COPD:
Complex Obstructive Pulmonary Disease

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The most recent chronic obstructive pulmonary disease (COPD) guidelines initiative comes from the Canadian Thoracic Society (CTS).[1]

COPD comprises a spectrum of chronic respiratory diseases, including chronic bronchitis and emphysema, characterized by cough, sputum production, dyspnea, airflow limitation and impaired gas exchange.[2] By the year 2020, COPD is predicted to be the fifth leading cause of disability, and the third leading cause of death worldwide. COPD is the only leading cause of death with a rising prevalence (an observation that likely reflects the impact of increased cigarette smoking during the 20th century). For similar reasons, COPD is also undergoing a gender shift, as its prevalence and consequences continue to rise in women. COPD is, however, underdiagnosed. Recent estimates have put the overall prevalence of physician-diagnosed COPD in Canada at 3.5%, representing approximately 500,000 to 750,000 cases.[3] This underestimation is significant, as COPD has an insidious onset, and is often unrecognized.

Seventy per cent of smokers see a physician at least once a year, yet COPD frequently goes unrecognized. In a recent Canadian survey, 18% of smokers with some respiratory symptoms (mainly cough and phlegm), were found to have abnormal lung function that met diagnostic criteria for COPD, but only 25% of these individuals had been diagnosed with COPD.[4] In the U.S., the National Health and Nutrition Examination Survey observed that 25% of white male smokers met lung function criteria for a diagnosis of COPD.[5] For smokers aged 45 to 64, the COPD prevalence was 43% and it was almost 50% for those 75 to 85.

Michelle's morning cough

Michelle, 45, is in your clinic at the request of her husband, who is concerned about her health.

She has smoked a pack of ultra light cigarettes every day for over 20 years. She walks her dog for exercise, but is otherwise sedentary. She says she has no allergies and takes no medications. Her father died of pneumonia at 80 and was said to have emphysema. Michelle considers herself to be in good health, and for the past two years, has only had morning cough with clear secretions. The cough sometimes presents at other times during the day, but never at night. She does not have any dyspnea or orthopnea, and has never had exercise-induced chest pain. Michelle is a bit overweight, but her chest is clear and the cardiac examination is normal.

Does Michelle have a respiratory illness?

See page 70 for the outcome.

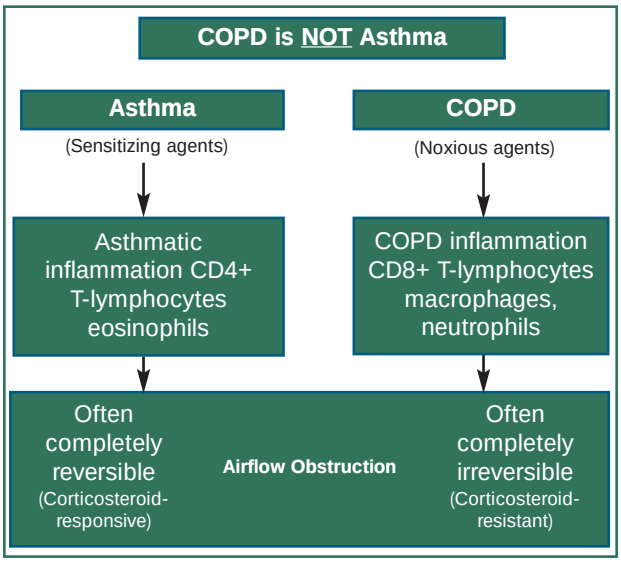

Figure 1. Fundamental differences between COPD and asthma.

Answers for Michelle

Michelle likely has early COPD and should be referred for spirometry to either establish or exclude the diagnosis.

The Canadian Lung Health Test is currently under development as a screening tool to facilitate earlier diagnosis of COPD. Smokers or ex-smokers who are over 40 and who answer "yes" to 2 or more of the following questions may have lung disease (especially COPD), and should have spirometry performed.

Canadian Lung Health Test

Answer "yes" or "no" to each of the following questions:

1. Do you cough regularly?
2. Do you cough up phlegm regularly?
3. Do even simple chores make you short of breath?
4. Do you wheeze when you exert yourself, or at night?
5. Do you get frequent colds that persist longer than those of other people you know?

