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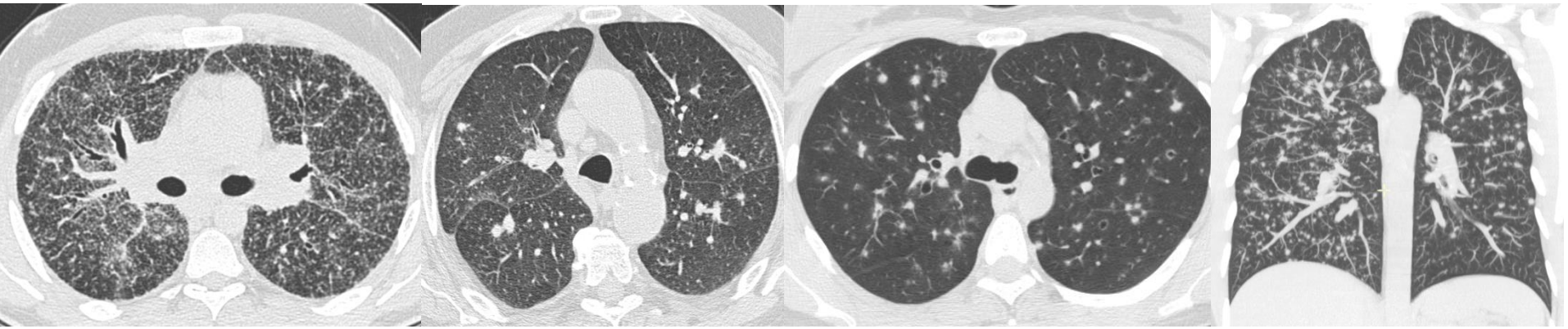

Micronodulations

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Learning objectives

- Understand pathophysiology behind the 3 main micronodular patterns on chest CT
  - Centrilobular (& tree-in-bud variant)
  - Peri-lymphatic
  - Random
- Describe how to differentiate these patterns
- List a differential diagnosis for centrilobular nodules and explain how clinical information can help to narrow the differential
- List the differential diagnosis for peri-lymphatic and random nodules

Definition

Radiology

Fleischner Society: Glossary of Terms for Thoracic Imaging[1]

David M. Hansell, MD, FRCP, FRCR
Alexander A. Bankier, MD
Heber MacMahon, MB, BCh, BAO
Theresa C. McLoud, MD
Nestor L. Müller, MD, PhD
Jacques Remy, MD

Members of the Fleischner Society compiled a glossary of terms for thoracic imaging that replaces previous glossaries published in 1984 and 1996 for thoracic radiography and computed tomography (CT), respectively. The need to update the previous versions came from the recognition that new words have emerged, others have become obsolete, and the meaning of some terms has changed. Brief descriptions of some diseases are included, and pictorial examples (chest radiographs and CT scans) are provided for the majority of terms.

[1] From the Department of Radiology, Royal Brompton Hospital, Sydney Street, London SW3 6NP, United Kingdom (D.M.H.); Department of Radiology, Beth Israel Deaconess Medical Center, Boston, Mass (A.A.B.); Department of Radiology, University of Chicago Hospital, Chicago, Ill (H.M.); Department of Radiology, Massachusetts General Hospital, Boston, Mass (T.C.M.); Department of Radiology, Vancouver General Hospital, Vancouver, British Columbia, Canada (N.L.M.); and Department of Radiology, CHRU de Lille, Hôpital Calmette, Lille, France (J.R.). Received April 21, 2007; revision requested May 29; revision received June 6; accepted August 7; final version accepted September 19. **Address correspondence to:** D.M.H. (e-mail: *d.hansell@rbht.nhs.uk*).

micronodule

CT scans.—A micronodule is a discrete, small, round, focal opacity. A variety of diameters have been used in the past to define a micronodule; for example, a diameter of no greater than 7 mm (86). Use of the term is most often limited to nodules with a diameter of less than 5 mm (87) or less than 3 mm (88). It is recommended that the term be reserved for opacities less than 3 mm in diameter. (See also *nodule, miliary pattern.*)

Figure 38

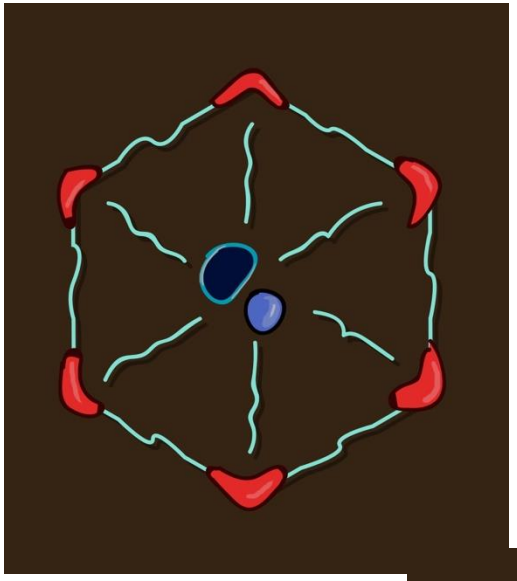
Figure 38: Magnified chest radiograph shows miliary pattern.

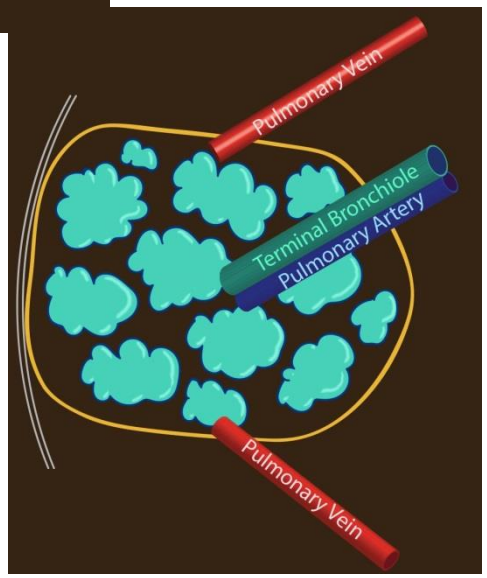
Lung infiltration

Round opacity: 1 à 30 mm
micronodule < 5 mm
5 mm < nodules < 30 mm

Solid: cellular-fibrosis
Confluent
Fibrosis
Excavated

Secondary pulmonary lobule

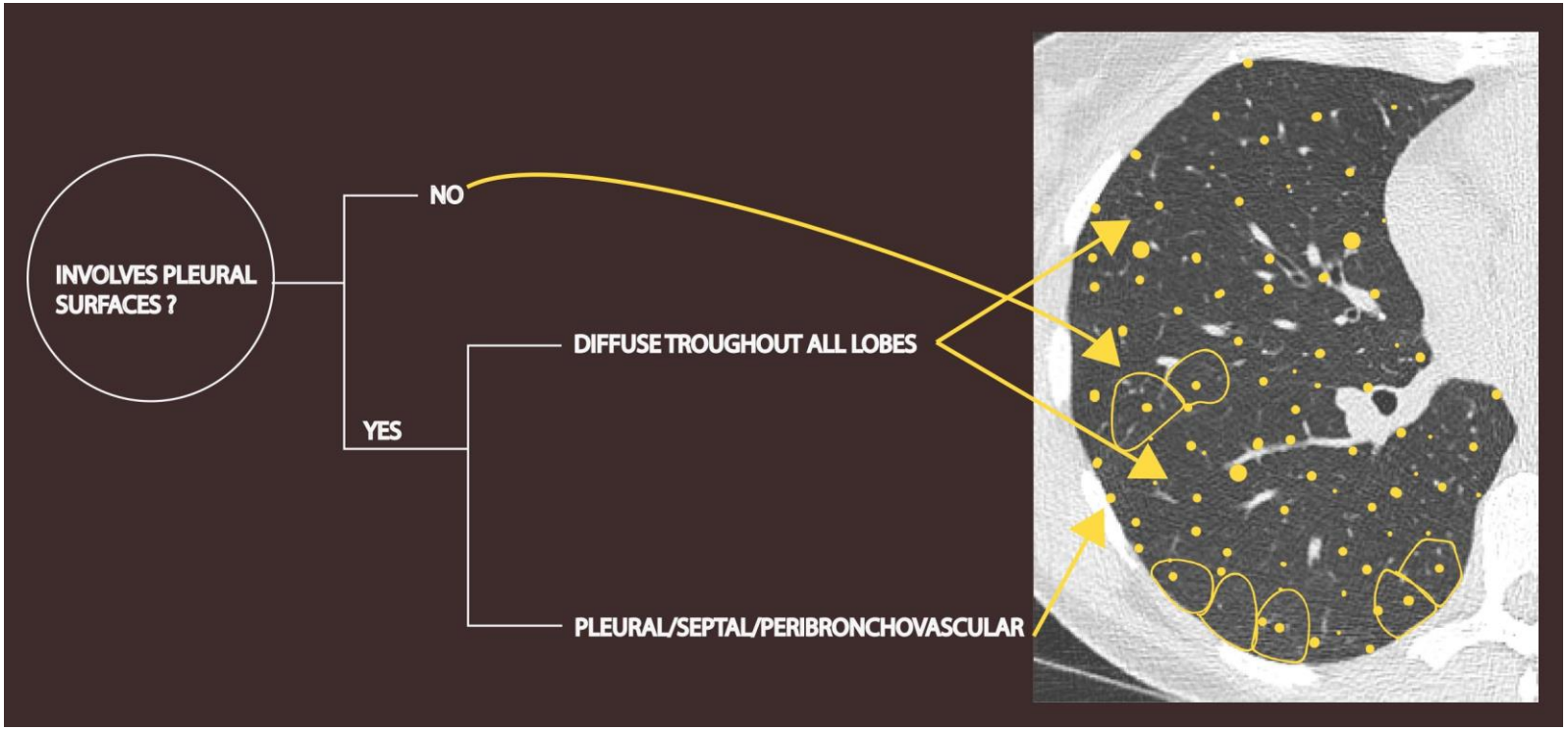




- Key for understanding micronodular patterns
- Basic anatomic unit of pulmonary structure and function
- 1-2 cm, contains 5-15 pulmonary acini

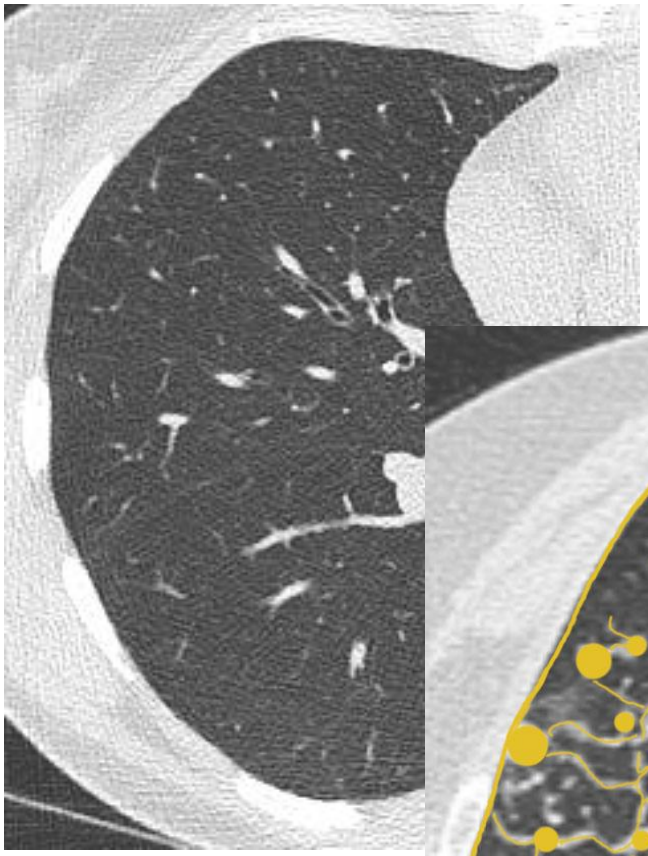
How to distinguish micronodular pattern?

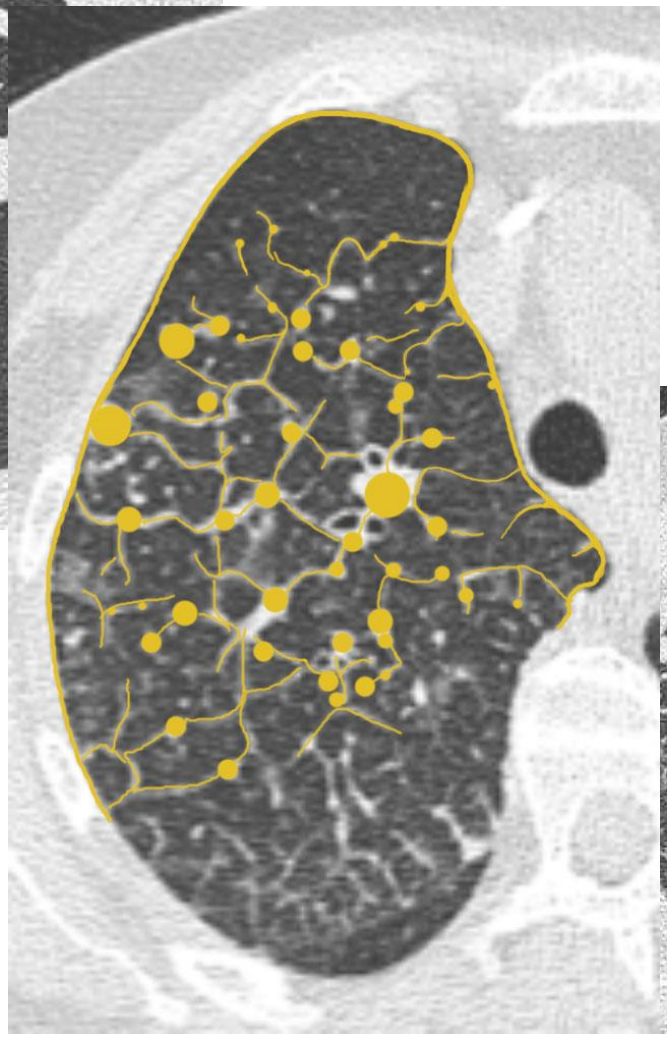
- Distribution of nodules is KEY to diagnosis

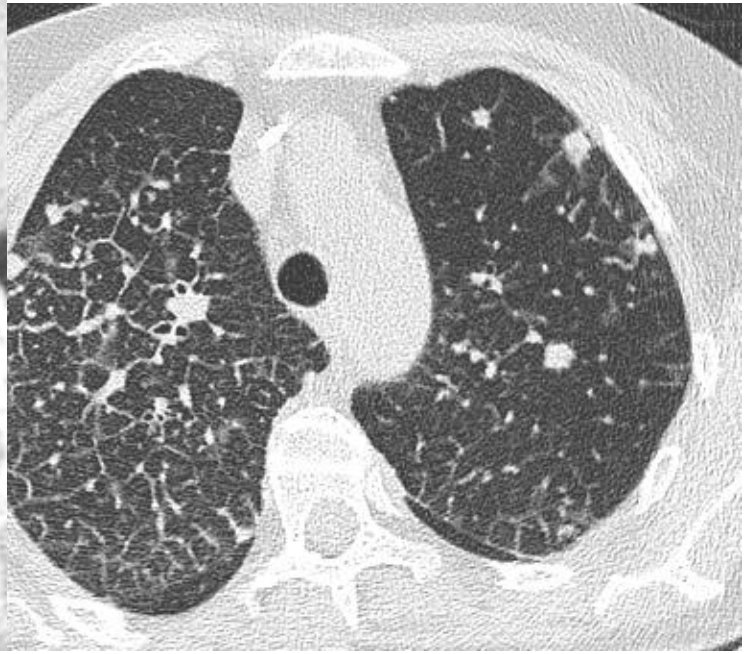


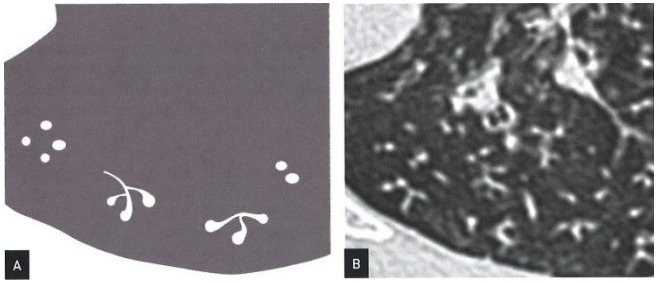
Drawings are from Dr Marin Halut, Cliniques Universitaires St-Luc-Brussels

Distribution of nodules is KEY to diagnosis



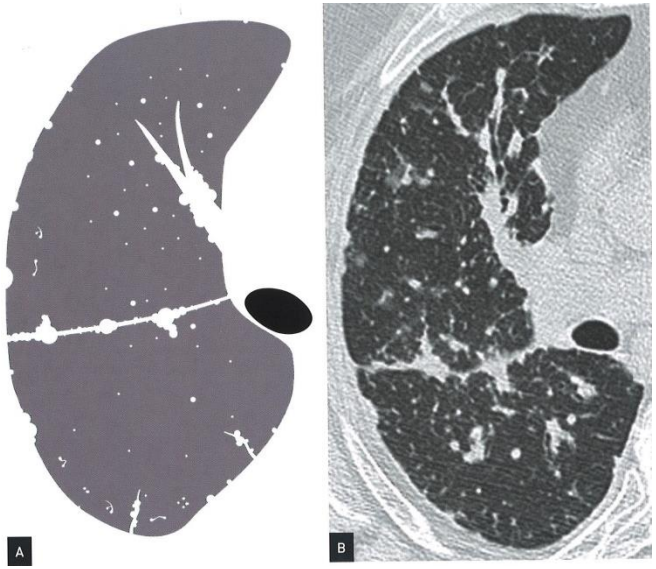






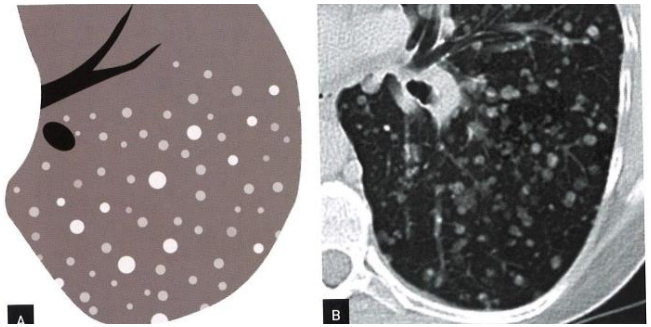
Centri-lobular

Nodules originate from the structures found in the middle of lobules
Typically situated no closer than 5-10 mm from the pleural surface



Peri-lymphatic

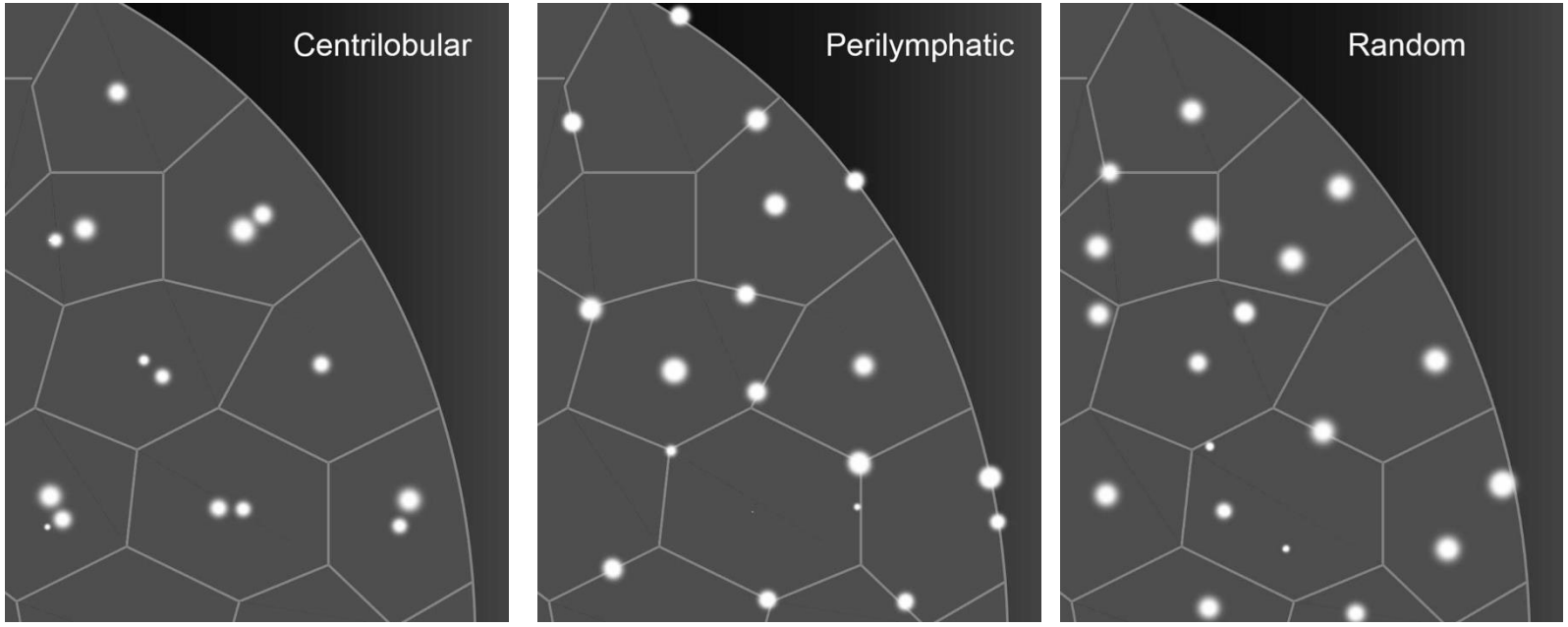
Nodules are well defined and solid
Distributed along lymphatics, in the subpleural, peribronchovascular, perihilar areas and along the interlobular septae



