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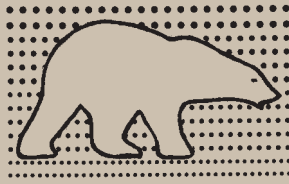
Welcome to the Snowdrift Frontline Treatment Monographs. The authors welcome you to this series of monographs that aim to disseminate worldwide new knowledge about common pulmonary disorders. We offer our messages to anyone who will find them useful in the diagnosis and treatment of the many pulmonary disorders that continue to plague mankind around the world. We invite you to download these monographs and use them in your teaching and practice of medicine. We feel a fraternal connection to all practitioners who serve the suffering. We hope that we can move toward the prevention of disease as an alternative to premature morbidity and mortality.

The Authors.

Mission Statement

The Snowdrift Pulmonary Conference is a not-for-profit corporation that is dedicated to the dissemination of knowledge about the lungs and lung diseases. Composed of both private practice pulmonologists and academicians, the conferees have launched a consumer-oriented program for primary care practitioners and the patients they serve. As a result, the following concise and authoritative monographs have been written.

Snowdrift Pulmonary Conference



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Frontline Cardiopulmonary Topics

Dyspnea

The Authors

J. Kern Buckner, MD	Denver, CO
Roy V. Ditchey, MD	Redding, CA
James T. Good, Jr., MD	Englewood, CO
Richard A. Matthay, MD	New Haven, CT
Douglass Morrison, MD	Tucson, AZ
Thomas L. Petty, MD*	Denver, CO
Sidney C. Smith, Jr., MD*	Chapel Hill, NC

*Co-Editors

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Preface

A series of monographs called the *Frontline Treatment* series has been well received by primary care physicians. Collectively, *Frontline Treatment of COPD (2nd ed)*, *Asthma*, *Common Respiratory Infections*, *Venous Thromboembolism*, *Assessment of Common Pulmonary Presentations*, *Assessment of Lung Cancer and Occupational Pulmonary Diseases*, and *Pulmonary Procedures and Interventions* provide a compact and practical library for the frontline practitioner. Now members of the original *Frontline Treatment* group, comprised of pulmonologists, are joined by cardiologists from academia and the private practice sector to discuss symptoms, presentations, and management of disease entities that involve the heart/lung interface. Drawing on extensive experience in diagnosing and treating patients with dyspnea, we have written this monograph mainly for primary care physicians and others involved or otherwise interested in this common and distressing symptom.

The purpose of the monograph is to present an approach to evaluating dyspnea. We focus on a practical, clinical protocol commencing with office evaluation of the patient with dyspnea. This is followed by a description of necessary studies that can help elucidate the cause(s) of dyspnea in a patient. Finally, we present a series of cases to emphasize the appropriate evaluation and management of patients with dyspnea. ■

The Authors

Pearls

- The cause of dyspnea can be determined in many patients by a careful history and physical.
- Spirometry should be performed in all patients who complain of dyspnea.
- Always obtain a chest x-ray (CXR) in a patient with dyspnea.
- In acute dyspnea, consider acute myocardial infarction, airflow obstruction, pulmonary embolism (PE), or pneumothorax as underlying causes.
- New-onset wheezing in men more than 40 years old suggests cardiac dyspnea.
- Nocturnal dyspnea suggests congestive heart failure (CHF), airflow obstruction, or sleep-disordered breathing.
- Dyspnea is the most common symptom of acute PE.
- Resting and exercise pulse oximetry should be obtained in patients with chronic dyspnea.
- Spirometry is to dyspnea as an electrocardiogram (ECG) is to chest pain.
- Syncope and dyspnea in young women suggest primary pulmonary hypertension (PPH) or PE.
- The ventilation-perfusion $\dot{V}\dot{Q}$ scan is the diagnostic study of choice for PE in patients with a normal CXR and no history of lung disease.
- Acute dyspnea and a reading of S1, Q3, and T3 on an ECG suggest PE.

- New-onset atrial fibrillation, wheezing, and paroxysmal nocturnal dyspnea suggest mitral stenosis.
- Dyspnea from anxiety improves with exercise.
- High-resolution computed tomography of the chest can confirm idiopathic pulmonary fibrosis.
- A restrictive ventilatory defect may be due to CHF.
- Think cost/benefit when ordering tests for dyspnea. ■

A. Mechanisms of Dyspnea

One of the most common reasons why patients consult physicians and other healthcare workers, dyspnea is responsible for substantial disability in millions of patients each year. Although many definitions for dyspnea exist, our working explanation is, “a person’s uncomfortable sensation associated with breathing.” Dyspnea is thus a perception by the individual and is entirely subjective. It is not a clinical observation, nor does it relate directly to any physiological or laboratory test. It is the patient’s interpretation of a reduction in pleasant breathing.

Dyspnea may occur normally in states of intense exercise, such as running, mountain climbing, lifting, rowing, and swimming, where the stress of breathing is a direct result of intense physical effort and not a consequence of a cardiopulmonary or metabolic disorder. At the other extreme, the sensation of uncomfortable breathing may occur at rest, with or without associated anxiety or other provocation, when an advanced cardiac or pulmonary disorder is usually present. There are other causes of dyspnea that do not involve the cardiopulmonary systems (e.g., psychogenic dyspnea).

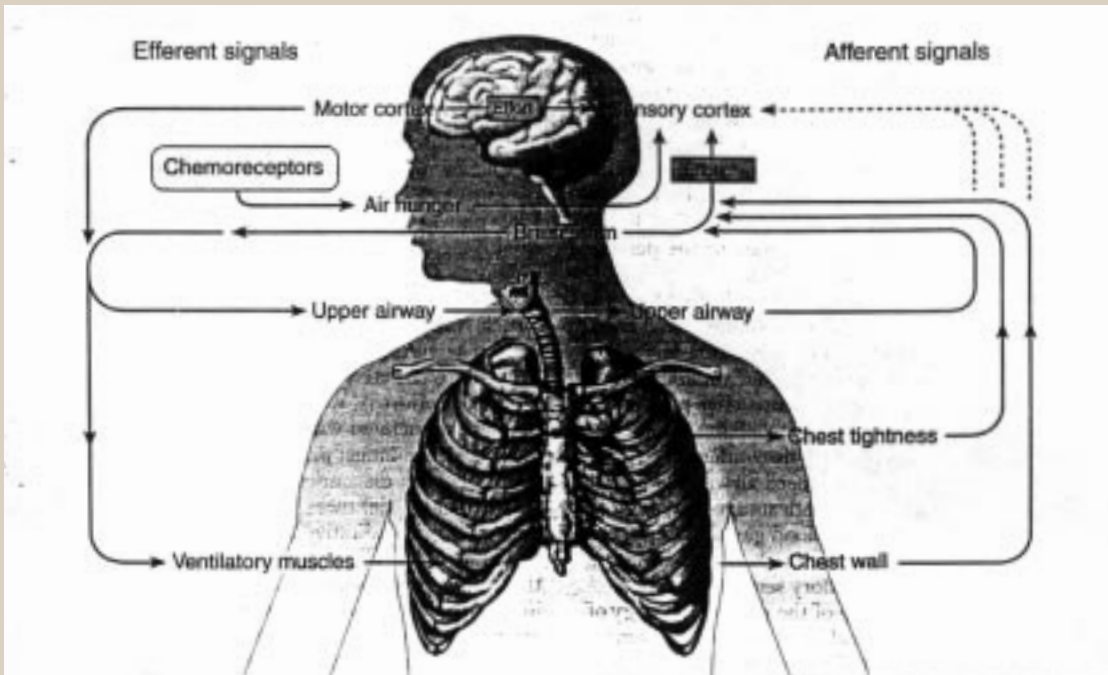
The disorder is a result of an imbalance between the respiratory drives that originate from the complex respiratory center and the responses of the cardiopulmonary systems. The work of breathing must be appropriate to the task and in the context of the resultant cardiovascular and respiratory responses. Respiratory work has two major components: the first is related to the resistance of moving air through bronchi and is known as resistive load; the second is the load imposed by elasticity and recoil of the lungs, thorax, and respiratory musculature, called elastic load. Both resistive loads and elastic loads can be increased in cardiovascular as well as pulmonary diseases.

The respiratory center receives many signals, including the powerful chemical stimuli from the carotid and aortic bodies that sense pH, PCO₂, and PO₂. Mechanical signals are also sent to the respiratory center during physical activity by the stretch receptors of the lungs and the muscles of the body. At the same time, the respiratory center receives numerous messages from the cerebral cortex. Thus, a barrage of afferent signals affects the intrinsic rhythmicity of the respiratory center, which responds with efferent signals that control the rate and depth of respiration.

Dyspnea is most commonly encountered in conditions where the respiratory drive is increased or the respiratory system is excessively loaded. These conditions are characterized by a perception of “air hunger” or increased effort of breathing. Figure 1 nicely summarizes the exquisite balance between efferent and afferent signals that contribute to the sensation of dyspnea.

Cardiac and pulmonary diseases create disturbances in the balance between respiratory drives, the work of breathing, and how well the cardiorespiratory apparatus responds to the physiologic requests of the body at rest and with exercise. Congestive heart failure (CHF) is probably the most common cause of dyspnea on exertion and of paroxysmal nocturnal dyspnea (PND). The next most common causes of dyspnea are diseases of the lungs that are characterized by airflow obstruction, such as bronchial asthma, chronic obstructive pulmonary disease (COPD), and a wide variety of less common obstructive diseases. Dyspnea also accompanies the full spectrum of interstitial lung diseases and is often found with pulmonary hypertension (PH) regardless of the underlying cause. Neuromuscular diseases, anemia, physical deconditioning, metabolic disorders, responses to pharmacologic agents, and anxiety may all be associated with dyspnea. In several of these and other

Figure 1. Efferent and Afferent Signals That Contribute to the Sensation of Dyspnea



The sense of respiratory effort is believed to arise from signals transmitted from the motor cortex to the sensory cortex coincidentally with the outgoing motor command to the ventilatory muscles. The arrow from the brain stem to the sensory cortex indicates that the motor output of the brain stem may also contribute to the sense of effort. The sense of air hunger is believed to arise, in part, from increased respiratory activity within the brain stem, and the sensation of chest tightness probably results from stimulation of vagal-irritant receptors. Although afferent information from airway, lung, and chest-wall receptors most likely passes through the brain stem before reaching the sensory cortex, the dashed lines indicate uncertainty about whether some afferents bypass the brain stem and project directly to the sensory cortex. (Reprinted with permission from Manning HL, Schwartzstein, RM. Mechanisms of disease: Pathophysiology of dyspnea. *New Engl J Med.* 1995;333:1548.)

associated disorders, dyspnea is the limiting factor in exercise—in up to one third of patients with cardiac disease, for example.

The evaluation of the dyspneic patient requires the acquisition of a detailed history describing the conditions under which the patient has been or is currently experiencing dyspnea. In addition, a physical examination, a chest radiograph, and measurements of pulmonary mechanics are usually required to make a clinical diagnosis. In some cases, cardiovascular physiological performance tests are also required. The case studies in Section F focus on the likely mechanism(s) of dyspnea that are commonly encountered by the clinician. ■

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B. Office Evaluation of the Patient: History and Physical Examination

Shortness of breath is a common symptom and frequently occurs to such a degree that patients seek medical attention. Except in acute emergencies, patients usually present to the physician's office for the initial evaluation. If the physician can accurately and efficiently evaluate the patient, a more involved study requiring multiple sophisticated and expensive tests can often be avoided (see Section D). On the other hand, when office screening does not result in an etiological explanation for the dyspnea, complex studies are required. The purpose of this section is to outline an efficient office workup of patients presenting with dyspnea.

Patient History

For many patients, the symptom of dyspnea may have several different meanings. Physicians classically refer to dyspnea as "shortness of breath." But many patients may have less obvious complaints, such as weakness, fatigue, lack of energy, chest tightness, decreased exercise tolerance, inability to take a deep breath, and "just getting old." These symptoms may in fact be what are occurring when the patient describes shortness of breath. In taking a history, it is important to establish:

- How long symptoms have been present;
- Whether symptoms are stable or escalating; and
- Why the patient chose this exact time to see the physician.

