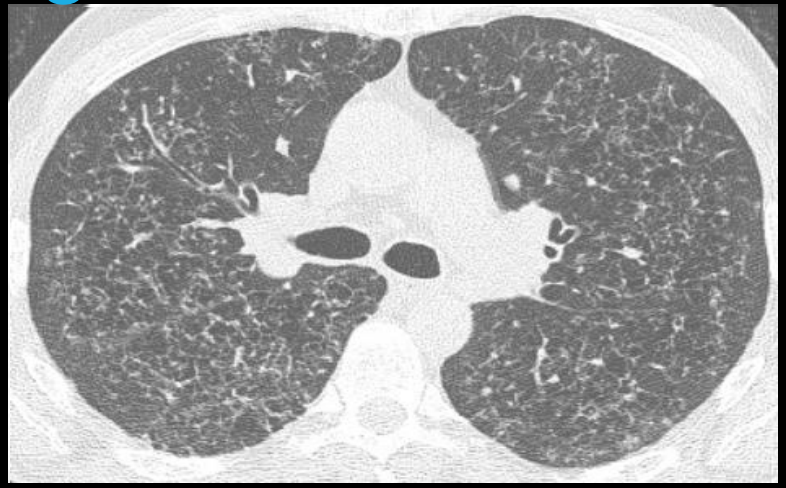
PLCH: Progressive





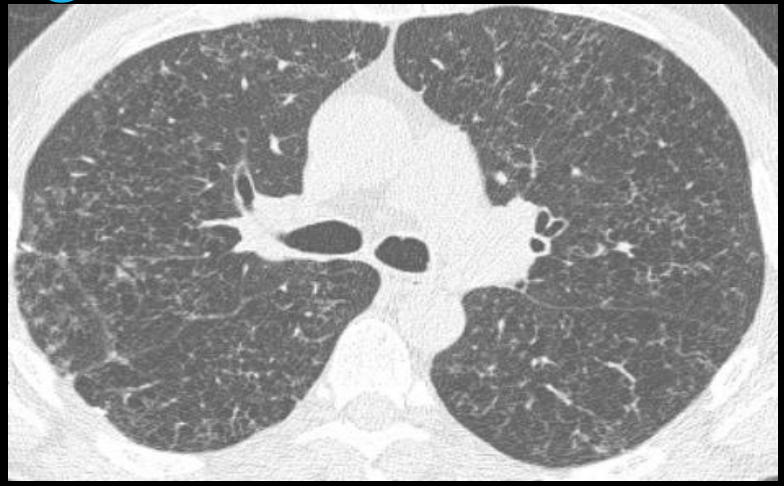
1 year later

PLCH: Progressive



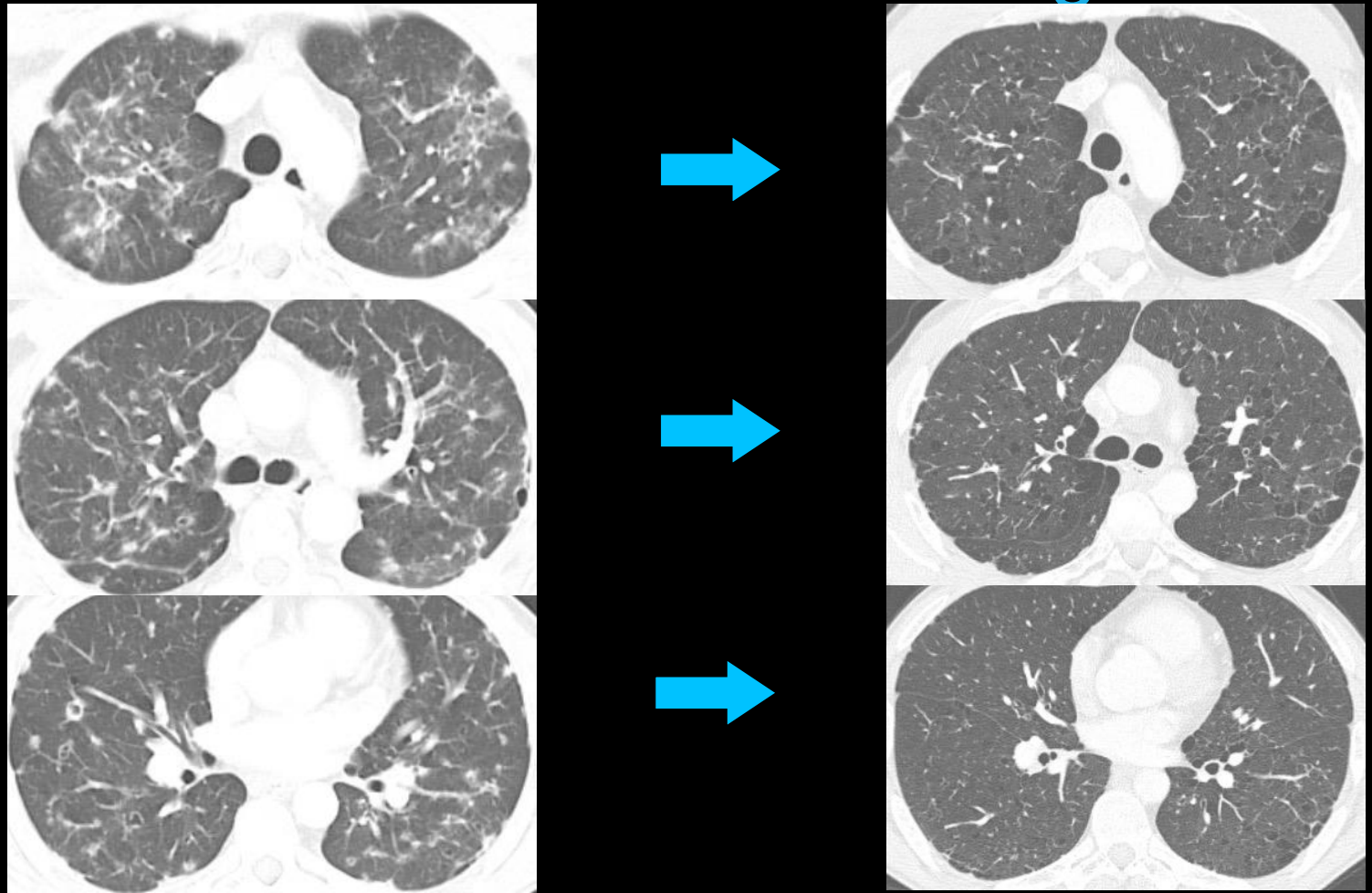
2 years later

PLCH: Progressive



3 years later

PLCH: Resolving



Pulmonary Langerhans Cell Histiocytosis (PLCH)

- Prognosis
  - End-stage disease may require lung transplant
  - Pulmonary hypertension portends poor prognosis

Cystic Lung Disease

Diagnosis	Distribution	Morphology	Other Findings	Clinical
PLCH	Upper zone	Irregular, thick wall	Nodules, ground-glass	Cigarette smoking

Lymphangioleiomyomatosis (LAM)

- Low-grade multicentric, malignant neoplasm characterized by infiltration of neoplastic smooth-muscle like cells
  - Lungs
  - Lymphatics
- Associated with angiomyolipomas (AML)
  - Kidney most common
  - Liver and spleen

Lymphangioleiomyomatosis (LAM)

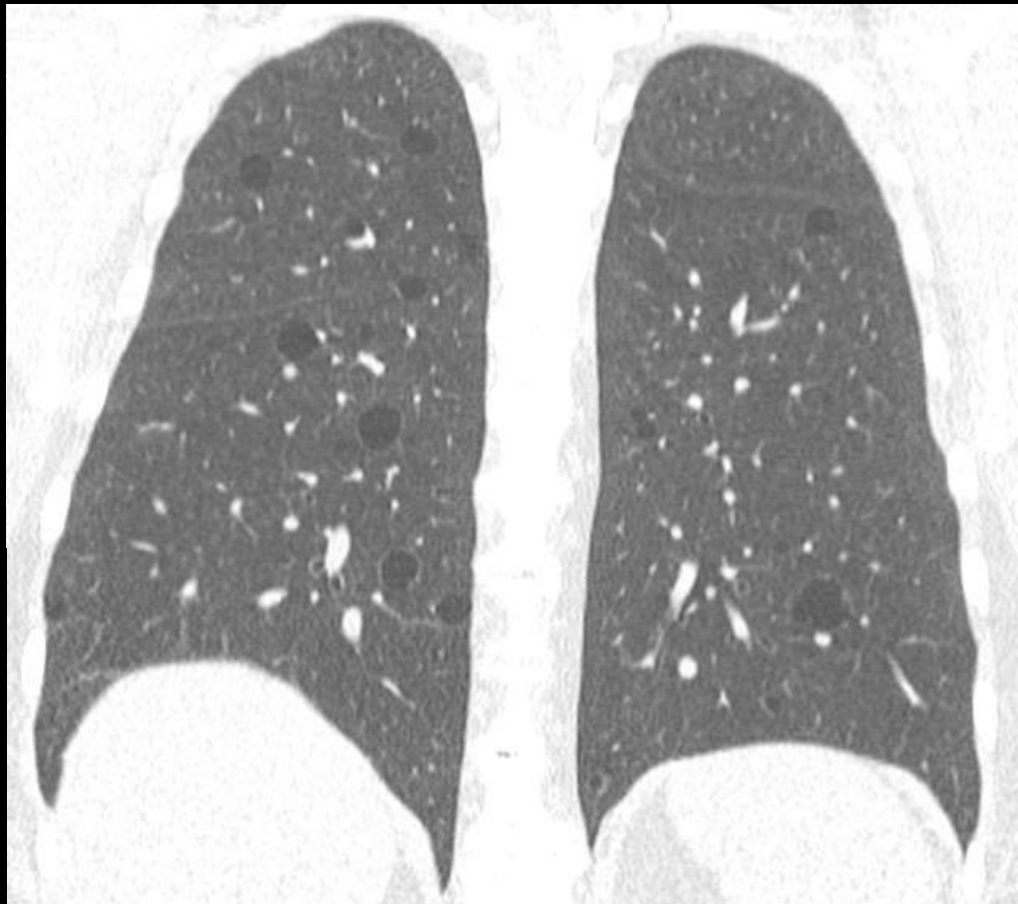
- Two types of LAM
  - Tuberous sclerosis complex (TSC-LAM): Autosomal dominant
    - Affects up to 40% of women with TSC
    - Affects 10-15% of men with TSC
      - Rarely symptomatic
    - Brain, skin, heart, lungs, kidneys, and liver lesions
  - Sporadic (S-LAM)
    - 3-5/1,000,000 women
    - Single case report of S-LAM in male

LAM

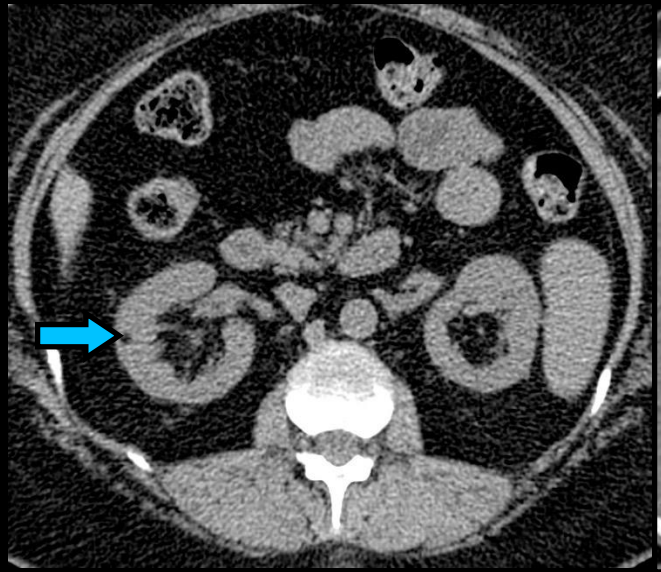
- Diffuse thin-walled cysts
  - 2-20 mm diameter
  - No zonal predominance
- Small nodules
  - Muscle or pneumocyte hyperplasia (rare)
- Ground-glass opacity
  - Hemorrhage
  - Hemosiderosis
  - Smooth muscle proliferation

Lymphangioleiomyomatosis (LAM)

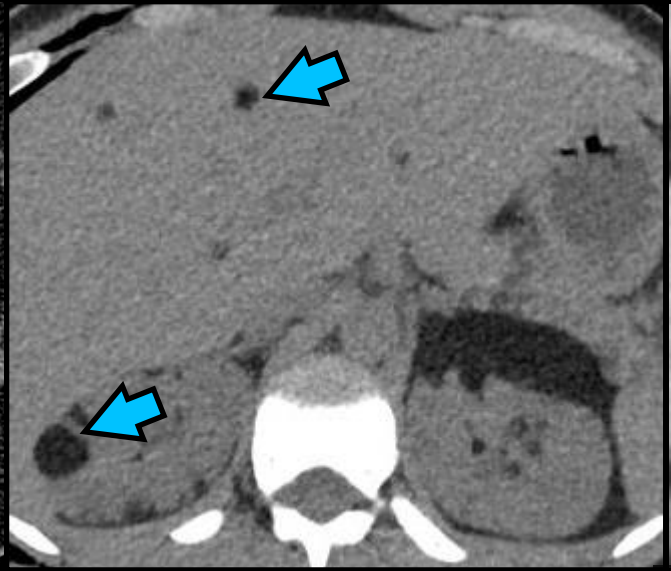
- 35-years-old mean age diagnosis
- Progressive dyspnea on exertion
- Obstructive physiology
- Pneumothorax
- Chylothorax
- Incidental



Lymphangioleiomyomatosis (LAM)



Angiomyolipoma



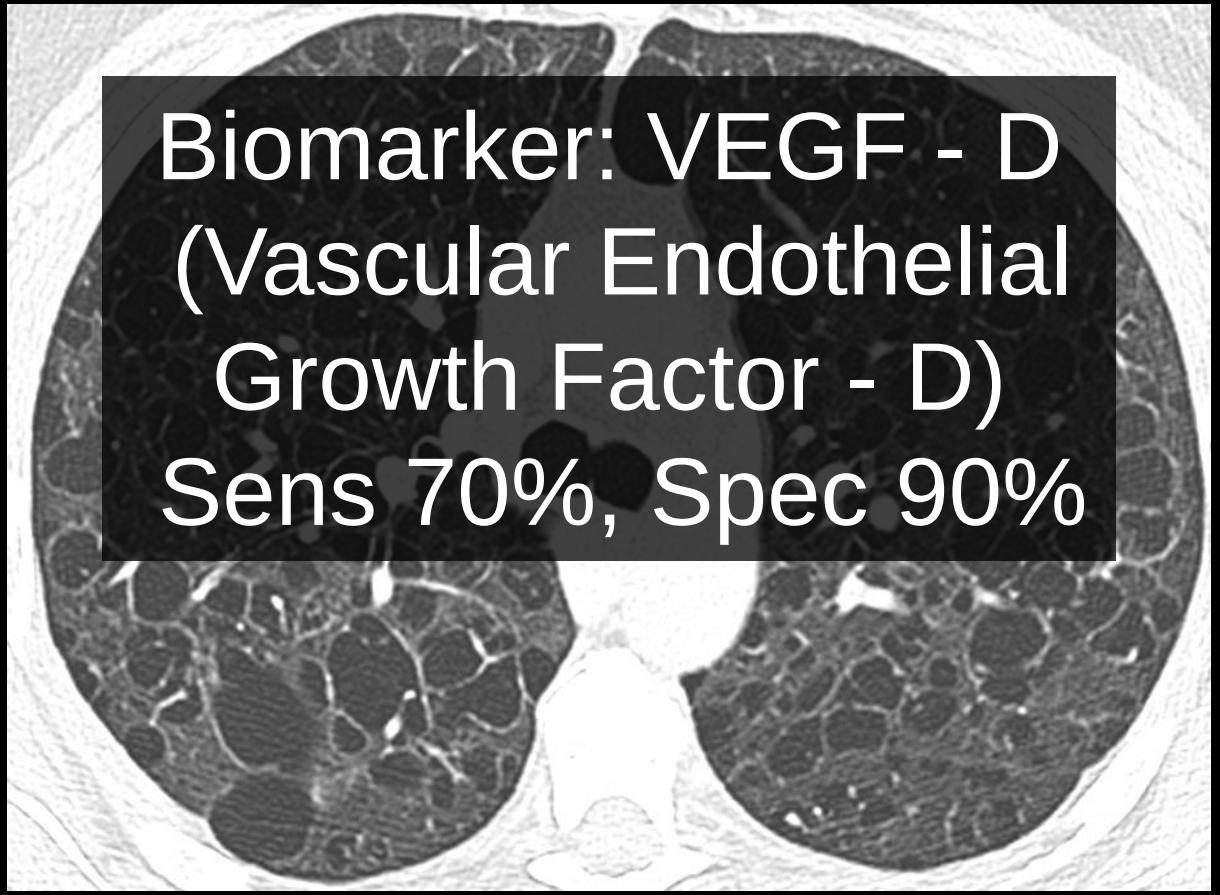
Angiomyolipoma

Cystic Lymphangioleiomyomas [1]