Random

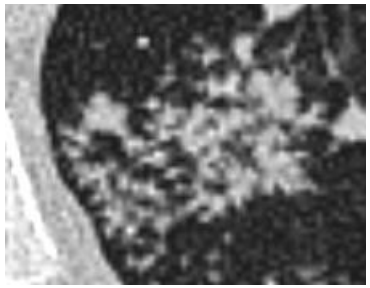
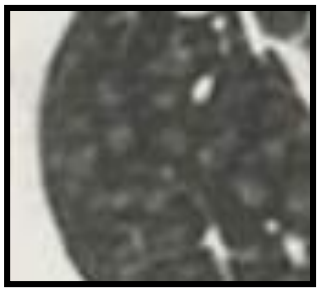
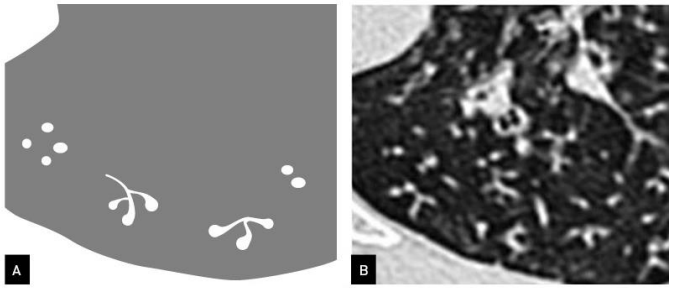
The nodules are located interstitially
Are relatively uniformly spread in the parenchyma
Individual nodules are also found close to the pleural surface and next to fissures

HRCT. Pattern recognition and differential diagnosis of lung disease. Carl Lamm, Frederic Ahlfors Trombone, Hungary 2013

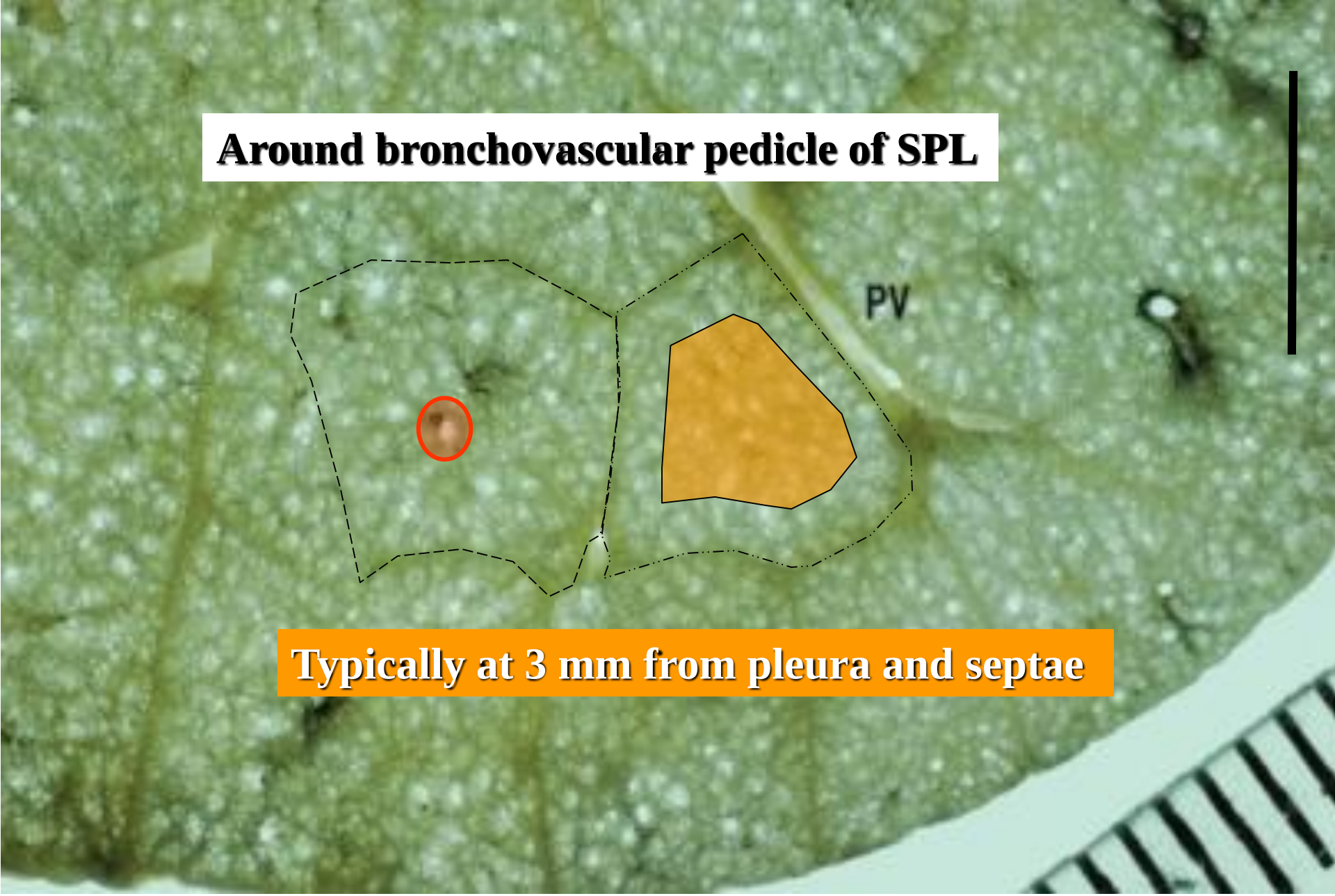

Centrilobular
Perilymphatic
Random

A.Centrilobular nodules

- boundaries : well defined and regular / fuzzy

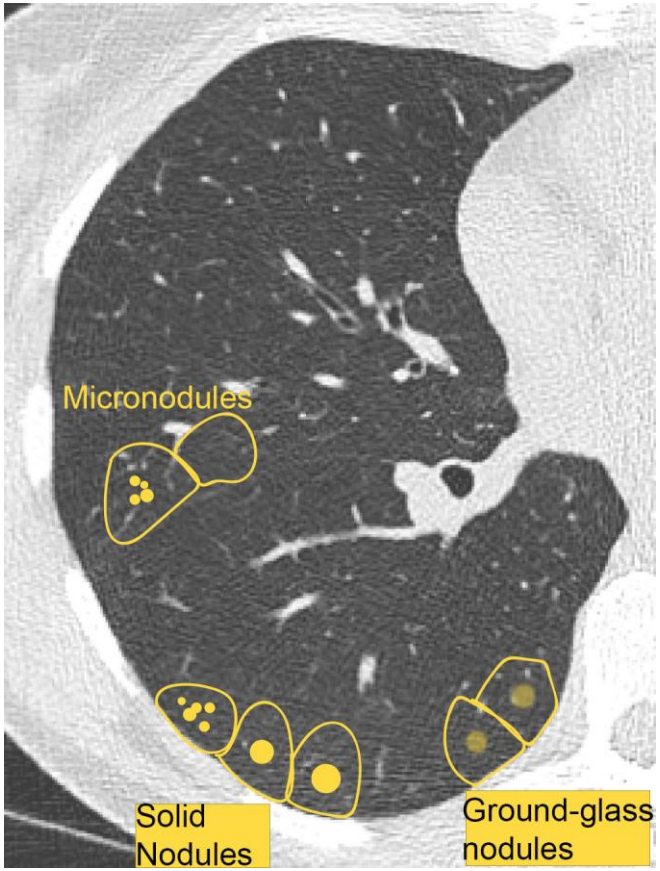




- Density : tissu / ground glass opacity



From Takahashi M. Imaging of pulmonary emphysema: a pictorial review. Int J Chron Obstruct Pulmon Dis. 2008;3(2):193-204.

CENTRILOBULAR NODULES



- **Inflammatory**
  - Aspiration
    - Hypersensitivity Pneumonitis
  - Pan-bronchiolitis
    - Respiratory bronchiolitis
    - Follicular bronchiolitis
- **Infectious**
  - Viral/bacterial pneumonia
  - Post-primary TB
  - MAI
- **Vascular**
  - Pulmonary edema
  - Cholesterol granulomas in pulm HTN
  - Pulmonary arteriolar aneurysms
  - Talc granulomatosis
  - Arterial or peri-lympathic tumor
  - Pulmonary capillary hemangiomatosis

Modified from poster RSNA 2018. Micronodular patterns on HRCT. Kim J, et al. Brigham and women's hospital. Harvard Medical School

Centrilobular nodules Differential by Distribution

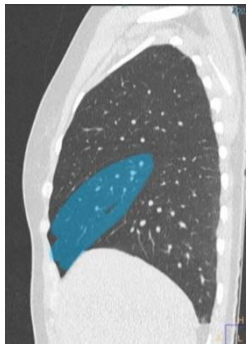
Lower lobe predominance

Upper lobe predominance

Middle lobe (RML and lingula)

Perihilar

Difuse



- **Inflammatory**
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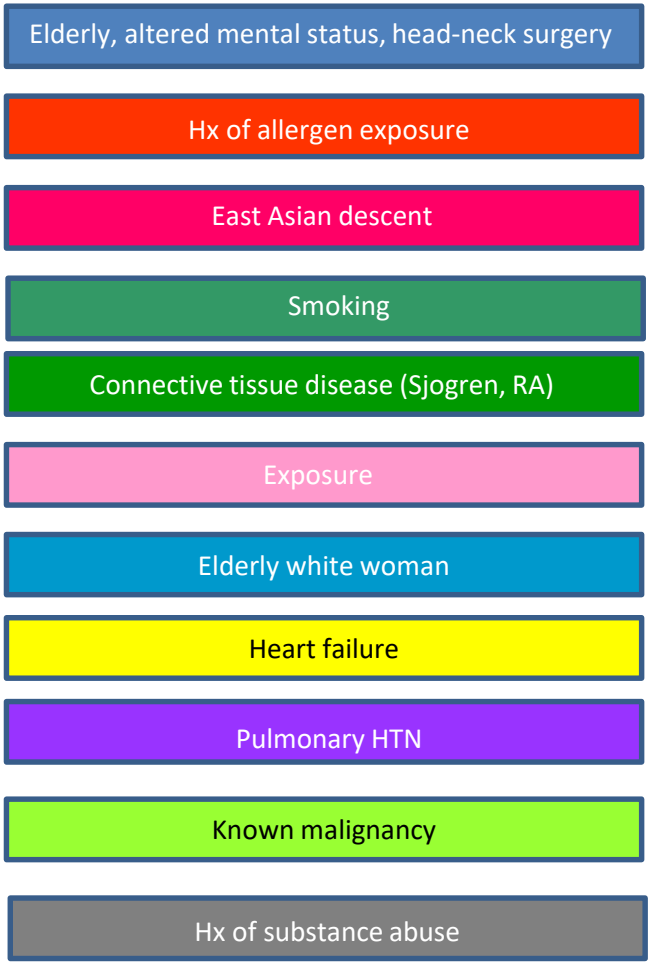
  - Pulmonary edema
    Cholesterol granulomas in pulm HTN
    Pulmonary arteriolair aneurysms
    Talc granulomatosis
    Arterial or peri-lympathic tumor
    Pulmonary capillary hemangiomatosis

Centrilobular nodules Differential by Clinical History



- **Inflammatory**
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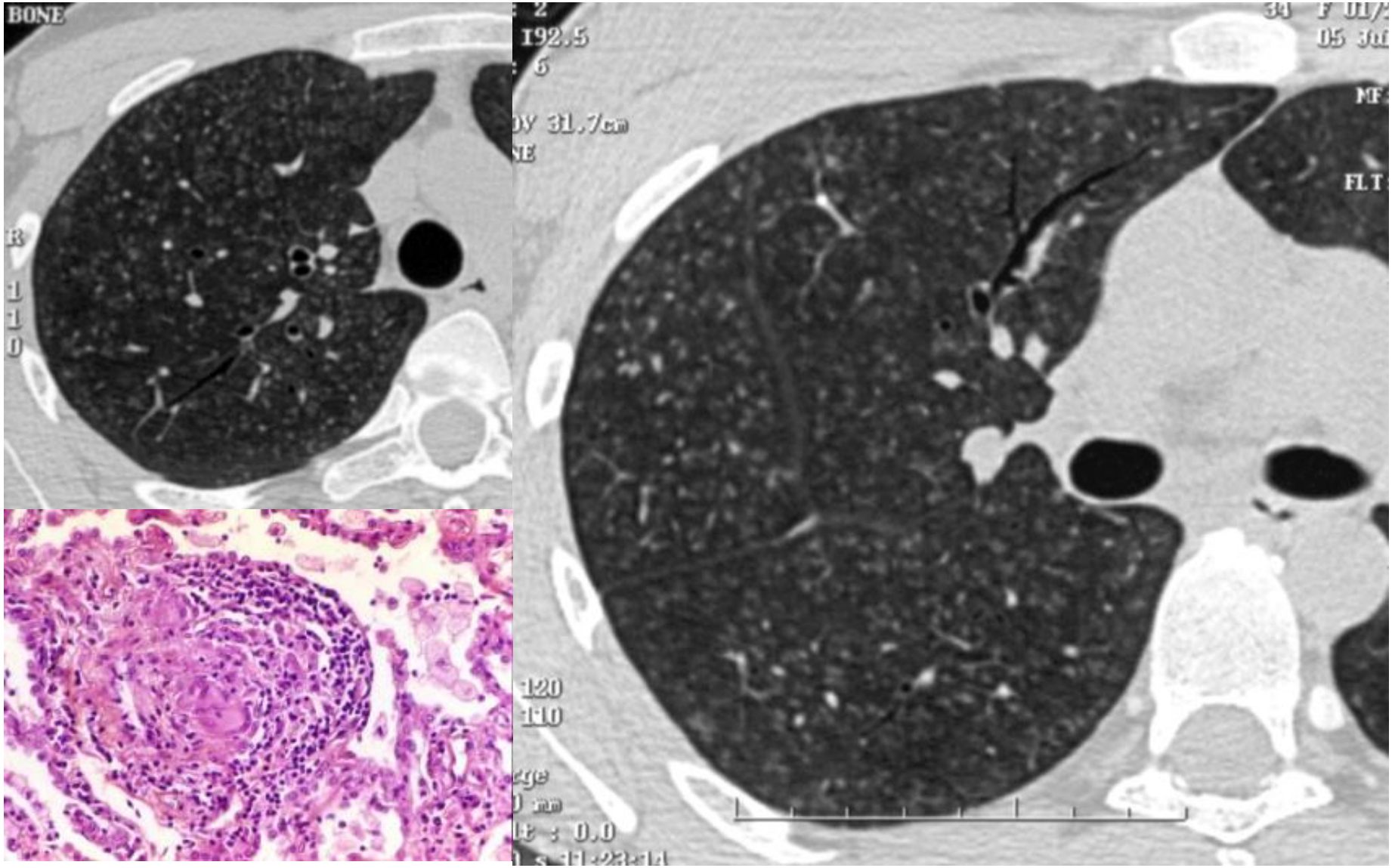
  - Talc granulomatosis

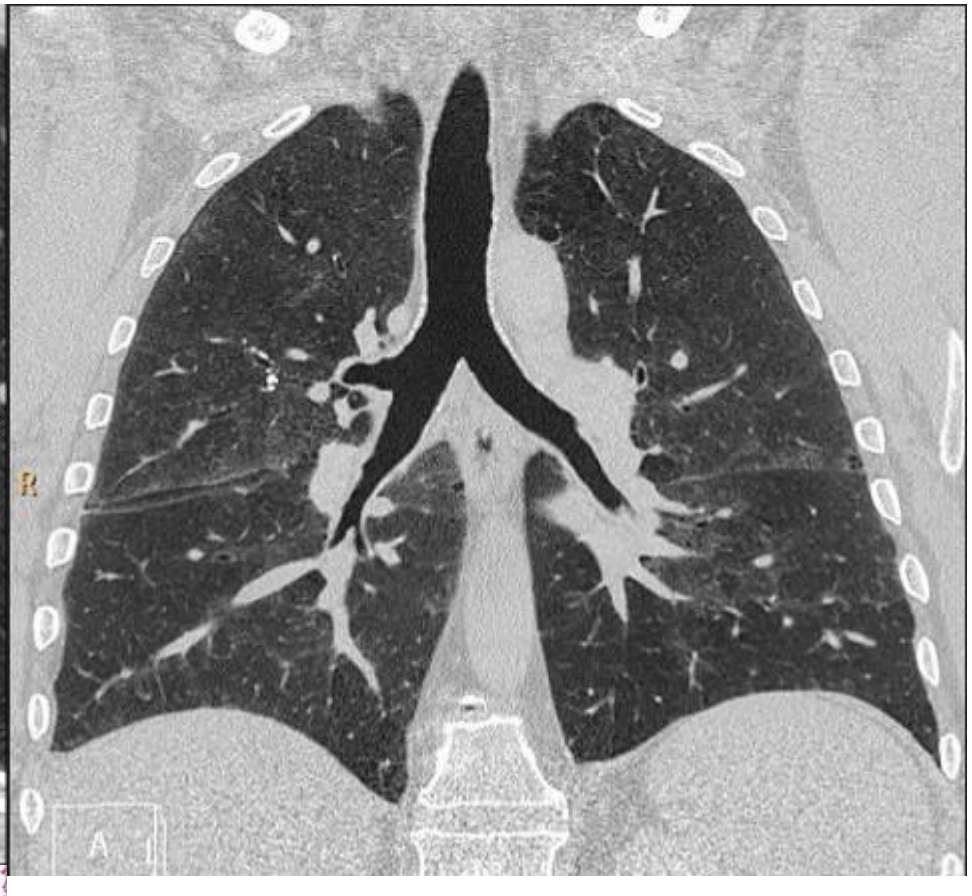
Modified from poster RSNA 2018. Micronodular patterns on HRCT. Kim J, et al. Brigham and women's hospital. Harvard Medical School

