



Brigham and Women's Hospital

Founding Member, Mass General Brigham

Pulmonary Board Review

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- Clinical focus: Bronchiectasis, cystic fibrosis, inflammatory lung disease
- Research focus: role of inflammation in lung disease

DISCLOSURES

- I have no relevant conflicts of interest.



Key Objectives

- Review the clinical presentation and treatment of inflammatory and interstitial lung diseases and pneumoconioses.
- Review categories and treatment options for obstructive sleep apnea.
- Review pulmonary function testing and role in diagnosis of obstructive lung disease.
- Review presentation and management of acute respiratory distress syndrome (ARDS).
- Review of testing and treatment of respiratory infections, including non-tuberculous mycobacteria and latent tuberculosis infection



Question 1

75-year-old smoker (1 ppd x 40 years, quit 15 years ago) presents with progressive exertional dyspnea over the past 6 months. He endorses a non-productive cough, worse in the morning, without fever, chest pain, hemoptysis or constitutional symptoms. He denies orthopnea, PND, or swelling of his lower extremities.

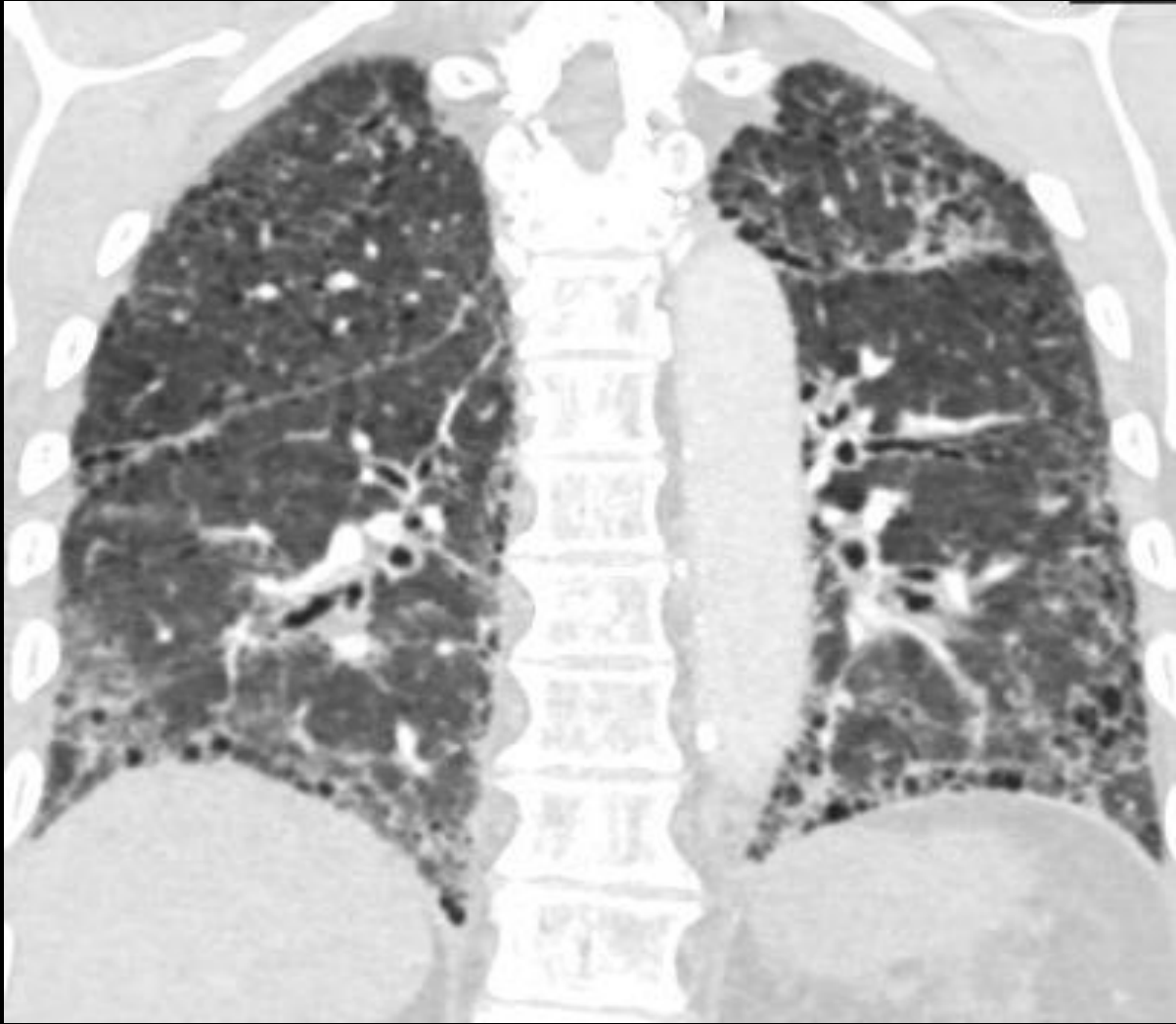
He has retired from his work as a lawyer. He has no unusual exposures at home, no arthritic complaints or symptoms of Raynaud's disease.



Question 1 (con't)

- His exam is notable for digital clubbing and fine inspiratory crackles in bilateral lower lung zones.
- His oxygen saturation is 95% at rest. He desaturates to 87% with ambulation.
- Spirometry demonstrates moderate restriction.
- Chest x-ray is notable for increased linear markings, predominantly in the lower lung zones. Chest CT scan shows demonstrates basilar honeycombing and traction bronchiectasis.