The important initial finding relates to dyspnea at rest versus dyspnea with exercise. Dyspnea at rest suggests either severe cardiopulmonary disease or possible anxiety. Dyspnea with exercise is by far the more common complaint and may be associated with cardiac, pulmonary, or metabolic disorders or deconditioning as opposed to anxiety.

(continued)

B. Office Evaluation of the Patient: History and Physical Examination (*continued*)

Key questions to ask during the history can be divided into three main areas:

1. *Cardiac questions.* The physician should inquire about the presence or absence of chest pain, orthopnea, paroxysmal nocturnal dyspnea (PND), edema, weight gain, and any cardiac medications or cardiac diagnoses of the patient.
2. *Pulmonary questions.* The physician should also ask about the presence or absence of wheezing, chest tightness, cough, sputum production, pleuritic pain, sleep patterns (apneas), and a history of tobacco smoking.
3. *Other.* In addition, the patient should be asked about any history of cirrhosis, renal insufficiency, anemia, or endocrine abnormalities, all of which can be quickly reviewed.

In many situations, the distinction between cardiac and pulmonary dyspnea is difficult. Cardiac dyspnea is the result of left atrial hypertension and an increased Starling gradient of pulmonary venous hypertension. Pulmonary dyspnea typically results when chemoreceptors are stimulated (low PaO₂ or high PaCO₂) or other pulmonary receptors (stretch, irritant, or J receptors) are involved.

The major important historical finding of cardiac dyspnea is dyspnea aggravated by recumbency (orthopnea). Paroxysmal nocturnal dyspnea (PND) may be common to both heart and lung disease, especially chronic obstructive pulmonary disease (COPD). When it is of cardiac origin, PND is due to acute interstitial edema and is characterized by an overwhelming and frightening sensation of suffocation. Cough, if present, follows the dyspnea. Symptom relief is achieved only with sitting or standing to allow gravity to compensate. On the other

hand, PND of pulmonary origin is due to the collection and plugging of secretions in the airways. Patients usually present with an initial paroxysm of coughing, followed by dyspnea. Relief of symptoms is achieved with expectoration of secretions.

Dyspnea on exertion is a common initial complaint in both the cardiac and pulmonary forms. The symptom of chest tightness or feeling of oppressiveness in the chest experienced with angina pectoris may be confused for dyspnea, but careful questioning can quickly establish the difference. Dyspnea as an anginal equivalent may be the sentinel symptom of ischemic heart disease in the COPD patient. The new onset of asthma in a previously healthy patient over 40 years old should alert the physician to a possible cardiac origin.

Dyspnea at rest may reflect severe and often end-stage cardiopulmonary disease but needs to be differentiated from the heightened sensation of breathlessness and hyperventilation experienced during anxiety. The diagnosis of dyspnea associated with pulmonary embolism deserves special consideration because the signal findings of tachycardia, hypoxemia, and pleurisy may not always be present.

Physical Examination

One minute of dedicated observation is paramount. Are the eyes bright with a sparkle, or dull and lethargic? Does the patient speak with authority or have difficulty talking because of conversational dyspnea? Skin color, muscle tone, use of accessory muscles of respiration, and whether there is the presence of clubbing, jugular venous distension, edema and abdominal swelling, barrel chest, and thoracic skeletal abnormalities such as kyphoscoliosis can all be quickly assessed.

(continued)

B. Office Evaluation of the Patient: History and Physical Examination *(continued)*

Pulmonary Examination

The chest examination should consist of inspection, palpation, percussion, and auscultation:

- *Inspection* includes observation of rate and depth of breathing and any chest wall abnormalities, use of pursed-lipped breathing, or presence of a respiratory pattern that includes Kussmaul (rapid and deep breathing), Cheyne-Stokes (a regularly irregular pattern), and Biot's (irregularly irregular) respirations. Kussmaul respirations are usually associated with severe metabolic acidosis, Cheyne-Stokes respirations are commonly seen in congestive heart failure (CHF), and Biot's respirations are associated with neurologic diseases such as meningitis. The presence of clubbing should raise suspicion of interstitial lung disease, bronchiectasis, or lung cancer.
- *Palpation* allows for evaluation of chest expansion and tracheal location, identification of tactile fremitus (increased with consolidation and decreased with pleural effusion, pneumothorax, and atelectasis), and detection of any presence of subcutaneous emphysema and pleural friction rubs.
- *Percussion* allows for assessment of lung resonance and dullness. Hyperresonance occurs in patients with emphysema and asthma, while dullness is associated with consolidation, atelectasis, pleural effusion, and diaphragmatic paralysis.
- *Auscultation* of the chest with the stethoscope identifies both normal and abnormal sounds. Vesicular breath sounds are heard over normally functioning lung tissue and multiply with increased depth of respiration. Bronchial or tubular breath sounds normally occur over the upper airway, but they indicate consolidation when heard over the remainder of the chest. Rales or crackles indicate abnormalities within the alveoli and small airways,

and they are associated with atelectasis, pneumonia, CHF, interstitial lung disease, and alveolar hemorrhage. Rhonchi are sounds that originate in the larger airways and are usually associated with the accumulation of mucus. Wheezes are high-pitched whistling sounds resulting from partial airway obstruction, usually of mid-sized airways, and are associated with asthma and COPD.

Cardiac Examination

As with the pulmonary examination, inspection, palpation, percussion, and auscultation are important in assessing the condition of the heart. Initial palpation of the radial pulse gives insight into cardiac hemodynamics. *Pulsus alternans* reflects low cardiac output, an irregularly irregular heartbeat suggests atrial fibrillation, and bounding pulses suggest valvular heart disease (aortic insufficiency).

- *Inspection* is best carried out with the patient in the supine or slightly lateral decubitus position. The point of maximal impulse (also known as the “apical” impulse) should be seen in the fourth intercostal space at the midclavicular line. The precordium is observed for any abnormal pulsations or movements frequently associated with right and left ventricular enlargement. Asymmetrical enlargement of the left chest may reflect chronic heart enlargement of any cause. The clinician should also observe for jugular venous distention, ascites, and pedal edema.
- *Palpation* is used to confirm the findings of inspection and to anticipate auscultation. Third and fourth heart sounds can be palpated, reflecting abnormal systolic and diastolic function. Thrills (vibratory sensations detected by the palm of the hand) can be associated with both systolic and diastolic murmurs, suggesting severe valvular heart disease or cardiac shunts. Parasternal lifts indicate

B. Office Evaluation of the Patient: History and Physical Examination *(continued)*

significant enlargement of the right ventricle and possible underlying pulmonary hypertension (PH).

- *Percussion* of the heart is often not necessary due to the immediate availability of chest x-rays (CXR) to most clinicians. However, when it is performed, percussion is used primarily to detect cardiomegaly or a pericardial effusion.
- *Auscultation* of the heart forms the mental image many people have when envisioning a visit to the doctor. Recognition of normal heart sounds, physiologic sounds, and pathologic findings can be very difficult. Because a discussion of all possibilities is not possible in this monograph, readers should refer to a basic physical diagnosis text.

When evaluating the patient with dyspnea, certain cardiovascular findings are key. The physical findings of left atrial hypertension may be subtle or even absent early in the disease process. Initially, there may be a soft fourth heart sound at the apex, reflecting elevated left atrial and left ventricular end-diastolic pressure (LVEDP). With more advanced and chronic disease, other physical findings usually become manifest. The apical impulse may become abnormal in location and contour, possibly with palpable gallops, reflecting structural disease, and elevated cardiac pressures. Jugular pressure may be elevated or, in absence of abnormal jugular distention, there may be the finding of hepatojugular reflux. Auscultation of the heart may be remarkable for murmurs of valvular heart disease or intracardiac shunt. A third heart sound usually develops as left atrial pressure and LVEDP, exceeding 25 mm Hg or, if tachycardia is present, a third plus fourth heart sound known as “summation gallop.” Examination of the abdomen may be remarkable for a distended and tender liver of passive congestion, the presence of shifting dullness, or the fluid wave of

ascites. The lower extremities may show pitting edema and chronic stasis changes.

Office Studies

The history and physical examination may direct the physician to specific screening tests that can be performed in the doctor's office:

Oximetry/Oxygen Saturation. Measurement of O₂ saturation (usually by a portable oximeter) is key because low values indicate abnormal physiology. If the resting O₂ saturation is normal, then the patient should be exercised to determine if desaturation occurs with activity.

Chest X-ray. The CXR screens for anatomical abnormalities, including cardiomegaly, pulmonary vascular congestion and pulmonary edema, CHF, pulmonary infiltrates and atelectasis, interstitial lung diseases, hyperinflation, COPD and asthma, and PH.

Electrocardiogram (ECG). The ECG may identify ischemia, chamber enlargement, arrhythmias, bundle branch block, and metabolic abnormalities.

Office Spirometry. One of the most useful, yet underutilized diagnostic techniques in all of medicine, spirometry is appropriate in the evaluation of many patients who present with dyspnea. Yet, all too often, patients with unexplained dyspnea receive only a CXR and/or an ECG during their initial evaluation. Neither test is of much value in evaluating pulmonary mechanics.

Spirometry simply measures airflow from fully inflated lungs. It can also measure inspiratory airflow (see Section C). The most common measurements are the record of airflow and volume from fully inflated lungs. Measurements of the forced vital capacity (FVC) and the forced expiratory volume in one second (FEV₁) are performed to diagnose both obstructive (decreased

B. Office Evaluation of the Patient: History and Physical Examination *(continued)*

FEV₁ and decreased FEV₁/FVC ratio) and restrictive (decreased FVC and normal or increased FEV₁/FVC ratio) lung disease.

Complete Blood Count (CBC). Metabolic and systemic disorders can be screened by a CBC biochemistry panel, including liver and renal function studies and a thyroid panel.

If the above studies do not allow for a diagnosis and subsequent therapeutic plan, then the more complex studies covered in Section D should be considered.

Other Causes of Dyspnea

Dyspnea that is not of cardiac or pulmonary origin occurs because of decreased O₂ delivery to the tissues, increased utilization of O₂, or, in the absence of pathology, either deconditioning or anxiety. Key components of a history taken for other causes of dyspnea should center on the presence of systemic disease, especially anemia, neoplastic disease, and metabolic disorders. A patient with a normal heart will experience dyspnea at strenuous levels of exercise as the Starling gradient transiently exceeds the dyspnea threshold, or the anaerobic threshold is achieved. In a deconditioned but normal heart, dyspnea may be experienced with less than strenuous exercise.

The dyspnea of anxiety is always present at rest and usually improves with exercise and activity. The patient with anxiety will often sigh and complain of “not being able to get enough air into my lungs.” The heightened sensation of breathing may be accompanied by a sharp and stabbing (usually nonexertional) inframammary chest pain. Hyperventilation may also

be present in the anxious patient and be accompanied by circumoral and extremity paresthesias. Having the patient hyperventilate with reproduction of symptoms establishes the diagnosis.

In summary, while the history and physical examination usually give an excellent insight into the cause of the patient's dyspnea, the few simple office screening tests described in this section are usually quite helpful in establishing the diagnosis. ■

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C. Office
Evaluation of the
Patient:
Initial Studies—
Spirometry

The Basis of
Pulmonary
Mechanics

When patients take a large breath, they create a negative pressure in the pleural space. This creates the force for airflow to fill the lungs to the point of maximum inflation. Expiratory airflow is initiated by forceful effort. Much of the expiratory airflow is a function of elastic recoil and the conductance of air through small and large airways. Following the initiation of forced exhalation, the alveoli empty into small airways, and small airways empty into large airways. The resultant airflow is recorded by a spirometer. The forced expiratory volume in 1 second (FEV_1) is a flow test. The entire forced expiration, or forced vital capacity (FVC), is a volume test.

