

COPD: (CLINICAL FEATURES AND CLINICAL DIAGNOSIS

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○ CLINICAL FEATURES

□ SYMPTOMS



- Individuals with early COPD are often asymptomatic. However, as the disease progresses, dyspnea, wheezing, cough and sputum production typically become more prominent.
- Any of these features should trigger an evaluation including spirometry both for diagnosis, if not already established, and for disease staging.
- Early in the disease course, dyspnea may be experienced only with exertion and patients may attribute these symptoms to other factors and not seek treatment.
- In fact, patients' activity may be severely limited even when they believe their disease process is still mild.
- Eventually, however, as the disease progresses, dyspnea may ultimately be present with activities of daily living.

- ✓ The mechanism for dyspnea in COPD is likely multifactorial, exercise-induced air trapping otherwise known as “dynamic hyperinflation” likely plays a significant role (Fig. 44-1).

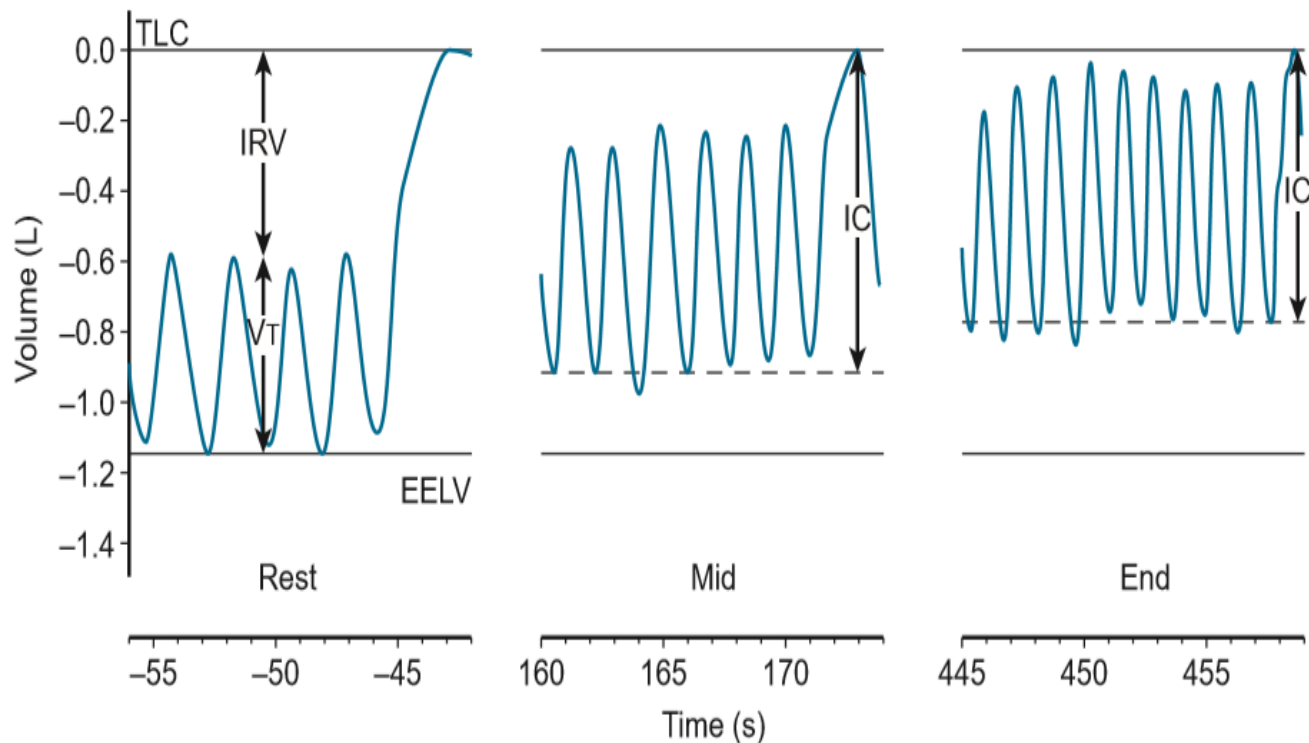


Figure 44-1 Dynamic hyperinflation. Volume tracing from a patient with severe COPD who demonstrated ventilatory dependent dynamic hyperinflation. Inspiratory capacity (IC) decreases and end-expiratory lung volume (EELV) increases as ventilation increases during exercise. IRV, inspiratory reserve volume; TLC, total lung capacity; VT, tidal volume. (From Dolmage TE, Evans RA, Goldstein RS: Defining hyperinflation as 'dynamic': moving toward the slope. *Respir Med.* Mar 7, 2013. Figure 1.)

- As with dyspnea, patients may attribute cough to other factors such as smoking and therefore may not complain about this symptom unless prompted.
- In general, current smokers have more sputum production, which paradoxically may increase transiently after smoking cessation.
- Sputum, when present, tends to be mucoid, clear to white in appearance, and more purulent with exacerbations.
- Excessive sputum production (more than 2 to 3 tablespoons daily) may indicate the presence of bronchiectasis, which has been reported to range in prevalence between 29% and 52% in moderate- to-severe COPD and has been associated with increased mortality.

- Hemoptysis may be seen with both chronic bronchitis and bronchiectasis, particularly during COPD exacerbations.
- However, the presence of hemoptysis in a patient with COPD should raise concern for other possible causes, including **lung cancer**, given the increased risk for lung cancer in this patient population.

- Several instruments have been developed to assess health status in COPD, most notably the St. George's Respiratory Questionnaire (**SGRQ**) and the COPD Assessment Test (**CAT**) (Fig. 44-2).
- Both are multidimensional instruments encompassing symptoms such as cough and sputum production as well as breathlessness and activity limitation.
- The **Modified Medical Research Council scale** is a 5-point dyspnea scale that, while not developed specifically for COPD, is relevant because it relates to mortality in COPD alone or when used to calculate the **BODE** (BMI, obstruction, dyspnea, exercise capacity) index, a mortality predictor in COPD (Table 44-1).

