A Stepwise Approach to the Interpretation of Pulmonary Function Tests

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Office-based pulmonary function testing, also known as spirometry, is a powerful tool for primary care physicians to diagnose and manage respiratory problems. An obstructive defect is indicated by a low forced expiratory volume in one second/forced vital capacity (FEV_1/FVC) ratio, which is defined as less than 70% or below the fifth percentile based on data from the Third National Health and Nutrition Examination Survey (NHANES III) in adults, and less than 85% in patients five to 18 years of age. If an obstructive defect is present, the physician should determine if the disease is reversible based on the increase in FEV_1 or FVC after bronchodilator treatment (i.e., increase of more than 12% in patients five to 18 years of age, or more than 12% and more than 200 mL in adults). Asthma is typically reversible, whereas chronic obstructive pulmonary disease is not. A restrictive pattern is indicated by an FVC below the fifth percentile based on NHANES III data in adults, or less than 80% in patients five to 18 years of age. If a restrictive pattern is present, full pulmonary function tests with diffusing capacity of the lung for carbon monoxide testing should be ordered to confirm restrictive lung disease and form a differential diagnosis. If both the FEV_1/FVC ratio and the FVC are low, the patient has a mixed defect. The severity of the abnormality is determined by the FEV_1 (percentage of predicted). If pulmonary function test results are normal, but the physician still suspects exercise- or allergen-induced asthma, bronchoprovocation (e.g., methacholine challenge, mannitol inhalation challenge, exercise testing) should be considered. (*Am Fam Physician.* 2014;89(5):359-366. Copyright © 2014 American Academy of Family Physicians.)

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Pulmonary function tests (PFTs) are useful for diagnosing the cause of unexplained respiratory symptoms and monitoring patients with known respiratory disease. Many organizations, including the National Asthma Education and Prevention Program, Global Initiative for Chronic Obstructive Lung Disease (GOLD), and American Thoracic Society (ATS), recommend using these tests.[1-3] Office equipment required to perform PFTs includes a computer, PFT software, pneumotach, printer, disposable mouthpiece, disposable nosepiece, and a 3-L syringe for calibration. There is no difference between PFT measurements obtained in the office (spirometry) and those obtained in a pulmonary function laboratory, as long as trained personnel calibrate, administer, and interpret the results.

PFTs take approximately 15 minutes for adults, 15 to 30 minutes for children, 45 minutes for pre- and postbronchodilator testing, and one hour for full PFTs with diffusing capacity of the lung for carbon monoxide (DLCO) testing. Five years is usually the youngest age at which children are able to cooperate with PFT procedures.[1] Some PFT software will interpret the patient's results automatically, but these machines should be used with caution because they may not follow current guidelines.

Physicians can use the following stepwise approach to not only interpret PFTs from their office or a pulmonary function laboratory, but also determine when to order further testing and how to use PFT results to formulate a differential diagnosis. *Figure 1* is an algorithm based on this approach. *Table 1* includes common terms related to PFTs.[4]

BEST PRACTICES IN PULMONARY MEDICINE: RECOMMENDATIONS FROM THE CHOOSING WISELY CAMPAIGN

Recommendation	*Sponsoring organization*
Do not diagnose or manage asthma without spirometry.	American Academy of Allergy, Asthma and Immunology

Source: For supporting citations, see http://www.aafp.org/afp/cw-table.pdf. To search Choosing Wisely recommendations relevant to primary care, see http://www.aafp.org/afp/recommendations/search.htm.