Recently, new terminology has been added to simple spirometry. Since normal lungs empty in 6 seconds, a recent convention has substituted the FEV_6 (also known as FVC_6) for the FVC, to make testing more convenient for both the patient and the spirometer technician. Normally, the FEV_1/FVC is 70% or more. A low ratio of FEV_1 to FVC identifies patients at risk of accelerated losses in absolute FEV_1 over time. The same is true for FEV_1/FEV_6 .

Obstructive Lung
Diseases

Table 1 lists the common diseases characterized by expiratory airflow obstruction. In obstructive diseases, the FEV_1/FVC (FEV_6) is <70%, and the absolute FEV_1 is usually <80% of predicted. Examples of the normal volume-time and flow-volume curves are presented in Figure 2. Both expressions present the same data but in a different format. The advantage of the volume-time convention is that the FEV_1 and FVC can be directly visualized. The advantage of the flow-volume display is that the peak flow can be directly visualized as an indication of a good expiratory effort. Clinicians should be comfortable using either form of expiratory airflow recording. Examples of normal flow volume and time-volume curves are presented in Figure 2 (A&B). Examples of mild, moderate,

Table 1. Common Obstructive Ventilatory Disorders

Asthma

Asthmatic bronchitis

Chronic obstructive bronchitis

Chronic obstructive pulmonary disease*

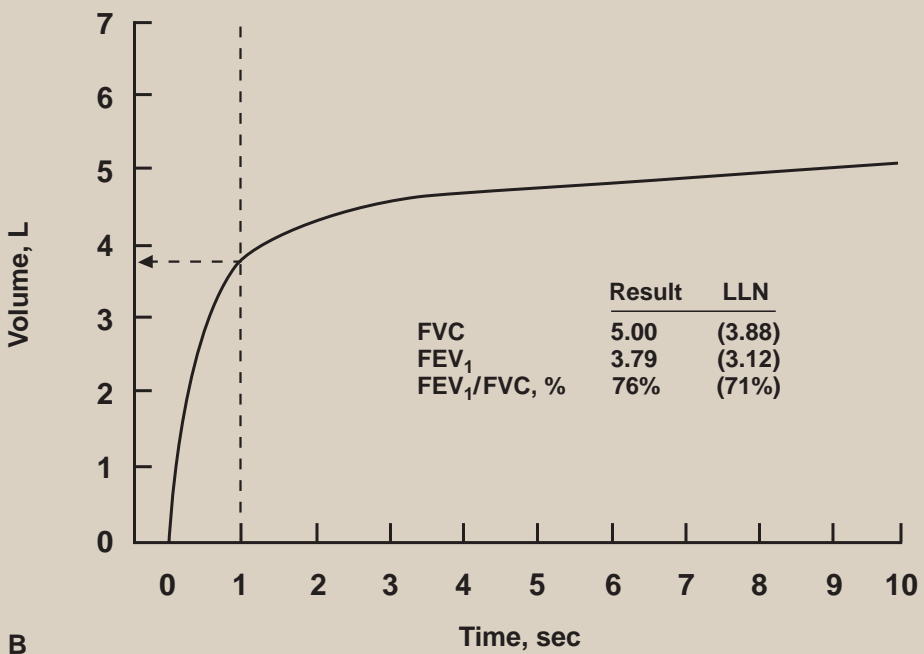
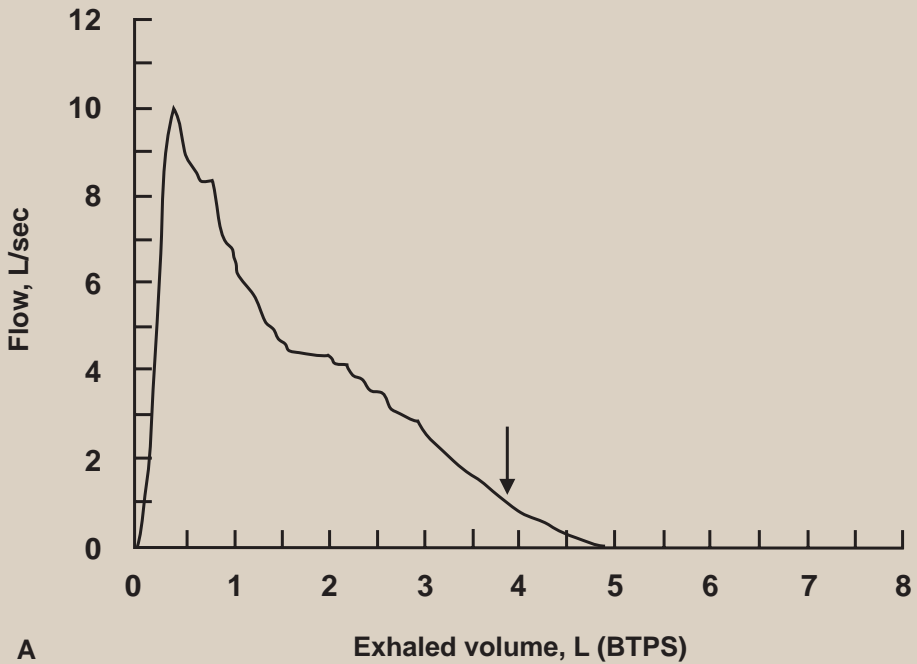
Cystic fibrosis

Emphysema

*This is a generic term that includes asthmatic bronchitis, chronic bronchitis, bronchiectasis, and emphysema. These states commonly overlap.

Adapted with permission from Petty TL. *Simple Spirometry for Frontline Practitioners*. Fairfield, NJ: Laennec Publishing Inc; 1998:18.

Figure 2. Normal Volume-time and Flow-volume Curves



BTPS indicates body temperature pressure saturated; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; LLN, lower limits of normal.

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and severe expiratory airflow obstruction are shown in Figures 3, 4, and 5.

Restrictive Ventilatory Disorders

In restrictive ventilatory disorders, the FVC (or FEV₆) is <80% of predicted, and the ratio of FEV₁/FVC is usually >70%, often >80%, 90%, or even higher. Examples of moderate and severe ventilatory restriction are presented in Figures 6 and 7. The common restrictive ventilatory defects are listed in Table 2.

Inspiratory flow obstruction will suggest vocal cord dysfunction, tracheal tumors, or tracheal stenosis, which sometimes follows intubation. A few other rare conditions result in inspiratory airflow obstruction. When these conditions are believed to be present, consultation with a pulmonologist and/or an otolaryngologist is advised.

Algorithm for Interpretation of Spirometry

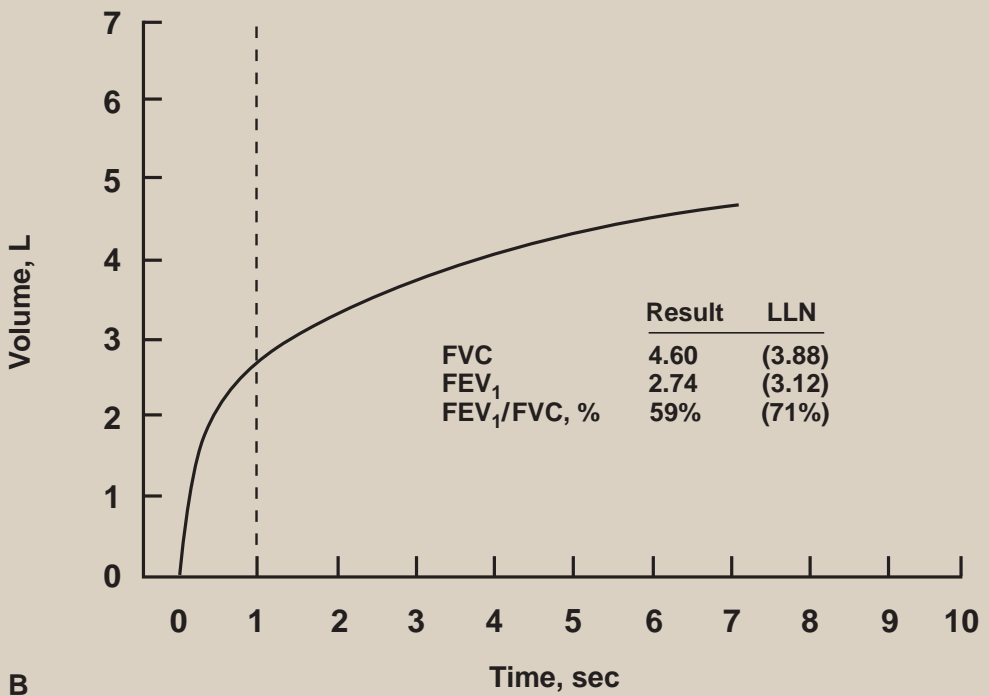
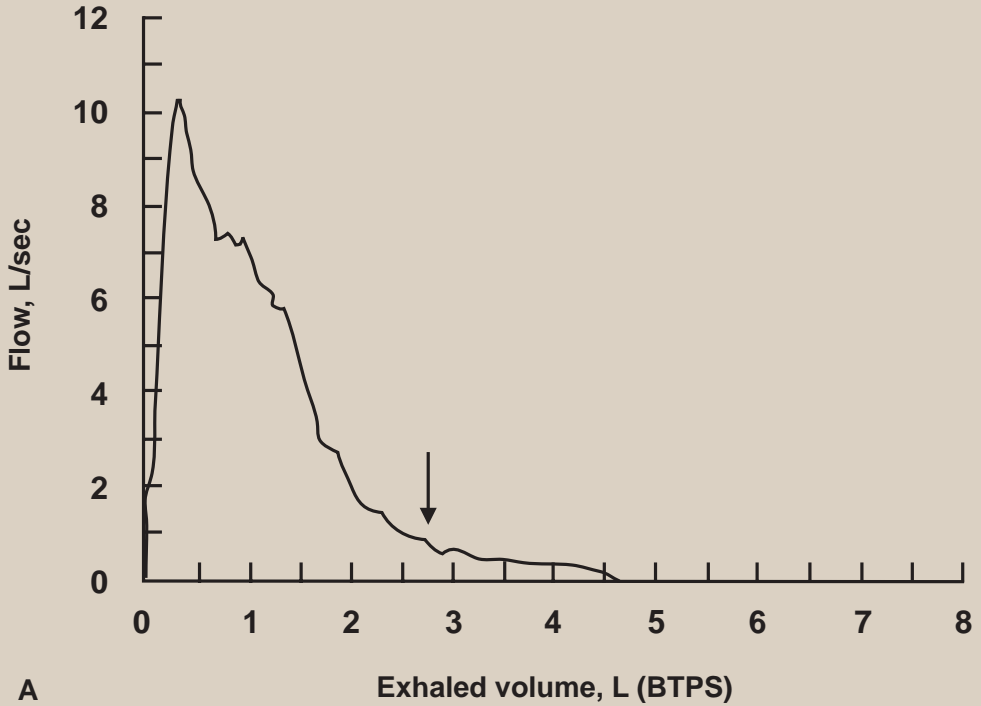
A simple algorithm for identifying restrictive and obstructive ventilatory disorders is shown in Figure 8. Lung volume measurements may be needed to adequately evaluate restrictive pulmonary disease states.

Spirometry and Clinical Diagnosis

It should be stressed that spirometric measurements do not make a clinical diagnosis. Spirometric abnormalities indicate a physiological impairment, very much like blood pressure (BP), blood urea nitrogen, creatinine, etc., from which the physician must derive the diagnosis. It has been traditional to label reversible airflow obstruction as asthma and irreversible airflow disorders as chronic obstructive pulmonary disease (COPD). Overlaps are common. Responses to therapy, including the use of bronchoactive drugs (e.g., bronchodilators, corticosteroids, and other new agents), will help determine how to establish the diagnosis of reversibility or irreversibility. Consultation is advised in complex situations.

(continued)

Figure 3 Mild Expiratory Airflow Obstruction



BTPS indicates body temperature pressure saturated; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; LLN, lower limits of normal.

