

# Making the Diagnosis of Asthma

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**Diagnostic tests can only increase or decrease the probability of the asthma diagnosis, so a thorough history is very important. In patients with asthma-like symptoms, spirometric evidence of airway obstruction plus a large bronchodilator response makes asthma much more likely. However, normal spirometry is common in patients with mild asthma who are not symptomatic at the time of testing, and patients with poorly controlled asthma may lack substantial bronchodilator response. Inhalation challenge test often helps confirm asthma in patients with normal spirometry. Adult smokers with intermittent respiratory symptoms may have either asthma or chronic obstructive pulmonary disease (COPD). Normal post-bronchodilator spirometry rules out COPD. In patients with airway obstruction, a low diffusing capacity of the lung for carbon monoxide increases the probability of COPD and makes asthma much less likely. A high exhaled nitric oxide level makes allergic asthma more likely. Response to inhaled corticosteroids makes asthma more likely and COPD less likely. Key words: asthma, spirometry, methacholine, bronchodilator, pulmonary function, diagnosis. [Respir Care 2008;53(5):583–590. © 2008 Daedalus Enterprises]**

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Dr McCormack reports no conflicts of interest related to the content of this paper. Dr Enright has received approximately 3 free lunches or dinners per year during the past 5 years from companies that make or distribute office spirometers, but he has received no consulting or travel expense reimbursement from such companies. He received about \$10,000 from Pfizer during the 24 months leading up to this conference, for

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Table 1. Signs and Symptoms of Asthma

Symptoms
Cough
Wheeze
Shortness of Breath
Chest tightness
History
Environmental triggers
Atopic/allergic history
Symptoms with exercise
Sensitivity to aspirin or nonsteroidal anti-inflammatories
Nasal polyposis
Family history of asthma or allergies
Physical Examination Findings
Hyperexpansion of the chest cavity
Prolonged expiratory time
Expiratory wheezing
Decreased air movement
Use of accessory respiratory muscles
Rash/eczema

Table 2. Differential Diagnosis of Asthma

Chronic obstructive pulmonary disease
Heart failure
Post-nasal drip
Gastroesophageal reflux disease
Vocal cord dysfunction
Cystic fibrosis
Bronchiolitis obliterans
Lymphangioleiomyomatosis
Allergic bronchopulmonary aspergillosis
Churg-Strauss syndrome

## Introduction

Asthma is a common, chronic disease of airway inflammation that manifests clinically with recurrent episodes of coughing, breathlessness, wheezing, and chest tightness. These episodes are associated with airflow obstruction that is at least partially reversible. There is no accepted standard diagnostic test for asthma. Making the diagnosis of asthma requires a critical evaluation of the patient's symptoms, medical history, physical examination, and diagnostic tests.

## Signs and Symptoms

The first step in making the diagnosis of asthma is reviewing the patient's history and formulating the pre-test probability of asthma (Table 1). Patients typically present with intermittent symptoms of cough, wheeze, dyspnea, and/or chest discomfort. These symptoms are often exacerbated by identifiable triggers, such as tobacco smoke, perfume, pets, workplace exposure, or upper-respiratory-tract infection. Patients may experience symptoms during the daytime, nighttime, or with exercise, and the symptoms may vary depending on the time of year.

Asthma is often associated with a history of atopy, and this association in a symptomatic patient is one of the strongest predictors of asthma.<sup>1</sup> Thus, personal and family histories of allergies are key components of the medical history. Other important information to elicit includes early childhood breathing problems, occupational exposures, sensitivity to aspirin or nonsteroidal anti-inflammatory pain relievers, nasal polyposis, or sinusitis.

Cough-variant asthma is a subset of asthma characterized by cough as the predominant or sole symptom.<sup>2</sup> In patients with chronic cough, asthma should always be considered as a possible diagnosis. The diagnostic and therapeutic approaches are similar to those for the typical form of asthma. The diagnosis of cough-variant asthma should be confirmed by the resolution of cough in response to asthma therapy.