How is your COPD?

For each item below, place a mark (v) in the box that best describes your experience.

Example: I am very happy

0	1	2	3	4	5
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I am very sad

		SCORE							
I never cough	<table border="1"><tr><td>0</td><td>1</td><td>2</td><td>3</td><td>4</td><td>5</td></tr></table>	0	1	2	3	4	5	I cough all the time	<input type="checkbox"/>
0	1	2	3	4	5				
I have no phlegm (mucus) in my chest at all	<table border="1"><tr><td>0</td><td>1</td><td>2</td><td>3</td><td>4</td><td>5</td></tr></table>	0	1	2	3	4	5	My chest is completely full of phlegm (mucus)	<input type="checkbox"/>
0	1	2	3	4	5				
My chest does not feel tight at all	<table border="1"><tr><td>0</td><td>1</td><td>2</td><td>3</td><td>4</td><td>5</td></tr></table>	0	1	2	3	4	5	My chest feels very tight	<input type="checkbox"/>
0	1	2	3	4	5				
When I walk up a hill or one flight of stairs I am not breathless	<table border="1"><tr><td>0</td><td>1</td><td>2</td><td>3</td><td>4</td><td>5</td></tr></table>	0	1	2	3	4	5	When I walk up a hill or one flight of stairs I am very breathless	<input type="checkbox"/>
0	1	2	3	4	5				
I am not limited doing any activities at home	<table border="1"><tr><td>0</td><td>1</td><td>2</td><td>3</td><td>4</td><td>5</td></tr></table>	0	1	2	3	4	5	I am very limited doing activities at home	<input type="checkbox"/>
0	1	2	3	4	5				
I am confident leaving my home despite my lung condition	<table border="1"><tr><td>0</td><td>1</td><td>2</td><td>3</td><td>4</td><td>5</td></tr></table>	0	1	2	3	4	5	I am not at all confident leaving my home because of my lung condition	<input type="checkbox"/>
0	1	2	3	4	5				
I sleep soundly	<table border="1"><tr><td>0</td><td>1</td><td>2</td><td>3</td><td>4</td><td>5</td></tr></table>	0	1	2	3	4	5	I don't sleep soundly because of my lung condition	<input type="checkbox"/>
0	1	2	3	4	5				
I have lots of energy	<table border="1"><tr><td>0</td><td>1</td><td>2</td><td>3</td><td>4</td><td>5</td></tr></table>	0	1	2	3	4	5	I have no energy at all	<input type="checkbox"/>
0	1	2	3	4	5				

SCORE

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Table 44-1 The BODE Index

Variable	Points on the BODE index			
	0	1	2	3
B—Body mass index (kg/m^2) ^a	>21	≤ 21	—	—
O—FEV ₁ (% of predicted) ^b	≥ 65	50–64	36–49	≤ 35
D—Distance walked in 6 min (m)	≥ 350	250–349	150–249	≤ 149
E—MMRC dyspnea scale (score)	0–1	2	3	4

○ CLINICAL FEATURES

□ PHYSICAL EXAMINATION

- Early in the course of the disease, no specific abnormalities may be noted on physical examination.
- **Wheezing** may or may not be present and does not necessarily relate to the severity of airflow obstruction.
- **Prolonged expiratory time** is a more consistent finding in COPD, particularly as the disease progresses.
- **A forced expiratory time of more than 6 seconds corresponds to an FEV₁/forced vital capacity (FVC) ratio of less than 50% to 60%.**

- In very severe disease, patients develop physical signs indicative of hyperinflation, including a **barrel-shaped chest**, **decreased breath sounds**, **distant heart sounds**, and **increased resonance** to percussion.
- Patients may breathe in a **“tripod” position** in which the individual leans forward and supports his or her upper body with extended arms. This maneuver takes advantage of the accessory muscles of the neck and upper chest to increase air movement.
- Patients with severe disease may also use pursed-lip breathing, which involves exhaling through tightly pressed, **pursed lips**. This technique creates back-pressure and is thought to reduce dynamic hyperinflation although it may also work by reducing bronchoconstriction via neutrally mediated mechanisms.

- In patients with severe disease, other systemic manifestations may include signs of **cor pulmonale**, or right-sided heart failure, leading to lower extremity edema.
- An **accentuated P2** or pulmonic component of the second heart sound may also be appreciated.
- **Tar stains on the fingers** from cigarette smoking may be present.
- ✓ Clubbing is not a typical feature of COPD, even when hypoxemia is present, and should suggest evaluation for other comorbidities including lung cancer.

- ✓ Two commonly recognized COPD subtypes are the “pink puffers” and “blue bloaters.”
- Pink puffers, typically associated with significant emphysema, compensate by hyperventilation and often manifest muscle wasting and weight loss. Compared with blue bloaters, pink puffers are less hypoxemic and therefore appear “pink.”
- Blue bloaters typically have chronic bronchitis and tend to have decreased ventilation and greater ventilation-perfusion (V/Q) mismatch than pink puffers, leading to hypoxemia and hence cyanosis and to cor pulmonale with edema or “bloating.”

- PULMONARY FUNCTION TESTING
AND DIAGNOSIS

□ Spirometry

- Pulmonary function testing and, in particular, spirometry is essential to establish a diagnosis of COPD.
- Spirometry can be performed in the physician's office and should be done in any patient with symptoms (e.g., cough, sputum, dyspnea) and risk factors.
- COPD is defined by a reduction in the FEV₁/FVC ratio.
- The degree of FEV₁ reduction defines the severity of airflow obstruction.
- The flow volume loop in COPD typically has a concave appearance and the volume time curve demonstrates a prolonged expiratory time.

