BMJ Best Practice

Evaluation of chronic cough

Straight to the point of care

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Summary

Cough is one of the most common presenting symptom in primary practice.[1] Subacute cough is defined as cough persisting for 3-8 weeks, and chronic cough as that persisting for more than 8 weeks in adults.[2] [3] [4] Chronic cough in children has been defined as the presence of cough every day for 4 weeks or more.[5] Subacute cough is most often self-limited, but chronic cough may provide significant challenges for effective evaluation and management. The difficulty is in determining the cause of cough, because some "etiologies" are syndromes without accurate diagnostic tests. The cause is determined instead by typical historical features, elimination of alternative causes, and response to targeted therapies (therapeutic trials serve as tests). Nonetheless, a careful history and examination, followed by carefully selected therapeutic trials and/or diagnostic evaluations, may satisfactorily resolve cough in most cases.

However, for children ages ≤14 years, common causes of chronic cough may be different to those in adults; the child's age, cough characteristics, clinical history, and geographical setting should be taken into account.[5] Detailed recommendations regarding diagnostic algorithms and therapeutic trials for children may also differ from those for adults.[5]

Nontargeted cough suppressant therapy is rarely effective for chronic cough.

Etiology

All chronic cough begins as subacute, and differential diagnosis includes all causes of subacute cough. Postinfectious cough is the most common etiology of subacute cough.[6] Most cases will be self-limited. Once cough duration has exceeded 8 weeks, a systematic approach to elucidating cause and best treatment is needed.

Common etiologies

In most nonsmoking adults with a normal chest x-ray who do not take ACE inhibitors, chronic cough is caused by one or more of four conditions:[2] [3][7] [8]

- Upper airway cough syndrome (formerly postnasal drip syndrome)
- Asthma
- Gastroesophageal reflux disease
- Nonasthmatic eosinophilic bronchitis.

More than one cause of chronic cough is often present. Truly idiopathic cough is rare and is a diagnosis of exclusion.[9] [10]

Cough as a principal or sole symptom of asthma, known as cough-variant asthma, is present in a subgroup of patients.[11] The cough may be productive and may be worse at night or with exercise.[11] Evidence of airflow limitation may only be present during bronchial provocation testing.[11]

These commonest causes account for most patients presenting to specialty clinics with chronic cough and should generally be considered first if there are no signs or symptoms pointing to alternative diagnoses.

Other common causes include the following.

- ACE inhibitors: dry cough, typically associated with a tickling or scratching sensation in the throat. The reported incidence varies.[12] ACE inhibitor-induced cough is more frequent in women than men and is associated with increasing age.[13] [14]
- Postinfectious cough: postinfectious cough is the most common etiology of subacute cough.[6] A history typical for postinfectious cough should prompt watchful waiting and symptomatic therapy as necessary.
- Chronic bronchitis: adult with a history of chronic productive cough lasting for more than 3 months of the year and for at least 2 consecutive years when other diagnoses have been ruled out.[15] Chronic bronchitis is one of the manifestations of chronic obstructive pulmonary disease. Predisposing factors include nicotine and marijuana smoking, second-hand exposure to nicotine smoke, and environmental exposure to toxins.[8][16]
- Bordetella pertussis: when local epidemiology indicates a high rate of pertussis infection, testing for *Bordetella pertussis* is recommended. If tests are supportive of pertussis, specific antimicrobial therapy is indicated.

Less common etiologies

Diagnoses to consider are those that impart cough through stimulation of airway mechanical and chemical receptors that feed into the vagus nerve, including afferent nerves located in the chest wall, diaphragm, esophagus, abdominal wall, and external auditory meatus.[8] Other potential causes therefore are:

- Disorders that distort or irritate the airway (e.g., bronchiectasis, chronic suppurative lung disease, endobronchial tumors, granulomatous disease, foreign bodies)
- Disorders of lung parenchyma (e.g., interstitial lung disease resulting from hypersensitivity pneumonitis, occupational/environmental exposure, or autoimmune diseases such as systemic lupus erythematosus)
- Systemic diseases (e.g., rheumatoid arthritis, sarcoidosis) or autoimmune diseases such as systemic lupus erythematosus
- Chronic vagal neuropathy (e.g., vitamin B12 neuropathy, diabetic neuropathy, herpes zoster infection, chemical irritant exposure)
- Irritation of the external ear canal by an infection, wax, or hearing aids may produce cough, through a reflex mediated by Arnold's nerve

Obstructive sleep apnea may cause repeated drops in intrapleural pressure, resulting in episodes of nocturnal aspiration, throat irritation and cough.[17]

Oral-pharyngeal dysphagia that results in recurrent aspiration of foods and liquids may also cause cough. Patients with cough who report difficulty swallowing should be further evaluated for such etiology.

Zenker diverticulum can cause chronic cough, accompanied by dysphagia, regurgitation, aspiration, and weight loss.[18]

Bronchiolitis should also be considered, and may result from infection, or may be drug/toxin-related. Diffuse panbronchiolitis should be considered in patients from East Asia.[19] [20]

Neurologic conditions affecting the medulla oblongata or cerebellum may increase the cough reflex (e.g., brainstem space-occupying lesions, Tourette syndrome, neuromyelitis optica spectrum disorder, cerebellar neurodegenerative diseases).[21]

In areas of endemic infection with fungi or parasites, diagnostic evaluation for these should be undertaken when more common causes of cough have been ruled out. Slow enlargement of intrathoracic blood vessels, such as an aortic aneurysm, may cause chronic cough.[22]

People who work with their voice (e.g., teachers, call center operators, actors, singers, coaches) may experience chronic cough and hoarseness.[16]

Coronavirus disease 2019 (COVID-19) may be associated with long-term symptoms, most commonly cough, low grade fever, and fatigue, and/or organ dysfunction.[23] The definition and time frame of "postacute COVID-19 syndrome" or "long COVID" has not been universally determined. In the UK, "ongoing symptomatic COVID-19" has been defined as signs and symptoms of COVID-19 from 4-12 weeks. "Post-COVID-19 syndrome" is defined as signs and symptoms that develop during or after COVID-19 and continue for more than 12 weeks.[24] Incidence, natural history, and etiology data continue to emerge. See Coronavirus disease 2019 (COVID-19).

Chronic cough that persists in spite of therapeutic trials and is otherwise unexplained by extensive evaluations is labeled as refractory chronic cough or unexplained chronic cough. In the literature, it is also referred to as neurogenic cough, cough hypersensitivity syndrome, or somatic cough.[25] [26]

Urgent considerations

(See **Differentials** for more details)
Chronic cough as a sole symptom typically lasts for months or years before presentation and does not usually represent an urgent medical condition. Faster and more comprehensive evaluation (rather than empiric treatment) should take place if other symptoms are present (such as dyspnea, hemoptysis, weight loss, fever, or chest pain) or if the patient is immunosuppressed.

Lung carcinoma

Cough is the most common symptom of lung cancer and is often accompanied by other symptoms such as weight loss, hemoptysis, chest pain, dyspnea, or hoarseness. Patients may also present with nonspecific symptoms such as fatigue and anorexia. Lung cancer is more likely in current or prior smokers.

UK guidelines recommend urgent chest x-ray to assess for lung cancer in people age ≥40 years if they have two or more of the following unexplained symptoms, or one or more unexplained symptom(s) if they have ever smoked:[27]

- Cough
- Fatigue
- Shortness of breath
- Chest pain
- Weight loss
- Appetite loss

Diagnosis is confirmed by radiography and pathology, and treatment may involve surgery, chemotherapy, and radiation therapy.[28]

Asthma

Timely diagnosis of asthma is important to reduce the risk of exacerbations and long-term airway remodelling.[29]

Diagnosis follows a structured clinical assessment that may demonstrate:[11] [30] [31]

- chronic cough accompanied by episodic dyspnea, wheezing and chest tightness that worsens at night, on exposure to allergens, cold, or fumes
- previous documented symptom variability
- clinical findings of bronchoconstriction, and
- variable expiratory airflow (ideally confirmed by spirometry).

If asthma is poorly controlled at diagnosis, a short course of oral corticosteroids may be used prior to starting inhaled corticosteroids. In an acute exacerbation of asthma, bronchodilators and corticosteroids should be administered to relieve airflow obstruction. If the patient has signs of a severe exacerbation, arrange immediate transfer to the emergency department, or to intensive care if the patient is drowsy, confused or has a silent chest.[11] Careful monitoring is essential.[11] Treatment in these situations includes a short-acting beta-2 agonist, early corticosteroid, and oxygen.[11] Ipratropium should be used for severe exacerbations.[11] [32] Intravenous magnesium sulfate may be considered in patients with severe exacerbations if they are unresponsive to initial therapy.[11] [33]

Pneumonia

May follow a prodrome of chronic cough and, in that instance, is typically manifested with a change in the character of cough, appearance of sputum purulence, and fever. Less commonly, hemoptysis, chest pain, or dyspnea may be present. Diagnosis is based on clinical findings of lung consolidation, along with radiographic findings of an infiltrate. Treatment consists of antibiotics.[34]

Tuberculosis

Chronic cough accompanied by night sweats and weight loss may indicate tuberculosis (TB), especially in a patient living in or visiting an area with high prevalence of this disease. Adults account for approximately 90% of all cases; there are more cases among men than women (55% vs. 33% respectively).[35] People at increased risk for TB infection include those with underlying conditions that affect their immune status such as HIV infection, patients receiving immunosuppressant medications, transplant recipients, individuals with diabetes, and patients receiving dialysis.[36]

Epidemiological risk factors include recent immigrant or refugee status, being in prison, and having a "contact" with active TB. These risk factors are associated with a particularly high risk of active TB if a test for latent TB (e.g., tuberculin skin test, interferon-gamma release assay) is positive.

TB is typically accompanied by radiographic infiltrative, fibrotic, or cavitating changes and confirmed by demonstration of *Mycobacterium tuberculosis* bacilli in sputum.

Confirmed TB should be treated promptly with antitubercular drugs to cure the patient and prevent transmission to others.

Bordetella pertussis infection

Paroxysmal cough, inspiratory whooping, and post-tussive vomiting raise a possibility of *B pertussis* infection. Diagnosis is suspected in household contacts of whooping cough and confirmed with microbiologic or serologic testing.

First line treatment is with a macrolide antibiotic or, in the presence of contraindications or bacterial resistance, with trimethoprim/sulfamethoxazole.

Interstitial lung disease

Cough accompanied by progressive dyspnea may indicate the presence of interstitial lung disease. Diagnosis is further suspected with signs of dry crackles and clubbing, and is confirmed clinically or pathologically. Radiography shows a plethora of interstitial changes, and pulmonary function testing typically demonstrates a restrictive pattern. Treatment depends on the specific clinical and pathological pattern of disease.

Approach

Patients may present with a subacute cough, most commonly postinfection; however, in most patients, postinfectious cough is self-limited.[6] Observation and, if required, symptomatic therapy may be all that is needed in these patients. Once the cough persists for longer than 8 weeks, further evaluation is indicated.[37] [38] Several validated tools of cough assessment are available, although these are used mostly for research purposes.[39]

Pursuing the cause and resolution of chronic cough requires ongoing commitment to the patient. The approach to an individual patient with chronic cough may vary from full initial diagnostic evaluation for common associated diseases, to empiric but targeted therapy for common conditions known to cause chronic cough, with limited or no diagnostic efforts.[10] Choice of the specific approach may be individualized, and depends on type and duration of symptoms, the patient's preference, and availability of resources. Limiting diagnostic testing, treating assumed etiologies, and applying sequential empiric trials of therapy is most cost-effective, but leads to the longest time to resolution of cough and may be associated with increased patient anxiety.[10] [40] [41] In practice, diagnostic and therapeutic processes are often applied simultaneously. It is best to involve the patient in choosing the best approach and to explain the expected duration and course of diagnostic and therapeutic trials.

History and examination

A detailed history is essential, and should include:

- Time and clinical setting of onset
- Exacerbating factors
- Associated symptoms
- Prior history suggestive of atopic disease
- A complete medical, smoking, drug, and exposure history
- Occupational and family history
- What measures have already been tried, and to what effect.

The history substantially influences the clinician's impression as to which (if any) of the four most common etiologies (upper airway cough syndrome [UACS], asthma, gastroesophageal reflux disease [GERD], or nonasthmatic eosinophilic bronchitis [NAEB]) are most likely.

A careful examination is, unfortunately, unlikely to inform the clinician regarding the commonest causes of chronic cough, but is essential for early detection of less common causes, such as bronchiectasis, interstitial lung disease, neoplastic disorders, or chronic infectious pulmonary diseases.

Although no specific history or physical exam findings are reliably associated with specific etiology of chronic cough, they may direct further testing or therapeutic trials.

The symptoms and findings associated with the common causes (asthma, UACS, GERD, or NAEB) may direct further diagnostic evaluation toward confirming that cause.

Asthma

May present with wheezing, chest tightness, or dyspnea apart from paroxysms of cough, or exacerbation of cough by seasonal exposures, specific irritants, or nonspecific respiratory irritants such as cold air, aromatic vapors, or dusty environments. In patients who do not ever wheeze, another cause should be

considered.[10] There may be variability of symptoms, nocturnal exacerbation of cough, or a strong family history of asthma or atopic disease.[42] Cough-variant asthma, in which persistent cough is the principal or sole symptom, tends to be worse at night or with exercise.[11][43]

UACS

A clinical syndrome and diagnosis is based on the clinical picture (which includes frequent throat clearing, postnasal drip, nasal discharge, nasal obstruction, and sneezing) and response to therapy.[44] Potential causes of UACS include allergic rhinitis, perennial nonallergic rhinitis, postinfectious rhinitis, bacterial sinusitis, allergic fungal sinusitis, rhinitis due to anatomic abnormalities, nasal polyposis, rhinitis due to physical or chemical irritants, occupational rhinitis, rhinitis medicamentosa, and rhinitis of pregnancy.[44]

GERD

May present with heartburn, dysphagia, acid regurgitation, and an associated cough with slouched posture. Suggestive symptoms may include cough on phonation, cough on rising from bed, or association with certain foods or with eating in general.[10] Reflux disease is clinically silent in up to 75% of cases.[45] Extra-esophageal symptoms of GERD (chronic cough, asthma, laryngitis, and dental erosions) can occur without typical GERD symptoms.[46]

NAEB

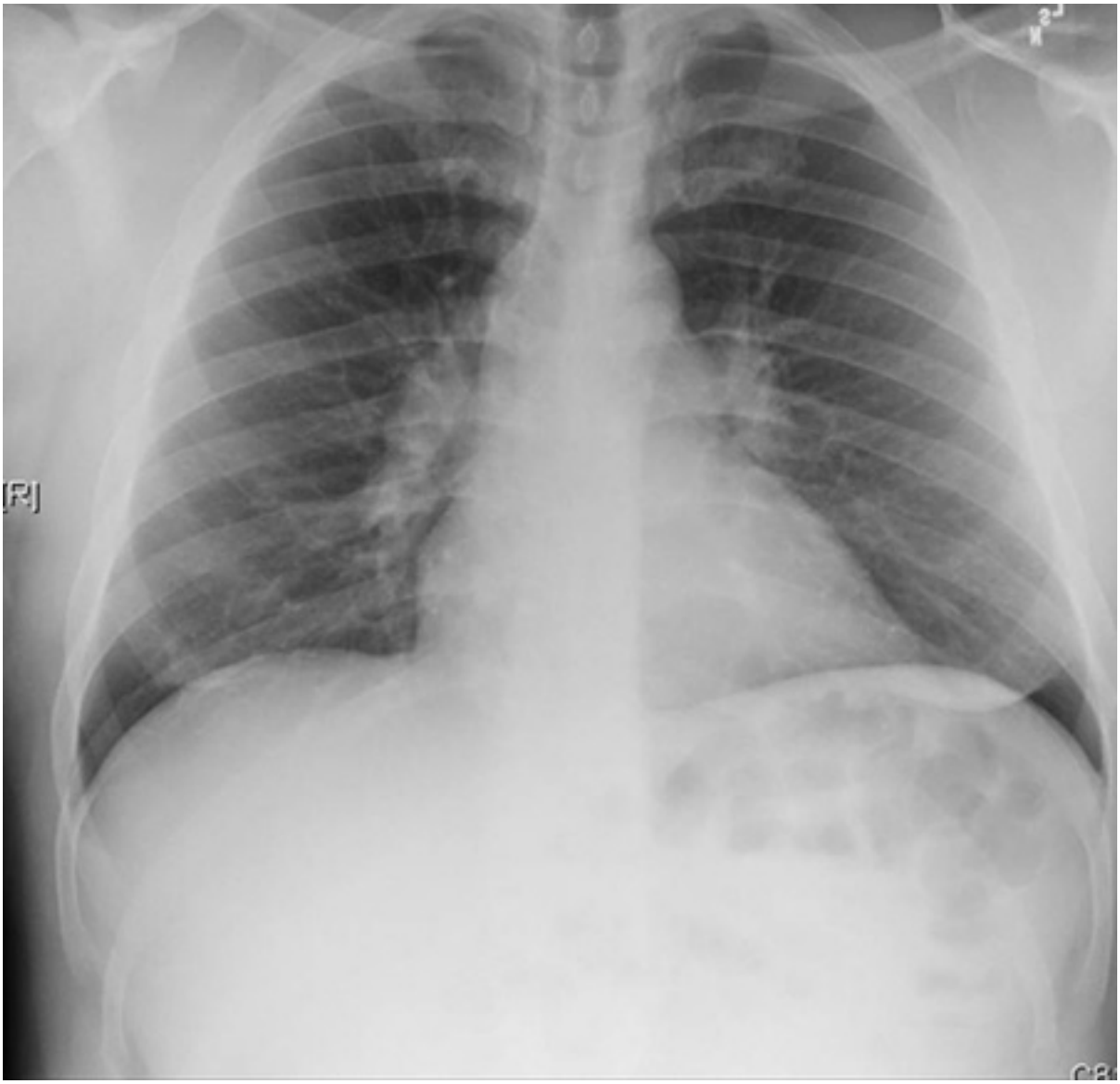
Presents with a chronic, generally scantily productive or nonproductive cough without prominent features of asthma or reliable cough triggers, although patients may complain of wheezing at times.

ACE inhibitor cessation

The cough from an ACE inhibitor may begin within days or months of onset of ACE inhibitor therapy. If use of ACE inhibitors is suspected as the cause, use should be stopped if at all possible. Diagnosis is then confirmed by the resolution of cough, usually within 1 to 4 weeks (although it may be up to 3 months).[47] Angiotensin receptor blocking agents do not appear significantly related to chronic cough symptoms.

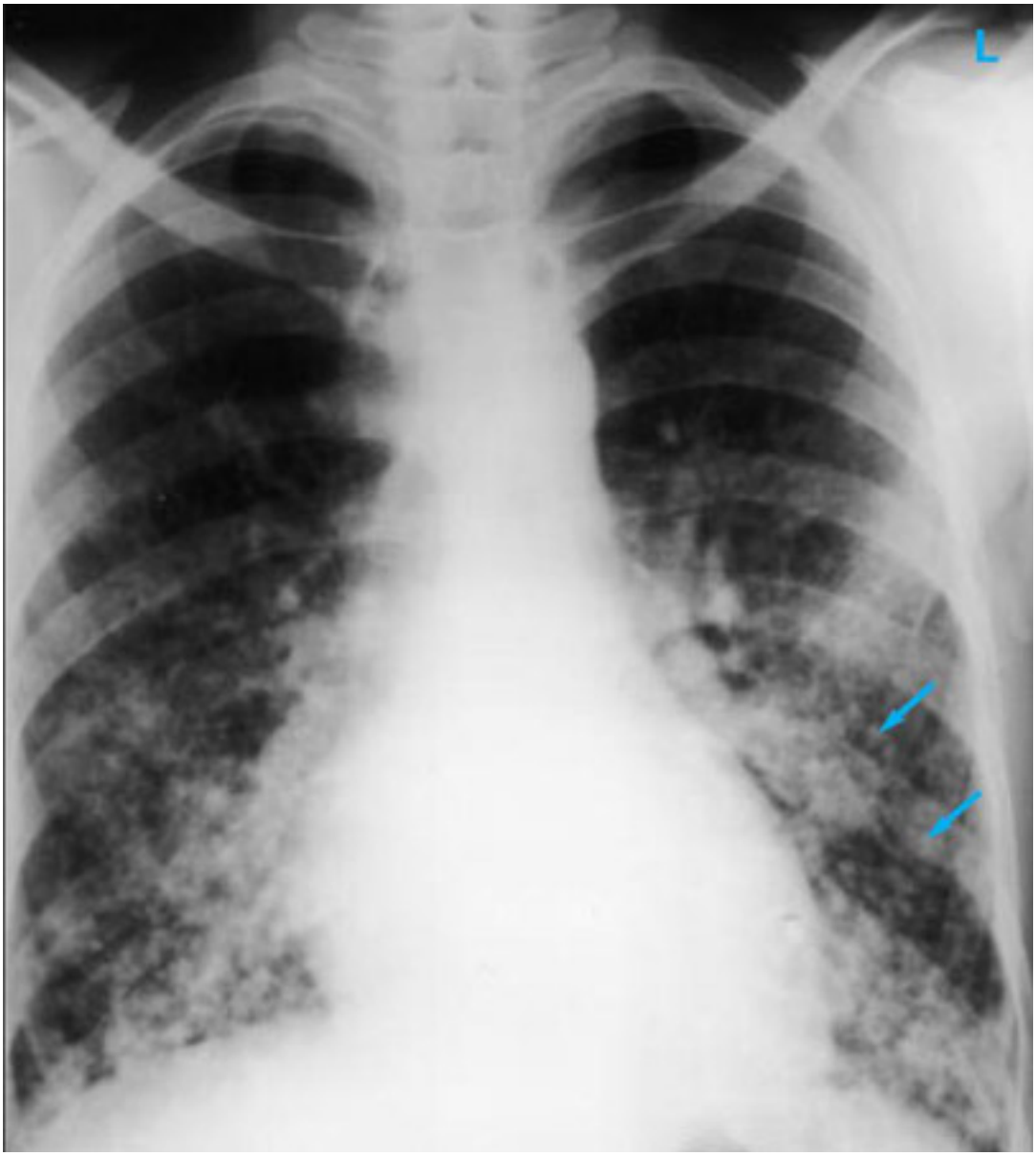
Chest x-ray

A chest x-ray should be obtained early in the evaluation of chronic cough.[38] Although it is not diagnostic of the most common causes, findings may quickly divert the evaluation to causes of greater gravity, such as structural lung diseases. These include lung cancer, tuberculosis, bronchiectasis, pneumonia, aspiration, and sarcoidosis.