AML: LAM-TSC ~80% >>> Sporadic LAM ~30%

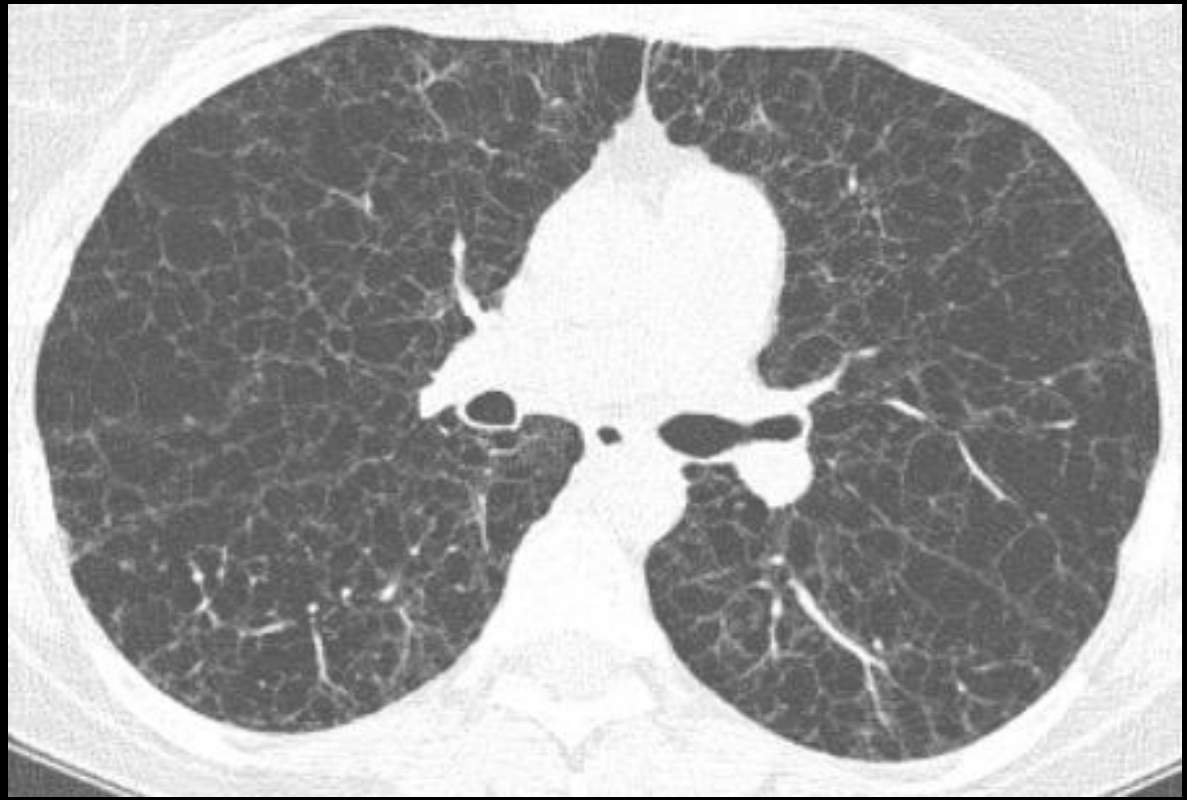
[1] Pallisa et al. Radiographics, 2002.

Lymphangioleiomyomatosis (LAM)



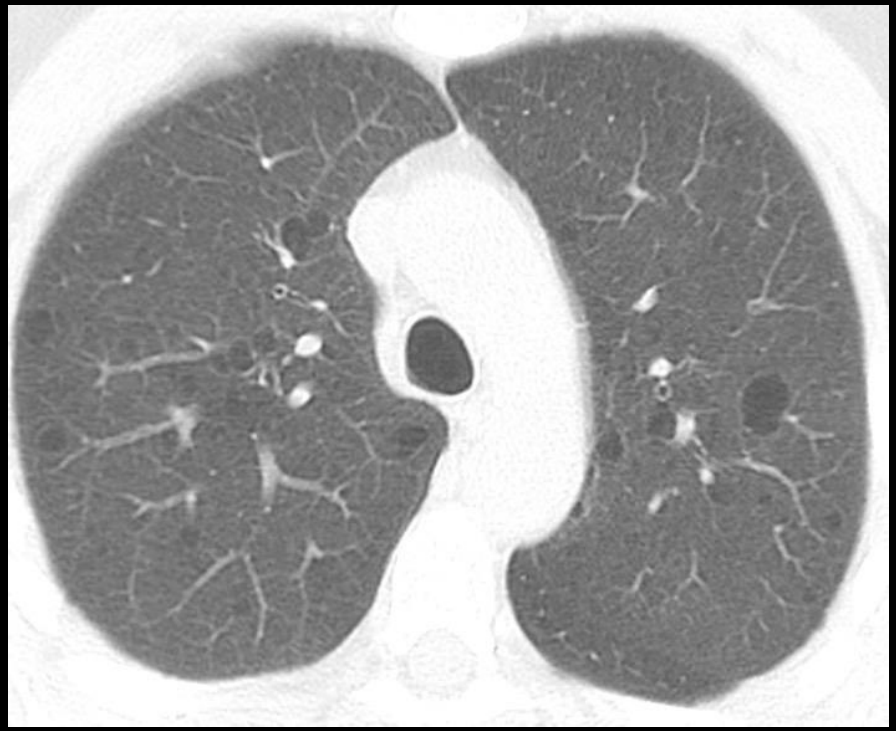
Lymphangioleiomyomatosis (LAM)

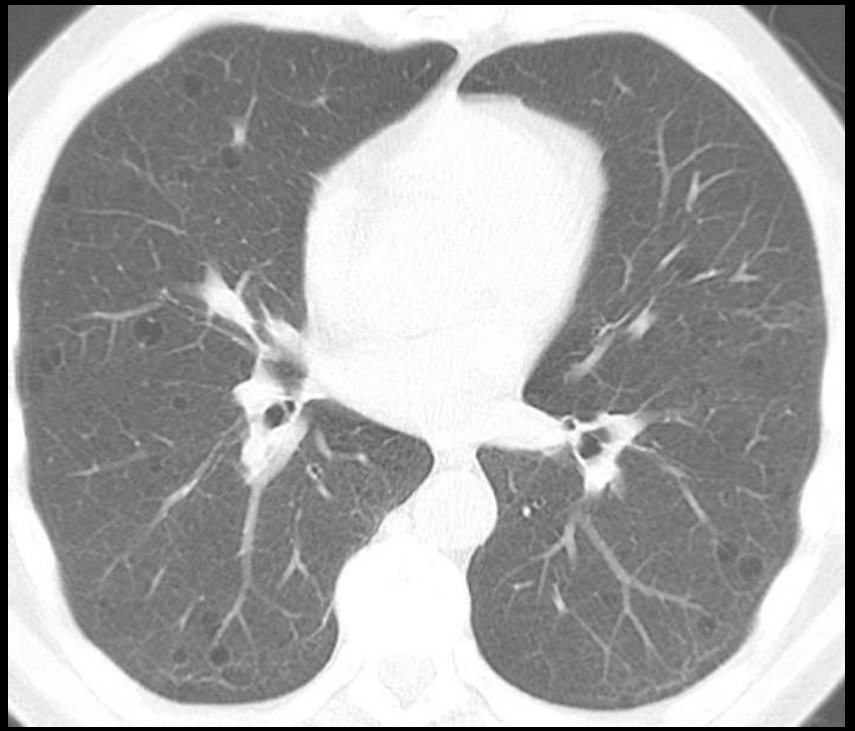
- 55% patients SOB with daily activities at 10 years*
- Dyspnea with daily activities, recurrent PTX, and hypoxia requiring oxygen develop in most patients within 10 years of symptom onset



- Gupta et al. *Am J Respir Crit Care,* 2014
- McCormack et al. *Am J Respir Crit Care,* 2016

TSC-LAM



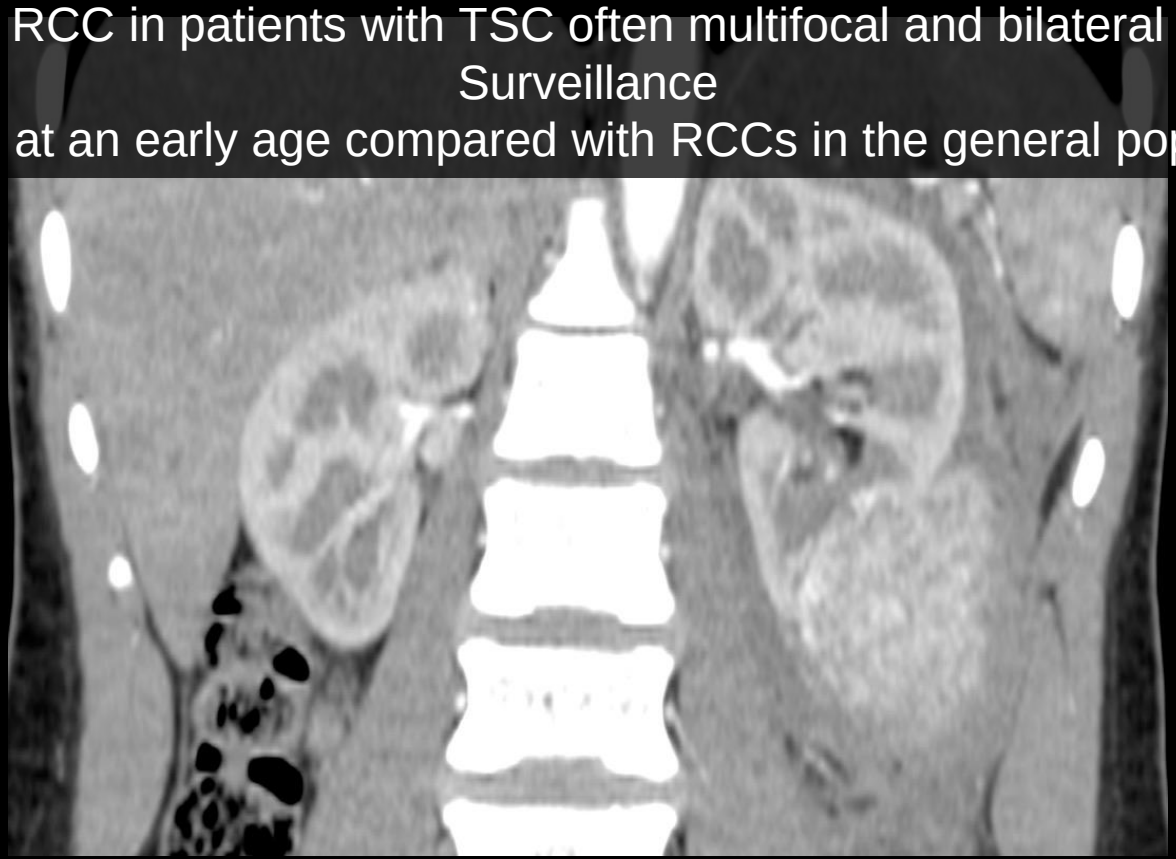


TSC-LAM

RCC in patients with TSC often multifocal and bilateral

Surveillance

Develop at an early age compared with RCCs in the general population

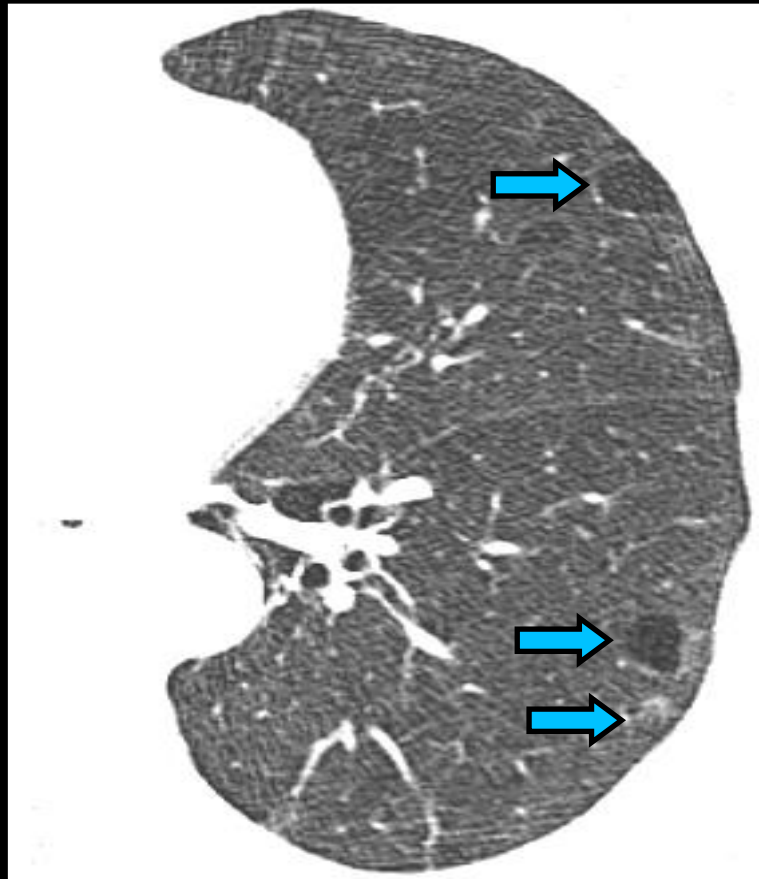


Cystic Lung Disease

Diagnosis	Distribution	Morphology	Other Findings	Clinical
PLCH	Upper zone	Irregular, thick wall	Nodules, ground-glass	Cigarette smoking
LAM	Diffuse	Uniform, thin wall	AML	Female, TSC, ↑VEGF-D

Lymphoid Interstitial Pneumonia (LIP)

- Diffuse or focal interstitial infiltration with lymphocytes and plasma cells
  - Polyclonal
  - Usually mature T or B lymphocytes
  - Primarily affects alveolar septae