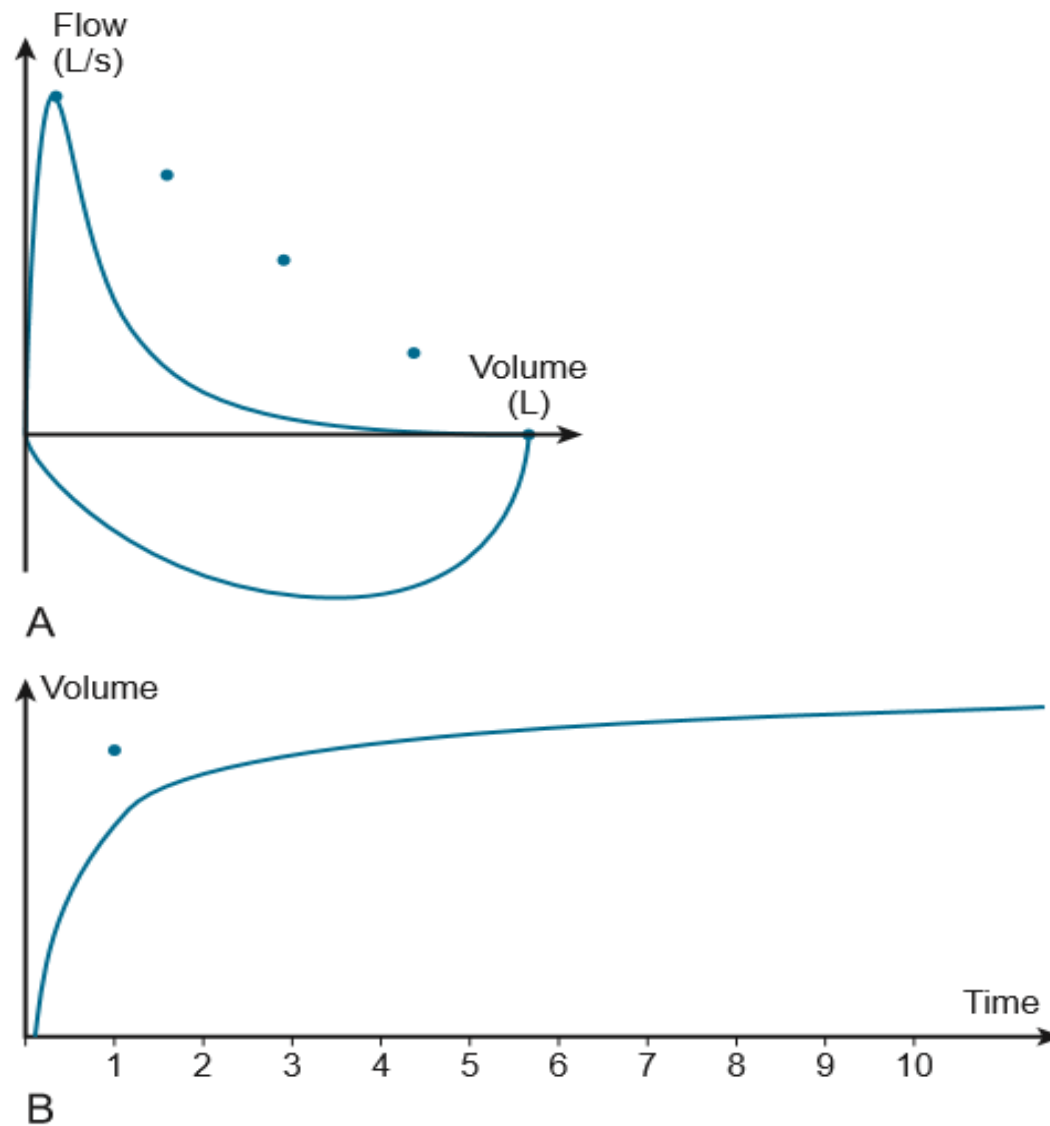


Figure 44-3 Flow volume loop in COPD. A, The tracing shows a concave flow volume loop with reduction of flow at all lung volumes. The dots indicate the expected flow at various lung volumes. **B,** The volume-time curve shows a prolonged expiratory time. The dot demonstrates the predicted FEV₁.