Q1: Which of the following actions would you take?

- A. Refer to Pulmonary for transbronchial lung biopsy
- B. Refer to Thoracic Surgery for thoracoscopic lung biopsy
- C. Begin anti-inflammatory therapy with high-dose prednisone
- D. Begin immunosuppressive therapy with prednisone and azathioprine
- E. Begin anti-fibrotic therapy with pirfenidone, nintedanib or nerandomilast.



Q1: Which of the following actions would you take?

- A. Refer to Pulmonary for transbronchial lung biopsy
- B. Refer to Thoracic Surgery for thoracoscopic lung biopsy
- C. Begin anti-inflammatory therapy with high-dose prednisone
- D. Begin immunosuppressive therapy with prednisone and azathioprine
- ☒ E. Begin anti-fibrotic therapy with pirfenidone, nintedanib or nerandomilast.



Q1: MOC reflective statement

- A clinical diagnosis of idiopathic pulmonary fibrosis (IPF) can be made if patient has characteristic clinical presentation (age >60, bibasilar crackles, progressive dyspnea, w/ or w/o digital clubbing); high resolution chest CT demonstrates usual interstitial pneumonia (UIP) or probable UIP; no suggestive clinical symptoms/history of rheumatologic disease or environmental exposures.
- High-resolution CT findings c/w UIP: subpleural and basal predominant honeycombing with or without peripheral traction bronchiectasis
- Lung biopsy is not required if clinical and radiographic criteria are met.
- Immunosuppressive therapy with prednisone was shown to be a deleterious treatment for patients with IPF
- Currently available anti-fibrotic therapies: pirfenidone, nintedanib or nerandomilast.



Q2: Conditions commonly associated with cystic fibrosis include each of the following except:

- A. Bronchiectasis
- B. Sinusitis
- C. Chronic otitis media
- D. Airflow obstruction
- E. Azoospermia



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Q3: Typical manifestations of asbestos-related intra-thoracic disease include each of the following except:

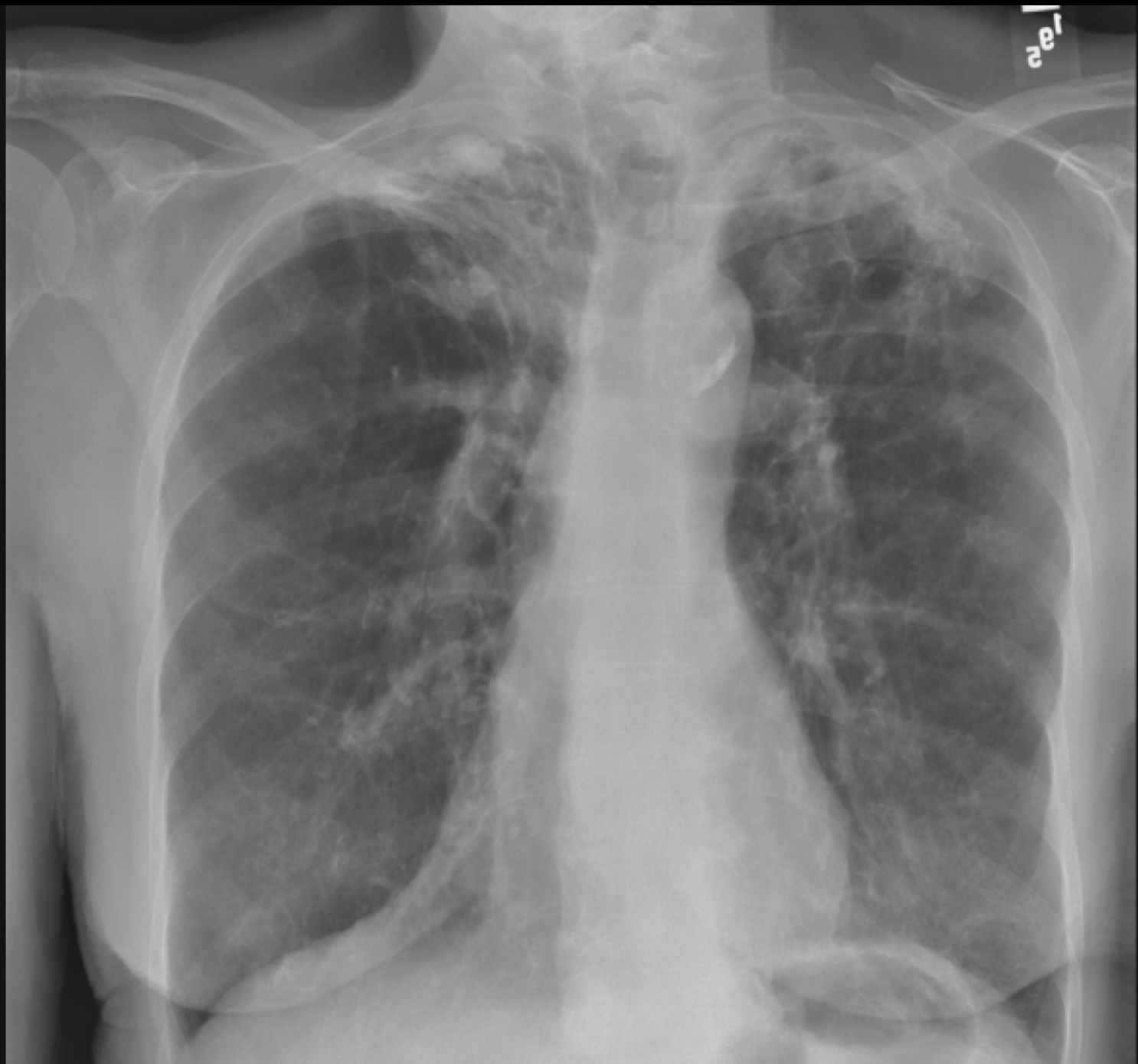
- A. Fibrocalcific parenchymal disease, predominantly involving the upper zones of the lung
- B. Pleural plaques
- C. Malignant mesothelioma
- D. Benign pleural effusions
- E. Bronchogenic carcinoma

