

Bronchiolitis and Non-Cystic Fibrosis Bronchiectasis

Christopher H. Fanta, M.D.

Pulmonary and Critical Care Division

Brigham and Women's Hospital

Partners Asthma Center

Harvard Medical School



Disclosure of Conflicts of Interest

None.

Bronchiolitis: Definition

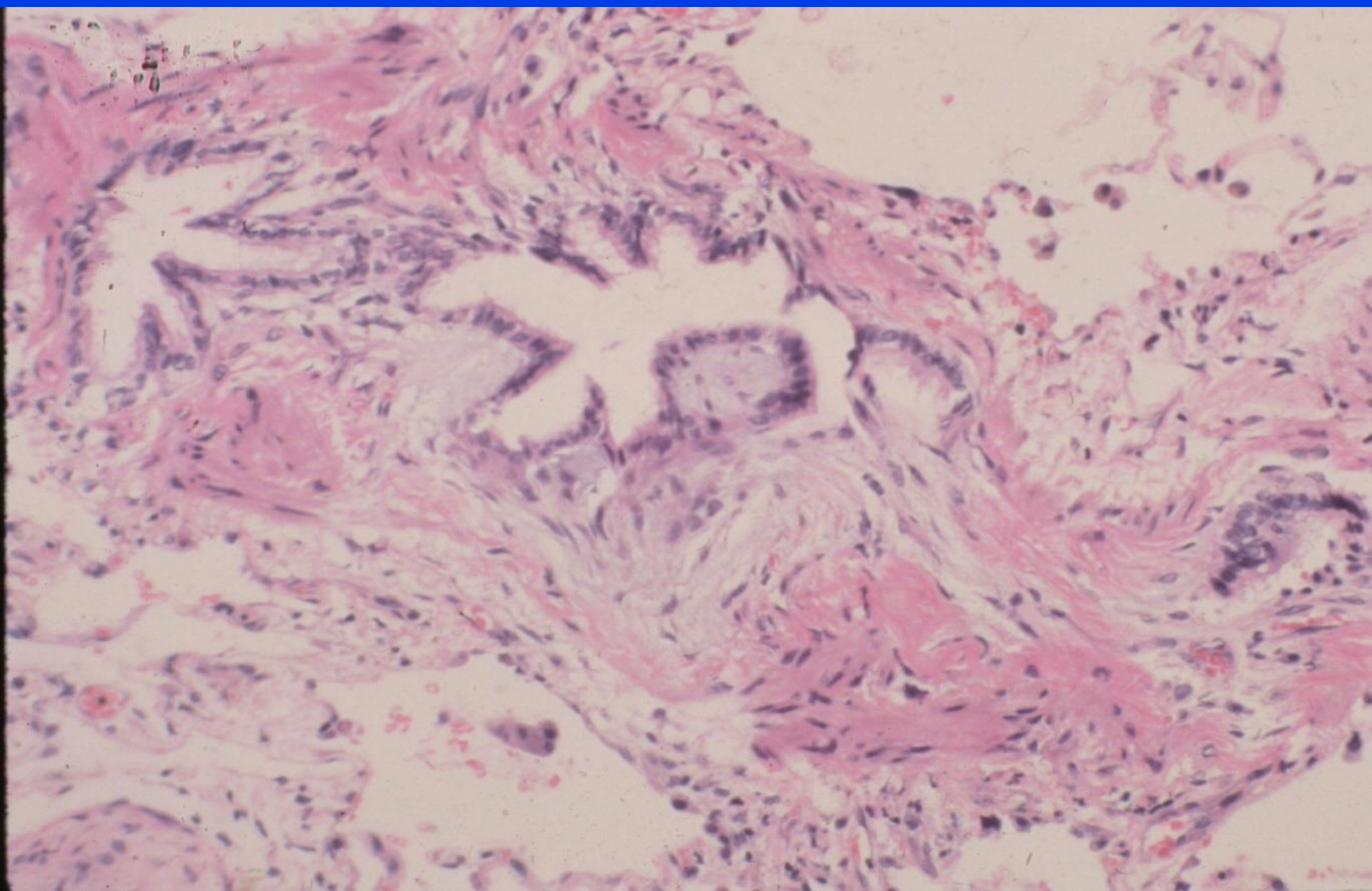
Acute or chronic cellular inflammation or fibrosis of the bronchiolar walls.

Acute: Viral (e.g., RSV), mycoplasma
Aspiration

Chronic: Follicular bronchiolitis (C-V diseases)
Mineral dust bronchiolitis
Cigarette smoke respiratory bronchiolitis
Diffuse panbronchiolitis (Japan)
Bronchiolitis obliterans

Bronchiolitis Obliterans: Etiologies

- Toxic fume inhalation (e.g., nitrogen oxides in silo filler's lung disease; diacetyl in workers exposed to artificial butter flavoring for popcorn; vaping)
- Post-infectious (e.g., viral, mycoplasma)
- Immune-mediated
 - Rheumatoid arthritis
 - Ulcerative colitis
 - Paraneoplastic pemphigus/other autoimmune blistering diseases
 - S/P transplantation (e.g., lung, allogeneic bone marrow)



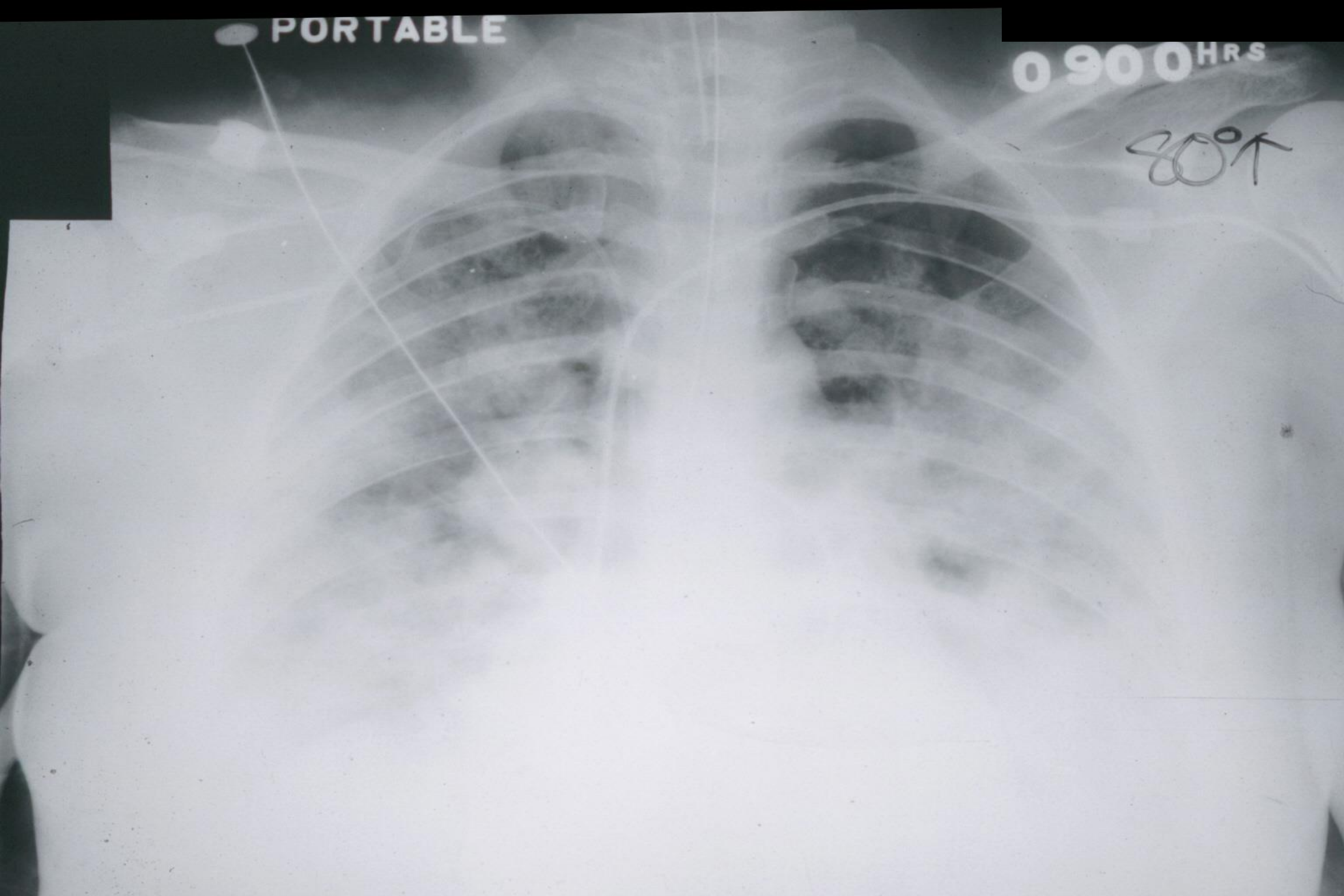
Bronchiolitis Obliterans: Clinical Features

