Spirometry for Chronic Obstructive Pulmonary Disease Case Finding in Primary Care?

The American Thoracic Society's (ATS) "Spirometry Task Force" was initiated in partnership with the American Academy of Family Physicians, the American College of Physicians, and the American Academy of Pediatrics* to determine whether evidence justifies recommending spirometry as a routine tool in the practice of primary care. The three criteria developed to support a positive recommendation were that (*1*) accurate, inexpensive, rugged, and "user friendly" spirometers be available; (*2*) acceptable test performance and interpretation be achievable in the primary care setting; and (*3*) important clinical benefits accrue.

To assess whether the third criterion is met when spirometry is used for case finding and management of chronic obstructive pulmonary disease (COPD) in the primary care setting, a systematic review of the evidence was needed. To this end, the task force submitted a request to the Agency for Health Care Research and Quality (AHRQ) to conduct a review through its network of evidence-based practice centers. The request was accepted, a review was performed, and the findings are now available (*see* "Spirometry for COPD" at www.ahrq.gov). The results suggest a need for high-quality research before a positive recommendation can be made.

The AHRQ's review will provoke controversy for concluding that spirometry for case finding of COPD among adults with persistent respiratory symptoms or with a history of exposure to risk factors (especially cigarette smoking) will add greatly to overall health care costs without adding much benefit to patients.

This conclusion was drawn from a systematic review, evaluation, and analysis of English-language literature since 1966 on four specific questions:

1. What is the prevalence of COPD and of airflow obstruction?
2. Does spirometry substantially improve smoking cessation rates?
3. Does the effectiveness of any COPD intervention vary based on impairment of lung function, as determined by spirometry?
4. Does spirometry provide independent prognostic value for important outcomes?

The answer to the first question, at least as provided by weighted interpretation of the best available literature, was that 7 to 14% of the U.S. adult population have airflow obstruction (depending on the definition). This obstruction is severe or very severe (Global Initiative for Chronic Obstructive Lung Disease stages III and IV, with $FEV_1 < 50\%$ predicted) in only 1.5% (1). Cough, phlegm, wheeze, or dyspnea are reported by about one third, but fewer than half of those reporting one or more of these cardinal respiratory symptoms are found to have airflow obstruction by spirometry. Conversely, symptoms are not necessarily reported by those who have airflow obstruction. The infrequency of severe and very severe airflow obstruction becomes important when the answers to the other questions posed are considered.

The answers to the remaining three questions are not supportive of spirometry. The evidence that COPD case finding substantially improves smoking cessation rates was considered inadequate. Existing therapies for COPD were found on average to cause little sustained improvement in quality of life or to reduce exacerbation rates except in patients with severe or very severe obstruction. As for forecasting future respiratory impairment, the evidence suggests that symptoms, especially related to dyspnea, are stronger predictors than abnormal spirometric values for maximal expiratory flow.

When the evidence report estimated the number of patients evaluated by spirometry per unit of benefit achieved, the case for broad application of spirometry for COPD case detection was found wanting. Using Third National Health and Nutrition Examination Survey data, about two thirds of U.S. adults meet the case-finding criteria proposed by the National Lung Health Education Program: ever-smokers older than age 45 and all adults with respiratory symptoms such as chronic cough, episodic wheezing, and exertional dyspnea (2). The report's calculations indicated that, in a population of 10,000 adults, 6,588 would qualify for spirometry by these criteria, but only 150 cases of severe or very severe obstruction would be identified. Of these 150, only 129 would also have symptoms and fit the characteristics of the only population that the review found to benefit from therapy. From the evidence reviewed, the report estimates that, in this group, current inhaled medications achieve at best a 20% reduction in exacerbation rate, so that only eight exacerbations would be prevented per year if all such patients were prescribed an inhaled medication and were compliant.

The report offers "hard" evidence in two senses. "Hard" in the sense of being an unimpeachable review of the evidence, and also hard to accept, especially for those like ourselves, who cannot conceive of practicing without objective assessment of pulmonary function. We were disappointed that the evidence was found to be so limited for a physiologic test so long and so widely used. The review highlights gaps in the evidence that need to be filled by carefully designed studies of sufficient size.

In considering the findings, the focus on COPD and the particular questions addressed need to be kept in mind, as the review does not address other clinical circumstances in which spirometry may be valuable. The main limitation is the review's focus on COPD—a disease defined by its irreversibility—rather than on the patients who undergo spirometric testing for diverse clinical indications. Exclusion of mislabeled COPD in symptomatic persons by a finding of normal spirometry avoids inappropriate labeling and therapy. Saving the cost of even a month of unnecessary inhaler use would more than offset the costs of spirometry for such individuals. For those with dyspnea, normal spirometry directs attention elsewhere, with the attendant benefit of appropriate treatment. Another group that should benefit from spirometry comprises those with other causes of airflow obstruction, especially asthma. For this group, the benefits of treatment are substantial. Finally, limiting spirometry to those who volunteer

* Other societies participating in the ATS Spirometry Task Force include the American Academy of Asthma Allergy and Immunology, the American Association of Respiratory Care, the American College of Chest Physicians, and the National Association of Directors of Respiratory Care.