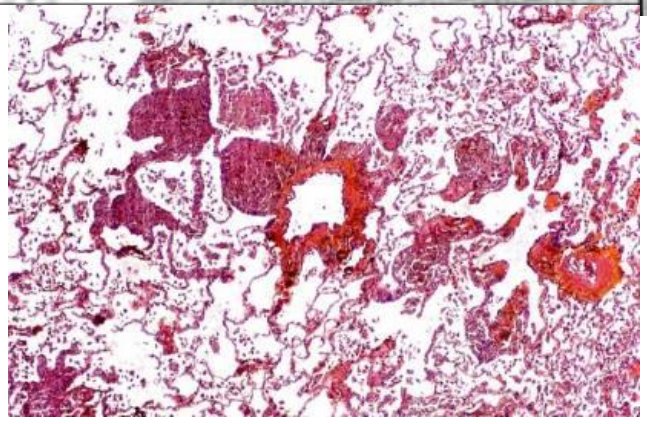
Acute extrinsic alveolitis



Courtesy G.Ferretti-CHU Grenoble

Respiratory bronchiolitis



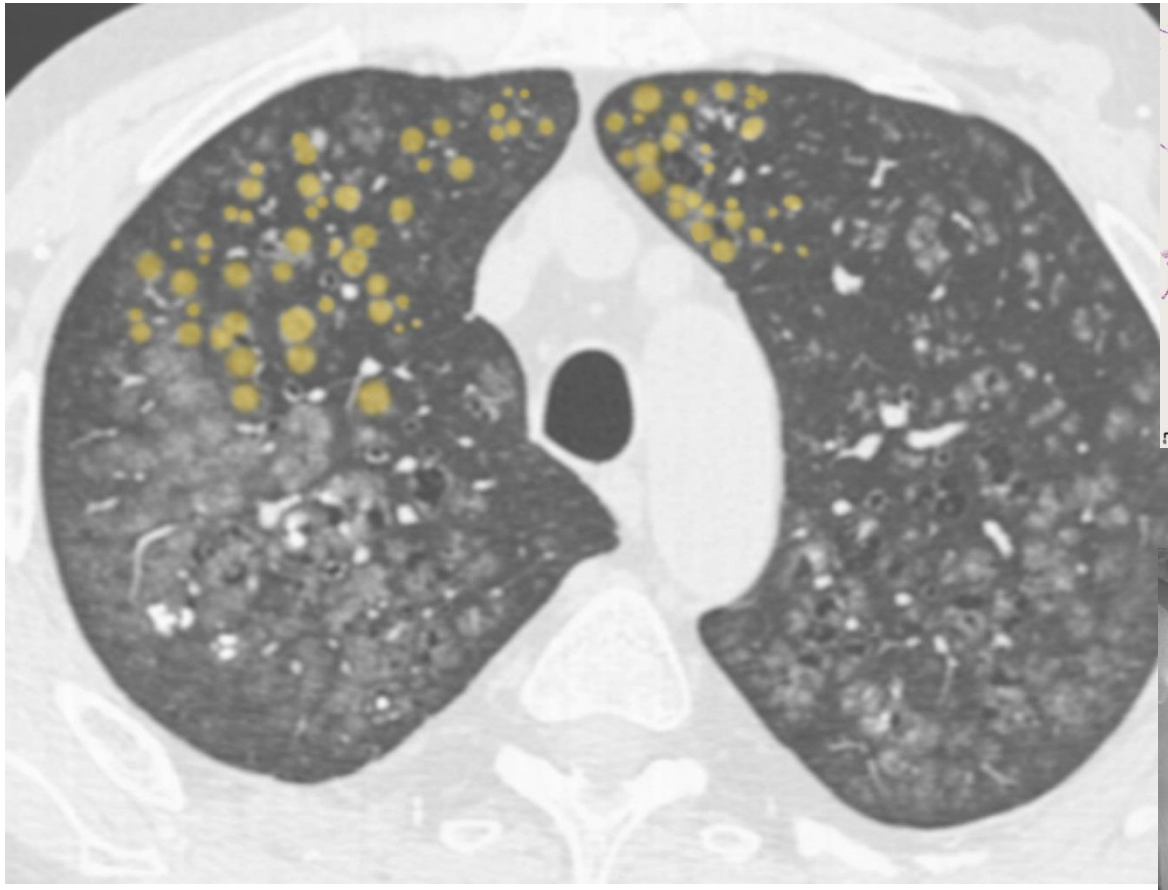


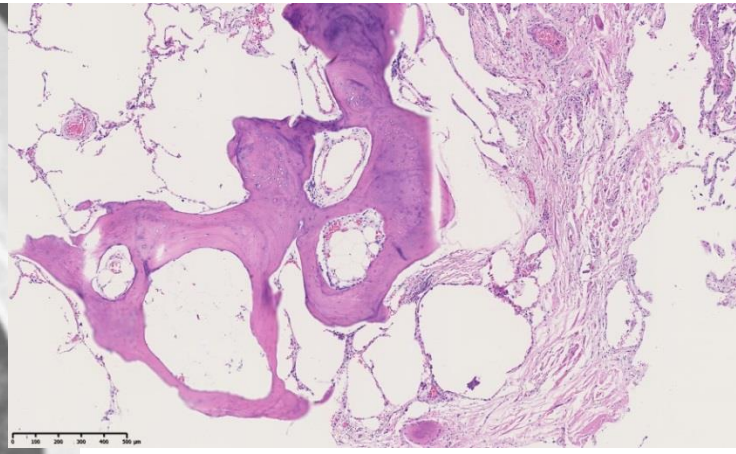
Courtesy G.Ferretti-CHU Grenoble

Respiratory bronchiolitis

Cannabis Consumption

Courtesy C.Beigelman-CHU Lausanne

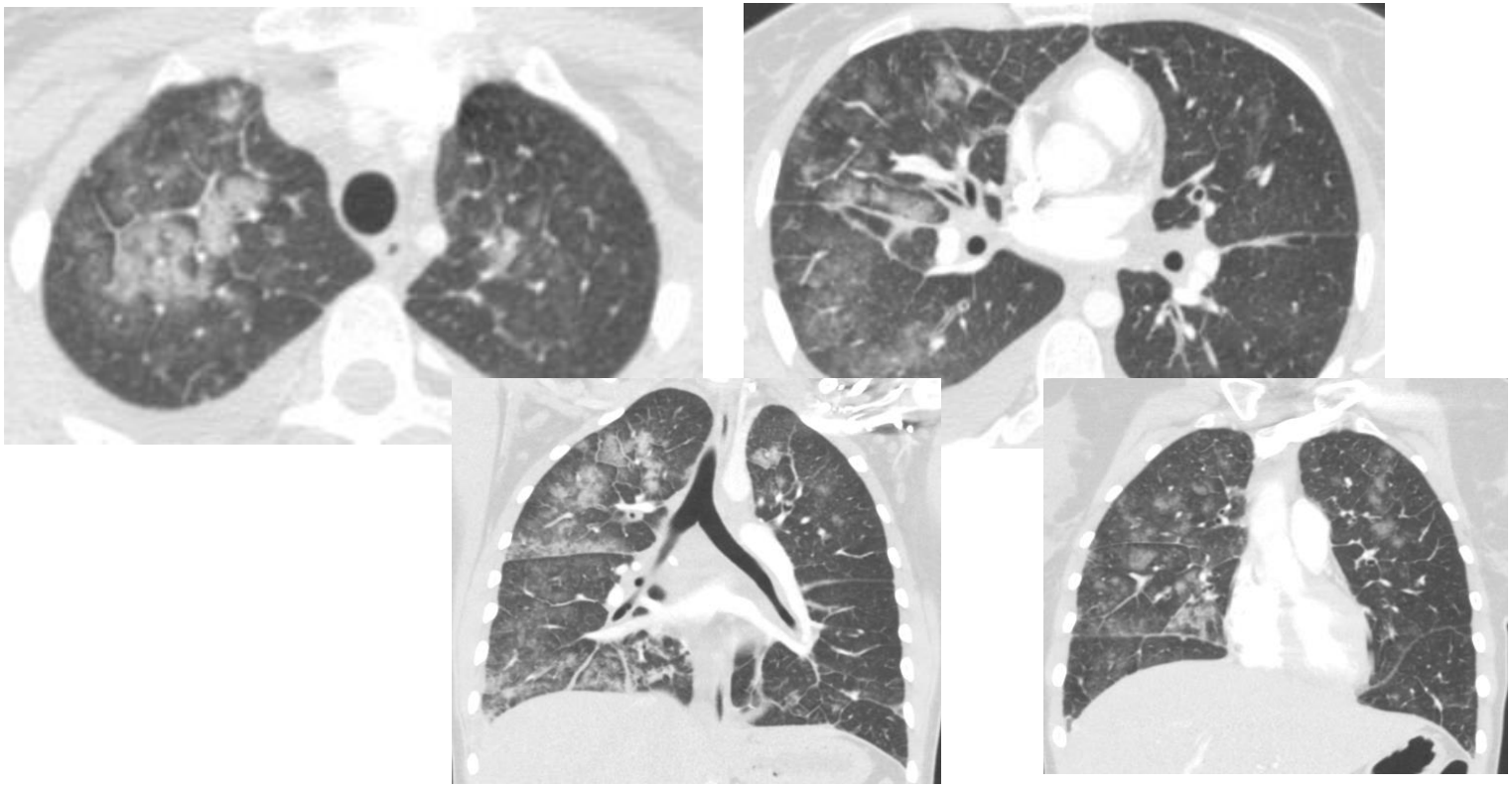




Metastatic calcifications

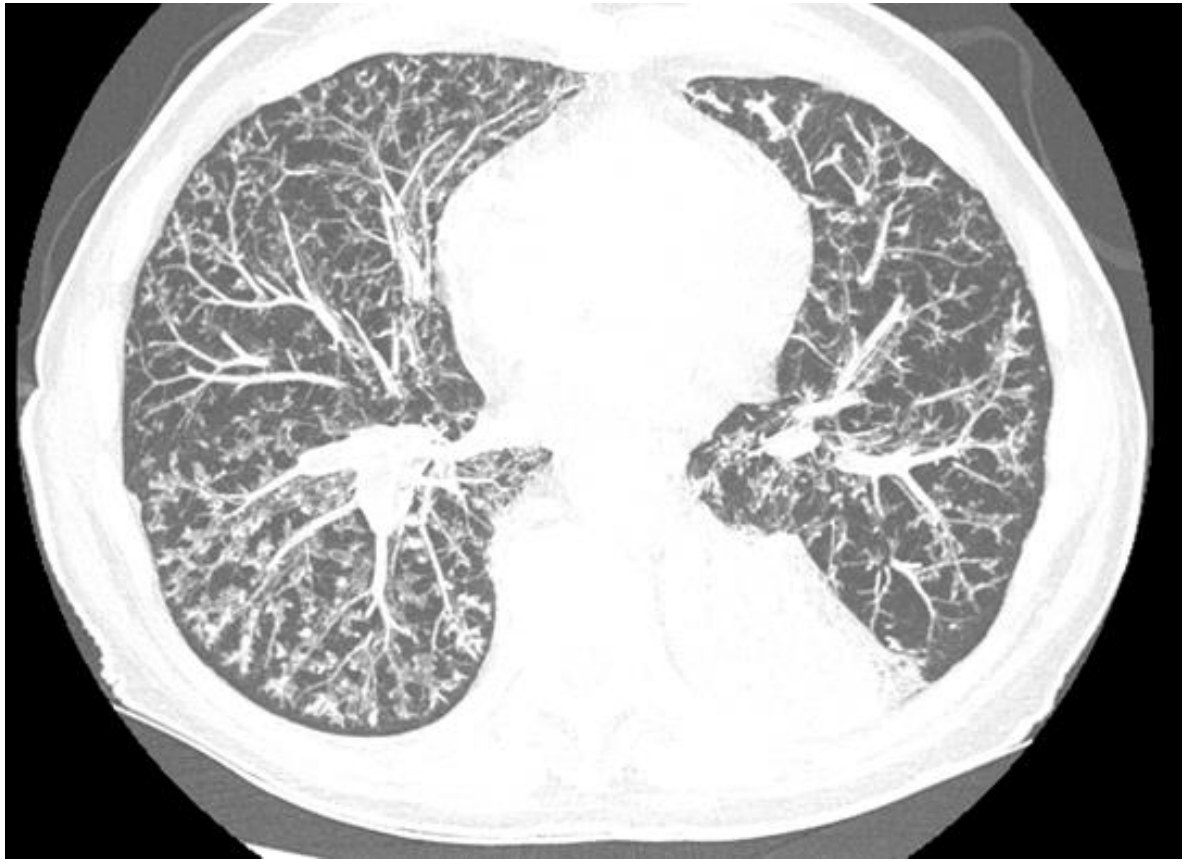
End stage renal disease
Hyperparathyroidism
Myeloma
Upper lobes because alcalinity

Centrilobular nodules ddx – Viral-baterial infection



- 21-year old female, hypoxemia and chest pain
- Chest CT : centrilobular nodules and thickened septal lines
- <u>Dx: Infectious pneumonia</u>
  - Resolution with empirical antibiotherapy (Augmentin + Biclar)
  - No identitified germ

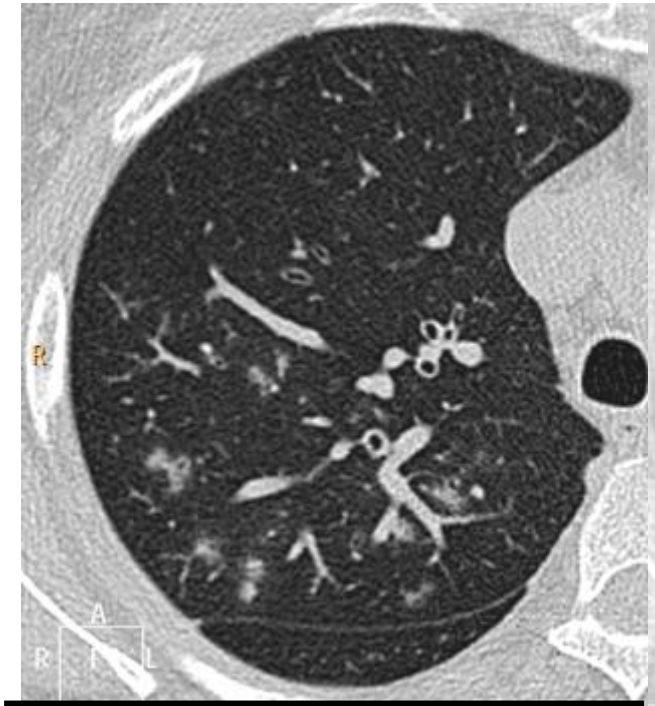
Centrilobular nodules ddx – Viral-baterial infection

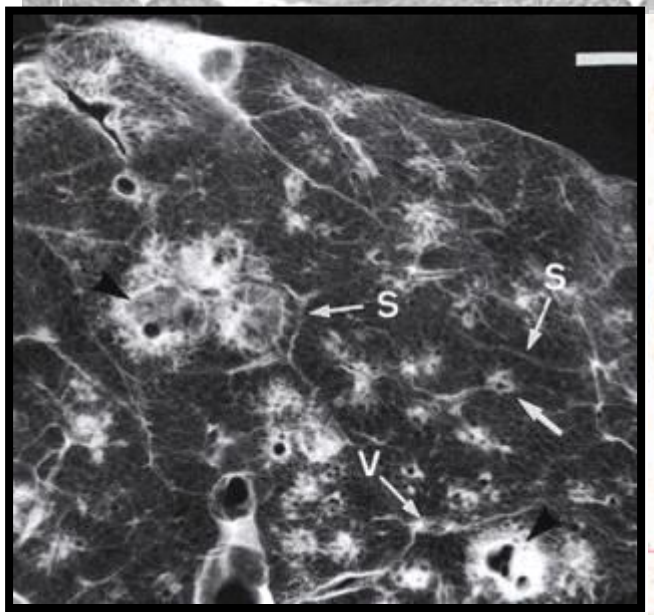


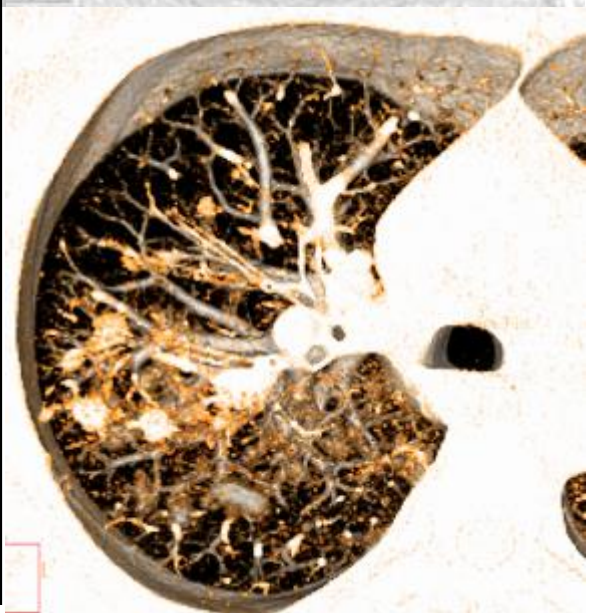
MIP

Diffuse bronchiolitis and bronchiectasis/pseudomonas + Achromobacter Xyloxosidans