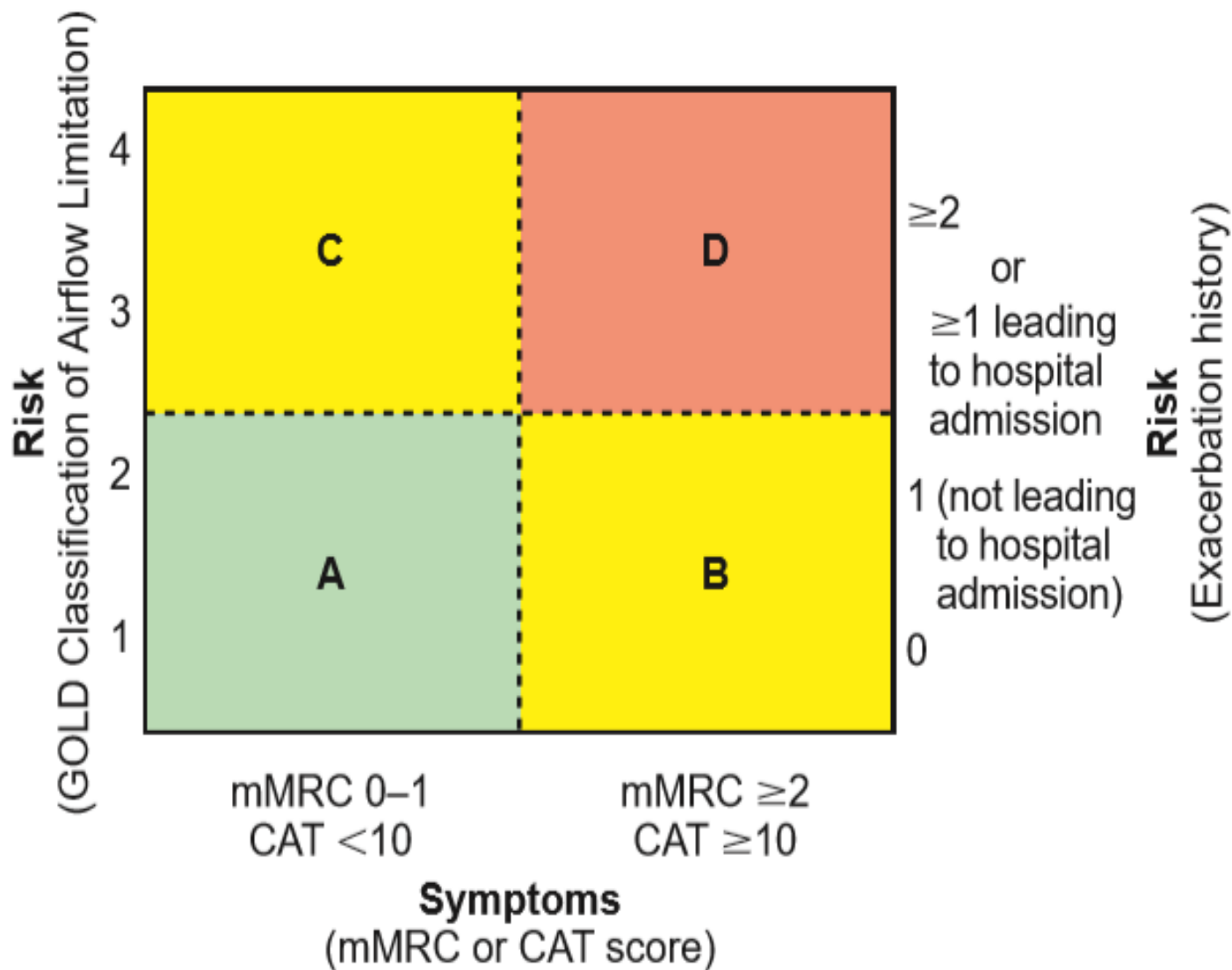
- The ATS and the Global Initiative for Chronic Obstructive Lung Disease (GOLD) recommend that **post-bronchodilator values** be used to help distinguish COPD from asthma.
- **GOLD recommends an FEV₁/FVC less than 0.70 as the threshold for presence of airflow obstruction.**
- **Rather than using the fixed ratio, the ATS/ERS recommends using the fifth percentile for the lower limit of normal.**
- In general, the fixed ratio approach leads to overdiagnosis in older subjects because the FEV₁/FVC ratio declines with age, even in healthy individuals.
- However, the fixed ratio approach carries the advantage of simplicity.

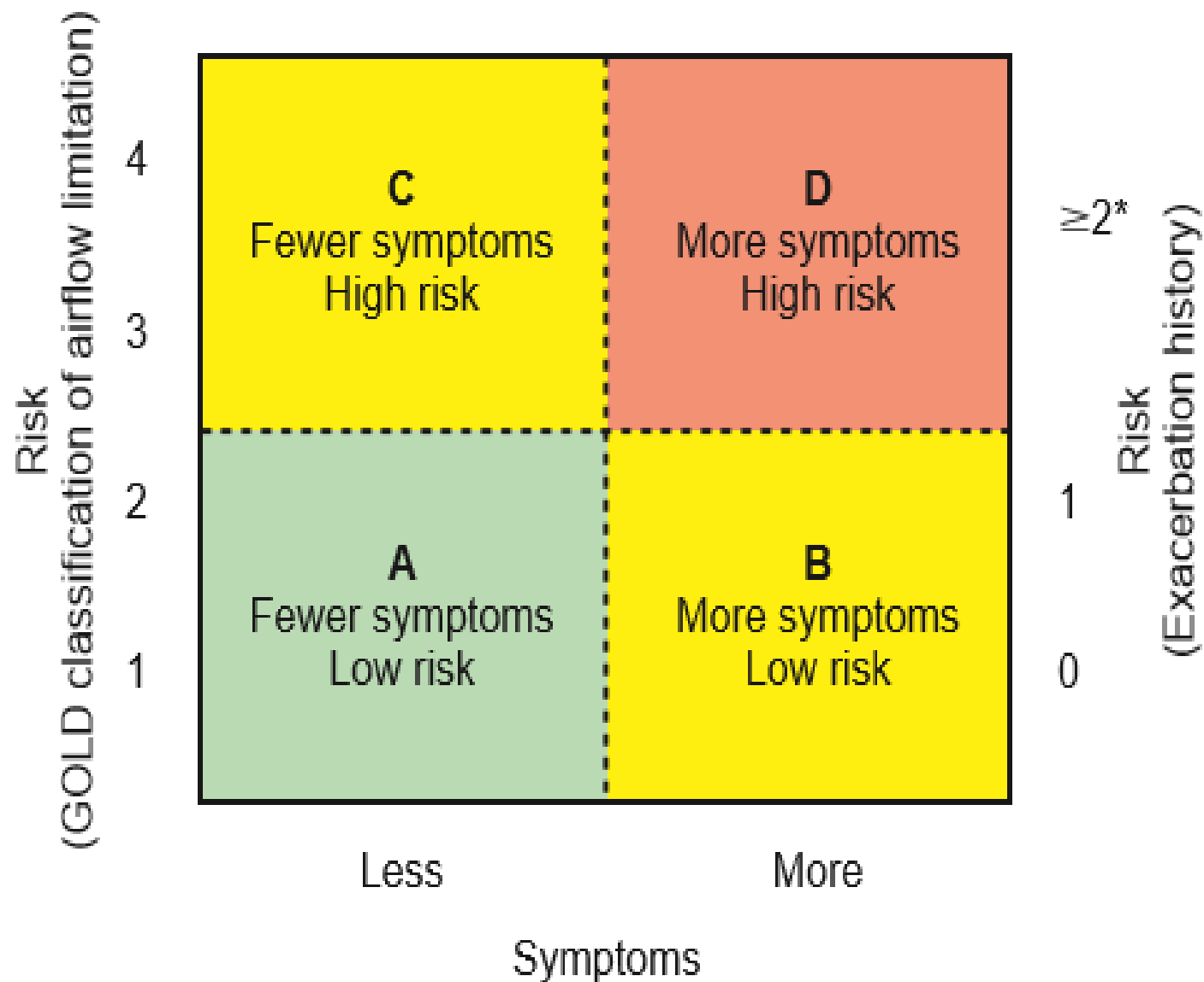
- ✓ While COPD severity has typically been graded based on FEV₁% predicted, which is part of the GOLD and ATS/ERS recommendations, recent updates to the GOLD recommendations now incorporate symptoms and exacerbation risk as part of disease staging.