- Hx: dyspnea, non-productive cough
- P.E.: inspiratory crackles; mid-inspiratory squeak; expiratory wheezes
- CXR: hyperinflation; \pm small patchy parenchymal infiltrates

● PORTABLE

0900 HRS

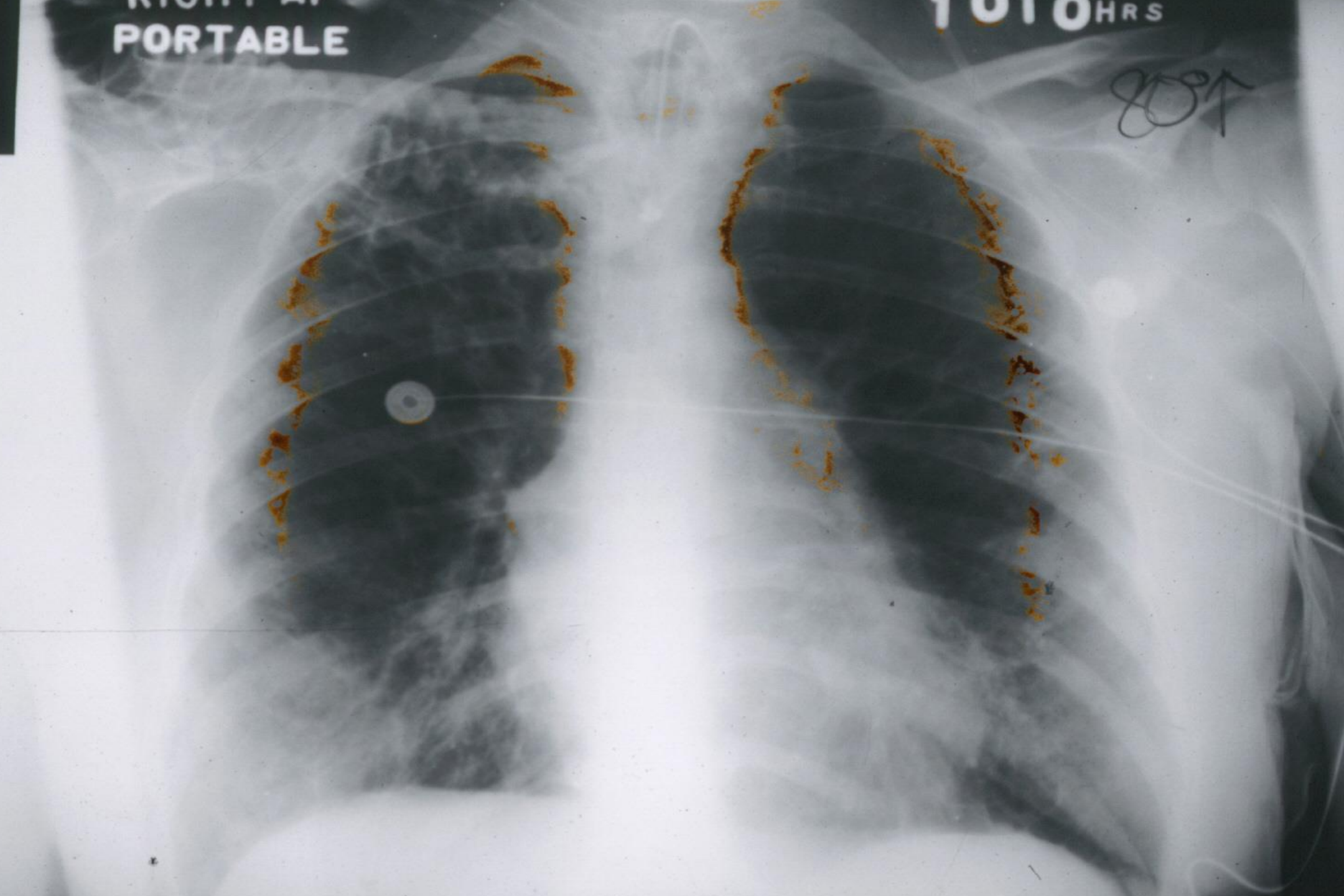
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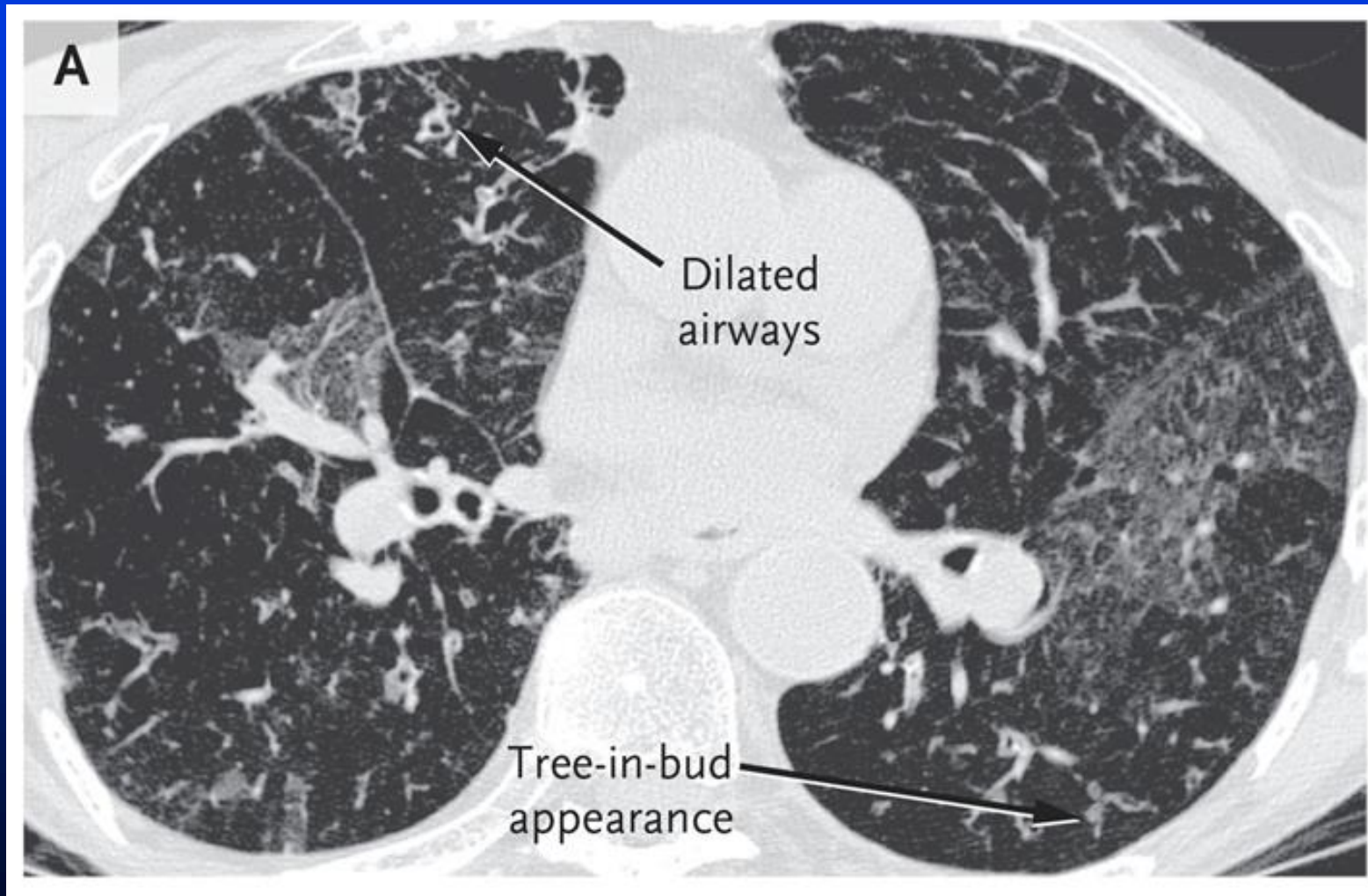