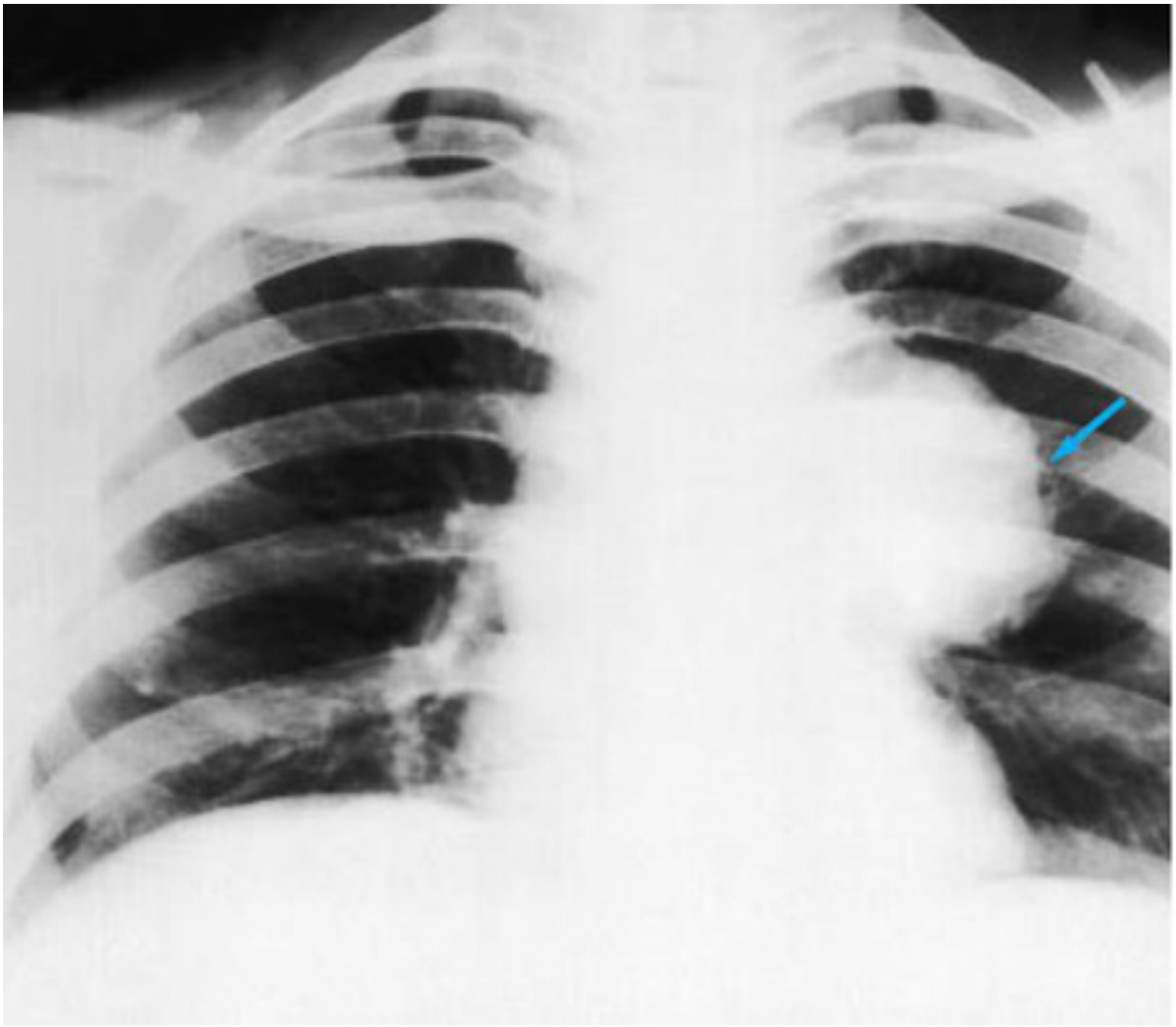
Chest x-ray showing bilateral hilar adenopathy in a patient with sarcoidosis

From the personal collection of Dr M.P. Muthiah, Division of Pulmonary and Critical Care and Sleep Medicine, University of Tennessee



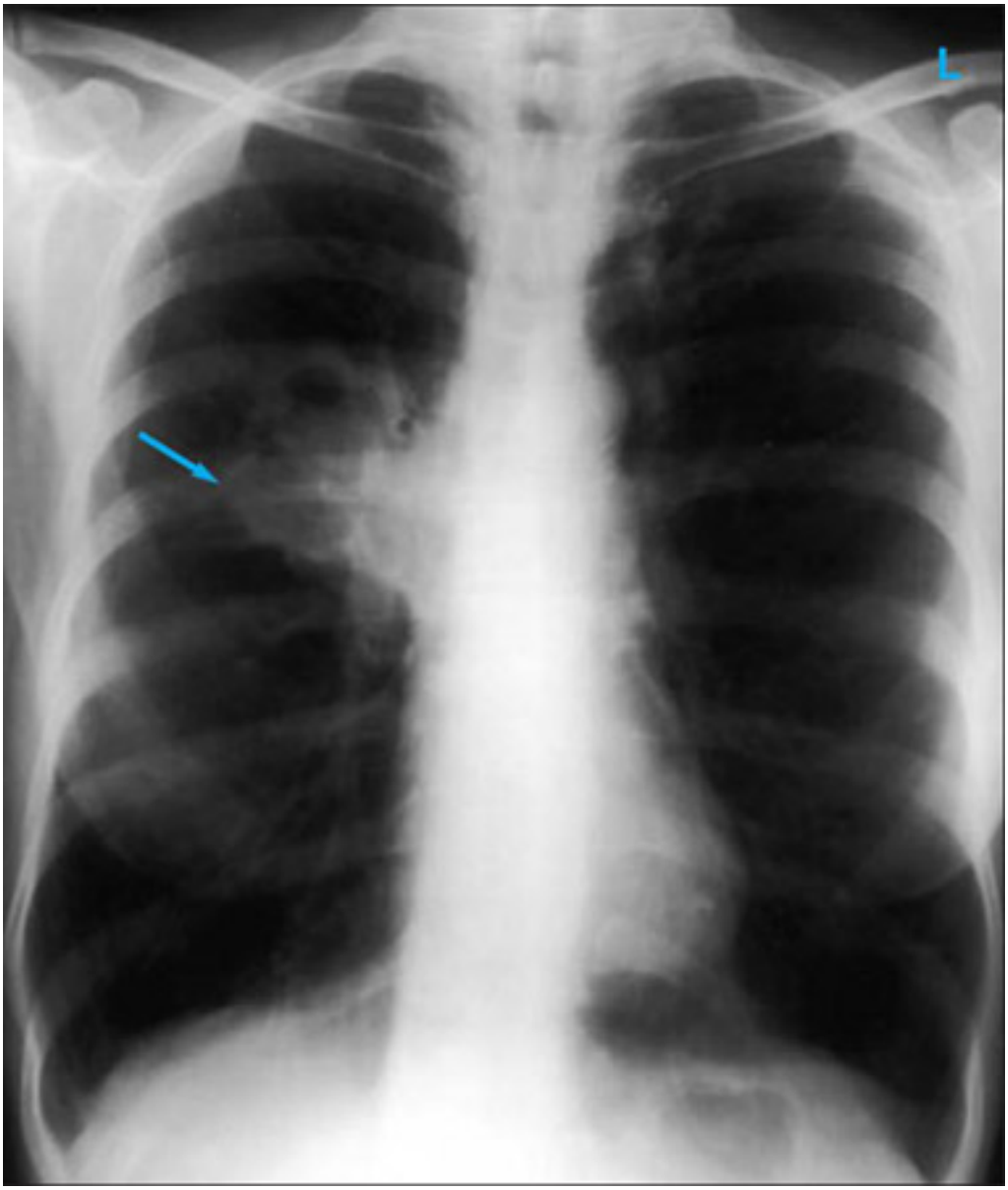
Chest x-ray showing multiple miliary lung metastases (arrows). The primary tumor was a thyroid carcinoma

E. Dick, Student BMJ. 2001;9:10-12



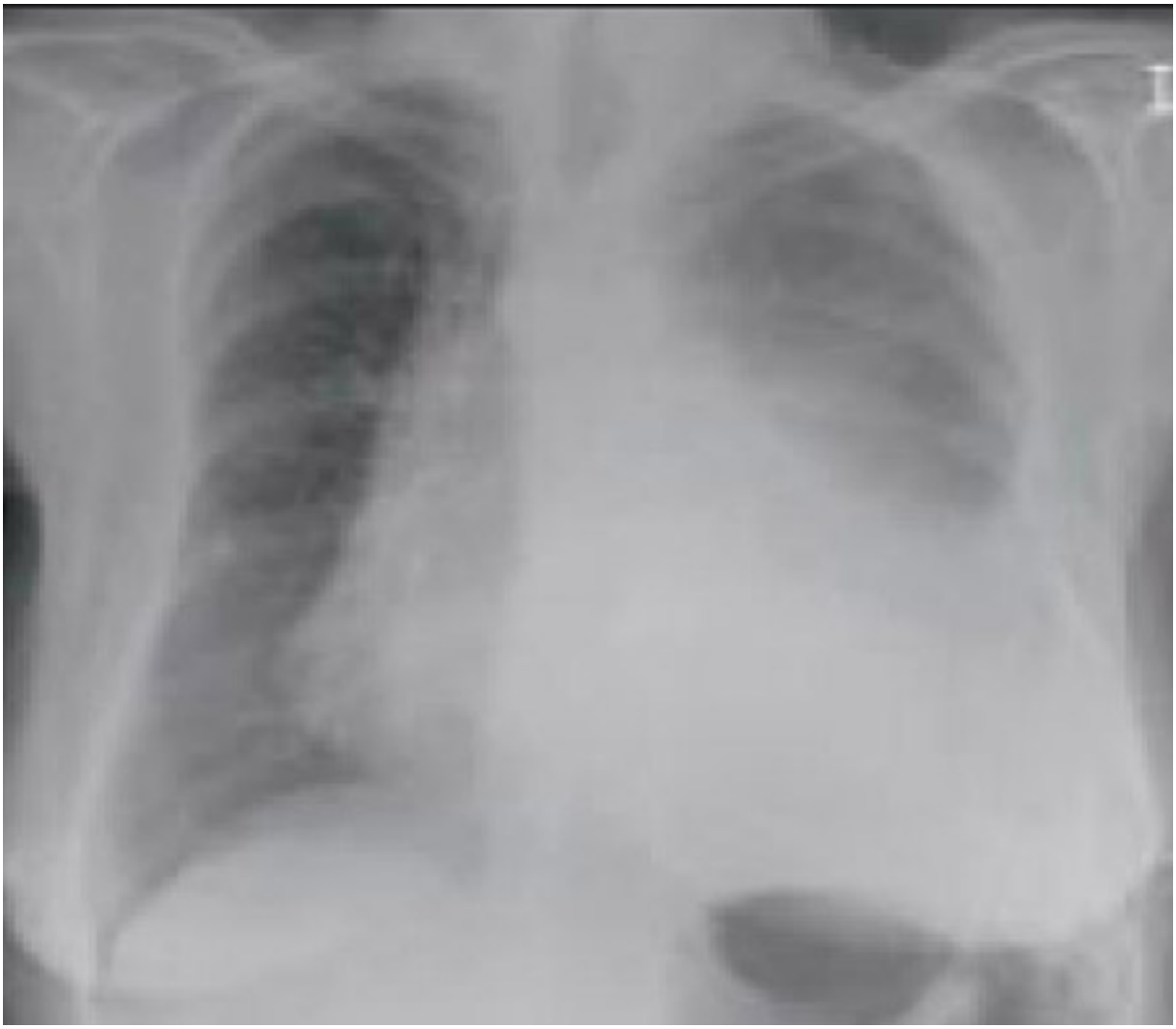
Chest x-ray showing left hilar carcinoma (arrow)

From: E. Dick, Student BMJ. 2000;8:358-360



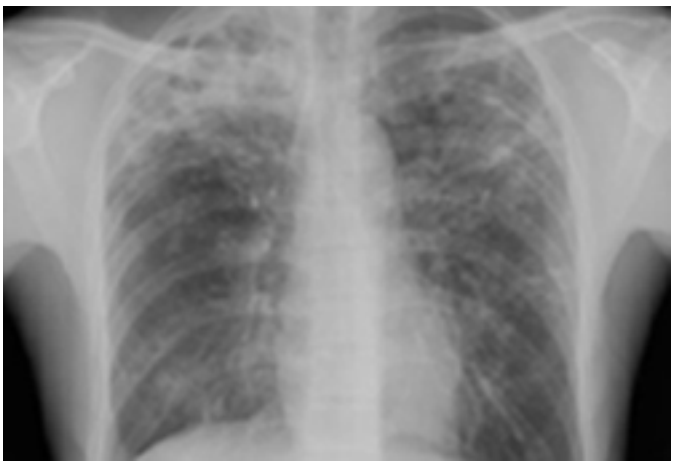
Chest x-ray showing a cavitating right hilar carcinoma (arrow)

E. Dick, Student BMJ. 2001;9:10-12



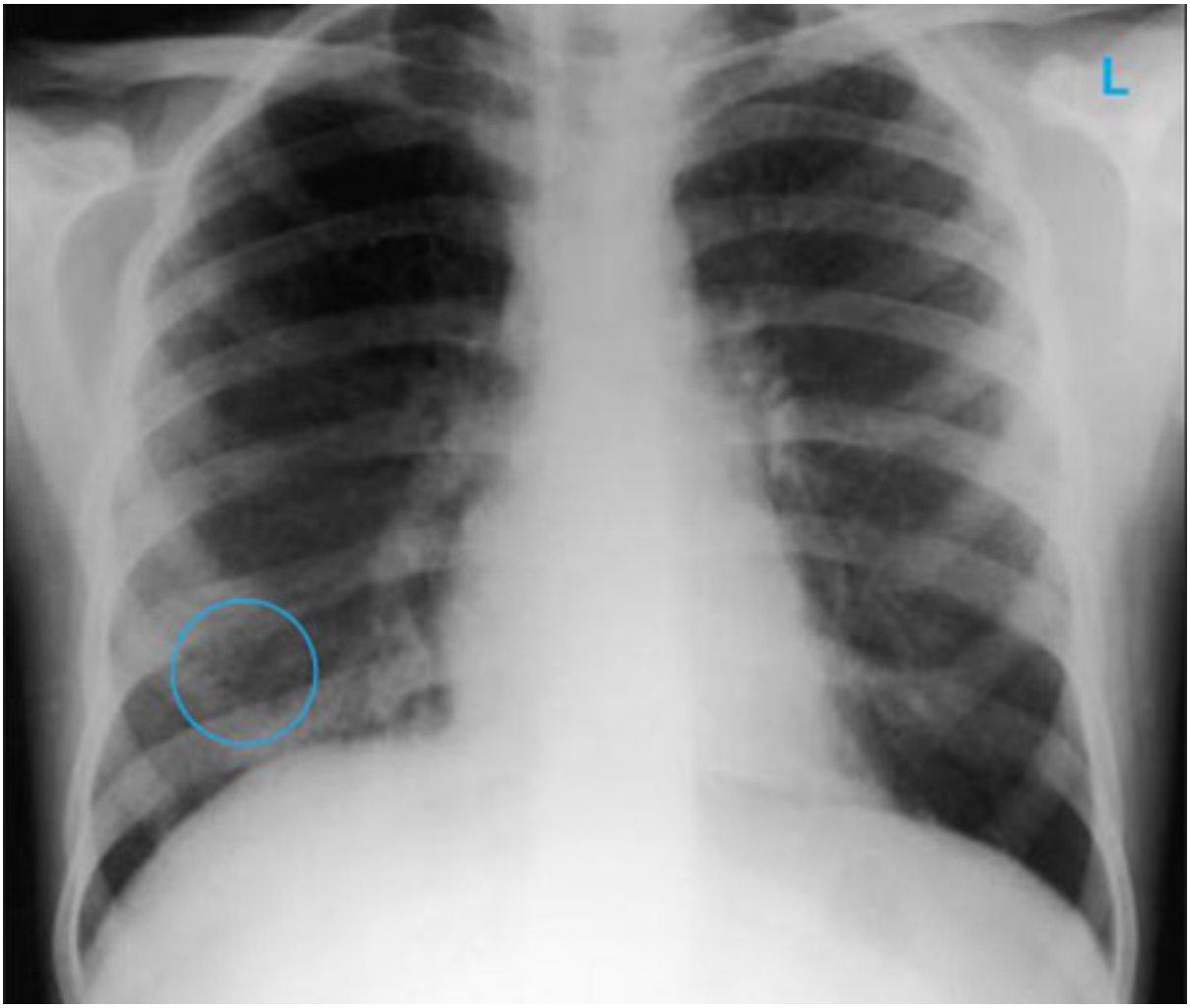
Chest x-ray in a patient with bronchogenic carcinoma showing a left-sided pleural effusion

From: R. Thakkar, Student BMJ. 2001;9:458



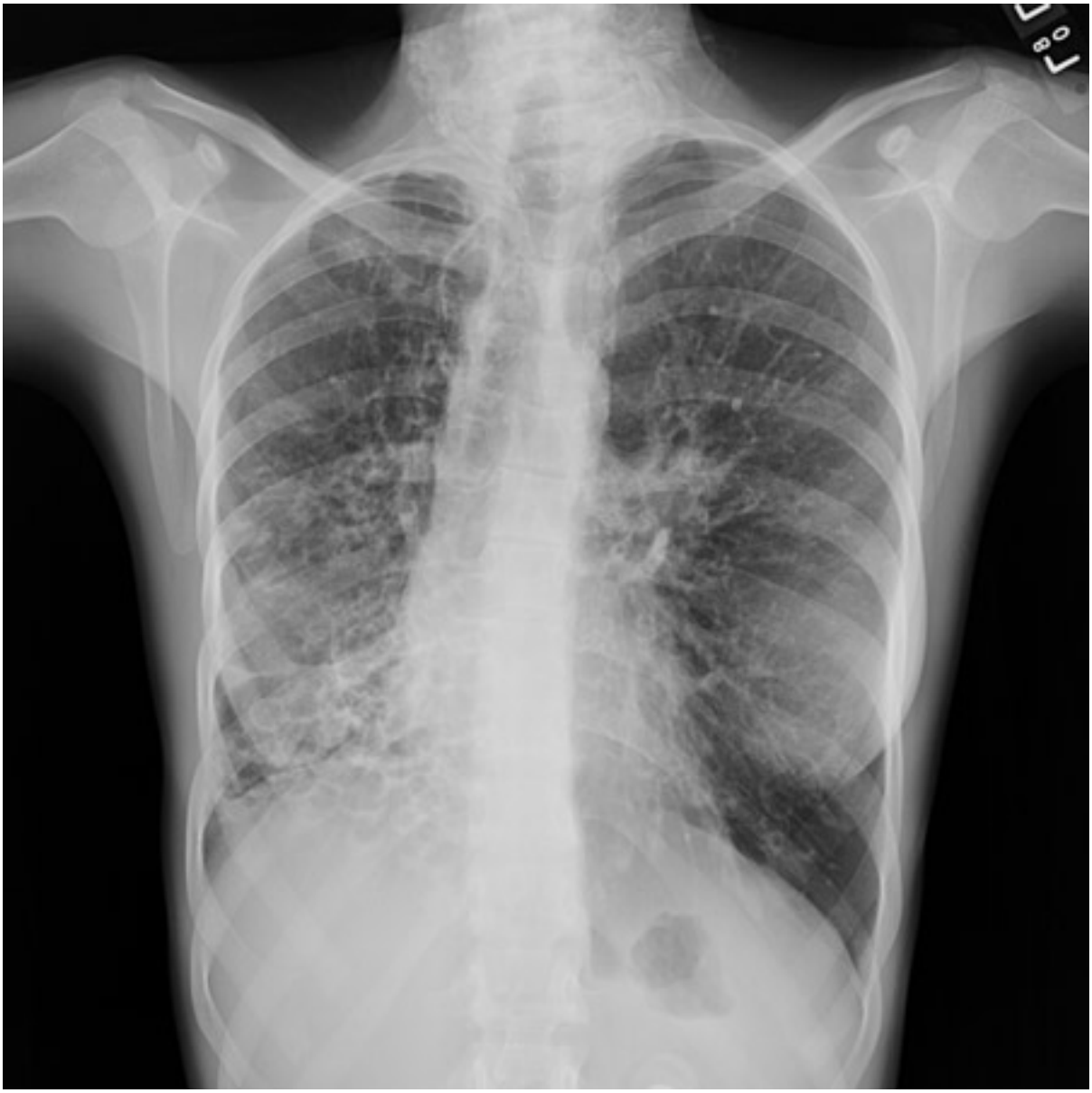
Chest x-ray showing pulmonary tuberculosis with cavitation

From the personal collection of Dr M. Narita, Department of Pulmonary and Critical Care Medicine, University of Washington



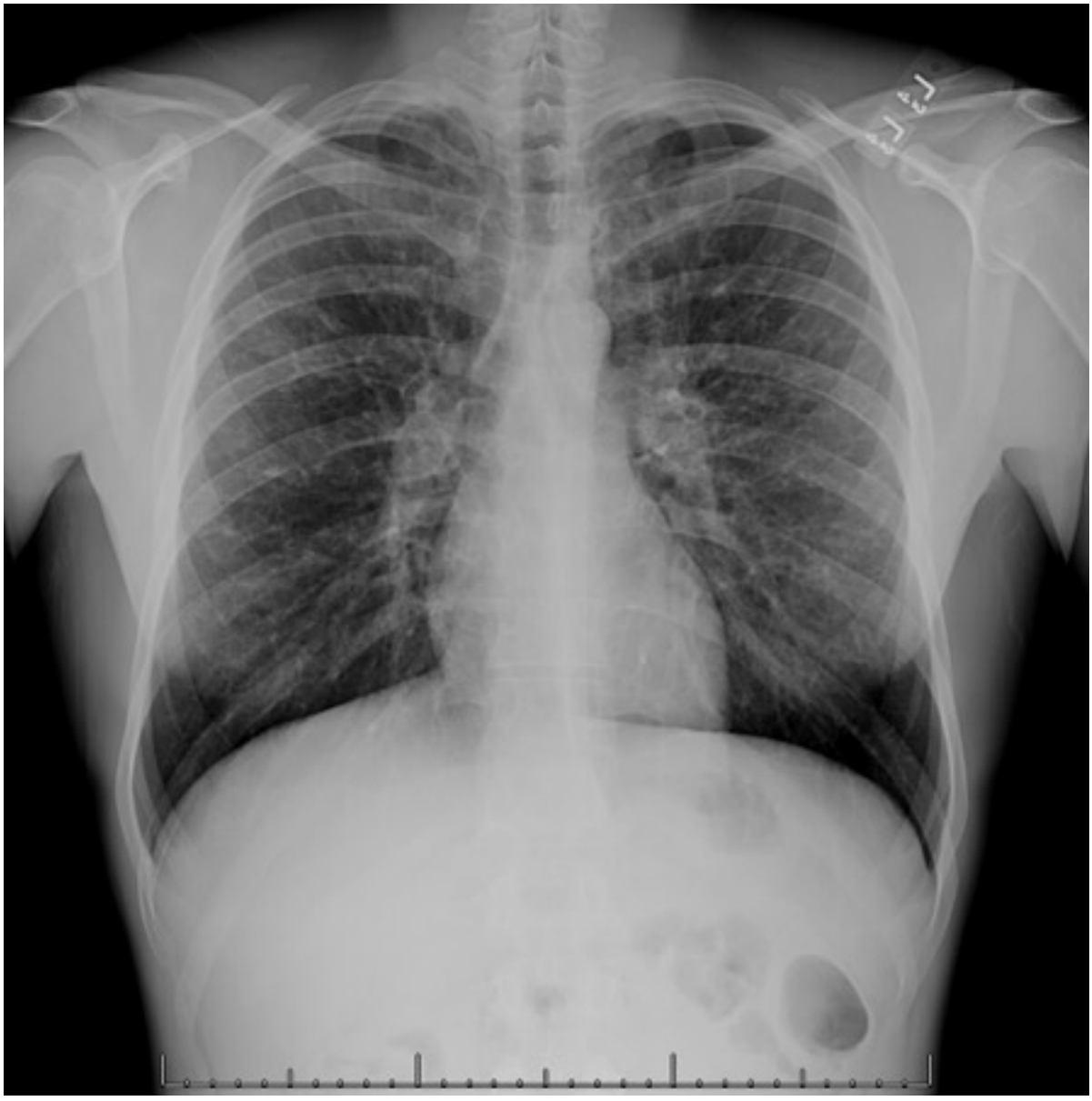
Chest x-ray showing multiple discrete nodules throughout both lungs (one of which is circled) in a patient with miliary tuberculosis

E. Dick, Student BMJ. 2001;9:10-12



Chest x-ray with lack of normal tapering producing a tram line in a patient with bronchiectasis

From the personal collection of Dr S.M. Bhorade, University of Chicago Medical Center; used with permission