Table 44-2 GOLD Classification of Severity of Airflow Limitation in COPD, Based on Post-Bronchodilator FEV_1

In Patients with $FEV_1/FVC < 0.70$

GOLD 1: mild	$FEV_1 \geq 80\%$ predicted
GOLD 2: moderate	$50\% \leq FEV_1 < 80\%$ predicted
GOLD 3: severe	$30\% \leq FEV_1 < 50\%$ predicted
GOLD 4: very severe	$FEV_1 < 30\%$ predicted





□ Lung Volumes

- ✓ Other lung volumes including total lung capacity (TLC) and residual volume (RV) must be measured via plethysmography, which is typically performed in a pulmonary function laboratory.
- **TLC is increased in COPD**, particularly in the presence of emphysema where there is significant loss of elastic recoil, resulting in lung hyperinflation.
- **Increases in RV and functional residual capacity** may also be seen.
- RV tends to increase to a greater extent than TLC, leading to an **increase in the RV/TLC ratio**.
- **Vital capacity in COPD is also typically decreased** because of hyperinflation.

□ Diffusing Capacity

- Diffusing capacity for carbon monoxide (DLCO) is decreased in the presence of emphysema.
- Near-normal spirometry and lung volumes in the setting of severely reduced diffusing capacity and radiographic evidence of emphysema should suggest a possible diagnosis of combined pulmonary fibrosis emphysema syndrome.

□ Exercise Testing

- The 6-minute walk test (6MWT) is probably the most frequently employed exercise test in COPD.
- While a 6MWT is not required to make a diagnosis of COPD, it allows the clinician to assess oxygenation during ambulation and the potential need for supplemental oxygen.
- 6MWD is also frequently employed during lung transplant evaluation to gauge functional status and prognosis.
- 6MWD has been demonstrated to relate to mortality in COPD and is a component of the BODE mortality index.
- The 6MWT however does not provide diagnostic information regarding specific causes for dyspnea or exercise limitation.

□ IMAGING

- Chest radiography and computed tomography (CT) are the two imaging modalities most commonly used in COPD.
- While not required to diagnose COPD, imaging can be helpful to rule out concomitant processes.
- Chest radiography is not particularly sensitive or specific for the diagnosis of COPD.
- ✓ Radiolucency, diaphragmatic flattening, and increased retrosternal airspace on the lateral radiograph may be seen when hyperinflation is present.
- Occasionally large bullae may manifest as radiolucent areas.

