

Recognizing and Destigmatizing COPD in the 21st Century

There is a lot we can do with the tools that are currently available to improve quality of life in our patients.



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Chronic obstructive pulmonary disease, or COPD, is the fourth leading cause of morbidity and mortality in the United States. However, prevalence in morbidity data greatly underestimate the total COPD burden because the disease is frequently not diagnosed until it is clinically apparent and moderately advanced. New understanding of the pathophysiology of COPD has led to interventions that may have the potential to modify or control disease progression and prevent or delay its effects.

This clinical discussion is intended to help you recognize the challenges of preventing, diagnosing, and treating COPD and to apply current evidence-based guidelines in selecting appropriate screening, testing, education, and treatment options to improve patient care.

Dr. Rotello: Thank you for joining us today, Dr. Sutherland. To begin, the onset of COPD may be insidious and unsuspected in early stages. However, accurate diagnosis and early intervention with optimal therapy can improve the patient's symptoms, quality of life, and survival. How frequently does COPD affect patients?

Dr. Sutherland: Thank you, Dr. Rotello. As you mention, early diagnosis and intervention are critical. We have a number of good data that suggest that there is a fairly wide age distribution of COPD in the United States. Data from 2002 suggests that about one-third of all cases of COPD—including emphysema and chronic bronchitis—occur in patients

Learning Objectives

Upon completion of this course, you should be able to:

- ◆ Differentiate COPD from asthma in adult patients
- ◆ Describe the changes in COPD management that have made it a more treatable disease
- ◆ Articulate the advantages of early COPD diagnosis and treatment

For information about earning credit for this activity, see page 2. Completion of this self-study activity should take about 1 hour.

Course ID: AB0489

between the ages of 18 and 44 years. Then, of course, the majority occurs after that, and we certainly think about COPD as a disease of middle age and later life.

Dr. Rotello: We often see patients who present with respiratory distress. What are the important points to look for in the differential diagnosis of COPD and asthma?

Dr. Sutherland: Well, of course, careful history taking and physical examination are critical to the evaluation of any patient with a respiratory distress (Table 1). If any prior history of exertional dyspnea, hypoxia, smoking,

or other features that commonly suggest COPD are present, then that is certainly one feature that can tip off the providing clinician to the fact that COPD may be active. In the very acute setting, both diseases—COPD and asthma—manifest with expiratory airflow limitation and respiratory difficulty. Hypoxemia and hypoventilation can also occur. Of course, the initial treatment for acute bronchodilation and, potentially, systemic corticosteroids is very similar between the two. It really depends on a number of things, including the medical history, physical examination findings, and clinical judgment with regard to exposure to risk factors and other epidemiologic issues (Table 2).

Table 1. Differential Diagnosis

Diagnosis	Suggestive features
COPD	<ul style="list-style-type: none"> ◆ Midlife onset ◆ Slowly progressing symptoms ◆ Long history of smoking ◆ Dyspnea during exercise ◆ Largely irreversible airflow limitation
Asthma	<ul style="list-style-type: none"> ◆ Early onset ◆ Varying symptoms ◆ Symptoms during the night/early morning ◆ Allergy, rhinitis, and/or eczema also present ◆ Family history ◆ Airflow limitation that is largely reversible
Congestive heart failure	<ul style="list-style-type: none"> ◆ Fine basilar crackles on auscultation ◆ Dilated heart, pulmonary edema on chest radiography ◆ Volume restriction, not airflow limitation, on PFTs
Bronchiectasis	<ul style="list-style-type: none"> ◆ Large volume of purulent sputum ◆ Commonly associated with bacterial infection ◆ Coarse crackles on auscultation ◆ Bronchial dilation and bronchial wall thickening on chest radiography/CT ◆ Clubbing
Tuberculosis	<ul style="list-style-type: none"> ◆ Onset all ages ◆ Lung infiltrates or nodular lesions on chest radiographs ◆ Microbiological confirmation ◆ High local prevalence of tuberculosis

Modified from: American Thoracic Society. Differential Diagnosis of COPD [American Thoracic Society Web site]. Available at www.thoracic.org/COPD.

Table 2. Risk Factors for COPD

Exposures
<ul style="list-style-type: none"> ◆ Tobacco smoke ◆ Environmental pollution ◆ Occupational materials
Host Factors
<ul style="list-style-type: none"> ◆ Childhood respiratory infections ◆ Genetics (eg, α_1-antitrypsin deficiency) ◆ Airway hyperresponsiveness ◆ Lung growth
Other
<ul style="list-style-type: none"> ◆ Socioeconomic status ◆ Family history

Dr. Rotello: Do you think COPD is often misdiagnosed as asthma, or vice versa?