Chest x-ray with dilated and thickened airways in a patient with bronchiectasis

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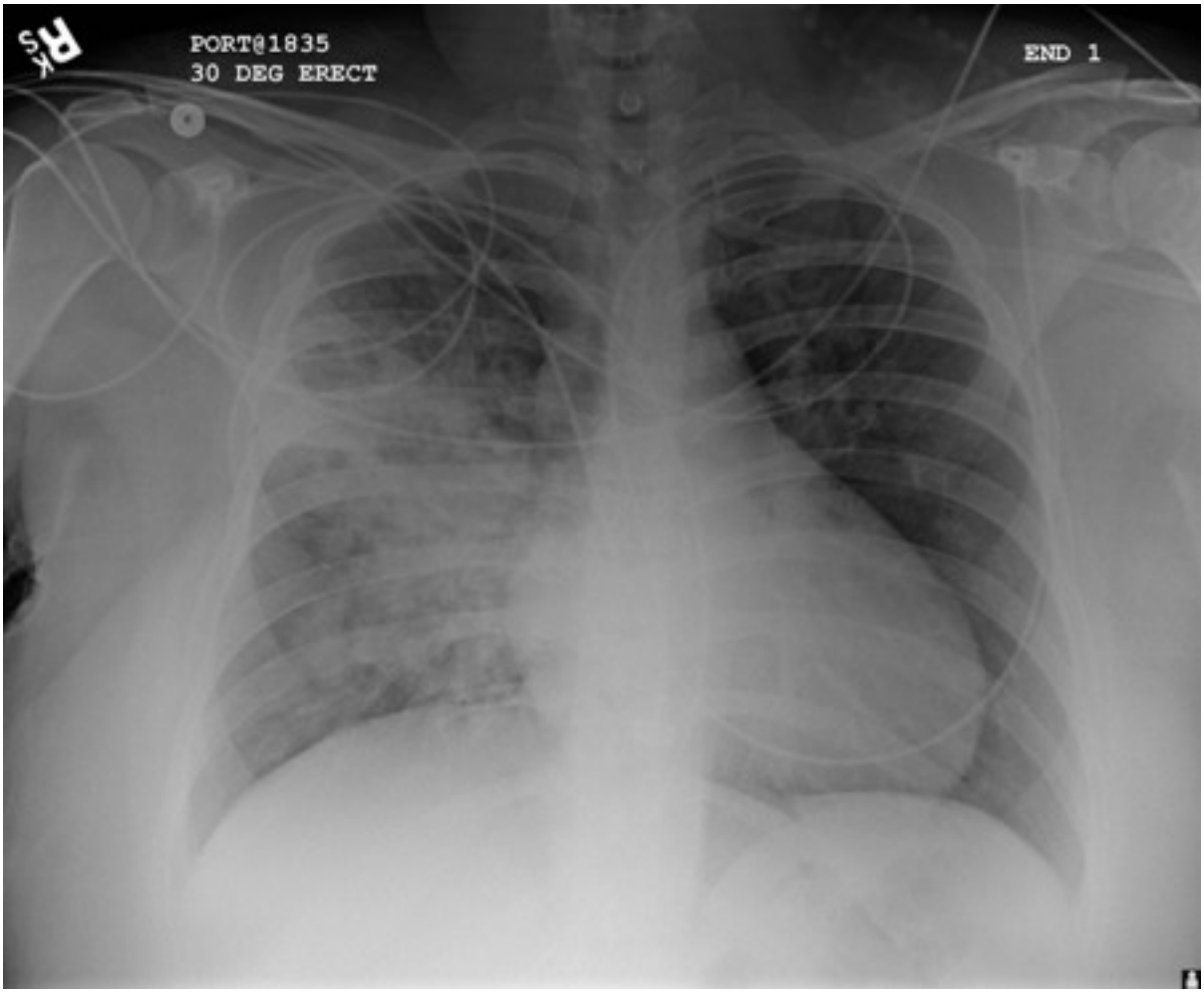
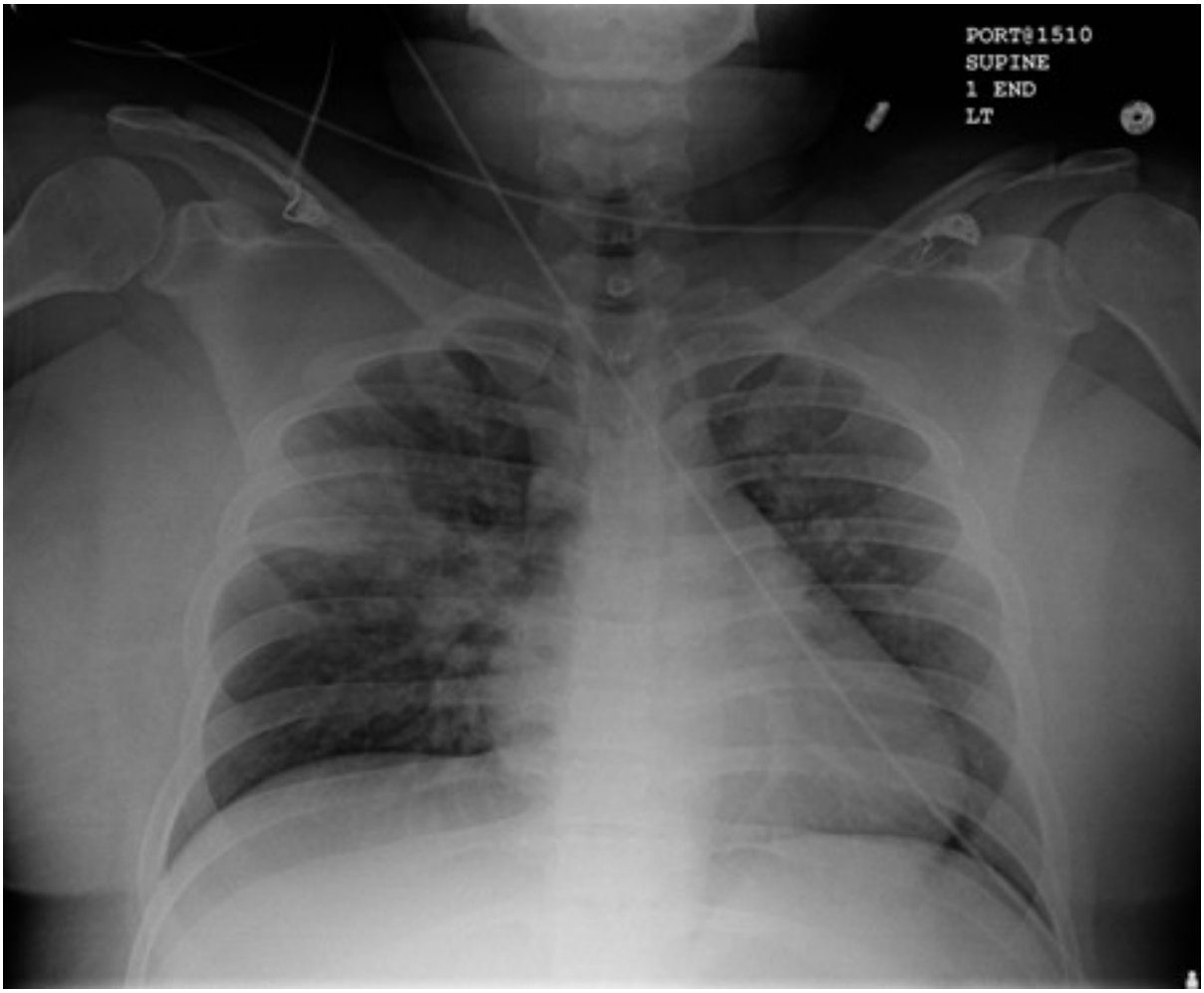


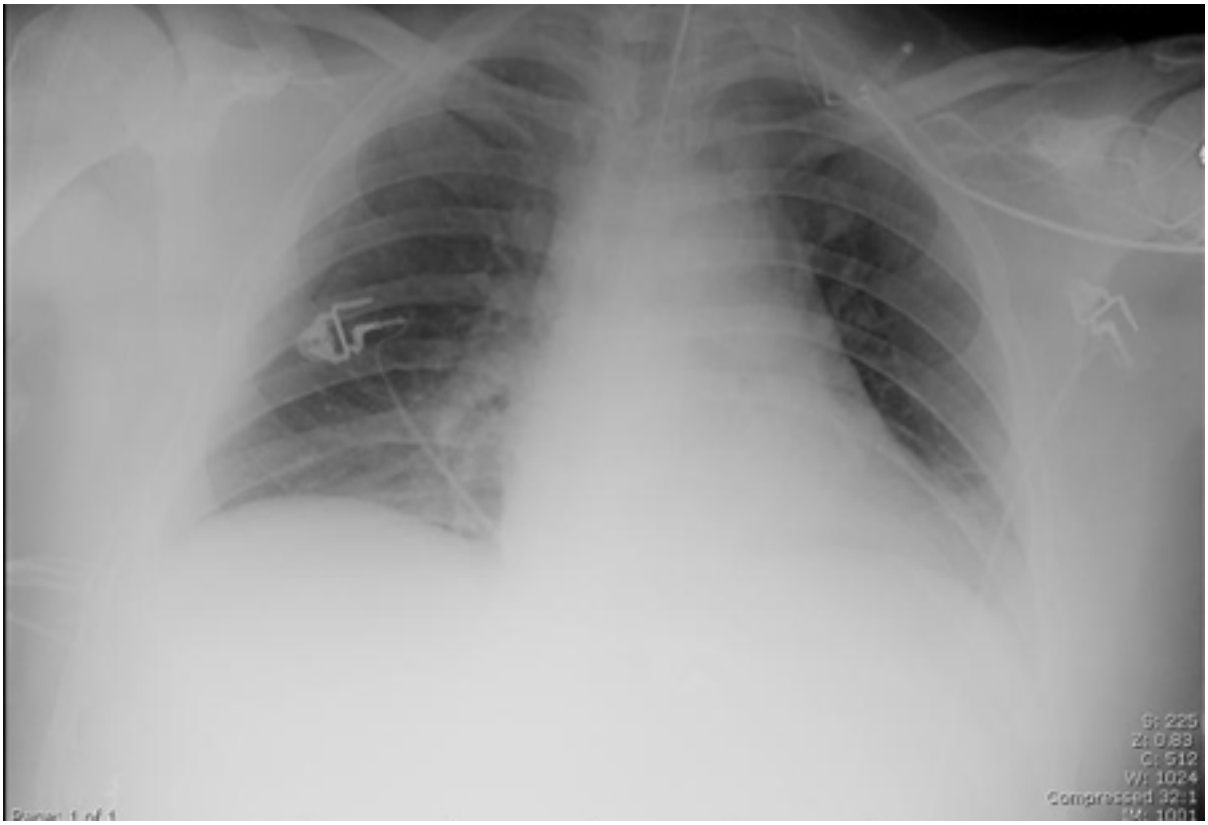
Chest x-ray showing increased opacification of the right perihilar region and superior segment of the right lower and upper lobes consistent with worsening aspiration pneumonia

From the personal collection of Dr R. Kanner, University of Utah School of Medicine



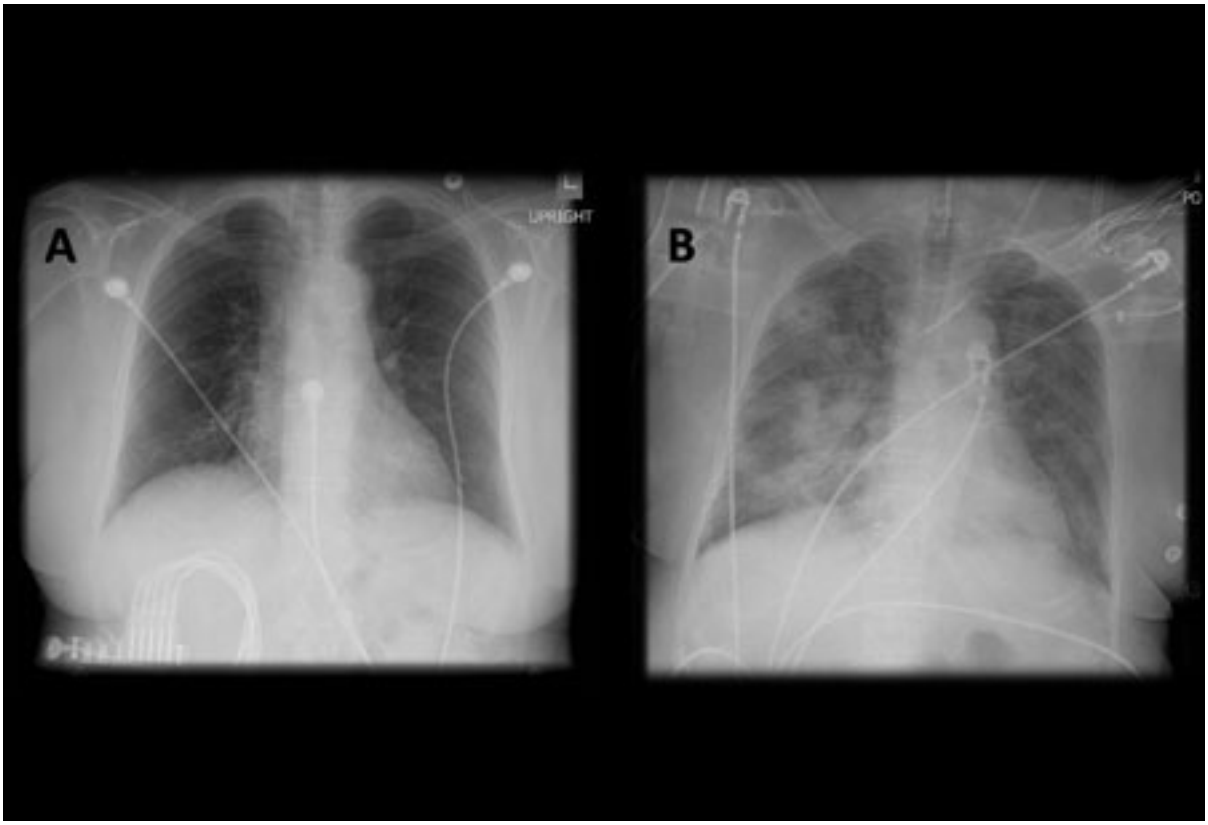
Chest x-ray showing early ill-defined opacities of the right upper lobe above the minor fissure consistent with early changes of aspiration pneumonia

From the personal collection of Dr R. Kanner, University of Utah School of Medicine



Portable chest x-ray with bibasilar opacities, worse on the right than the left, in a patient with hospital-acquired pneumonia

From the personal collection of Dr F.W. Arnold, Division of Infectious Diseases, Department of Medicine, University of Louisville School of Medicine



A. Portable upright chest x-ray before aspiration; B. Chest x-ray 1 hour after aspiration, showing bilateral diffuse alveolar infiltrates, worse at the bases on the right side

From the personal collection of Dr S. Murgu and Dr H. Colt, University of California at Irvine Medical Center

Choice of diagnostic testing or therapeutic trials

Following chest x-ray, the choice of either diagnostic testing or therapeutic trials depends on the clinician's assessed probability of a specific etiology and the patient's preferred approach.[38] Unless the history, physical examination, and chest x-ray indicate otherwise, efforts should be concentrated on one or more of the four most common causes (asthma, UACS, GERD, NAEB).

For example, if the history is most suggestive of asthma, then spirometry or assessment of peak expiratory flow (to test for airway obstruction) and bronchodilator variability testing would be appropriate first tests.[11] [30][31] Other investigations include fractional exhaled nitric oxide and bronchoprovocation challenge testing (e.g., methacholine inhalation test). Noninvasive tests to predict response to inhaled corticosteroids also include blood and sputum eosinophil counts, and blood and sputum eosinophilic cationic protein (ECP).[43] In the presence of raised blood or sputum eosinophil counts, negative reversibility tests should prompt consideration of a diagnosis of NAEB.

If UACS is suspected, a therapeutic trial aimed at resolving rhinosinusitis and reducing excessive secretions is indicated.

A therapeutic trial of proton pump inhibitors (PPIs) is recommended for patients with typical GERD symptoms (heartburn and regurgitation).[48] Diagnostic testing (including esophageal pH monitoring and endoscopy) may be considered according to clinician or patient preference in those refractory to a therapeutic trial of PPIs, or where there is a strong clinical suspicion of reflux-related cough.[48] [49] In patients with extra-

esophageal manifestations of GERD without typical GERD symptoms, consideration should be given toward diagnostic testing for reflux before initiation of PPI therapy.[46]

Laboratory tests

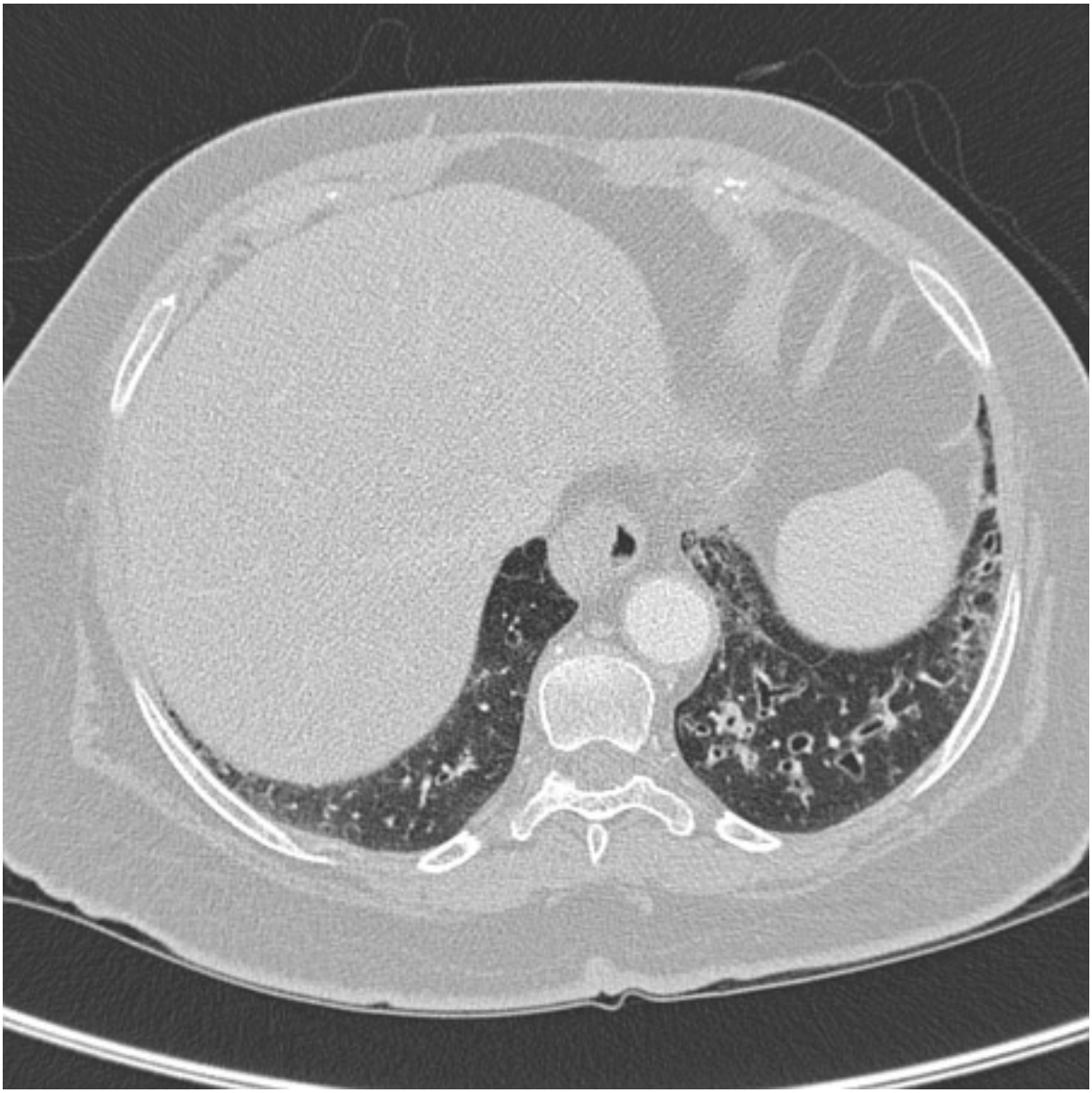
Laboratory assessment of sputum production is a key factor in narrowing the differential, as it can indicate presence of an infectious cause. If the cough is productive, a sputum sample should be sent for Gram stain and culture. Depending upon the history and examination, the following blood tests might be taken: CBC, WBC count, CRP, total IgE blood test for allergic bronchopulmonary aspergillosis.

Further diagnostic evaluation

If none of the four most common causes seem likely after thorough assessment, other tests to consider include:

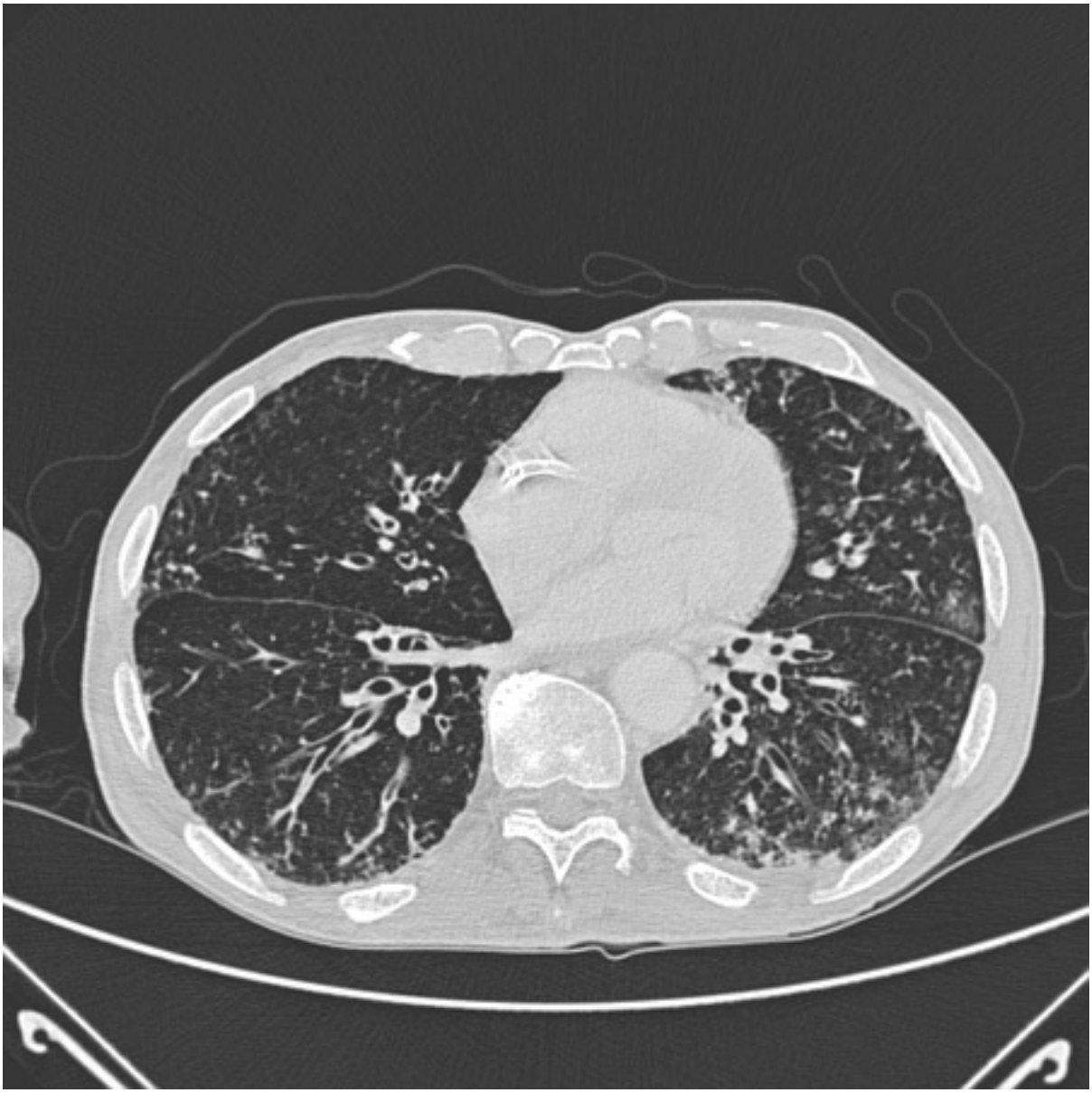
- High-resolution CT imaging of the chest to look for bronchiectasis (which does not always promote a productive cough), foreign body aspiration, pulmonary fibrosis, or other structural lung disease (which may not show well on chest x-ray). Chronic suppurative lung disease is diagnosed in patients with clinical symptoms of bronchiectasis but no radiographic evidence of bronchiectasis.[50] CT imaging may also indicate the presence of an aortic aneurysm or Zenker diverticulum. The diagnostic yield of the CT scan of the chest in a patient with chronic cough and normal chest x-ray is expected to be low.[3] [Evidence C] There is no high-quality evidence to support the use of chest CT in the initial evaluation of patients presenting with chronic cough.[38]
- Bronchoscopy to search for endobronchial pathology.
- CT sinuses or nasendoscopy.
- 24-hour esophageal pH and/or impedance monitoring to rule out silent GERD.
- Serum ferritin and iron, because iron deficiency has been associated with chronic cough.[51]
- Serum alpha-1 antitrypsin (AAT) levels should be quantified in individuals with possible AAT deficiency. However, AAT is an acute phase reactant, meaning that normal serum AAT levels can be misleading, especially in the setting of inflammatory processes.[52]
- Polysomnography or polygraphy to rule out obstructive sleep apnea.