Radiographic Findings on CT Imaging

- Centrilobular micronodules (often tree-in-bud distribution)
- Bronchiolectasis
- Bronchial wall thickening
- Mosaic attenuation

Winningham PJ, et al., *RadioGraphics* 2017;
37:777–94.

CT Scan in Bronchiolitis



Barker AF et al.
N Engl J Med
2014;370:1820-28.

Bronchiolitis Obliterans: Diagnosis

- Typically, a clinical diagnosis (without biopsy).
- Based on airflow obstruction in the appropriate setting and in the absence of alternative etiologies (such as asthma or COPD).
- Lung biopsy infrequently employed (exception = s/p lung transplantation).

Bronchiolitis Obliterans: Treatment

- Corticosteroids (systemic/inhaled); bronchodilators; O₂ as needed.
- (Post-transplant: extracorporeal photopheresis; etanercept; montelukast)
- Experimental: anti-IL-1R; inhaled liposomal cyclosporine A

Bronchiolitis obliterans is often refractory to therapy.

Mystery Case

67-year-old woman with chronic cough and exertional dyspnea for more than 10 years.

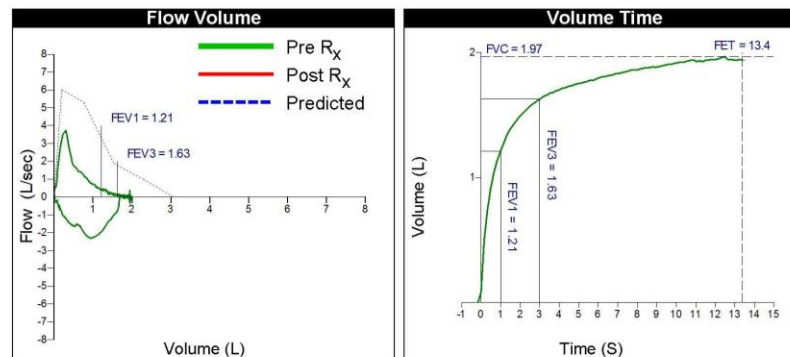
- Lifelong non-smoker; MM alpha-1 AT phenotype.
- Allergy testing negative.
- Treated for asthma without improvement.
- Treated for GERD, including fundoplication, with little change.
- No family history of lung disease; retired school administrator.

Mystery Case – cont.

Physical exam is normal.

Spirometry:

Spirometry		Predicted Range		Pre Bronchodilator	
		Mean	95%	Actual	% Pred
FVC Effort Time		----	----	16:27	----
FEV ₁	L	2.39	1.76	1.21	51
FVC	L	3.07	2.27	1.97	64
FEV ₁ / FVC	%	78	66	61	78
FEV ₆	L	3.08	2.38	1.80	58
FEV ₁ / FEV ₆	%	80	71	67	84
FEF ₂₅₋₇₅	L/s	2.05	0.98	0.56	27
PEFR	L/s	6.01	4.25	4.25	71
PIFR	L/s	4.01	----	2.32	58



Spirometer Calibration to ATS

By: Jennys Mindy Frias
Same Day - 12:52 PM

Exhaled Nitric Oxide Assay:

Measured eNO (single exhalation at 3L/min): **13** (ppb)





Diagnosis: Diffuse Idiopathic Pulmonary Neuroendocrine Cell Hyperplasia (DIPNECH)

- Proliferation of neuroendocrine cells along airway epithelium, with multiple carcinoid tumorlets (<5 mm) or carcinoid tumors (>5 mm), and constrictive obliterative bronchiolitis.
- Treatment: systemic steroids; somatostatin analogs (e.g., octreotide, lanreotide).

Bronchiectasis: Definition

Irreversible airway wall damage and dilatation (-ectasis) of the bronchi, usually associated with chronic airway infection

Clinical Presentations: Historical Features

- Chronic productive cough
- Recurrent hemoptysis
- Recurrent focal pneumonia
- Associations: sinusitis, infertility