Physical examination can be normal but often reveals wheezing, chest hyperinflation, or a prolonged expiratory phase, especially when patients are symptomatic. The use of accessory muscles may be apparent during a more severe exacerbation. Examination for signs of allergic rhinitis, conjunctivitis, and dermatitis should also be done.

## Differential Diagnosis

In patients who present with a chronic cough as the predominant symptom, it is important to consider other common causes of cough, such as post-nasal drip and gastroesophageal reflux disease.<sup>3</sup> Chronic obstructive pulmonary disease (COPD) is another common disease in the differential diagnosis for asthma, especially among adults with a history of tobacco use. In older patients, heart failure can present with intermittent symptoms of wheezing and breathlessness. Less common diseases that may present similarly to asthma include vocal cord dysfunction, bronchiolitis obliterans, cystic fibrosis, lymphangioleiomyomatosis, and allergic bronchopulmonary aspergillosis. Asthma can also occur as part of a systemic disorder such as Churg-Strauss syndrome (Table 2).

## Diagnostic Testing

### Spirometry

Spirometry is a pulmonary function test (PFT) that measures the amount (volume) or speed (flow) of air that can be inhaled and exhaled. The patient is typically asked to breathe normally and then to take the deepest possible breath and then exhale as quickly and as hard as possible.

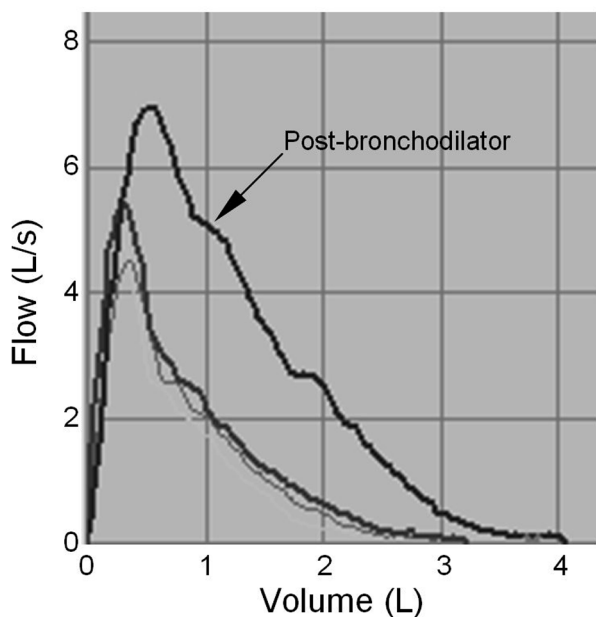


Fig. 1. Flow-volume curves characteristic of asthma airflow obstruction and post-bronchodilator improvement.

From that maneuver the forced expiratory volume in the first second ( $FEV_1$ ) of exhalation is measured and compared to the entire volume of air that can be expelled in a forced expiration (forced vital capacity [FVC]). Spirometry is indicated as part of the initial diagnostic evaluation for asthma in all patients  $\geq 5$  years old to test for airflow obstruction, the severity, and the short-term reversibility.<sup>4</sup> Spirometry provides an objective assessment of airflow obstruction. Though physicians can generally categorize pulmonary abnormalities as obstructive based on the clinical history, they are less able to correctly predict the severity of obstruction and the degree of reversibility.<sup>5,6</sup>