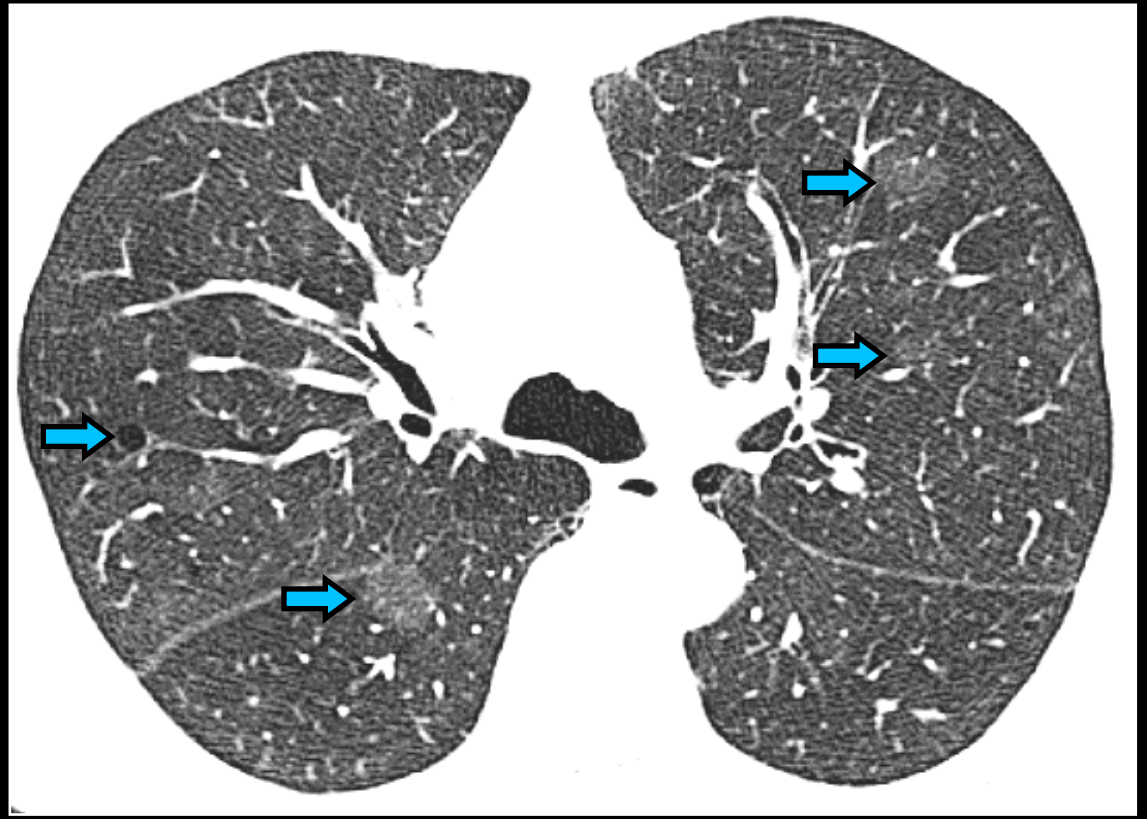


LIP

- Cysts
  - 1-30 mm
  - +/- elongated
  - Perivascular
  - Basilar predominant
  - Fewer in number than LAM

LIP

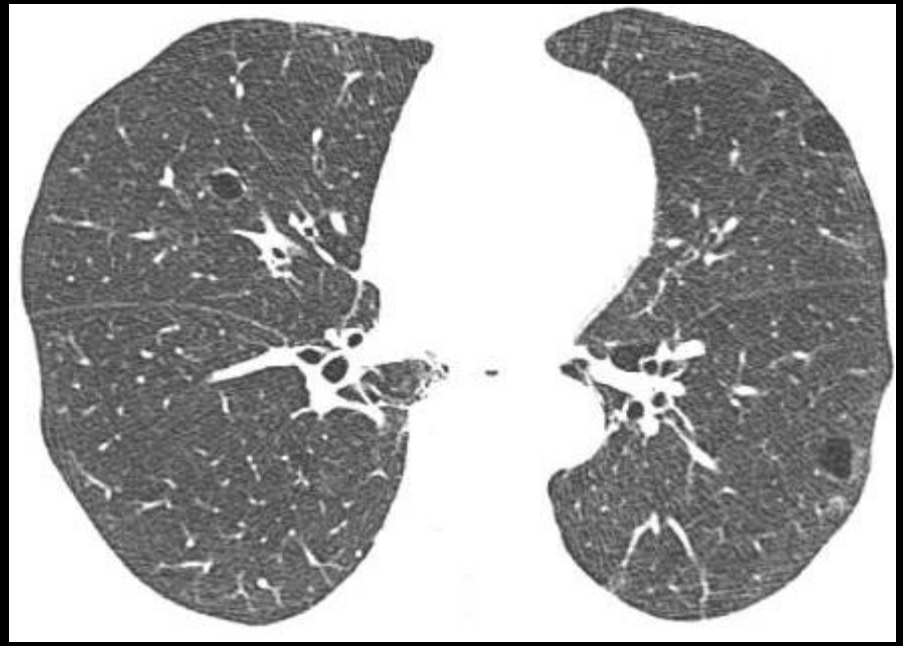
- Associated findings
  - Poorly-defined centrilobular nodules
  - Septal thickening
  - Subpleural nodules
  - Bronchovascular thickening
  - Ground-glass opacities



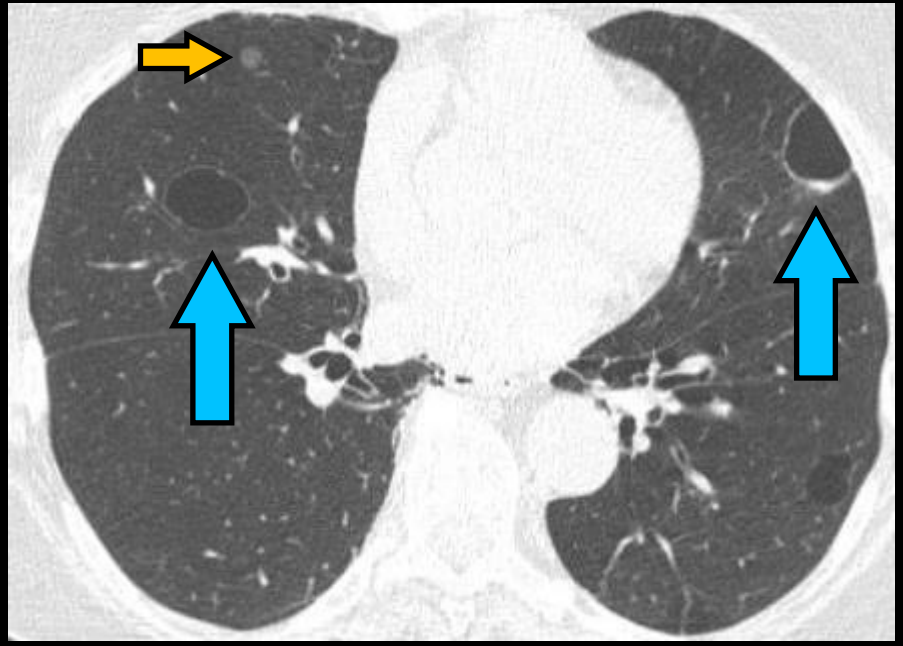
LIP

- Incidental or slowly worsening cough and dyspnea
- Underlying disease
  - Sjögren syndrome (25%)
  - AIDS (especially children)
  - Dysproteinemias
  - Other autoimmune disease
  - Infection
  - Graft-versus-host disease
  - Idiopathic

Lymphoid Interstitial Pneumonia

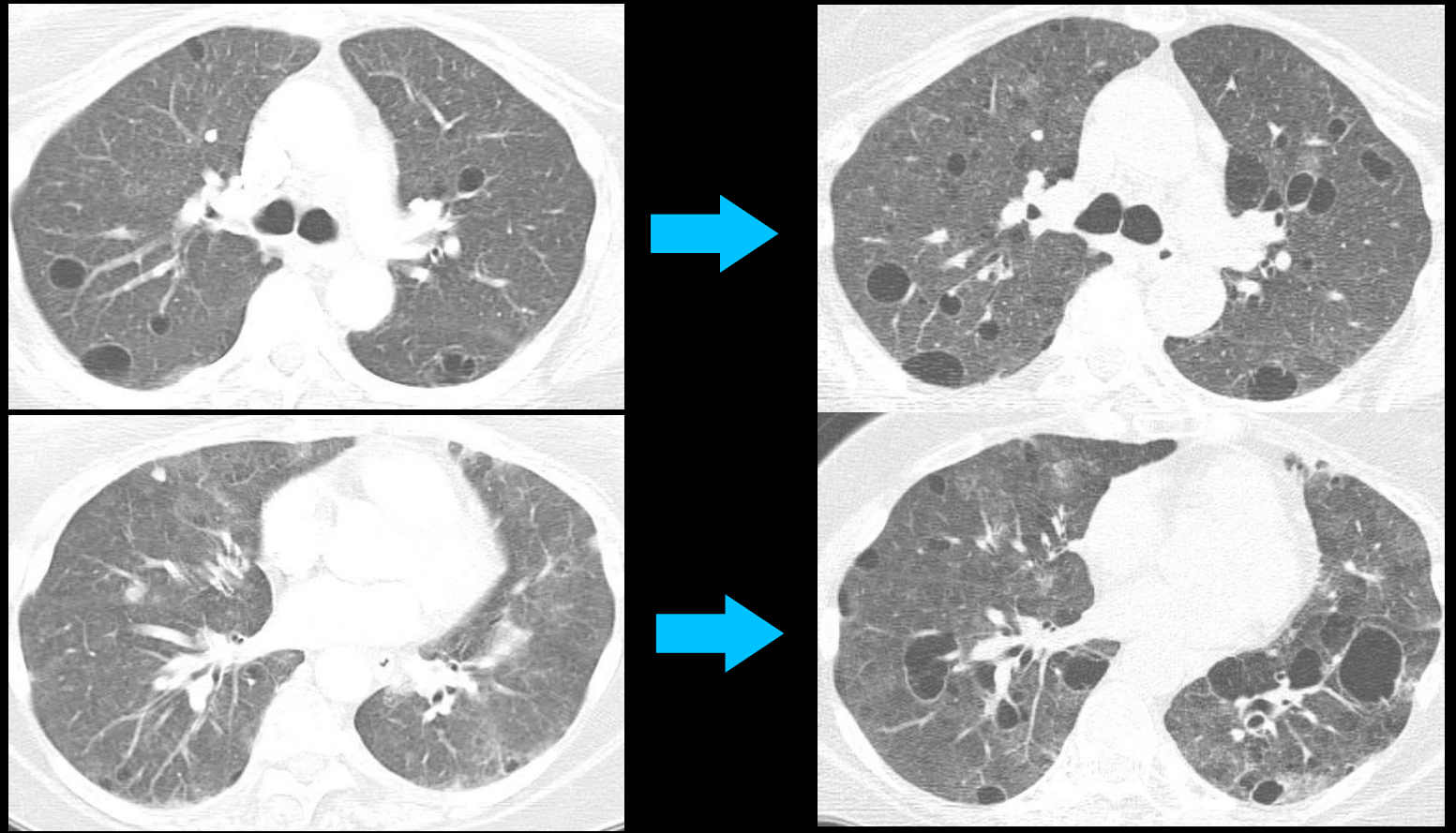


Baseline



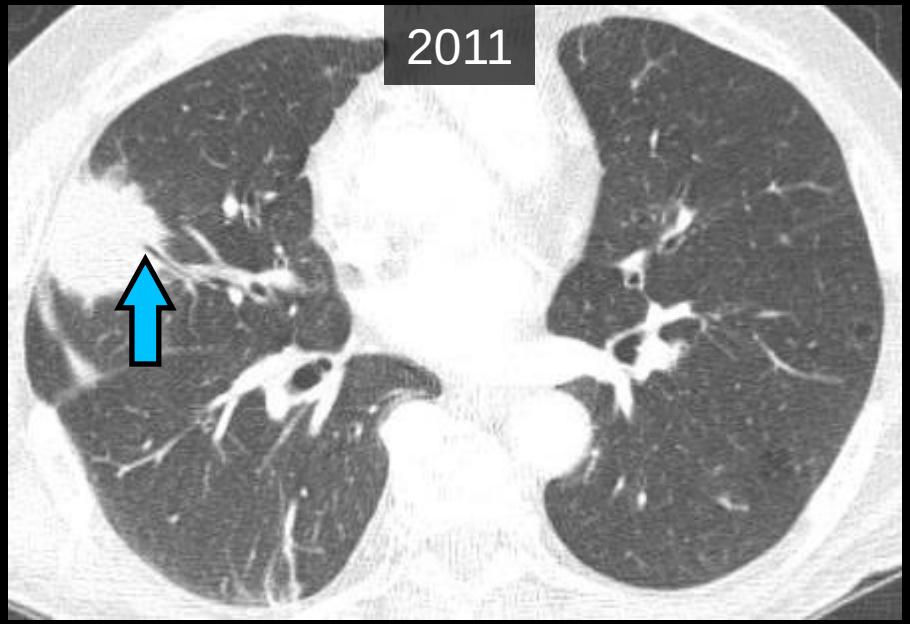
6 years

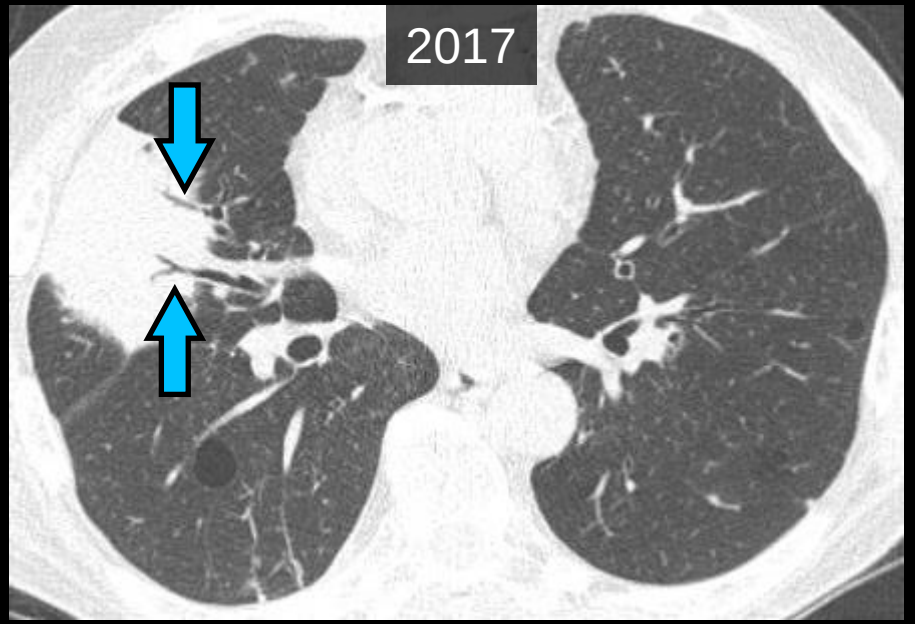
Lymphoid Interstitial Pneumonia



- Consolidation
- Nodules > 11 mm
- Growing nodules
- Pleural effusion

Sirajuddin A, et al. Primary Pulmonary Lymphoid Lesions: Radiologic and Pathologic Findings. *RadioGraphics*. 2016