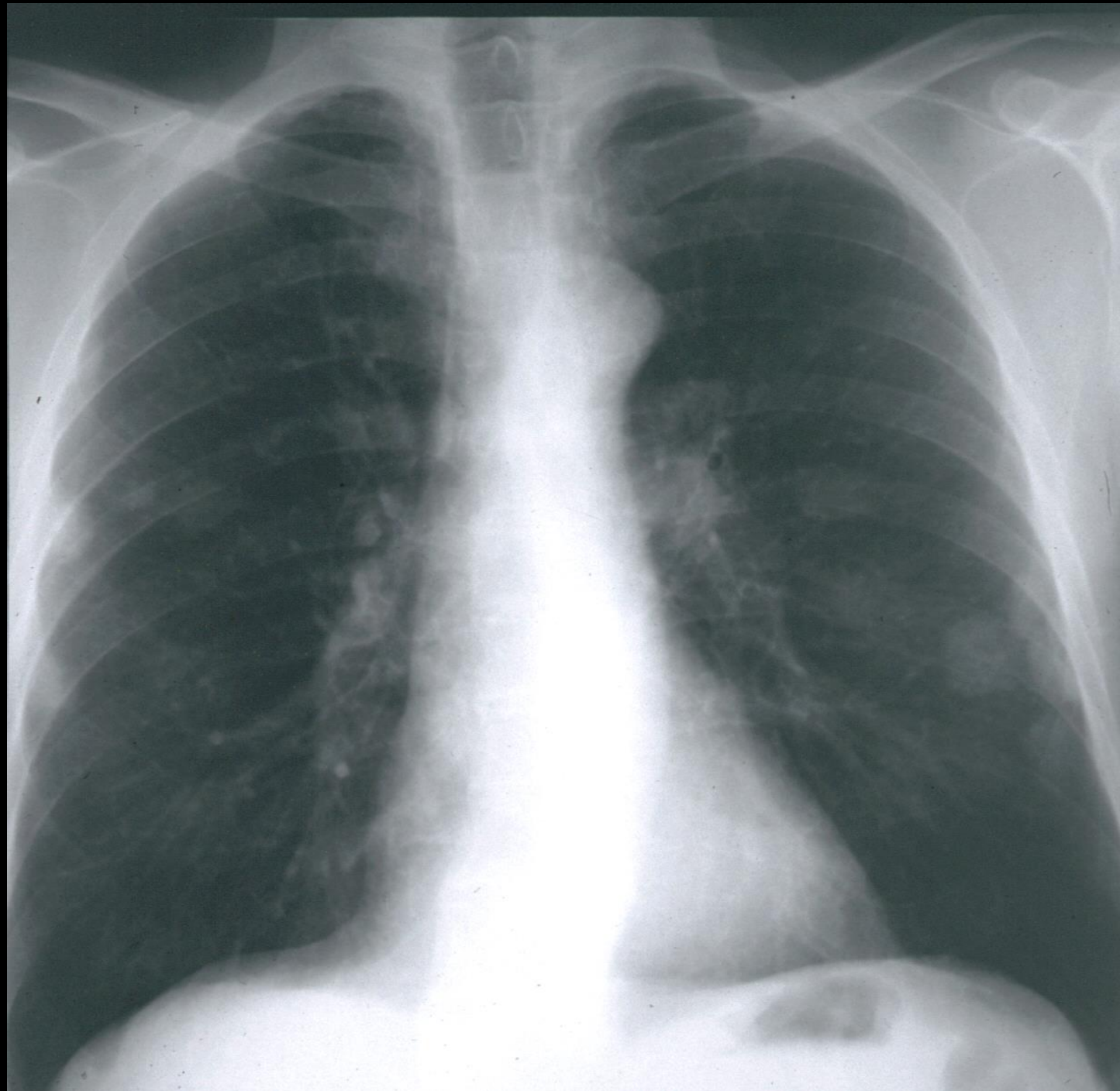


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- E. Bronchogenic carcinoma







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Q3: MOC reflective statement

Pleuroparenchymal manifestations of asbestos-related lung disease:

- Pleural plaques
- Benign pleural effusions
- Asbestosis (chronic, diffuse fibrotic lung disease caused by inhalation of asbestos fibers)
- Malignancy: malignant mesothelioma and non-small cell and small cell lung carcinoma



Question 4:

In December, a 63-year-old man with a 60 pack-year history of cigarette smoking noticed an increase in the amount of his usual sputum production and a change to yellow-green sputum. Findings on physical examination were normal; temperature was 37.8°C (100°F). A chest x-ray was normal.