If you answered "yes" to two or more of these questions you should ask your doctor to test you for COPD.

COPD is not asthma

Asthma and COPD are fundamentally different and should not be confused, nor lumped together. Although airflow obstruction is common to both conditions, the obstruction is caused by different mechanisms, and responds differently to various types of drug therapy (Figure 1).[2,6]

One consequence of the chronic airflow obstruction in COPD is air-trapping or hyperinflation (Figure 2). Because expiratory airflow is compromised in COPD, the lungs become chronically overdistended. This trapped air generates an internal pressure in the lungs, called intrinsic positive end-expiratory pressure (intrinsic PEEP), and this pressure acts as an impedance or resistance to inspiration. Because of this, and because hyperinflation pushes the diaphragm down, reducing its efficiency as an inspiratory muscle, patients with advanced COPD can have extreme chronic breathlessness, which is mainly manifested as difficulty with inspiration and high work of breathing. In asthma, hyperinflation can usually be prevented or treated and so is reversible. In COPD on the other hand, it is not so readily treated, and so becomes chronic, and worsens during exercise due to additional dynamic hyperinflation.

Clinically, making the distinction between asthma and COPD in a given patient is usually relatively straightforward. A careful history will usually uncover the important differences, which can be confirmed by simple spirometry (Table 1). In asthma, especially if the inflammatory component is not

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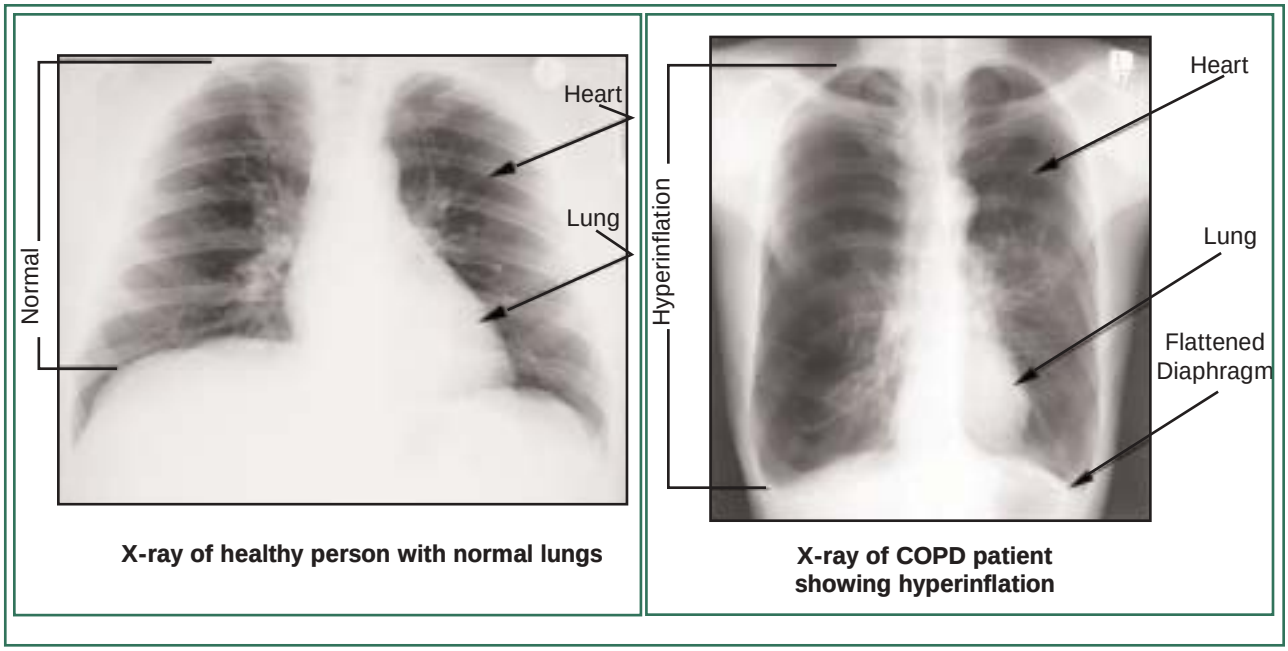

Figure 2. Hyperinflation in COPD compared to normal lung volumes in healthy individuals.