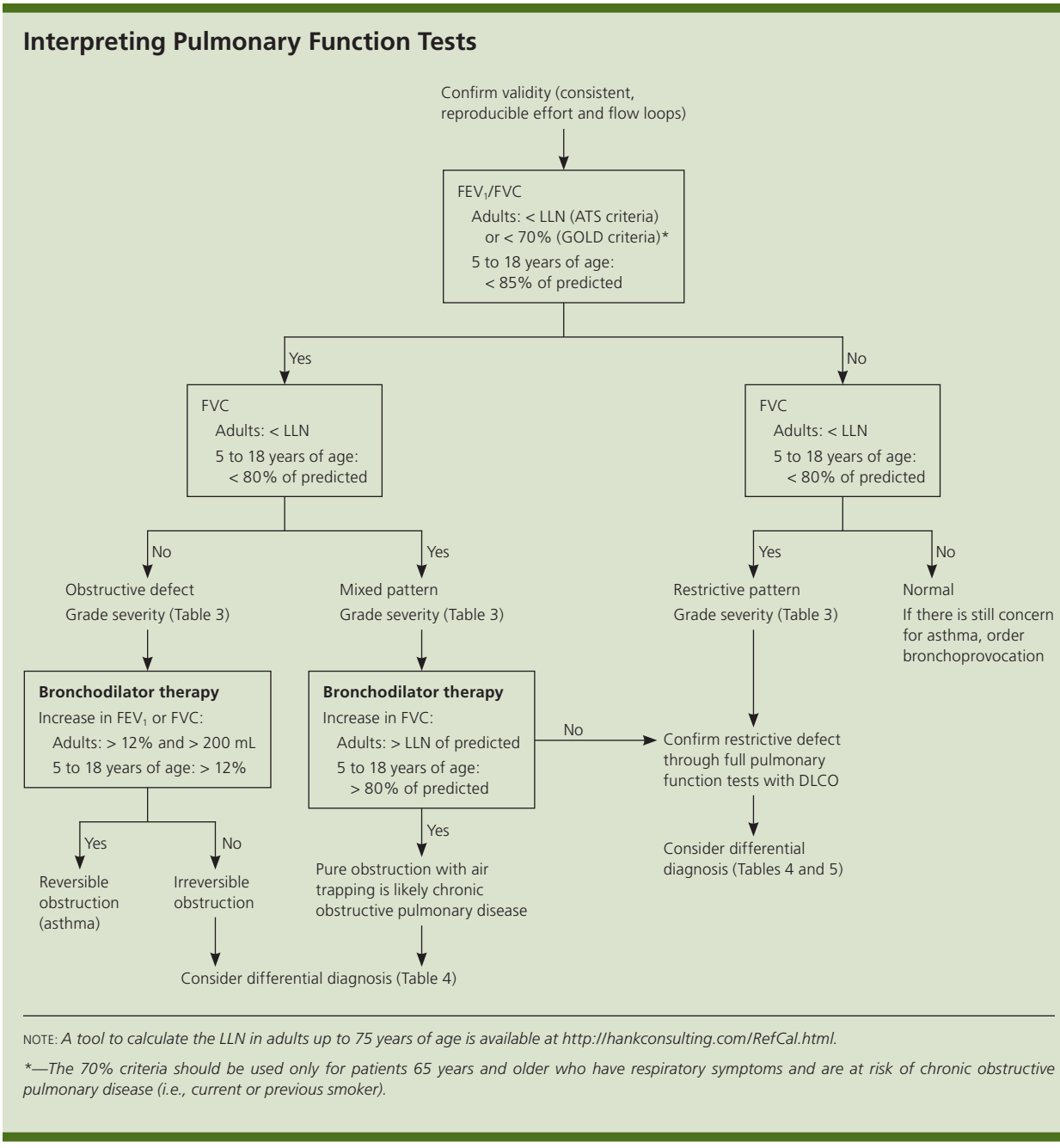


Figure 1. Algorithm for interpreting pulmonary function test results. (ATS = American Thoracic Society; DLCO = diffusing capacity of the lung for carbon monoxide; FEV_1 = forced expiratory volume in one second; FVC = forced vital capacity; GOLD = Global Initiative for Chronic Obstructive Lung Disease; LLN = lower limit of normal.)

Getting Started

Before PFT results can be reliably interpreted, three factors must be confirmed: (1) the volume-time curve reaches a plateau, and expiration lasts at least six seconds *(Figure 2)*; (2) results of the two best efforts on the PFT are within 0.2 L of each other *(Figure 3)*; and (3) the flow-volume loops are free of artifacts and abnormalities.[5] If the patient's efforts yield flattened flow-volume loops, submaximal effort is most likely; however, central or upper airway obstruction should be considered.