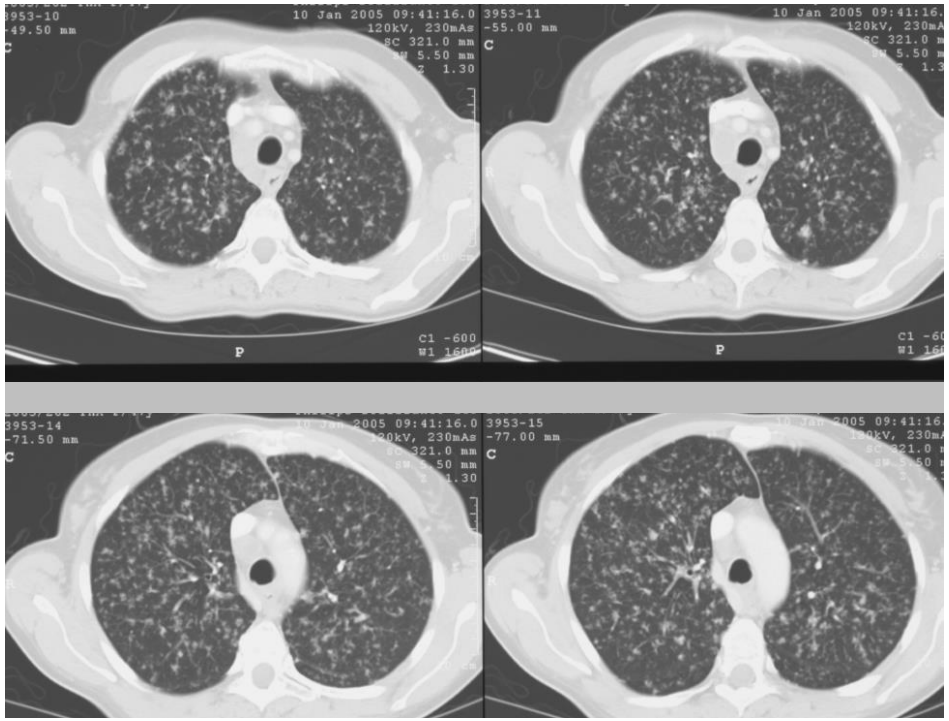
Influenza bronchopneumonia



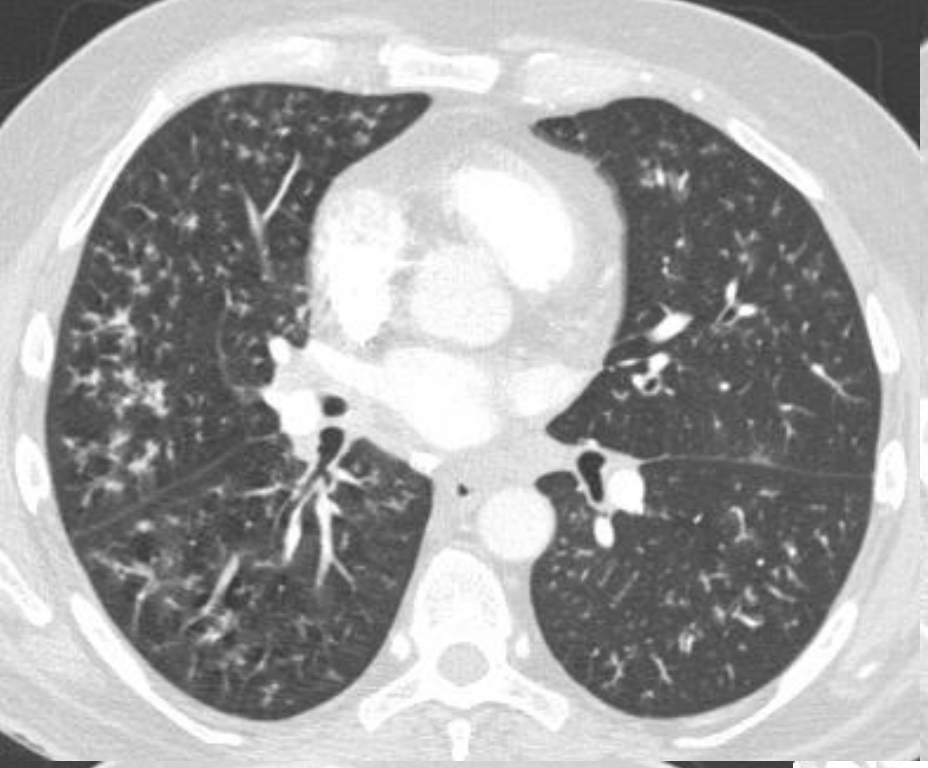


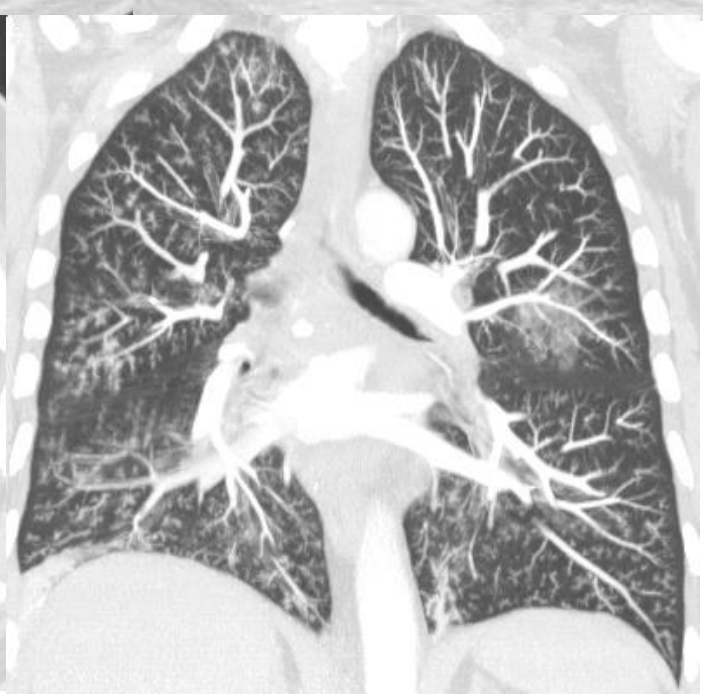


Centrilobular nodules ddx – Tuberculosis



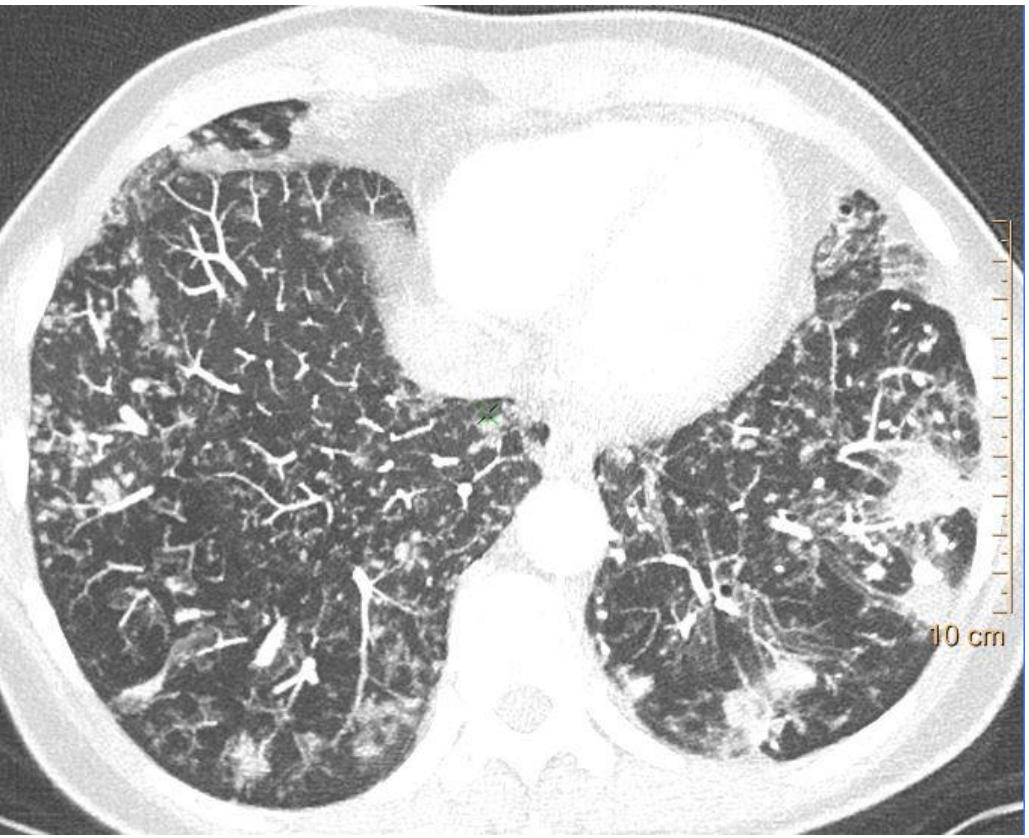
- 21-year old female, long standing fever and cough
- Chest CT : tree-in-bud nodules
- <u>Dx: tuberculosis</u>



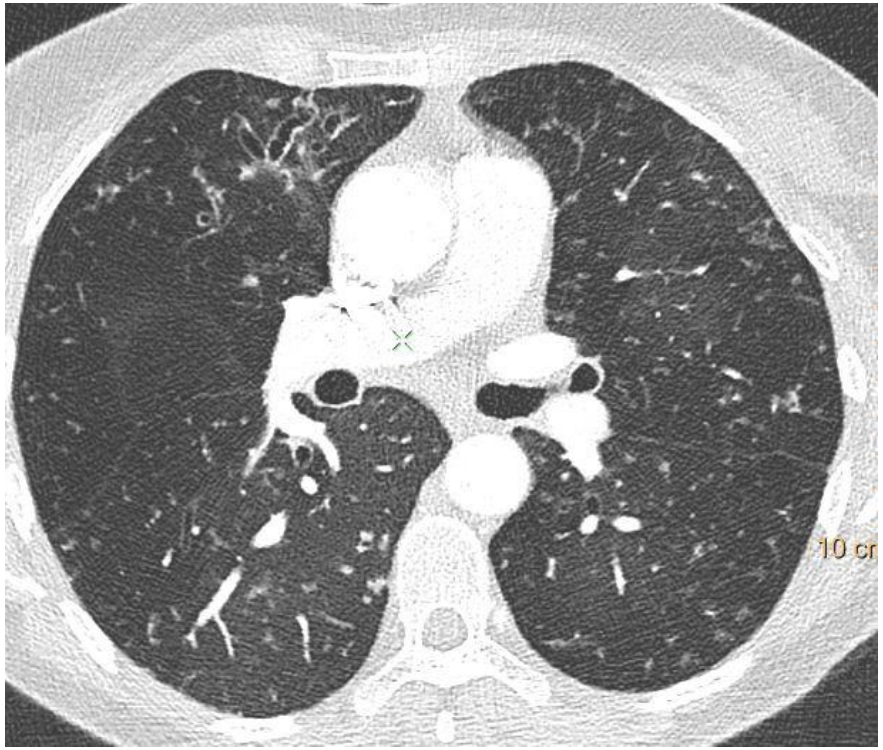


56-year old man
Fever
Hypoxemia (74 mm Hg)
Potential Chlamydia pneumoniae

Centrilobular nodules ddx – MAI



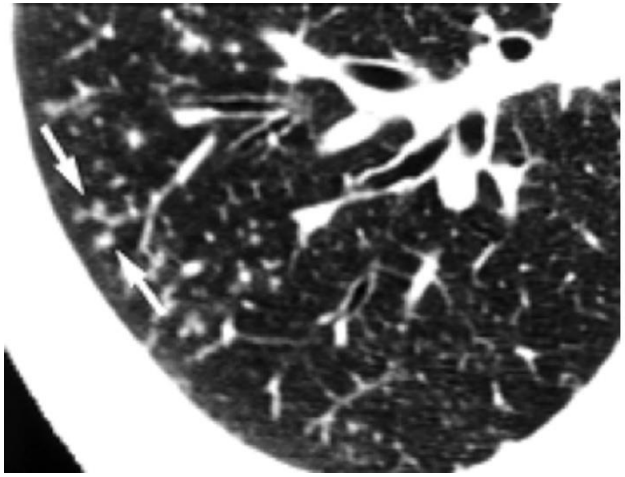
Mycobacterium Abcessus

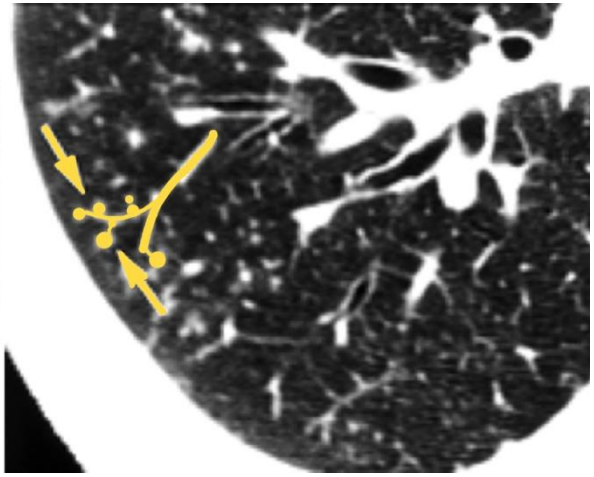


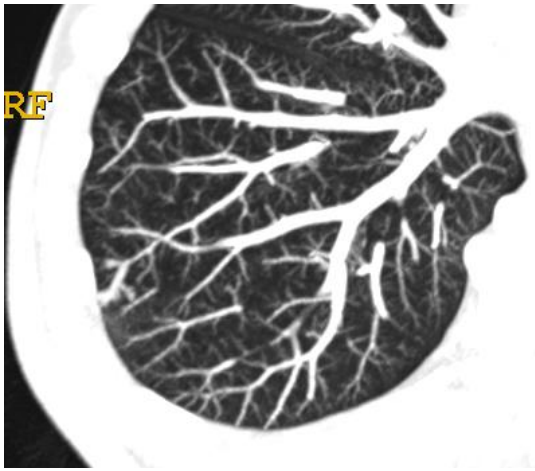
53-year old woman
Long history of ABPA
Long standing fever + cough

MIP

Tree-in-bud » sign = Non specific finding:







1. Small airway disease

2. Small arteries disease

Tree-in-bud pattern

- Peripheral airway disease
  - Infection
    - Bacterial
      - *Mycobacterium tuberculosis*
      - *M avium-intracellulare* complex
      - *Staphylococcus aureus*
      - *Haemophilus influenzae*
    - Fungal
      - *Aspergillus*
    - Viral
      - Cytomegalovirus
      - Respiratory syncytial virus
  - Congenital disorders
    - Cystic fibrosis
    - Kartagener syndrome
  - Idiopathic disorders
    - Obliterative bronchiolitis
    - Diffuse panbronchiolitis
  - Aspiration
  - Inhalation
    - Toxic fumes and gases
  - Immunologic disorders
    - Allergic bronchopulmonary aspergillosis
  - Connective tissue disorders
    - Rheumatoid arthritis
    - Sjögren syndrome
- Peripheral pulmonary vascular disease
  - Neoplasms
    - Gastric cancer
    - Breast cancer
    - Ewing sarcoma
    - Renal cancer

Previous Article

May-June 2005
Volume 25, Issue 3

Next Article

RSNA Education Exhibits

Tree-in-Bud Pattern at Thin-Section CT of the Lungs: Radiologic-Pathologic Overview

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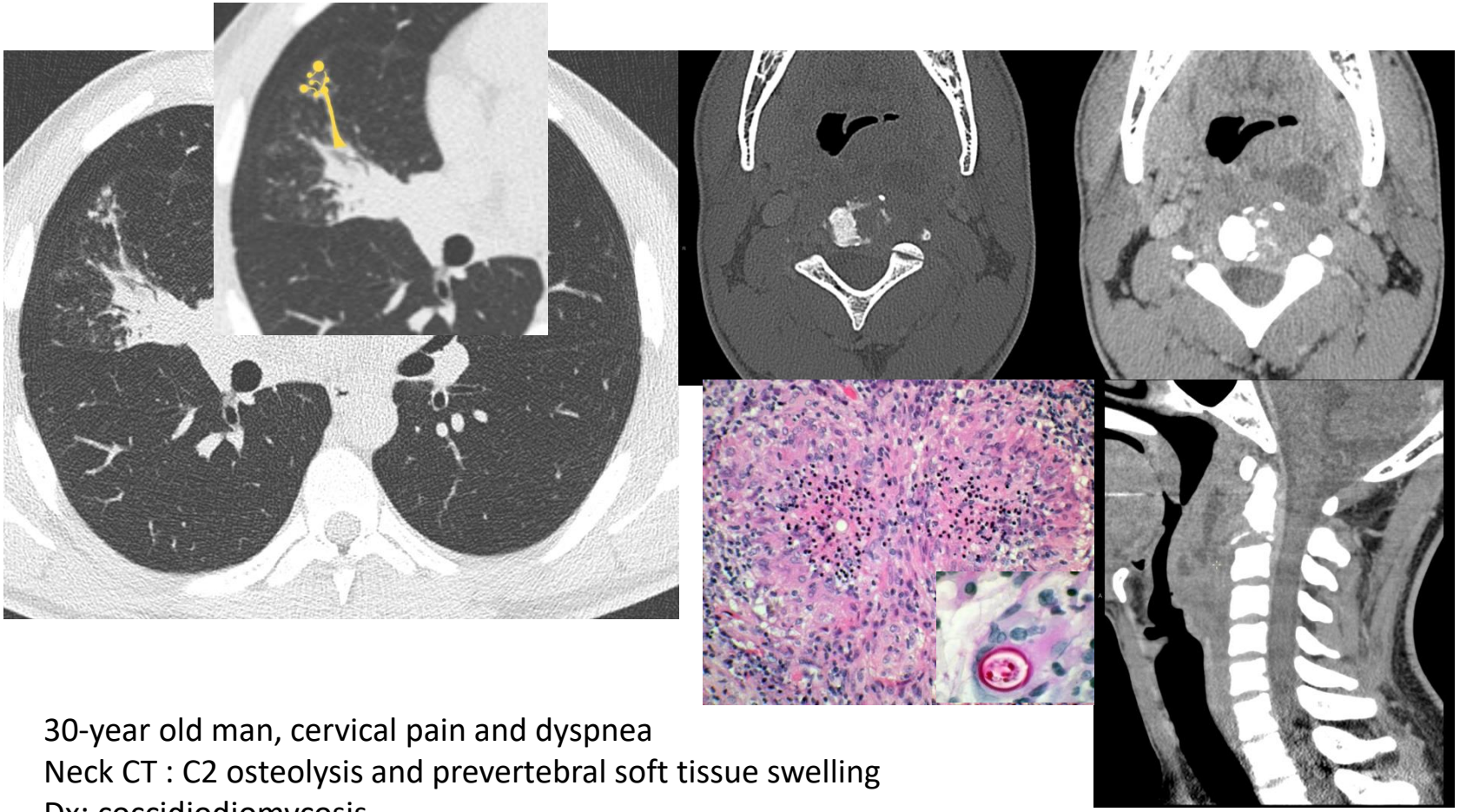
[1]From the Department of Radiology, Centro de Diagnostico Dr Enrique Rossi, Arenales 2777, CP 1425, Buenos Aires, Argentina (S.E.R., M.V., G.A.); and the Department of Radiology, Hospital de Sant Pau, Universidad Autónoma de Barcelona, Barcelona, Spain (T.F., A.G.).
Recipient of a Certificate of Merit award for an education exhibit at the 2003 RSNA Scientific Assembly. Received May 26, 2004; revision requested August 26 and received November 29; accepted December 6. All authors have no financial relationships to disclose.

DOI: http://dx.doi.org/10.1148/rg.253045115

Centrilobular nodules ddx – Tree-in-bud pattern

- A 60-year-old man presented for routine follow-up colon tumor surgically resected 15 years ago. Clinical examination, laboratory tests, including CEA and inflammatory parameters and chest X-Ray were normal
- <u>Dx: endovascular metastases</u>
  - Tree-in-bud pattern
  - Rare presentation

Centrilobular nodules ddx - Coccidiodiomycosis



- 30-year old man, cervical pain and dyspnea
- Neck CT : C2 osteolysis and prevertebral soft tissue swelling
- Dx: coccidiodiomycosis
- Thoracic manifestations of acute coccidioidomycosis include pulmonary parenchymal abnormalities, intrathoracic adenopathy, and pleural effusion. Pulmonary parenchymal abnormalities occur in most symptomatic cases and consist of consolidation, nodules, cavities, and peribronchial thickening

RadioGraphics

Pulmonary Coccidioidomycosis: Pictorial Review of Chest Radiographic and CT Findings

Cecilia M. Jude, MD • Nita B. Nayak, MD • Maitraya K. Patel, MD • Monica Deshmukh, MD • Poonam Batra, MD

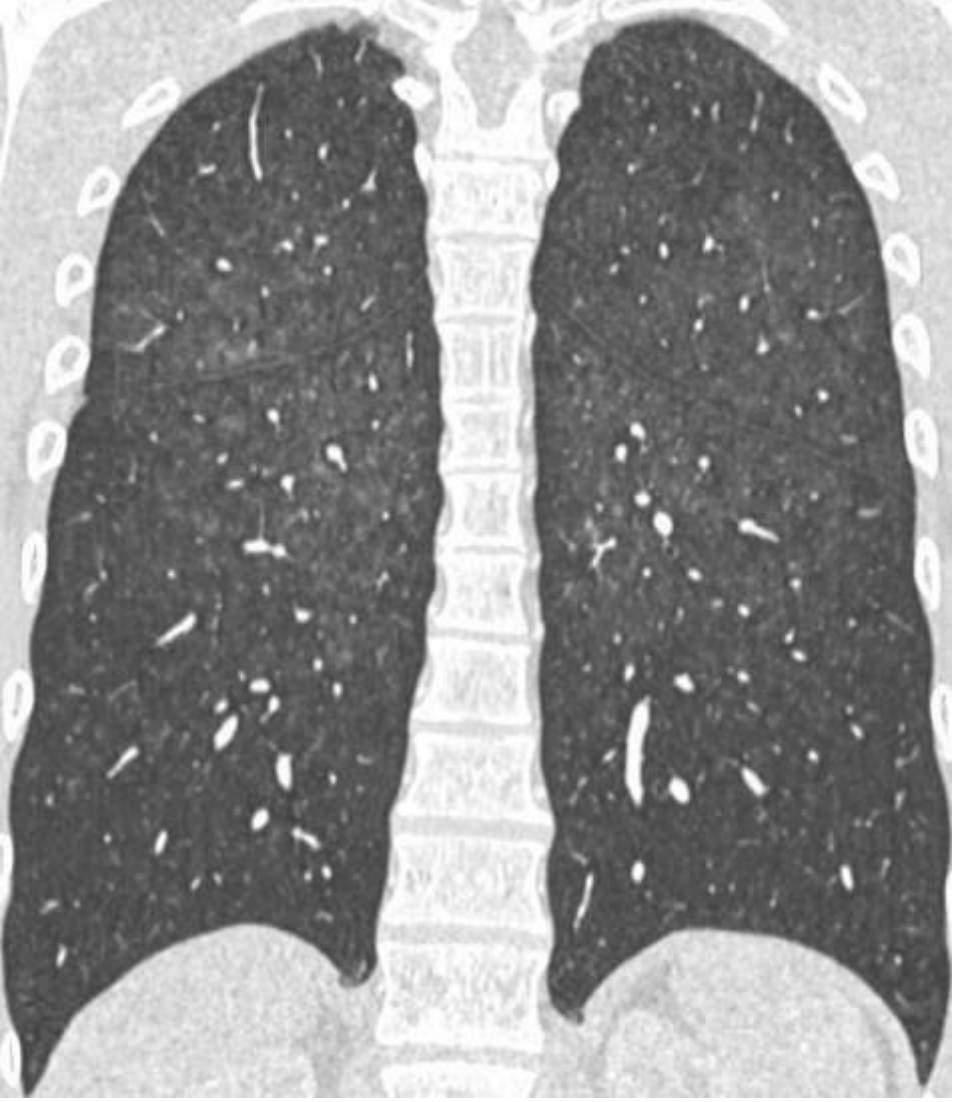
RadioGraphics 2014; 34:912–925 • **Published online** 10.1148/rg.344130134 • **Content Codes:** CH CT

Page 913
The lungs are the target organ in coccidioidomycosis and are involved in a wide spectrum of clinical and imaging manifestations that are categorized as acute, disseminated, or chronic disease. Acute coccidioidomycosis is responsible for up to 29% of cases of community-acquired pneumonia in endemic areas and is mostly self-limited. Disseminated or chronic disease occurs in a minority of cases and is associated with significant morbidity and mortality.