In addition, pulmonary and/or ENT consultation should be considered. In cases where the patient also has features of stridor, laryngospasm, or paradoxical vocal fold motion, early involvement of a speech pathologist is appropriate, because treatment directed at underlying causes may speed resolution of chronic cough as well.[53]



Chest CT with presence of signet ring on left in a patient with bronchiectasis

From the personal collection of Dr S.M. Bhorade, University of Chicago Medical Center



Chest CT with dilated and thickened airways and peripheral tree-in-bud pattern in a patient with bronchiectasis

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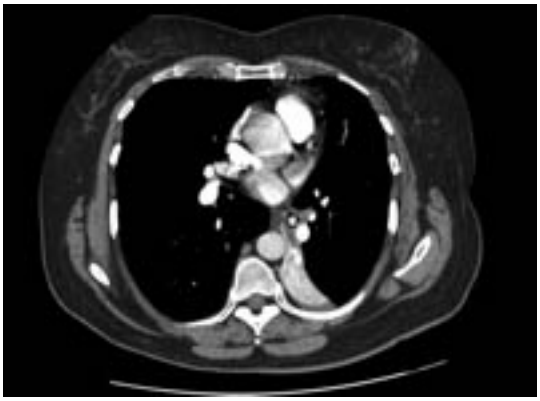
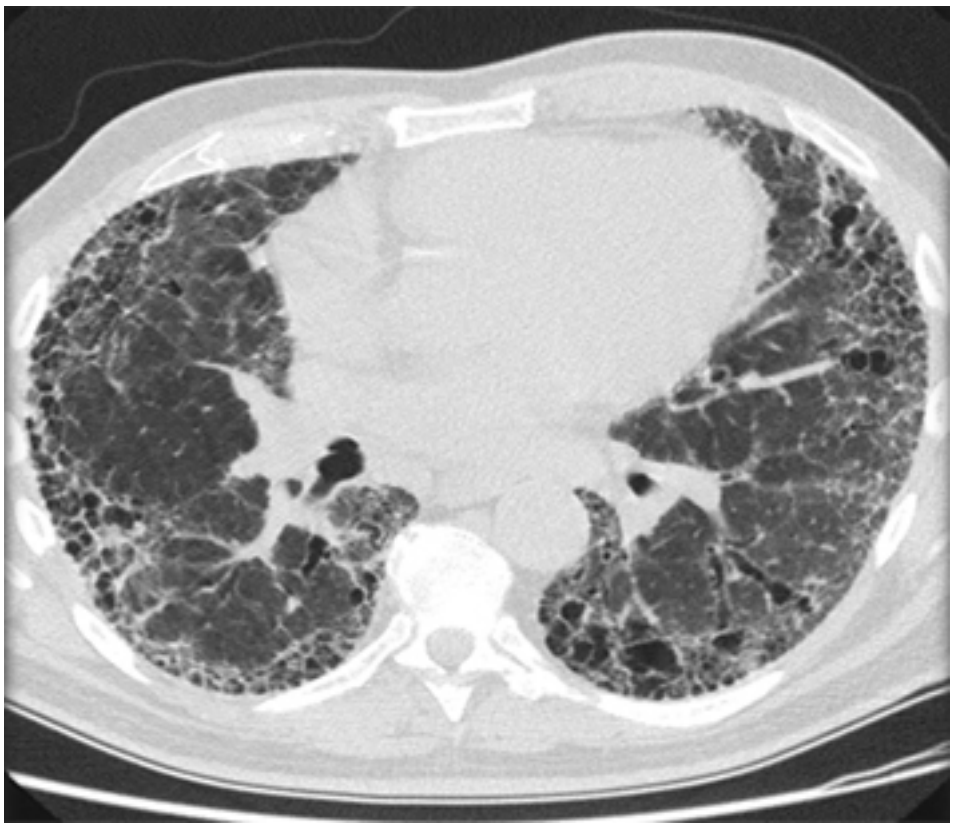


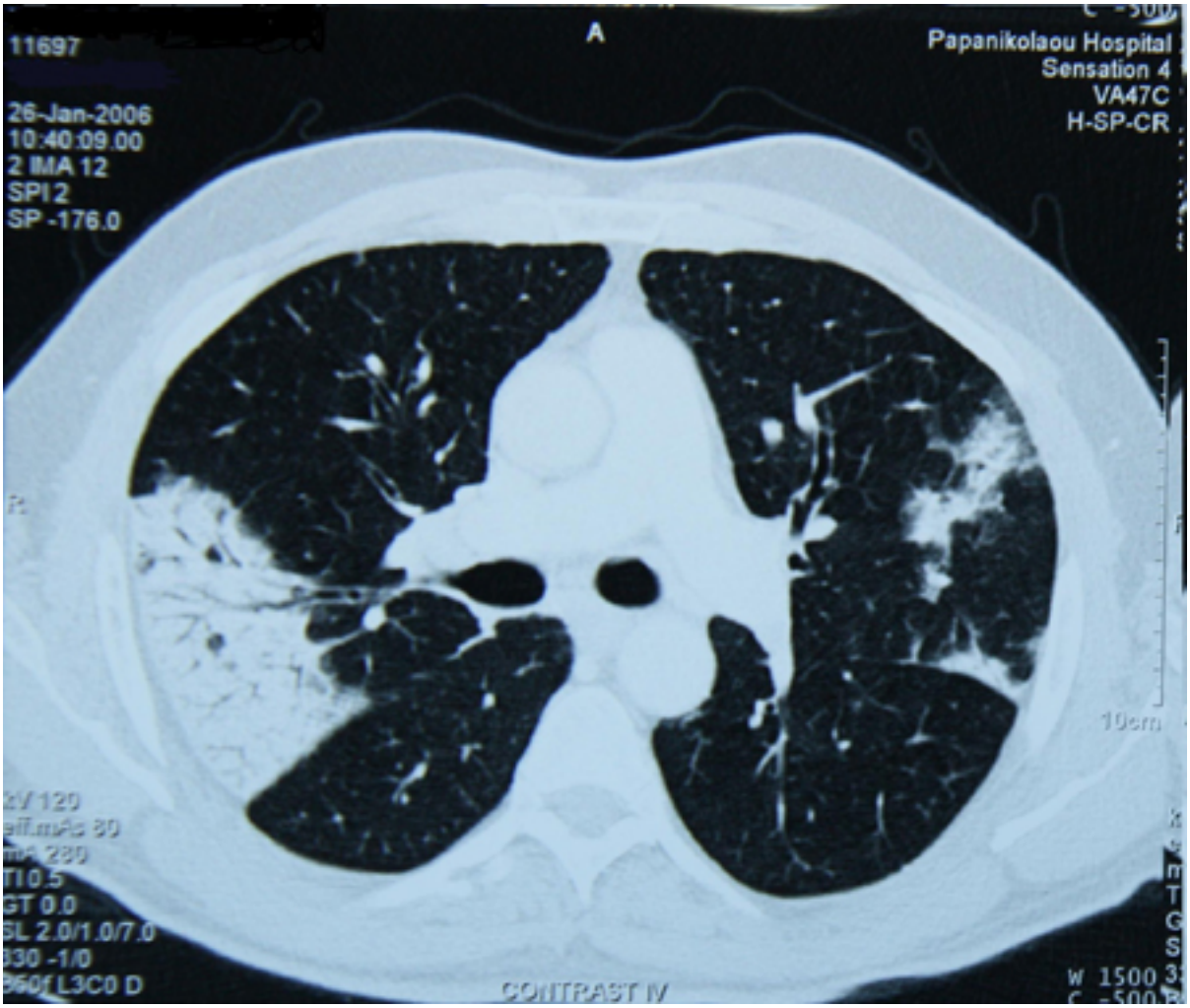
CT of the chest with intravenous contrast material showing complete left lower lobe collapse with a radiopaque object within the left lower main bronchus surrounded by a halo of air

BMJ Case Reports 2008 (doi:10.1136/bcr.06.2008.0013). Copyright 2008 BMJ Publishing Group Ltd



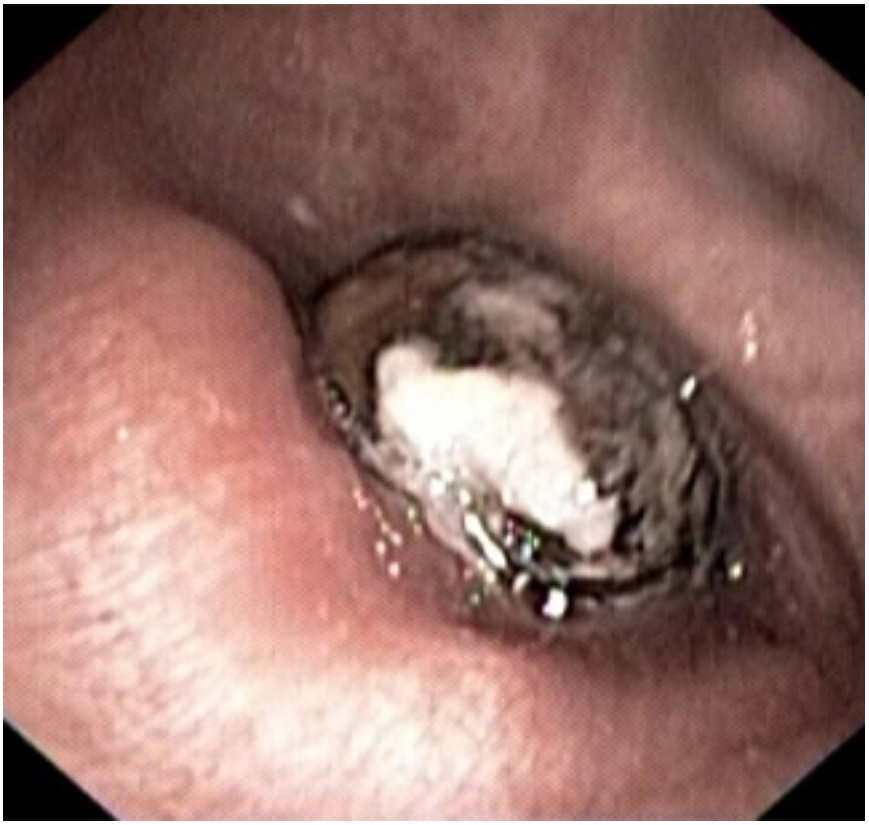
Chest CT showing idiopathic pulmonary fibrosis

From the personal collection of Dr J.C. Munson, Center for Clinical Epidemiology and Biostatistics, University of Pennsylvania School of Medicine



Chest CT of a patient with amiodarone pulmonary toxicity, showing asymmetric opacities with a peripheral distribution

From the personal collection of Dr A. Pataka and Professor P. Argyropoulou, Aristotle University, Thessaloniki, Greece



Bronchoscopy image showing a loquat seed completely occluding the bronchus intermedius

From the personal collection of Dr S. Murgu and Dr H. Colt, University of California at Irvine Medical Center

Therapeutic trials

Therapeutic trials are selected based on clinical impression, at times supported by diagnostic testing. The patient's response to the trial must be assessed and the cough resolved before a given etiology may be assigned with certainty. A partial response may indicate that more than one etiology is in play. In this event, further testing and/or additional therapeutic trials may be indicated, while the partially successful therapy should be continued. Lack of a response requires reassessment both of suspected etiology and of treatment adherence and effectiveness. High placebo effect has been reported in empiric trials in chronic cough.[54]

Empiric therapeutic trials may be undertaken sequentially (starting with the most likely etiology first), with subsequent selections made according to patient response. Alternatively, trials may be undertaken simultaneously when multiple etiologies are suspected from the outset, with subsequent sequential withdrawal of therapies once the cough is controlled. The following are considered:

1. UACS: a trial of an antihistamine plus a decongestant should be undertaken. Failure of response to appropriate therapeutic trials should prompt a sinus computed tomography (CT) scan and an ear, nose, and throat (ENT) referral, particularly if other etiologies have been considered and deemed very unlikely.
2. Asthma or NAEB: noninvasive measurement of airway inflammation (such as fractional exhaled nitric oxide (FeNO) sputum and blood eosinophilia, and sputum and blood eosinophilic cationic protein) is suggested as a useful tool to predict response of cough to inhaled corticosteroid (ICS), based on moderate supporting evidence.[43] If eosinophilic airway inflammation is found, it is likely to respond to corticosteroids.[43] Since the availability of these noninvasive tests is limited, an empiric trial of ICS is commonly used in clinical practice. Failure of response to 2-4 week trial of an ICS should

prompt an increase in the dose of the ICS with the addition of a therapeutic trial of a leukotriene receptor antagonist.[43] Beta agonists may also be considered with ICS.[43] Treatment adherence, anti-inflammatory effectiveness (measured by FeNO and peak-flow variability, as appropriate), and conditions that contribute to ongoing poor asthma control such as GERD, sinus disease, or ongoing allergen exposure, should be reevaluated.[43]

3. GERD: failure of response to an appropriate therapeutic trial (e.g., 8-12 weeks with a proton-pump inhibitor) should prompt confirmatory testing (if not already done), and careful assessment of effectiveness of acid suppression and/or other factors contributing to ongoing nonacid reflux.[46] [48] [49]
4. Cough hypersensitivity syndrome: a therapeutic trial of a neuromodulator drug, such as gabapentin, pregabalin, amitriptyline, or baclofen could be considered if previous investigations do not produce a conclusive diagnosis and cough hypersensitivity syndrome is suspected.[26]

Differentials overview

Common
Upper airway cough syndrome (UACS; postnasal drip)
Asthma
Gastroesophageal reflux disease (GERD)
Nonasthmatic eosinophilic bronchitis (NAEB)
Chronic bronchitis/COPD
Angiotensin-converting enzyme inhibitor (ACE inhibitor)
Pneumonia
Postinfectious cough
Bordetella pertussis infection

Uncommon
Lung cancer
Bronchiectasis and chronic suppurative lung disease
Interstitial lung disease
Sarcoidosis
Tuberculosis (TB)
Recurrent aspiration
Zenker diverticulum
Thoracic aortic aneurysm (TAA)
Foreign body
Hypersensitivity pneumonitis
Bronchiolitis

Uncommon

Tropical filarial pulmonary eosinophilia
Cough hypersensitivity syndrome (somatic cough, psychogenic cough, unexplained chronic cough, refractory chronic cough)
Obstructive sleep apnea/hypopnea syndrome (OSAHS)

Differentials

Common

◊ Upper airway cough syndrome (UACS; postnasal drip)

History	Exam	1st Test	Other tests
frequent throat clearing, postnasal drip, nasal discharge, nasal obstruction or sneezing typical, halitosis	mucopurulent secretions in the nasopharynx and oropharynx or cobblestone appearance of posterior oropharynx	»**therapeutic trial:** response to empiric therapy with antihistamine and decongestant There is no definitive test that can prove or disprove the presence of UACS; a combination of symptoms, physical examination findings, and response to therapy is required for diagnosis.[44] When a specific cause for UACS (e.g., allergic rhinitis or nasal polyposis) is suspected based on history and physical exam, therapy should first be directed toward those entities.	

Asthma

History	Exam	1st Test	Other tests
wheezing, chest tightness, dyspnea, symptom variability, strong family history of asthma/atopic disease, cough, paroxysms, exacerbation by irritants or seasonal exposures; cough may sometimes be the principal or sole symptom, usually worse at night (cough-variant asthma)	wheezing and prolonged expiratory phase on pulmonary exam	»**spirometry (FEV1/FVC ratio and bronchodilator reversibility [BDR] test):** FEV1/forced vital capacity (FVC) ratio: below the lower limit of normal (LLN; if available) or <70% (if LLN not available) is positive for airflow obstruction; BDR test: improvement in FEV1 of 12% or more in response	»**fractional exhaled nitric oxide (FeNO):** elevated (>40 parts per billion) In an untreated patient, absence of elevated FeNO would make asthma unlikely.[62] »**other noninvasive airway inflammation biomarkers (blood and sputum eosinophil counts**

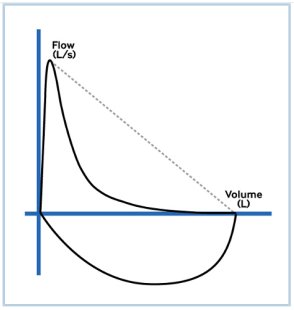
Common

Asthma

History	Exam	1st Test	Other tests
		to beta agonists (or to a treatment trial with corticosteroids), together with an increase in volume of 200 mL or more is positive for reversibility of airway obstruction FEV1/FVC ratio (spirometry) is the primary diagnostic test.[11] A bronchodilator reversibility test may demonstrate reversibility of airflow obstruction in response to short-acting bronchodilators.[11][31][59] Spirometry can be normal in some patients.[31] If normal, further investigations such as bronchoprovocation testing are recommended.	**and eosinophilic cationic protein):** elevated »**therapeutic trial:** improvement in symptoms following a 2-4 week course of an inhaled corticosteroid or a leukotriene receptor antagonist »**bronchoprovocation testing:** provocative concentration of methacholine causing a 20% fall in FEV1 (PC20) <4 mg/mL Increased airway responsiveness to inhaled methacholine is a moderately sensitive but not specific feature of asthma.[11][31] Negative methacholine challenge while not receiving inhaled corticosteroids essentially excludes asthma.[11][63] »**CBC:** normal or elevated eosinophils and/or neutrophilia »**serum IgE antibodies:** elevated antigen-specific IgE antibodies For suspected work-related asthma, perform testing before and

Common

Asthma

History	Exam	1st Test	Other tests
		 *Flow-volume loop (spirogram) in obstructive lung disease, such as asthma or COPD: peak expiratory flow may be normal, but a concave shape is seen following the point of maximal flow due to the low flow rate in relation to lung volume* *Created by BMJ Knowledge Centre* »**peak expiratory flow (PEF):** may be reduced; may be variability (>10%) of measurements recorded at different times of the day PEF should be measured in patients with normal spirometry. Variability of airway obstruction can be used to support the diagnosis of asthma.[31] [60][61] The diagnosis of asthma is supported if there is excessive	after exposure, i.e., at the end of a regular working week and after vacation.[16] »**skin-prick allergy testing:** may be positive for allergen May be done to support diagnosis and gauge treatment.

Common

Asthma

History	Exam	1st Test	Other tests
		variability in twice daily PEF over 2 weeks. In adults, an average daily diurnal variability in PEF of >10% is considered excessive. An increase in PEF by >20% from baseline after 4 weeks of treatment also indicates excessive variability.[11]	

◊ Gastroesophageal reflux disease (GERD)

History	Exam	1st Test	Other tests
heartburn, dysphagia, acid regurgitation, association of cough with slouched posture, phonation, rising from bed, or eating suggest reflux disease; may be silent	no differentiating features on exam, may be overweight or obese	»**therapeutic trial of proton-pump inhibitors (PPIs):** relief of symptoms Alleviation of symptoms may require 8 weeks of PPI therapy, so the trial should not be considered "negative" before 8 weeks; in rare cases, this improvement may take up to 3 months.[46] [48] [49] As reflux disease is clinically silent in 75% of cases, empiric therapy with a PPI should precede formal testing.[45] [49] Patients should also be advised to lose weight if overweight or obese, to elevate the head	»**24-hour esophageal pH monitoring:** pH <4 for 4% or more of monitoring time and coinciding with cough is consistent with pathologic acid exposure Most sensitive and specific for reflux disease-related cough. Testing first may be considered as an alternative to a PPI trial. Controversy exists in this regard.[49] Testing should be performed if a PPI trial does not resolve symptoms but GERD is still considered likely. A detailed assessment of symptom correlation with reflux events is

Common

◊ Gastroesophageal reflux disease (GERD)

History	Exam	1st Test	Other tests
		of the bed, and avoid meals within 3 hours of bedtime.[49]	most supportive of the diagnosis.[49] »**barium esophagram:** reflux May be indicated in suspected GERD; however, the presence of reflux on a barium esophagram has poor sensitivity and specificity for GERD, compared with pH testing.[48] [64]

◊ Nonasthmatic eosinophilic bronchitis (NAEB)

History	Exam	1st Test	Other tests
chronic nonproductive cough; no differentiating features on history	no differentiating features on exam	»**sputum or bronchoalveolar lavage (BAL) differential count:** eosinophilia Eosinophilia in sputum or BAL without obstruction on spirometry, without peak flow variability or hyperreactivity on bronchoprovocation testing, suggests NAEB.[43] [65]	»**FeNO:** elevated Sensitive in patients not treated with inhaled corticosteroids.[66] »**therapeutic response to inhaled steroids:** present Cough due to NAEB improves after a course of inhaled steroids for 4-6 weeks.

◊ Chronic bronchitis/COPD

History	Exam	1st Test	Other tests
history of smoking may be present; cough may produce sputum; dyspnea, especially exertional,	mild cases: most respiratory exams are normal, may show quiet breath sounds, prolonged expiratory phase, rhonchi, or	»**spirometry:** reduced FEV1 and forced vital capacity (FVC); postbronchodilator FEV1/FVC ratio <0.70 (airflow limitation)	»**chest x-ray:** hyperinflation, but may not be present in some cases

Common

◊ Chronic bronchitis/COPD

History	Exam	1st Test	Other tests
may accompany the cough	wheezes; advanced cases: cyanosis, barrel chest, use of accessory muscles of inspiration, increased S2 over left sternal border, or peripheral edema	Required for diagnosis of COPD.[67] Obstructive ventilatory deficit may or may not be reversible after bronchodilator use. Postbronchodilator FEV1/FVC ratio <0.70 confirms airflow limitation.[67] The 2026 Global Initiative for Chronic Obstructive Lung Disease (GOLD) report recommends a repeat spirometry test on a separate occasion if the postbronchodilator FEV1/FVC ratio is between 0.6 and 0.8.[67] The 2026 GOLD report states that prebronchodilator spirometry can be used as an initial test to investigate whether symptomatic patients have airflow obstruction.[67] If this doesn't show obstruction, then postbronchodilator spirometry is not required unless there is a very high clinical suspicion of COPD, in which case an FVC	Not useful in diagnosis, but may be useful to exclude other conditions or for diagnosing comorbidities.[67] »**pulmonary function tests:** increased residual volume (RV), increased total lung capacity (TLC), decreased diffusing capacity of lung for carbon monoxide (DLCO) Air-trapping (increased RV) and hyperinflation (increased TLC) are typically present in patients with emphysema. »**ABG:** hypoxemia, hypercapnia Should be done if pulse oximetry measurements ≤92%.[67] Hypercapnia typically accompanies severe cases of COPD.