The presence of airflow obstruction (a reduced  $FEV_1$  to FVC ratio) is consistent with the diagnosis of asthma. However, as asthma can be intermittent and asthma airflow obstruction is (by definition) reversible, spirometry is often normal when the patient is not experiencing respiratory symptoms. The American Thoracic Society guidelines recommend comparing the patient's spirometry results to the reference equations from the National Health and Nutrition Examination Survey.<sup>7</sup> Airway obstruction is defined as an  $FEV_1/FVC$  less than the 5th percentile.<sup>7</sup> The use of other indices, such as forced expiratory flow during the middle half of the forced vital capacity maneuver, cause misclassification. The use of a fixed threshold, such as 0.70 for  $FEV_1/FVC$ , to define airway obstruction also causes misclassification.<sup>8</sup> Airway obstruction due to poorly controlled asthma may also be recognized by a characteristic "scooped out" appearance of the expiratory limb of the spirometry flow-volume curve (Fig. 1). During symp-

tomatic episodes of vocal cord dysfunction, variable reduction in forced inspiratory flow may be seen on the flow-volume loop, with normal forced expiratory flow.<sup>9,10</sup>

As spirometry has become more widely available, it is now performed in some primary care offices with technical adequacy and accurate interpretation.<sup>11</sup> Good-quality spirometry can also be obtained in the emergency department during an asthma exacerbation.<sup>12</sup> The introduction of spirometry into more clinical settings has the advantage of increasing the use of spirometry for diagnostic testing, which is emphasized by the 2007 National Asthma Education and Prevention Program's Expert Panel Report 3, Guidelines for the Diagnosis and Management of Asthma.<sup>4</sup> However, there are limitations to spirometry in primary care settings. Primary care offices do not have adequate time to perform post-bronchodilator spirometry, which is indicated for patients with airflow obstruction. Thus, patients found to have airflow obstruction via office spirometry should be referred to a PFT laboratory for further assessment, including bronchodilator response and possibly plethysmography and diffusing capacity of the lung for carbon monoxide ( $D_{LCO}$ ). In asthma (as well as COPD), lung volumes often show hyperinflation.<sup>13</sup>  $D_{LCO}$  is normal or increased in patients with asthma, but decreased in patients with COPD (emphysema).<sup>7</sup>

Peak flow meters should not be used in the diagnostic evaluation for asthma. Spirometers are much more accurate than peak flow meters (3% vs 10%), and  $FEV_1$  is less effort-dependent than peak flow measurements.<sup>14,15</sup> The quality of spirometry is verified from the graphs. Peak flow meters are still used for home monitoring by some patients with moderate-to-severe asthma, but the increased availability of spirometers, especially inexpensive pocket spirometers designed for use by patients, has made the portability and low cost of peak flow meters less of an advantage.<sup>16,17</sup>

### Bronchodilator Response Testing

Patients who have airflow obstruction on spirometry should undergo bronchodilator-response testing. This is done by administering 2–4 puffs from an albuterol inhaler (90  $\mu$ g/puff), via a spacer or valved holding chamber. After waiting for 10–15 min, spirometry is repeated. Short-acting anticholinergic agents can also be used but require a delay of more than 30 min before repeating spirometry. An improvement of  $> 12\%$  or  $> 0.2$  L in baseline  $FEV_1$  or FVC has traditionally defined reversible airflow obstruction.<sup>7</sup> An increase of  $\geq 10\%$  of the predicted value is another criterion that has been used, and this may be less subject to bias (see Fig. 1).<sup>18,19</sup>

The presence of airflow obstruction and a good bronchodilator response is consistent with the diagnosis of asthma, but lack of a bronchodilator response does not rule

Table 3. Methacholine Challenge Interpretation

PC <sub>20</sub> (mg/mL)	Interpretation*
>16	Normal bronchial responsiveness
4.0–16	Borderline bronchial hyperresponsiveness
1.0–4.0	Mild bronchial hyperresponsiveness
< 1.0	Moderate-to-severe bronchial hyperresponsiveness

\* The following assumptions must be met prior to applying this interpretation scheme: (1) no baseline airway obstruction, (2) good quality spirometry, (3) post-challenge recovery of forced expiratory volume in the first second (FEV<sub>1</sub>).

PC<sub>20</sub> = provocation concentration that produces a 20% FEV<sub>1</sub> decrease.