Clinical Presentations: Physical Examination

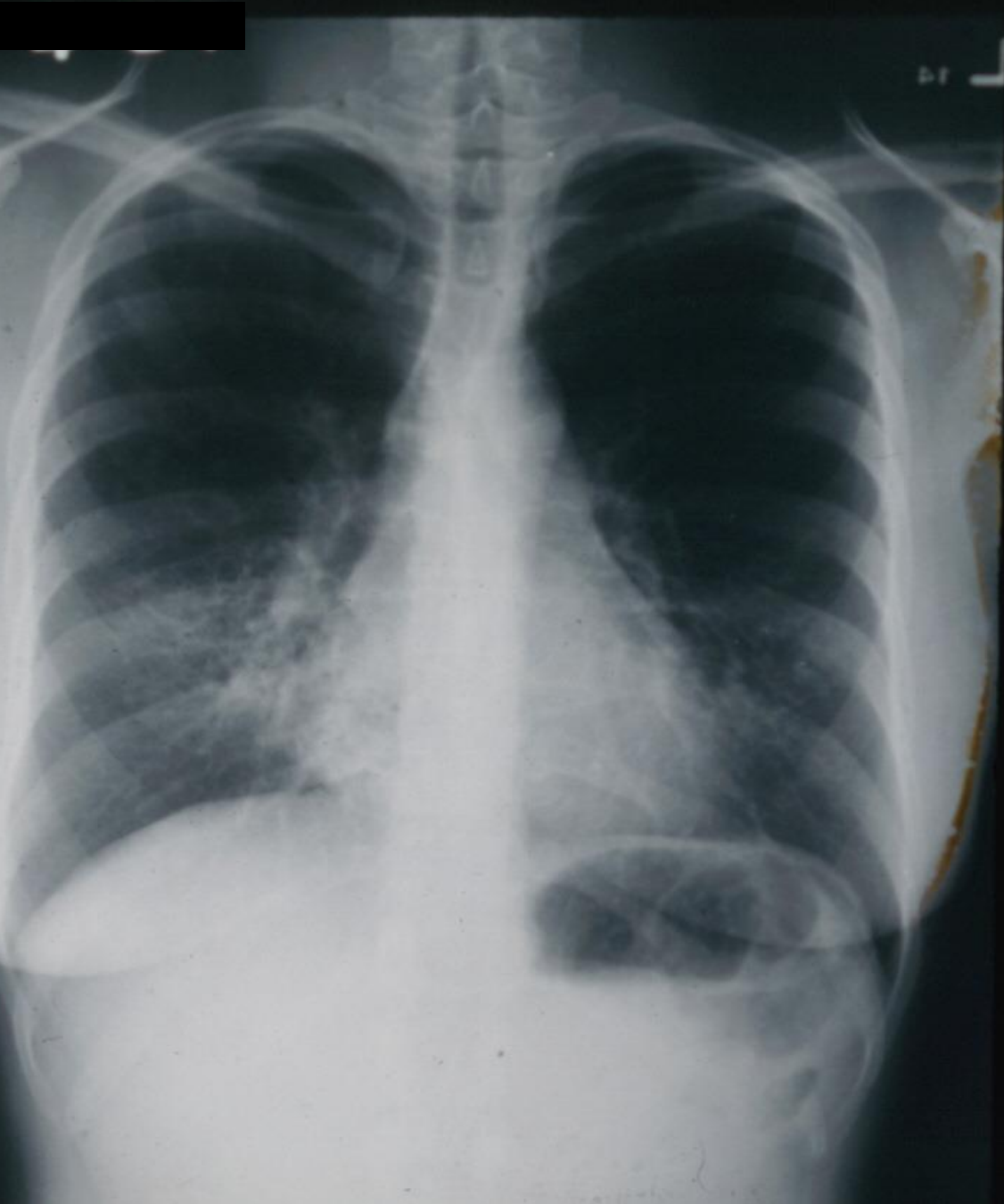
- Focal inspiratory crackles
- Low-pitched wheezing (“rhonchi”)
- Clubbing

Clinical Presentations: Laboratory Data

- Purulent sputum
- Typical bacterial isolates, especially *Pseudomonas*
- Abnormal chest radiograph / CT scan
- Pulmonary function:
 - variable: obstruction, restriction, mixed obstructive and restrictive patterns

Chest Radiography

- Focal non-homogeneous infiltrate with orientation of markings in direction of bronchovascular bundles
- Volume loss
- “Tram lines”
- Other: cyst formation; mucoid impaction





Primary Ciliary Dyskinesia (Immotile Cilia Syndrome) (Kartagener's Syndrome)

- Bronchiectasis
- Sinusitis
- Situs inversus (50%)
- Immotile sperm

Classic description: ultrastructural abnormality of cilia
(e.g., absence of dynein arms)

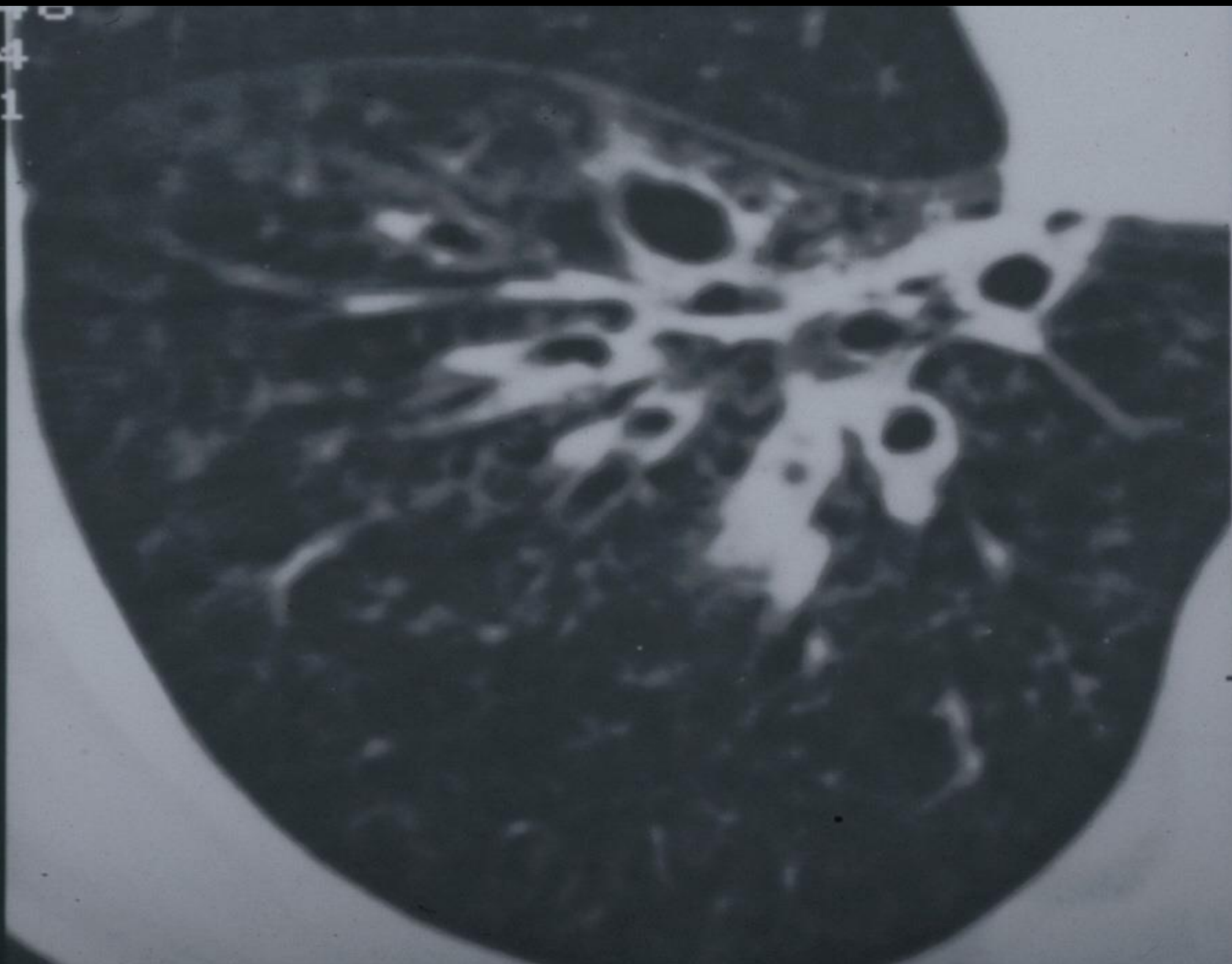
Diagnostic Techniques in Primary Ciliary Dyskinesia

- Transmission electron microscopy
- Videomicroscopy
- Immunofluorescence labeling
- Low nasal nitric oxide concentration
- Genetic analysis