Dr. Sutherland: As I mentioned, there is an overlap between the two disorders with regard to some of their clinical manifestations, as well as with their physiologic manifestations. It can be challenging, both in the acute and the more stable outpatient setting, to differentiate between the two disorders. From an epidemiologic standpoint, individuals who are older, who have a significant exposure to tobacco or potentially some occupational exposures, or who have a genetic or family history of early-onset emphysema or COPD are those in whom one might consider a diagnosis of COPD rather than asthma. There are some clinical differences with regard to the pace of the disease, with asthma being a more intermittent disease. It can occur over the entire life span, whereas COPD is sometimes considered a more chronic, progressive disease that starts in middle life and then progresses insidiously throughout the remainder of the life span. From a physiologic standpoint, one of the features that we look at to differentiate the two disease states is expiratory airflow limitation, which they both share as a clinical feature. However, a number

of reports in the literature suggest that the bronchodilator responsiveness and the airway hyperresponsiveness that are typical features of asthma are less prominent features of COPD.

Exercise 1

Mr. Smith, a 50-year-old man, presents with shortness of breath that has been worsening for years and especially over the last month. He has a history of smoking (30 pack-years) but no history of pneumonia. His lungs are clear on auscultation, with no cough or wheeze. He takes no medications other than aspirin. What is the likely diagnosis?

- a. COPD
- b. Asthma
- c. Congestive heart failure
- d. Bronchiectasis

Answer on page 16.

Dr. Rotello: Do you believe there is a relationship between childhood asthma and the development of COPD later in life?

Dr. Sutherland: That relationship has been hypothesized and forms the foundation of the Dutch hypothesis that asthma and COPD are potentially part of a disease continuum. However, we are not yet sure whether or not that is the case. There are certainly differences between certain phenotypes, if you will, of the two disorders that suggest that distinct epidemiologic and genetic risk factors predispose certain individuals to develop asthma and certain individuals to develop COPD. From the standpoint of COPD, of course, the single most important exposure or risk factor is the exposure to tobacco smoke. One can also consider environmental exposures and potentially α_1 -antitrypsin deficiency as other risk factors.

Dr. Rotello: Regarding pathophysiology, there is a strong emphasis on the role of inflammation in asthma. What about the role of inflammation in more chronic diseases, such as emphysema and chronic bronchitis?

Dr. Sutherland: That major risk factor I just mentioned, exposure to tobacco smoke, induces a very powerful inflammatory response in the lungs. The oxidative stress that is induced by tobacco smoke overwhelms the lungs' antioxidant defenses and initiates a severe inflammatory response that becomes chronic. It is certainly chronic in the face of continued exposure to tobacco smoke, and it can actually continue even after an individual has discontinued or stopped smoking. So, we know that tobacco smoke is a key inflammatory stimulus that leads to chronic airway inflammation, which then leads to the development of COPD. There are some differences between COPD and asthma with regard to the inflammatory cell phenotype. In asthma, we think about eosinophils as being the predominant effector cell, with lymphocytes and macrophages playing a role, whereas in COPD, we have traditionally thought about neutrophils and macrophages, and perhaps less commonly lymphocytes and eosinophils, as playing roles. This, of course, has implications for anti-inflammatory therapy.

Dr. Rotello: How do the underlying pathophysiologies of COPD and asthma differ?

Dr. Sutherland: They differ to some extent with regard to the inflammatory phenotype that I talked about. The physiologic manifestations that I mentioned previously with regard to differences, particularly between airway hyperresponsiveness and bronchodilator responsiveness, certainly exist. We know

that over time—or there is at least a suggestion in the literature—there are differences between the pathologic lesions that underlie COPD, chronic bronchitis, emphysema, and asthma. We know that, in emphysema, there can be destruction of the lung parenchyma and also involvement of the large and small airways. In asthma, we think more about a chronic inflammatory process that potentially leads to collagen deposition, and narrowing of the airway. Of course, this is then associated with a predisposition to bronchoconstriction.

Dr. Rotello: Especially in exacerbations, it is often difficult to determine exactly what is going on with the patient and whether you are dealing with a COPD exacerbation or an asthmatic exacerbation. Do these two conditions frequently coexist in some patients?

Dr. Sutherland: They certainly can. That clinical observation is, to some extent, what has led to the hypothesis that these diseases may be related to each other in some way. We certainly all have clinical experience in which we have patients who had early-life asthma and who smoked, and who later in life developed a clinical syndrome that very much appears to be COPD. Although we think of these distinctions as physiologically

Abbreviations

ATS/ERS	American Thoracic Society/ European Respiratory Society
COPD	chronic obstructive pulmonary disease
FEV₁	forced expiratory volume in 1 second
FVC	forced vital capacity
GOLD	Global Initiative for Chronic Obstructive Lung Disease
TRICC	Transfusion Requirements in Critical Care trial

Table 3: Classification of COPD Severity

Stage	GOLD	ATS/ERS
0: At Risk	◆ Chronic symptoms, cough, sputum production, normal spirometry results	Smoking or exposure to pollutants, cough, sputum production or dyspnea, family history of respiratory disease, normal spirometry results
I: Mild COPD, with or without chronic symptoms	◆ FEV ₁ >80% of predicted	
II: Moderate COPD, with or without chronic symptoms	◆ FEV ₁ 50–80% of predicted	
III: Severe COPD, with or without chronic symptoms	◆ FEV ₁ 30–50% of predicted	
IV: Very Severe COPD	◆ FEV ₁ <30% of predicted or ◆ FEV ₁ <50% of predicted plus chronic respiratory failure	FEV ₁ <30% of predicted

A defining characteristic of COPD at all levels of severity is an FEV₁ / FVC ratio of <70%.