(Adapted from Reference 22.)

out asthma. For example, some patients do not exhibit substantial bronchodilator reversibility until they are on therapy and their asthma is under better control. The bronchodilator response is not necessarily helpful in distinguishing asthma from other forms of airway obstruction, because patients with COPD and other obstructive lung diseases often have at least a small bronchodilator response.<sup>20</sup> However, normal spirometry after an inhaled bronchodilator rules out COPD.<sup>21</sup>

### Inhalation Challenge Test

To assess bronchial hyperactivity, inhalation-challenge tests are safe and useful diagnostic tools.<sup>22</sup> Typically, the patient is exposed to an agent or activity that could provoke bronchoconstriction during serial spirometry. Methacholine is used to directly stimulate airway smooth muscle. Other agents or activities indirectly provoke bronchoconstriction by inducing an airway inflammatory response (eg, mannitol, cold air, hypertonic saline, exercise). Methacholine challenge is best used in patients with no baseline obstruction who can perform good-quality spirometry. The interpretation is based on the provocation concentration of methacholine that induces a 20% decrease in baseline FEV<sub>1</sub> (PC<sub>20</sub>) (Table 3). A normal methacholine challenge test (PC<sub>20</sub> > 16 mg/mL) usually rules out asthma. However, the pre-test probability of the asthma diagnosis and the clinical circumstances of the test should be considered in interpreting the results, especially if the patient has taken any symptom-modifying drugs (eg, inhaled corticosteroids) or if the patient has not been experiencing recent symptoms (eg, has the aeroallergen season during which the patient experiences symptoms already passed?). See the Appendix for an example of how test results alter the probability of asthma.

A positive methacholine challenge test (PC<sub>20</sub> < 4 mg/mL, depending on the method used) indicates airway hyperresponsiveness, which is consistent with asthma but can also be present in other diseases.<sup>23</sup> Borderline bron-

chial hyperresponsiveness should be interpreted within the clinical context of the presentation, in an attempt to shift the probability toward or away from the diagnosis of asthma. In patients with suspected paradoxical vocal cord dysfunction, laryngoscopy during methacholine challenge may be needed to confirm vocal cord dysfunction.<sup>24</sup>

Other agents can also be used to provoke reversible airflow obstruction. Histamine has a shorter half-life than methacholine but is more likely to cause adverse effects such as voice changes, flushing, and headache, in addition to the chest tightness, dizziness, and cough that are common to both agents.<sup>25,26</sup> Powdered mannitol is more specific for diagnosing asthma<sup>27</sup> and may predict responsiveness to inhaled corticosteroids. It is currently awaiting United States Food and Drug Administration clearance for this use.<sup>28,29</sup> Cold air challenge is less sensitive than mannitol challenge.<sup>30</sup>

Exercise challenge test can be used to assess exercise-induced bronchoconstriction. The patient can exercise on a treadmill or a bicycle ergometer. A decrease to < 90% of baseline FEV<sub>1</sub> at 5–20 min after the end of the exercise confirms exercise-induced bronchoconstriction.<sup>22</sup> Exercise challenge is less sensitive than methacholine in diagnosing asthma.<sup>31,32</sup>

### Radioallergosorbent Test and Allergen Skin Test

Atopy, a high total immunoglobulin E (IgE), any positive allergen skin test, or any high specific IgE level increases the probability of asthma in a patient with respiratory symptoms.<sup>33,34</sup> Elevated IgE is consistent with the diagnosis of asthma, but very high IgE (> 1,000 ng/mL) should prompt consideration of allergic bronchopulmonary aspergillosis.<sup>35</sup> Skin testing or in vitro testing for specific IgE antibodies should be based on a careful history to ascertain likely aeroallergen exposures. This is important because the results will guide patient education about allergen avoidance and possibly immunotherapy. Skin testing and in vitro testing for specific IgE antibodies are equally sensitive, and each has advantages. Skin testing is performed by introducing an allergen into the skin and observing for wheal and flare. Skin-test results are available within one hour and are visible to the patient, which may encourage compliance with environmental control practices. However, this approach requires training and the availability of allergen extracts. In vitro assays, such as the radioallergosorbent test and the fluorescent enzyme immunoassay test, are blood tests used to identify specific IgE antibodies to suspected allergens in the serum. In vitro tests are more expensive but can be performed for patients who are taking medications that suppress skin-test reactions, such as antihistamines and some antidepressants; these tests do not entail a risk of systemic reactions and can be performed in patients with extensive eczema.<sup>36,37</sup>