Step 1: Determine If the FEV_1/FVC Ratio Is Low

The first step when interpreting PFT results is to determine if the forced expiratory volume in one second/forced vital capacity (FEV_1/FVC) ratio is low, indicating an obstructive defect. Physicians have two options to determine if this ratio is low.

The first option is to follow the GOLD criteria, which use a cutoff of less than 70%.[2] For patients five to 18 years of age, the National Asthma Education and Prevention Program guideline says that a ratio of less than 85% is

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	*Evidence rating*	*References*
Physicians should use the Global Initiative for Chronic Obstructive Lung Disease criteria (FEV_1/FVC ratio less than 70%) to diagnose obstructive lung disease in patients 65 years and older who have respiratory symptoms and are at risk of COPD (i.e., current or previous smoker).	C	6, 7
Physicians should use the American Thoracic Society criteria (FEV_1/FVC ratio less than the lower limit of normal) to diagnose obstructive lung disease in patients younger than 65 years (regardless of smoking status) and in nonsmokers 65 years and older.	C	8, 9
If an obstructive defect is present, the physician should determine if it is reversible based on the increase in FEV_1 or FVC after bronchodilator treatment (i.e., increase of more than 12% in patients five to 18 years of age, or more than 12% and more than 200 mL in adults).	C	3
If pulmonary function test results are normal but the physician still suspects exercise- or allergen-induced asthma, bronchoprovocation (e.g., methacholine challenge, mannitol inhalation challenge, exercise testing) should be performed.	C	15, 16

COPD = chronic obstructive pulmonary disease; FEV_1 = forced expiratory volume in one second; FVC = forced vital capacity.

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to http://www.aafp.org/afpsort.

consistent with an obstructive defect as long as the patient has symptoms consistent with obstructive lung disease.[1]

The second option is to follow the ATS criteria, which use the lower limit of normal (LLN) as the cutoff for adults.[3] The LLN is a measurement less than the fifth percentile of spirometry data obtained from the Third National Health and Nutrition Examination Survey (NHANES III). Most modern PFT software can calculate the LLN. Alternatively, the calculator at http://hankconsulting.com/RefCal.html can be used for adults up to 75 years of age. Although the U.S. Food and Drug Administration has not approved this calculator for clinical use, it appears to be accurate and valid.

GOLD VS. ATS CRITERIA

A large cohort study found that using the GOLD criteria (FEV_1/FVC less than 70%) for diagnosis of chronic obstructive pulmonary disease (COPD) in U.S. adults 65 years and older was more sensitive for COPD-related obstructive lung disease than using the ATS criteria (FEV_1/FVC less than the LLN).[6] This finding was based on evidence that adults who met the GOLD criteria but not the ATS criteria (FEV_1/FVC less than 70% but greater than the LLN) had greater risk of COPD-related hospitalization (hazard ratio = 2.6; 95% confidence interval, 2.0 to 3.3) and mortality (hazard ratio = 1.3; 95% confidence interval, 1.1 to 1.5).[7] Another cohort study looking at adults 65 years and older found that, compared with the ATS criteria, the GOLD criteria had higher clinical agreement with an expert panel diagnosis for COPD and better identified patients with clinically relevant events (e.g., COPD exacerbation, hospitalization, mortality).[7] Until better criteria for the diagnosis of COPD are found, physicians should use the GOLD criteria to diagnose obstructive lung disease in patients 65 years and older with respiratory symptoms who are at risk of COPD (i.e., current or previous smoker).[6,7]

Other studies have found that using the GOLD criteria can miss up to 50% of young adults with obstructive lung disease and leads to overdiagnosis in healthy nonsmokers.[8,9] Based on these studies, physicians should use the ATS criteria to diagnose obstructive lung disease in patients younger than 65 years regardless of smoking status, and in nonsmokers who are 65 years and older.[8,9]

Table 1. Glossary of Terms Related to Pulmonary Function Testing

Spirometric values

FEV_1: forced expiratory volume in one second; total volume of air a patient is able to exhale in the first second during maximal effort