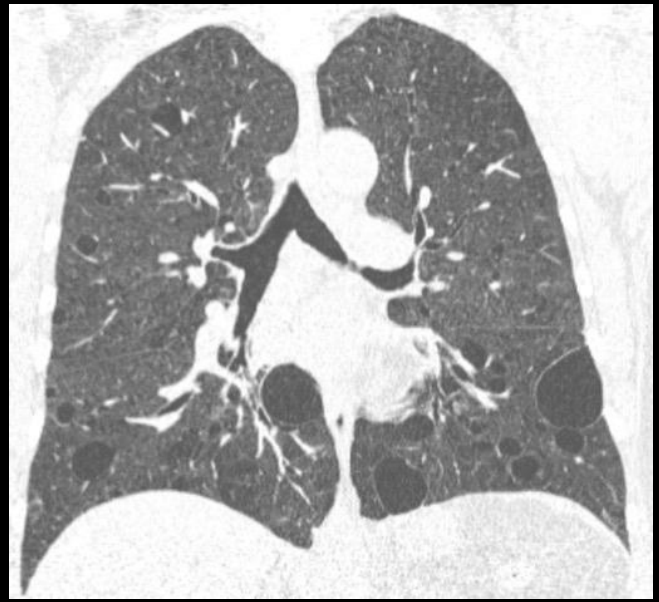


MALT Lymphoma

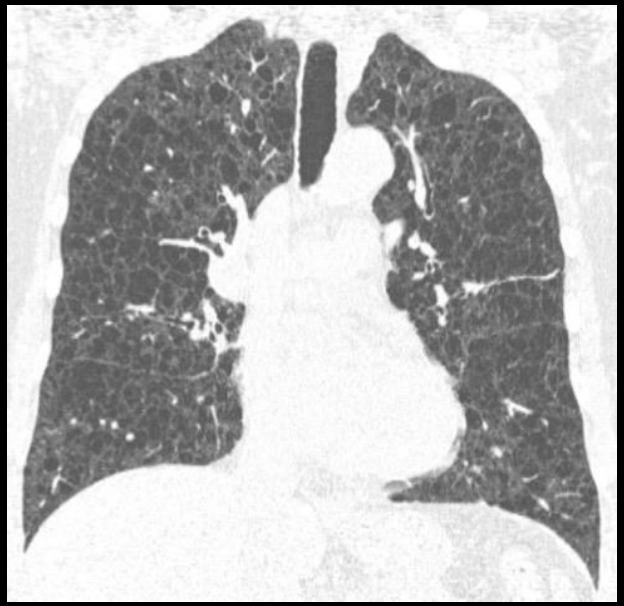
Cystic Lung Disease

Diagnosis	Distribution	Morphology	Other Findings	Clinical
PLCH	Upper zone	Irregular, thick wall	Nodules, ground-glass	Cigarette smoking
LAM	Diffuse	Uniform, thin wall	AML	Female, TSC, ↑VEGF-D
LIP	Basal	Perivascular	Nodules, ground-glass, septal lines	Sjögren syndrome, autoimmune, HIV

LIP vs. LAM vs. PLCH



LIP

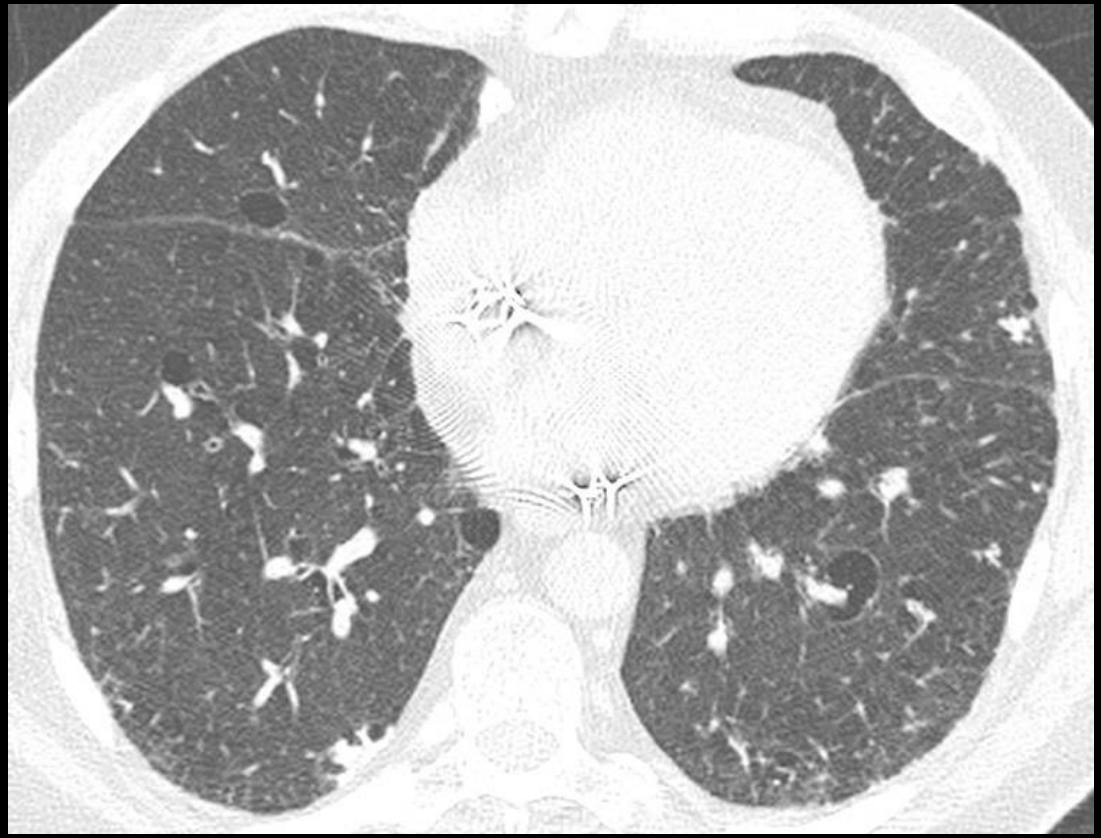


LAM

PLCH

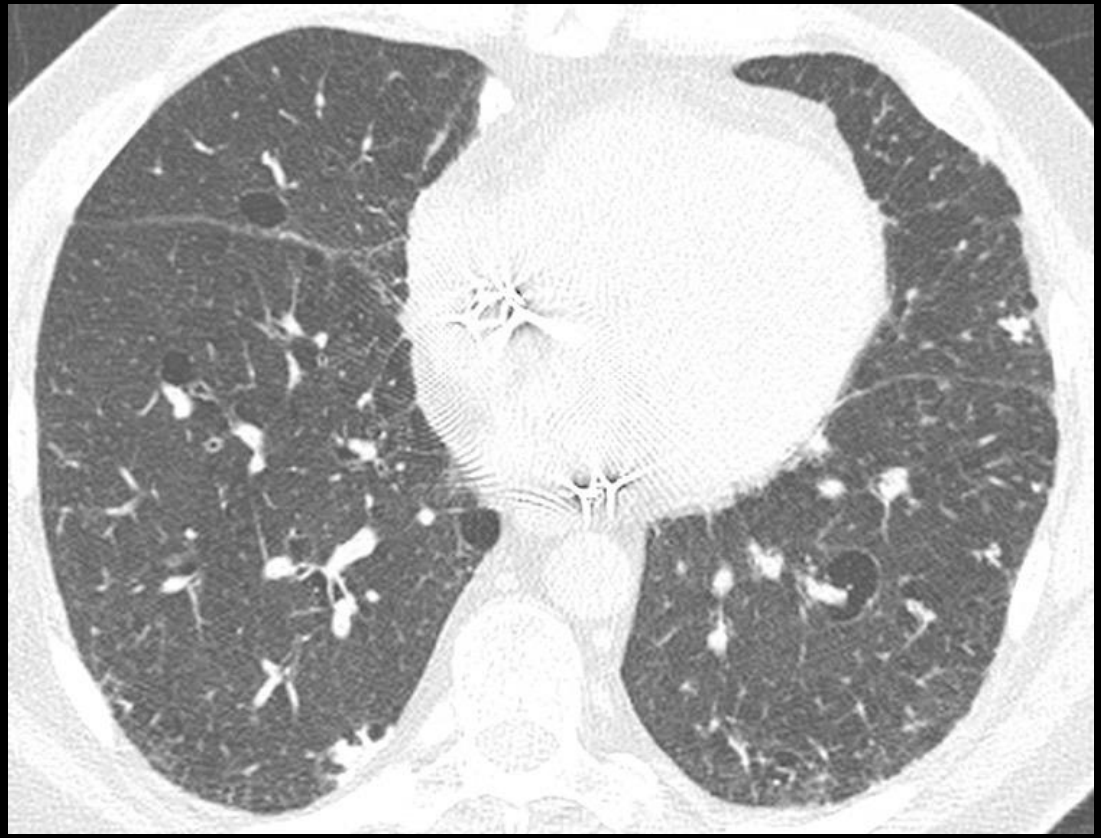
Amyloidosis

- Extracellular deposition of β-pleated sheets of protein
  - Localized (10-20%)
  - Systemic (80-90%)
    - Primary (multiple myeloma, macroglobulinemia)
    - Secondary (autoimmune, tuberculosis, cystic fibrosis, etc.)

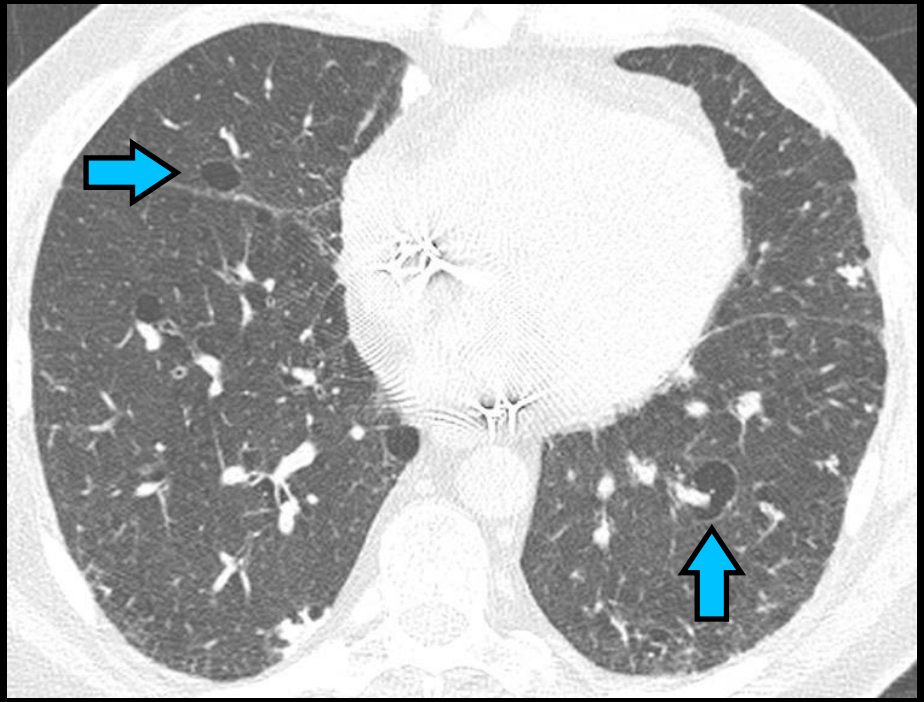


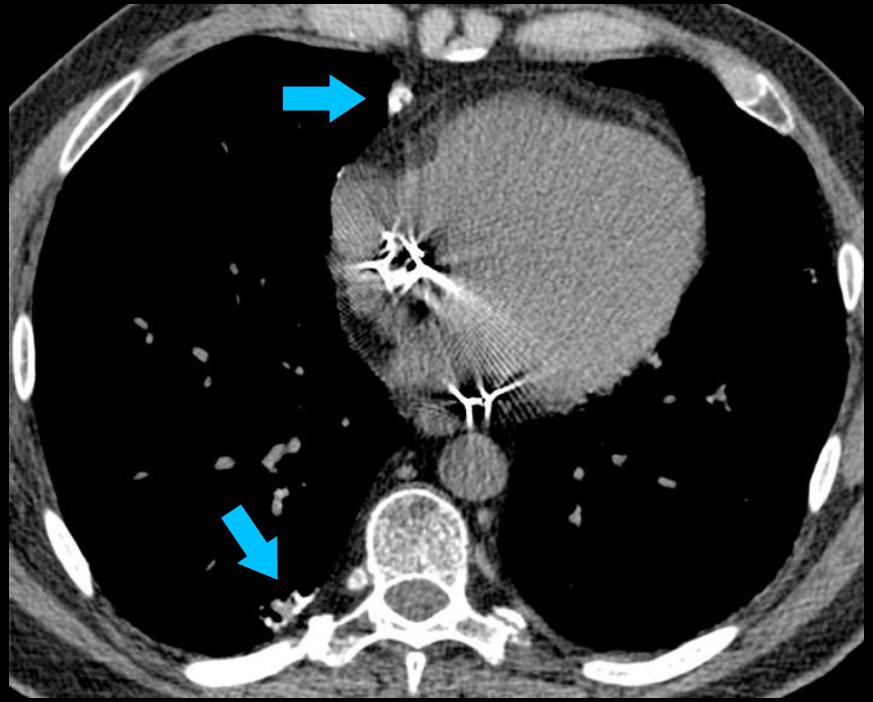
Amyloidosis

- Tracheobronchial
- Lung nodule(s)
- Lung cysts (usually Sjögren syndrome)
- Diffuse alveolar septal
- Lymph node enlargement
- Persistent pleural effusions
- Pulmonary hypertension (rare)

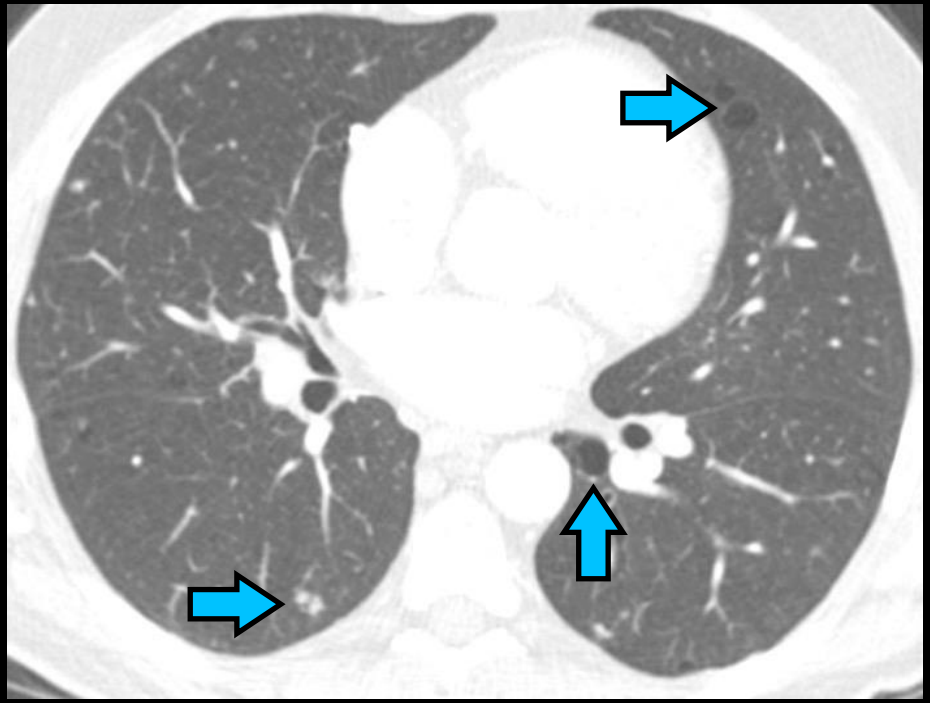


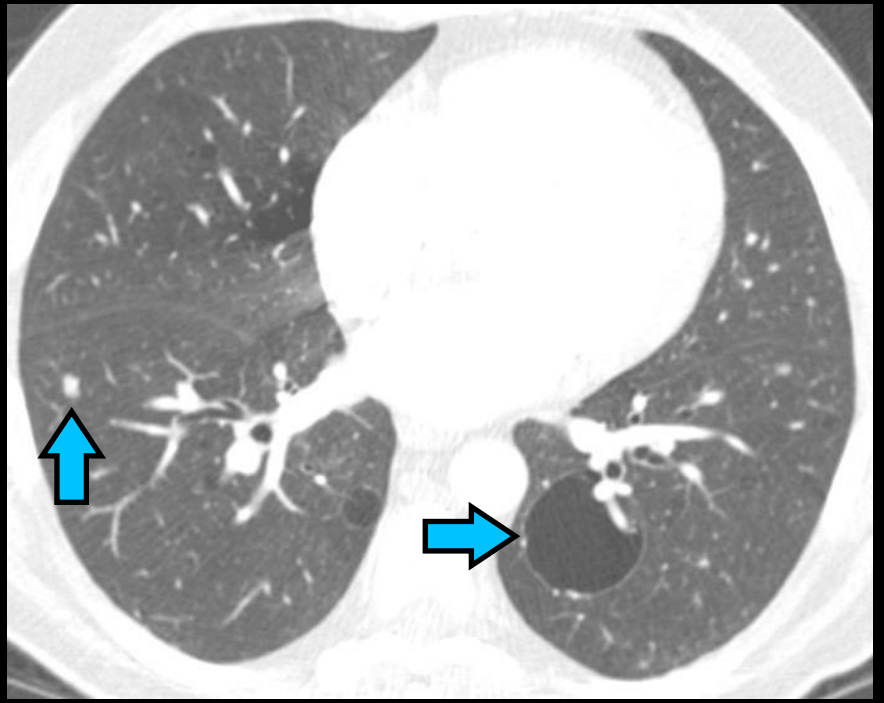
Amyloidosis





Amyloidosis





Light Chain Deposition Disease

- Rare cause of pulmonary disease
- Deposition of light chain proteins in walls of alveoli, vessels, and airways
- Associated with multiple myeloma or macroglobulinemia (75%)
- Renal involvement common