## Exhaled Nitric Oxide

The measurement of certain biomarkers in the diagnosis and assessment of asthma has gained increased attention. These include induced sputum, exhaled gases, and exhaled breath condensate. Induced sputum is collected by asking the patient to inhale nebulized saline (often hypertonic) and to then expectorate. Exhaled gases, such as nitric oxide, are measured by having the patient exhale to maintain a specified flow into a balloon or a measuring device. Exhaled breath condensate is obtained by passive breathing through a cooling device that contains a tube to collect the liquid sample. Of these, sputum eosinophil count and exhaled nitric oxide have shown the most promise for diagnosing asthma. Induced sputum eosinophil count can distinguish patients with and without asthma and predict responsiveness to inhaled corticosteroids.<sup>38,39</sup> However, the methods for obtaining and processing the samples are time-consuming and not standardized, so the use of induced sputum for assessing asthma is still most appropriate in the clinical research setting.

Exhaled nitric oxide is an index of eosinophilic airway inflammation. In asthma, exhaled nitric oxide correlates well with more invasive and less convenient measures of airway eosinophilia, such as induced sputum,<sup>40</sup> bronchoalveolar lavage,<sup>41</sup> and bronchial biopsy.<sup>42</sup> One of the more recent advances in asthma diagnosis is the application of exhaled nitric oxide assessment as a diagnostic tool.<sup>43</sup> Studies in selected populations have reported sensitivity and specificity of better than 80%.<sup>44-46</sup> A high exhaled nitric oxide predicts a good response to inhaled corticosteroids.<sup>47,48</sup> The Current Procedural Terminology code 95012 became available in January 2007 for exhaled nitric oxide test, which made the test reimbursable.<sup>49</sup> Third-generation, less expensive, hand-held exhaled-nitric-oxide analyzers will soon be marketed in the United States.<sup>50,51</sup>

## Radiographic Imaging

Chest radiographs and high-resolution computed tomography are often used in diagnosing asthma, to rule out other lung diseases.<sup>52</sup> The chest radiograph is typically normal in patients with asthma.<sup>53</sup> Radiographic abnormalities can help identify alternative diseases, such as heart failure (pulmonary vascular congestion) and COPD (emphysematous changes). Parenchymal abnormalities can be detected in diseases such as cystic fibrosis and lymphangioleiomyomatosis.

### Asthma Versus Chronic Obstructive Pulmonary Disease

One of the challenges in diagnosing asthma can be distinguishing asthma from COPD. Smoking can cause

asthma, and many adult and adolescent patients with asthma are smokers. Only about 20% of smokers ever develop COPD. Many patients with chronic respiratory symptoms and airway obstruction are erroneously diagnosed as having COPD by applying the Global Initiative for Chronic Obstructive Lung Disease (GOLD) COPD guidelines<sup>54</sup> to pre-bronchodilator spirometry results without taking the time to perform post-bronchodilator spirometry.<sup>55,56</sup> Applying the pre-test probability formulated from the clinical history and physical examination to the results of the diagnostic testing further increases the likelihood of arriving at the correct diagnosis. In interpreting the PFT results it is important to consider the degree of bronchodilator reversibility and any abnormalities in the  $D_{LCO}$ . A decreased  $D_{LCO}$  makes COPD much more likely than asthma.<sup>57,58</sup> In the future, biomarkers may have an increased role in distinguishing between COPD and asthma. For example, a patient with COPD will typically have a normal exhaled nitric oxide concentration, even during an exacerbation.<sup>59,60</sup> However, the utility of exhaled nitric oxide and other biomarkers in distinguishing between asthma and COPD has not been validated.