Page 913
Suppression of cellular immunity is a major risk factor for increased disease severity and dissemination. The most substantial risk factors are HIV infection, immunosuppressive medications, and high-dose glucocorticoid administration.

Pages 914–915
Thoracic manifestations of acute coccidioidomycosis include pulmonary parenchymal abnormalities, intrathoracic adenopathy, and pleural effusion. Pulmonary parenchymal abnormalities occur in most symptomatic cases and consist of consolidation, nodules, cavities, and peribronchial thickening.

Page 917
The classic pulmonary manifestation of disseminated coccidioidal infection is miliary nodules caused by hematogenous spread. The original focus of parenchymal consolidation is seen occasionally, and hilar and mediastinal adenopathy is usually present. The lung nodules often progress to confluent opacities. Acute respiratory distress syndrome (ARDS) is an infrequent complication that usually occurs in immunocompromised hosts.



Alveolar Hemorrhage

Hémosidérosis

Courtesy F. Laurent-CHU Bordeaux

Lung talcosis

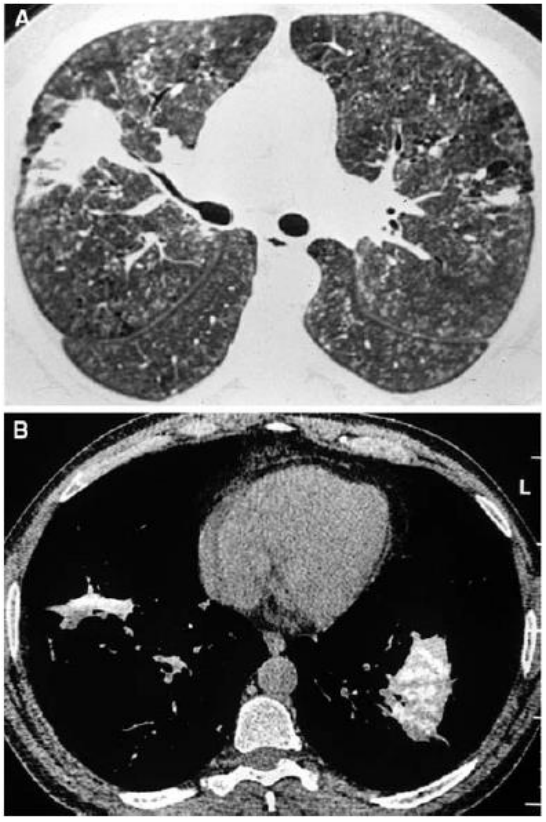


Fig. 2 A 45-year-old man with a 2-year history of occupational exposure to talc in a talc factory. **a** High-resolution CT image at the subcarinal area level shows numerous bilateral small nodules in a predominantly centrilobular distribution. Also note a conglomerate mass in the right lung. **b** High-resolution CT image with mediastinal window settings at the level of the lower lobes shows increased attenuation within the conglomerate masses, consistent with talc deposition

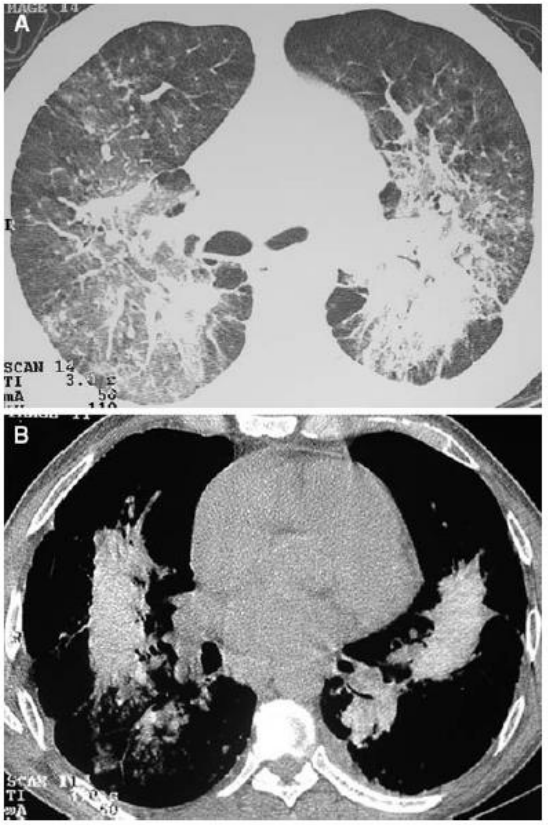
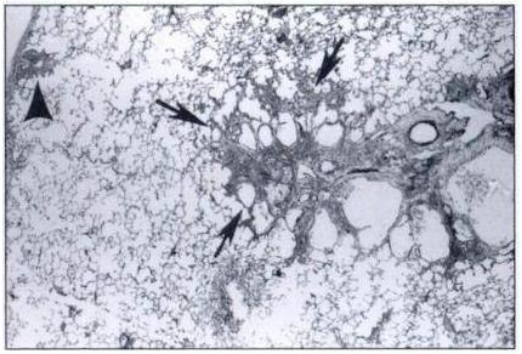


Fig. 3 A 41-year-old male with an 8-year history of occupational exposure to talc in a magnesium silicate mineral-processing industry. **a** High-resolution CT scan at the level of the main bronchi shows bilateral conglomerate masses and ground-glass opacities. **b** Scan obtained with mediastinal window settings at the level of the lower lobes shows high attenuation within the conglomerate masses

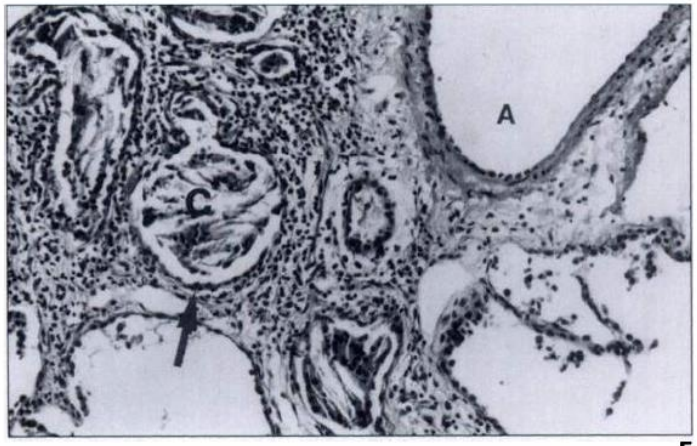
Marchiori E, et al. Pulmonary talcosis: Imaging findings. Lung (2010);188:165-171

Cholesterol granuloma

C



D

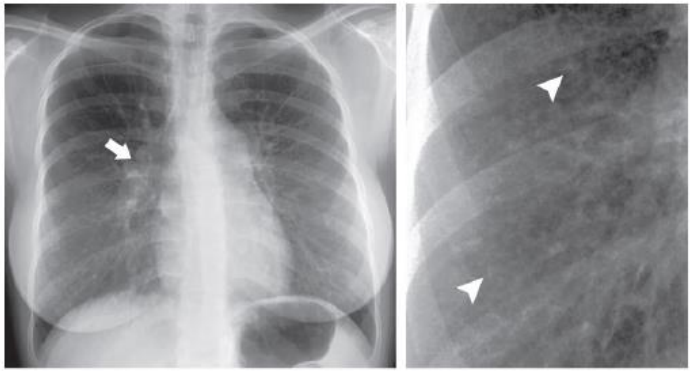


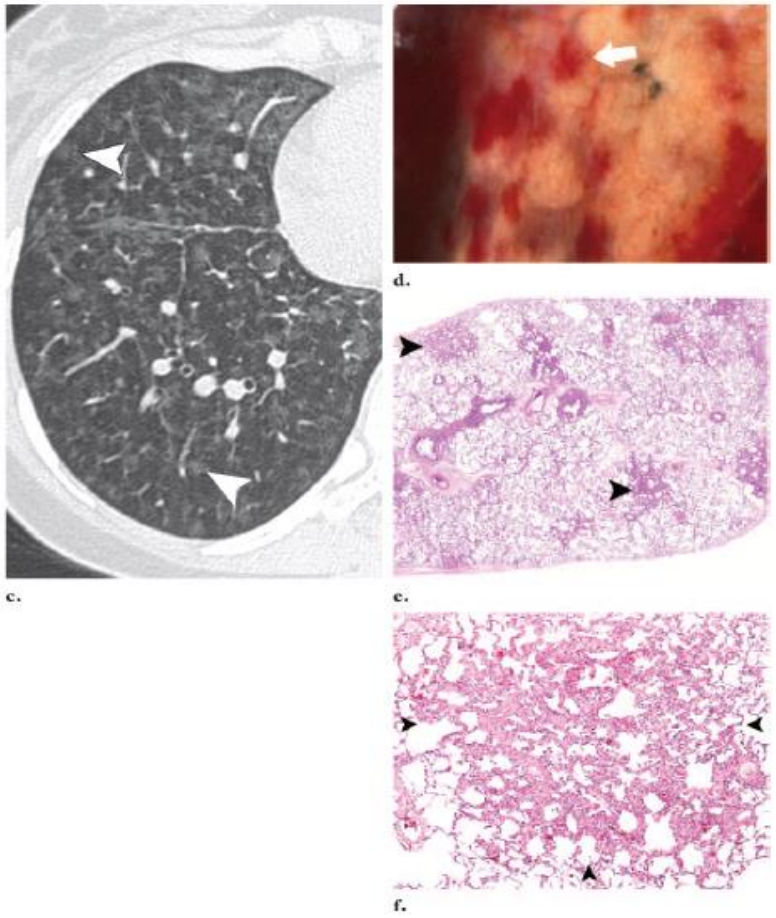
E

Fig. 1.—Pulmonary cholesterol granulomas in 30-year-old woman with primary pulmonary hypertension.
A, Posteroanterior chest radiograph shows marked cardiomegaly, severe enlargement of pulmonary artery, and diffuse 2- to 3-mm-diameter nodules.
B, Cone-down radiographic view of right lower lobe shows multiple 2- to 3-mm-diameter nodules.
C, Chest CT (3-mm collimation, lung window) shows multiple, poorly defined centrilobular nodules (*arrowheads*). Patient received unilateral lung transplant 4 days later.
D, Low-power photomicrograph of resected lung specimen shows centrilobular distribution of poorly defined granulomatous lesion (*arrows*). Note small, subpleural granuloma (*arrowhead*). (H and E, ×11)
E, High-power photomicrograph of resected lung specimen shows intraalveolar needlelike cholesterol clefts (C) associated with foreign body giant cells. Note chronic inflammatory cells in thickened, fibrotic interstitium. Also note hyperplastic type II cells (*arrow*) and adjacent thin-walled pulmonary artery (A). (H and E, ×200)

Nolan L, et al. Pulmonary cholesterol granulomas in patients with pulmonary hypertension: chest radiographic and CT findings. AJR Am J Roentgenol. (1999);172(5):1317-9.

Pulmonary capillary hemangiomatosis





Frazier AA, et al. From the archives of the AFIP: pulmonary veno-occlusive disease and pulmonary capillary hemangiomatosis. Radiographics (2007);27(3):867-82

Summary

Centrilobular nodules → Distribution

Distribution:

- Upper lobe
- RML & Lingula
- Lower lobe

- Upper lobe
  - Hypersensitivity pneumonitis
  - Respiratory bronchiolitis
  - Post-primary TB
- RML & Lingula
  - MAI
- Lower lobe
  - Aspiration
  - Pan-bronchiolitis
- Diffuse
  - Viral/bacterial pneumonia
  - Pulmonary edema
  - Cholesterol granulomas in pulm HTN
  - Pulmonary arteriolar aneurysms
  - Talc granulomatosis
  - Arterial or peri-lympathic tumor
  - Pulmonary capillary hemangiomatosis

Patient & hx

Age

- Elderly
  - MAI
  - Aspiration

PMH

- Autoimmune
  - Follicular bronchiolitis
- Heart failure
  - Pulmonary edema
- Pulm HTN
  - Cholesterol Granulomas
  - Pulmonary capillary hemangiomatosis
  - Pulmonary arteriolar aneurysms

Modified from poster RSNA 2018. Micronodular patterns on HRCT. Kim J, et al. Brigham and women's hospital. Harvard Medical School

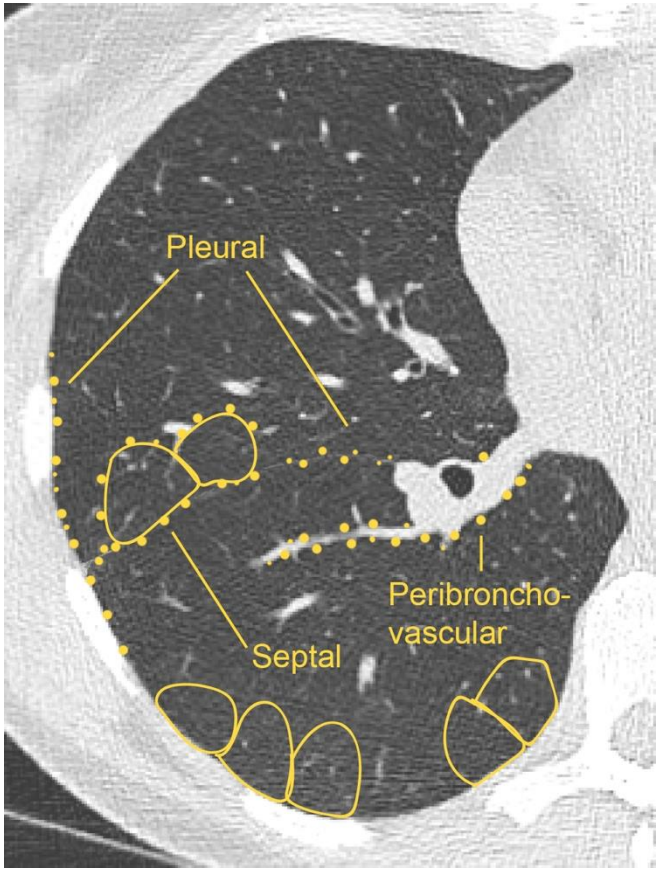
Social hx

- Smokers
  - Respiratory bronchiolitis
- IVDU
  - Talc granulomatosis
- Allergen
  - Hypersensitivity pneumonitis

Ethnicity

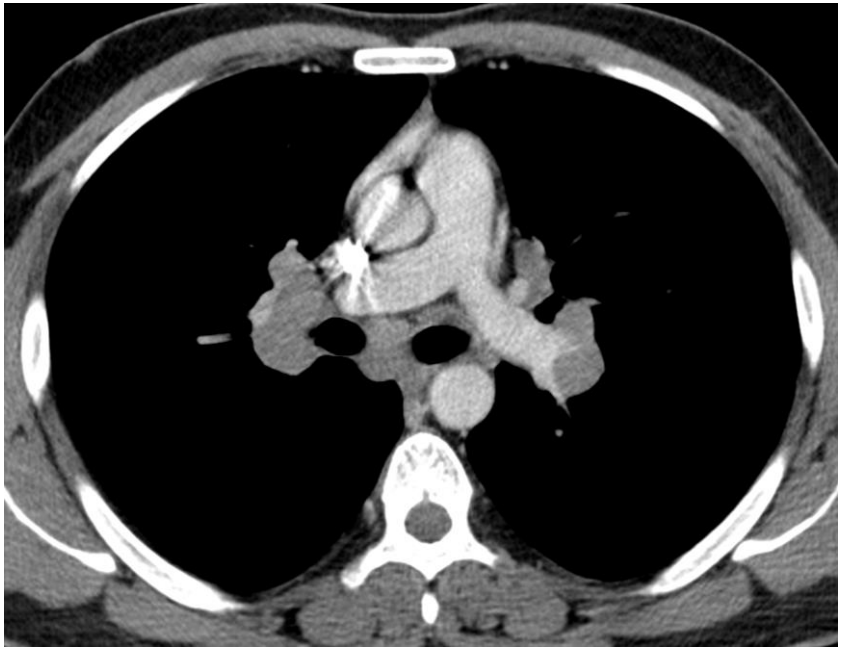
- East Asian
  - Pan-bronchiolitis

B. Peri-lymphatic nodules Differential Diagnosis



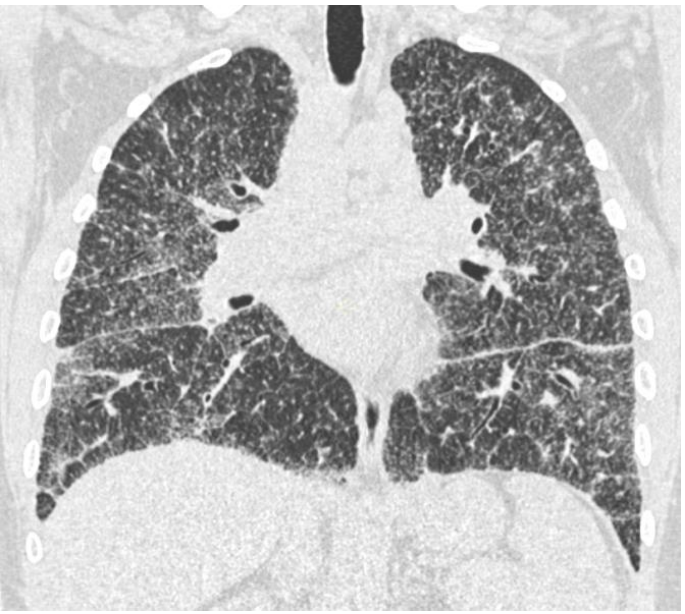
- **<u>Sarcoidosis</u>**
- **<u>Pneumoconioses</u>**
  - Silicosis
  - Coal worker's pneumoconiosis
  - Berylliosis
  - Very similar to sarcoidosis, but there is history of exposure
- **<u>Lymphangitic carcinomatosis</u>**

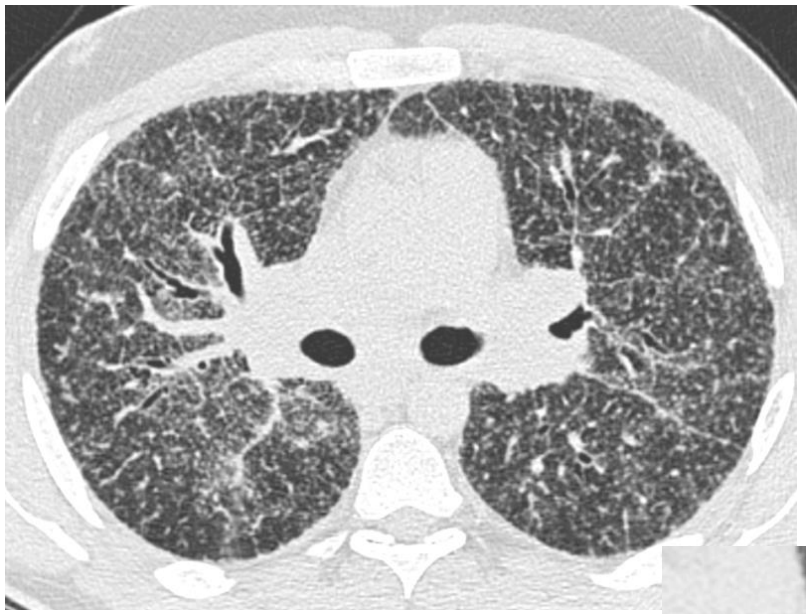
Peri-lymphatic nodules ddx - Sarcoidosis

