Think of COPD as a Multisystem Disease

BY BRUCE JANCIN
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SALT LAKE CITY — It's high time to recognize that chronic obstructive pulmonary disease is a multisystem disorder extending well beyond the lungs, Dr. Stanley B. Fiel said at a satellite symposium held in conjunction with the annual meeting of the American College of Chest Physicians.

Chronic obstructive pulmonary disease (COPD) is best viewed as a systemic inflammatory disorder, not merely an inflammatory disorder of the respiratory tract. The extrapulmonary systems where COPD takes its heaviest toll are the cardiovascular, muscular, and skeletal.

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Even among patients with severe COPD, only about one-quarter of deaths are due to COPD. Among those with moderate COPD, it's closer to 5%. The predominant cause of mortality in COPD patients is atherosclerotic cardiovascular disease, added Dr. Fiel, chairman of medicine at Morristown (N.J.) Memorial Hospital. He has served as a consultant to Altana Pharma, which sponsored the satellite symposium.

Cardiovascular Risk

Major contributions to understanding the association between COPD and cardiovascular risk have been provided by Dr. Don D. Sin of the University of British Columbia, Vancouver, and his coinvestigators. They showed in an analysis of 1,861 participants in the first National Health and Nutrition Examination Survey Epidemiologic Followup Study that a reduced forced expiratory volume in 1 second (FEV_1) is a risk factor for cardiovascular hospitalization or mortality independent of smoking history, Framingham risk score, and other potential confounders. Individuals in the lowest FEV_1 quintile had a 5.6-fold increased risk of fatal ischemic heart disease, compared with those in the top quintile. That was true even across a relatively narrow range of FEV_1 declines, from a mean of 109% to 88% of predicted (Chest 2005;127:1952-9).

As part of the same report, the Canadian investigators conducted a meta-analysis of 12 large published cohort studies that looked at cardiovascular mortality based on FEV_1 in nearly 84,000 subjects. Those in the worst FEV_1 quintile had an adjusted 75% increased risk of cardiovascular mortality, compared with those in the best quintile.

"So why don't primary care physicians do more routine measuring of FEV_1? It's a good question, since we know that just as blood pressure is an independent risk factor for cardiovascular mortality, so is FEV_1 in patients regardless of whether they smoke or don't smoke," Dr. Fiel said.

One major difference between high blood pressure and low FEV_1 as cardiovascular risk factors, however, is that as yet there are no prospective data demonstrating how to intervene effectively in COPD patients to reduce their cardiovascular risk, he conceded. Investigative interest in potential targets for preventive therapy is focused on the elevated levels of fibrinogen, neutrophils, platelets, and C-reactive protein that Dr. Sin and his coworkers documented in patients with stage 3 and 4 COPD (Circulation 2003;107:1514-9).

Bone Abnormalities

British investigators have reported a dual-energy x-ray absorptiometry study showing that osteoporosis or osteopenia was present in fully 89% of a group of COPD patients with an FEV_1 less than 50% of predicted, corresponding to Gold stage 3 or 4 disease. Among patients with COPD and an FEV_1 greater than 50% of predicted, osteoporosis or osteopenia was present in 69% (Am. J. Respir. Crit. Care Med. 2004;170:1286-93).

Other data have shown that the bone density abnormalities in COPD can't be explained away as being a result of prolonged use of corticosteroids. Such abnormalities are present in most steroid-naive patients with advanced COPD.

Skeletal Muscle Atrophy

Loss of fat-free mass in COPD patients is associated with reduced endurance, poor quality of life, and decreased exercise ability. Dutch researchers have reported the prevalence of abnormal body composition (low body mass index and/or low fat-free mass index) was 43% in women and 21% in men in a cohort of 389 outpatients with moderate to severe COPD (Respir. Med. 2006;100:1349-55). The intermediary between systemic inflammation and cachexia in COPD is thought to be the nuclear transcription factor, kappa beta, Dr. Fiel said. ■

CLINICAL GUIDELINES FOR FAMILY PHYSICIANS

Management of Cough

BY NEIL S. SKOLNIK, M.D., AND ADRIAN WILSON, D.O.