## Asthma Severity

Once the diagnosis of asthma is made, the clinical history and spirometry results are used to assess the severity of disease. This assessment is generally made before the patient is prescribed long-term control medication. Patients are asked about the symptoms during the previous 2–4 weeks, or, if the patient is presenting with an exacerbation, during the period before the exacerbation. This information is combined with spirometry findings to categorize the asthma severity.<sup>4</sup>  $FEV_1$  provides an objective index of disease severity, correlates somewhat with symptoms,<sup>61</sup> and provides additional information that is useful to determine disease severity. This was demonstrated in a large study where one third of children with moderate-to-severe asthma were reclassified to a more severe category when  $FEV_1$  was added to symptom assessment.<sup>62,63</sup>

### Summary: Take-Home Messages for the Respiratory Therapist

Making the diagnosis of asthma requires a systematic approach to reviewing the patient's medical history and interpreting diagnostic tests. Considering the diagnosis of asthma in patients with a history of suggestive symptoms, such as wheeze, cough, chest tightness, and shortness of breath, is a critical first step. Patient report of triggers or history of allergies with these symptoms further suggests the diagnosis of asthma. The diagnostic testing can shift the probability in favor of or against the asthma diagnosis. Among symptomatic patients, aspects of the evaluation



that support a diagnosis of asthma include spirometry evidence of airflow obstruction that is largely reversible with bronchodilators, or a positive response to bronchoprovocation in a patient with normal spirometry. In distinguishing COPD from asthma, normal post-bronchodilator spirometry results rule out COPD, whereas a decreased  $D_{LCO}$  strongly suggests COPD. Biomarkers such as exhaled nitric oxide may have a greater role in asthma diagnosis in the future.

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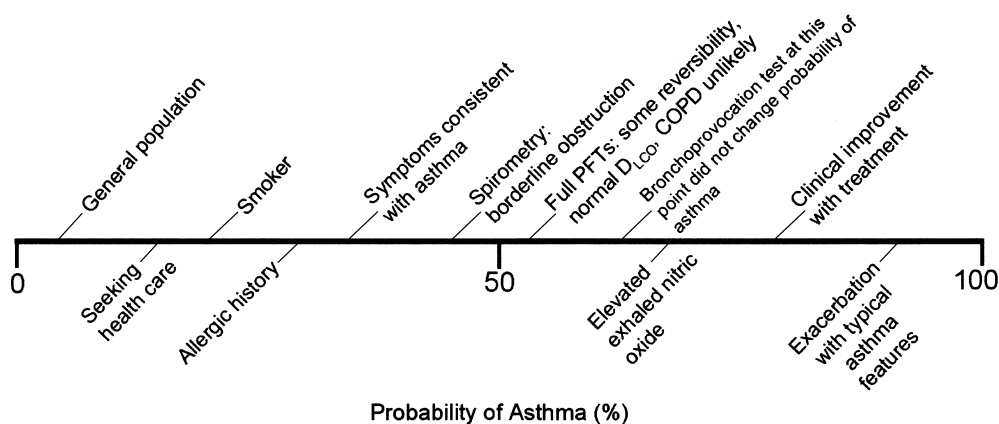
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Appendix