FVC: forced vital capacity; total volume of air a patient is able to exhale for the total duration of the test during maximal effort

FEV_1/FVC ratio: the percentage of the FVC expired in one second

FEV_6: forced expiratory volume in six seconds

$FEF_{25–75\%}$: forced expiratory flow over the middle one-half of the FVC; the average flow from the point at which 25% of the FVC has been exhaled to the point at which 75% of the FVC has been exhaled

Other terms

DLCO: diffusing capacity of the lung for carbon monoxide

EIB: exercise-induced bronchoconstriction

LLN: lower limit of normal, defined as below the fifth percentile of spirometry data obtained from the Third National Health and Nutrition Examination Survey

TLC: total lung capacity; the volume of air in the lungs at maximal inflation

VC: vital capacity; the largest volume measured on complete exhalation after full inspiration

Information from reference 4.

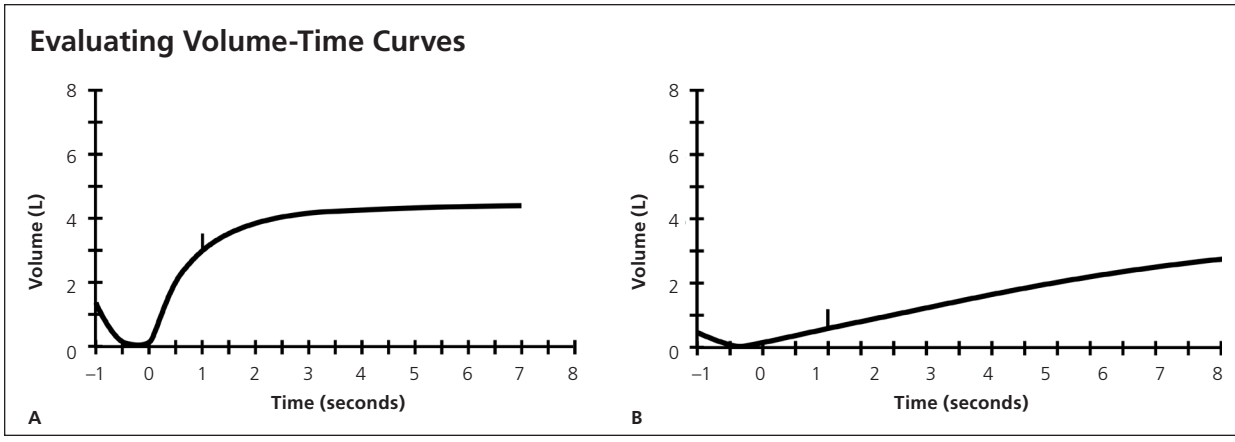


Figure 2. Volume-time curve showing *(A)* normal plateau of the volume of air expired at one or two seconds (total expiration lasts at least six seconds), and *(B)* no plateau; the volume continues to increase throughout expiration (this spirometry result should be interpreted with caution).

Determining the Validity of Pulmonary Function Tests

	Predicted	*Best*	*% of predicted*	*1*	*2*	*3*
FVC (L)	3.66	3.04	83	2.93	3.04	2.94
FEV_1 (L)	2.96	2.12	72	2.09	2.12	2.02
FEV_1/FVC (%)	83	70	84	71	70	69
$FEF_{25\%-75\%}$ (L per second)	3.36	1.36	40	1.44	1.36	1.23
PEF	6.65	4.71	71	5.07	4.71	4.67