(ATS) American Thoracic Society; (ERS) European Respiratory Society; (GOLD) Global Initiative for Chronic Obstructive Lung Disease

differentiating asthma from COPD, they certainly both have airflow limitation as their cardinal physiologic manifestation, and even though we think about airway hyperresponsiveness and bronchodilator

responsiveness as being less prominent in COPD, they certainly exist. Depending on the data or on the clinical trial that you look at, airway hyperresponsiveness to a stimulus like methacholine or histamine and improvement with a bronchodilator are seen. When it comes back to taking care of the individual patient, sometimes we have to use our clinical judgment and combine not only the physiologic manifestations but also the clinical features and histologic and epidemiologic features to really differentiate COPD and asthma. This is not just a moot point, if you will; it is important, particularly with regard to the initiation of anti-inflammatory therapy, to understand whether a patient has a predominantly asthmatic phenotype or more of a COPD chronic phenotype.

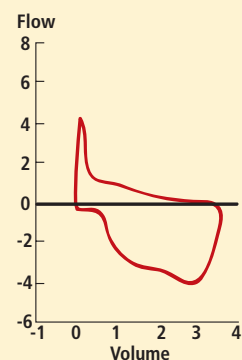
Dr. Rotello: How about spirometry? How do you use that test in your patients, and do you think, in general, that it is underused as a diagnostic and screening tool?

Dr. Sutherland: Spirometry is a cardinal clinical tool that we have for the

diagnosis of COPD. It is, I think, underutilized. A number of guidelines and other consensus statements have recommended the use of spirometry as a screening tool for the diagnosis of COPD in adult smokers with significant smoking histories—that is, 10 pack-years or greater. Now, it is hard to show that something like spirometry is cost-effective in diagnosing COPD because, clearly, you have to screen a lot of patients to make the diagnosis. This is also a disease that occurs and takes place over the adult life span. So, the impact of any single spirometry evaluation from a cost-effectiveness standpoint is difficult to justify. This is one of two tools that we have to evaluate and diagnose COPD.

Exercise 2

Mr. Smith undergoes pulmonary function testing with spirometry. What does his flow-volume loop show?



- Normal results
- Fixed upper-airway obstruction
- Normal inspiration but decreased expiration flow
- Decreased inspiration flow but normal expiration

Answer on page 16.

What we know is that there is a significant association between symptoms and physiologic impairment in COPD. The majority of patients do not actually

New HEDIS Measures Related to COPD

In addition to chronic obstructive pulmonary disease (COPD) guidelines from GOLD and ATS/ERS, the National Committee for Quality Assurance (NCQA) recently released specifications for COPD in their 2006 edition of its Health Plan Employer Data and Information Set (HEDIS®). According to the measures outlined by HEDIS:

- ◆ It is widely agreed that spirometry is the most accurate means of diagnosing COPD
- ◆ The use of corticosteroids have been shown to shorten recovery periods, prevent relapses, and reduce COPD-related mortality

To learn more about these two measures, as well as other measures in the 2006 edition of HEDIS, please visit www.ncqa.org.

present to clinical attention until their lung function is approximately 50% of normal. What that means is, unless you have known your patient for a very long time or unless you have frequently queried them about symptoms over a long period of time, you and the patient may not notice small symptomatic changes or small changes in activity levels or exercise tolerance that have occurred. These changes may not be accompanied by cough or sputum production or any other prominent clinical feature. So, if one relies on clinical manifestations alone and does not perform spirometry, it is very hard to find patients with COPD early. We think about spirometry as a key tool for screening for the disease, along with clinical evaluation, but it is also a key tool for evaluating the disease over time. We are certainly using recommendations from the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines and from the American Thoracic Society/European Respiratory Society (ATS/ERS) (Table 3) guidelines

to use spirometry as a tool for staging the disease. It is also something that we can use to follow the natural history of the disease over time and potentially something that we can use to evaluate therapeutic response as well. Spirometry has a number of roles, both in screening for diagnosis and in managing the disease, and it should be liberally utilized in the care of our patients with COPD.

Exercise 3

Mr. Johnson has an FEV₁ of 84% of predicted value and an FEV₁/FVC ratio of 70%. What stage of COPD does he have?

- a. 0, At risk
- b. I, Mild
- c. II, Moderate
- d. III, Severe
- e. IV, Very severe

Answer on page 16.

Dr. Rotello: We spoke a little bit earlier in relation to the special situations of some

patients. Are there specific populations who should be screened for α_1 -antitrypsin deficiency, for example?