Courtesy of Howard Mann, M.D. (Salt Lake City, UT)

Light Chain Deposition Disease

- Scattered small lung cysts
- Nodules
- Lymphadenopathy

Courtesy of Howard Mann, M.D. (Salt Lake City, UT)

Light Chain Deposition Disease

Cystic Lung Disease

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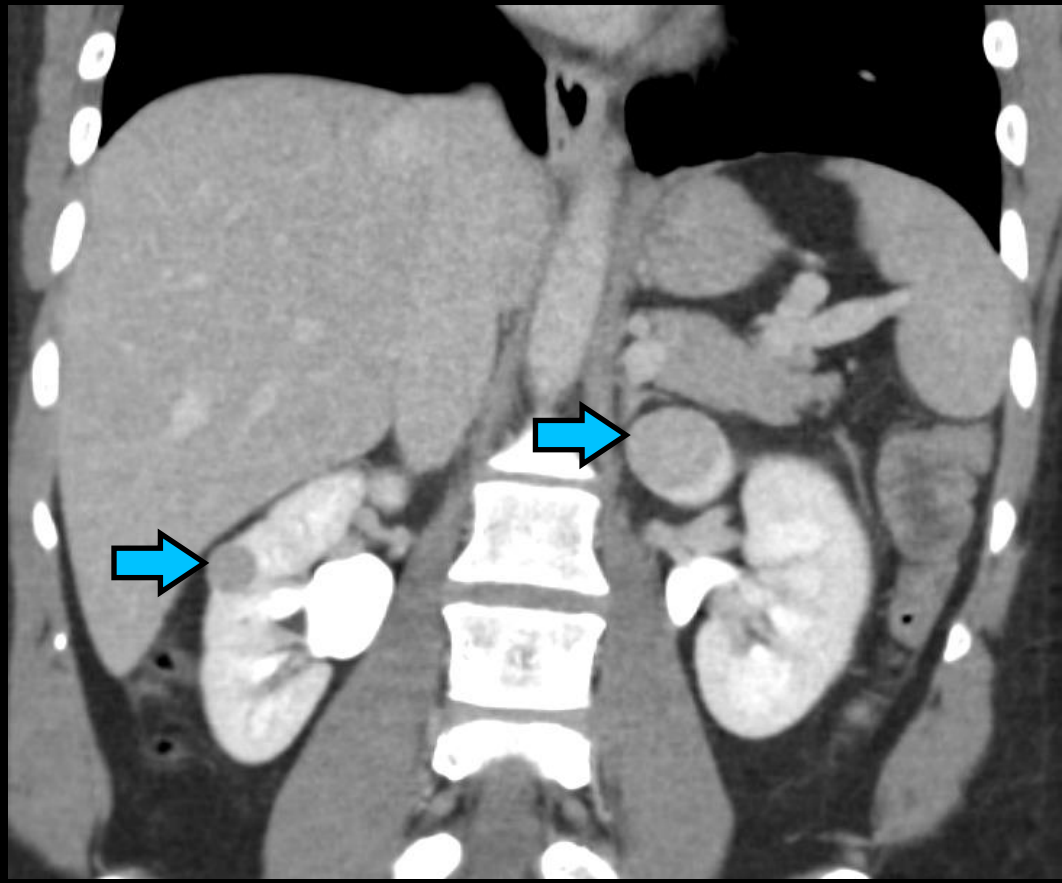
LAM	Diffuse	Uniform, thin wall	AML	Female, TSC, ↑VEGF-D
LIP	Basal	Perivascular	Nodules, ground-glass, septal lines	Sjögren syndrome, autoimmune, HIV
Amyloidosis	Basal	Perivascular	Nodules, calcium	Multiple myeloma, macroglobulinemia

Birt-Hogg-Dubé Syndrome

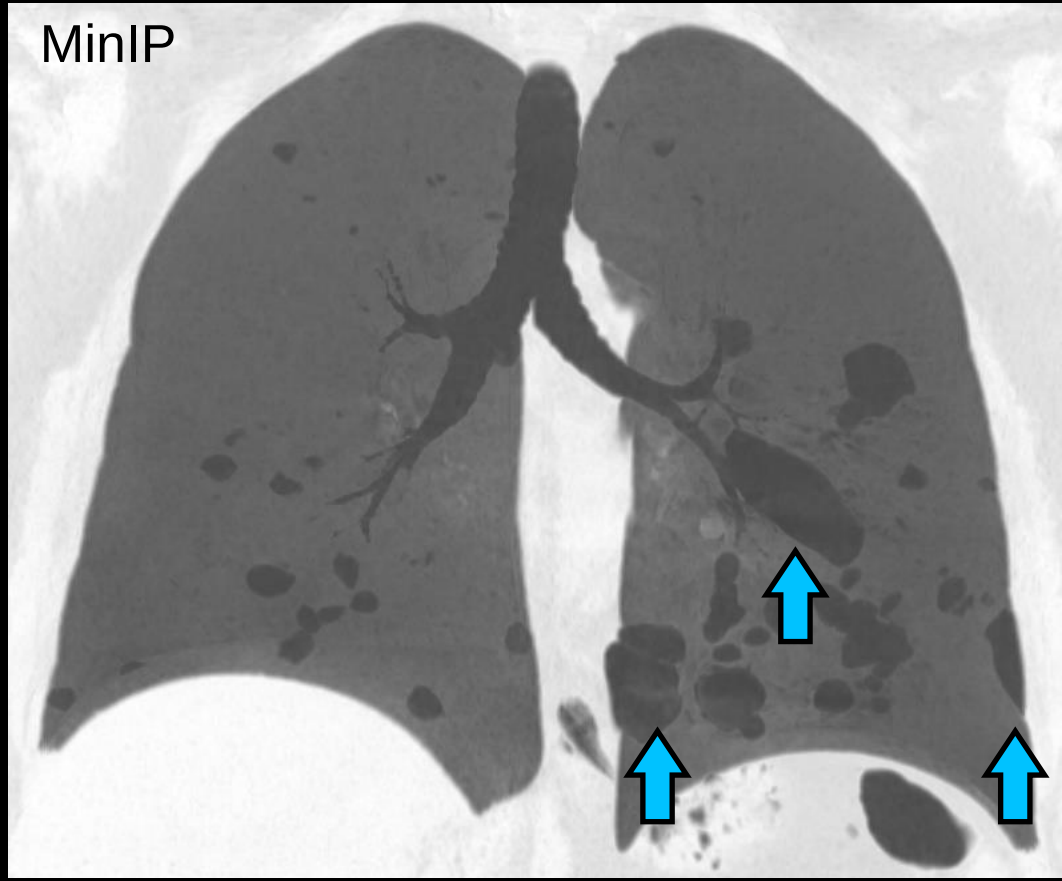
- Rare autosomal dominant syndrome
  - Skin lesions
    - Fibrofolliculomas
    - Trichodiscomas
    - Acrochordons
  - Kidneys
    - Renal neoplasms (~30%)
  - Lungs
    - Cysts (80%)
    - Spontaneous pneumothorax (25%)



29 F with bilateral solid renal masses and incidental lung cysts

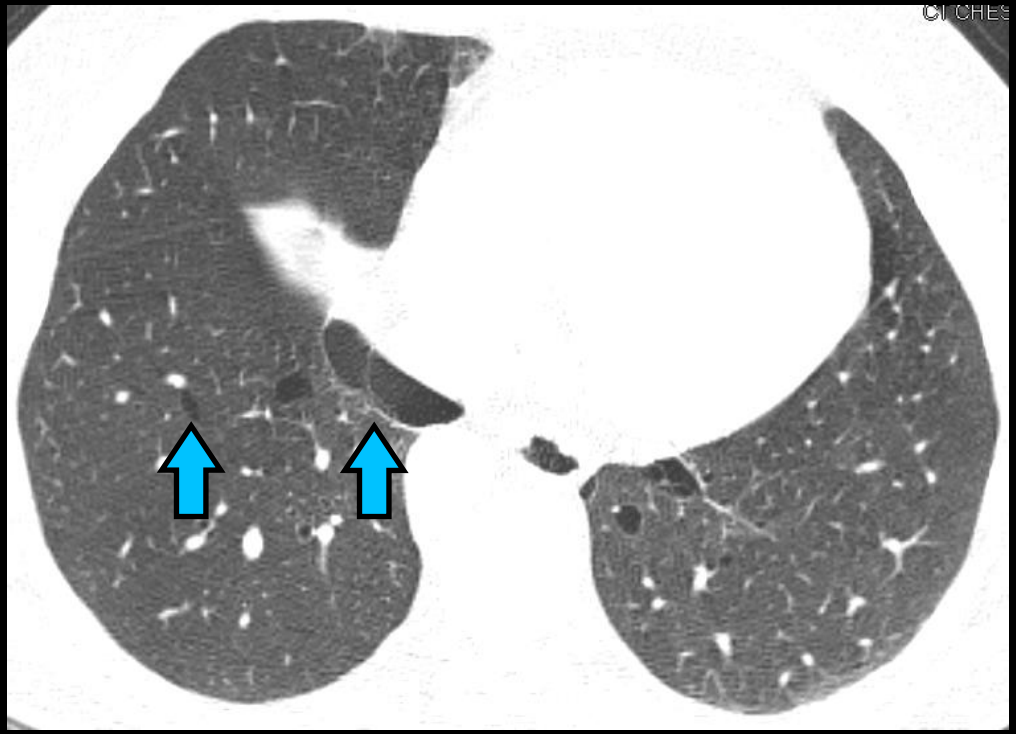
Birt-Hogg-Dubé Syndrome

- Thin-walled cysts
  - Bilateral (~90%)
  - Basal predominant (~90%)
  - Variable size
  - Round, lentiform
  - Septations



Distribution and shape ≠ LAM

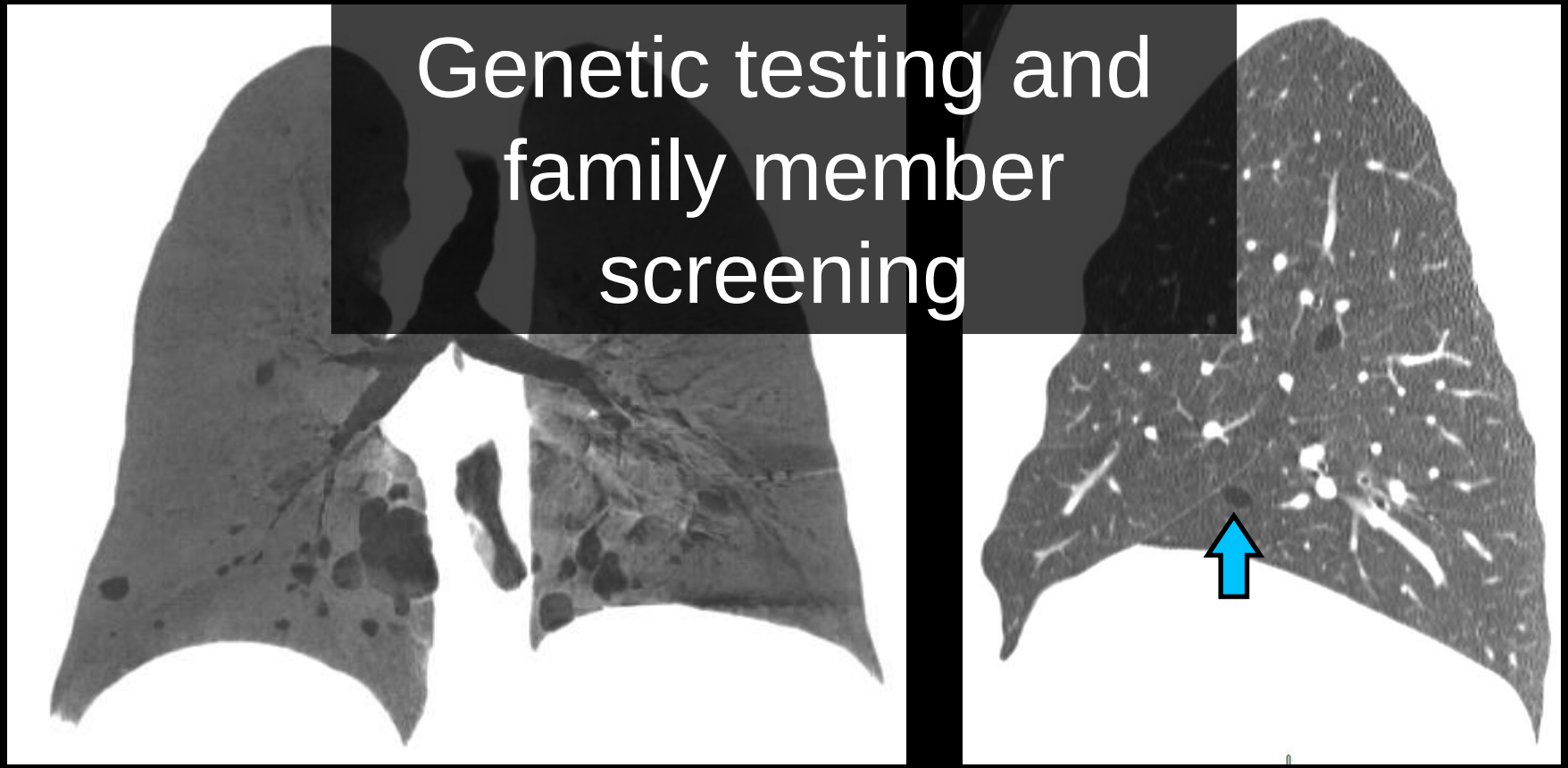
Birt-Hogg-Dubé Syndrome



Birt-Hogg-Dubé Syndrome

Birt-Hogg-Dubé Syndrome

Genetic testing and family member screening



56 M with history of RCC, rule out metastasis

Birt-Hogg-Dubé Syndrome

Courtesy of Arlene Sirajuddin, M.D. (Bethesda, MD)

Birt-Hogg-Dubé Syndrome

Courtesy of Arlene Sirajuddin, M.D. (Bethesda, MD)