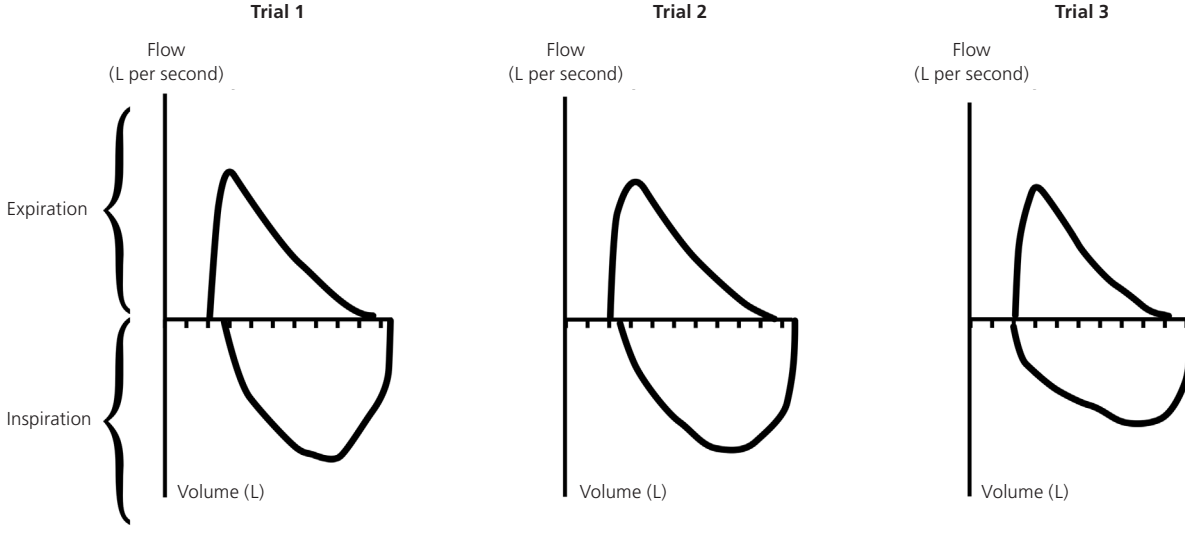


Figure 3. The FEV_1 and FVC measurements are within 0.2 L of each other during the two best efforts. Consistent, reproducible effort and flow loops confirm validity. ($FEF_{25\%-75\%}$ = forced expiratory flow at 25% to 75% of FVC; FEV_1 = forced expiratory volume in one second; FVC = forced vital capacity; PEF = peak expiratory flow.)

Step 2: Determine If the FVC Is Low

The physician must determine if the FVC is less than the LLN for adults or less than 80% of predicted for those five to 18 years of age, indicating a restrictive pattern.[3,10,11] The LLN can be determined using the calculator at http://hankconsulting.com/RefCal.html. A restrictive pattern can indicate restrictive lung disease, a mixed pattern (if a patient has an obstructive defect and a restrictive pattern), or pure obstructive lung disease with air trapping. *Table 2* summarizes the first two steps of PFT interpretation.[1-3,10,11]

Step 3: Confirm the Restrictive Pattern

If the patient's initial PFT results indicate a restrictive pattern or a mixed pattern that is not corrected with

Table 2. Pulmonary Function Test Interpretation

Test results based on age		
FVC	*FEV_1/FVC ratio**	*Suggested diagnosis*
5 to 18 years: ≥ 80% Adults: ≥ LLN	5 to 18 years: ≥ 85% Adults: ≥ LLN or ≥ 70%	Normal
5 to 18 years: ≥ 80% Adults: ≥ LLN	5 to 18 years: < 85% Adults: < LLN or < 70%	Obstructive defect
5 to 18 years: < 80% Adults: < LLN	5 to 18 years: ≥ 85% Adults: ≥ LLN or ≥ 70%	Restrictive pattern
5 to 18 years: < 80% Adults: < LLN	5 to 18 years: < 85% Adults: < LLN or < 70%	Mixed pattern

FEV_1 = forced expiratory volume in one second; FVC = forced vital capacity; LLN = lower limit of normal (defined as below the fifth percentile of spirometry data obtained from the Third National Health and Nutrition Examination Survey).

**—The 70% criteria should be used only for patients 65 years and older who have respiratory symptoms and are at risk of chronic obstructive pulmonary disease (i.e., current or previous smoker).*

Information from references 1 through 3, 10, and 11.

Table 3. American Thoracic Society Grades for Severity of a Pulmonary Function Test Abnormality

Severity	*FEV_1 percentage of predicted*
Mild	> 70
Moderate	60 to 69
Moderately severe	50 to 59
Severe	35 to 49
Very severe	< 35

FEV_1 = forced expiratory volume in one second.