Figure 4. Moderate Expiratory Airflow Obstruction

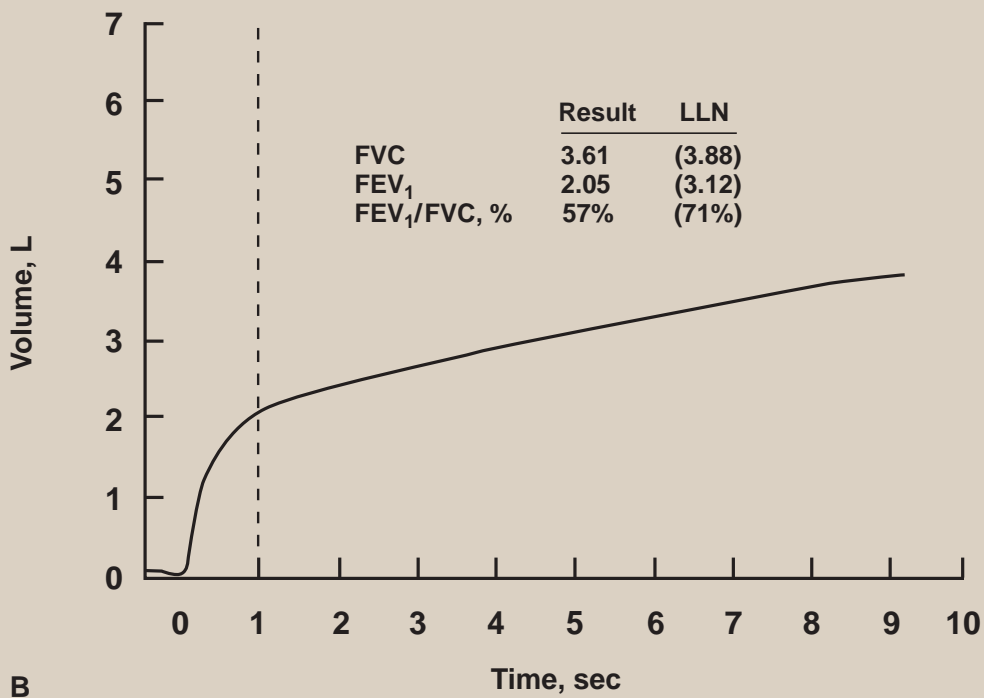
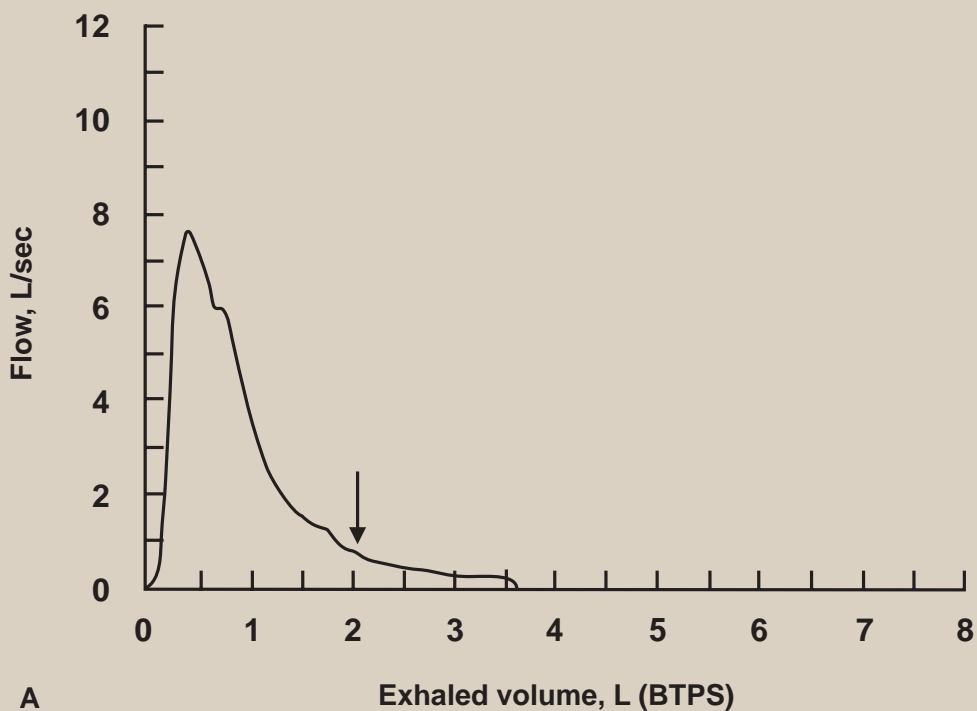
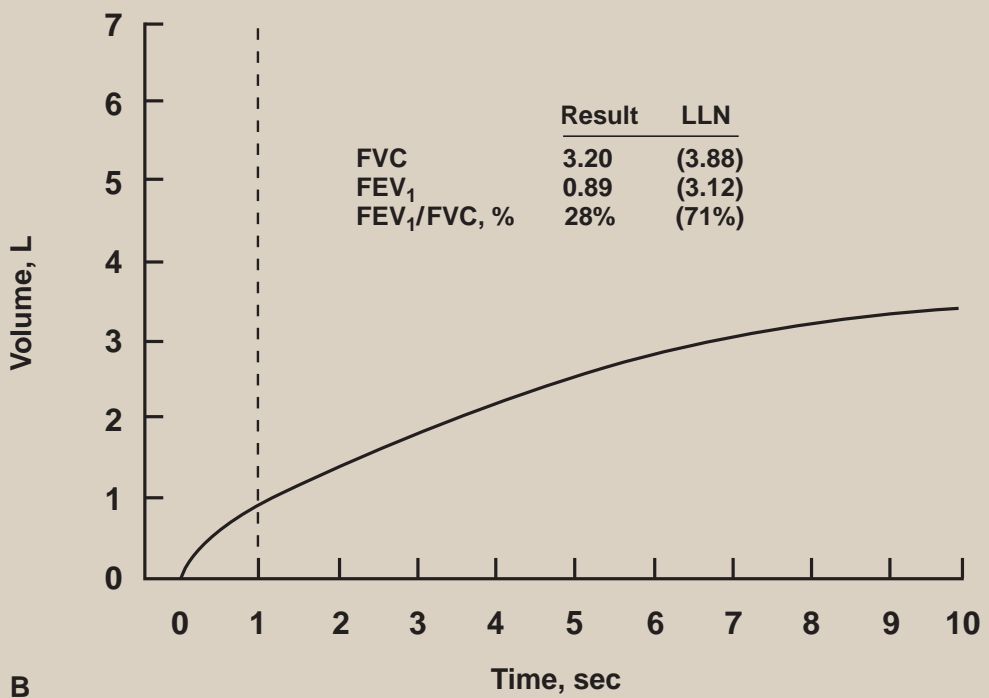
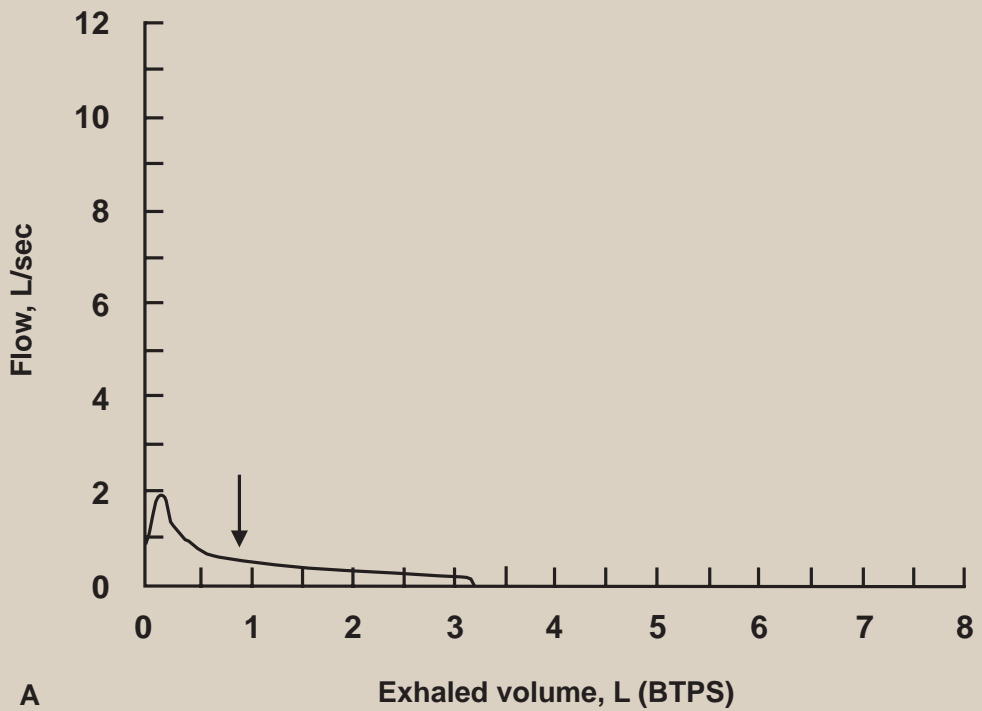


Figure 5. Severe Expiratory Airflow Obstruction



BTPS indicates body temperature pressure saturated; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; LLN, lower limits of normal.