Cough is a common symptom that leads to a large number of visits to primary care physicians every year. It is the chief complaint of over 2.5 million patients presenting to their doctors with acute bronchitis each year, but it is also associated with an extensive list of other illnesses. Both alone and in conjunction with illnesses such as asthma, gastroesophageal reflux disease (GERD), chronic obstructive pulmonary disease (COPD), or heart failure (HF), cough and its etiology present a diagnostic dilemma that requires a systematic approach in order to have appropriate diagnosis and management. The guidelines of the American College of Chest Physicians describe recommendations based on the duration of cough (Chest 2006;129(suppl. 1):222S-31S).

Guidelines are most useful when they are available at the point of care. A concise yet complete handheld computer version of this guideline is available for download, compliments of FAMILY PRACTICE NEWS, *at www.redi-reference.com.*

Acute cough typically lasts fewer than three weeks, and although it can be associated with life-threatening illnesses—such as pneumonia, HF, or pulmonary embolism—it is typically caused by one of four main disease processes: upper airway cough syndrome (UACS), asthma, GERD, or nonasthmatic eosinophilic bronchitis (NAEB). Exacerbations of an underlying illness, such as COPD, or infection with influenza, *Bordetella pertussis*, acute bronchitis, or the common cold may also trigger acute cough.

Subacute cough is defined as lasting 3-8 weeks, and chronic cough is defined as lasting longer than 8 weeks. Subacute cough is often caused by a postinfectious upper respiratory irritation, increased mucus production, or postnasal drip. A chronic cough is often linked to more than one condition's being present simultaneously. In addition to the common causes of acute cough, possible causes of chronic cough include tobacco use; ACE-inhibitor use; COPD; infectious etiologies such as tuberculosis; HF; interstitial lung disease; and lung cancer, among others.

Acute/Subacute Cough

A careful medical history and examination are important in ruling out potential causes of cough, including smoking, medication effect, or life-threatening illness such as HF or pneumonia. An important early goal is to determine whether cough is a manifestation of a life-threatening illness, an exacerbation of underlying illness, an environmental exposure, or a new non–life-threatening process. Good evidence supports the cessation of cough-inducing medicines such as ACE-inhibitors, even if symptoms began prior to medicine initiation, and the cessation of smoking.

The next goal is to determine if a cough is postinfectious in etiology. If it is postinfectious, the next goal is to determine if it is from UACS, transient bronchial hypersensitivity, asthma exacerbation, acute bronchitis, or pertussis. If the subacute cough is not postinfectious, it should be managed like a chronic cough.

For cough caused by asthma, there is good evidence to support the use of inhaled corticosteroids, inhaled β-agonists, or oral leukotriene inhibitors, ideally after a bronchoprovocation challenge test—such as a methacholine challenge—is administered to confirm the diagnosis.

Chronic Cough

For chronic cough, there is good evidence supporting empirical, additive, sequential steps of therapy, given the frequency of multifactorial etiology. Empirical treatment should include advice about smoking cessation if the patient smokes. The next step addresses UACS with the addition of an oral first-generation antihistamine and decongestant combination. If symptoms persist, the diagnosis of asthma should be pursued, using office spirometry and bronchoprovocation challenge if needed. If the latter is not available, empirical treatment of asthma is the next step. If treatment of UACS and asthma do not improve the cough, one should rule out NAEB with an induced sputum test for eosinophils. If this is not possible, consideration can be given to empirical treatment with corticosteroids.

For patients with chronic cough who have not responded to interventions for UACS, asthma, and NAEB, the treatment of GERD is the next step. Initial treatment for GERD includes an antireflux diet and a proton pump inhibitor. If symptoms persist beyond several months, further evaluation with endoscopy, esophageal pH monitoring, or a barium swallow study may be necessary. Ultimately, if all treatment options and diagnostic studies have been completed and there is still no identifiable cause of cough symptoms, patients should be referred to a cough specialist.

The Bottom Line

Cough is common, and the list of causes is formidable. A sequential, systematic approach is recommended whereby clinicians can identify dangerous sources when present, and target the more common causes in most cases. A search for common reversible causes—such as tobacco use, ACE-inhibitor use, and environmental irritants—is always the first step. The next step is a systematic approach advocating a combination of limited diagnostic testing and empirical treatment. Treat UACS with an antihistamine/decongestant combination; treat asthma with inhaled corticosteroids or β-agonists; and treat GERD with proton pump inhibitors and diet modification.

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