How Additional Information Changes the Probability of Asthma

- The patient is a 50-year-old female who presents to her primary care doctor for evaluation. She has a history of hay fever and cat allergies. She currently smokes one pack of cigarettes each day. She describes chronic cough that occasionally produces clear or whitish sputum. She occasionally experiences chest tightness and associated shortness of breath. Her probability of having asthma increases with the addition of each of these items from her history. Smokers can develop either asthma or chronic obstructive pulmonary disease (COPD) or both.
- Office spirometry reveals borderline obstruction. Her primary care doctor refers her to the pulmonary function laboratory at the local hospital. After bronchodilator her forced expiratory volume in the first second (FEV<sub>1</sub>) increased by 8%, and her ratio of FEV<sub>1</sub> to forced vital capacity (FVC) normalized. Her total lung capacity (TLC) is normal, but the ratio of residual volume to TLC is slightly elevated, at 105% of predicted. Her diffusing capacity of the lung for carbon monoxide (D<sub>LCO</sub>) is normal. At this point her probability of having asthma is about 50%, and COPD is ruled out because of her lack of post-bronchodilator airway obstruction and normal D<sub>LCO</sub>.
- She is referred for an exercise test. Her FEV<sub>1</sub> decreases by 8% after exercising on the treadmill. This is an equivocal result, so it does not change her probability of asthma.
- A methacholine challenge test is then performed and the PC<sub>20</sub> (provocational concentration that produces a 20% FEV<sub>1</sub> decrease) is 8 mg/mL. This is also an equivocal result, so it does not change her probability of having asthma.
- Her primary care doctor measures her exhaled nitric oxide at 100 ppb. This result makes allergic asthma more likely.
- During this time she is diagnosed with asthma, counseled about smoking cessation, started on pharmacotherapy for smoking cessation and daily inhaled corticosteroids, and given a short-acting bronchodilator for use as needed. She returns 3 months later and has successfully quit smoking. She has not had cough or chest tightness during that period. A repeat exhaled nitric oxide measurement is 20 ppb. This improvement on asthma therapy and reduction in exhaled nitric oxide now makes asthma even more likely.
- Six months later she returns to her doctor to follow up after a recent emergency department visit, where presented with wheezing and dyspnea and was found to have airflow obstruction. She was treated with a short course of oral steroids and is now feeling improved one week later. The probability of asthma is now nearly 100%.





## Discussion

**Stoloff:**\* Paul, You said that the majority of people have intermittent or mild asthma.

**Enright:** Well, I “see” them on the Web MD asthma message board. The majority of people with intermittent asthma don’t actually see a doctor about it, but may purchase Primatene Mist over the counter to treat their intermittent symptoms.

**Stoloff:** The papers that have been published clearly identify that when questions are asked of patients—consistent with the 1997 and 2007 NAEPP [National Asthma Education and Prevention Program] asthma guidelines,<sup>1,2</sup> or any other document on that level—the majority have mild-to-moderate asthma, with a far greater population who have severe asthma based on the concept of impairment, let alone risk. We can’t clearly identify the people with intermittent or mild asthma who do not present.

When someone comes into my office with asthma, it’s not mild or intermittent, because the impairment is enough that it’s affecting their daily life, so it’s moderate, because it’s causing a change in their behavior and to seek medical care.

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[gov/guidelines/asthma/asthgdln.pdf](http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf). Accessed February 29, 2008.

**Enright:** Good point. I am talking about estimates of prevalence rates from population-based samples from epidemiologic studies.

**Stoloff:** The other question is the issue of the percentage of primary care providers who use spirometry or have spirometers.

**Enright:** In Italy the percentage is very low.<sup>1</sup> There is also a new publication<sup>2</sup> on this topic, from a small group of primary care physicians in the United States, that is more encouraging.

1. Lusuardi M, De Benedetto F, Paggiaro P, Sanguinetti CM, Brazzola G, Ferri P, Donner CF. A randomized controlled trial on office spirometry in asthma and COPD in standard general practice: data from spirometry in asthma and COPD: a comparative evaluation Italian study. *Chest* 2006; 129(4):844-852.
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**Stoloff:** A survey on this topic was conducted about a decade ago by the American Academy of Family Physicians, but, unfortunately, they decided not to publish because the statistics were so low. Only 5% of the respondents said that they did spirometry. Now approximately 20% of clinicians in primary care specialties do spirometry, but less than 50%—more like 40%—of them say they do post-bronchodilator spirometry. And when they’re questioned on how they were trained in the interpretation of either the pre-bronchodilator or post-bronchodilator results, few actually understand it.