Figure 6. Moderate Ventilatory Restriction

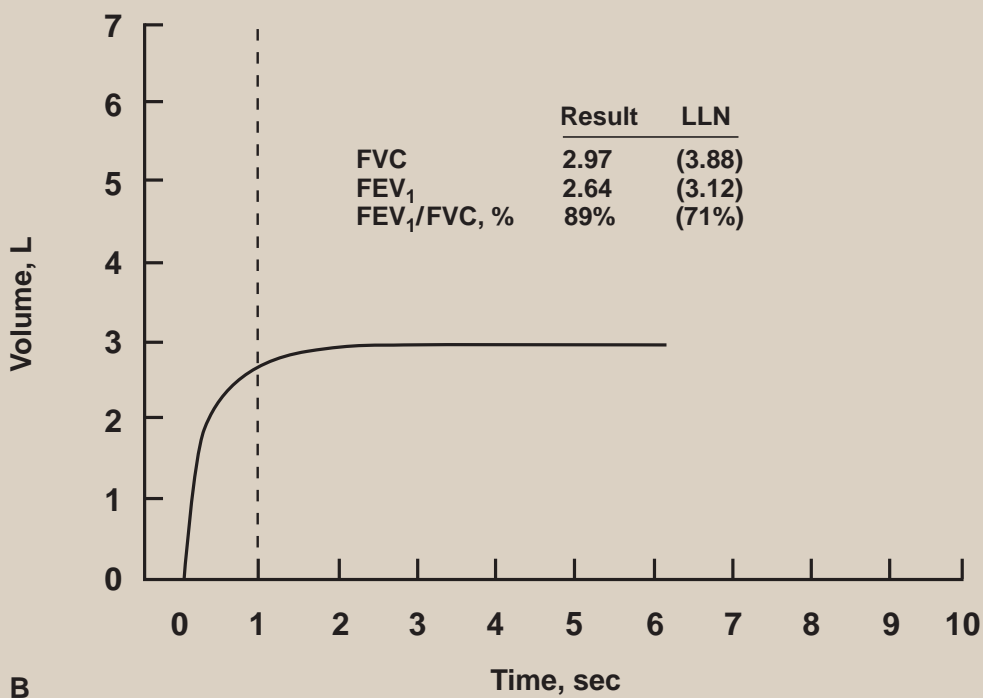
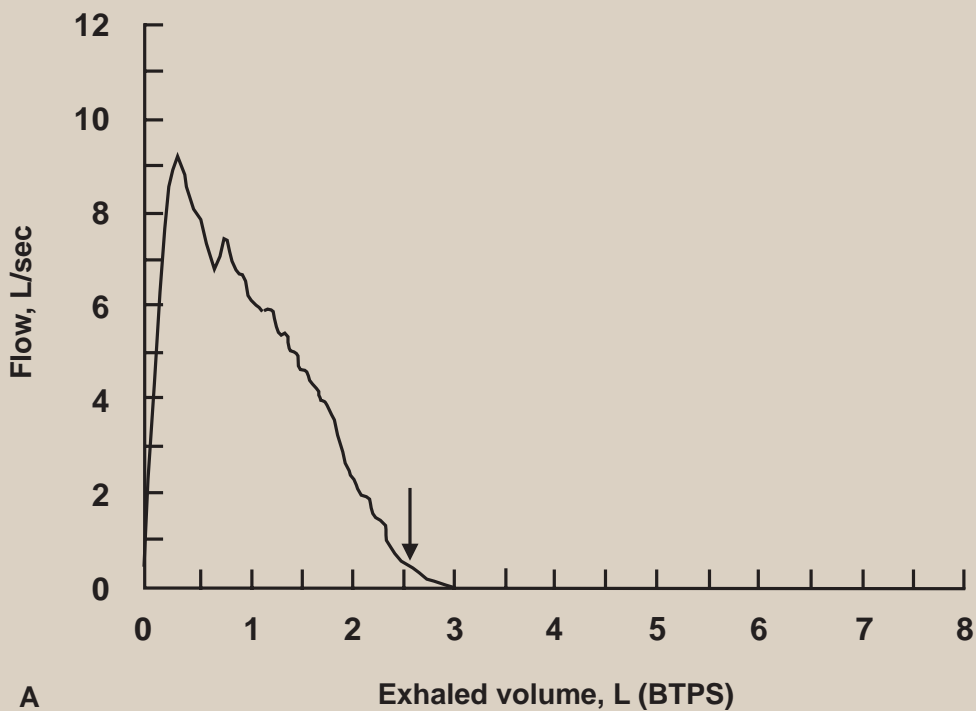
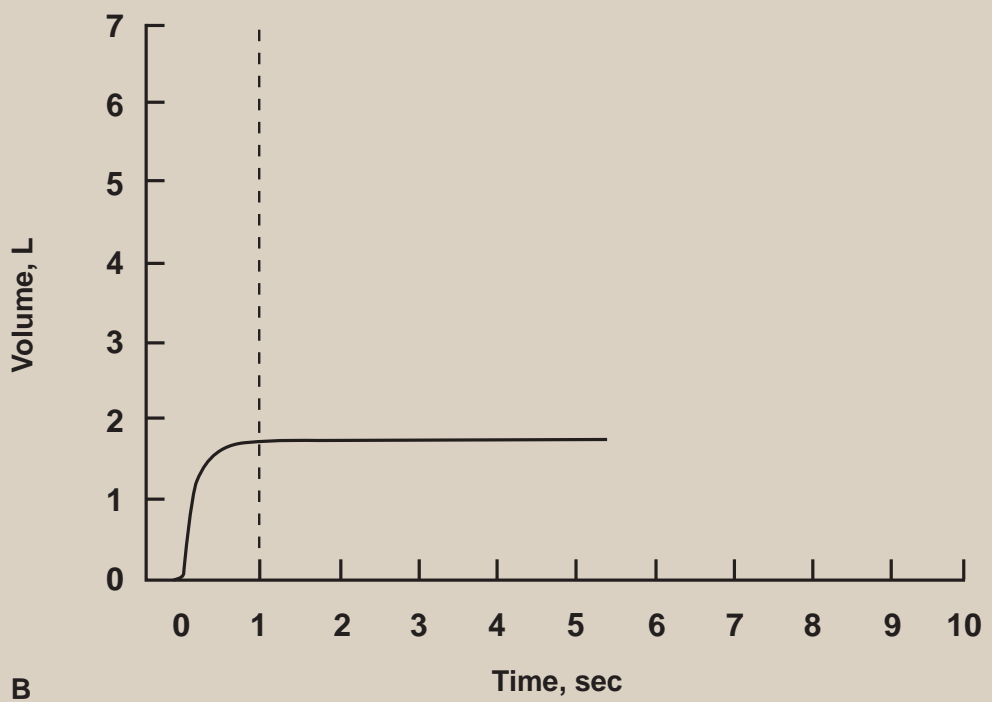
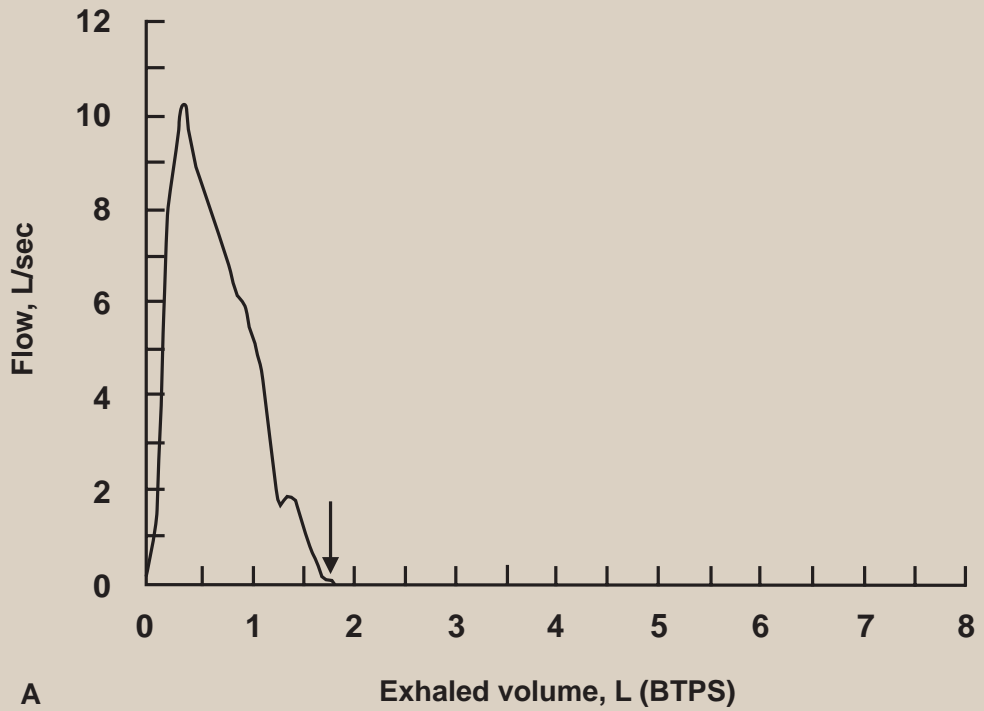


Figure 7. Severe Ventilatory Restriction



BTPS indicates body temperature pressure saturated; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; LLN, lower limits of normal.

Table 2. Common Restrictive Ventilatory Disorders

Interstitial pneumonitis and fibrosis*

Fibrotic residue of disseminated granulomas (e.g. tuberculosis, histoplasmosis)

Sarcoidosis

Thoracic deformities

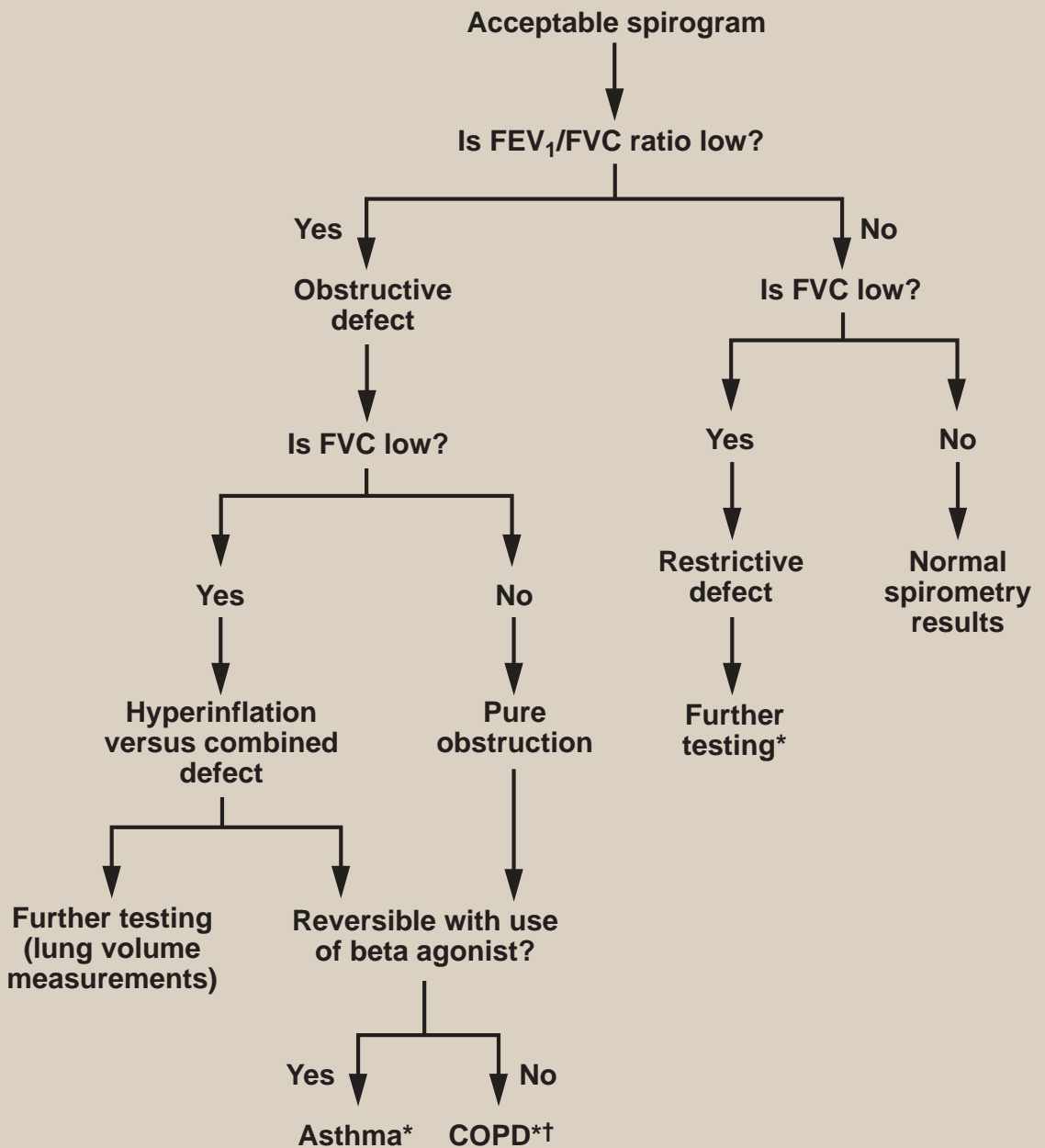
Congestive heart failure (CHF)

Neuromuscular disorders

*Associated with drug reactions, such as to bleomycin (Blenoxane®), or with occupational exposures (e.g., asbestosis) or with collagen diseases (e.g., rheumatoid arthritis).

Adapted with permission from Petty TL. *Simple Spirometry for Frontline Practitioners*. Fairfield, NJ: Laennec Publishing Inc; 1998:18.

Figure 8. Algorithm for Identifying Restrictive and Obstructive Ventilatory Disorders



*If clinical correlation present.

†Some cases of chronic obstructive pulmonary disease (COPD) may have a reversible component.

Table 3. High-Risk Diseases Associated With Spirometric Abnormalities

Disease State	Reference
Heart attack	<i>J Chron Dis.</i> 1987;40:849-856. <i>Am J Respir Crit Care Med.</i> 1995;151:390-398.
Lung cancer	<i>Ann Intern Med.</i> 1986;105:503-507. <i>Am Rev Respir Dis.</i> 1990;141:613-617.
Stroke	<i>Brit Med J.</i> 1991;302:84-87.
Chronic obstructive pulmonary disease	<i>Am Rev Respir Dis.</i> 1987;135:788-793.
All-cause mortality	<i>Am J Epidemiol.</i> 1994;140:398-408.

Spirometric abnormalities are predictive of increased risk of many diseases and all-cause mortality. The major diseases related to spirometric abnormalities are listed in Table 3, with citations. Note that heart attack, lung cancer, stroke, and COPD are the four most common causes of death!