Dr. Sutherland: We certainly think about α_1 -antitrypsin deficiency as a form of emphysema that occurs in early life. This, of course, is a deficiency in an antitrypsin that allows neutrophil elastase in the lung to essentially work unchecked. That results in destruction of the lung parenchyma and leads to emphysema. It is estimated that α_1 -antitrypsin deficiency accounts for about 1% to 3% of all cases of COPD, and it is certainly something we think about in patients with early-onset disease in our patients who have onset between the ages of 30 and 55 years. It is also something that we should think about in any nonsmoker who develops emphysema at any point in their life. It is important to think about α_1 -antitrypsin deficiency as probably the best understood genetic factor. There are very likely other genetic factors that we have yet to identify, and certainly,

Table 4: Recommended Treatment for Each Stage of COPD

Stage	0: At risk	I: Mild	II: Moderate	III: Severe	IV: Very Severe
Characteristics	<ul style="list-style-type: none"> ◆ Chronic symptoms ◆ Risk factors ◆ Normal spirometry 	<ul style="list-style-type: none"> ◆ FEV₁/FVC < 70% ◆ FEV₁ ≥ 80% ◆ With or without symptoms 	<ul style="list-style-type: none"> ◆ FEV₁/FVC < 70% ◆ 50% ≤ FEV₁ < 80% ◆ With or without symptoms 	<ul style="list-style-type: none"> ◆ FEV₁/FVC < 70% ◆ 30% ≤ FEV₁ < 50% ◆ With or without symptoms 	<ul style="list-style-type: none"> ◆ FEV₁/FVC < 70% ◆ FEV₁ < 30% or FEV₁ < 50% of predicted plus chronic respiratory failure
Treatment	Avoidance of risk factors; influenza vaccination				
	Add a short-acting bronchodilator when needed				
	Add regular treatment with ≥1 long-acting bronchodilators Add rehabilitation				
	Add inhaled glucocorticoids if repeated exacerbations				
	Add long-term oxygen if chronic respiratory failure Consider surgical treatments				

Source: The Global Initiative for Chronic Obstructive Lung Disease (GOLD). www.goldcopd.org/Guidelineitem.asp?l1=2&l2=1&intId=1116

environmental and occupational exposures have been associated with the development of COPD as well.

Dr. Rotello: What effect do you think an earlier diagnosis of COPD has on patients' outcomes?

Dr. Sutherland: Well, I emphasized earlier the importance of spirometry and clinical evaluation as means of diagnosing COPD early. The major importance of diagnosing COPD early has to do with the fact that this is a disease with a natural history that we can modify by initiating smoking cessation. We think that we can modify it with regard to symptoms, quality of life, and potential exacerbations by optimizing pharmacologic therapy. Particularly in the case of supplemental oxygen, we know that appropriate intervention can also modify survival. As I mentioned, a number of patients present to medical attention when their lung function is already 50% of predicted or less. What that means is that we have missed a huge window of opportunity in these patients

in terms of diagnosing the disease early and potentially modifying the natural history of the disease. So, early diagnosis, screening, and thinking about this as a potential diagnosis in any of our adult patients who have smoked are key factors because early intervention leads to significant benefits in our patients.

Dr. Rotello: When a younger patient presents with COPD, what type of aggressive management—pharmacologic or otherwise—do you usually institute in these patients?

Dr. Sutherland: That is a good question. It is interesting that pharmacologic therapy and aggressive therapy are important across all patients with COPD. So, there is little suggestion in the literature that intervention based on age alone makes any difference; however, what is suggested in the literature is that early intervention makes a difference. If we can identify those patients who we might not normally see until they are 60 years old or until they have an FEV₁ (forced expiratory volume in 1 second)

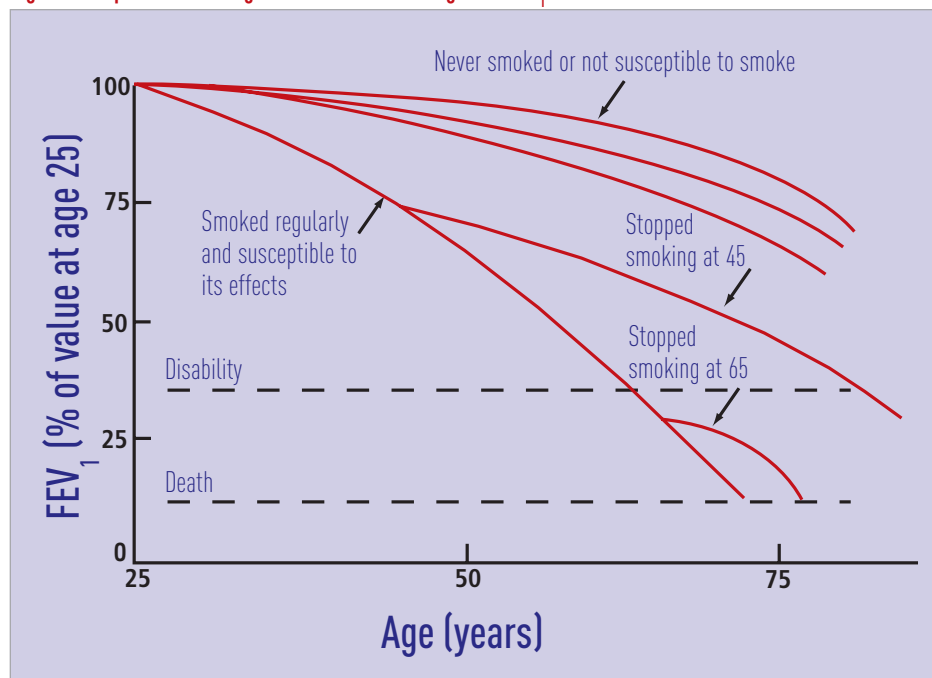
of 50% predicted, we will hopefully find them at an earlier stage of life and at an earlier stage of the disease, and this will allow the implementation of aggressive pharmacologic therapy. Now, pharmacologic therapy is really pretty much tied to the degree of symptomatic impairment and the degree of airflow limitation. Depending on which guidelines you like to use and depending on the degree of clinical and physiologic impairment that your patient is experiencing, pharmacologic therapy is very much tied to that.