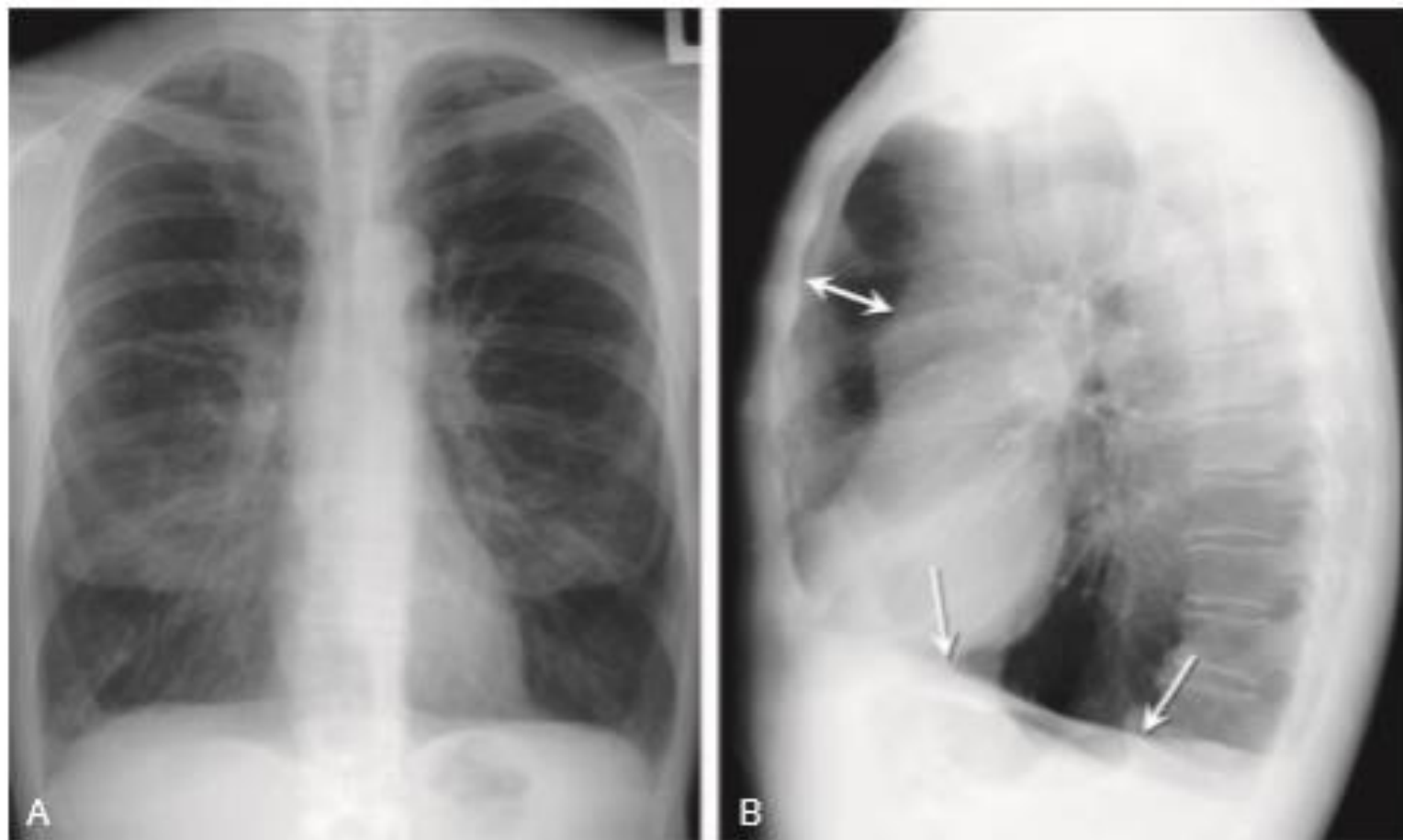
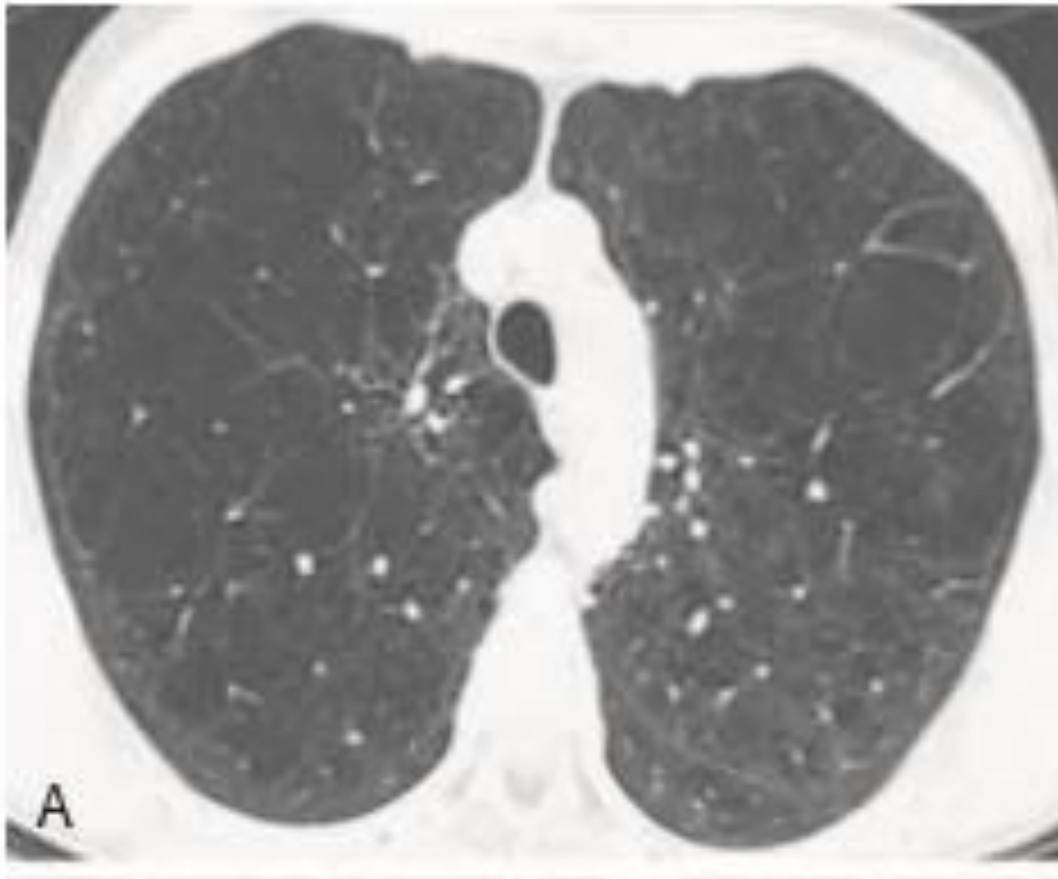


Figure 44-4 Centriacinar emphysema. Frontal (A) and lateral (B) chest radiograph in a 54-year-old female smoker with centriacinar emphysema. Note the very large lung volumes, with hyperlucency primarily seen in the upper lobes, consistent with a centriacinar emphysema pattern. Flattening of the diaphragms (arrows), a prominent retrosternal clear space on the lateral radiograph (double arrow), and a small-appearing heart on the frontal radiograph are findings consistent with abnormally increased lung volumes and are typical of advanced emphysema. The upper lobe lucency typical of centriacinar emphysema contrasts with the lower lobe predominant lucency seen in patients with panacinar emphysema. See [Video 44-1](#) for CT video of this patient.

- Chest CT allows better detection and quantification of emphysema than does traditional chest radiography.
- Areas of low attenuation are a marker of emphysema; thickened airways indicative of bronchial thickening may also be seen.
- If expiratory views are obtained, areas of air trapping indicative of small airway obstruction and emphysema may also be seen.
- CT is not indicated in the routine diagnosis or evaluation of COPD, but can be helpful when evaluating individuals with very severe COPD.

- Individuals with very severe COPD undergoing transplant evaluation typically require a chest CT to rule out the presence of lung cancer and aid with surgical planning.
- CT imaging is also helpful when the clinician is concerned about a concomitant process such as interstitial lung disease which may be suggested on pulmonary function testing or when hemoptysis or other unexplained changes in symptoms develop.
- Bronchiectasis, which may be reflected by copious sputum production and cough and has been associated with increased mortality, is also best assessed on CT.