Prognostic Value

No doctor would prescribe antihypertensive agents without BP measurements, antiarrhythmics without evidence of cardiac rhythm disturbances, insulin without measurements of blood sugar, or warfarin without prothrombin measurements. It is, therefore, not prudent to treat obstructive or restrictive lung diseases without spirometry. Spirometry is as fundamental to the diagnosis and management of pulmonary diseases as the sphygmomanometer is to the assessment and management of hypertension.

According to the Spirometry Committee of the National Lung Health Education Program (NLHEP), all smokers over the age of 45 and individuals of any age with symptoms of dyspnea, mucus hypersecretion, or wheeze should have spirometry. The NLHEP aims to identify COPD and related diseases in their early stages in primary care physicians' offices. Whereas there are approximately 9,000 board-certified pulmonologists in North America, there are approximately 220,000 primary care providers. Every year, these professionals see at least 70% of the 47,000,000 smokers in the United States for some medical problem. Of course, all smokers should be strongly advised to stop, and those who have already developed signs of airflow abnormalities have an additional urgent need to stop—to help prevent future problems. ■

References

Anthonisen NR, Connett JE, Kiley JP, et al. Effects of smoking intervention and the use of an inhaled anticholinergic bronchodilator on the rate of decline of FEV₁: the Lung Health Study. *JAMA*. 1994;272: 1497-1505. This landmark study showed an improvement in FEV₁ and a gradual decline in FEV₁ over 5 years when patients stopped smoking. Subjects who continued to smoke lost FEV₁ at a much faster rate.

Burrows B, Knudson RJ, Camilli AE, et al. The “horse-racing effect” and predicting decline in forced expiratory volume in one second from screening spirometry. *Am Rev Respir Dis*. 1987;135:788-793. This study demonstrated that a rapid rate of decline in FEV₁ was predictive of premature mortality from COPD.

Ferguson GT, Enright PL, Buist AS, et al. Office spirometry for lung health assessment in adults: a consensus statement from the National Lung Health Education Program. *Chest*. 2000;117:1146-1161. This NLHEP consensus statement recommends testing all smokers over the age of 45 and anyone with dyspnea, cough, mucus hypersecretion, or wheeze.

Hankinson JL, Odencrantz JR, Fedan KB. Spirometric reference values from a sample of the general US population. *Am J Respir Crit Care Med*. 1999; 159:179-187. These latest normal values were derived from the third National Health and Nutrition Examination Survey (NHANES III), which includes an explanation of the reason that the FEV₆ is a surrogate for the FVC.

Lange P, Nyboe J, Appleyard M, et al. Ventilatory function and chronic mucus hypersecretion as predictors of death from lung cancer. *Am Rev Respir Dis.* 1990;141:613-617. This is one of several studies that documents an increased prevalence of lung cancer in smokers with airflow obstruction.

Rodriguez BL, Masaki K, Burchfiel C, et al. Pulmonary function decline and 17-year total mortality: the Honolulu Heart Program. *Am J Epidemiol.* 1994; 140:398-408. This report relates abnormal lung function to premature deaths from all causes.

Skillrud DM, Offord KP, Miller RD. Higher risk of lung cancer in chronic obstructive pulmonary disease: a prospective, matched, controlled study. *Ann Intern Med.* 1986;105:503-507. This study documents a much higher prevalence of lung cancer in smokers with airflow obstruction compared with those who smoke with equal intensity and have the same occupational risk and a similar family history of lung cancer but who have normal airflow.

Sorlie P, Lakatos E, Kannel WB. Influence of cigarette smoking on lung function at baseline and at follow-up in 14 years: the Framingham Study. *J Chronic Dis.* 1987;40:849-856. This study demonstrates a relationship between spirometric abnormalities and premature death from coronary artery disease.

Strachan DP. Ventilatory function as a predictor of fatal stroke. *Brit Med J.* 1991;302:84-87. This summary documents an increased risk of stroke in smokers with airflow obstruction.

(continued)

C. Office Evaluation of the Patient: Initial Studies—Spirometry (*continued*)

Swanney MP, Jensen RL, Crichton DA, et al. FEV₆ is an acceptable surrogate for FVC in the spirometric diagnosis of airflow obstruction and restriction. *Am J Respir Crit Care Med.* 2000;162:917-919. The reproducibility of FEV₆ was superior to the FVC. The FEV₆ is an accurate and reliable surrogate for FVC in the spirometric assessment of ventilatory disorders.

Tockman MS, Pearson JD, Fleg JL, et al. Rapid decline in FEV₁: a new risk factor for coronary heart disease mortality. *Am J Respir Crit Care Med.* 1995; 151:390-398. This article shows evidence that rapid decline of FEV₁ is predictive of excess risk of death from coronary artery disease.

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Studies**

**Arterial Blood
Gases (ABGs)**

In patients with dyspnea, especially those with pulmonary abnormalities such as acute and chronic bronchitis, emphysema, infections, asthma, or left ventricular (LV) disease leading to congestive heart failure, arterial hypoxemia may be present. Most often, the arterial hypoxemia in these disease entities is due to ventilation-perfusion (\dot{V}/\dot{Q}) mismatch. In patients with an atrial septal defect (ASD) or pulmonary arteriovenous malformations, right to left shunt ($\dot{V}/\dot{Q} = 0$) may be the major reason for arterial hypoxemia. Other pulmonary diseases such as sarcoidosis and idiopathic pulmonary fibrosis (IPF) may be associated with arterial hypoxemia due either to a \dot{V}/\dot{Q} mismatch, a diffusion abnormality, or both.

If hypercapnia accompanies arterial hypoxemia, alveolar ventilation is reduced. Entities associated with this combination include an exacerbation of chronic obstructive pulmonary disease (COPD) and severe acute asthma. Less common entities include those conditions affecting respiratory center function (e.g., strokes, drug ingestions, tumors) or primary hypoventilation syndrome. Additional causes of hypercapnia include spinal cord disease, neuromuscular diseases (e.g., myasthenia gravis), or muscular disorders (e.g., muscular dystrophy).

Complete Pulmonary Function Studies. Pulmonary function tests (PFTs) are indicated to determine whether dyspnea is due to diseases of the lung and/or respiratory muscles or the cardiovascular system. Spirometry, lung volumes, and diffusion capacity measurements should be obtained as the initial tests to determine whether an obstructive or restrictive ventilatory defect, or both, are present, and to quantify the degree of impairment. In addition, to assess the gas-exchange function of the lungs, arterial blood gases (ABGs) are indicated. If tests of mechanical function are within normal limits, further evaluation should be done to rule out pulmonary

D. Office Evaluation of the Patient: Additional Studies *(continued)*

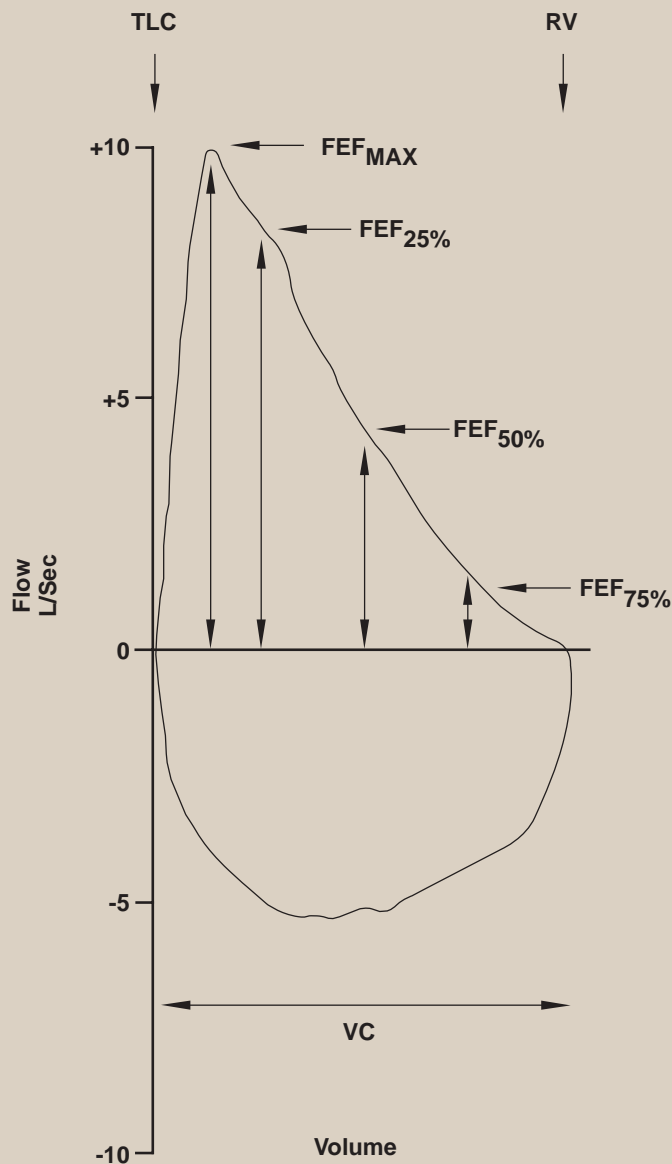
vascular, neuromuscular, or cardiovascular causes of dyspnea. Such evaluations may include cardio-pulmonary exercise testing, bronchoprovocation testing, and measurements of diaphragmatic strength and endurance.

Flow-volume Loops. Flow-volume loops are frequently reported as part of simple spirometric testing (see Figures 9 and 10 and Section C). However, they provide the same information as conventional spirometry, which expresses volume over time. Flow-volume curves express this information in a different way (see also Section C). The shape of the expiratory limb of the curves may be characteristic of either obstructive or restrictive disease. The flow-volume loop may also detect patient-induced artifacts caused by improper inspiratory and/or expiratory maneuvers, such as coughing during expiration.

In individuals with an obstructive ventilatory defect, the expiratory flow-volume curves are coved with respect to the x axis (volume), and the vital capacity (VC) is reduced (see Figure 10A and 10B). Assessing the shape of the flow-volume curve and the flows in inspiration and expiration (see Figure 10C) can make a diagnosis of upper airway obstruction. In contrast, in patients with restrictive disease, the expiratory flow-volume curve appears compressed relative to normal curves, and the VC is also reduced (see Figure 10D). A flat expiratory limb, a reduced peak flow, and a normal inspiratory limb suggest an intrathoracic airway obstruction, such as an intratracheal neoplasm. A flat inspiratory limb in association with reduced inspiratory flow is suggestive of an extrathoracic obstruction, as might be seen with a vocal cord neoplasm.