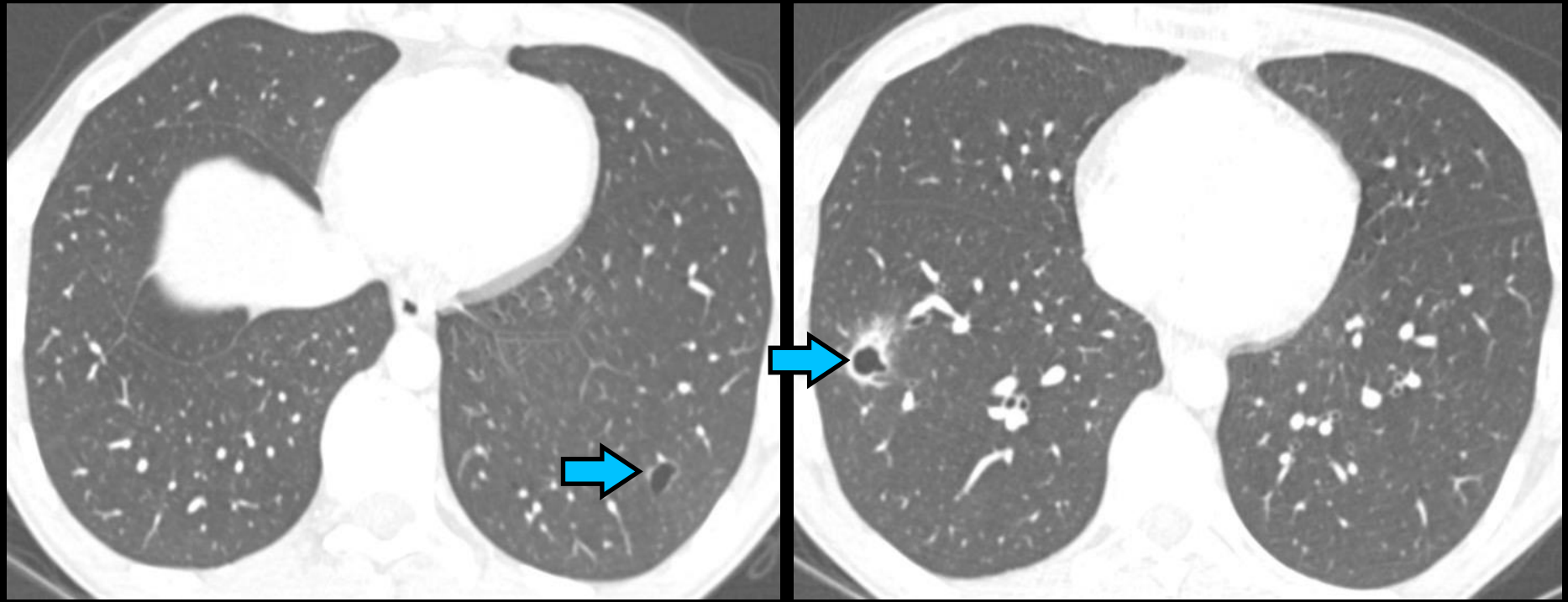
Cystic Lung Disease

Diagnosis	Distribution	Morphology	Other Findings	Clinical
PLCH	Upper zone	Irregular, thick wall	Nodules, ground-glass	Cigarette smoking
LAM	Diffuse	Uniform, thin wall	AML	Female, TSC, ↑VEGF-D
LIP	Basal	Perivascular	Nodules, ground-glass, septal lines	Sjögren syndrome, autoimmune, HIV
Amyloidosis	Basal	Perivascular	Nodules, calcium	Multiple myeloma, macroglobulinemia
Birt-Hogg-Dubé	Basal, Perivenous, septal, subpleural	Lentiform, round, ovoid	Renal mass	Skin lesions, family history of renal malignancy

Cystic Metastases

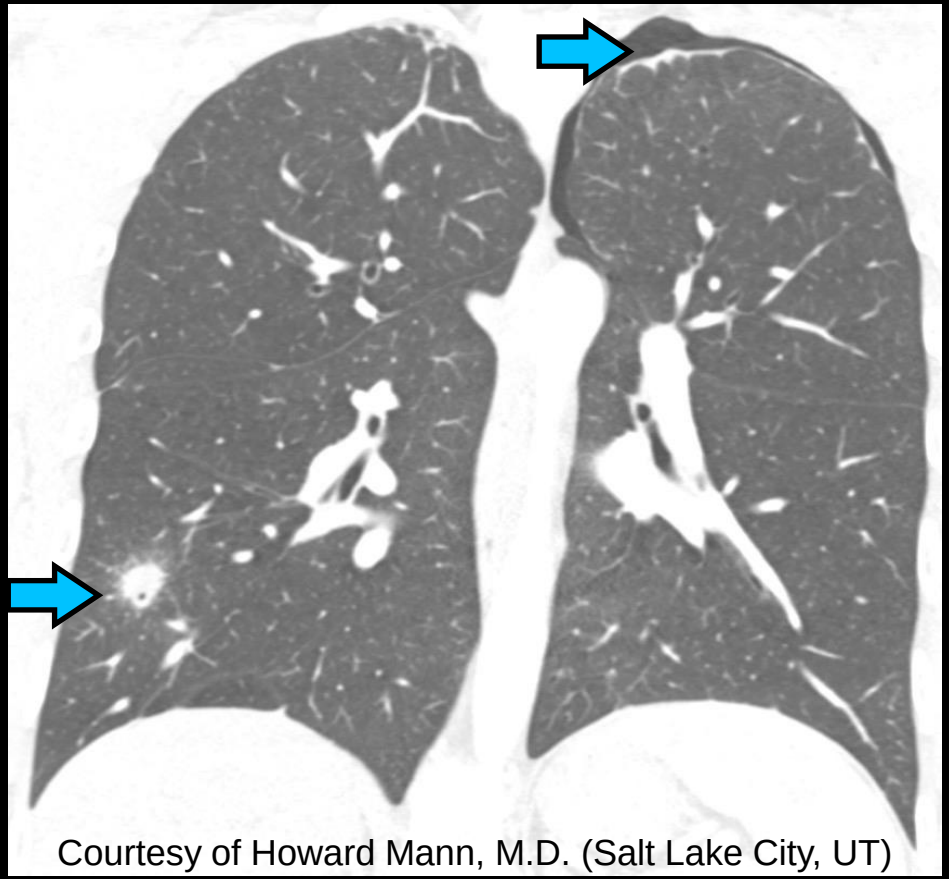
- Rare
  - Appropriate clinical history
  - Change over time
- Epithelial neoplasms most common

Epithelioid Sarcoma



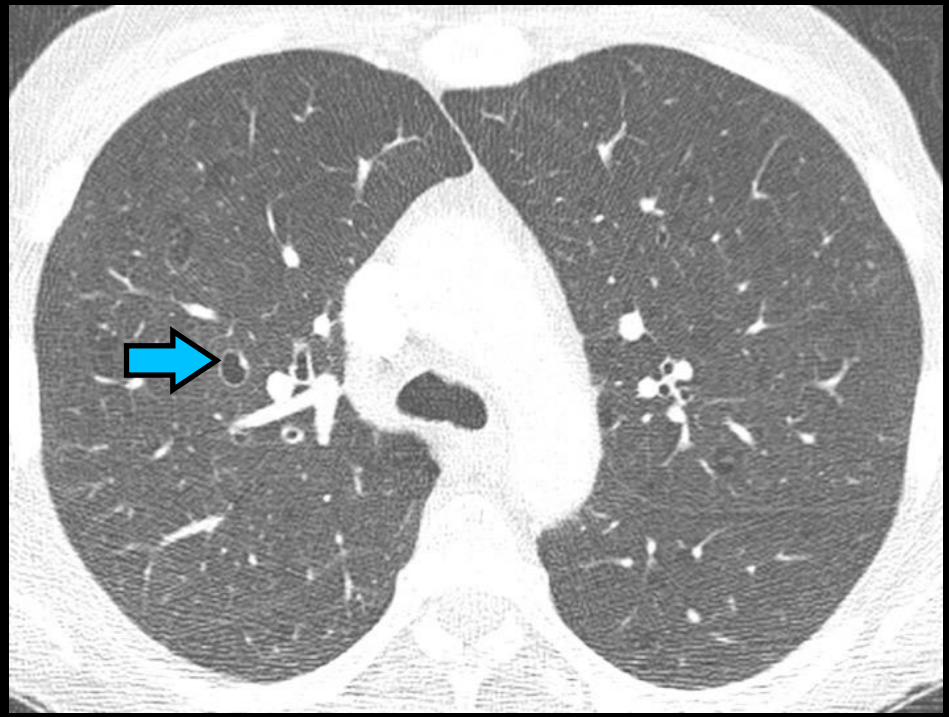
Courtesy of Howard Mann, M.D. (Salt Lake City, UT)

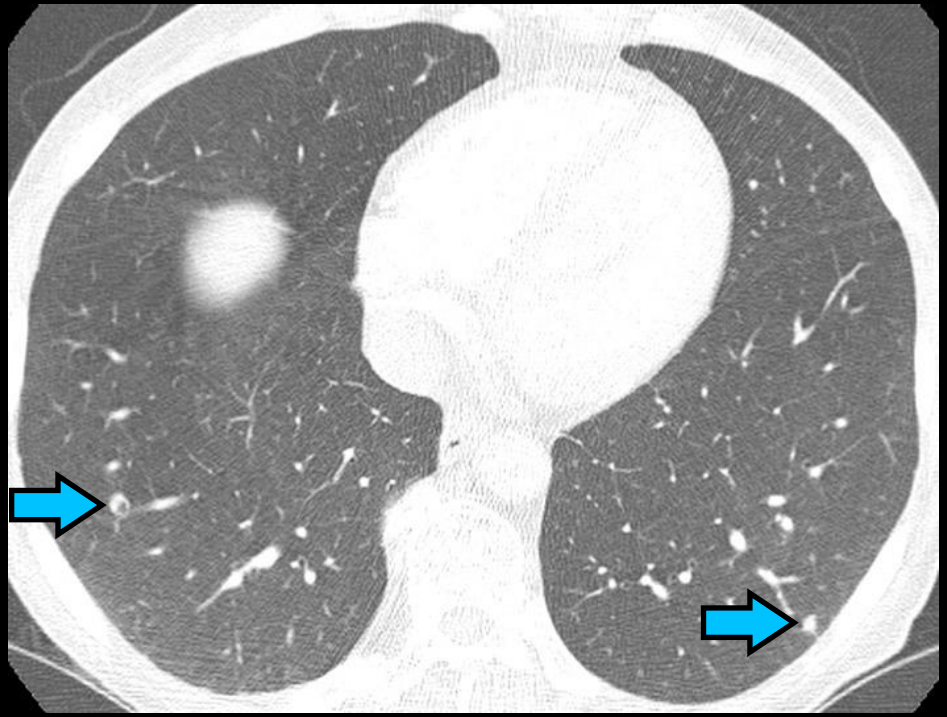
Epithelioid Sarcoma



Courtesy of Howard Mann, M.D. (Salt Lake City, UT)

Rectal Adenocarcinoma





Cystic Lung Disease Summary

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Birt-Hogg-Dubé	Basal, Perivenous, septal, subpleural	Lentiform, round, ovoid	Renal mass	Skin lesions, family history of renal malignancy
Metastases	Random	Variable	Solid nodules, lymph node enlargement	Known malignancy

Smoking-related Lung Disease

Introduction

- Cigarette smoking has been linked to variety of diseases that affect the lung
- Considerable overlap of histopathologic patterns of injury exists
- Leads to overlap of CT findings

Smoking Related Lung Injury

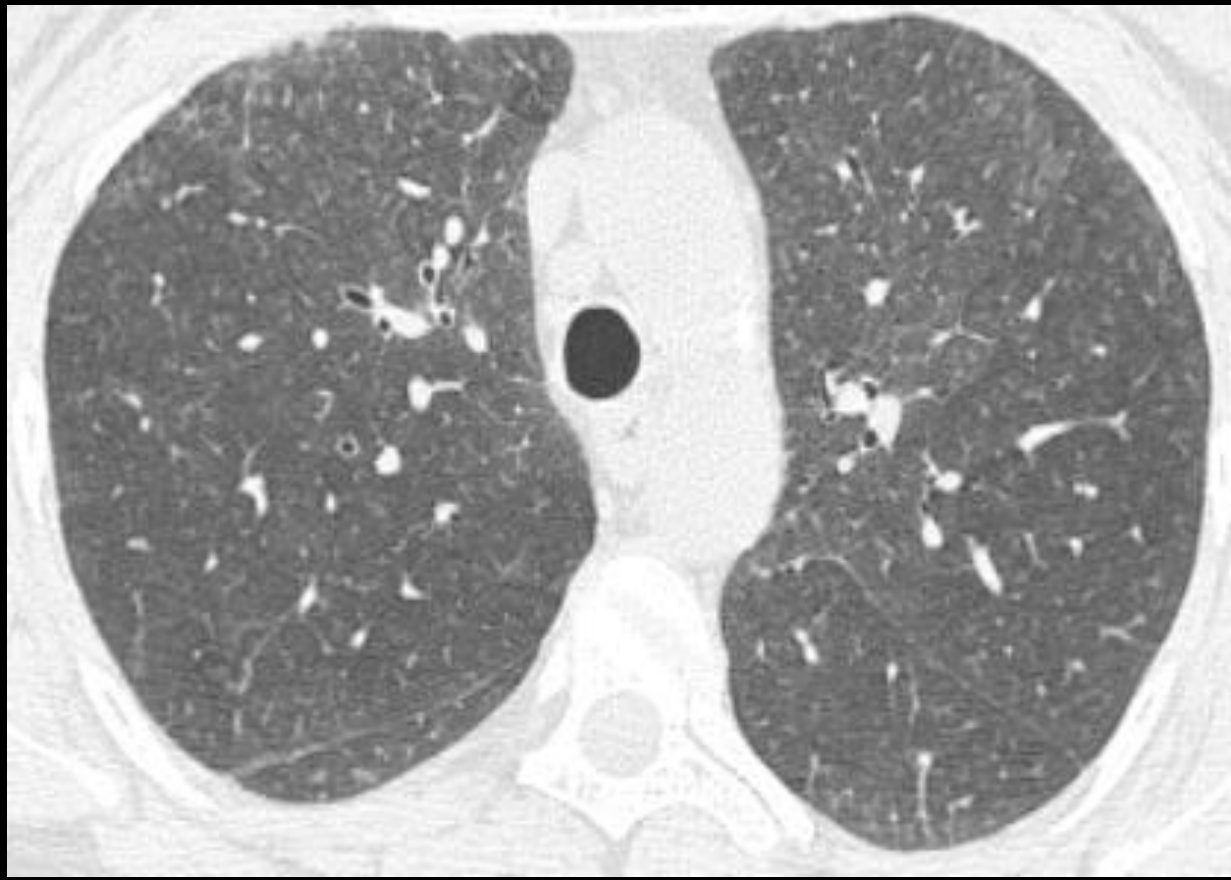
- Cigarette smoke affects all components of the respiratory system
  - Destruction
  - Remodeling
  - Repair
- Range of lung injury from cigarette smoking is wider than previously described

Lesions

- Respiratory bronchiolitis
- Pulmonary Langerhans cell histiocytosis
- Desquamative interstitial pneumonia
- Emphysema
- Airspace enlargement with fibrosis