well-controlled, there will be a significant improvement (> 15% to 20%) in peak expiratory flow rates (PEFRs), or in the forced expiratory volume in one second (FEV_1) in response to inhalation of a ß2 adrenergic bronchodilator, such as salbutamol. In COPD, PEFR changes are unreliable and FEV_1 usually only improves by < 10%. The other characteristic of asthma is airway hyperresponsiveness (AHR), or twitchy airways. Asthmatic airways are much more likely to suddenly constrict when exposed to senstizing agents, such as allergens, strong smells, fumes, dusts, vapours, cold air, and even exertion. AHR also exists in COPD, but is much less prominent than in asthma, unless there is co-existing asthma (in about 10% of COPD patients).

Staging COPD severity

Classifying COPD is not as intuitive, nor as straightforward as it may sound. Traditionally, staging of COPD has been done by lung func-

Table 1
Clinical differentiations between patients with asthma and COPD

Clinical markers	Asthma	COPD
Age at onset/recognition	Usually < 40 years old	Usually > 40 years old
Smoking history	Not causal	Usually smoke > 10 packs a year
Cough	Intermittent, usually dry	Cough productive of phlegm
Symptom pattern	Intermittent, variable	Persistent and progressive
Lung function	Often normalizes	Never normalizes
Allergic triggers	Common	Infrequent
Disease course	Stable (with exacerbations)	Progressive worsening (with exacerbations)

tion[2] (usually FEV_1), but we know that lung function measurement is infrequently done in primary care, especially in early COPD. Staging COPD by symptoms is a more discriminating predictor of survival than is FEV_1. Because of this, a symptomatic approach to COPD staging that would facilitate earlier recognition, diagnosis, and following response to therapy has been suggested by the CTS[1] (Table 2). Smokers or ex-smokers with symptoms defining the "at risk" group in the CTS guidelines should be suspected of having COPD and should be referred for lung function testing. If early COPD is confirmed, serious efforts at smoking cessation must be continued. The patient should be more closely followed and pharmacotherapy should be instituted.

What are COPD risk factors?

COPD is associated with an accelerated age-related decline in lung function[7,8] (Figure 3). In industrialized countries, cigarette smoking dominates all other etiologic factors for the development of COPD. It is frequently stated that only 15% to 20% of smokers develop COPD, but this reflects data from cross-sectional studies of smokers. When longitudinal studies are done, it appears that a higher percentage of regular smokers develop recognizable COPD with time, indicating that smoking burden is very important. In the Lung Health Study,[8] approximately 25% of current smokers (aged 35 to 59) were observed to have moderate airflow obstruction (FEV_1 < 50% predicted). In a study from Sweden, 50% of elderly smokers met lung function criteria for COPD.[9] Clearly, individual susceptibility to cigarette smoke is important and involves multiple co-factors.[10] For example, it appears that only smokers who manifest the CD8+ T-cell response to injury from cigarette smoke are likely to manifest COPD. Passive exposure to environmental tobacco smoke (ETS) during childhood, and especially inutero, can affect lung growth and is associated with an increased risk of COPD in later life.[11] ETS exposure in the household and workplace is associated with deterioration in lung function in adults, but epidemiologic reviews concerning COPD causation remain inconclusive.

Genetic susceptibility factors are likely to be important, but currently, the only genetic abnormality known to enhance risk for emphysema is α1-antitrypsin deficiency, and this is felt to make up no more than 1% of all individuals with COPD. Family members of patients with COPD have a 1.2 to three times increased risk for developing the disease. There is little evidence that ethnic groups