Common

◊ Chronic bronchitis/COPD

History	Exam	1st Test	Other tests
		volume response may reveal obstruction.[67]	

◊ Angiotensin-converting enzyme inhibitor (ACE inhibitor)

History	Exam	1st Test	Other tests
dry cough, typically associated with tickling or scratching sensation in the throat; cough may begin within days or months of initiating ACE inhibitor therapy	no specific exam findings	»**stop ACE inhibitor use:** resolution of cough Stopping ACE inhibitors resolves cough in 1-12 weeks, typically 1-4 weeks.[47]	

Pneumonia

History	Exam	1st Test	Other tests
fever, malaise, cough, usually productive of sputum, chest pain	dullness to percussion, decreased breath sounds, and presence of rales	»**chest x-ray:** infiltrate suggestive of pneumonia	»**WBC (blood):** usually elevated but nonspecific »**serum C-reactive protein (CRP):** may be elevated CRP >10 mg/L has a sensitivity of 90% and a specificity of 48% for diagnosing community-acquired pneumonia.[72] »**sputum Gram stain and culture:** presence of microorganisms and leukocytes in a good sputum sample (<25 squamous epithelial cells per field) supports the diagnosis of respiratory tract infection

Common

◊ Postinfectious cough

History	Exam	1st Test	Other tests
cough of duration between 3 and 8 weeks following symptoms of acute respiratory infection; nasal/ sinus congestion, nonpurulent nasal discharge, sore throat	diagnosis is clinical and one of exclusion	»**chest x-ray:** normal, rules out pneumonia	»**WBC (blood):** usually elevated but nonspecific »**sputum Gram stain and culture:** presence of microorganisms and leukocytes in a good sputum sample (<25 squamous epithelial cells per field) supports the diagnosis of respiratory tract infection

Bordetella pertussis infection

History	Exam	1st Test	Other tests
paroxysms of cough, post-tussive vomiting, or inspiratory whooping sound; more likely if local epidemiology suggests increased prevalence	petechiae and conjunctival hemorrhages may result from cough paroxysms; lung examination is typically normal	»**nasopharyngeal culture (if symptoms <2 weeks):** positive In presence of symptoms, pertussis should be diagnosed using appropriate tests when available, unless another diagnosis is proven.[80] Patient should be isolated for 5 days and case reported to public health authorities. Enriched media is required for culturing.	»**polymerase chain reaction, and/ or serology (if symptoms present >4 weeks):** positive

Uncommon

Lung cancer

History	Exam	1st Test	Other tests
history of tobacco smoking, change in character of chronic	central lung cancers may cause unilateral localized wheezing;	»**chest x-ray:** presence of the lesion	»**CT chest:** presence of the lesion and locoregional disease

DIAGNOSIS

Uncommon

Lung cancer

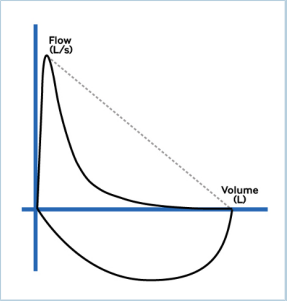
History	Exam	1st Test	Other tests
cough, hemoptysis, hoarseness, chest pain, weight loss, superior vena cava syndrome (localized edema of face and upper extremities, facial plethora, distended neck and chest veins), symptoms related to distant metastases and advanced stages of cancer	superior vena cava syndrome; cachexia and symptoms related to distant metastases (e.g., bone pain) are late symptoms	Up to 26% of the parenchyma may not be adequately visualized on a CXR.[68]	»**sputum cytology:** may document presence of malignant cells »**bronchoscopy:** presence of tumor Allows visualization of extent of tumor and collection of material for biopsy.

◊ Bronchiectasis and chronic suppurative lung disease

History	Exam	1st Test	Other tests
cough productive of large amounts of mucopurulent sputum, diurnal variation (e.g., worse in the morning), positional worsening; dyspnea, wheezing, hemoptysis; paroxysmal cough nonproductive of sputum may sometimes be present	crackles and wheezing, predominantly over lower lobes; clubbing in a minority of patients	»**chest x-ray:** increased bronchovascular markings May be appropriate for evaluation of associated conditions and exclusion of diseases that cause similar symptoms, and useful as a baseline investigation in suspected bronchiectasis.[69] [70] »**high-resolution CT chest:** bronchial dilatation, size of the bronchi exceeding the size of the accompanying artery,	»**pulmonary function tests:** irreversible obstructive defect, with FEV1/ forced vital capacity (FVC) <70% Peak expiratory flow may be normal, but a concave shape is seen following the point of maximal flow due to the low flow rate in relation to lung volume.

Uncommon

◊ Bronchiectasis and chronic suppurative lung disease

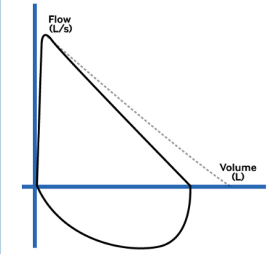
History	Exam	1st Test	Other tests
		lack of tapering of the bronchi at the lung peripheries Should be the first exam if available. Conventional high-resolution CT or volumetric thin-slice CT, are preferred for evaluation of suspected bronchiectasis.[69][70][71]	 *Flow-volume loop (spirogram) in obstructive lung disease, such as asthma or COPD: peak expiratory flow may be normal, but a concave shape is seen following the point of maximal flow due to the low flow rate in relation to lung volume* *Created by BMJ Knowledge Centre*

Interstitial lung disease

History	Exam	1st Test	Other tests
dyspnea of subacute onset dominates the clinical picture; cough typically dry	dry, velcro crackles, typically over lung bases; clubbing may be present	»**chest x-ray:** increased interstitial markings First test if high-resolution CT not available. »**high-resolution CT chest:** interstitial pneumonitis: patchy, predominantly basilar and subpleural reticular changes with honeycombing and traction bronchiectasis	»**pulmonary function tests:** restrictive pattern with total lung capacity <80%, functional residual capacity <80%, and vital capacity <80%, with diffusion capacity for CO <80% Flow-volume loop (spirogram) in restrictive lung disease (e.g., interstitial pulmonary fibrosis).

Uncommon

Interstitial lung disease

History	Exam	1st Test	Other tests
		in later stages of the disease Confirmatory, sensitive and specific. Findings depend on specific interstitial pathology. Interstitial pneumonitis is the most common form.	 *Flow-volume loop (spirogram) in restrictive lung disease (e.g., interstitial pulmonary fibrosis): peak expiratory flow may be normal or low. The shape of the curve is generally normal, but the loop is narrowed and the forced vital capacity is low because of the reduced lung volume.* *Created by BMJ Knowledge Centre* »**biopsy:** pattern of usual interstitial pneumonia

◊ Sarcoidosis

History	Exam	1st Test	Other tests
most patients asymptomatic; symptomatic patients: shortness of breath, dyspnea on exertion, and chest pain are present in minority of patients; low-grade fever; other symptoms	most often normal; skin lesions (erythema nodosum and maculopapular skin lesions), enlargement of lacrimal glands, lymphadenopathy in cervical, supraclavicular, or axillary areas; redness	»**chest x-ray:** various findings, bilateral hilar and mediastinal lymphadenopathy, reticular infiltrates; fibrosis with decreased lung volumes in late sarcoidosis	»**chest CT with high-resolution cuts:** bilateral hilar and mediastinal lymphadenopathy, interstitial infiltrates »**pulmonary function tests:** often normal, but may show

Uncommon

◊ Sarcoidosis

History	Exam	1st Test	Other tests
reflect involvement of various organs	of eye, tearing, and photophobia may represent uveitis	Severity of radiographic lung involvement may not correlate with severity of physiologic deficit.	nonspecific reduction in diffusion capacity, obstruction, restriction, or mixed picture Not sensitive or specific for this disorder, but results may influence therapeutic choices once coupled with clinical and radiographic data. »**bronchoscopy with biopsy:** noncaseating granuloma is supportive, but other granulomatous disorders should be reasonably excluded with special stains and clinical assessment When pulmonary involvement is present, has a high sensitivity.

Tuberculosis (TB)

History	Exam	1st Test	Other tests
residence in/visit to high-prevalence area; immunosuppressed status (e.g., HIV infection, immunosuppressant medication, transplant recipients, diabetes, dialysis treatment); epidemiological risk factors, particularly close contact with active TB; history of anorexia, malaise, weight loss, fever, or night sweats; chronic cough productive of sputum, occasionally	fever, cachexia, tachycardia; asymmetry in chest movement and dullness to percussion due to pleural effusion, bronchial breathing, crackles, rales due to an infiltrate or rhonchi in presence of significant bronchial purulence; palpable extrathoracic lymphadenopathy is uncommon	»**chest x-ray:** may demonstrate atelectasis from airway compression, pleural effusion, consolidation, pulmonary infiltrates, mediastinal or hilar lymphadenopathy, upper zone fibrosis Evidence of unrecognized pulmonary TB or evidence of old healed TB (e.g., upper lobe fibrosis) may be present; such abnormalities	»**bronchoscopy and bronchoalveolar lavage:** positive for acid-fast bacilli Bronchoalveolar lavage may be indicated in patients in whom sputum induction is unsuccessful or in whom smear and NAAT are negative. Bronchoscopy is useful when other diagnoses are strongly considered or in patients in whom pulmonary TB is

DIAGNOSIS

Uncommon

Tuberculosis (TB)

History	Exam	1st Test	Other tests
associated with hemoptysis		should prompt sputum collection for smear, culture, and nucleic acid amplification testing. »**sputum acid-fast bacilli smear and culture:** presence of acid-fast bacilli (Ziehl-Neelsen stain) in specimen Testing of 3 specimens (minimum 8 hours apart, including an early morning specimen) is recommended in many countries; consult local guidance.[73] Sputum specimen should be tested in patients with suspected extrapulmonary TB, as active pulmonary TB is seen in 15% to 20% of patients with extrapulmonary TB.[74] [75] [76] Culture of *Mycobacterium tuberculosis* typically takes several weeks (up to 8 weeks), decisions on treatment are usually made before culture results are known. »**nucleic acid amplification tests**	still suspected after other methods proved nondiagnostic. Transbronchial lung biopsies are useful in the diagnosis of miliary disease as granulomas may be visible. »**lateral flow urine lipoarabinomannan (LF-LAM) assay:** positive WHO recommends concurrent testing with LF-LAM to assist in the diagnosis of active TB in adults living with HIV, adolescents, and children with signs and symptoms of TB, or who screen positive for TB.[77] WHO also recommends concurrent testing with LF-LAM in adults and adolescents living with HIV who are seriously ill or have advanced HIV.[77] One Cochrane review found the LF-LAM assay to have a sensitivity of 42% in diagnosing TB in people living with HIV with TB symptoms, and 35% in people living with HIV not assessed for TB symptoms.[79]

Uncommon

Tuberculosis (TB)

History	Exam	1st Test	Other tests
		(NAAT): positive for M tuberculosis NAAT should be performed on at least one respiratory specimen when a diagnosis of pulmonary TB is being considered.[77] NAAT may speed the diagnosis in smear-negative cases and may be helpful to differentiate nontuberculous mycobacteria when sputum is AFB smear positive but NAAT negative.[78] Genotyping might be considered useful in outbreaks of TB to identify transmission of TB, especially when contact had not been appreciated in the course of epidemiologic investigations. Several rapid NAATs are available for the diagnosis of TB and some are also able to detect genes encoding resistance to TB drugs.[77]	»**contrast-enhanced chest computed tomography scan:** primary TB: mediastinal tuberculous lymphadenitis with central node attenuation and peripheral enhancement, delineated cavities; postprimary TB: centrilobular nodules and tree-in-bud pattern Bronchiectasis can be seen in chronic cases. Hemoptysis usually originates from bronchial arteries, but Rasmussen aneurysms from a pulmonary artery adjacent to a cavity can be the source of bleeding. Residual bronchiectasis from old TB can cause hemoptysis.

Uncommon

Recurrent aspiration

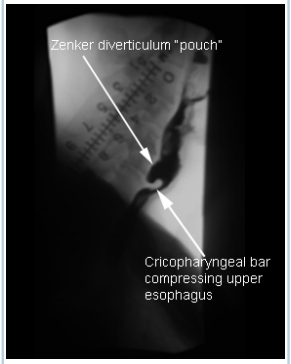
History	Exam	1st Test	Other tests
dysphagia, association of cough with eating/ drinking, fear of choking with eating/drinking; may have history of neurologic disease including stroke, multiple sclerosis, Parkinson disease	signs of neurologic disease such as stroke, multiple sclerosis, Parkinson disease	»**chest x-ray:** persistent lower lobe infiltrates »**swallow evaluation:** aspiration Patient should be referred to speech-language pathologist for this evaluation.	

◊ Zenker diverticulum

History	Exam	1st Test	Other tests
dysphagia present in the majority of patients; regurgitation of bland undigested food; frequent aspiration; noisy deglutition (gurgling); halitosis; voice changes	halitosis, voice changes	»**barium esophagram:** positive contrast within the structure connected to the posterior wall of esophagus is consistent with a diverticulum	»**endoscopy:** visualization of diverticulum

Uncommon

◊ Zenker diverticulum

History	Exam	1st Test	Other tests
		 *Zenker diverticulum: lateral view with barium esophagram* *From the collection of Dr S. Charous, Clinical Professor of Otolaryngology - Head and Neck Surgery, Loyola University Medical Center; used with#permission.*	

Thoracic aortic aneurysm (TAA)

History	Exam	1st Test	Other tests
most patients have no symptoms attributable to TAA at the time of diagnosis; most common initial symptom is vague pain, which can occur in the chest, back, flank, or abdomen; hoarseness due to stretching or compression of left recurrent laryngeal nerve; tracheal deviation, persistent cough, or other respiratory symptoms such as shortness of	generally no obvious physical findings in chest area unless tracheal deviation is present; patients with an abdominal component may have a pulsatile abdominal mass similar to pure abdominal aortic aneurysms; signs of arterial perfusion differentials in both upper and lower extremities; evidence of visceral ischemia; focal neurologic deficits;	»**chest radiograph:** widened mediastinum, prominence of the aortic knob, or tracheal deviation	»**spiral CT of chest with three-dimensional reconstructions:** visualization of aneurysm, seen as an increase in size of a section of the aorta »**MRI and magnetic resonance angiography:** visualization of aneurysm, seen as an increase in size of a section of the aorta

Uncommon

Thoracic aortic aneurysm (TAA)

History	Exam	1st Test	Other tests
breath or chest pain; dysphagia (uncommon) due to compression of the esophagus by the aneurysm; sudden and catastrophic hemoptysis or hematemesis; neurologic deficits including paraplegia	murmur of aortic regurgitation; bruits		

Foreign body

History	Exam	1st Test	Other tests
abrupt onset, more common in young children	may be asymptomatic or show signs of airways obstruction, including cough, wheeze, decreased breath sounds, dyspnea, or fever	»**laryngoscopy/ bronchoscopy:** visualization of foreign body »**chest x-ray:** visualization of foreign body (if object is radiopaque)	»**chest CT:** visualization of foreign body

◊ Hypersensitivity pneumonitis

History	Exam	1st Test	Other tests
occupational/ environmental exposure to allergens (e.g., farmers, bird breeders), progressive dyspnea, fatigue, and weight loss	clubbing, increased respiratory rate, inspiratory crackles over lower lung fields	»**chest x-ray:** fibrotic changes; loss of lung volume particularly affecting the upper lobes	»**chest CT:** features of fibrosis »**IgG testing:** high titers with antigen-specific antibodies

◊ Bronchiolitis

History	Exam	1st Test	Other tests
age <1 year, cough, wheeze, and dyspnea, history of prematurity, underlying cardiopulmonary disease or immunodeficiency	high respiratory rate, accessory muscle use, retractions, wheezes, crackles, purulent secretions on bronchoscopy	»**chest x-ray:** consolidation and atelectasis in severe disease	»**virology:** may be positive for respiratory syncytial virus Rarely useful in making management decisions.

Uncommon

◊ Bronchiolitis

History	Exam	1st Test	Other tests
			»**high-resolution CT scan:** signs of small airways disease

◊ Tropical filarial pulmonary eosinophilia

History	Exam	1st Test	Other tests
Travel to endemic area (sub-Saharan Africa, Indian subcontinent, southeast Asia, Oceania); dry, paroxysmal cough, frequently nocturnal	frequently normal; wheezing, rhonchi, crackles may be present on lung exam; some patients develop hepatosplenomegaly	»**blood count with differential:** eosinophilia »**chest x-ray:** increased interstitial markings	»**filarial antibody levels:** elevated »**serum IgE:** elevated

◊ Cough hypersensitivity syndrome#somatic cough, psychogenic cough, unexplained chronic cough, refractory chronic cough)

History	Exam	1st Test	Other tests
extensive evaluation has ruled out other causes; patients may report an urge to cough triggered by itch, scratchy throat, tickle or globus sensation; cough improves following behavior modification	usually unremarkable	»**none:** extensive evaluation has already ruled out other causes Cough improves following behavior modification, speech therapy, trial of opioids or neuromodulators such as gabapentin, pregabalin, amitriptyline, or baclofen, or psychiatric therapy.[26]	

◊ Obstructive sleep apnea/hypopnea syndrome (OSAHS)

History	Exam	1st Test	Other tests
snoring, diurnal somnolence, agitation and sweating at night, headache, morning xerostomia (dry mouth) and sore throat,	elevated BP, obesity, nasal obstruction, macroglossia, tonsillar hypertrophy, obstruction by the palate, low soft	»**polysomnography:** apnea/hypopnea index ≥15 episodes/ hour (in the absence of symptoms) or ≥5 events/hour associated	»**fiber optic endoscopy:** may see nasal polyps or tumors, or hypertrophic lingual tonsils

Uncommon

◊ Obstructive sleep apnea/hypopnea syndrome (OSAHS)

History	Exam	1st Test	Other tests
depressed mood, irritability, loss of libido; total score of ≥11 on Epworth sleepiness scale supports the diagnosis	palate, retrognathism, micrognathia	with the typical symptoms of OSAM Polysomnography is the definitive test.[81] General parameters measured include electroencephalogram, electro-oculographic recording, air flow assessment, electromyogram, capnography, esophageal manometry, ECG, pulse oximetry, respiratory effort signals, synchronized polysomnography video, and body position.[82] Polysomnography may be a full night study or a split study. »**portable multichannel sleep tests:** Respiratory Event Index (REI) of ≥15 episodes/hour or REI ≥5 with symptoms or comorbidities Used for patients with higher probability of OSA and without complex comorbidities (e.g., cardiopulmonary disease, chronic opioid therapy, or neuromuscular disease). Portable tests typically include a smaller selection of channels than the	

Uncommon

◊ Obstructive sleep apnea/hypopnea syndrome (OSAHS)

History	Exam	1st Test	Other tests
		polysomnogram (nasal pressure, oximetry, thoracoabdominal effort sensors, heart rate), but usually do not measure sleep. Portable tests may underestimate the REI as obstructions are measured for recording time, not sleep time.	

Evidence tables

What is the diagnostic yield of chest computed tomography (CT) scan in people with chronic cough, normal chest x-ray and physical exam?[3]

This table is a summary of the analysis reported in a guideline (underpinned by a systematic review) that focuses on the above important clinical question.

View the full source guideline (https://erj.ersjournals.com/content/55/1/1901136.figures-only)

Evidence C *	Confidence in the evidence is very low or low where GRADE has been performed and the intervention may be less effective or likely to be more harmful than the comparison for key outcomes. However, this is uncertain and new evidence could change this in the future.

Population: People with chronic cough and normal chest x-ray and physical examination
Intervention: Chest CT scan
Comparison: No chest CT scan

Outcome	Effectiveness (BMJ rating)†	Confidence in evidence (GRADE)‡
Diagnostic yield	See note [a]	Very Low

Recommendations as stated in the source guideline
We suggest that clinicians do not routinely perform a chest CT scan in patients with chronic cough who have a normal chest radiograph and physical examination.

Note
[a] The content of this table is based on four observational studies. One prospective study found that the diagnostic yield of chest CT scan was 3/46 (6.5%) participants, while three retrospective studies produced the following results: 20/34 (58%) participants, 9/21 (43%) participants, and 21/59 (36%) participants.

The guideline task force noted that the variation in the above results, regarding the diagnostic yield of CT scan, were unlikely to explain the cause of coughs or influence treatment.

The guideline task force also noted that there is concern about the potential cancer risk from CT radiation exposure, particularly in children and women, which should be weighed against any diagnostic yields.

EVIDENCE TABLES

* Evidence levels

The Evidence level is an internal rating applied by BMJ Best Practice. See the EBM Toolkit (https://bestpractice.bmj.com/info/evidence-tables/) for details.

Confidence in evidence

A - High or moderate to high

B - Moderate or low to moderate

C - Very low or low

† Effectiveness (BMJ rating)

Based on statistical significance, which demonstrates that the results are unlikely to be due to chance, but which does not necessarily translate to a clinical significance.

‡ Grade certainty ratings

High	The authors are very confident that the true effect is similar to the estimated effect.
Moderate	The authors are moderately confident that the true effect is likely to be close to the estimated effect.
Low	The authors have limited confidence in the effect estimate and the true effect may be substantially different.
Very Low	The authors have very little confidence in the effect estimate and the true effect is likely to be substantially different.

BMJ Best Practice EBM Toolkit: What is GRADE? (https://bestpractice.bmj.com/info/toolkit/learn-ebm/what-is-grade/)

Key articles

- Morice AH, Millqvist E, Bieksiene K, et al. ERS guidelines on the diagnosis and treatment of chronic cough in adults and children. Eur Respir J. 2020 Jan;55(1):1901136. Full text (https://erj.ersjournals.com/content/55/1/1901136.long) Abstract
- Canning BJ, Chang AB, Bolser DC, et al. Anatomy and neurophysiology of cough: CHEST Guideline and Expert Panel report. Chest. 2014 Dec;146(6):1633-48. Full text (https://journal.chestnet.org/article/S0012-3692(15)51535-3/fulltext) Abstract
- Global Initiative for Asthma. Global strategy for asthma management and prevention (2025 update). May 2025 [internet publication]. Full text (https://ginasthma.org)
- American College of Radiology. ACR Appropriateness Criteria: chronic cough. Nov 2021 [internet publication]. Full text (https://acsearch.acr.org/docs/3158177/Narrative) Abstract
- Kahrilas PJ, Altman KW, Chang AB, et al. Chronic cough due to gastroesophageal reflux in adults: CHEST guideline and expert panel report. Chest. 2016 Dec;150(6):1341-60. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6026249) Abstract

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Images

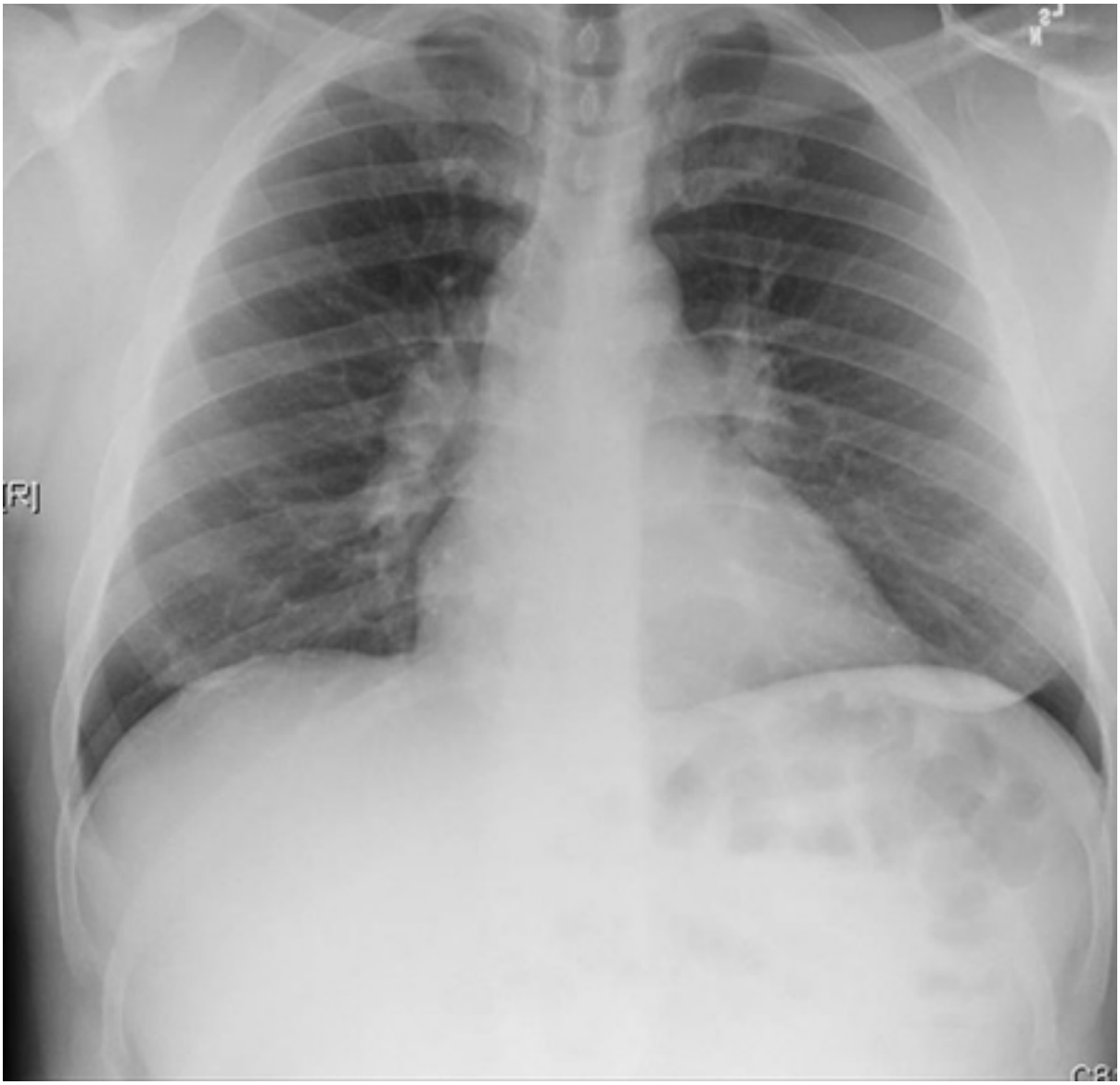

Figure 1: Chest x-ray showing bilateral hilar adenopathy in a patient with sarcoidosis