Adapted with permission from Pellegrino R, Viegi G, Brusasco V, et al. Interpretative strategies for lung function tests. Eur Respir J. *2005; 26(5):957.*

bronchodilators, the patient should be referred for full PFTs with DLCO testing. DLCO is a quantitative measurement of gas transfer in the lungs. Diseases that decrease blood flow to the lungs or damage alveoli will cause less efficient gas exchange, resulting in a lower DLCO measurement.

During the DLCO test, patients inhale a mixture of helium (10%), carbon monoxide (0.3%), oxygen (21%), and nitrogen (68.7%)[12] then hold their breath for 10 seconds before exhaling. The amounts of exhaled helium and carbon monoxide are used to calculate the DLCO. Carbon monoxide is used to estimate gas transfer instead of oxygen due to its much higher affinity for hemoglobin. A baseline hemoglobin level should be obtained before DLCO testing because results are adjusted for the hemoglobin level.

Full PFTs provide the patient's total lung capacity. The restrictive pattern is confirmed as a true restrictive defect if the total lung capacity is less than 80% of predicted in patients five to 18 years of age, or less than the LLN in adults. If full PFTs cannot be obtained, the FVC can be used to infer a restrictive defect; however, FVC has a poor positive predictive value.[13,14]

Step 4: Grade the Severity of the Abnormality

If an obstructive defect, a restrictive pattern, or a mixed pattern is present, as defined by steps 1 and 2, the physician should grade the severity of the abnormality based on the FEV_1 percentage of predicted. The ATS system for grading the severity of a PFT abnormality is summarized in *Table 3*.[3]

Step 5: Determine Reversibility of the Obstructive Defect

If the patient has an obstructive defect, the physician should determine if it is reversible based on the increase in FEV_1 or FVC after bronchodilator treatment (i.e., increase of more than 12% in patients five to 18 years of age, or more than 12% and more than 200 mL in adults).[3] *Figure 4* shows a fully reversible obstructive defect. Obstructive defects in persons with asthma are usually fully reversible, whereas defects in persons with COPD typically are not.

If PFTs show a mixed pattern and the FVC corrects to 80% or more of predicted in patients five to 18 years of age or to the LLN or more in adults after bronchodilator use, it is likely that the patient has pure obstructive lung disease with air trapping.

Step 6: Bronchoprovocation

If PFT results are normal but the physician still suspects exercise- or allergen-induced asthma, the next step is bronchoprovocation, such as a methacholine challenge, a mannitol inhalation challenge, exercise testing, or sometimes eucapnic voluntary hyperpnea testing.[15,16] When the FEV_1 is 70% or more of predicted on standard spirometry, bronchoprovocation should be used to make the diagnosis. If the FEV_1 is less than 70% of predicted, a therapeutic trial of a bronchodilator may be considered.[17]