Yesterday I was at a clinic for the underserved in Las Vegas. There are 3 physicians there, and they see about 210 patients a day. It is one of 4 clinics serving Latino Americans in the

Las Vegas area. They each have a spirometer, but none of them knows how to use it. Even if they ordered a spirometry test, the patient would have to go to a local hospital to have it done. They don’t even use peak flow meters, because they don’t know where to get them. So when you look at this conundrum it is far more critical than discussions of the appropriate place for methacholine challenge in the workup of a patient with asthma-like symptoms. I think we need to hone down to the key issues.

**Enright:** Granted. An analogy is that many people have a home gym apparatus but very few of them have used it in the last 3 months. I think they’re all just hoping that if they bought the gizmo, they’d lose weight.

**Colice:** How much bronchodilator do you give? Do you give 2 puffs of albuterol, or do you give 10 days of prednisone and Singulair [montelukast sodium] and albuterol on top of that?

**Enright:** There is short-term bronchodilator responsiveness, and people will give either 2 or 4 puffs of albuterol. Or if it’s an adult, they might be savvy enough to use Combivent [albuterol and ipratropium combination formula]. Do the 2007 NAEPP guidelines indicate what is considered an adequate clinical trial of asthma therapy—the duration and the mix of drugs?

**Stoloff:** No.

**Diette:** I like the idea you mentioned of taking the prior probability into account and trying to decide where you are along the continuum. One of the things you’ve probably wrestled with is what information you still have available. Collectively, I think we’ve been somewhat lazy about insisting that there’s a threshold—for example, that 12% bronchodilator response means something that 11% doesn’t, or that 13% is exactly the same as 12%.

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In your example there was an 8% bronchodilator response; that's not meaningless information; it just doesn't meet that threshold. It's different from 2% and it's different from 18%. It could be that somebody just needs to do the hard work of looking at the likelihood ratios that come from the different values of each of these continuous variables and then feed them to the clinician on these now very-easy-to-generate reports and say that a certain value indicates a 20% likelihood or a very low or very high probability, and use the full continuum of information instead of forcing it into a dichotomy.

**Enright:** And those of us who run pulmonary function laboratories

ought to ask, what specifically is the question asked by the clinician when she ordered the pulmonary function test, rather than just using these rather arbitrary thresholds for normal or abnormal bronchodilator responsiveness. It ought to be a mini-consultation.

**Colice:** My European colleagues tell me that they use bronchodilator reversibility to tell them how well the patient's asthma is controlled. So if they've got them on an inhaled corticosteroid and they bring them into the laboratory and give them a puff of albuterol and their FEV<sub>1</sub> increases by 14%, then they say the asthma is not well controlled.

**Enright:** I love to hate the topic of bronchodilator reversibility for diagnosis or as an index of asthma control. I don't think that we should push drugs on patients to achieve maximum lung function. We should only give them enough medication(s) to treat their symptoms and reduce the risk of future exacerbations.

**Moore:** I think this relates to the newer model that says that the inflammation process and airway hyperactivity aren't always necessarily linked, so persistent bronchodilator reversibility may not be a good marker of control. They may be doing a lot for inflammation, and it's independent of the airway hyperactivity they're seeing.



Inhalation Therapy Department supervisor performing  
screening spirometry on citizen volunteer  
as part of pilot project of Pennsylvania Tuberculosis and Health Society  
From Donohue WF: Routine Function Tests to Become as Common as Chest X-Rays  
*Inhalation Therapy*, Journal of the American Association of Inhalation Therapists Vol 9, No 4, August 1964