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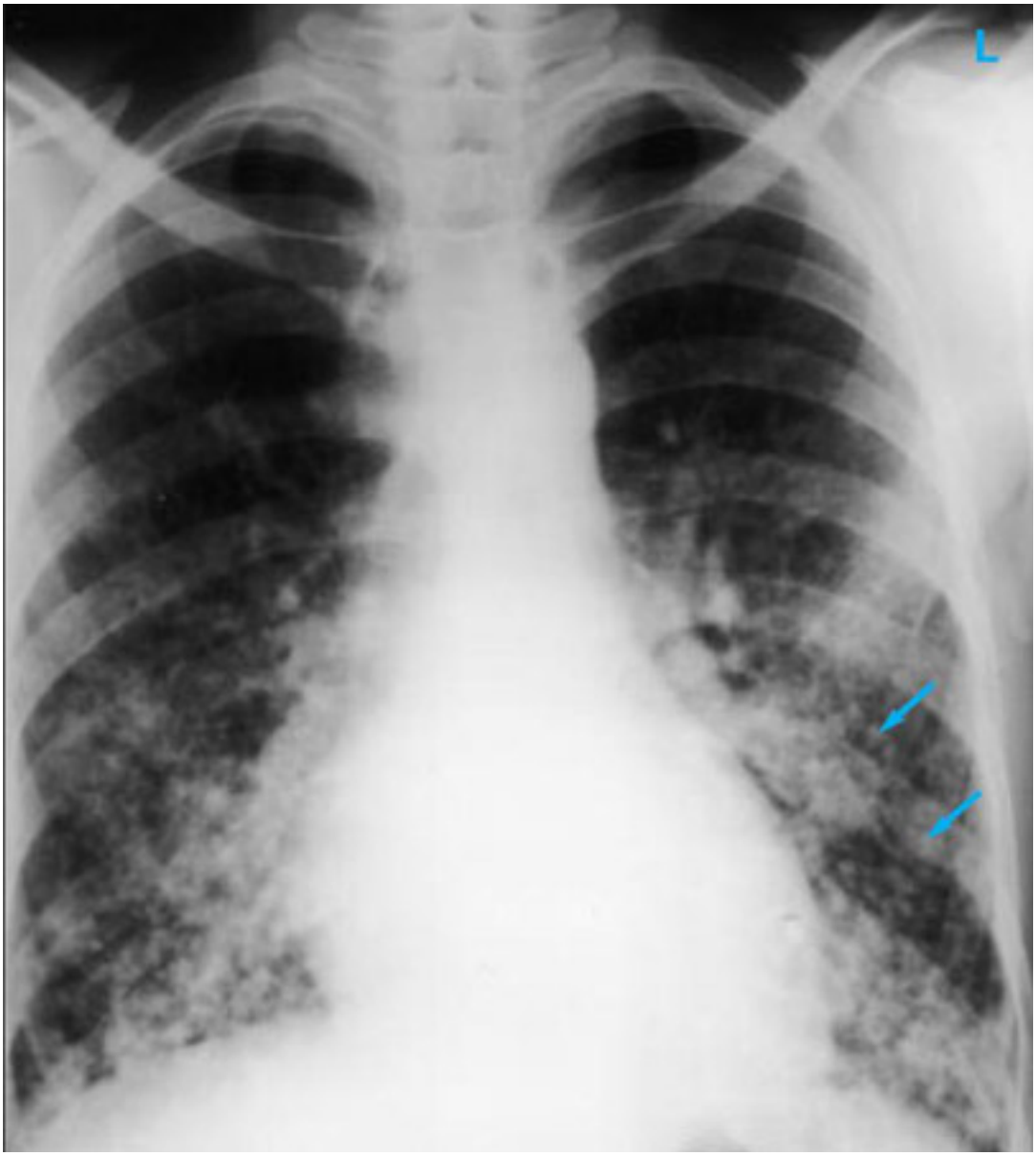

Figure 2: Chest x-ray showing multiple miliary lung metastases (arrows). The primary tumor was a thyroid carcinoma

E. Dick, Student BMJ. 2001;9:10-12

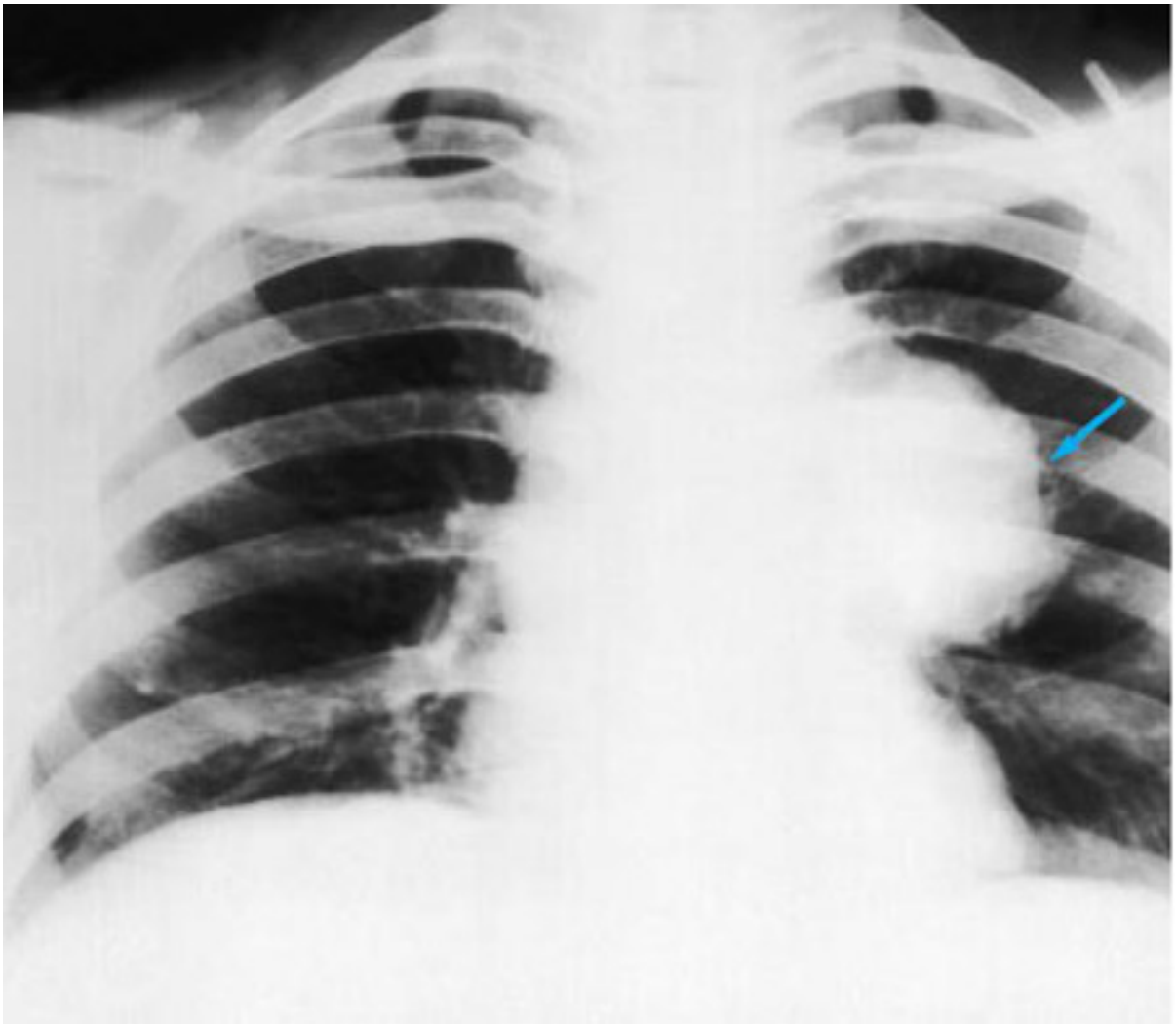

Figure 3: Chest x-ray showing left hilar carcinoma (arrow)

From: E. Dick, Student BMJ. 2000;8:358-360

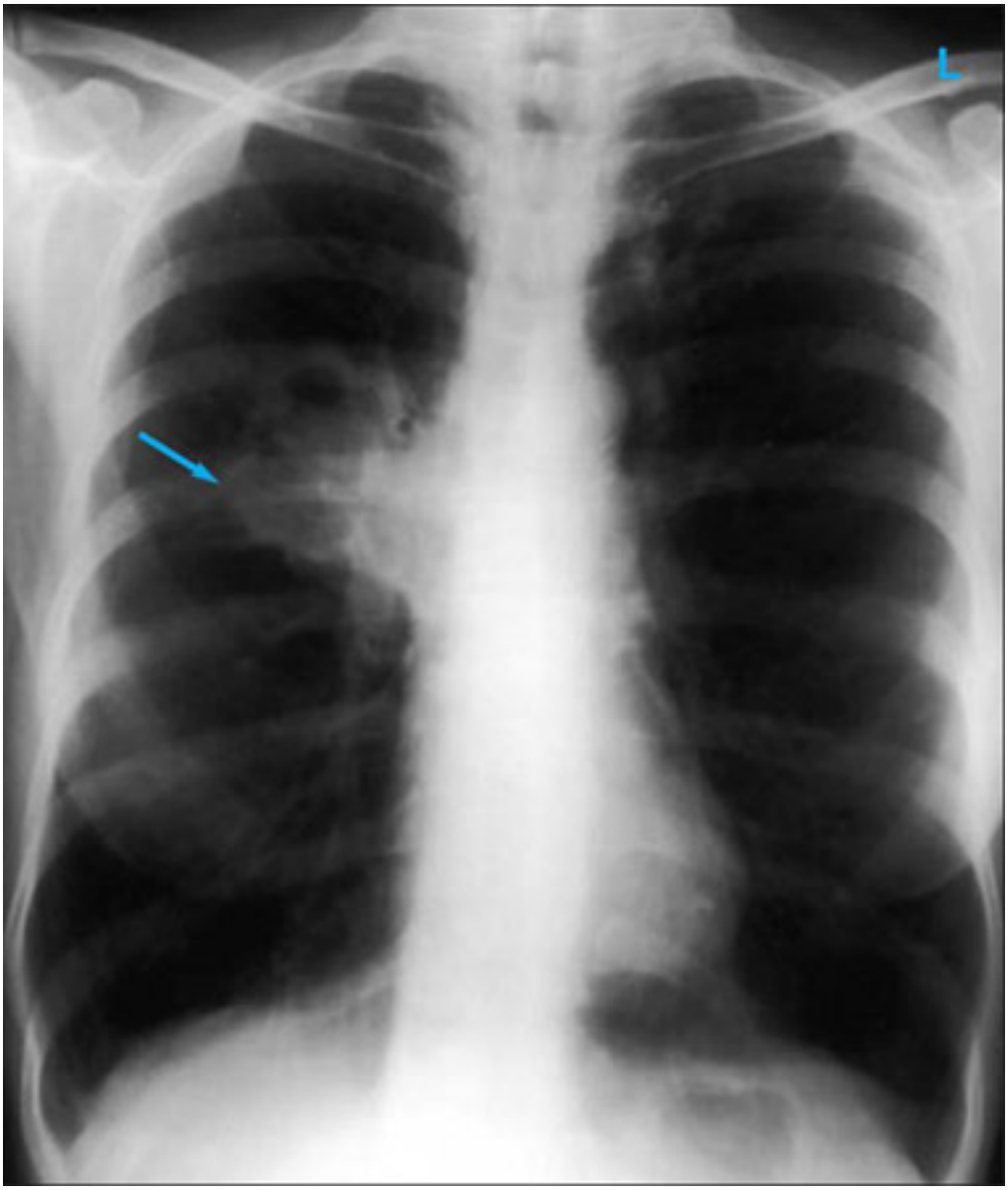

Figure 4: Chest x-ray showing a cavitating right hilar carcinoma (arrow)

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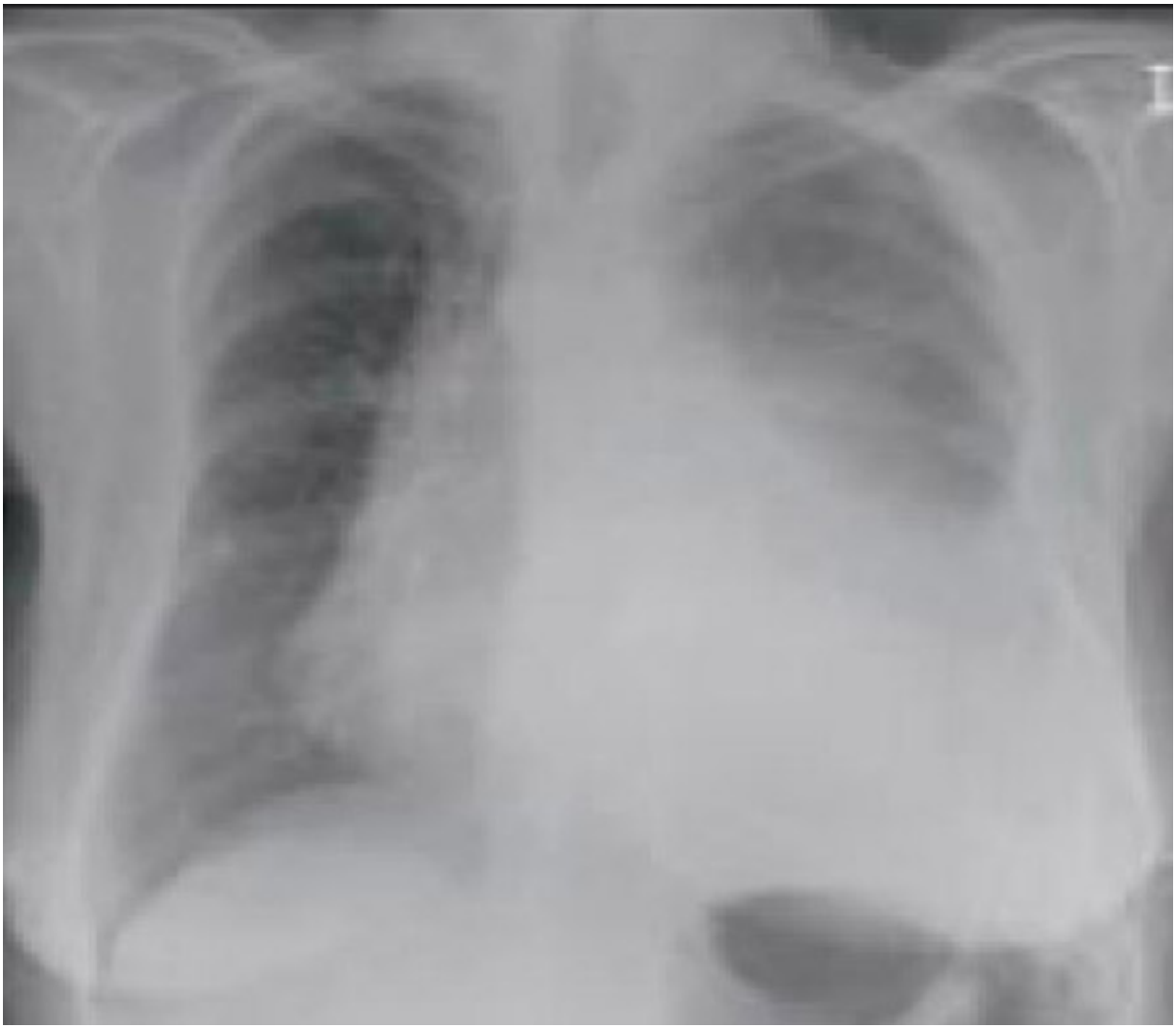

Figure 5: Chest x-ray in a patient with bronchogenic carcinoma showing a left-sided pleural effusion

From: R. Thakkar, Student BMJ. 2001;9:458

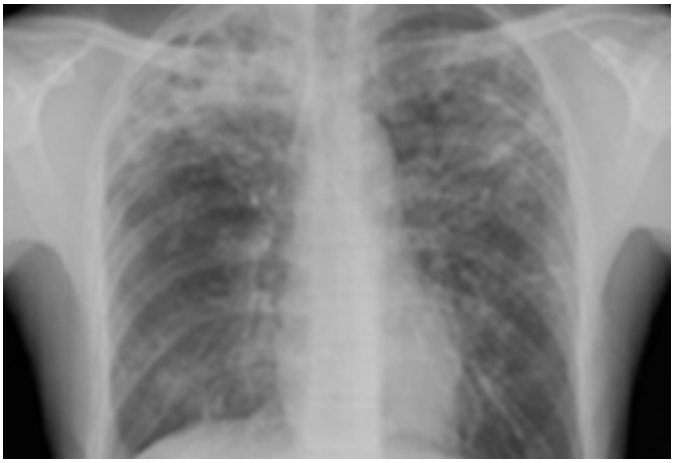

Figure 6: Chest x-ray showing pulmonary tuberculosis with cavitation

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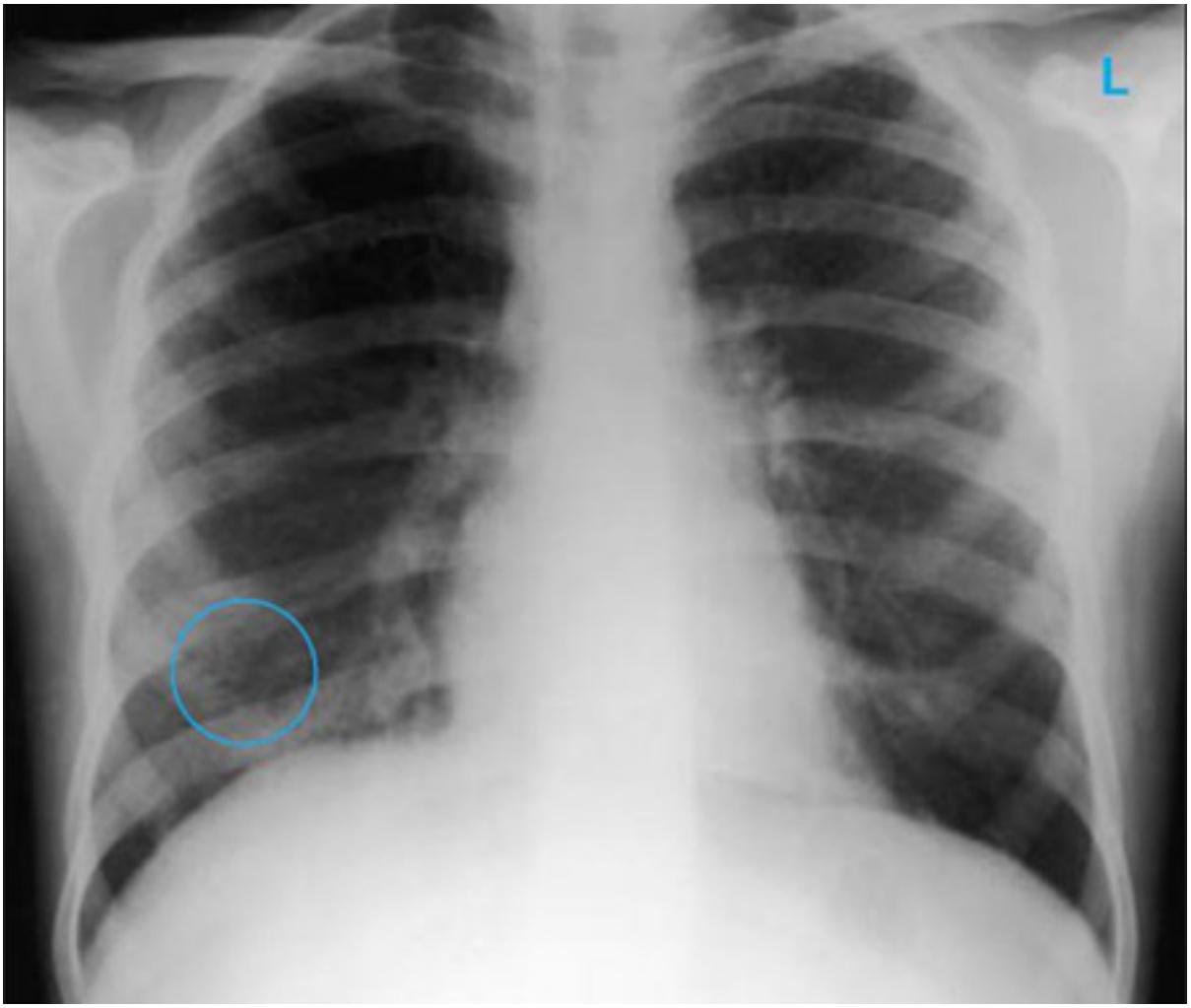

Figure 7: Chest x-ray showing multiple discrete nodules throughout both lungs (one of which is circled) in a patient with miliary tuberculosis

E. Dick, Student BMJ. 2001;9:10-12

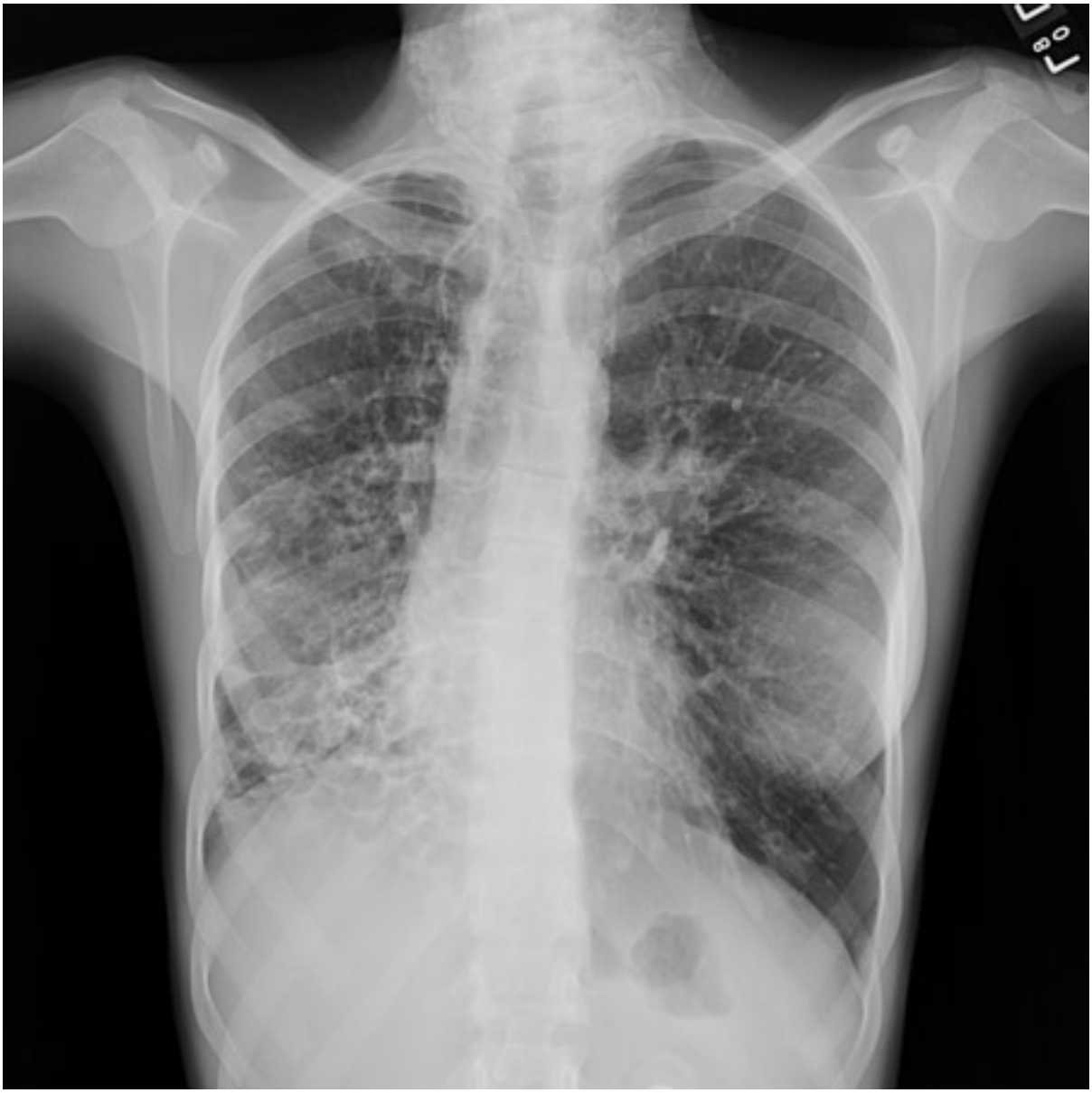

Figure 8: Chest x-ray with lack of normal tapering producing a tram line in a patient with bronchiectasis