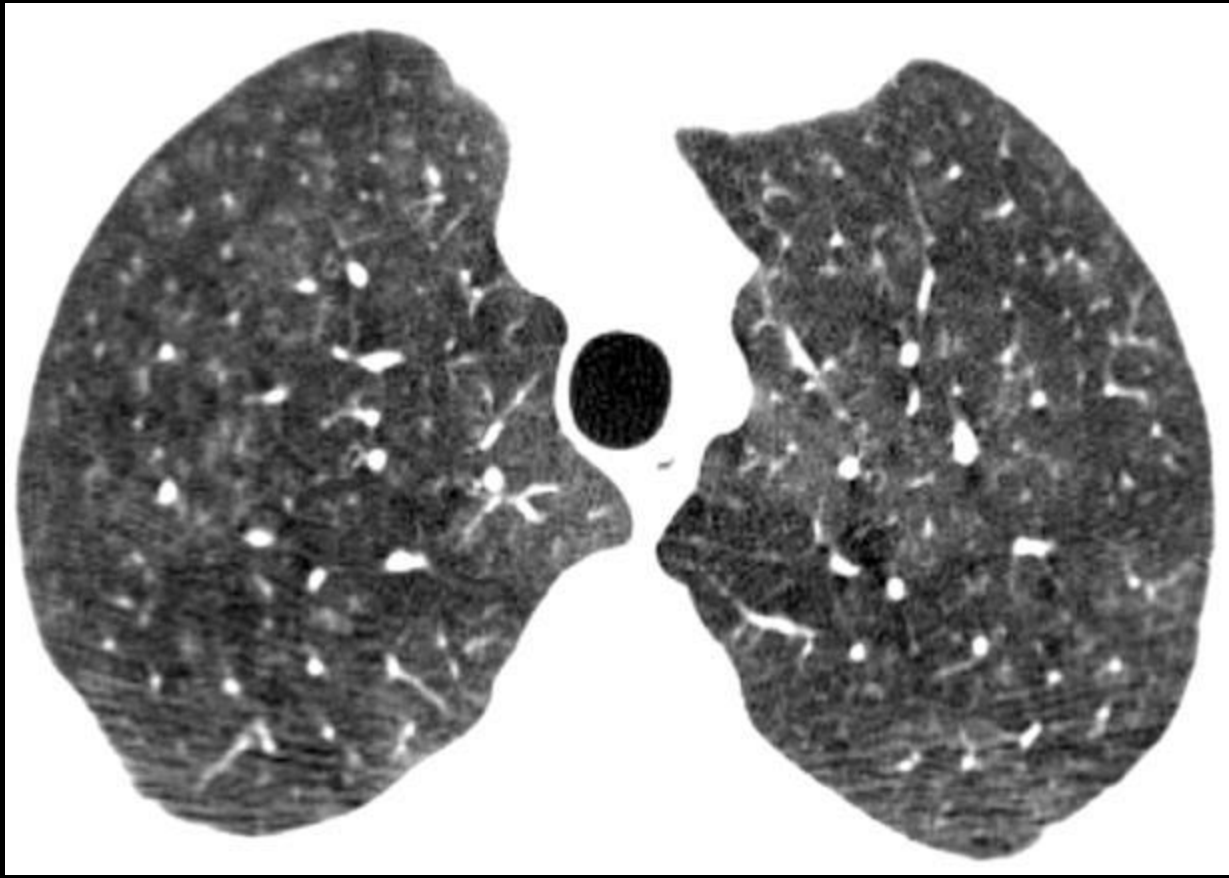
Respiratory Bronchiolitis: Pathology

- Pigmented macrophages in respiratory bronchioles
- Bronchiolocentric
- Peribronchiolar fibrosis
- Emphysema



Respiratory Bronchiolitis: Imaging

- Centrilobular GG nodules
- Patchy GGO
- Upper lobe predominant
- Current or former smokers
- +/- Emphysema



Desquamative Interstitial Pneumonia (DIP): Pathology

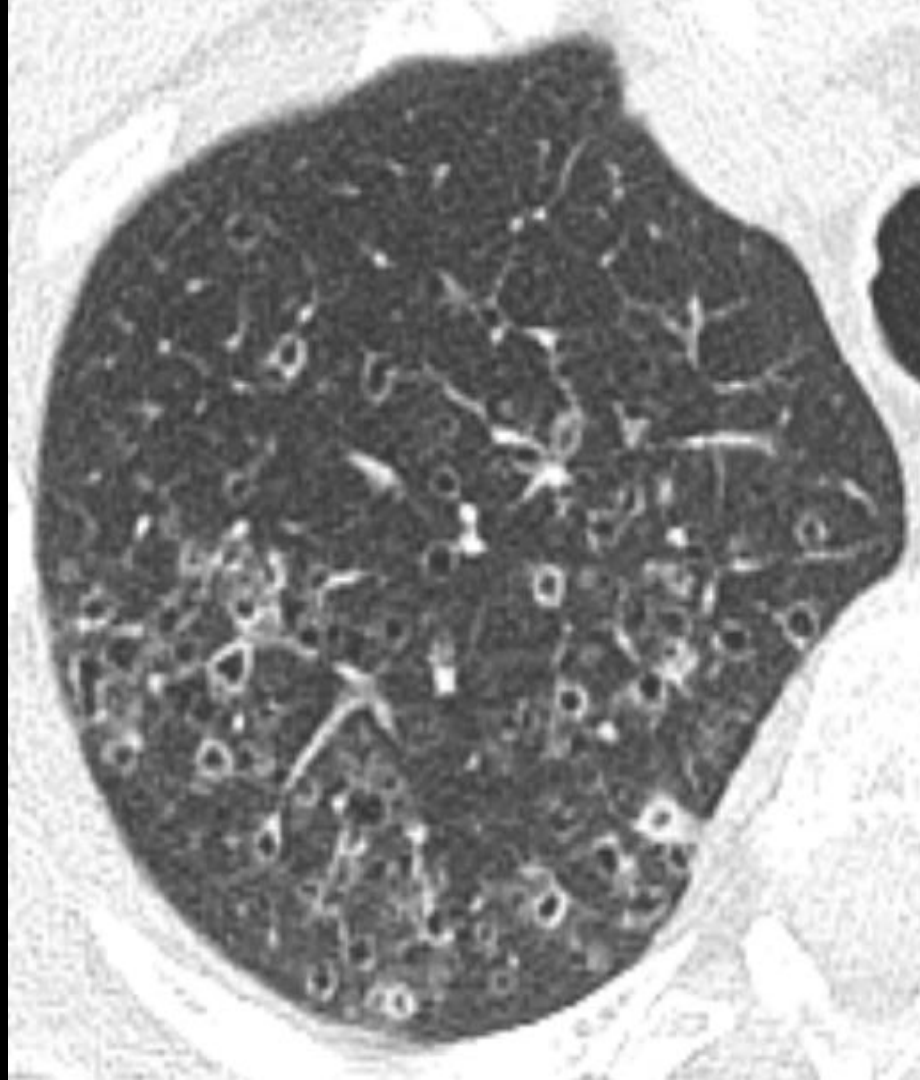
- Pigmented macrophages fill alveoli
- Diffuse involvement
- Homogenous
- Alveolar septal thickening
- Forms spectrum with RB
- Findings may overlap

DIP: Imaging

- Lower lobe, peripheral predominance
- GGO ±
  - Reticulation
  - Cysts
  - Emphysema

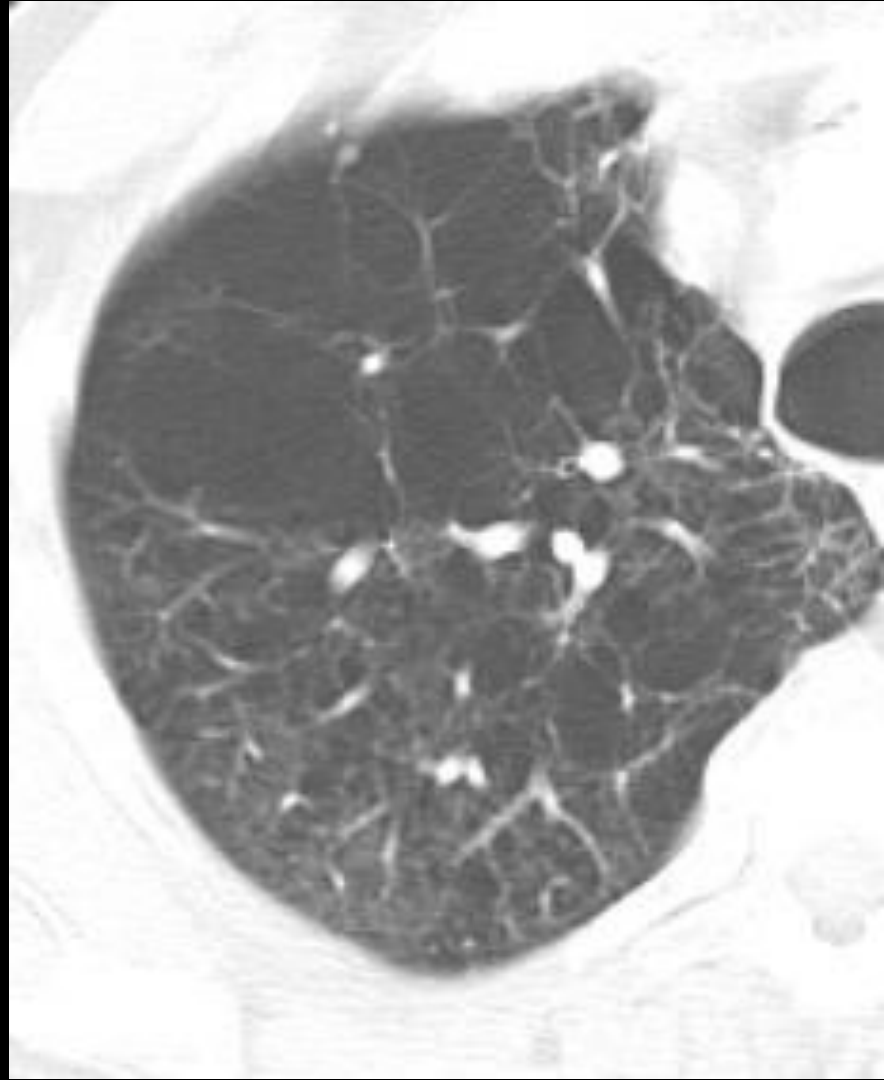
PLCH

- Solid nodules and/or cysts
- Upper and mid lung predominant
- Characteristic sparing of costophrenic sulci and anterior tips of lungs



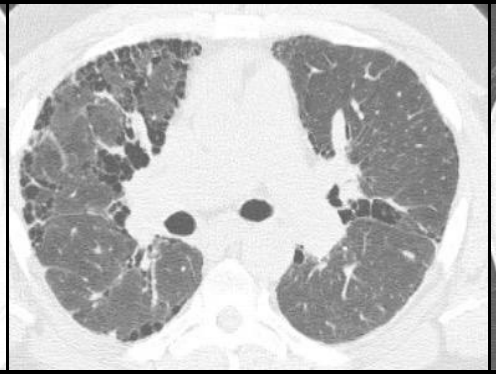
Emphysema

- Irreversible enlarged airspaces distal to and originating from the terminal bronchioles with destruction of the alveolar walls
- Cigarette smoking most common cause

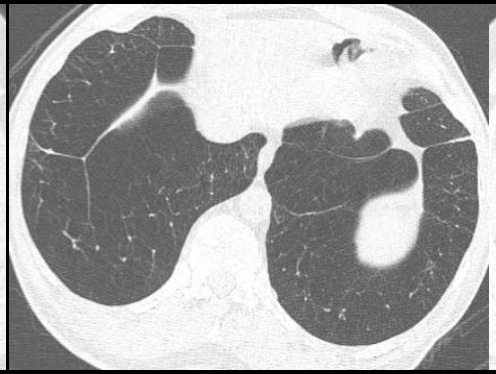


Classification of Emphysema

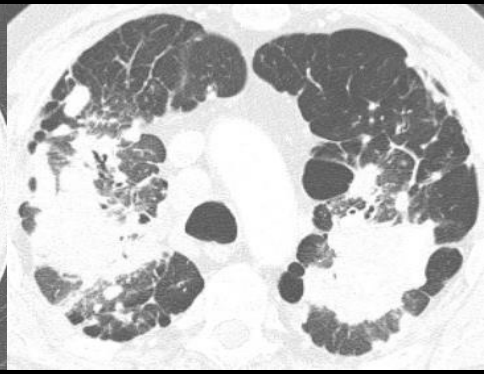
Centrilobular



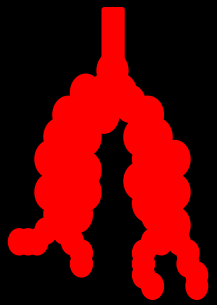
Paraseptal

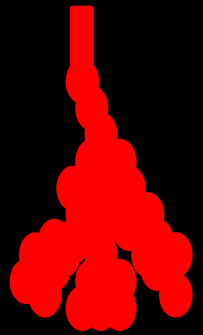


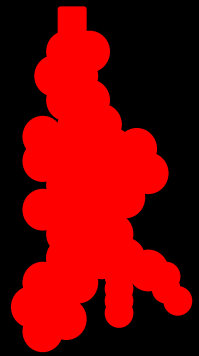
Panlobular



Irregular /
(para)cicatricial



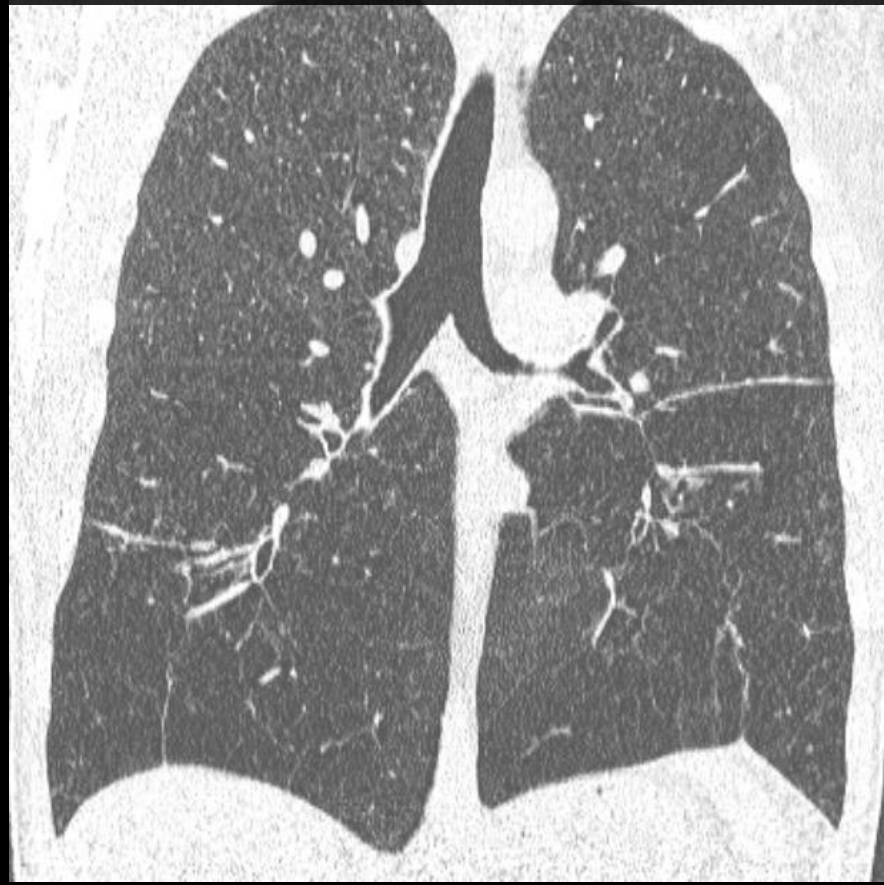




Emphysema: 10% of patients never or rarely smoked

- Alpha 1-antitrypsin deficiency
- Connective tissue disease (e.g. Ehlers-Danlos syndrome, Marfan syndrome)
- PMF, end-stage Sarcoid, sickle cell
- IV drug abuse (methadone, heroin, methylphenidate (Ritalin®))
- HIV
- Hypocomplementemic urticarial vasculitis syndrome
- Malnutrition and rare metabolic disorders