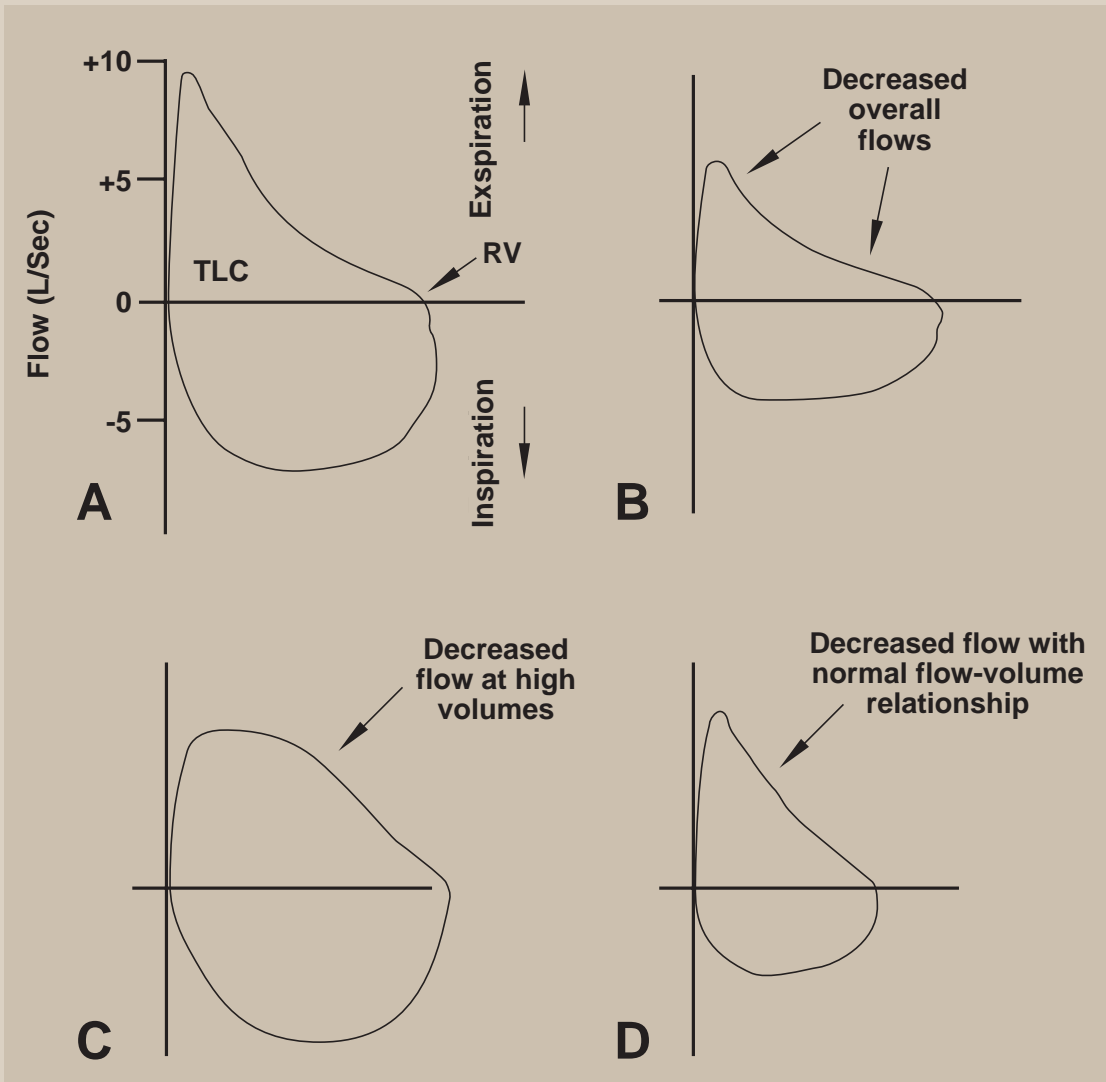
Response to Bronchodilator. Increases in forced vital capacity (FVC) and forced expiratory volume in 1

Figure 9. Normal Flow-volume Loop



A typical flow-volume loop from a normal subject showing both expiratory (upper) and inspiratory (lower) portions. Instantaneous flows (forced expiratory flow [FEF]) may be measured after 25% ($FEF_{25\%}$), 50% ($FEF_{50\%}$), and 75% ($FEF_{75\%}$) of the vital capacity (VC) has been exhaled. The peak flow is easily measured as the value of the peak of the graph. The measurements offer no advantages over the forced expiratory volume in 1 second (FEV_1), the forced vital capacity (FVC), and the FEV_1/FVC ratio, however. RV indicates residual volume; TLC, total lung capacity. (Reproduced with permission from Light RW. Clinical pulmonary function testing, exercise testing, and disability evaluation. In: George RB, Light RW, Matthay MA, Matthay RA, eds. Chest Medicine. 4th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2000:93.)

Figure 10. Abnormal Flow-volume Loops



Common examples of abnormal flow-volume loops. A, Mild obstructive airway disease characterized by decreased flow at low lung volume when elastic support is reduced. B, Significant obstructive airway disease characterized by decreased overall flows with a further decrease at low lung volumes. C, Variable intrathoracic large airway obstruction in which peak flow is decreased at higher lung volumes with preservation of normal flow-volume relationship at lower lung volumes. D, Restrictive pulmonary disease with decreased VC and flows, but preservation of normal flow-volume relationships. (Reproduced with permission from Light RW. Clinical pulmonary function testing, exercise testing, and disability evaluation. In: George RB, Light RW, Matthay MA, Matthay RA, eds. Chest Medicine. 4th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2000:93.)

second (FEV₁) of >12% following two inhalations of a bronchodilator are good evidence that reversible bronchoconstriction is present.

Lung Volume Measurements. The presence of a restrictive ventilatory defect is based upon the lung volume measurement termed total lung capacity (TLC). If the TLC is reduced below 80% of predicted, a restrictive ventilatory defect is present, and the degree of restriction is assessed by the degree of reduction in TLC (see Table 4). In the absence of a TLC measurement, a reduction in the FVC without a reduction in the FEV₁/FVC ratio by spirometry suggests the presence of a restrictive ventilatory defect. Interstitial lung diseases such as IPF and sarcoidosis often cause a restrictive ventilatory defect.

In patients with obstructive lung disease (e.g., asthma or emphysema), there are also frequently abnormalities in lung volumes. The VC may be normal but is often reduced, and both the residual volume (RV) and the RV/TLC ratio will be significantly increased as the result of air trapping due to the increased airway resistance.

Diffusion Capacity. The diffusion capacity measurement assesses the conductance of the alveolar-capillary membrane for a test gas, which is almost always carbon monoxide (CO). This gas is used because its partial pressure in blood is zero due to its high affinity for hemoglobin, whereas the PO₂ in the pulmonary capillaries varies. The diffusing capacity for carbon monoxide (DLCO) is the amount of CO driving pressure (mL/min/mm Hg) that diffuses across the alveolar-capillary membrane. The DLCO is dependent on age, body size, lung volume, hemoglobin concentration, and the presence of carboxyhemoglobin and changing body position. The DLCO is reduced in diseases that affect the interstitium of the lung because the alveolar-capillary membrane is reduced in total

Table 4. Example of Criteria for Assessing the Severity of Abnormalities*

A. Normal: The test is interpreted as “within normal limits” if both the VC and the FEV₁/VC are in the normal range.

B. Obstructive abnormality: This is interpreted when the FEV₁/FVC is below the normal range. The severity of the abnormality might be graded as follows:

May be a physiological variant	% Pred FEV ₁ 100
Mild	% Pred FEV ₁ <100 and 70
Moderate	% Pred FEV ₁ <70 and 60
Moderately severe	% Pred FEV ₁ <60 and 50
Severe	% Pred FEV ₁ <50 and 35
Very severe	% Pred FEV ₁ <35

C. Restrictive abnormality: This is most reliably interpreted on the basis of TLC. If this is not available, one may interpret a reduction in the VC without a reduction of the FEV₁/VC ratio as a “restriction of the volume excursion of the lung.” The severity of the abnormality might be graded as follows:

Based on the TLC

Mild	% Pred TLC <LLN but 70
Moderate	% Pred TLC <70 and 60
Moderately severe	% Pred TLC <60

Based on spirometry

Mild	% Pred VC <LLN but 70
Moderate	% Pred VC <70 and 60
Moderately severe	% Pred VC <60 and 50
Severe	% Pred VC <50 and 34
Very severe	% Pred VC <34

FEV₁ indicates forced expiratory volume in 1 second; FVC, forced vital capacity; LLN, lower limits of normal; Pred = predicted; TLC, total lung capacity; VC, vital capacity.

*This schema was contributed by Burrows and Lebowitz. It has been in use in the lung function laboratory at the Health Sciences Center in Tucson, Arizona, for clinical purposes. It is intended only as an example of a transparent schema for assessing severity. Other schema may also be acceptable. More work is required before any schema can be adopted as a standard. **Note:** All statements regarding severity should be accompanied by a disclaimer such as “as assessed by spirometry” or “physiologic assessments of severity may differ from clinical assessments.”

Reproduced with permission from American Thoracic Society. Lung function testing: selection of reference values and interpretative strategies. *Am Rev Respir Dis.* 1991;144:1213. (Table 13.)

area and/or because the thickness of the membrane is increased. The test is more sensitive to mild idiopathic lung disease (ILD) than measurements of lung volumes. The DLCO is useful for confirming the diagnosis and following the progression of the disease, on or off therapy. The DLCO is also reduced in patients with alveolar wall destruction from any cause (e.g., emphysema) and helps confirm this diagnosis in an individual with the appropriate clinical history, physical examination, chest radiographic findings, and other pulmonary function abnormalities such as an obstructive ventilatory defect. Disease processes that affect the pulmonary vasculature (e.g., pulmonary thromboemboli) also reduce the DLCO.

Bronchoprovocation Testing. In patients with dyspnea and normal spirometry and lung volumes, in whom hyperreactive airways disease is suspected, bronchoprovocation testing may be helpful. Patients being considered for bronchoprovocation testing should be seen by a pulmonologist or an allergist/immunologist who performs the test. Individuals are exposed to increasing doses of inhaled methacholine or histamine or to specific antigens or chemicals (e.g., toluene diisocyanate). Measurements are made every 3 to 5 minutes after the inhalation, and the results are compared to flow decrements noted after inhalational challenges of saline. A 20% decrement in FEV₁—or PD₂₀ (for “provocative dose” of methacholine)—at a dose of <10 mg should occur for a test to be positive. This response is considered nonspecific in that patients without symptoms of asthma also will respond to methacholine with a decrease in airflow. Accordingly, the test should be interpreted with caution.

Tests of Respiratory Muscle Function. In patients in whom diaphragmatic and accessory muscle function is potentially impaired and a contributing factor to their dyspnea (e.g., patients with

D. Office Evaluation of the Patient: Additional Studies *(continued)*

hypothyroidism or phrenic nerve injuries), tests of respiratory muscle function may be useful in delineating the respiratory muscle effects of these disorders. The maximum inspiratory pressure ($P_{i_{max}}$) measures the strength of diaphragmatic contraction. This test is performed by having a subject inhale to TLC and perform a forced expiration to the residual volume. The pressure developed at the mouth is then measured while the patient inspires against an occluded valve. Healthy subjects should generate a pressure > -60 cm H_2O , while patients with diaphragmatic impairment will generate pressures in the -20 to -60 cm H_2O range. The $P_{i_{max}}$ generated also depends on sex, age, height, and weight. The maximum expiratory pressure ($P_{e_{max}}$) measures the strength of muscles of expiration and is performed by having the subject inspire from the residual volume to TLC. Then the pressure developed at the mouth is measured while forced expiration is performed against an occluded valve. This test is abnormal in patients with decreased diaphragm and accessory muscle strength from any cause (e.g., myopathies and neuropathies).

The maximum transdiaphragmatic pressure ($P_{di_{max}}$) measurement is a definitive technique to assess diaphragmatic function. This invasive technique necessitates placement of an intra-esophageal balloon to measure pleural pressure and the simultaneous placement of a gastric balloon to measure intra-abdominal pressure. The difference between these pressures is the transdiaphragmatic pressure (P_{di}). Usually, the measurement is made at functional residual capacity.

Echocardiography. Echocardiography is a powerful noninvasive tool that can detect or exclude pulmonary hypertension (PH) and most cardiac causes of dyspnea. The major exception is transient myocardial ischemia, but this also can be detected in most patients when

echocardiography is combined with exercise or pharmacologic stress.

General categories of disorders associated with dyspnea that can be detected and evaluated by echocardiography are summarized in Table 5. Modern echocardiography is useful across this broad range of disorders because it combines several techniques that together allow comprehensive assessment of cardiac structure and function.

Two-dimensional and M-mode imaging allow direct visualization of cardiac chambers and great vessels, including measurement of dimensions and wall thicknesses throughout the cardiac cycle. Doppler color flow imaging superimposes computerized representation of blood flow patterns on two-dimensional images, using colors to denote flow direction and velocity. Quantitative analysis of continuous-wave and pulsed Doppler signals provides additional information on flow patterns at specific locations and allows estimation of pressure gradients across valves and other cardiac structures due to a predictable relationship between flow velocity and the pressure gradient providing the driving force for flow.