Chest CT Appearance

- Lack of bronchial tapering
- Bronchial dilatation (internal diameter $>$ 1.5 x diameter of accompany vessel)
- Visualization of bronchi in lung periphery (within 1 cm of pleura)
- Bronchial wall thickening may be present

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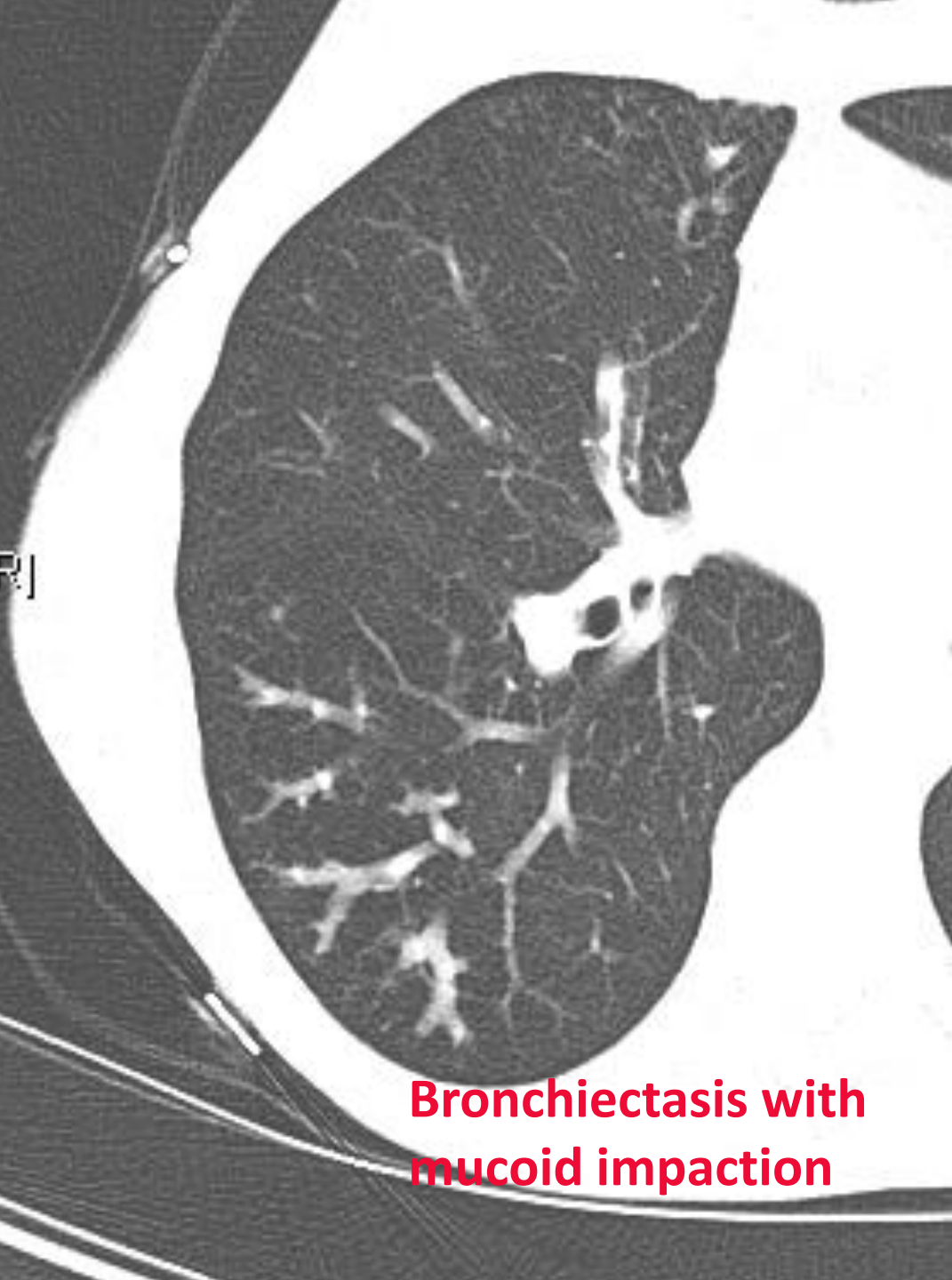


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**Bronchiectasis with
mucoid impaction**



Etiologies

- **Localized**
 - Post-pneumonic
 - Distal to bronchial obstruction
- **Widespread**
 - Cystic fibrosis
 - Primary ciliary dyskinesia
 - Hypogammaglobulinemia

Etiologies:

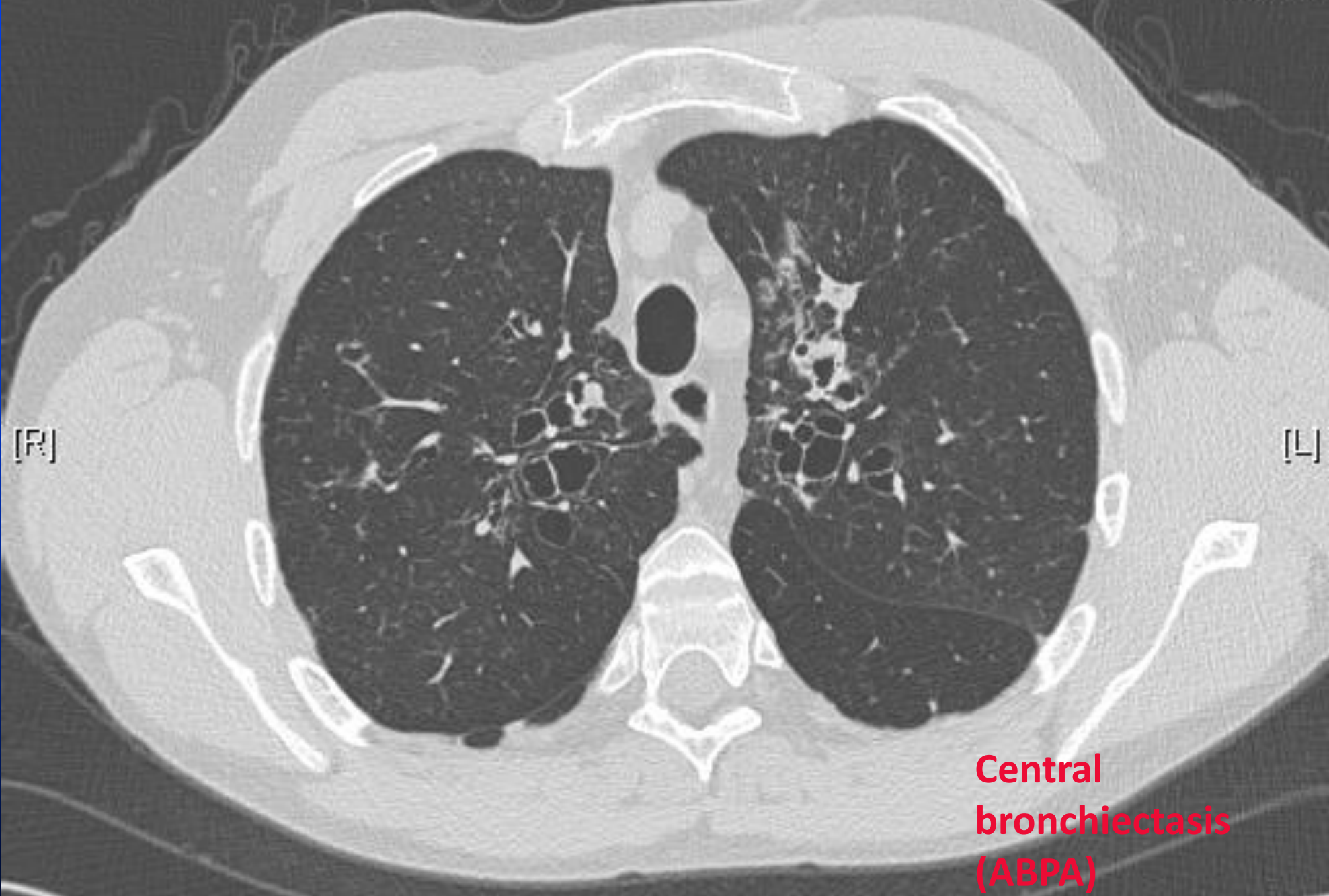
Special Syndromes

- Congenital anatomic defects
 - Williams-Campbell syndrome (bronchial cartilage deficiency)
 - Yellow nails syndrome (lymphatic hypoplasia)
 - Young's syndrome (bronchiectasis and azospermia)
 - Munier-Kuhn syndrome (tracheobronchomegaly: trachea >30 mm; right mainstem >20 mm, left mainstem >18 mm)
- Alpha-1 antitrypsin deficiency

Etiologies:

Other Observations

- AIDS
- Ulcerative colitis
- Rheumatoid arthritis
- Allergic bronchopulmonary aspergillosis
- Non-tuberculous mycobacterial infection



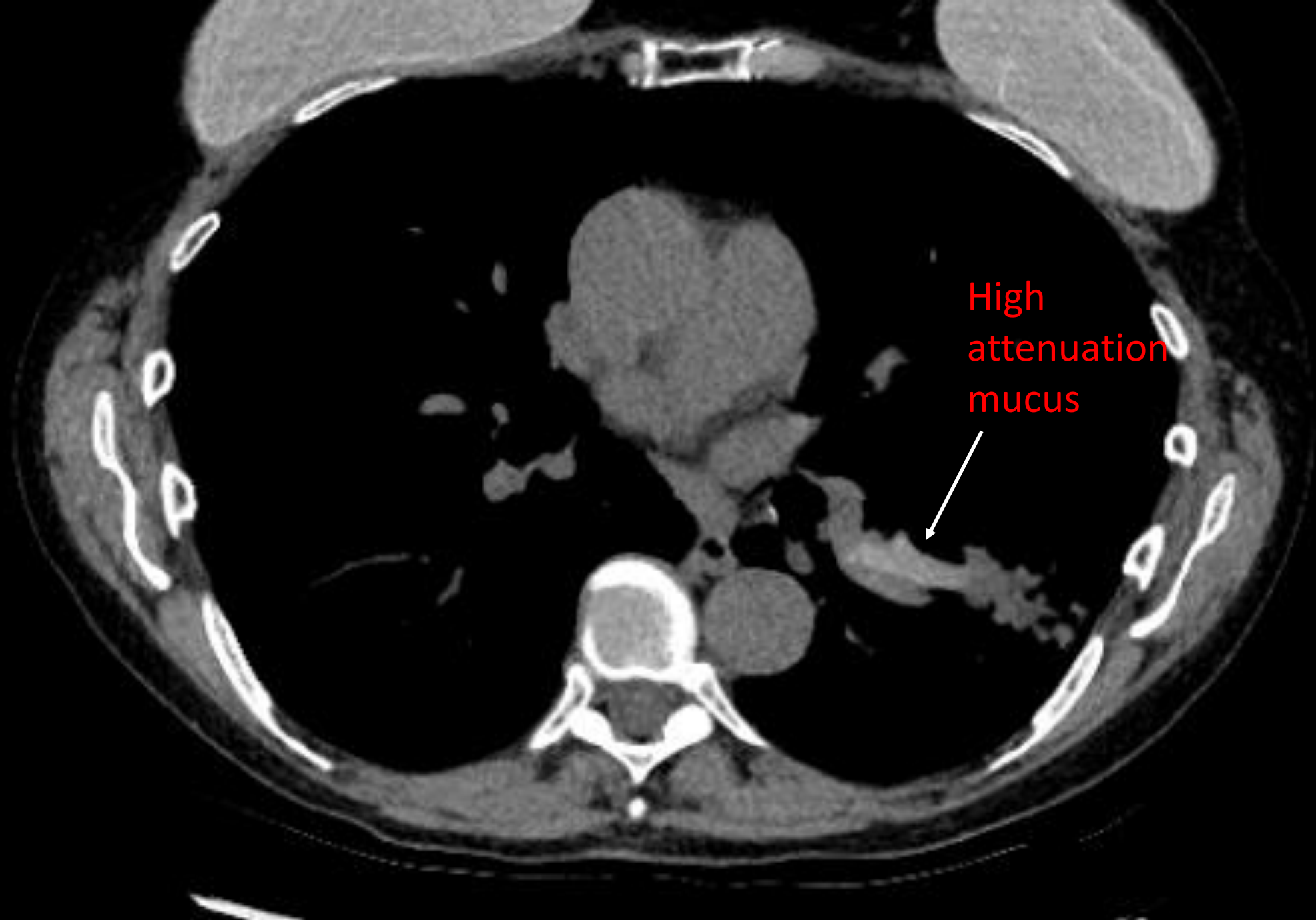
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**Central
bronchiectasis
(ABPA)**

Diagnosis of ABPA

- Asthma or cystic fibrosis
- ↑ IgE (>1000 IU/ml)
- Aspergillus-specific IgE (or skin test)
- Peripheral blood eosinophilia
- Aspergillus isolated from sputum
- Bronchiectasis; high attenuation mucus on chest CT imaging



High
attenuation
mucus

Patient Evaluation

- Chest X-ray/CT scan
- Pulmonary function/gas exchange
- Sputum cultures
- Immunoglobulin analysis
- Other: sweat chloride; genetic typing; semen analysis; nasal or bronchial biopsy; alpha-1 antitrypsin level; IgE and aspergillus-specific IgE
- Bronchoscopy (new, local disease)

Treatment

- Predisposing condition
 - Gammaglobulin replacement
 - Systemic corticosteroids/antifungals in ABPA
 - (?) α_1 -antitrypsin replacement in AAT deficiency
 - CFTR modulators

Treatment

- Bronchiectasis itself
 - I. Mild, intermittent symptoms
 - II. Persistent symptoms and morbidity
 - III. Acute-on-chronic exacerbations

Treatment

- Bronchiectasis itself
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Therapeutic Options

- Antibiotics
- Mucolytics
- Clearance of secretions
- Bronchodilators
- Anti-inflammatory Rx:
macrolide antibiotics; ? corticosteroids

Antibiotic Therapy

- Intermittent antibiotics
- Chronic, rotating antibiotics
- Inhaled antibiotics
- Intravenous antibiotics (for refractory infections or resistant pathogens)

Inhaled Antibiotics

- Tobramycin (nebulized, powder inhaler)
- Colistimethate (colomycin, Colistin)
- Aztreonam (Cayston)

Therapeutic Options

- Mucolytics
 - Iodides
 - Guaifenesin
 - Acetylcysteine (Mucomyst[®])
 - rh-DNase (Pulmozyme[®])
 - Hyperosmolar aerosols (3%-7% NaCl)