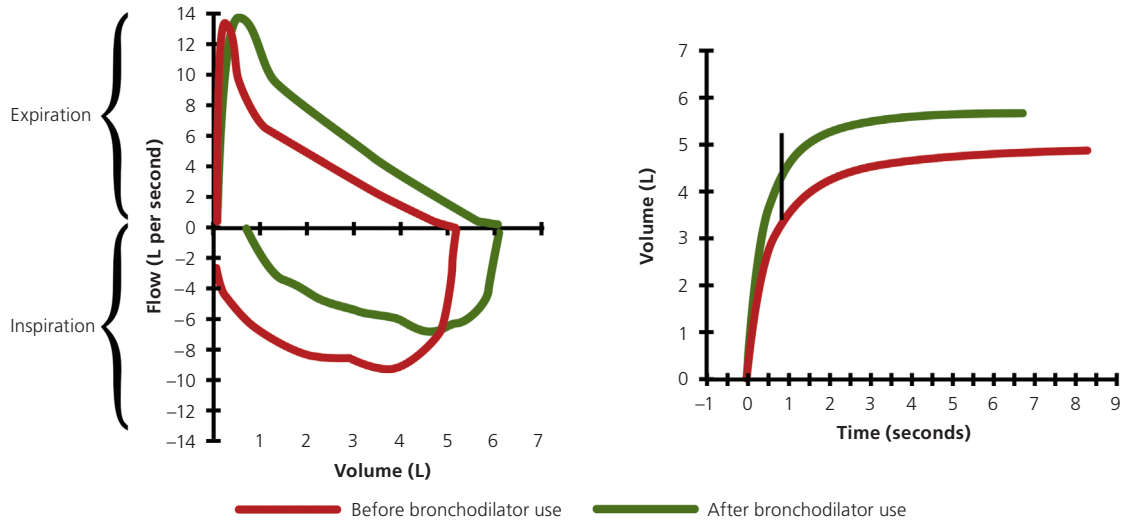
METHACHOLINE CHALLENGE

The methacholine challenge is highly sensitive for diagnosing asthma; however, its low specificity results in false-positive results.[15,17] A positive methacholine challenge result is defined as a greater than 20% reduction in FEV_1 at or before administration of 4 mg per mL of inhaled methacholine.[15] The result is considered borderline if the FEV_1 drops by 20% at a dose between 4 and 16 mg per mL.[15]

Obstructive Defect with Reversibility

Age: 26 years **Height:** 5 ft, 8 in **Weight:** 197 lb **Sex:** Male **Race:** Hispanic

	Prebronchodilators				*Postbronchodilators*		
Spirometry	*Predicted*	*LLN*	*Actual*	*% of predicted*	*Actual*	*% of predicted*	*% change*
FVC (L)	5.20	4.34	5.18[A]	99[D]	6.06[F]	116	+16[I]
FEV_1 (L)	4.37	3.64	3.55[B]	81[E]	4.64[G]	106	+30[J]
FEV_1/FVC (%)	84	75	68[C]	81	77[H]	91	+11
$FEF_{25\%-75\%}$ (L per second)	4.74	3.11	2.41	50	3.84	80	+59



A = FVC (before bronchodilators), this is > LLN and thus does not show a restrictive pattern
B = FEV_1 (before bronchodilators)
C = FEV_1/FVC ratio (before bronchodilators), this is < LLN and thus shows an obstructive defect
D = FVC percentage of predicted (before bronchodilators)
E = FEV_1 percentage of predicted (before bronchodilators)
F = FVC (after bronchodilators)
G = FEV_1 (after bronchodilators)
H = FEV_1/FVC ratio (after bronchodilators)
I = A 0.88-L increase in FVC is a 16% increase
J = A 1.09-L increase in FEV_1 is a 30% increase

The above indicates reversibility because at least one of the two (FVC or FEV_1) increased by at least 0.2 L and by at least 12%

Figure 4. The obstructive defect is reversible because at least one of the two measurements (FVC or FEV_1) increased by at least 0.2 L and by at least 12%. ($FEF_{25\%-75\%}$ = forced expiratory flow at 25% to 75% of FVC; FEV_1 = forced expiratory volume in one second; FVC = forced vital capacity; LLN = lower limit of normal.)

MANNITOL INHALATION CHALLENGE

The mannitol inhalation challenge has a lower sensitivity for the diagnosis of asthma or exercise-induced bronchoconstriction than the methacholine challenge, but has a higher specificity for the diagnosis of asthma.[16,17] A positive mannitol inhalation challenge result is defined as a greater than 15% decrease from baseline in FEV_1 at a cumulative dose of 635 mg or less of inhaled mannitol, or a 10% decrease between any two consecutive doses.[16,17]

EXERCISE TESTING

A treadmill exercise test has excellent sensitivity and specificity for the diagnosis of exercise-induced bronchoconstriction, but has only modest sensitivity and specificity for the diagnosis of asthma.[17] In this test, baseline spirometry is measured, followed by exercise on a treadmill. The goal is to achieve 80% to 90% of the maximum heart rate within two minutes, and maintain that heart rate for eight minutes.[17] Inhaled medical-grade dry air or an air-conditioned room, with air temperature between 60°F and 77°F (20°C and 25°C) and humidity level less than 50%, is recommended. The patient must wear a nose clip.