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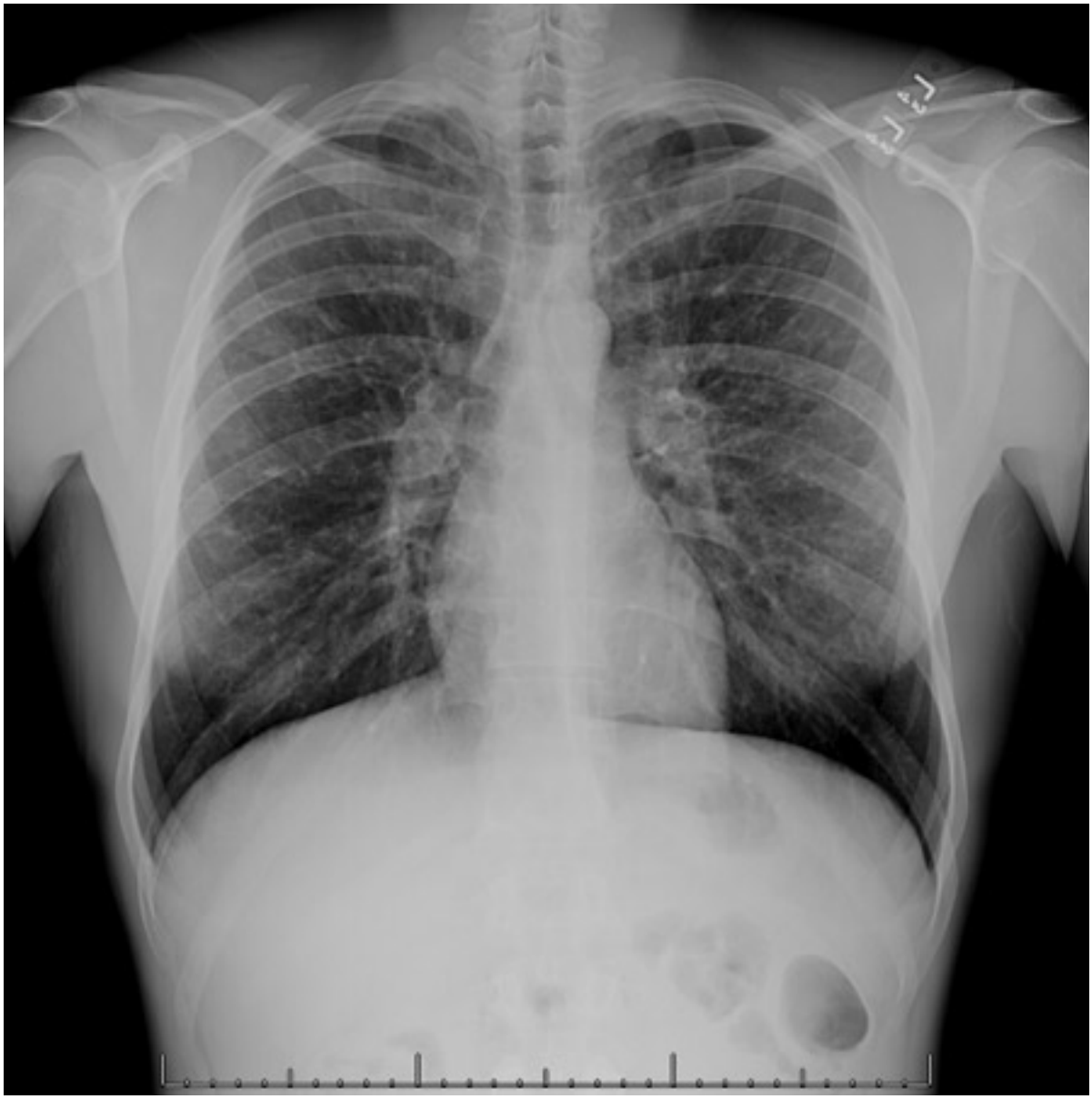

Figure 9: Chest x-ray with dilated and thickened airways in a patient with bronchiectasis

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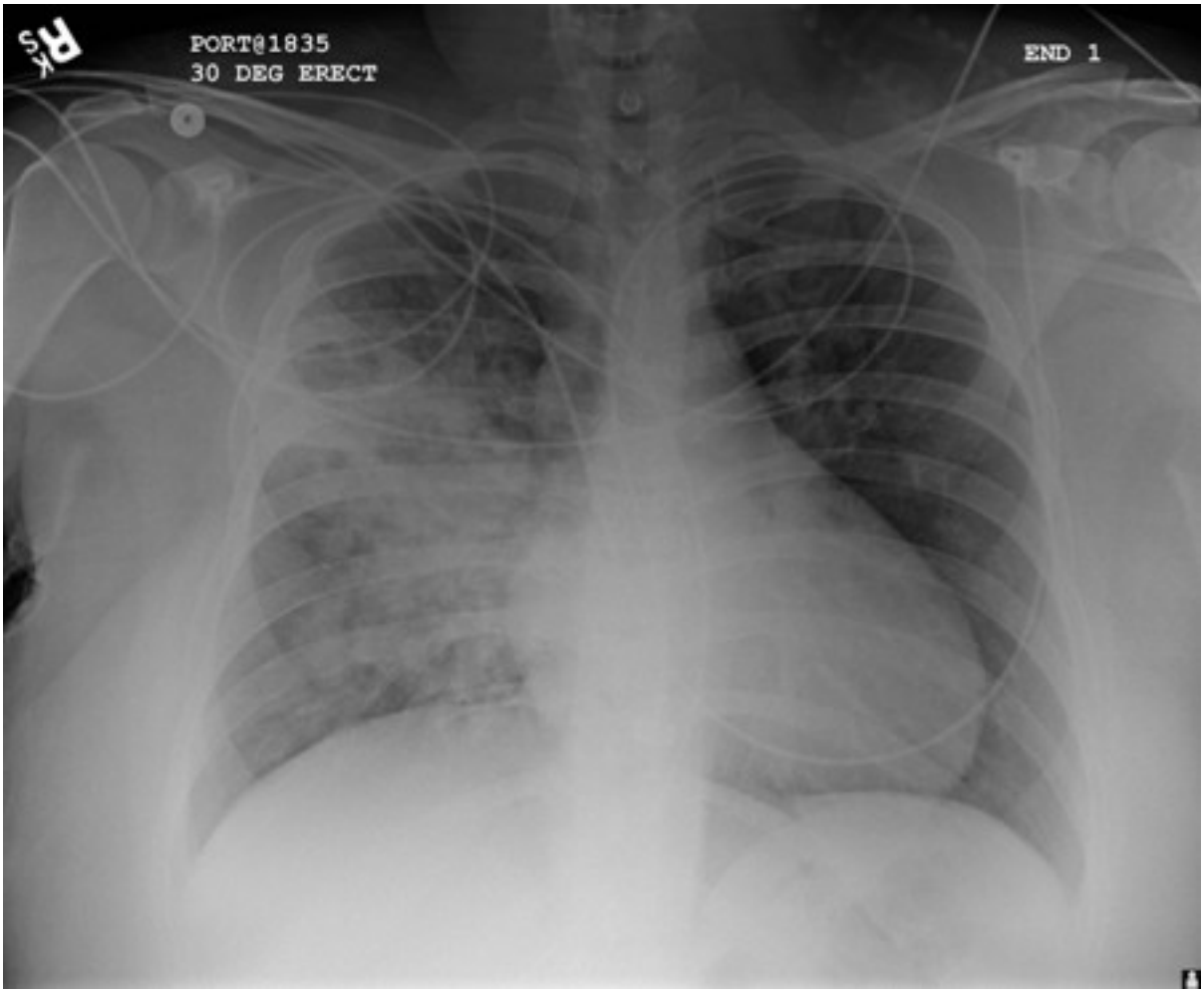

Figure 10: Chest x-ray showing increased opacification of the right perihilar region and superior segment of the right lower and upper lobes consistent with worsening aspiration pneumonia

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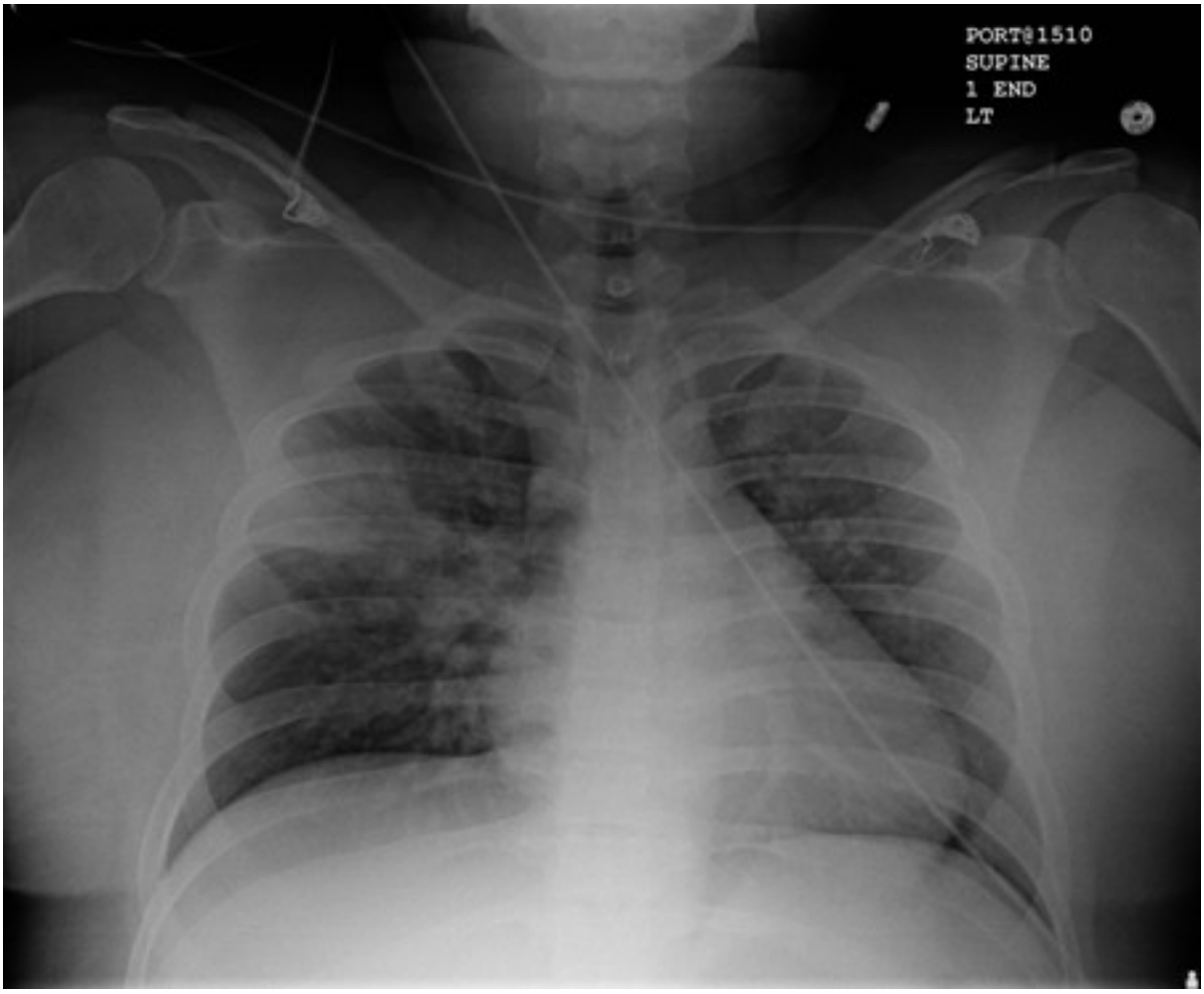

Figure 11: Chest x-ray showing early ill-defined opacities of the right upper lobe above the minor fissure consistent with early changes of aspiration pneumonia

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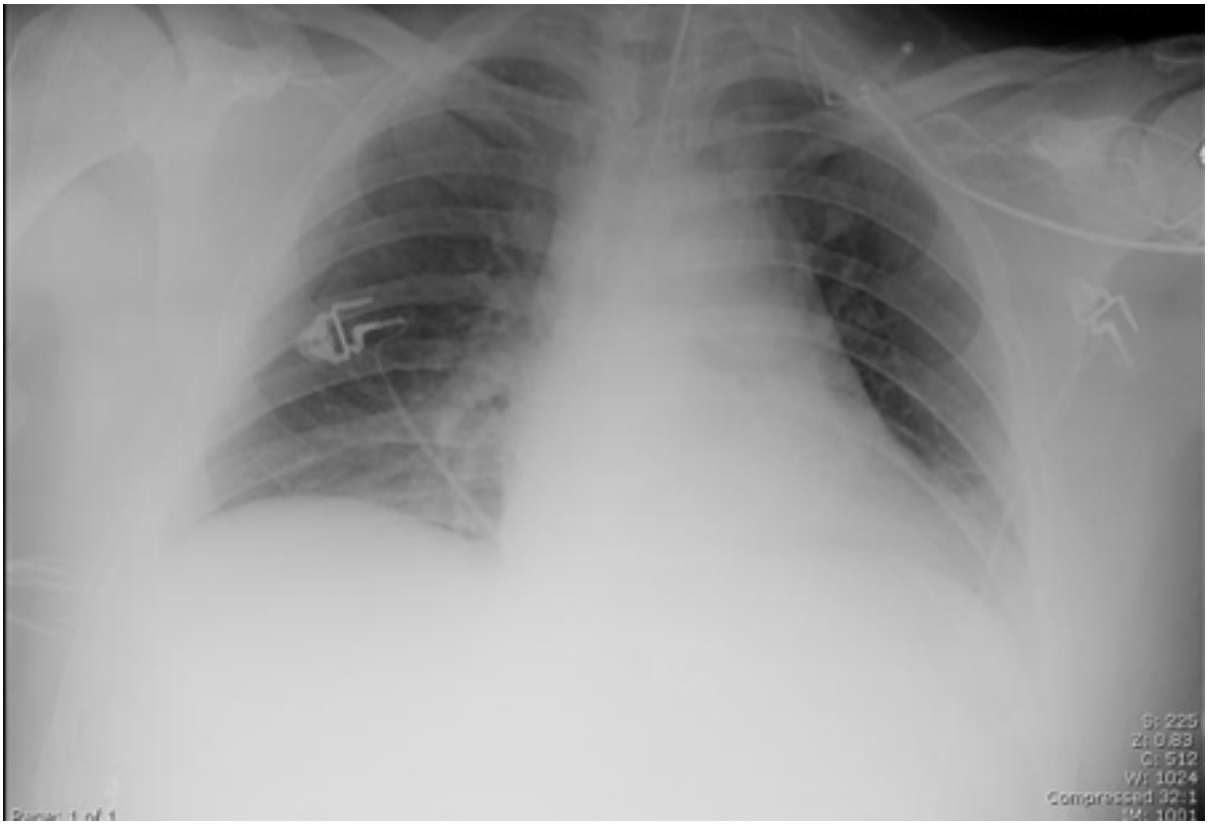

Figure 12: Portable chest x-ray with bibasilar opacities, worse on the right than the left, in a patient with hospital-acquired pneumonia

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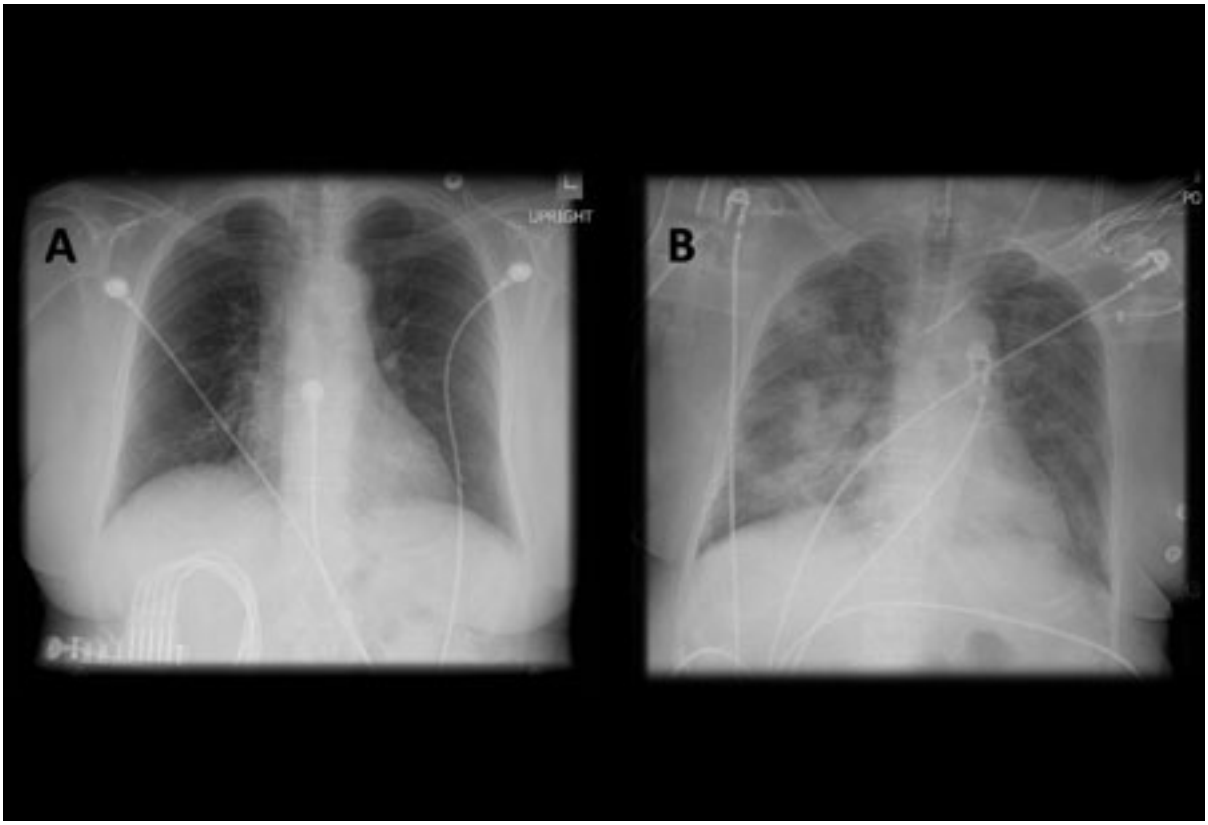

Figure 13: A. Portable upright chest x-ray before aspiration; B. Chest x-ray 1 hour after aspiration, showing bilateral diffuse alveolar infiltrates, worse at the bases on the right side

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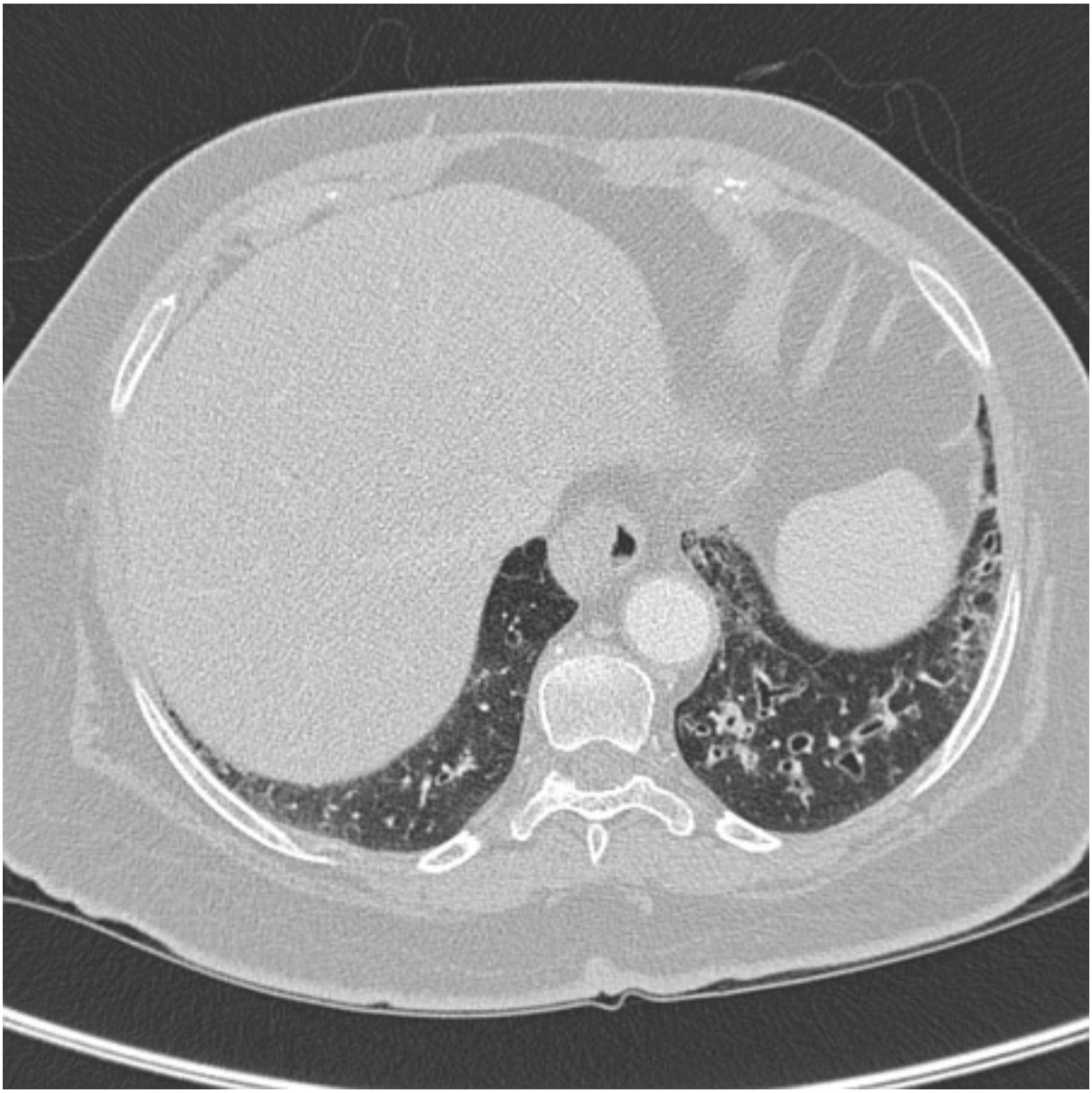

Figure 14: Chest CT with presence of signet ring on left in a patient with bronchiectasis