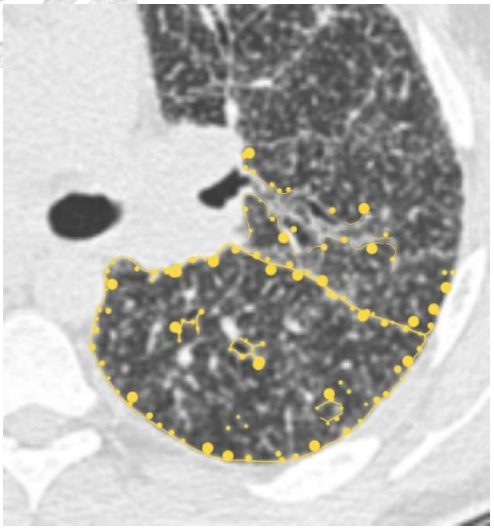


- 33 M with erythema nodosum
- <u>Dx: Sarcoidosis</u>
  - Upper lobe predominant peri-lymphatic nodules
  - Can be focal or localized small area
  - Confluent nodules create the galary sign
  - Mediastinal lymph nodes
  - Can see fribrosis in end stage

Peri-lymphatic nodules ddx – Sarcoidosis

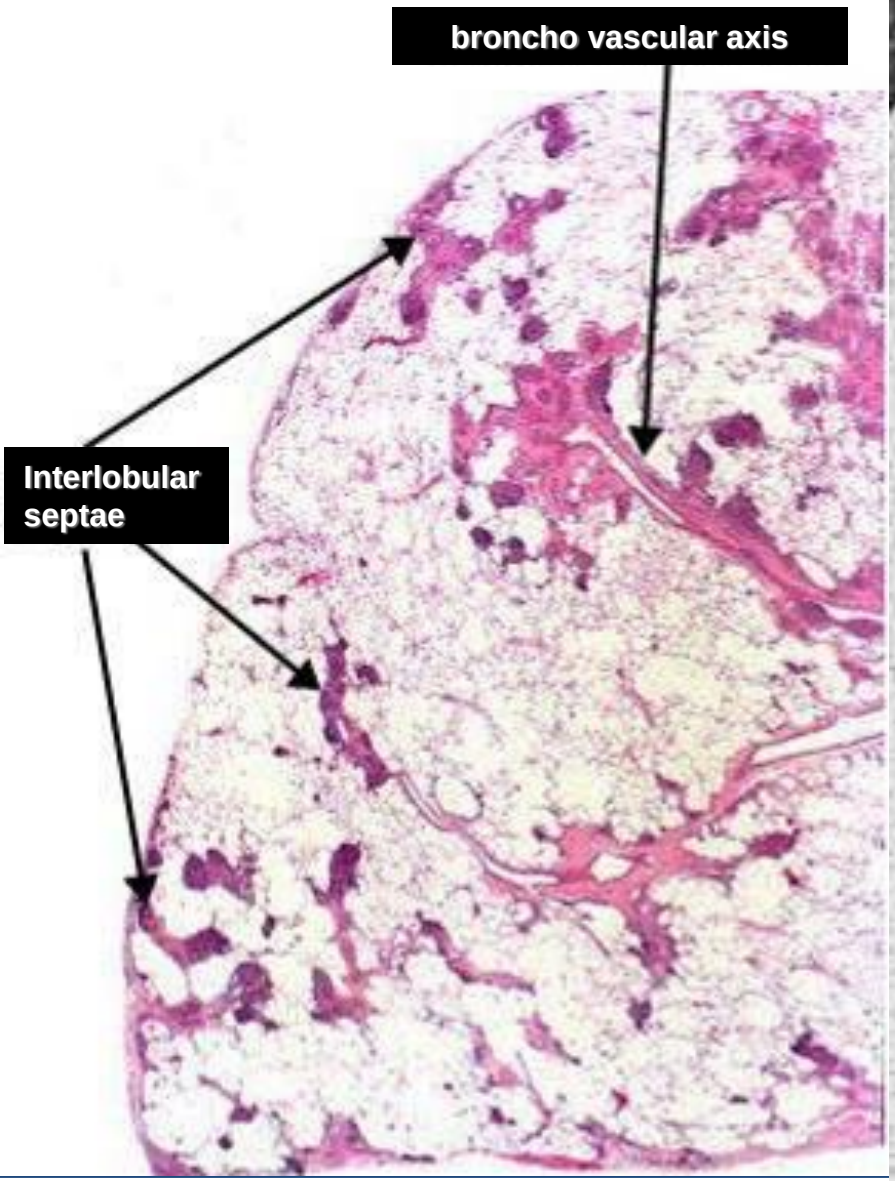


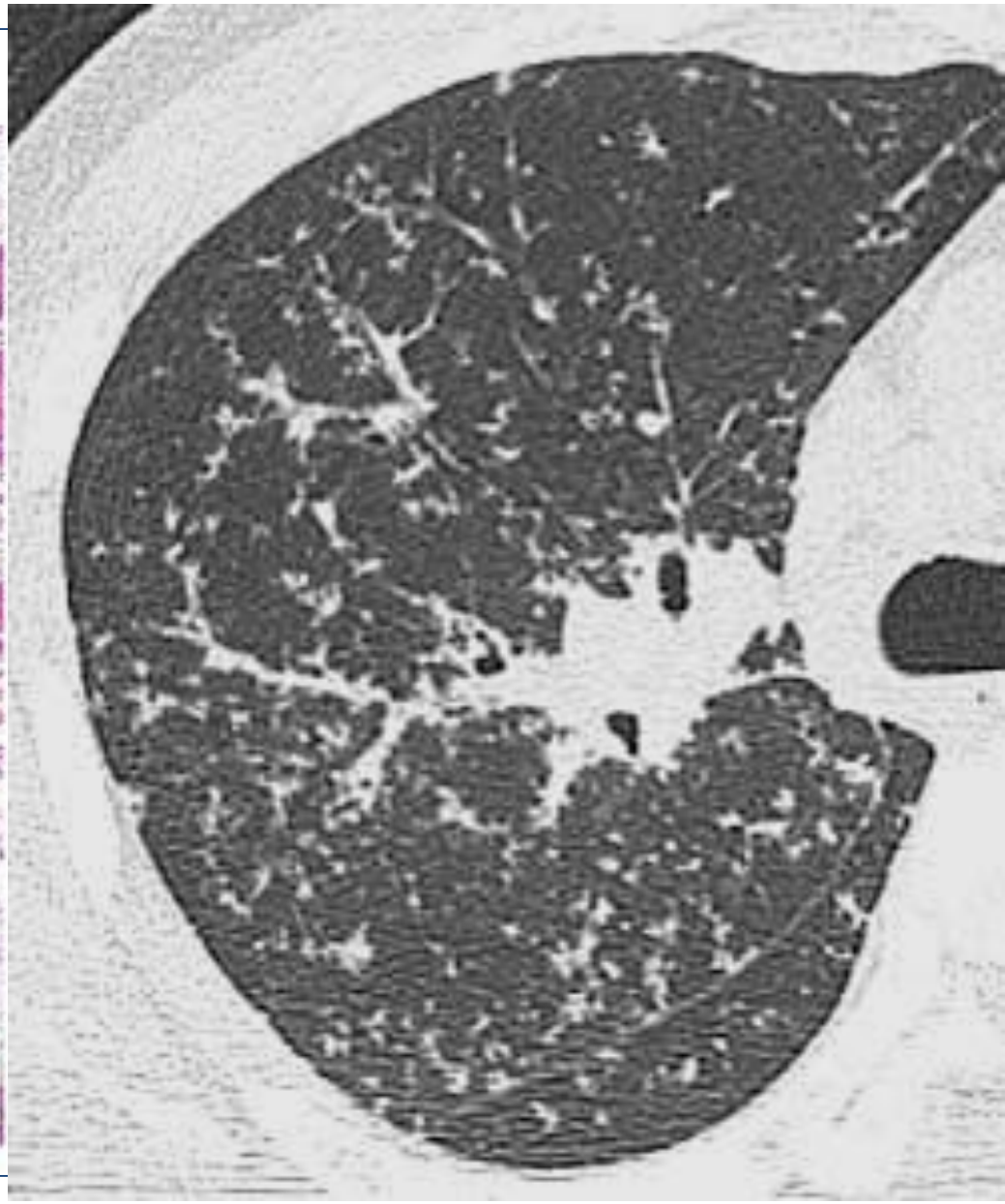




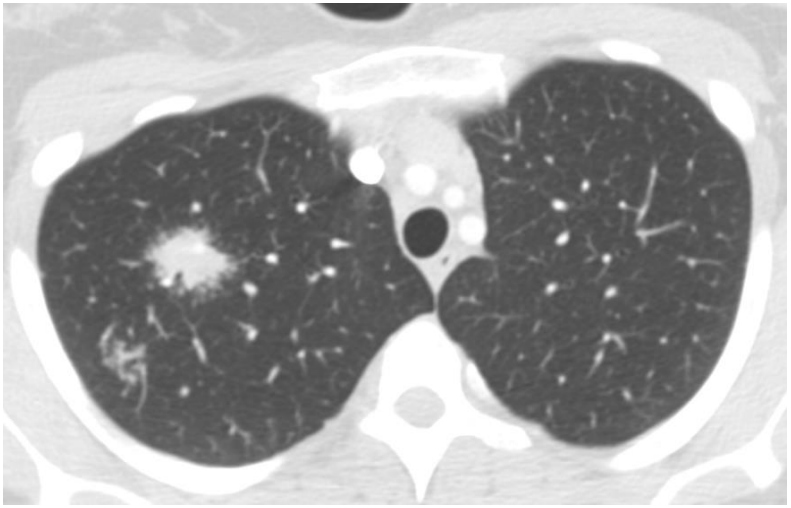
- 34 M with shortness of breath and Erythema Nodosum
- <u>Dx: Sarcoidosis</u>
  - Upper lobe predominant peri-lymphatic nodules
  - Can be focal or localized to small areas
  - Confluent nodules create the galaxy sign
  - Mediastinal lymph node (lambda sign on CXR)
  - Can see fibrosis in end stage

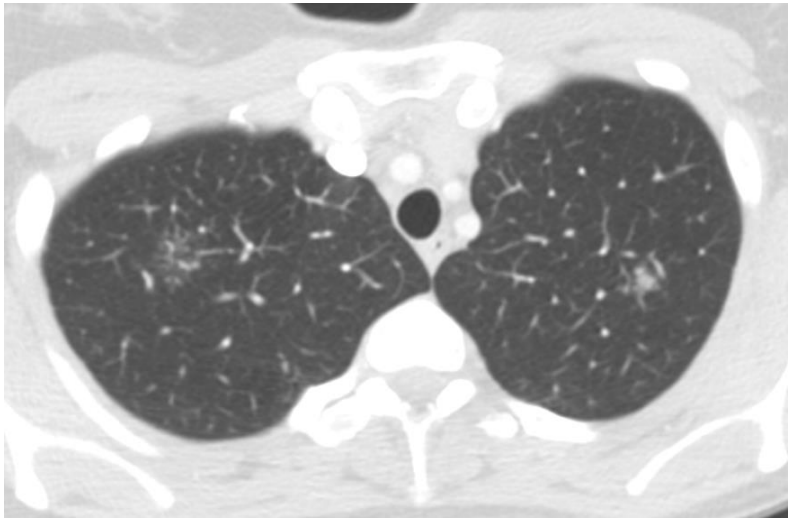
- Always think to sarcoidosis if unusual pattern!

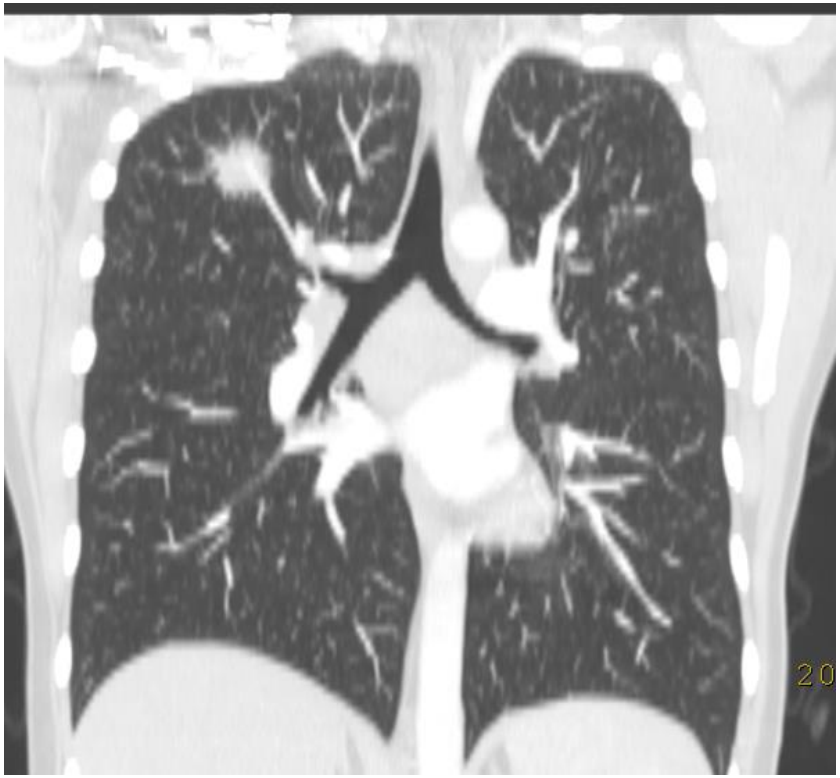


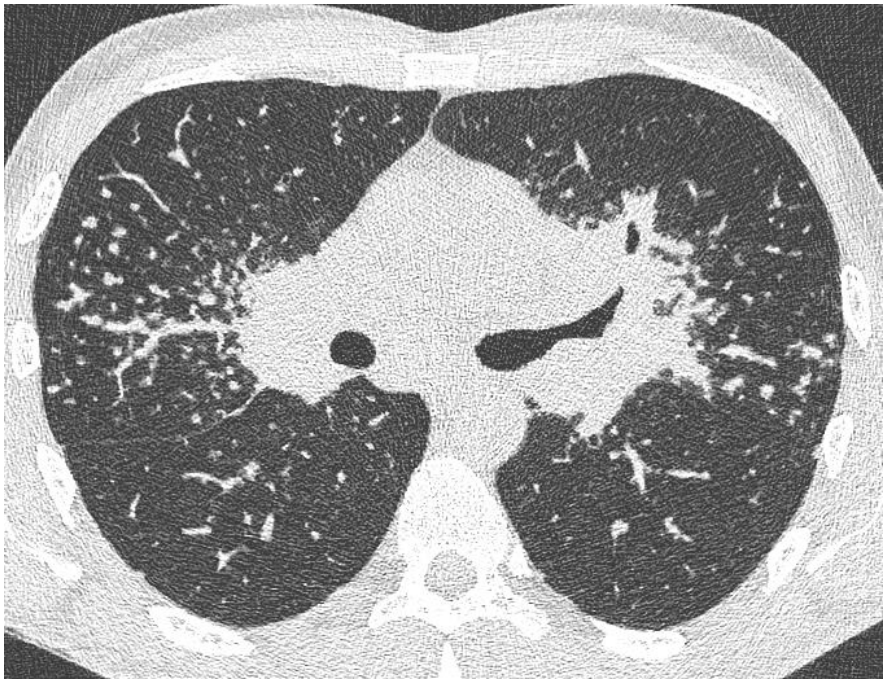


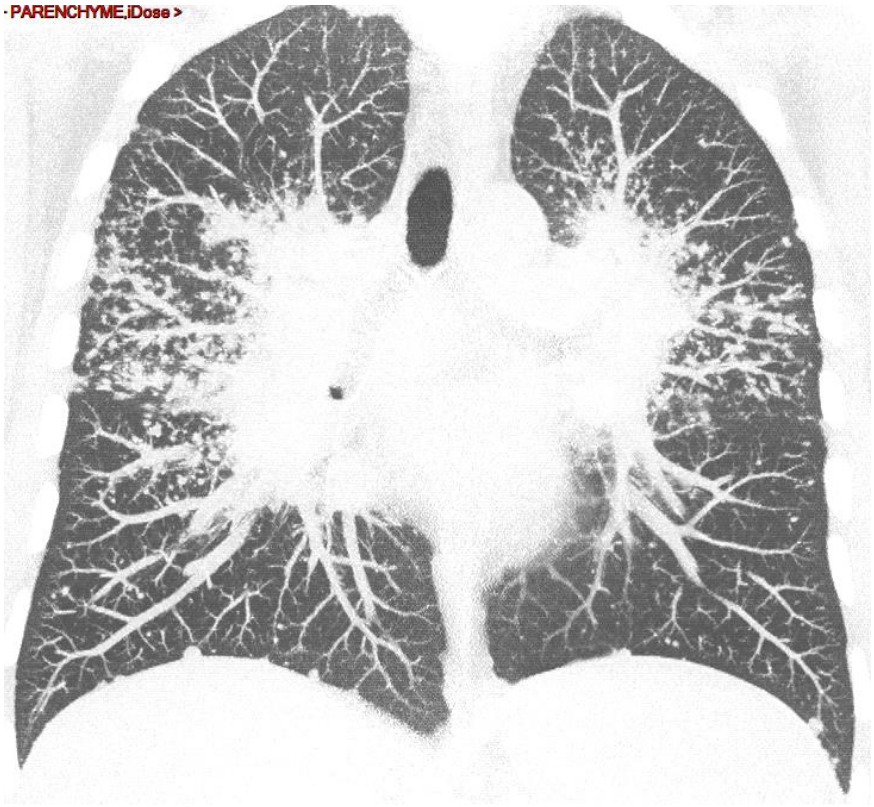
Courtesy of Gilbert Ferretti, CHU Grenoble, France