A sputum gram stain showed no squamous epithelial cells and many neutrophils per high-power field. The predominant organisms on the gram stain were gram-negative cocci in pairs.



Q4: Which of the following antibiotics would you prescribe?

- A. Ampicillin, orally
- B. Amoxicillin-clavulanic acid, orally
- C. Procaine penicillin G, intramuscularly twice a day
- D. Cefotaxime, intravenously
- E. Cephalexin, orally



Q4: Which of the following antibiotics would you prescribe?

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- C. Procaine penicillin G, intramuscularly twice a day
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- E. Cephalexin, orally



Q4: MOC reflective statement

- *Moraxella catarrhalis* is a gram negative cocci and common respiratory pathogen in patients with COPD
- 95% of strains of *Moraxella catarrhalis* are resistant to amoxicillin.
- Susceptibility testing is not routinely performed in most laboratories.

POLY: 3+ EPITH: NONE
MANY GM(+) COCCI IN CLUSTERS AND PAIRS
MODERATE GM(-) COCCI

-----CULTURE-----

2+ ORAL FLORA

4+ MORAXELLA (BRANHAMELLA) CATARRHALIS (BETA LACTAMASE POSITIVE)

SUSCEPTIBILITIES:

TET	CHL	STR	KAN	COL	SUL	TOB	CIP	KEF	AMP	GEN	MEZ
25	31	21	26	14	15	25	35	21	20	26	30
S	S	S	S	S	I	S	S	S	R	S	S



Q5: An intensive pulmonary rehabilitation program for patients with COPD after hospitalization for a COPD exacerbation has been shown to improve:

- A. Survival
- B. Cardiovascular function
- C. Exercise tolerance
- D. Expiratory flow rates
- E. A and C



Q5: An intensive pulmonary rehabilitation program for patients with COPD after hospitalization for a COPD exacerbation has been shown to improve:

- A. Survival
- B. Cardiovascular function
- C. Exercise tolerance
- D. Expiratory flow rates
- ☒ E. A and C



Question 6:

A 67-year-old woman complains of persistent productive cough with occasional blood-streaking of her sputum of more than 1 year's duration.

She has mild exertional dyspnea and reports 6-7 lb weight loss; no fever or chest pain. She is a lifelong non-smoker. She had pneumonia once approximately seven years ago.



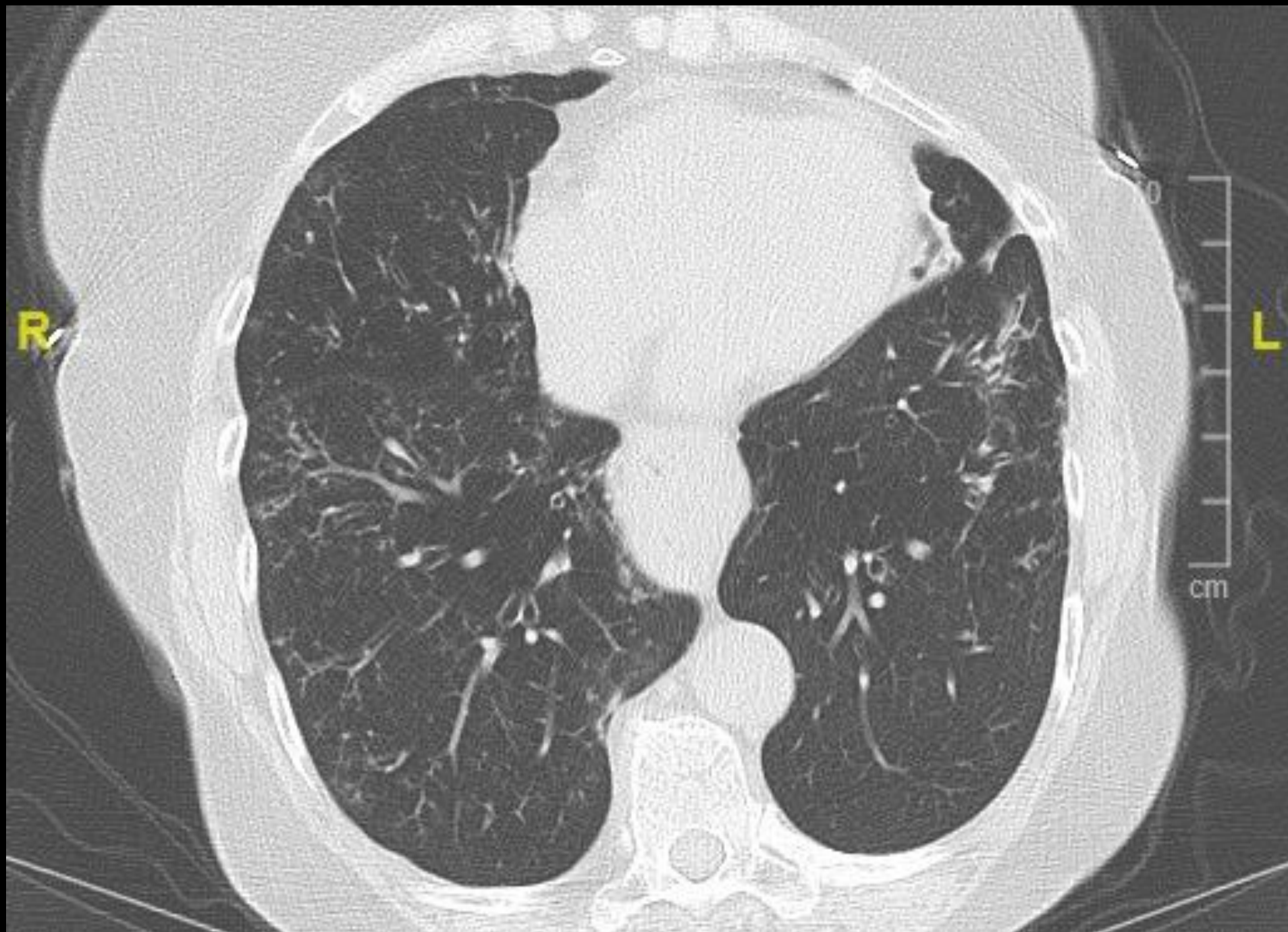
Question 6 (con't):