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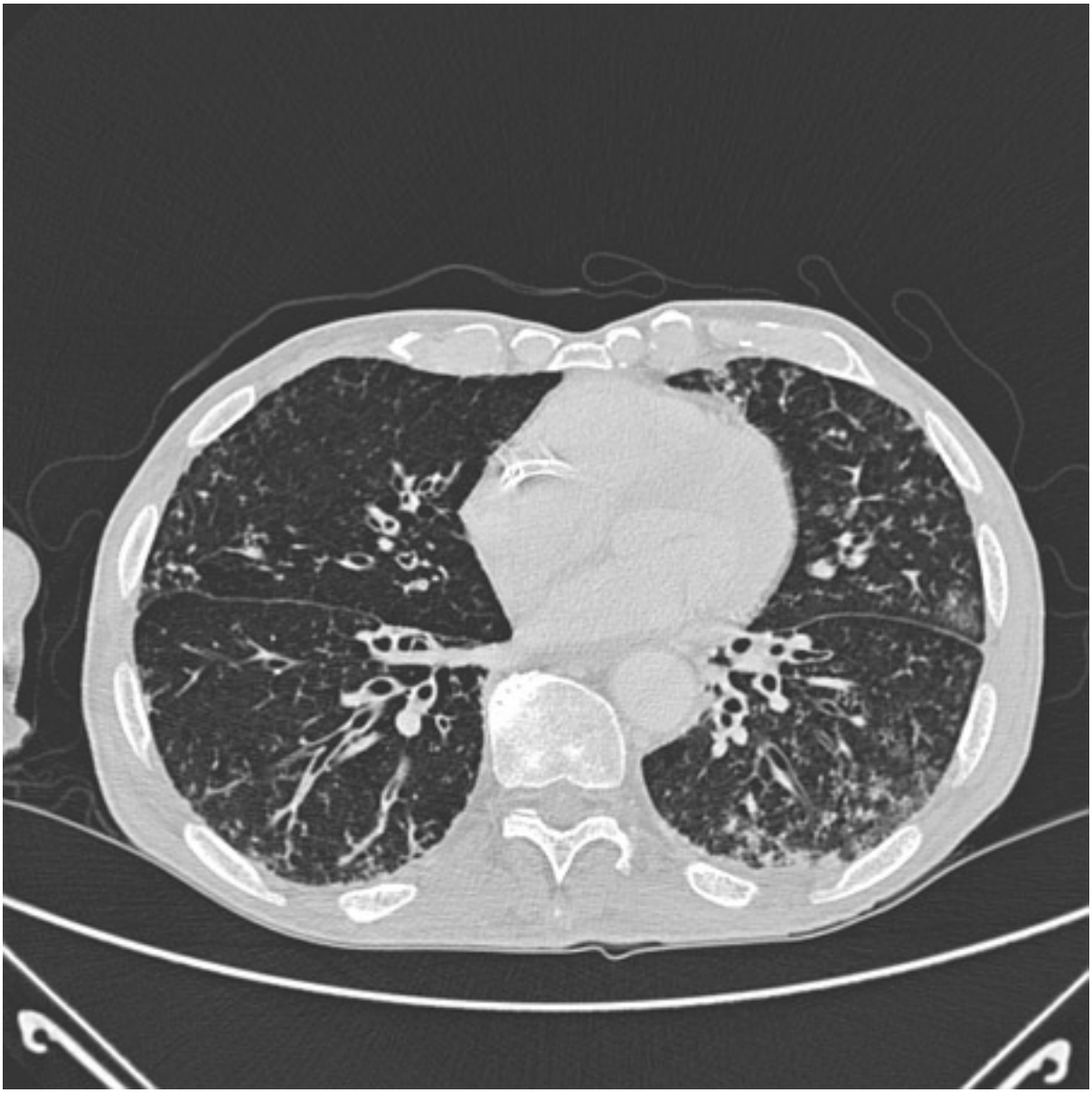

Figure 15: Chest CT with dilated and thickened airways and peripheral tree-in-bud pattern in a patient with bronchiectasis

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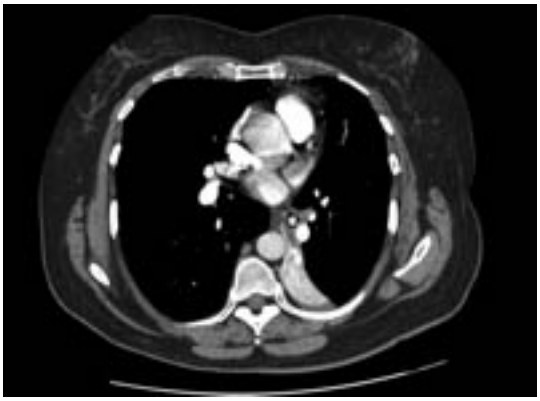

Figure 16: CT of the chest with intravenous contrast material showing complete left lower lobe collapse with a radiopaque object within the left lower main bronchus surrounded by a halo of air

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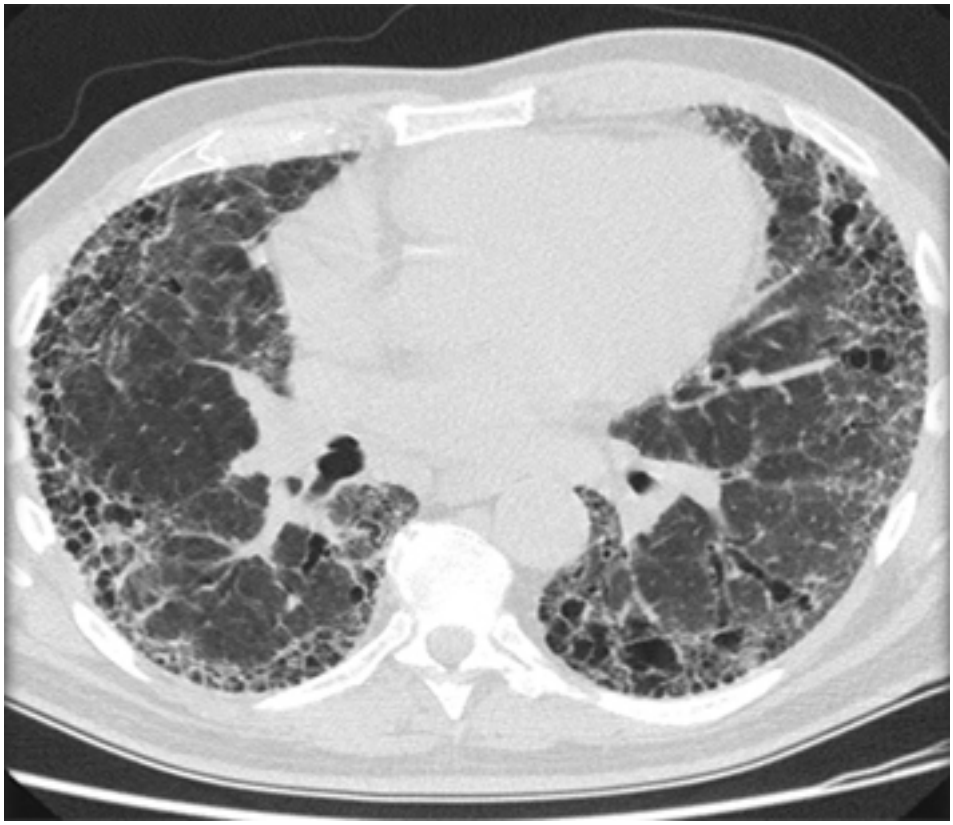

Figure 17: Chest CT showing idiopathic pulmonary fibrosis

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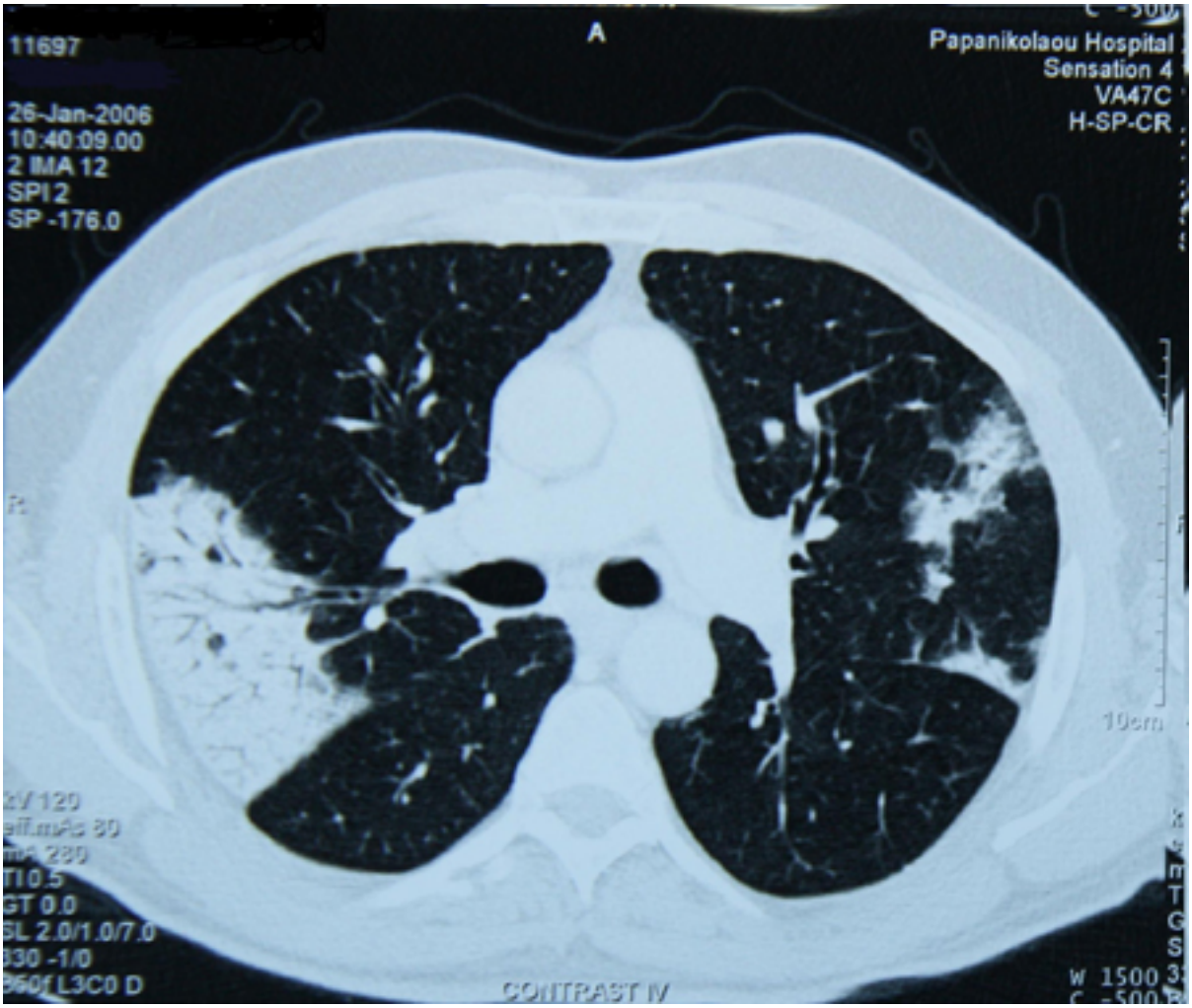

Figure 18: Chest CT of a patient with amiodarone pulmonary toxicity, showing asymmetric opacities with a peripheral distribution

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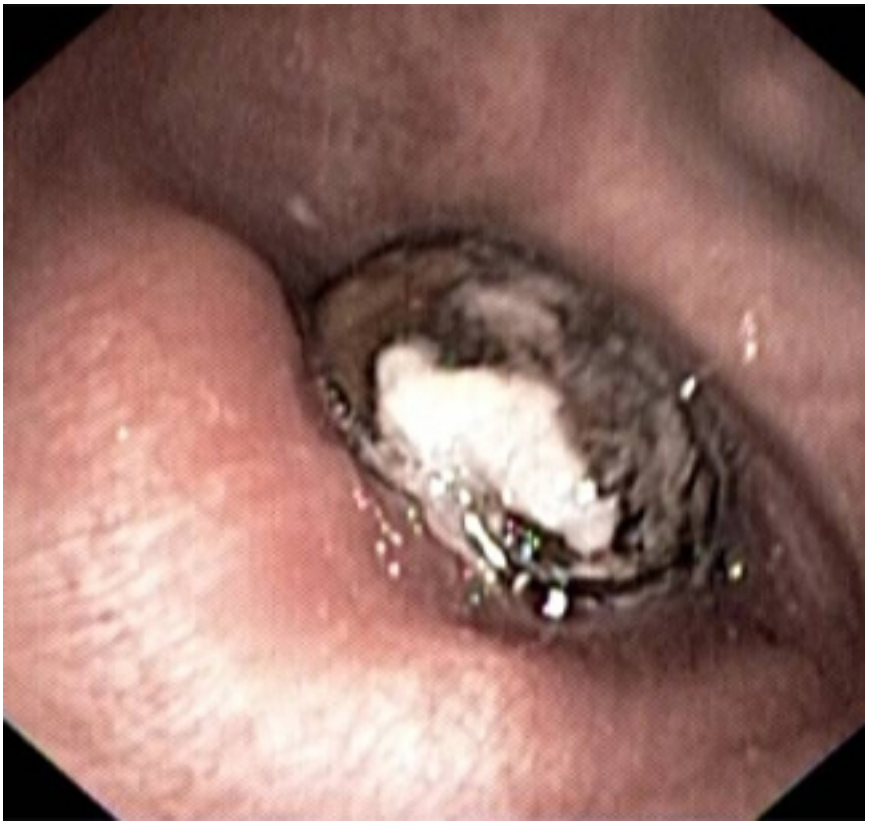

Figure 19: Bronchoscopy image showing a loquat seed completely occluding the bronchus intermedius

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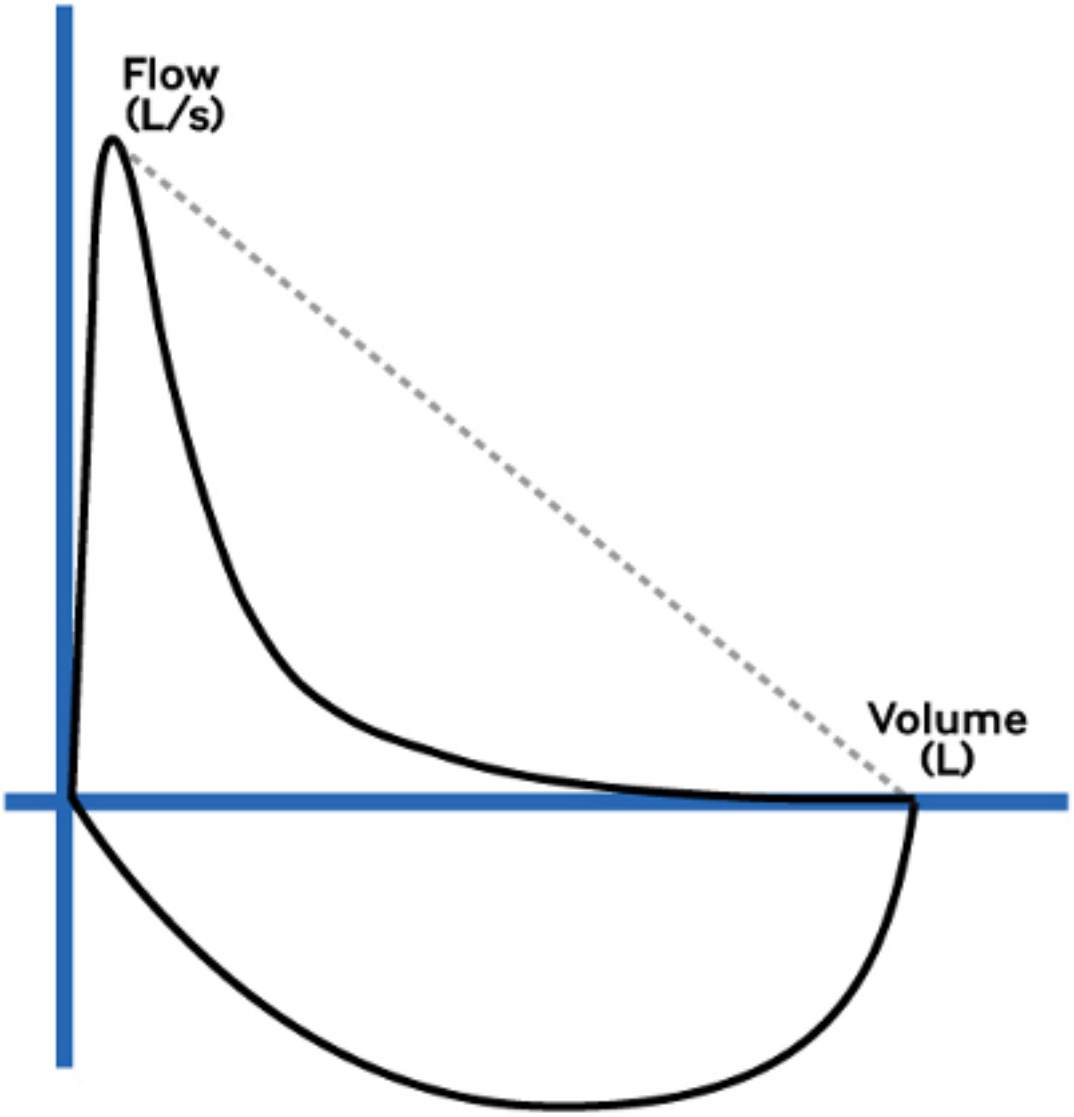

Figure 20: Flow-volume loop (spirogram) in obstructive lung disease, such as asthma or COPD: peak expiratory flow may be normal, but a concave shape is seen following the point of maximal flow due to the low flow rate in relation to lung volume

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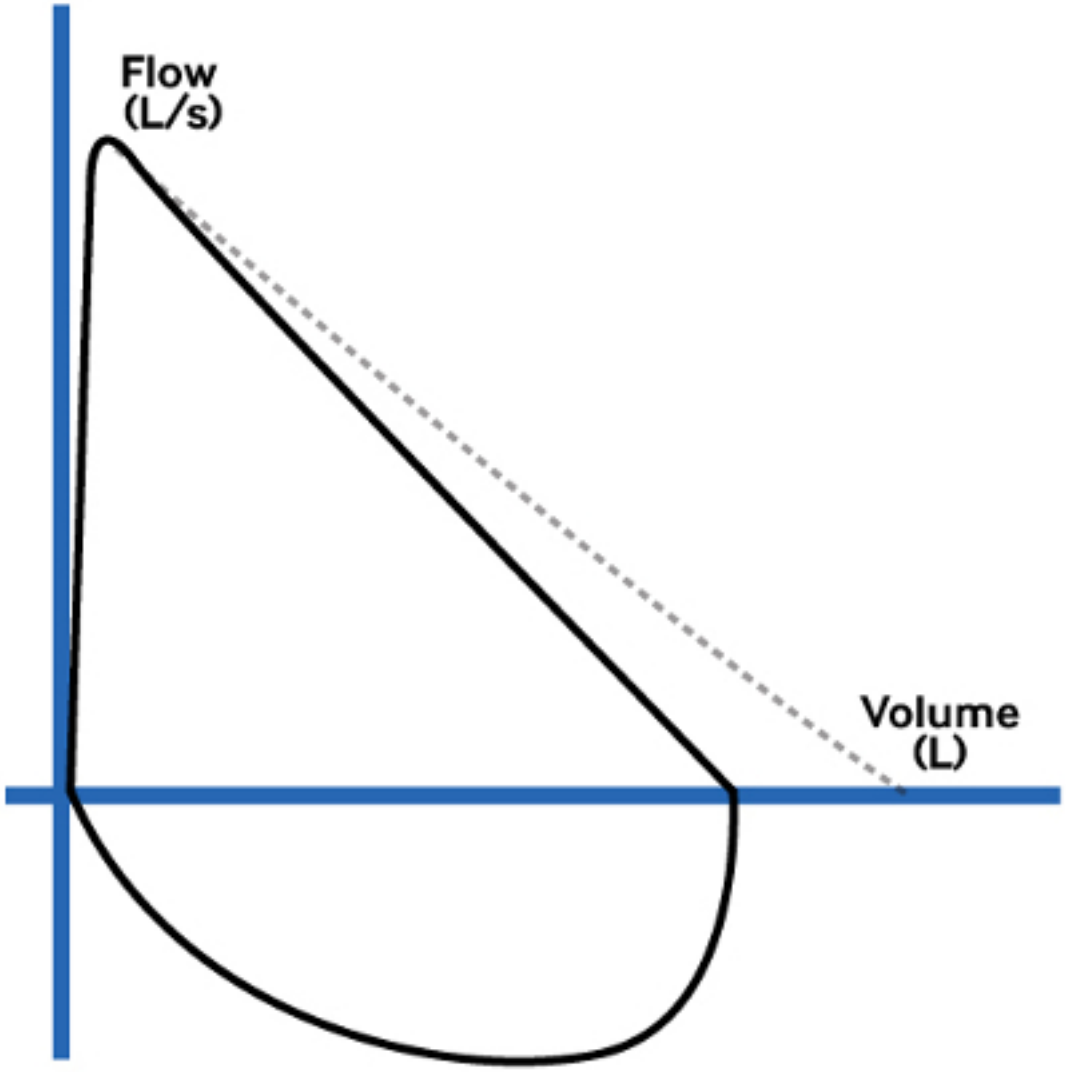

Figure 21: Flow-volume loop (spirogram) in restrictive lung disease (e.g., interstitial pulmonary fibrosis): peak expiratory flow may be normal or low. The shape of the curve is generally normal, but the loop is narrowed and the forced vital capacity is low because of the reduced lung volume.

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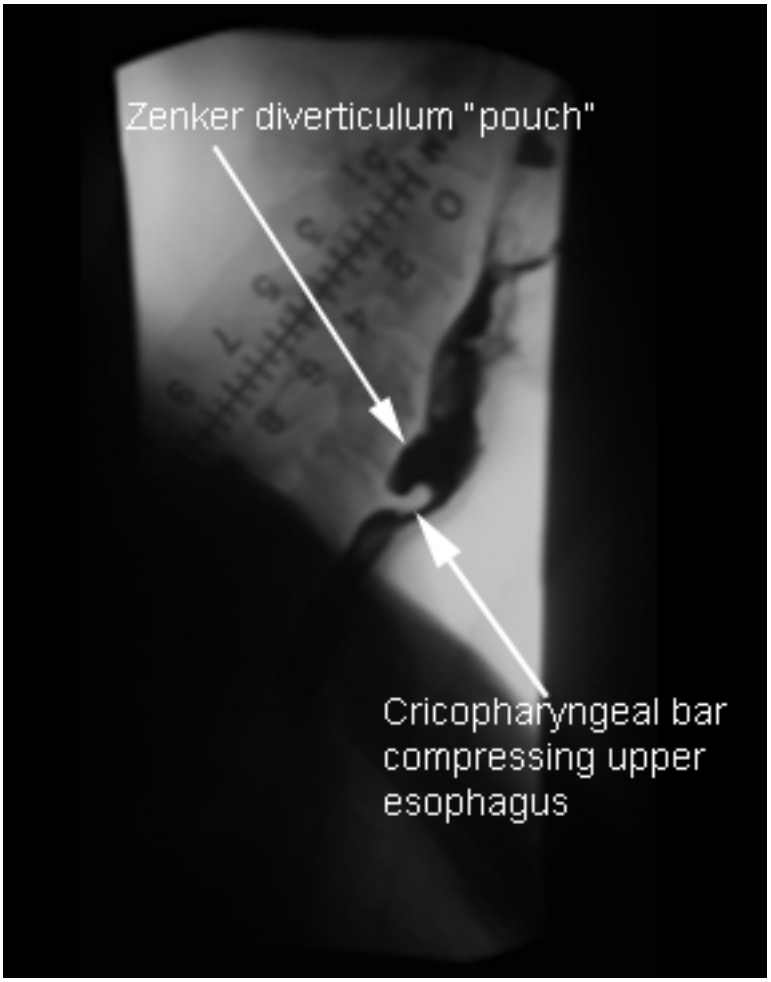

Figure 22: Zenker diverticulum: lateral view with barium esophagram

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