Therapeutic Options

- Clearance of secretions
 - Chest physiotherapy and postural drainage
 - PEP bronchial vibrating device
 - External electric vibrator
 - Pneumatic vest
 - Exercise

Cough-Assist Devices



Anti-Inflammatory Therapy

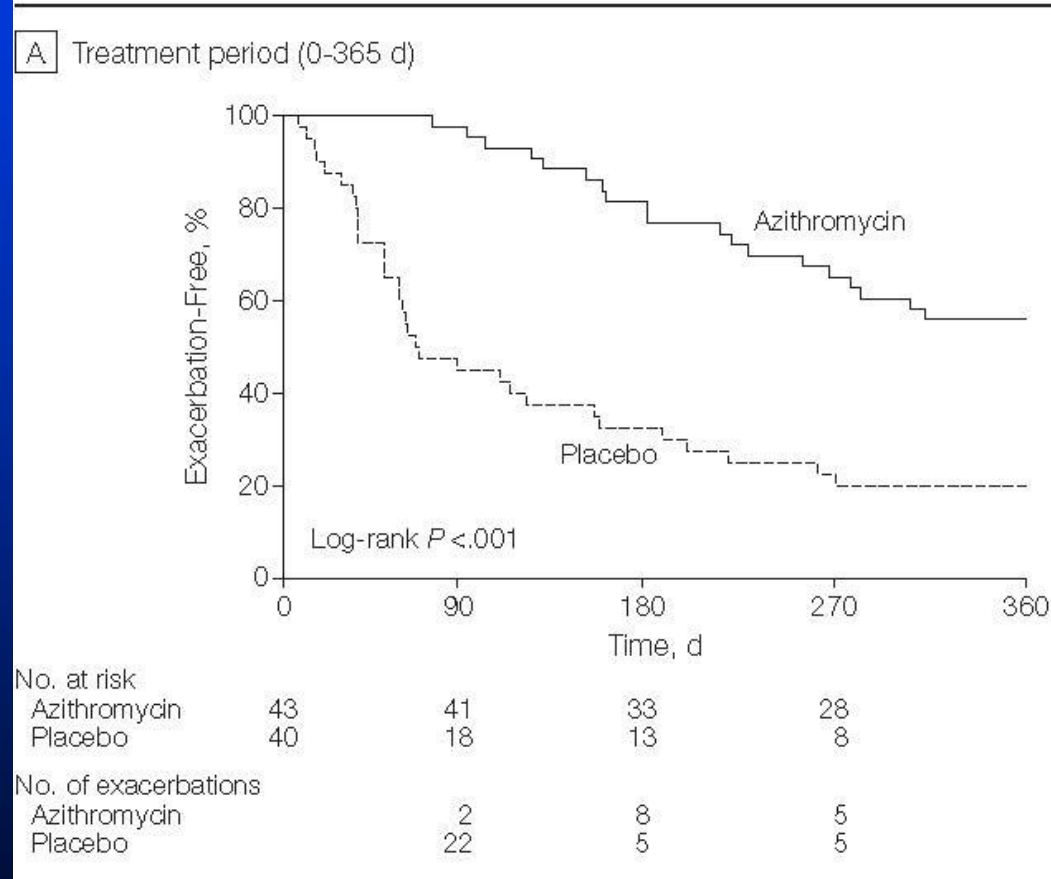
- Inhaled corticosteroids
- Macrolide antibiotics
 - Two randomized, placebo-controlled trials of azithromycin found fewer exacerbations over 1 year of observation compared with placebo.

Altenburg J, et al. *JAMA* 2013; 309:1251-9.

Wong C, et al. *Lancet* 2012; 380:660-7.

BAT Trial

Figure 2. Proportion of Patients Remaining Exacerbation Free



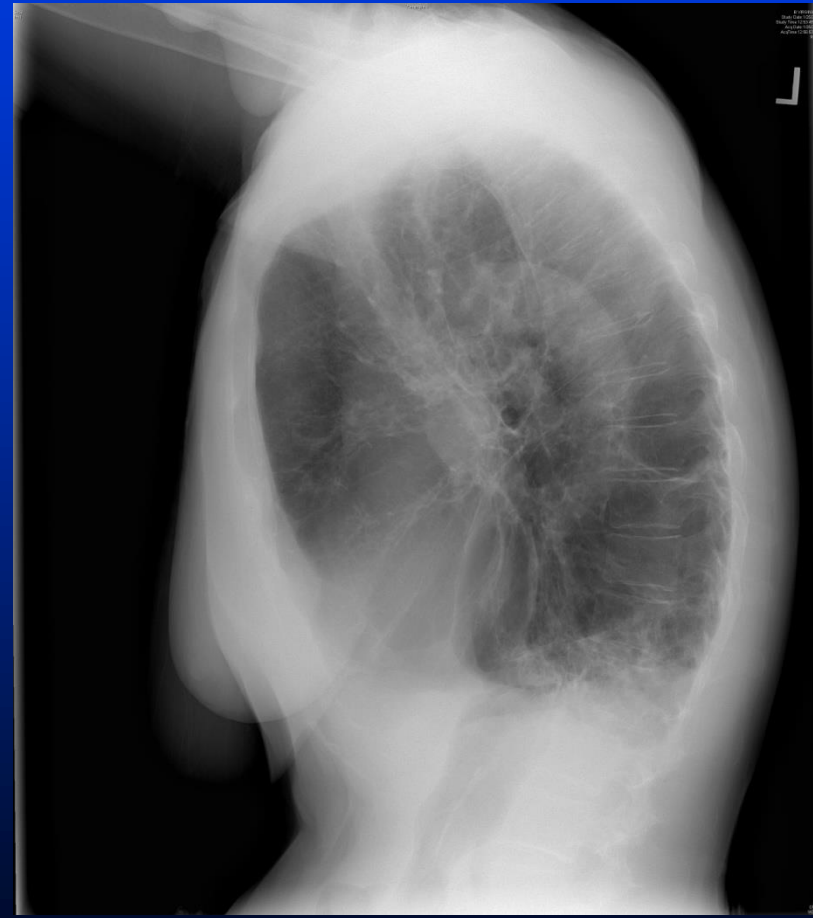
Complications

- Hemoptysis, including massive hemoptysis
- Infection with resistant organisms
- Hypercapnic respiratory failure
- Other: weight loss, mycetoma

Take Home Points

- In a patient with persistent airflow obstruction who does not have asthma or COPD, consider the possibility of bronchiolitis obliterans.
- Unlike treating COPD flares, antibiotic therapy in bronchiectasis should be guided by the results of sputum culture.

Multiple-Choice Question: 48-year-old cigarette smoker with productive cough.