Her chest exam reveals a transient expiratory rhonchus.

Chest x-ray demonstrates a lingula pneumonia.

Chest CT scan demonstrates bronchiectasis with tree-in-bud nodularity in the RML, lingula, and RLL. The radiologic interpretation raises the possibility of non-tuberculous mycobacterial infection.





Q6: Based on these findings, you recommend:

- A. Levofloxacin for a 2-week course
- B. Initiation of therapy for *M. avium-intracellulare* with azithromycin, ethambutol, and rifampin
- C. Initiation of therapy for *Mycobacterium tuberculosis* with isoniazid, ethambutol, rifampin, and pyrazinamide
- D. Sputum for AFB culture and smear x 3
- E. Anti-nuclear cytoplasmic antibody (ANCA) testing



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- ☒ D. Sputum for AFB culture and smear x 3
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Q6: MOC reflective statement

If pulmonary non-tuberculosis mycobacterial (NTM) pulmonary infection is suspected:

- Identification of the strain of mycobacteria and susceptibility testing is critical for treatment
- Identification of NTM is achieved by sputum AFB culture (2 positive sputum cultures) and/or positive bronchoalveolar lavage AFB culture
- Three sputum AFB cultures are typically ordered
- Although *M avium-intracellulare* is a frequent cause of NTM pulmonary infection, empiric treatment without identification and susceptibility testing is not appropriate
- Pulmonary NTM treatment requires multiple antibiotics, typically for 12+ months
- Bronchiectasis with tree-in-bud nodularity in mid to lower lung zones is a characteristic pattern



Question 7:

A 52-year-old schoolteacher presents for a check-up. She has recently moved to the area to assume a new teaching position. She has never smoked cigarettes and has been found healthy at previous annual check-ups.

Her physical examination and routine laboratory studies are normal. However, a routine posteroanterior and lateral chest x-ray shows a 1-cm x 1.8-cm smooth, well-demarcated lesion in the right middle lobe.



Q7: The appropriate initial step for the patient's internist would be:

- A. Obtain a chest PET-CT scan
- B. Order a transthoracic needle biopsy
- C. Refer to pulmonologist to perform bronchoscopy
- D. Obtain prior CXRs
- E. Order chest MRI



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Question 8:

A 47-year-old woman presents with a six-week history of nonproductive cough, moderate exertional dyspnea, and temperature to 38.3°C (101°F). She has smoked two packs of cigarettes per day for the last 25 years but is otherwise healthy. The patient received clarithromycin for 10 days on two occasions without improvement in her symptoms.