- The COPD patient population is at increased risk for lung cancer and the mortality benefit of screening CTs in smokers has now been established.
- ✓ Therefore a low-dose screening CT for lung cancer in individuals aged 55 to 74 years with at least a 30 pack-year smoking history, including those who quit in the preceding 15 years, may be appropriate.



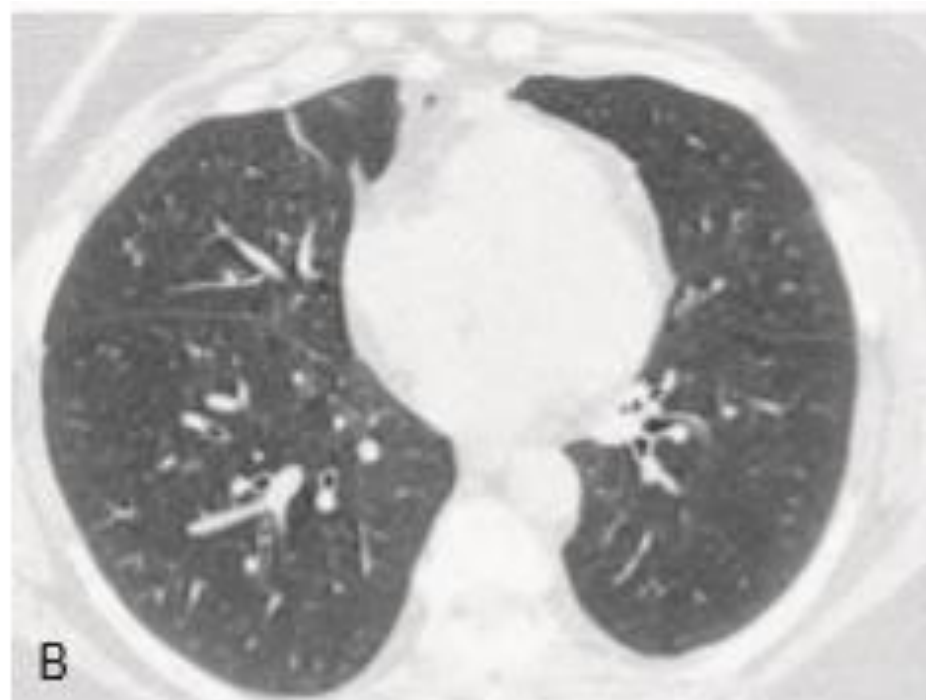


Figure 44-5 Two radiologic phenotypes of COPD. CT of two patients with COPD demonstrating the significant difference in the type of disease that may be present. Two patients with moderately severe disease are shown. **A**, The patient demonstrates predominantly emphysema whereas the patient shown in **B** demonstrates predominantly airway thickening. (From Han MK, Kazerooni EA, Lynch DA, et al: Chronic obstructive pulmonary disease exacerbations in the COPDGene study: associated radiologic phenotypes. *Radiology* 261:274-282, 2011.)

○ LABORATORY TESTING

□ Arterial Blood Gases

- Arterial blood gases (ABGs) are not indicated as part of the routine evaluation for patients with mild to moderate COPD.
- ABGs can be helpful to assess hypoxemia and to provide information regarding hypercapnia, particularly in individuals with more severe disease or during an acute exacerbation.
- ✓ Early in the disease course, mild to moderate hypoxemia without hypercapnia is typically seen.
- ✓ Later in the disease course, hypercapnia may develop, particularly in individuals with FEV₁ less than 1 L.

□ Erythrocytosis

- Elevated hemoglobin may be seen in COPD, particularly in the presence of chronic hypoxemia.
- A hemoglobin value is also helpful in the evaluation of dyspnea because anemia is a common cause of dyspnea that should be ruled out.
- In addition, DLCO is most accurate when adjusted for hemoglobin.

□ Serum Bicarbonate

- ✓ An elevated serum bicarbonate can suggest chronic hypercapnia; in the setting of hypercapnia, serum bicarbonate is increased due to compensatory metabolic alkalosis.

- Alpha1-Antitrypsin Deficiency

- ✓ The ATS guidelines recommend testing for A1AT deficiency for all individuals with persistent airflow obstruction.
- Clinical features suggestive of A1AT deficiency include emphysema at a young age, emphysema in an individual with minimal or no smoking history, lower lobe predominant emphysema, and a family history of emphysema.
- However, A1AT deficiency can also be present in patients with more typical COPD presentations. In individuals with established COPD, diagnostic testing is recommended.

- Concern for the diagnosis is raised based on A1AT serum levels below 11 micromol/L (approximately 50 mg/dL using nephelometry (i.e., immunoturbidimetry) and 80 mg/dL by radial immunodiffusion) but should be confirmed with genotyping (**high-risk genotypes include S, Z, and null alleles** as the most deficient).
- Occasionally the serum level and genotyping are discordant; in this situation, **protein phenotype analysis via electrophoresis** can identify alleles with abnormal protein migration patterns.
- ✓ **The chest radiograph and CT show the predominantly lower lobe distribution of emphysema, consistent with a panacinar pattern and different from the more common centriacinar pattern.**



Figure 44-6 Panacinar emphysema. Frontal chest radiograph in a 51-year-old woman with α_1 -protease inhibitor deficiency presenting for lung transplant evaluation. Note the very large lung volumes with hyperlucency primarily seen in the bases, consistent with panacinar emphysema, as well as flattening of the diaphragms. Contrast the lower lobe lucency in this radiograph with [Figure 44-4](#), which shows upper lobe lucency in a patient with centrilobular emphysema. See [CT Video 44-2](#) of this patient. ■

- Sputum evaluation

- ✓ Sputum evaluation is not indicated in the routine diagnosis and care of the COPD patient.
- In patients with stable disease, sputum examination typically reveals a predominance of macrophages and few bacteria.
- During exacerbations, the number of organisms on Gram stain typically increases. The most common pathogens identified on sputum culture include *Haemophilus influenzae*, *Moraxella catarrhalis* and *Streptococcus pneumoniae*.
- Bacteria identified in sputum during stable COPD have been associated with a greater exacerbation frequency and lung function decline. In general, exacerbations typically respond to empirical treatment.