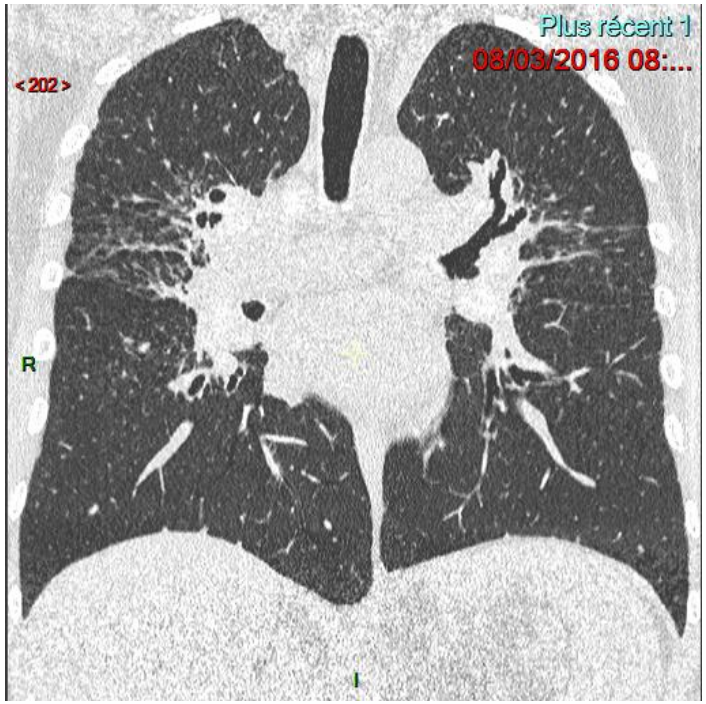






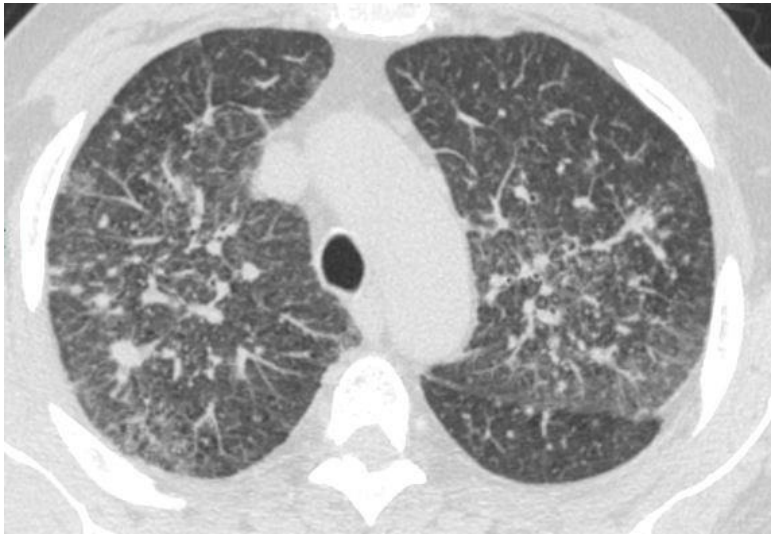


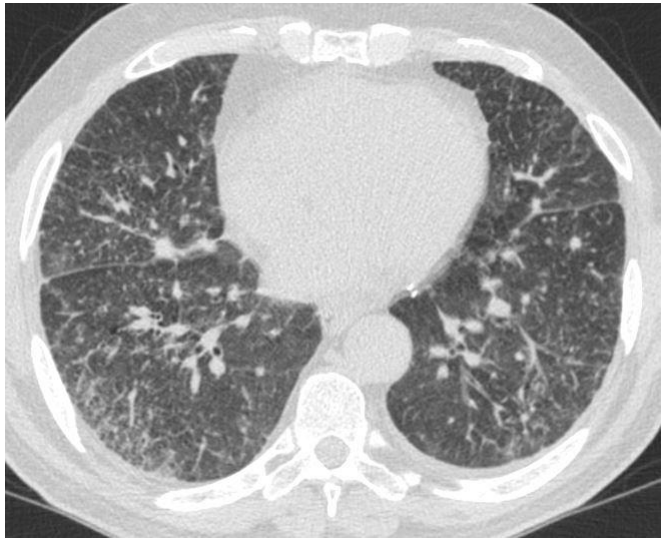
13/09/2013

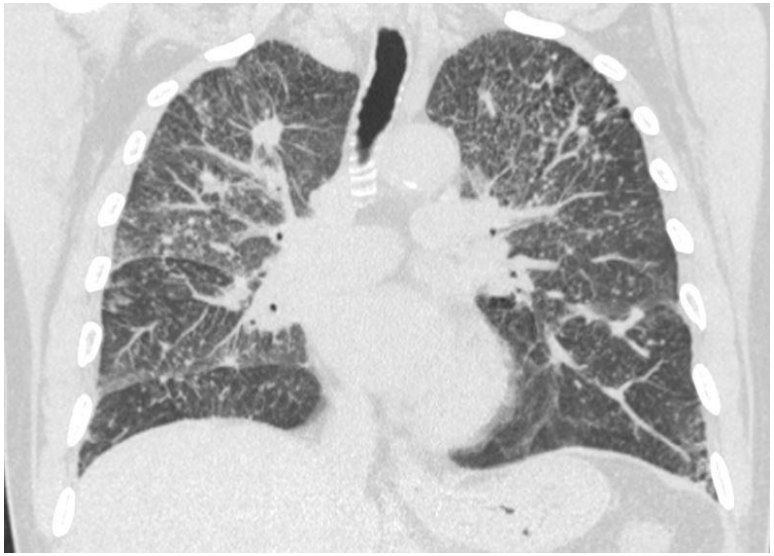


08/03/2016

Peri-lymphatic nodules ddx - Silicosis

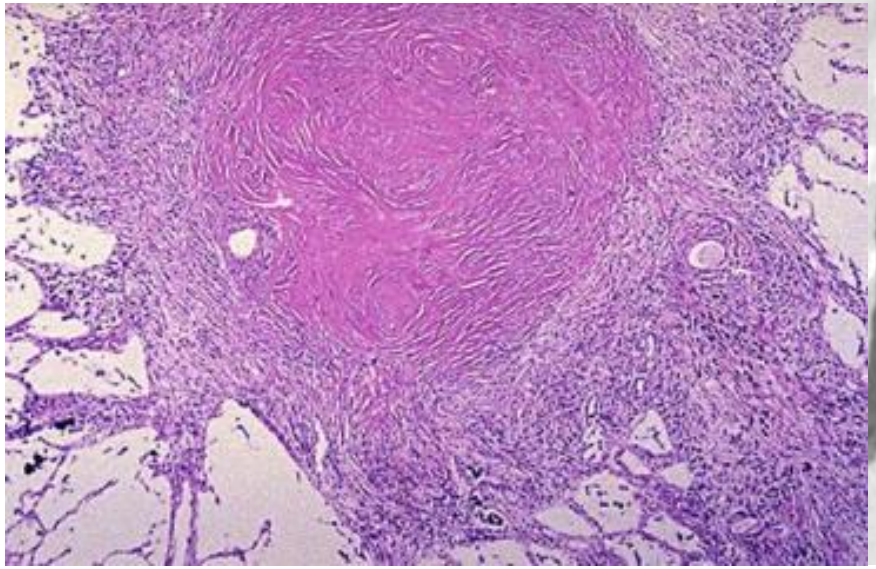


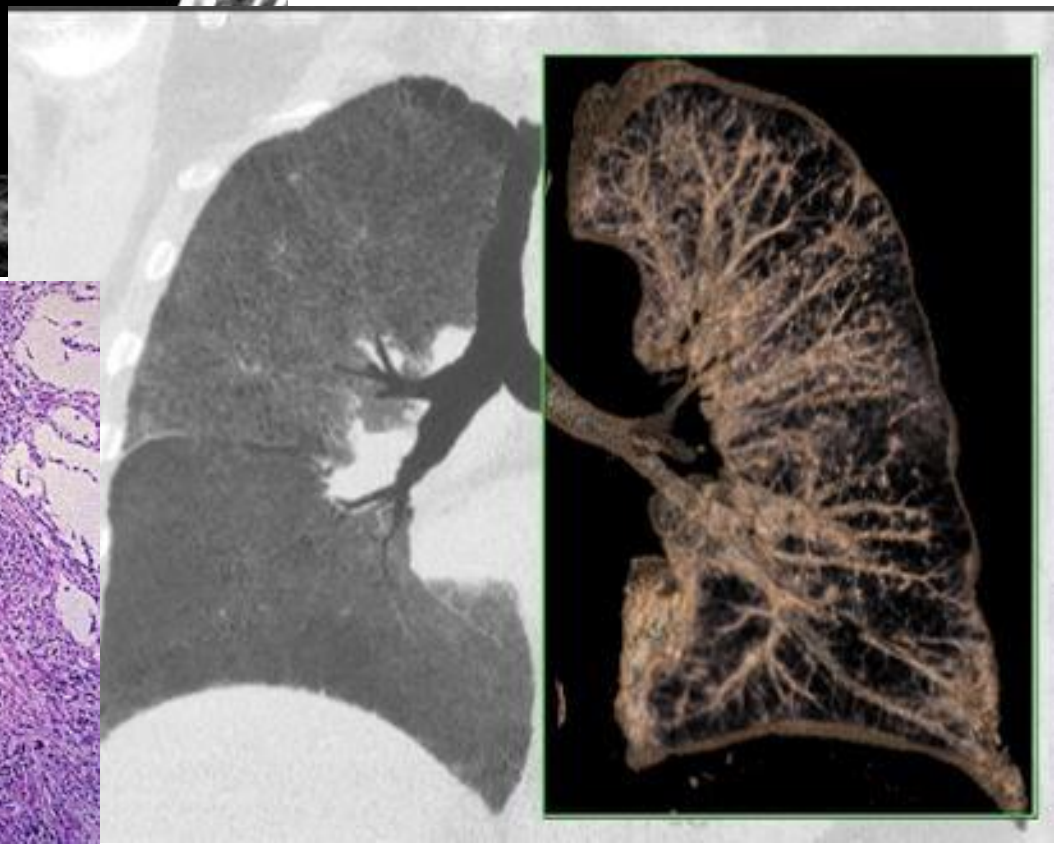




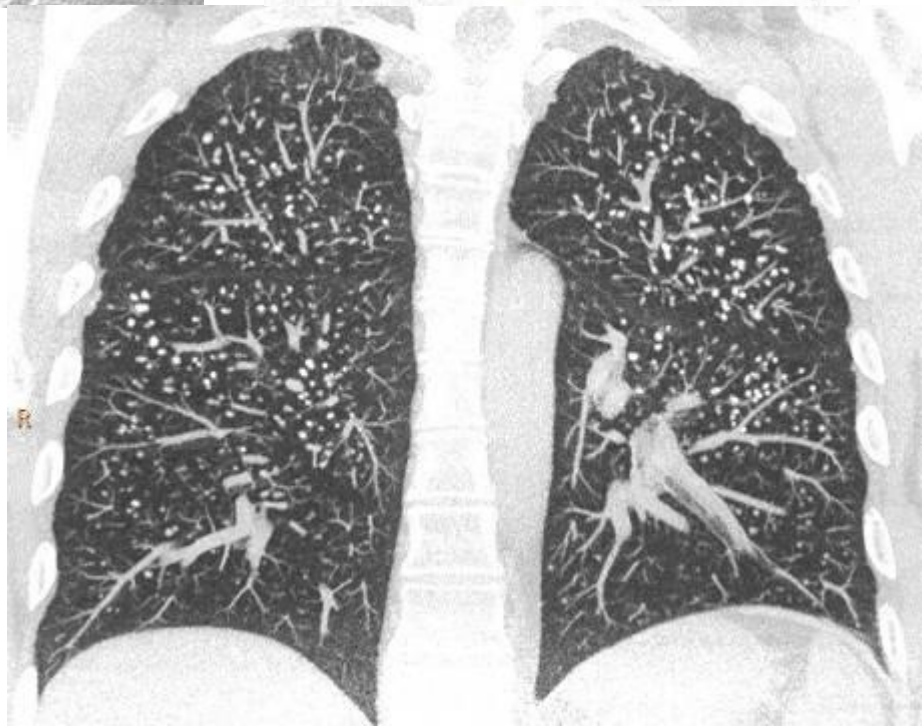
- 84-year old man, fever, known for anthracosilicosis
- <u>Dx: Silicosis</u>
  - Similar appearance to sarcoidosis but history of exposure (e.g. mining)
  - Upper lobe predominant peri-lymphatic nodules & lymphadenopathy
  - Confluent fibrosis refered to as progressive massive fibrosis
  - 5% of silicosis cases exhibit characteristic peripheral (egghell) calcifications of LNs

Associated emphysema
Calcified lymphnodes
Perilymphatic micronodules

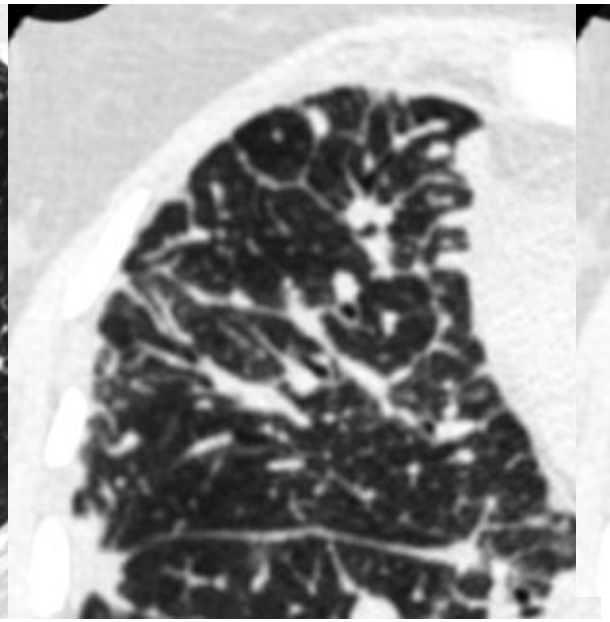


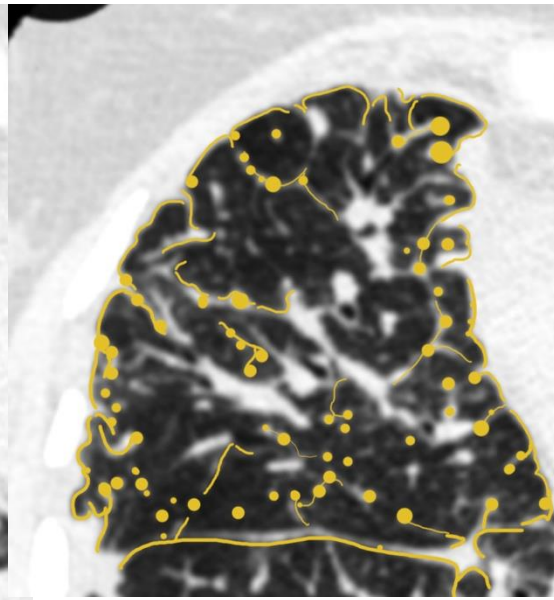


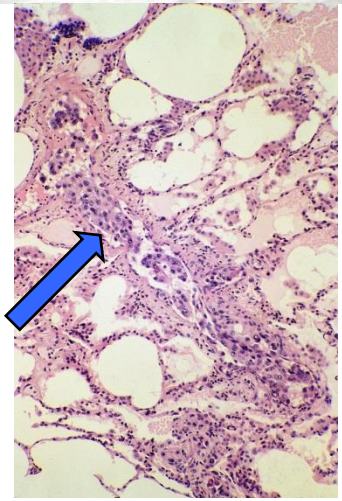
silicosis



Peri-lymphatic nodules ddx – Lymphangitic carcinomatosis

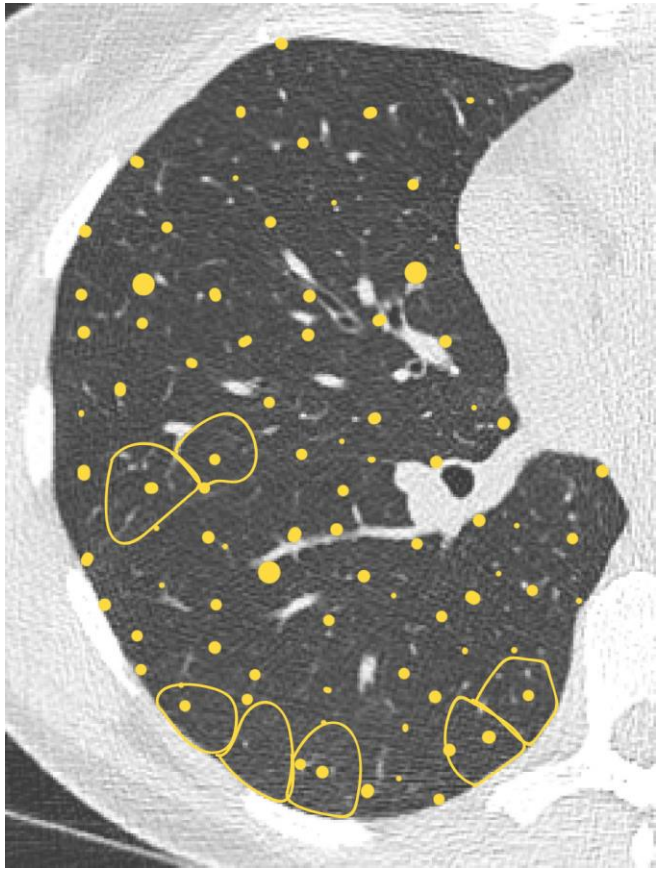






- 60 F with history of breast cancer
- <u>Dx: lymphangitic carcinomatosis</u>
  - Tumor growth in lymphatic system of lungs
  - Can be focal or unilateral in up to 50 % of patients

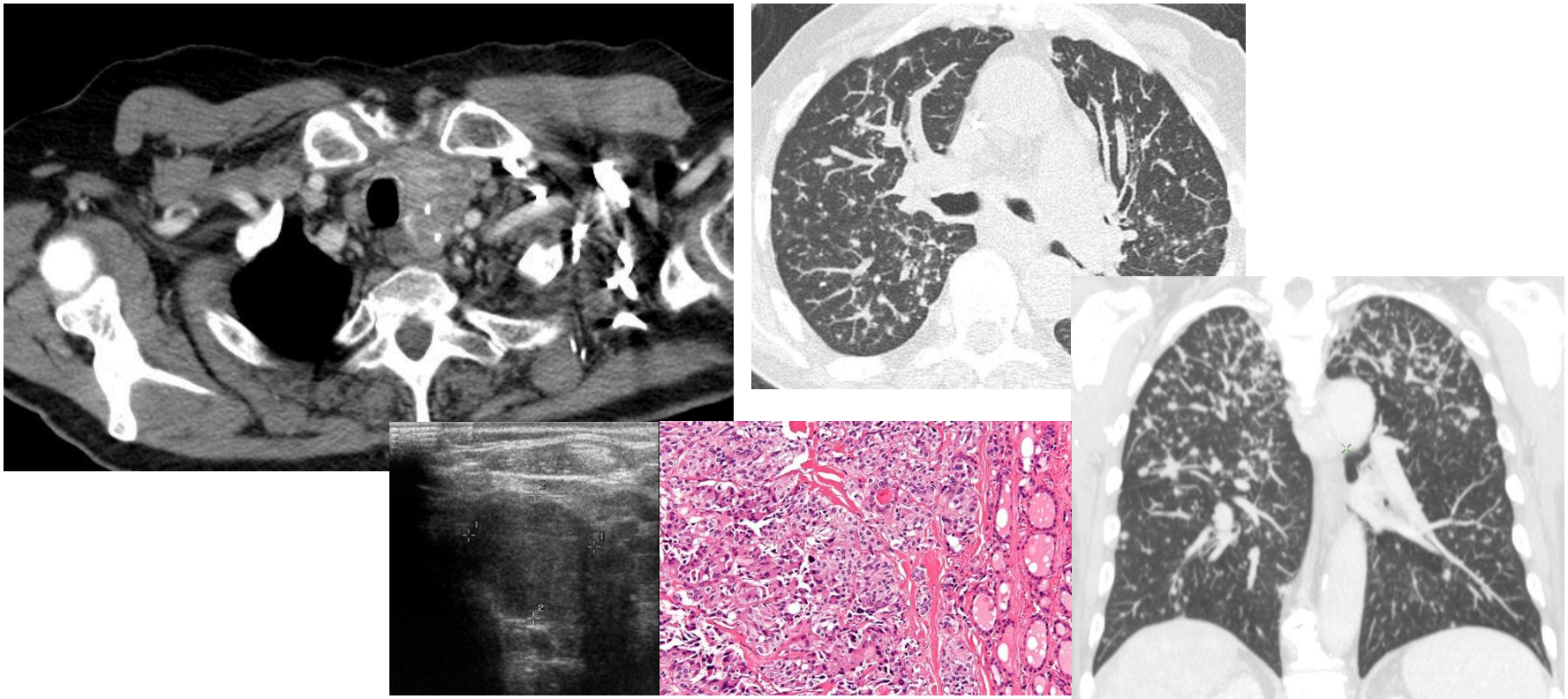
C. Random nodules Differential Diagnosis



Random distribution = hematogenous

- **<u>Hematogenous metastases</u>**
  - May occur in 20-30 % of malignancies
  - Most occur in outer 1/3 of the lung
- **<u>Hematogenous infections</u>**
  - Miliary tuberculosis
  - Disseminated fungal infection (e.g., histoplasmosis, candidiasis)