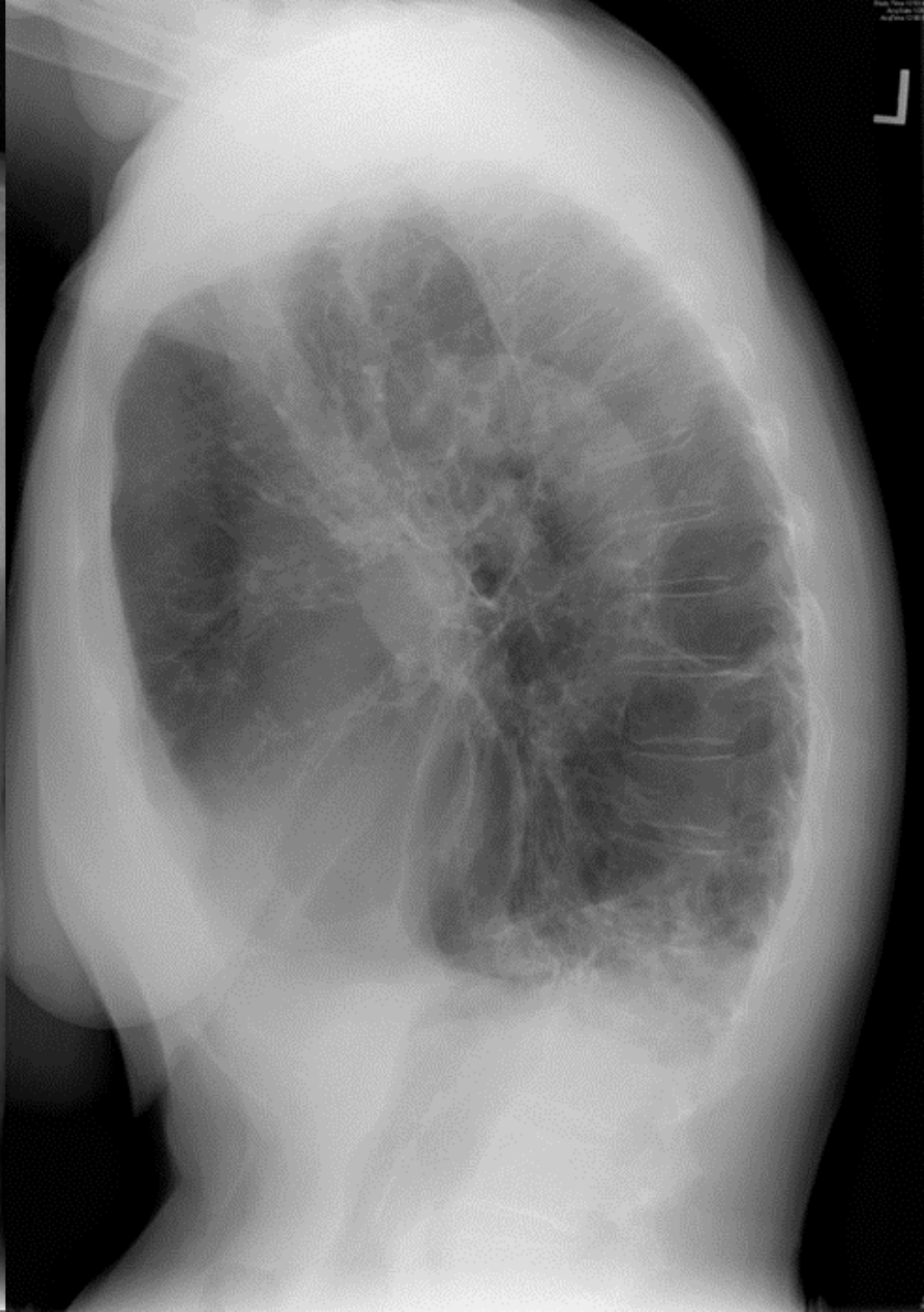
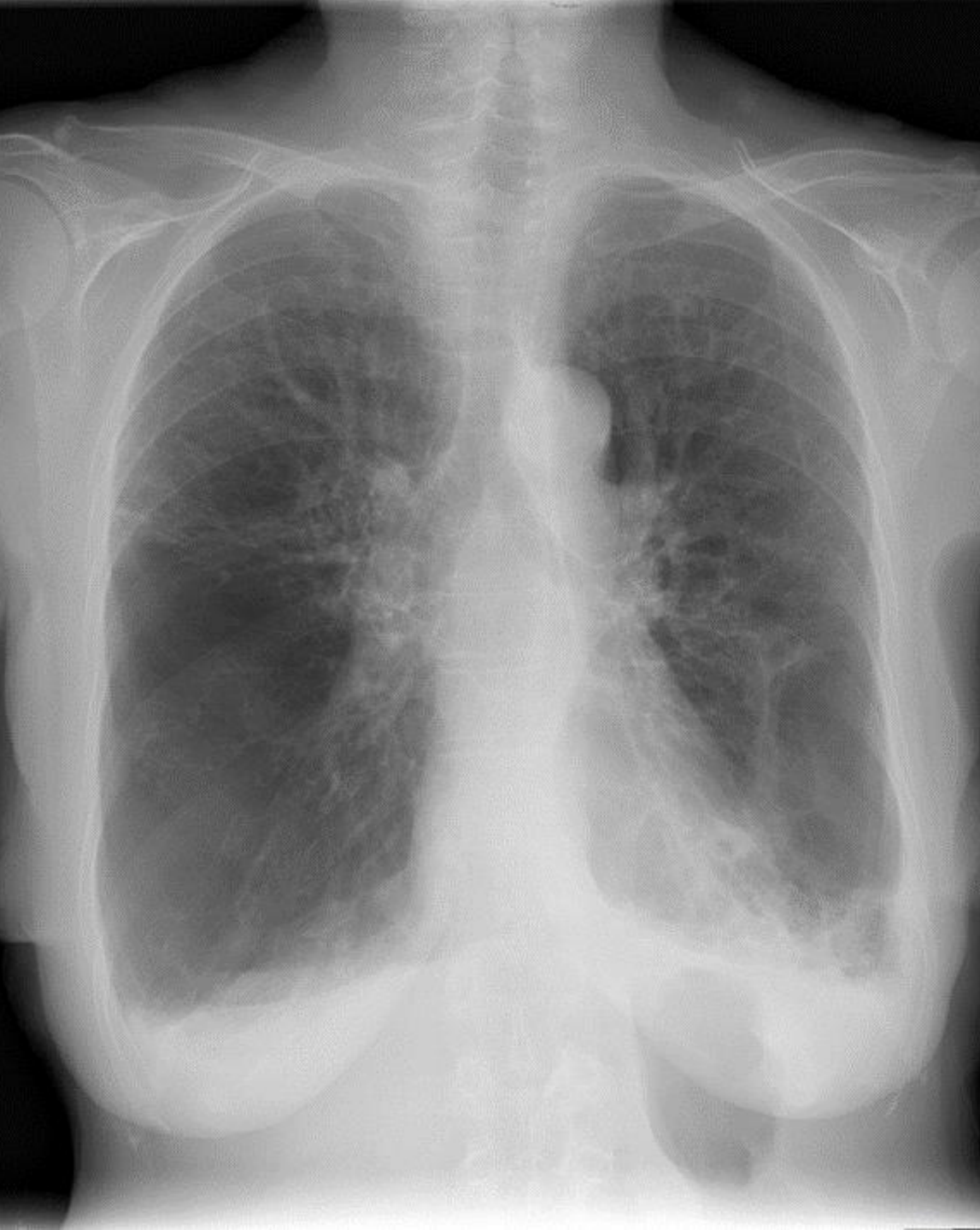
Multiple-Choice Question: Close-Up of left base



Question:

Which of the following blood tests is most likely to be helpful in assessment of this patient?

- A. Cystic fibrosis gene mutation
- B. ANCA
- C. Alpha-1 antitrypsin level
- D. VEGF-D
- E. Serum immunoglobulin E



Correct Answer:

Which of the following blood tests is most likely to be helpful in assessment of this patient?

- A. Cystic fibrosis gene mutation
- B. ANCA
- C. Alpha-1 antitrypsin level
- D. VEGF-D
- E. Serum immunoglobulin E

References

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