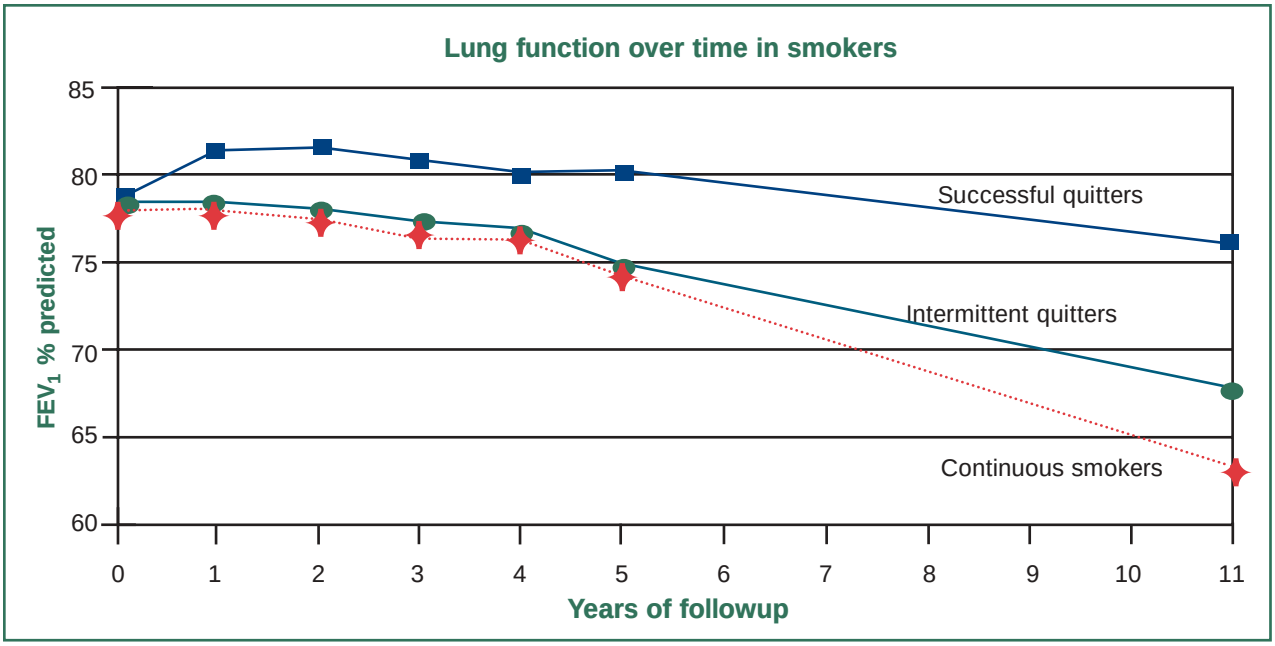

Figure 3. Accelerated age-related decline of lung function (FEV_1) in COPD and the beneficial effect of sustained smoking cessation. Adapted from: Anthonisen N, Connett J, Murray R: Smoking and lung function of Lung Health Study participants after 11 years. Am J Respir Crit Care Med 2002; 166:675-9.

vary in their susceptibility to smoking. Pulmonary viral infections (especially adenovirus) at a young age may result in altered lung growth and amplify cigarette smoke-induced lung inflammation, and so contribute to the pathogenesis of COPD. Cigar smoke is another independent predictor of COPD. Chronic marijuana smoking is also associated with airway inflammation similar to that seen in COPD.[12]

Smoking is not the main cause of COPD for 10% to 20% of patients, and other factors seem important. Some patients seem predisposed to AHR, and this may relate to atopy or an allergic tendency. A correlation between deteriorating lung function and increased immunoglobulin E levels has been observed. In the Lung Health Study, AHR was the third most important independent predictor of lung function, after smoking and

age.[8] Clearly, this makes distinction from asthma potentially difficult. In addition, people with asthma who continue to smoke are not only likely to develop fixed airflow obstruction over time, but also are less responsive to therapy with inhaled corticosteroids.[13] COPD is associated with occupational exposures to fibrogenic dusts (coal, silica, asbestos), mixed dust (organic and inorganic), and gas and fume exposures.[14] It remains controversial as to whether chronic exposure to levels of outdoor pollutants (air pollution or smog) in urban populations can cause COPD in the absence of smoking. In developing countries, indoor air pollution from cooking and heating fires in poorly ventilated dwellings can also be important causes of lung function deterioration.[15] In areas where access to health care is poor, chronic lower respiratory tract infection is common and can lead to COPD secondary to chronic release of inflammatory cytokines, such as IL-8 in the lower airways. Nutrition may be important, as there is some evidence that certain nutritional practices may be protective against lung disease. There is, as yet, no strong evidence that nutritional factors can contribute to the development of COPD, other than the observation of a correlation between alcohol consumption and the development of COPD.