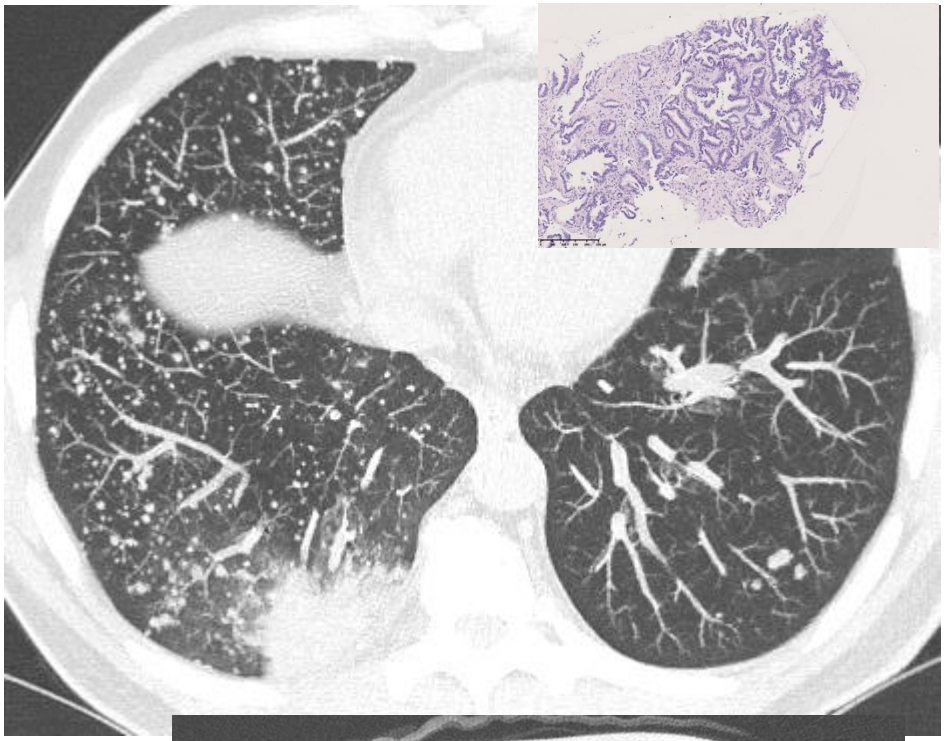
Random nodules ddx – Miliary metastasis

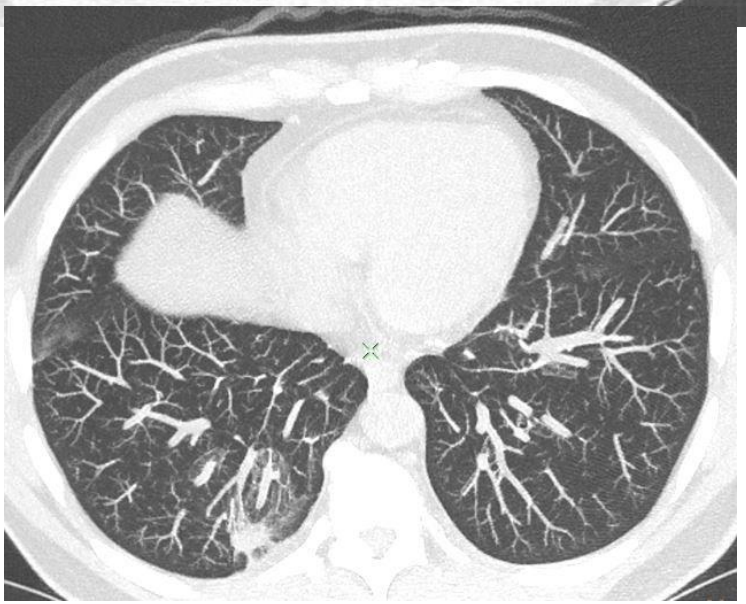


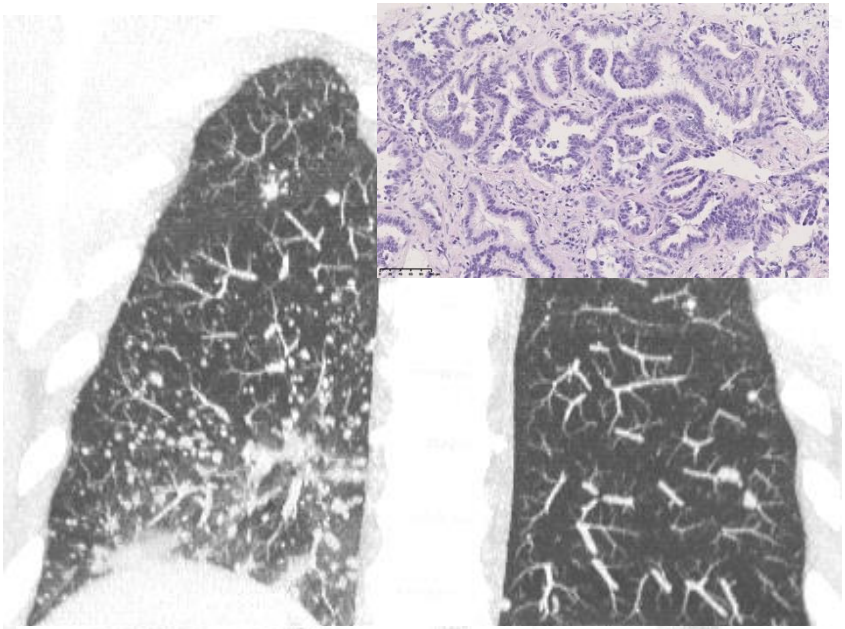
- 72 M with history of medullary thyroid cancer
- <u>Dx: Miliary metastases</u>
  - Most often seen with medullary thyroid carcinoma, melanoma, renal cell carcinoma, ovarian carcinoma

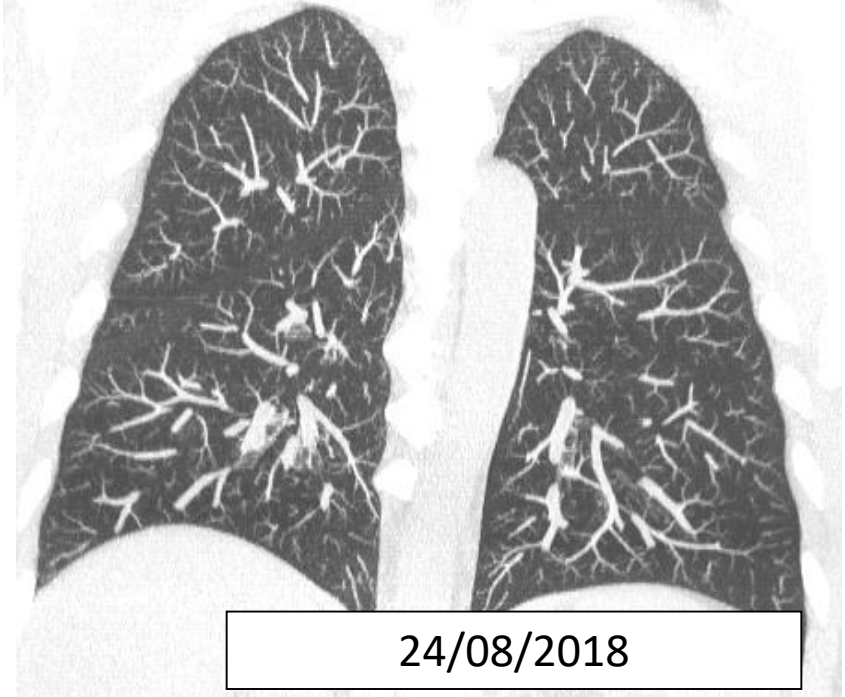
Lepidic adenocarcinoma

16/08/2016



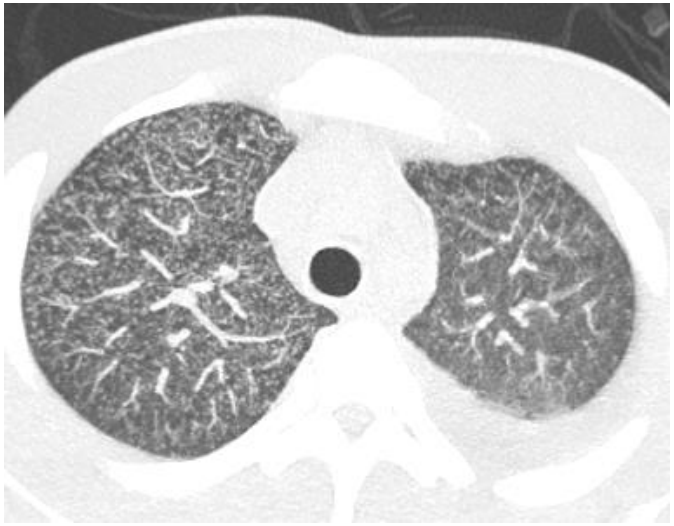


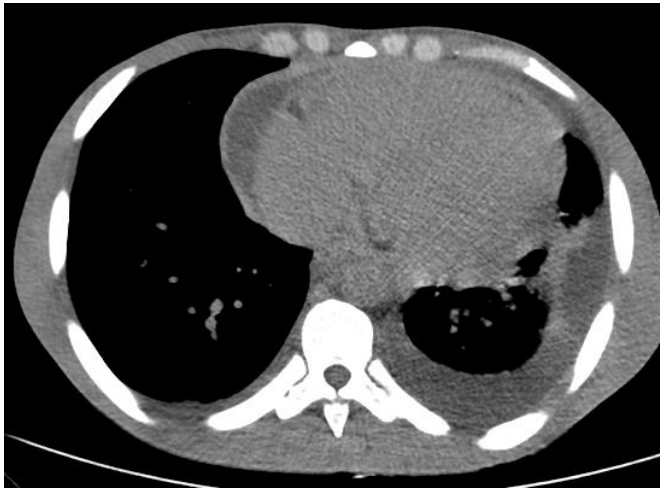




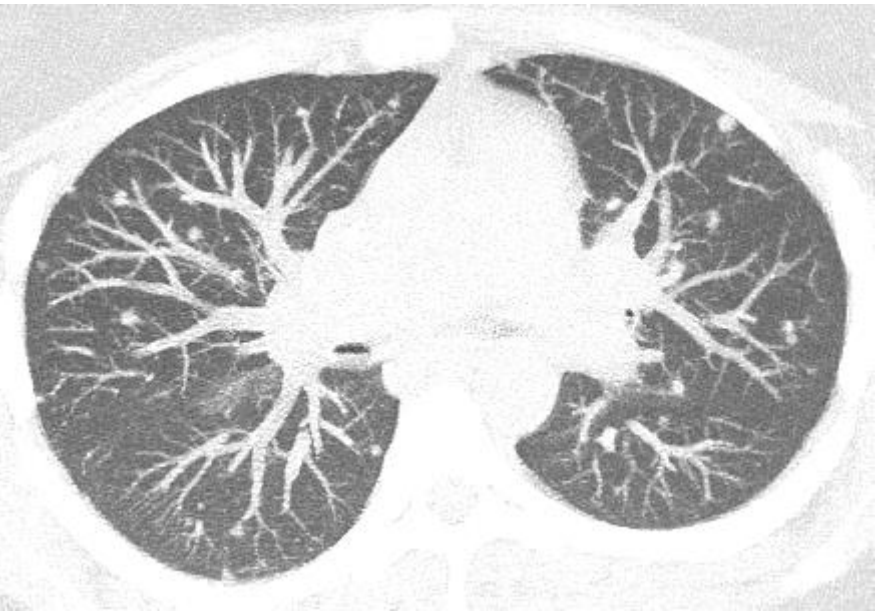
24/08/2018

Random nodules ddx – Miliary TB

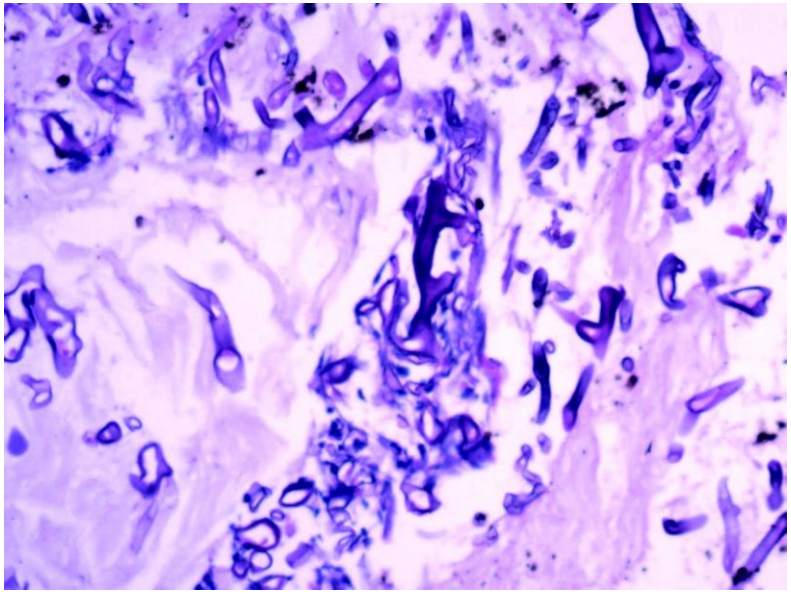




- 21 M with exusdative pleuro-pericarditis
- <u>Dx: Miliary tuberculosis</u>
  - Hematogenously disseminated TB
  - May affect any organ
  - Miliary nodules within the lung (diffuse uniform)
  - Commonly associated with necrotic lymphadenopathy
  - Higher risk of miliary spread in immunocompromised patients



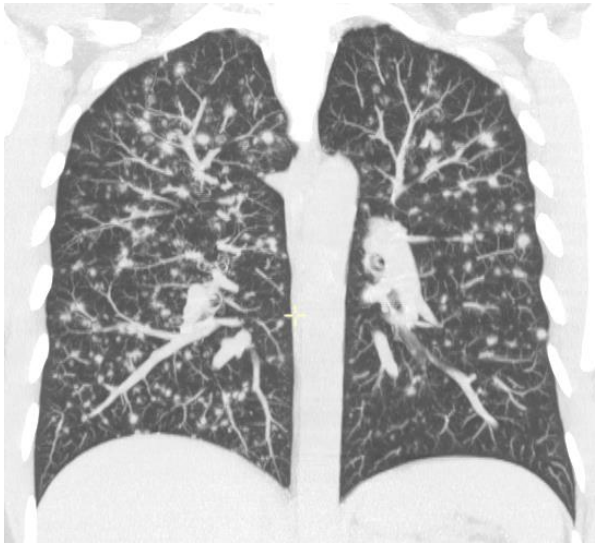
Random distribution



Mucormycosis

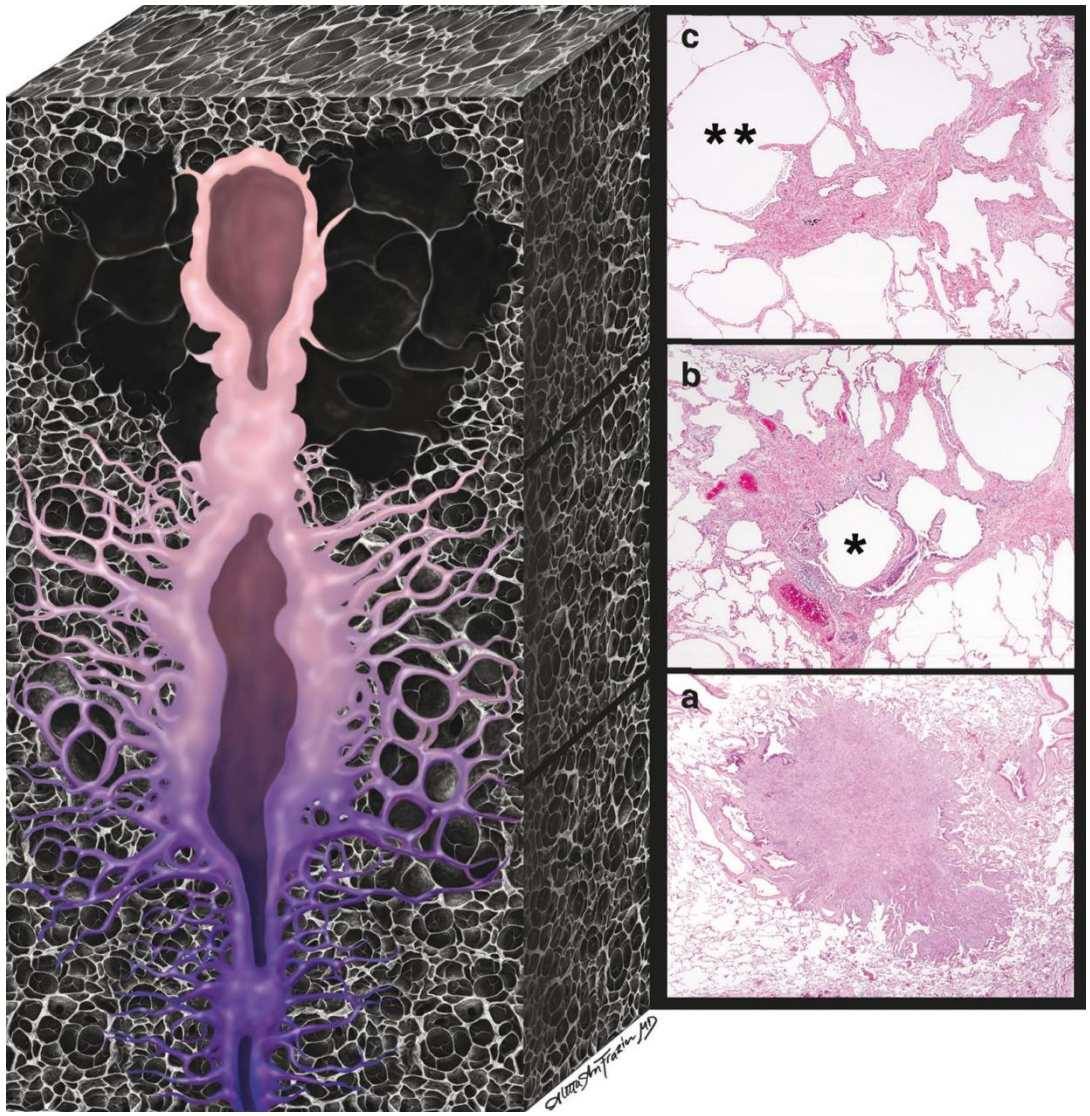
28-year old woman-fever-LLA under chemotherapy

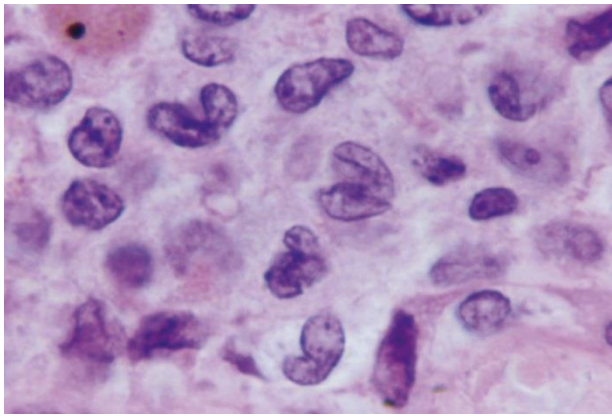
Random distribution: Histiocytosis

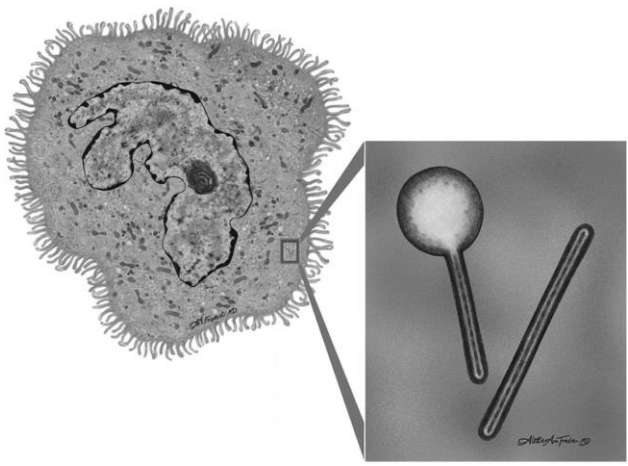


- 33 F with chest pain
- <u>Dx: Langerhans histiocytosis</u>
  - Micronodules in random distribution
  - First phases of the disease
  - Excavated nodules and cysts

Langerhans Histiocytosis







Abbot Radiographics 2004

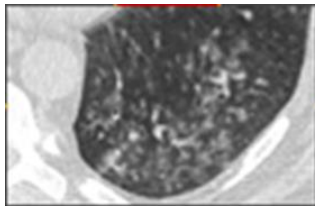
Take Home messages

- 3 main patterns to classify lung microndules
  - Centrilobular
  - Perilymphatic
  - Random
- Restrain differential diagnosis
  - By distribution
  - By clinical History
- Check associated findings

Summary Diagram

Involves pleura ?

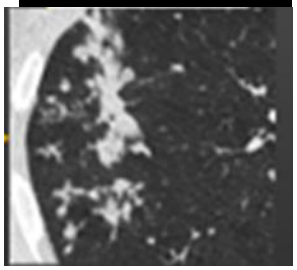
No



Centrilobular

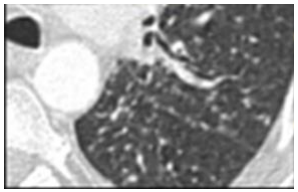
Use distribution & clinical info

Tree-in-bud



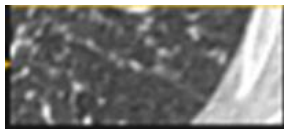
- Aspiration
- TB/MAI
- Viral infection

Yes



Pleura, fissure
Peri-bronchovascular

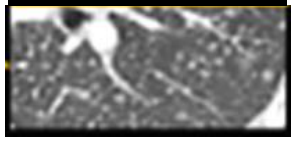
Peri-lymphatic



- Sarcoidosis
- Pneumoconioses
- Lymphangitic carcinomatosis

Diffuse, uniform

Ramdom



- Miliary metastasis
- Miliary TB
- Disseminated furgal infection

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