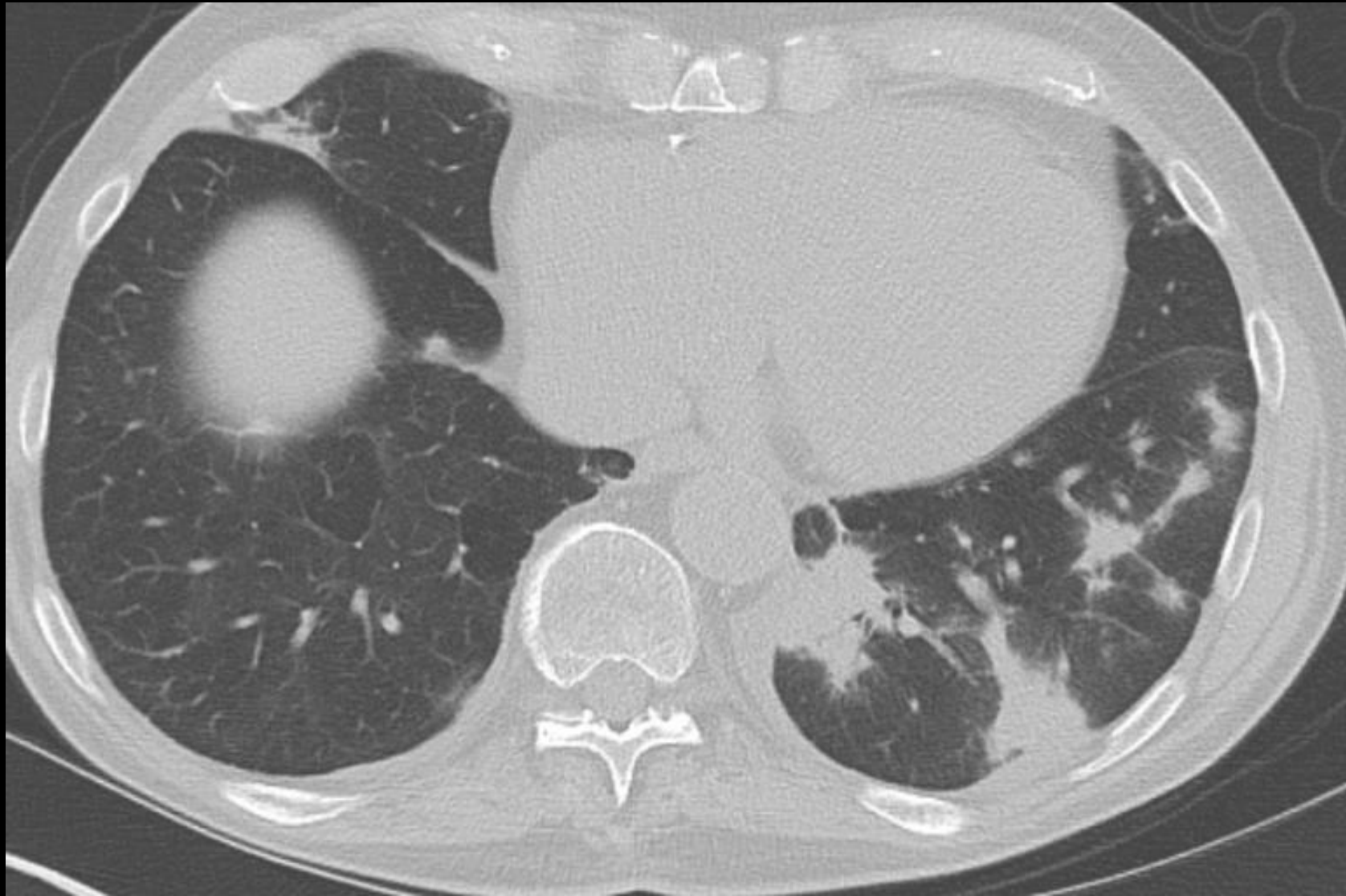
There is no history of ocular inflammation, exanthems or arthralgias.



Question 8 (con't):

- Physical examination demonstrates normal jugular venous pressure and no peripheral lymphadenopathy. Breath sounds are diminished over the lower lobes bilaterally. There are basilar crackles but no bronchial breathing, egophony, or wheezing.
- Laboratory studies are notable for creatinine 0.8 mg/dl, hematocrit 31%, white blood cell count 11,000/ μ L with 64% neutrophils and 7% band forms, 18% lymphocytes, 6% monocytes, 5% eosinophils. Urinalysis is normal.
- Chest imaging demonstrates nodular subpleural and peribronchial infiltrates.





Q8: The most likely diagnosis is:

- A. Legionnaire's disease
- B. Granulomatosis with polyangiitis
- C. *Streptococcus pneumoniae* pneumonia
- D. Idiopathic pulmonary fibrosis
- E. Cryptogenic organizing pneumonia (previously known as bronchiolitis obliterans organizing pneumonia)



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Q8: MOC reflective statement: Differentiating COP from Bronchiolitis Obliterans

	Cryptogenic Organizing Pneumonia (COP, BOOP)	Obstructive Bronchiolitis (OB or BOS)
<i>Presentation</i>	Pneumonia-like	COPD-like
<i>Chest x-ray</i>	Multifocal or diffuse pulmonary opacities	Hyperinflation
<i>Physiology</i>	Restrictive	Obstructive
<i>Response to corticosteroids</i>	Good	Poor



Question 9:

47-year-old male with history of hypertension, CAD, severe asthma, obesity with BMI of 48 and GERD undergoes sleep study for evaluation of snoring and excessive day time sleepiness. Polysomnogram is notable for Apnea-Hypopnea index (AHI) of 38 events/hour.



The first line of treatment for this patient is:

- A. Mandibular advancement device
- B. Continuous Positive Airway Pressure (CPAP)
- C. Weight management
- D. Average Volume-Assured Pressure Support (AVAPS)
- E. Hypoglossal nerve stimulator



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Q9: MOC reflective statement

Apnea-Hypopnea Index Score Classification for Adults

Apnea Severity	Apnea-Hypopnea Index (AHI) (Events/hour of sleep)
Normal	<5
Mild	$5 \leq \text{AHI} < 15$
Moderate	$15 \leq \text{AHI} < 30$
Severe	≥ 30

- Current guidelines recommend positive airway pressure as initial treatment for patients with moderate to severe OSA (AHI >15)
- Continuous positive airway pressure (CPAP) is the recommended modality



Questions 10 – 14:

- 10. A majority of cigarette smokers are affected
- 11. Reduced FEV_1/FVC ratio
- 12. Decreased diffusing capacity (DL_{CO})
- 13. Most patients have a deficiency of alpha-1 antitrypsin
- 14. Montelukast is useful in treatment