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the complaint of dyspnea might miss a substantial population who, in fact, are limited by airflow obstruction. The highly engineered environment of modern life enables people to modify their daily activities to avoid the unpleasant sensation of dyspnea, becoming more and more sedentary until they are unable to participate in valued life activities and quality of life declines (3, 4). At this point, they seek medical evaluation, but the disease has progressed to the point of severe airflow obstruction. Earlier spirometric evaluation that uncovers evidence of airflow obstruction could prompt a careful assessment by a skilled clinician concerning symptoms that the individual may have ignored, attributed to advancing age, or denied.

The AHRQ report acknowledges that the lack of evidence of benefit does not mean that benefit does not exist. The review highlights the gaps for which research that demonstrates benefit is needed on common clinical issues affecting the primary care in a U.S. adult population of 196 million. The report's authors even list some of the research questions they think need to be addressed. Approaching these research questions might show a way out of the quandary we now face. The burden and cost of COPD are enormous: 1.5 million emergency department visits, 750,000 hospitalizations, 120,000 deaths, and $39 billion in direct and indirect costs each year in the United States alone (www.cdc.gov/nchs/fastats/copd.htm). Means for reducing this burden are needed. Primary prevention of cigarette smoking is doubtless the best strategy for reducing the burden over the long term. For secondary prevention, aimed at detecting those in early stages of the disease, testing modalities that are better than spirometry alone are necessary for identifying those who are truly at risk, and effective treatments beyond smoking cessation are needed for preventing progression.

Although focused on the narrow question as to whether spirometry should be performed for "case finding" of COPD in primary care, the AHRQ's report nonetheless identifies deficiencies in the tools and treatments now available, and the gaps in knowledge that must be filled, for the burden of COPD to be reduced. For the ATS Spirometry Task Force, and for the many stakeholders interested in the diagnosis, management, treatment, and prevention of COPD, the report should be a call for action.

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Cardiopulmonary Health Effects of Air Pollution: Is a Mechanism Emerging?

Three articles appear in this issue of the *Journal* that further our understanding of the clinical consequences of air pollution, its physiologic effects, and its mechanisms. In the first article by Forastiere and colleagues (pp. 1549–1555), out-of-hospital cardiovascular death in Rome, Italy is shown to be positively associated with levels of ambient ultrafine particles, PM_{10} and CO (1). The exposure–risk relationship is linear, and aged adults are at highest risk. As such, the article shows a strong link between air pollution and out-of-hospital cardiac deaths, a result that differs from two previous studies conducted in the Seattle metropolitan area that found no association (2, 3). The second article by Schwartz and colleagues (pp. 1529–1533) provides evidence that oxidative stress transduces the physiologic response to particle air pollution (4). This conclusion is inferred from the observation that individuals lacking the gene glutathione S-transferase M1 (GSTM1), encoding an enzyme scavenging oxygen free radicals, show an increased sensitivity to inspired particulate matter as evidenced by greater changes in heart rate variability (HRV). Moreover, statins, which are known to have antioxidant and antiinflammatory properties in the cardiovascular system, mitigate against the effects of ambient particle air pollution to decrease HRV in subjects lacking the GSTM1 allele. In the third article, Romieu and colleagues (pp. 1534–1540) show that $PM_{2.5}$ is associated with decreased HRV in a cohort of aged Mexican adults, and dietary supplementation with n-3 polyunsaturated fatty acid (PUFA) abrogated this response (5). Together, the articles by Schwartz and Romieu show that genetic polymorphisms or drugs modulating oxidant stress can mitigate against the effect of particulate air pollution, thereby providing evidence for oxidant stress as one of the mechanisms explaining the effect of particle air pollution on the cardiovascular system.

The article by Forastiere and colleagues presents new data from Rome, Italy collected between 1998 and 2000, and associates out-of-hospital death due to coronary heart disease with levels of air pollution. Specifically, a case–crossover study design was used to investigate the relationship of out-of-hospital deaths to levels of several measured air pollutants: PM_{10}, $PM_{2.5}$, CO, NO_2, NO, SO_2, and O_3. Particle number count (PNC) was not measured directly, but was imputed based on a predictive model created by estimating the relationship between measured PNC during