○ COMPLICATIONS

- PNEUMOTHORAX
- GIANT BULLAE
- PNEUMONIA
- COR PULMONALE
- SLEEP DISORDERS

- **SYSTEMIC MANIFESTATIONS AND COMORBIDITIES**

- Cardiovascular Disease
- Osteoporosis
- Diabetes
- Gastroesophageal Reflux Disease
- Depression and Anxiety

COPD:

DIFFERENTIAL DIAGNOSIS

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- Several disorders may mimic aspects of COPD, and certainly many conditions may be associated with dyspnea.
- However, there are a handful of disorders that are particularly challenging because they may be associated with cough, sputum production, airflow obstruction, or emphysema-like radiographic changes.
- Careful clinical assessment can help differentiate these disorders from COPD although, in some instances, these disorders may be present in addition to COPD.

- ✓ CHRONIC OBSTRUCTIVE ASTHMA
- ✓ CHRONIC BRONCHITIS WITHOUT AIRFLOW OBSTRUCTION
- ✓ BRONCHIECTASIS
- ✓ BRONCHIOLITIS OBLITERANS
- ✓ DIFFUSE PANBRONCHIOLITIS
- ✓ LYMPHANGIOLEIOMYOMATOSIS

- CHRONIC OBSTRUCTIVE ASTHMA

- Chronic asthma may be associated with the development of persistent airflow obstruction that is not completely reversible (i.e., due to “remodeling”).
- **Chronic asthma may also coexist with COPD.**
- In general, the age of onset for asthma tends to be earlier.
- Asthmatic patients may have a history of atopy and a family history of asthma.
- Airflow obstruction abnormalities are usually less severe with asthma, with greater prevalence of reversibility.
- **Sputum production is less common in asthma.**
- These patients also tend to have less of a smoking history and greater steroid responsiveness than patients with COPD.
- Chronic asthma is also not associated with emphysema.
- **The DLCO is normal or increased in chronic asthma, whereas it is decreased in emphysema.**

- CHRONIC BRONCHITIS WITHOUT
AIRFLOW OBSTRUCTION

- Chronic cough and sputum production may be present in the absence of airflow obstruction.
- The accepted definition for chronic bronchitis is a productive cough for 3 months for 2 successive years.
- Diagnostically, this is often mistaken for COPD because chronic bronchitis even in the absence of airflow obstruction is often associated with smoking.
- Chronic exposure to poor air quality or industrial dusts/fumes also increase risk for this disorder.
- While no specific therapies have been developed for chronic bronchitis without airflow obstruction, the morbidity and mortality associated with this disorder should not be ignored.
- Such patients still experience poorer quality of life and increased risk of death as opposed to healthy controls.

- **BRONCHIECTASIS**

- Bronchiectasis is characterized by dyspnea and in particular copious mucopurulent sputum that tends to be greater than in typical COPD.
- It is not uncommon to see concurrent mild bronchiectasis in both COPD and asthma.
- Bronchiectasis in COPD is associated with increased mortality.
- Moderate to severe bronchiectasis should raise a clinician's concern for immunodeficiency, cystic fibrosis, rheumatic disorders, ciliary motility disorders, alpha1antitrypsin deficiency, allergic bronchopulmonary aspergillosis, and mycobacterial infection.

- BRONCHIOLITIS OBLITERANS

- Bronchiolitis obliterans (BO) is also known as constrictive bronchiolitis.
- BO is a known **complication of lung, heart, and bone marrow transplants** but also may be seen in association with **connective tissue diseases** and **inflammatory bowel disease**.
- Inhalation of dusts or **toxins**, **infection**, and **drug reactions** are less frequent causes of BO.
- As opposed to those with COPD, patients with BO may have no significant smoking history and typically do not have significant emphysema on CT, which may show only hyperinflation and air trapping.
- **Mosaic attenuation indicative of localized air trapping is common.** Bronchial wall thickening may also be present.
- Pulmonary function testing demonstrates **severe, progressive, and irreversible airflow obstruction** but is not typically associated with severe DLCO impairment.
- **Unfortunately, BO responds poorly to therapy.**

- **DIFFUSE PANBRONCHIOLITIS**

- Diffuse panbronchiolitis is a rare form of bronchiolitis **involving the upper and lower respiratory tracts** that is seen primarily in **Japan** and only rarely outside the Far East.
- Genetic factors, specific human leukocyte antigen (HLA) haplotypes, are thought to contribute to the pathogenesis and geographic distribution of this disease.
- Such patients typically present with chronic sinusitis, cough productive of copious sputum, dyspnea, wheezing, and weight loss.
- Airflow obstruction is a common feature, and HRCT may show **diffusely thickened** and **dilated bronchi** or **tree-in-bud opacities** corresponding to bronchiolitis.
- Confirming this diagnosis is important, because **diffuse panbronchiolitis often improves with macrolide antibiotics**.

○ LYMPHANGIOLEIOMYOMATOSIS

- Lymphangi leiomyomatosis is a rare disorder affecting women almost exclusively.
- It is caused by a mutation in the tuberous sclerosis-1 or -2 gene, either sporadically or in the setting of tuberous sclerosis, resulting in the proliferation of interstitial smooth muscle cells and pulmonary cyst formation.
- Other clinical characteristics include renal angiomyolipomas and chylous effusions.
- Lymphangi leiomyomatosis is also characterized by airflow obstruction and spontaneous pneumothoraces.
- Therefore it is not infrequently mistaken for emphysema.
- The presence of other characteristic clinical features can be helpful in the diagnosis.

با تشکر