Table 2
COPD staging by symptoms*

COPD stage/status	Symptoms*
At risk (does not yet fulfill diagnosis of COPD)	Asymptomatic smoker or ex-smoker, or chronic cough/sputum (predicted spirometry results: $FEV_1 \geq 80\%$ of predicted and/or $FEV_1/FVC \geq 0.7$).
Mild	Shortness of breath from COPD** when hurrying on the level or walking up a slight hill.
Moderate	Shortness of breath from COPD** causing the patient to stop for breath after walking 100 yards (or after a few minutes) on the level
Severe	Shortness of breath from COPD** resulting in the patient being too breathless to leave the house, or breathless when dressing, or the presence of chronic respiratory failure, or clinical signs of right heart failure.

* Post-bronchodilator $FEV_1/FVC < 0.7$ and $FEV_1 < 80\%$ predicted are both required for the diagnosis of COPD to be established.
** In the presence of non-COPD conditions that may cause shortness of breath (*e.g.,* cardiac dysfunction, anemia, muscle weakness, metabolic disorders), patient symptoms may not appropriately reflect COPD disease severity. Classification of COPD severity should be undertaken with care in patients with co-morbid diseases, or other possible contributors to shortness of breath.

Adapted from: O'Donnell D, Aaron S, Bourbeau J: Canadian Thoracic Society recommendations for management of chronic obstructive pulmonary disease. Can Respir J 2003; 10 (suppl A).

COPD as a systemic disease

COPD is more than just a lung disease, which is why I think of it as complex obstructive pulmonary disease. Like many chronic illnesses, COPD progressively imposes both physiologic and psychologic burdens that combine to result an overall deterioration in the patient's quality of life. COPD is considered to be a lung disease with significant systemic manifestations, such as poor nutrition, muscle wasting, and reduced exercise tolerance, not simply related to poor lung function.[16] For example, breathlessness with exertion is usually the main complaint of patients with COPD. Although this is partly the result of impaired lung mechanics, exercise performance remains substantially reduced even if both lungs are replaced. Peripheral muscle wasting and myopathy are features of COPD, and the muscles

Take-ho message

- Asthma and COPD are fundamentally different and should not be confused, nor lumped together. Although airflow obstruction is common to both conditions, the obstruction is caused by different mechanisms, and responds differently to various types of drug therapy
- If early COPD is confirmed, serious efforts at smoking cessation must be continued. The patient should be more closely followed and pharmacotherapy should be instituted.
- Clinically, making the distinction between asthma and COPD in a given patient is usually relatively straightforward. A careful history will usually uncover the important differences, which can be confirmed by simple spirometry.

of these patients manifest anaerobic metabolism and generate lactic acid at lower work rates than normal muscle. Muscle wasting in COPD is in part related to disuse and inactivity, and also due to a systemic inflammatory response. A generalized hypermetabolic state has also been postulated for COPD. The role of systemic inflammation in COPD is supported by the observation that COPD patients who fail to gain weight during refeeding programs have high levels of tumour necrosis factor (TNF) receptor and that skeletal muscle mass in COPD is inversely related to circulating levels of interleukin-6 and TNF-α. Recent data also suggest that recurrent exacerbations of COPD lead to a stepwise impairment of muscle function, which underscores the importance of therapies which reduce the frequency of acute exacerbations of COPD.

COPD as a psychosocial disease

COPD is a disease of loss—loss of youth, physical vitality, social interaction, self-worth, and hope. COPD does have important psychosocial manifestations. Patients become fearful of not being able to maintain their independence, with resultant anxiety and even depression over becoming a burden to their families and a burden upon society.

Indeed, as the disease evolves, its impact on the patient's family becomes part of the disease process itself, as caregivers of patients with chronic lung disease become overwhelmed by the chronicity of their burden. In helping to optimally manage COPD, the health-care professional must consider not only the pathophysiology and multiple exacerbations of this disease, but its psychosocial impact on patients and families as well. CME

t Readings

1. The Canadian Lung Association: *www.lung.ca*
2. American Lung Association: *www.lungusa.org*

www.stacommunications.com

For an electronic version of this article, visit: *The Canadian Journal of CME* online.

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