Dr. Rotello: A lot of recent data, specifically those in the GOLD guidelines, have suggested the stratification of disease processes based on severity of illness. Could you review for us the GOLD guidelines?

Dr. Sutherland: Sure. I will take that question and divide it into two. I think the important practice elements with regard to treating our patients with COPD provided by the GOLD guidelines have to do with diagnosing the disease, staging it appropriately, then implementing pharmacologic therapy and nonpharmacologic therapy and even health maintenance strategies across the disease spectrum (Table 4). As I mentioned earlier, the GOLD guidelines state that COPD is a disease that is associated with airflow limitation. That airflow limitation is not as responsive to a bronchodilator (like albuterol) as the airflow limitation that we see in asthma. This physiologic abnormality that underpins COPD is very much tied to chronic exposure to tobacco smoke, gases, or other particles that may occur in the environment or in the workplace.

When it comes to using physiology to define COPD, we think about a reduction in the FEV₁-to-FVC (forced vital capacity) ratio of less than 70%

Figure 1. Impact of Smoking Cessation Based on Age and FEV₁



Source: Fletcher C, Peto R. The natural history of chronic airflow obstruction. *Br Med J.* 1977;1:1645-1648.

and an FEV₁ less than 80% of predicted as the two physiologic criteria at which we start to think about mild disease. In the revision of the GOLD guidelines that occurred in 2003, the stages were changed somewhat, and we started to think about a stage that was actually a preclinical stage or an at-risk stage. That really ties into the issues of spirometry and smoking cessation and early diagnosis that I mentioned earlier, because we want to find these people, and we want to be able to modify their disease. So, there is an at-risk group in which spirometry results are normal, in which symptoms do occur, and in which significant exposure to risk factors has occurred. As we then go through the mild, moderate, severe, and very severe stages, we see the initiation of airflow limitation, as manifested by an FEV₁-to-FVC ratio of less than 70%. Then, we look at the FEV₁ and we look at a variety of ranges of that FEV₁ as a percentage of the predicted normal value. Individuals with mild COPD have a reduced FEV₁-to-FVC ratio but a preserved FEV₁ that is greater than or equal to 80% of predicted. To achieve moderate disease status, the FEV₁ has to range between 50% and 80% of predicted. To achieve severe status, the FEV₁ has to range between 30% and 50% of predicted. Individuals with very severe COPD are those who have an FEV₁ of less than 30% of predicted, or who have milder airflow limitation, but demonstrate the presence of chronic respiratory failure or right heart failure. Interestingly, because symptoms are variable in COPD, we see that there is actually a variation in the presence or absence of symptoms across the disease spectrum. So, if one looks at the GOLD guidelines for staging, one will see that, ranging from mild to severe disease, there is actually a range in the presence or absence of symptoms. In terms of how this ties into therapy, I think one good way of thinking about therapy is to divide it into healthcare

maintenance strategies. Those, of course, include smoking cessation, regular vaccination, and (potentially) routine evaluation of spirometry. Then, furthermore, we can divide it into pharmacologic and nonpharmacologic treatment strategies. What the GOLD guidelines recommend with regard to pharmacologic treatment strategies is that patients with mild disease receive therapy initiated with a short-acting bronchodilator on an as-needed basis. That can be continued as a rescue medication, if you will, across the disease spectrum, but as moderate disease develops, the addition of regular treatment with one or more long-acting bronchodilators should be considered. In patients who have more severe disease, that is, those with an FEV₁ of less than 50% who have frequent exacerbations, the addition of inhaled corticosteroids can be considered as well. Other pharmacologic therapies include theophylline, of course, and that can be used in severe and very severe disease. When we talk about nonpharmacologic therapy, we think about pulmonary rehabilitation, which is something that is recommended starting in the moderate disease category. Later on, with very severe disease or even severe disease accompanied by hypoxia, evaluation of the blood oxygen level and treatment with supplemental oxygen is important. Finally, as a measure in very, very severe patients, surgical therapy, including lung-volume reduction surgery in a subset of patients and lung transplantation, can be considered.