Postchallenge FEV_1 testing takes place at 1- to 3-, 5-, 10-, 15-, 20-, and 30- to 45-minute time points. The test is considered positive if a 10% or greater decline from baseline in FVC or FEV_1 occurs over any two consecutive time points in the 30 minutes following the cessation of exercise.[15,18]

EUCAPNIC VOLUNTARY HYPERPNEA TESTING

Eucapnic voluntary hyperpnea testing is available only at specialized centers and is used by the International

Table 4. Common Causes of Obstructive and Restrictive Lung Disease

Obstructive	**Restrictive** *(continued)*
α_1-antitrypsin deficiency	Interstitial lung disease
Asthma	Asbestosis
Bronchiectasis	Berylliosis
Bronchiolitis obliterans	Eosinophilic pneumonia
Chronic obstructive pulmonary disease	Hypersensitivity pneumonitis
Cystic fibrosis	Idiopathic pulmonary fibrosis
Silicosis (early)	Sarcoidosis
Restrictive	Silicosis (late)
Chest wall	Neuromuscular disorders
Ankylosing spondylitis	Amyotrophic lateral sclerosis
Kyphosis	Guillain-Barré syndrome
Morbid obesity	Muscular dystrophy
Scoliosis	Myasthenia gravis
Drugs (adverse reaction)	
Amiodarone	
Methotrexate	
Nitrofurantoin (Furadantin)	

Information from references 20 through 35.

Olympic Committee Medical Commission's Independent Panel on Asthma to identify exercise-induced bronchoconstriction in elite athletes desiring to use bronchodilators before competition.[19]

Step 7: Establish the Differential Diagnosis

Once PFT results have been interpreted, the broad differential diagnosis should be considered. *Table 4* lists common causes of lung disorders.[20-35] *Table 5* is the differential diagnosis based on DLCO results.[3,12,14,36-44]

Step 8: Compare Current and Prior PFT Results

If a patient's prior PFT results are available, they should be compared with the current results to determine the course of the disease or effects of treatment.

Data Sources: We conducted literature searches using Ovid, PubMed, the Cochrane database, and Essential Evidence Plus, focusing on the keywords spirometry and pulmonary function test(s), with an emphasis on the diagnosis and/or interpretation of results. The section on DLCO was reviewed in UpToDate in October 2011 to identify additional primary literature regarding this test. Search dates: September to October 2011, May 2012, and August 2013.

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Table 5. Differential Diagnosis Based on DLCO Results

DLCO results	*Differential diagnosis*
High DLCO	Asthma, left-to-right intracardiac shunts, polycythemia, pulmonary hemorrhage
Normal DLCO with restrictive pattern	Kyphoscoliosis, morbid obesity, neuromuscular weakness, pleural effusion
Normal DLCO with obstructive component	α_1-antitrypsin deficiency, asthma, bronchiectasis, chronic bronchitis
Low DLCO with restriction	Asbestosis, berylliosis, hypersensitivity pneumonitis, idiopathic pulmonary fibrosis, Langerhans cell histiocytosis (histiocytosis X), lymphangitic spread of tumor, miliary tuberculosis, sarcoidosis, silicosis (late)
Low DLCO with obstruction	Cystic fibrosis, emphysema, silicosis (early)
Low DLCO with normal pulmonary function test results	Chronic pulmonary emboli, congestive heart failure, connective tissue disease with pulmonary involvement, dermatomyositis/polymyositis, inflammatory bowel disease, interstitial lung disease (early), primary pulmonary hypertension, rheumatoid arthritis, systemic lupus erythematosus, systemic sclerosis, Wegener granulomatosis (also called granulomatosis with polyangiitis)

Interpretation: High = greater than 120% of predicted; Normal = LLN to 120% of predicted; Low (mild decrease) = greater than 60% of predicted and less than LLN; Low (moderate decrease) = 40% to 60% of predicted; Low (severe decrease) = less than 40% of predicted. If the laboratory does not report LLN, observational studies indicate that the LLN for men is approximately 80%, and the LLN for women is approximately 76%.[36]

DLCO = diffusing capacity of the lung for carbon monoxide; LLN = lower limit of normal.

Information from references 3, 12, 14, and 36 through 44.

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