Alpha 1-antitrypsin deficiency

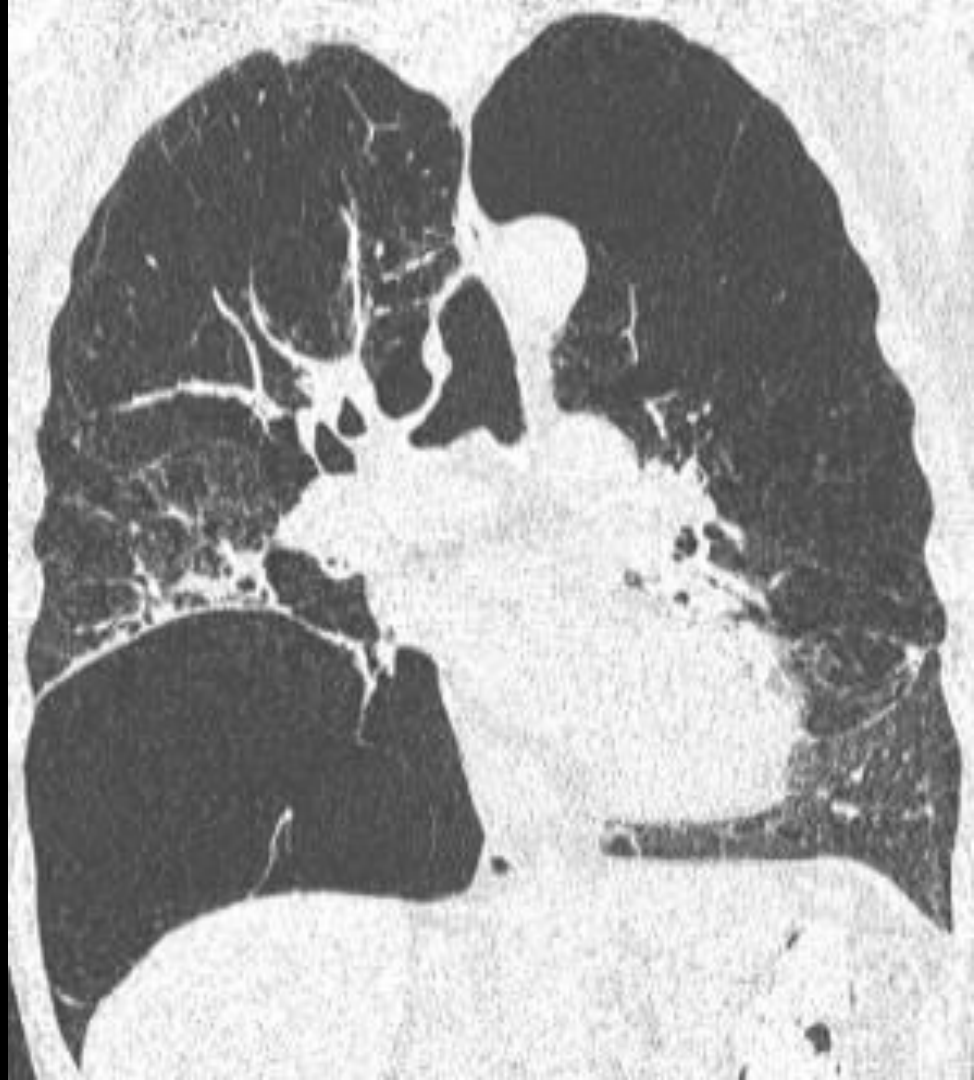


Giant Bullous Emphysema

- Also referred to as vanishing lung syndrome
- Young male smokers most commonly affected
- Usually bilateral, asymmetric
- Bullae 1-20 cm (usually 2-8 cm)

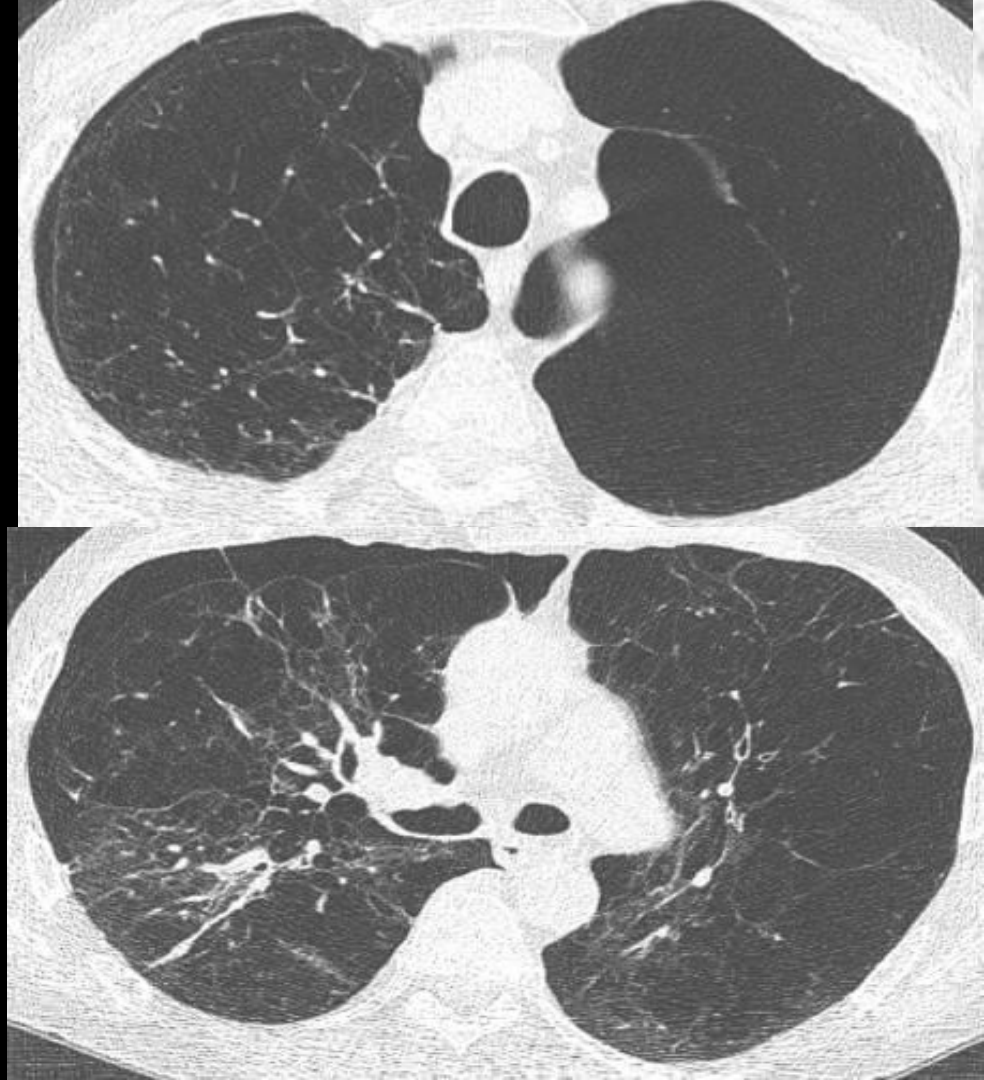
Giant Bullous Emphysema

- Complications
  - Pneumothorax
    - May require HRCT to distinguish from bullae
  - Pulmonary dysfunction
    - Hypoxemia, hypercapnia
    - ↓FEV_1/FVC, ↓DL_{CO}

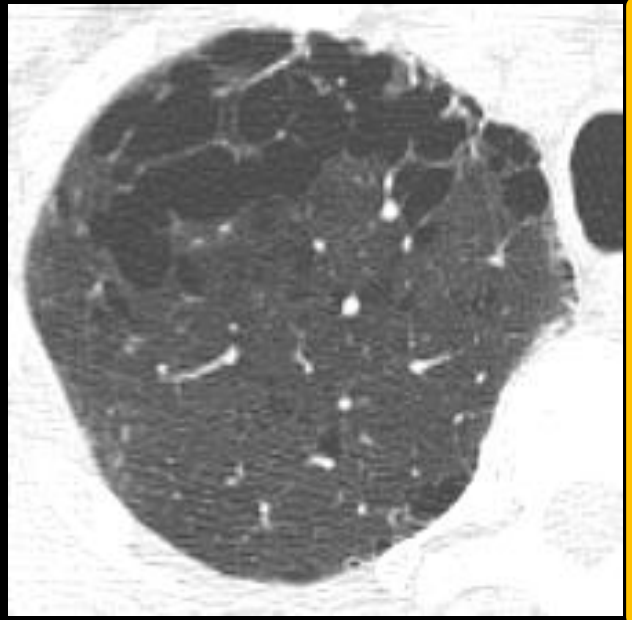


Giant Bullous Emphysema

- Bullectomy treatment of choice
  - Size of bullae proportional to physiologic improvement after bullectomy
- Some patients may require lung transplant



What is this?

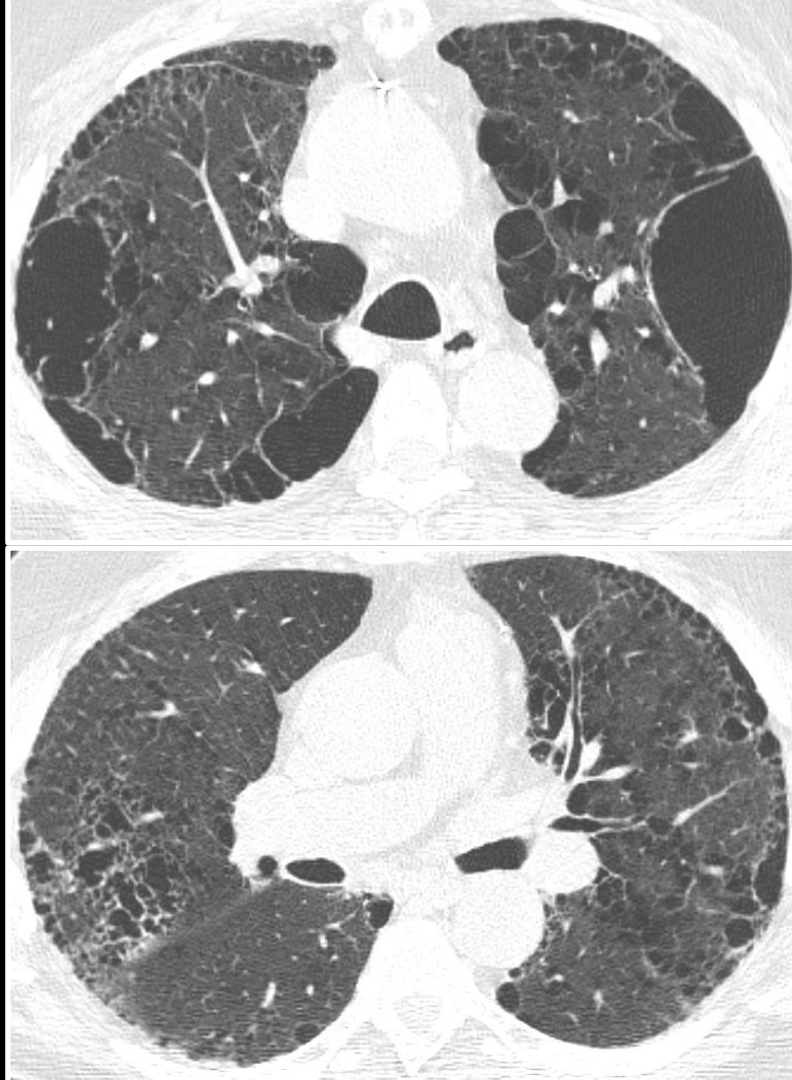


Emphysema

Honeycombing

Airspace enlargement with fibrosis (AEF)

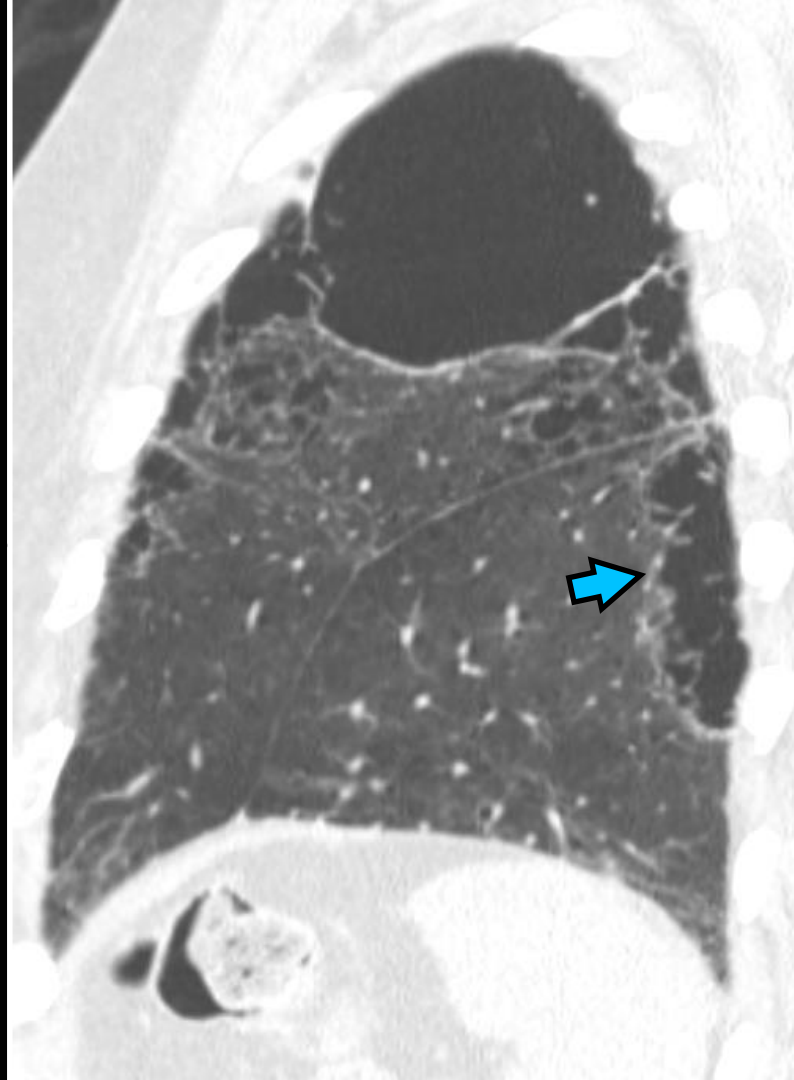
- Also called smoking-related interstitial fibrosis
- Not a form of idiopathic interstitial pneumonia
- Results from greater amount of fibrosis than usually described in the classic definition of emphysema



* Idiopathic Pulmonary Fibrosis (an Update) and Progressive Pulmonary Fibrosis in Adults. An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline. *Am J Respir Crit Care Med.*

Airspace enlargement with fibrosis (AEF)

- Clustered asymmetric cysts, larger and more irregular than typical honeycomb cysts
- No traction bronchiectasis or other signs of fibrosis
- Emphysema also present



Summary

- Cigarette smoke causes a variety of histopathologic lesions in the lung
- CT pattern depends on the dominant lesion
- Emphysema most often related to smoking but can occur from other causes
- Cumulative lung impairment from smoking-related lung injury → dyspnea, decreased diffusion, and altered physiology

Summary

- CT patterns of cystic disease can point to a specific diagnosis
- Integration of clinical information with CT findings can obviate need for lung biopsy
- Sometimes distinguishing cystic lung disease from emphysema can be challenging if not impossible

Cystic and Smoking-related Lung Disease

Questions?