Dr. Rotello: Do you think nonpharmacologic therapies, such as smoking cessation, have a role even in the population with severe or very severe disease?

Dr. Sutherland: Absolutely. I think there has, for a long time, been some nihilism about what we can do for our patient

with COPD. Although we realize that by the time most patients present, they are fairly well along with regard to airflow limitation, that does not mean that we cannot do anything for them. We can certainly modify the disease course. We think we can modify survival, and we can certainly modify symptoms and quality of life. How do we modify the disease course? Well, we implement smoking cessation.

Exercise 4

What do the GOLD and ATS/ERS guidelines recommend for the treatment of mild COPD?

- Avoidance of risk factors
- Influenza vaccination
- Short-acting bronchodilator when needed
- All of the above

Answer on page 16.

Of course we all know that this is a challenging clinical scenario. This is sometimes easier said than done, but what we know from data evaluated in the Lung Health Study is that smoking cessation reduces the progression of the disease. Specifically, it reduces the rate of decline in FEV₁ and actually returns the rate of decline in lung function to normal (Figure 1).

In terms of modifying survival or mortality, we know that supplemental oxygen is a key tool, as has been demonstrated in two good clinical trials. So, identifying hypoxemia when it occurs and adding supplemental oxygen for at least 15 hours a day has been shown to be associated with a mortality benefit in patients with COPD. In terms of modifying quality of life and symptoms, and potentially exacerbations and other important disease manifestations, we know that

inhaled bronchodilators—be they one of two pharmacologic classes (beta-agonist or anticholinergic) or of one of two durations (short-acting or long-acting)—have significant benefits with regard to health status, quality of life, symptoms scores, exercise tolerance, etc. We also think that the addition of inhaled corticosteroids, as demonstrated in a number of clinical trials, may not necessarily have an effect on lung function, but they can actually improve symptom scores and reduce exacerbations.

Dr. Rotello: As with many other disease processes, protocols and guidelines are often well-published and well-validated, but they can be difficult to put into practice. What is your advice to an institution or practice that is trying to implement GOLD guidelines in their treatment of patients?

Dr. Sutherland: I think the first issue is understanding who your patients are. We certainly all have different patient-population mixes, and it may be that these guidelines or disease management strategies vary, even between patients. So, it is difficult to make a blanket statement and a blanket recommendation for what works. What I do is, I take an approach that first evaluates the patients on the basis of clinical manifestations and physiologic abnormalities. I think about that, and in my own practice I actually try to implement the GOLD guidelines in terms of asking, can I make a diagnosis of COPD at this point? If I can, what is the stage, and what are the recommendations for treatment at that point? And then, with regard to breaking down treatment into its individual constituents, I go on to healthcare maintenance. In every patient, I think about smoking cessation, vaccination for influenza and *Pneumococcus*, and routine spirometry measurement. I

think about pharmacologic therapy by staging the patient's disease and by seeing what is appropriate with regard to bronchodilator therapy or, potentially, inhaled corticosteroids. Then I ask, how severe are they? Would they benefit from pulmonary rehabilitation? Would they benefit from supplemental oxygen in terms of considering nonpharmacologic therapy as well? So, I think these basic elements can really form the framework, or skeleton if you will, of the disease management program that then can be flexible enough to be individualized and made appropriate for each specific patient.

Dr. Rotello: A major treatment goal is, obviously, to reduce the number and severity of acute exacerbations, as most patients who experience these exacerbations can have either a temporary or a permanent decrease in their quality of life. What do the guidelines recommend as treatment for patients with acute exacerbations?

Dr. Sutherland: I think one key thing to understand before we talk about treatment is, how do we define an exacerbation? There are a number of

different definitions out there. The most recent come from the ATS/ERS, and they state that the definition of a COPD exacerbation is an acute change in the patient's baseline shortness of breath, cough, and/or sputum production beyond the variability that is normally seen day to day, and those changes have to be sufficient enough to warrant a change in therapy. This is really taking into account the fact that the disease can have some variability over a day or over a week, but that the real indicator of an exacerbation is a significant change in clinical or potentially functional status. What that does for us, as clinicians, is make us want to do something, and so a number of pharmacologic therapies can be initiated.

In terms of exacerbations, not all exacerbations are created equal, so the other thing that the ATS/ERS recommends is that we think about an operational classification with three levels of exacerbation. Level I exacerbations are those that are mild enough to be treated at home, potentially with just an increase in rescue bronchodilator use. Level II exacerbations are those that require hospitalization, and level III exacerbations are those severe exacerbations that are potentially associated with respiratory failure. The clinical response to these different levels of exacerbations varies, of course, by what you see when you are there at the bedside evaluating the patient, but also from a kind of general standpoint. Medical therapy for COPD exacerbation includes the addition of bronchodilators. So, for patients already using a long-acting bronchodilator, you might very well continue that, but you might also increase the use of short-acting rescue beta-agonists or anticholinergics. Conventionally, we use systemic corticosteroids—either oral or intravenous—at the onset of an exacerbation, and there is some