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- A. Emphysema
 - B. Asthma
 - C. Both
 - D. Neither



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Q10 – 14: MOC reflective statement

- As per CDC, “age-adjusted prevalence of COPD was 15.2% among current cigarette smokers, 7.6% among former smokers, and 2.8% among adults who had never smoked.”
- Alpha-1-anti-trypsin deficiency (A1AT) occurs in approximately 2-3% of patients with COPD and is frequently undiagnosed.
- Patients with COPD typically have obstructive physiology (reduced FEV1/FVC) on pulmonary function testing.
- Decreased diffusion capacity (DLCO), which is a metric that measures gas exchange, in patients with COPD was associated with increased symptoms, decreased exercise capacity and increased risk of exacerbations.
- As per the CDC, 8% of US adults have asthma.
- Patients with asthma often have obstructive physiology (reduced FEV1/FVC) on pulmonary function testing.
- The leukotriene inhibitor, montelukast, is one of the many treatments currently available for the treatment of asthma.



Q10 – 14: MOC reflective statement #2

Pulmonary Function Testing Severity Classification

Prior interpretation criteria		Current interpretation standards (Z-score)	
Mild	>70% predicted	Mild	-1.65 to -2.5
Moderate	60-69% predicted	Moderate	-2.51 to -4.0
Moderate to severe	50-59% predicted	Severe	< -4.1
Severe	35-49% predicted		
Very severe	<35% predicted		

Advantages of Z-score classification:

- Race neutral
- Accounts for lung function variability that is not constant across all age ranges and height
- Decreases misinterpretation of lung function, especially in young and elderly



Questions 15 – 18:

- 15. Diffuse lung infiltrates
 - 16. Commonly caused by sepsis and gastric aspiration
 - 17. Positive-pressure ventilation is an important treatment
 - 18. Corticosteroid therapy is beneficial in select subgroups
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- A. Acute respiratory distress syndrome
- B. Severe cardiogenic pulmonary edema
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- ☐ C. Both
- ☐ D. Neither



Q15 – 18: MOC reflective statement

- Diffuse pulmonary infiltrates in patients with severe acute hypoxemic respiratory failure can be caused by infection, acute respiratory distress syndrome (ARDS), severe pulmonary edema, inflammation or hemorrhage.
- Two of the most frequent causes of ARDS are sepsis and gastric aspiration.
- Positive-pressure ventilation is an important treatment modality in patients with respiratory failure. In patients with ARDS, it is administered with lung protective strategy/low tidal volume ventilation.
- Corticosteroids are recommended in patients with early (<14 days) moderate to severe ARDS with refractory shock, and ARDS due to COVID-19 or severe community-acquired pneumonia.



Questions 19 – 22:

- 19. Necrobiotic nodules
 - 20. Occurrence in women
 - 21. Diabetes insipidus
 - 22. Recurrent aspiration pneumonia
-

- A. Rheumatoid arthritis
- B. Scleroderma
- C. Langerhans cell histiocytosis (histiocytosis X; eosinophilic granuloma)
- D. Lymphangioleiomyomatosis
- E. Idiopathic pulmonary fibrosis



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- B. Scleroderma
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- B. Scleroderma
- ☒ C. Langerhans cell histiocytosis (histiocytosis X; eosinophilic granuloma)
- D. Lymphangioleiomyomatosis
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22. Recurrent aspiration pneumonia

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- B. Scleroderma
- C. Langerhans cell histiocytosis (histiocytosis X; eosinophilic granuloma)
- D. Lymphangiomyomatosis
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22. Recurrent aspiration pneumonia

- A. Rheumatoid arthritis
- ☒ B. Scleroderma
- C. Langerhans cell histiocytosis (histiocytosis X; eosinophilic granuloma)
- D. Lymphangiomyomatosis
- E. Idiopathic pulmonary fibrosis



Q19 – 22: MOC reflective statement

- The pulmonary manifestations of rheumatoid arthritis include interstitial lung disease, rheumatoid nodules, pleural disease, bronchiectasis and bronchiolitis.
- Scleroderma (systemic sclerosis) can cause interstitial lung disease, pulmonary hypertension, pleural disease, and indirectly recurrent aspiration pneumonia/lung injury due to impaired esophageal motility.
- Pulmonary Langerhans cell histiocytosis (histiocytosis X; eosinophilic granuloma) in adults is a disease primarily of smokers that can cause diffuse cystic lung disease and extrapulmonary manifestations: including diabetes insipidus, bone and skin lesions.
- Lymphangioleiomyomatosis (LAM) is a rare disease that occurs almost exclusively in women of childbearing age that causes cystic lung disease, pneumothorax, and in some patients can progress to respiratory failure.



Questions 23 – 27: Detection and Treatment of Asymptomatic (Latent) Tuberculosis Infection

- Presence of *M. tuberculosis* without clinical evidence of active infection = latent tuberculous infection (LTBI).
- Most cases of active TB are due to reactivation of LTBI – 5-10% lifetime risk of LTBI reactivation if untreated.
- Treatment of LTBI can eradicate TB mycobacteria and prevent reactivation.