Table 5. Common Symptoms of Depression

- ◆ Changes in appetite
- ◆ Changes in sleep patterns (eg, insomnia or early waking)
- ◆ Feelings of guilt, hopelessness, and despair
- ◆ Fatigue
- ◆ Withdrawal from others
- ◆ Lack of enjoyment in once pleasurable activities
- ◆ Thoughts of death and suicide
- ◆ Coexistent anxiety

suggestion that intervening with corticosteroids early in the course of an exacerbation is likely to have the greatest benefit. If there is a significant increase in sputum production or a change in the characteristics of the sputum that suggest a bacterial infection, then antibiotic therapy is certainly warranted. Usually, broad-spectrum antibiotic therapy to cover commonly encountered organisms is appropriate. Finally, brief or acute changes in airflow limitation and physiologic status may not just change airflow but also result in a reduction in blood oxygen level or even an increase in blood carbon dioxide levels. So, evaluating your patient for abnormal gas exchange, and particularly treating hypoxemia when it is present, is another key feature of medical therapy for COPD exacerbations.

Dr. Rotello: In patients who present to the hospital with severe exacerbations, when do you usually use BiPAP (bilevel positive airways pressure)?

Dr. Sutherland: That is a good question, and again, I think it probably varies patient to patient. There is some suggestion, certainly in the literature on more chronic, stable disease, that using noninvasive positive-pressure ventilation is a means of supporting patients. It may even result in reduction in carbon dioxide levels, but it potentially comes with a risk of actually increasing hyperinflation. That, I think, is the major concern, not just with noninvasive ventilation but also with invasive mechanical ventilation in patients who have acute exacerbations of any disease that is associated with airflow limitation. I think, when BiPAP or other forms of noninvasive positive-pressure ventilation are used, it is important to frequently reassess the patient. It is also important to come up with some rational clinical targets, whether that is a reduction in carbon dioxide, an

improvement in the oxygen level, or an overall global assessment. I think a key to implementing these therapies, if you have chosen to do so, is to do it when you can stay at the bedside or when you can have a reliable surrogate, such as a respiratory therapist, at the bedside. Frequently reevaluate the patient and make a decision about whether this is the kind of patient who is improving with noninvasive positive-pressure ventilation or if this is the kind of patient who is continuing to progress to a more severe, level III exacerbation and really requires more aggressive ventilatory support.

Dr. Rotello: When these patients do deteriorate to the point of needing mechanical ventilation and when you are at the point of weaning them off the ventilator and liberating them from the endotracheal tube, do you routinely extubate these patients directly to BiPAP?

Dr. Sutherland: I think that the use of noninvasive positive-pressure ventilation after extubation is a good idea and one that can potentially temporize and prevent reintubation. This has been studied recently in a more global patient population that did not include a large component of COPD patients, and I think there is still some debate about whether extubating to BiPAP really does prevent reintubation or reduce reintubation rates. I think that it is something to consider, and I think it is something to consider in the setting of continued aggressive medical management and continued frequent evaluations, if not continuous evaluations at the bedside, as you work toward extubating these patients.

Dr. Rotello: In patients who do require intubation and mechanical ventilation, do you routinely prescribe broad-spectrum antibiotics?

Dr. Sutherland: Yes.

Dr. Rotello: What do you generally use to monitor the efficacy of your treatment? Do you use spirometry and quality-of-life questionnaires?

Dr. Sutherland: Right. This is, again, a very important question in the clinical setting, not just in the acute setting, of course, but in the chronic stable disease setting as well. I think that going back to those elements of the clinical and physiologic manifestations is a key way of approaching this. So, I will look at lung function, I will ask about symptom scores, and I will ask about quality of life and activity levels. I do not personally implement a lot of the more research-based quality-of-life instruments in my clinical practice, but a lot of the constituents can impact overall symptoms. Again, activity tolerance and exercise limitation are key clinical features that can supplement the measurement of FEV₁ and allow us to monitor not only disease course across time but also changes, be they improvements or exacerbations.

Dr. Rotello: Obviously, being given a diagnosis of COPD has a huge effect on a patient when they are first presented with it. Do you think patients' emotional responses to their diagnosis affect their self-management or their outcomes?

Dr. Sutherland: I certainly think it is something to be aware of as a clinician. It is very important in COPD, and in many other chronic illness for that matter, to be aware of comorbid depression or anxiety as features that may need and require individualized treatment and that may actually affect overall systemic or host function and also modify specific diseases like COPD (Table 5). I think that, as with any chronic disease, being told that you have a new diagnosis is a shock and



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requires some adjustment in life, and it is certainly something that as clinicians we need to be aware of and to support our patients through. Again, I would extend this even to the evaluation of comorbid psychiatric disorders, including anxiety and depression, because these are certainly common in patients with severe and very severe disease. We think that treating these disorders improves overall quality of life in patients with COPD.

Dr. Rotello: In these patients in particular, do you think that they feel stigmatized because their smoking history has significantly contributed to their illness?

Dr. Sutherland: I think it is a real possibility. I know that, to some extent, there is again a nihilistic approach to this disease because it is “something that people do to themselves,” but I think that is, of course, not the most constructive way to approach it. I often reassure my patients and talk to them about how we know that tobacco, and particularly cigarettes, are addictive, how it is hard to quit, and how this is not something that we can treat very usefully by focusing on what happened in the past. What we need to do now is focus on where we are, how severe things are, how we need to address smoking cessation, and what we need

to do in terms of pharmacologic and nonpharmacologic therapy and healthcare maintenance to target and focus on all of these areas of potential improvement.

Exercise 5

In addition to depression and anxiety, what other comorbidities are common in patients with COPD?

- Sleep disturbance
- Malnutrition
- Gastroesophageal reflux disease
- All of the above

Answer on page 16.

Dr. Rotello: How can clinicians help patients and their families accept their disease? Are there support groups out there or other areas that families and patients can access to help them better deal with their disease?

Dr. Sutherland: There certainly are support groups, and I know that many practices and hospitals offer support groups and counseling groups for patients with COPD. Certainly, your local American Lung Association chapter is another way of identifying resources in the community that help provide the kind of support that people often need in dealing with a chronic illness. I think that the other thing that clinicians can do is take the recommendations from the GOLD guidelines and from other guidelines and summarize them for their patients, and show them that this disease is something we have a handle on, that it is something we can evaluate and stage, that it is something for which we have a number of effective treatments, and that we are not going to give up on this. Yes, COPD is a chronic disease, but it is something that, by invoking and developing a strong partnership between the clinician and the patient, can really be addressed and managed fairly well, I think, over time.

Dr. Rotello: There is a tremendous amount of ongoing research related to COPD and its treatment and management. What are some of the newer therapies currently under investigation, and what is on the horizon?

Dr. Sutherland: I think answering this question is really one way of pointing out that things are getting better and going to continue to get better for patients with COPD. In terms of what is on the horizon, I think, again, one way to look at this is to look at the disease spectrum and to look at features across the disease spectrum that could be treated. There is a lot of research going on with regard to smoking cessation and coming up with more effective ways to have our patients address and be able to deal with overcoming the addiction that is caused by cigarette smoking. So, I think that is a very exciting area, and it really ties into early diagnosis and potentially long-term modification of disease risk. Other things that are important are coming up with new ways of making the diagnosis, and I talked about how patients may not present to clinical attention until their lung function is at 50% of predicted. So, again, we try to use clinical features, and we try to use physiology to find patients early, but it would be nice if there were some blood test, radiographic study, or novel way of evaluating our patients and identifying not only who has the disease but also who is potentially at risk for developing the disease. A lot of work is going on in the area of radiology and genetic evaluation to understand risk and to be able to classify our patients more accurately in terms of their risk for developing the disease. Once the disease is in place, then we have to focus on the inflammatory basis of the disease, so drug companies are aggressively looking at modifying the inflammatory basis of COPD with anti-inflammatory therapy. Bronchodilation is another

important feature that we implement now in the treatment of our patients, and new versions of old bronchodilators and new bronchodilators are also under investigation. I think there is a lot to look forward to, both in terms of diagnosis and risk assessment, as well as, potentially, pharmacologic therapy for the treatment of COPD.

Dr. Rotello: That is very encouraging for our patients. In closing, do you have any final thoughts regarding the future management and treatment of COPD?

Dr. Sutherland: I think we have spent a lot of time today summarizing some of the important clinical and physiologic features of this disorder, and what I have tried to do is present them in a way that really helps us, as clinicians, to focus on this disease, understand its diagnosis and staging, understand its impact on patients, and understand what we as clinicians can do to help our patients, so I think there is a lot that we can do just with the tools that are currently available to improve quality of life in our patients. I, as do many clinicians, look forward to new progress and new discoveries in terms of pharmacologic and other therapies to help our patients and improve their overall quality of life and symptoms, and to reduce the impact of this disease.

Dr. Rotello: Dr. Sutherland, I would like to thank you for joining us today and for helping us gain a better understanding of this very important disease process.

Dr. Sutherland: Thank you. ♦

For More Information, Visit These Web Sites

α_1 -antitrypsin (AAT) deficiency

www.alphaone.org

American Association for Respiratory Care (AARC)

www.aarc.org

American College of Chest Physicians (ACCP)

www.chestnet.org

American Lung Association (ALA)

www.lungusa.org

American Thoracic Society (ATS)

www.thoracic.org

COPD-Alert

www.copd-alert.com/COPD.html

National Heart, Lung, and Blood Institute (NHLBI)

www.nhlbi.nih.gov/health/dci/Diseases/Copd/Copd_WhatIs.html

National Lung Health Education Program (NLHEP)

www.nlhep.org

National Respiratory Training Center—USA (NRTC)

www.nrtc-usa.org

United States National Library of Medicine (NLM)

www.nlm.nih.gov/medlineplus/copdchronicobstructivepulmonarydisease.html