Q23-27: Indications for Treating Latent TB Infection

- Household contact
- Recent “convertor” to positive status = recently infected
- X-ray with findings consistent with inactive TB, never treated with TB drugs
- Special circumstances for those at increased risk (*e.g., diabetes, HIV, dialysis, immunosuppression, major weight loss, silicosis, recent immigration from an endemic area*)



Defining a Positive Purified Protein Derivative (PPD) Skin Test

Risk	Induration	Population
Low	≥ 15 mm	- Immunocompetent patients without risk factors
Moderate	≥ 10 mm	- Residents / employees of prisons, nursing homes, homeless shelters, healthcare facilities - Recent immigrant (<5 yrs) from an endemic area - Mycobacteriology lab personnel - Intravenous drug users - Children < 5 yrs old or exposed to high-risk adults
High	≥ 5 mm	- HIV or immunosuppression - Recent close TB contact - Scarring on CXR c/w inactive disease



Interferon Gamma Release Assays, BCG Vaccine

- Interferon Gamma Release Assay (IGRA) and Tuberculin skin tests (TST) can be used interchangeably
- Bacillus Calmette–Guérin (BCG) vaccine does not cause a false positive IGRA result
- IGRAs are less likely to be positive from cross-reactivity with atypical mycobacteria



Questions 23 – 27:

Treatment of latent tuberculous infection should be given in which of the following cases?

23. A 21-year-old healthcare worker with a TB skin test reaction of 15 mm induration. Chest X-ray is normal. The skin test was positive 5 years ago at 10 mm induration.

A. Yes

B. No



Questions 23 – 27:

Treatment of latent tuberculous infection should be given in which of the following cases?

23. A 21-year-old healthcare worker with a TB skin test reaction of 15 mm induration. Chest X-ray is normal. The skin test was positive 5 years ago at 10 mm induration.

☒ A. Yes

B. No



Questions 23 – 27:

Treatment of latent tuberculous infection should be given in which of the following cases?

24. An asymptomatic 74-year-old man, who is HIV negative with no known TB exposure, has a TB skin test of 4 mm induration on routine testing. A repeat skin test 1 week later shows a 16 mm induration. A chest x-ray is obtained and is normal.

- A. Yes
- B. No



Questions 23 – 27:

Treatment of latent tuberculous infection should be given in which of the following cases?

24. A 74-year-old man, who is HIV negative with no known TB exposure, has a TB skin test of 4 mm induration on routine testing. A repeat skin test 1 week later shows a 16 mm induration. A chest X-ray is obtained and is normal.

A. Yes

 B. No

Booster Phenomenon

A person previously exposed to TB has a negative result on initial testing but, on repeat testing one to three weeks later, has a positive test.

The initial result is a “false negative” due to waning cellular immunity; the latter is a true positive due to “boosting” of the immune response by the recent re-exposure to tuberculin protein.

Booster phenomenon should be distinguished from a recent conversion. Screening (e.g., in nursing homes, hospitals) often uses an initial two-step PPD testing procedure, with repeat testing 1-3 weeks after an initial negative result.



Questions 23 – 27:

Treatment of latent tuberculous infection should be given in which of the following cases?

25. A 45-year-old man who previously used intravenous drugs and is HIV positive has a clear chest X-ray. His TB test is 5 mm induration. Prior skin tests were reported as “equivocal.”

- A. Yes
- B. No



Questions 23 – 27:

Treatment of latent tuberculous infection should be given in which of the following cases?

25. A 45-year-old man who previously used intravenous drugs and is HIV positive has a clear chest X-ray. His TB test is 5 mm induration. Prior skin tests were reported as “equivocal.”

- ☒ A. Yes
- ☐ B. No



Questions 23 – 27:

Treatment of latent tuberculous infection should be given in which of the following cases?

26. A 53-year-old woman with no known medical illnesses and a clear chest x-ray has a TB skin test reaction of 8 mm. She did not have prior TB skin testing. She is now tested because her husband was recently diagnosed with active TB after a 6-month illness.

- A. Yes
- B. No



Questions 23 – 27:

Treatment of latent tuberculous infection should be given in which of the following cases?

26. A 53-year-old woman with no known medical illnesses and a clear chest x-ray has a TB skin test reaction of 8 mm. She did not have prior TB skin testing. She is now tested because her husband was recently diagnosed with active TB after a 6-month illness.

- A. Yes
- B. No



Questions 23 – 27:

Treatment of latent tuberculous infection should be given in which of the following cases?

27. A 26-year-old homeless man has a positive IGRA TB test. He is asymptomatic. Chest x-ray demonstrates a left upper lobe infiltrate.

- A. Yes
- B. No



Questions 23 – 27:

Treatment of latent tuberculous infection should be given in which of the following cases?

27. A 26-year-old homeless man has a positive IGRA TB test. He is asymptomatic. Chest x-ray demonstrates a left upper lobe infiltrate.

A. Yes

☒ B. No



Additional Recommendations for Treatment of Latent Tuberculous Infection

- **Shorter (3-4 month) regimens are now preferred therapy.**
 - Rifampin daily for 4 months
 - Isoniazid (INH) + rifampin daily for 3 months
 - Isoniazid (INH) + rifapentine once weekly for 3 months
- Alternative is INH for 6 months or 9 months
- Rifamycin-based regimens are preferred
- Routine laboratory monitoring (LFTs) is indicated for:
HIV infection; pregnancy; chronic liver disease; history of elevated LFTs; current use of injectable drugs or regular alcohol use.



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THANK YOU

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