Two-dimensional imaging allows direct assessment of global LV systolic function and regional wall-motion. A normal ejection fraction excludes chronic LV systolic dysfunction as a cause of dyspnea. The presence of a regional wall-motion abnormality suggests underlying coronary artery disease and the possibility that dyspnea is an angina equivalent. A new wall-motion abnormality when echocardiography is repeated after exercise or pharmacologic stress is evidence of physiologically important coronary disease. Although not specific, certain mitral inflow velocity patterns are associated with impaired LV relaxation and decreased compliance and suggest the possibility of LV diastolic dysfunction. In addition, clinically important diastolic

Table 5. General Causes of Dyspnea Detectable by Echocardiography

Left ventricular (LV) systolic dysfunction
LV diastolic dysfunction
Aortic and mitral valve disease
Congenital heart disease
Tumors
Pericardial diseases
Pulmonary hypertension
Myocardial ischemia

dysfunction usually occurs in association with increased LV wall thicknesses, which can be detected reliably by two-dimensional and M-mode imaging. Left atrial enlargement in the absence of LV systolic dysfunction, significant valvular disease, or other structural abnormalities is another potential clue to the presence of LV diastolic dysfunction.

Aortic and mitral valve disease can be evaluated thoroughly with combined imaging and Doppler techniques. Valve gradients and effective orifice areas can be determined for stenotic lesions. Color flow imaging allows semiquantitative assessment of mitral regurgitation and aortic insufficiency. In addition, echocardiography can help assess the physiologic importance of aortic and mitral valve disease by determining whether there is left atrial enlargement or evidence of significant LV pressure or volume overload, as indicated by LV enlargement or hypertrophy, respectively.

Two-dimensional imaging also allows detection of congenital structural abnormalities, pericardial effusions and thickening, and tumors that compress cardiac structures or obstruct LV inflow or outflow. Color flow imaging can detect intracardiac shunts and estimate their magnitude and the direction of shunt flow.

Finally, quantitative Doppler techniques can detect or exclude PH in the majority of patients because even normal subjects typically have a small or physiologic degree of tricuspid regurgitation. The tricuspid regurgitant flow velocity signal reflects the pressure gradient between the right ventricle and atrium during systole. As a result, adding an estimate of central venous pressure to the measured tricuspid regurgitant gradient can approximate right ventricular systolic pressure. Two-dimensional imaging also may reveal consequences of PH, such as right ventricular

D. Office Evaluation of the Patient: Additional Studies *(continued)*

enlargement and hypokinesis, significant tricuspid regurgitation, and right atrial enlargement.

Studies Used to Diagnose Venous Throm- boembolism (VTE)

Establishing a diagnosis of venous thromboembolism (VTE) remains a challenge for physicians. In the clinical setting of dyspnea, pleuritic chest pain, and hypoxemia, many studies may suggest a diagnosis of VTE (e.g., new right-axis deviation, right bundle branch block, wedged-shaped pulmonary infiltrate, and elevation of d-dimer products), but none confirm it.

Currently, the four most commonly used studies to document VTE include:

1. Noninvasive vascular assessment (NIVA) of the lower extremities by ultrasound and impedance plethysmography;
2. Ventilation-perfusion (\dot{V}/\dot{Q}) scan;
3. Spiral (helical) computed tomography (CT);
4. Pulmonary angiography; and
5. High-resolution CT scanning.

When clinical suspicion of deep venous thrombophlebitis (DVT) exists, lower-extremity ultrasound with color Doppler allows for the diagnosis of acute DVT, flow abnormalities, and an evaluation of chronic venous insufficiency. When pulmonary signs and symptoms exist, additional imaging is necessary.

For years, \dot{V}/\dot{Q} scans have been the most commonly used initial study to diagnose VTE. Unless the lung scan is normal or there is high probability in conjunction with high clinical suspicion, considerable doubt exists about the presence or absence of pulmonary embolism. In the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) trial, almost 705 patients had nondiagnostic studies. Those with chronic lung disease and those with abnormal chest x-rays (CXRs) will have abnormal scans, which are usually nondiagnostic, thus limiting the usefulness of \dot{V}/\dot{Q} scanning in these patients.

The recent development and widespread availability of spiral CT technology with the addition of intravenous (IV) contrast allows for direct visualization of the pulmonary vasculature and is an excellent method for assessing patients with suspected acute and chronic thromboembolic disease. In contrast to conventional CT scans that produce a single axial image, the spiral technique computes a helical volume of data over the entire thorax in seconds. Rather than viewing static images, the radiologist is able to dynamically scan serial computer images and identify thrombi at the segmental and subsegmental level.

In many institutions that have spiral CT technology, this study has replaced the \dot{V}/\dot{Q} scan as the initial diagnostic study for PE in patients who are critically ill (e.g., patients on ventilators), have chronic lung disease, or have abnormal CXRs. The \dot{V}/\dot{Q} scan remains the initial study of choice for stable patients with normal CXRs and without chronic lung disease.

Occasionally, even after NIVA, \dot{V}/\dot{Q} scans, and spiral CT are completed, doubt may exist about the presence or absence of PE. In this situation, pulmonary angiography should be performed as the final deciding test.
(continued)

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Conventional and spiral CT scans provide excellent anatomical definition of the thorax and its structures. The addition of IV contrast allows blood vessels and other vascular structures to be differentiated from nonvascular structures such as mediastinal nodes, masses, and soft tissue densities. With conventional CT scanning, serial coronal images are taken every 8 to 10 mm from the apices to the bases of the lungs. Nodules, masses, infiltrates, atelectasis, pleural effusions, and lymphadenopathy are identified in much greater detail than with the CXR.

The high-resolution CT scan is a refinement of conventional CT scanning and provides extreme detail of the lung parenchyma. Because of this high resolution, it is extremely helpful in defining abnormalities of the lung parenchyma such as interstitial lung disease and emphysema. The key determinants contributing to the fine detail are narrow beam collimation (section thickness) and a high-spatial reconstruction algorithm. For routine high-resolution CT scanning, a section thickness of 1 to 1.5 mm is optimal. Table 6 provides the indications for the use of imaging techniques in evaluating dyspnea.

Cardio- pulmonary Stress Testing

Cardiopulmonary exercise testing may be helpful in patients with dyspnea on exertion in whom a history and physical examination, routine blood studies, chest radiograph, and routine PFTs have not provided an explanation. Among the entities identified with cardiopulmonary exercise testing are: cardiac diseases (e.g., ischemic heart disease), pulmonary diseases (e.g., reactive airways or interstitial lung disease), deconditioning and/or obesity, and those due to psychogenic causes (normal tests).

Stress Testing. Exercise testing is a generic term for the qualitative and quantitative evaluation of a subject's exercise performance. A variety of specific means of

Table 6. Imaging Techniques Used to Evaluate Dyspnea

Imaging Technique	Clinical Indication for Study
Chest x-ray (CXR)	All patients should have a CXR prior to other imaging techniques.
Computed tomography (CT) with contrast	Evaluates lung masses, nodules, hilar and mediastinal structures (including aorta), pleural disease, and pulmonary infiltrates.
CT without contrast	Used when the patient is allergic to contrast imaging. It is the follow-up procedure to determine the size of lung nodules.
High-resolution CT (HRCT)	Evaluates parenchymal lung disease such as interstitial lung disease, bronchiectasis, and emphysema.
Spiral CT with contrast	Evaluates for acute and chronic thromboembolic disease in patients with nondiagnostic lung scans, abnormal CXR, or chronic lung disease.
Low-radiation-dose CT	Screens high-risk patients (e.g., smokers with airflow obstruction) for lung cancer.

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assessing mechanisms of exercise limitation can be performed. Qualitative assessment may be as simple as watching a patient walk down a hall or up a flight of stairs. For patients who cannot walk without assistance, upright or supine bicycle ergometry or arm ergometry are alternative exercise methods.

For patients with significant cardiac or pulmonary conditions, exercise testing should involve electrocardiogram (ECG) and blood pressure (BP) monitoring and be performed by persons trained in cardiopulmonary resuscitation and exercise testing methods. Resuscitative devices, including a defibrillator, oxygen, and intubation equipment, should be readily available.

In order to evaluate exercise capacity, a graded form of exercise involving the large muscles of the legs, such as walking or cycling, is most often used. In clinical practice, a treadmill test employing a standard protocol, whereby speed and grade of walking are progressively increased, is the most common form of exercise testing. A variety of protocols that have been performed in large numbers of subjects and have become standardized are available. The Bruce protocol, for example, has been used in thousands of subjects with and without heart disease. The average exercise durations of age- and gender-specific cohorts are available.

Because exercise involves a stress on the cardiopulmonary system, there are absolute and relative contraindications to exercise testing.

Absolute contraindications to exercise testing include:

- Acute myocardial infarction within 2 days;
- Unstable angina;

- Uncontrolled symptomatic arrhythmia;
- Uncontrolled hyper- or hypotension;
- Decompensated heart failure;
- Severe symptomatic fixed cardiac output (aortic stenosis [AS], pulmonic stenosis, severe PH, etc.);
- Acute PE;
- Acute myocarditis or pericarditis; and
- Acute aortic dissection.

Relative contraindications to exercise testing include:

- Left main coronary stenosis;
- Severe electrolyte abnormalities;
- Severe hypertension;
- Tachycardic or bradycardic arrhythmias;
- Hypertrophic cardiomyopathy;
- High-grade atrioventricular block; and
- Mental or physical impairment that preclude exercising.

Graded exercise is often continued until the patient reaches his or her symptom limit, provided the care provider feels it is safe. This allows comparison of performance over time or against the nomograms of age- and gender-matched subjects.

Indications for terminating exercise testing include:

- Drop in systolic BP >10 mm Hg from baseline;
- Moderate or severe angina;
- Nervous system signs (ataxia, dizziness, or pre-syncope);
- Cyanosis or pallor;
- Technical difficulties with monitoring either BP or ECG;
- Sustained ventricular tachycardia;
- New ST segment elevation; and
- The patient's desire to stop.

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Relative indications for terminating exercise testing include:

- 2 mm ST depression;
- Arrhythmias other than sustained ventricular tachycardia;
- Fatigue, severe shortness of breath, leg cramps, or claudication;
- Development of conduction delay that cannot be distinguished from ventricular tachycardia;
- Increasing chest pain; and
- Hypertensive response to exercise (e.g., 220/110 mm Hg).

A standard exercise test report should include:

- The patient's exercise duration on a specific protocol;
- Rest and peak exercise heart rate and BP measurements;
- The patient's report of perceived exertion;
- Report of any cardiac arrhythmias; and
- Report of ECG changes with exercise, specifically ST segment depression or elevation.

These data allow for a quantitative description of severity of exercise limitation (if any). They also provide some information relative to cardiac pump function (ability to increase systolic pressure >30 mm Hg), myocardial O₂ demand (double the product of peak heart rate multiplied by the peak systolic pressure), and presence of myocardial ischemia (ST segment shifts).

Additional noninvasive observations particularly relevant to pulmonary mechanisms include recording of respiratory rate (RR) (as well as observation of ventilatory pattern and auscultation) and oximetry to assess SaO₂. Inappropriately high RR, a fall in SaO₂, and the development of wheezing all suggest

pulmonary limitation, whereas the development of rales raises the likelihood of left heart problems.

Exercise Exhaled Gas Measurements. Collection of the patient's exhaled gases, by means of a noseclip and tightly fitting mouthpiece, allows for measurement of O_2 consumption. This is a more objective measure of exercise capacity and has been used in training studies and assessment of heart failure patients, for example. Collection of exhaled gases also permits measurement of exercise ventilation that can be compared to maximum voluntary ventilation in the pulmonary function laboratory. A high ratio of exercise ventilation/maximum voluntary ventilation and a high RR at maximal exercise are two useful means of inferring predominantly ventilatory limitation to exercise. Relating the maximal O_2 consumption to the maximal heart rate (O_2 pulse) is another way of trying to determine if exercise limitation is predominantly circulatory or ventilatory.

Exercise Ventriculography. The left and right ventricles can be simultaneously visualized using either radionuclide imaging (see below) or two-dimensional echocardiography during or immediately following graded exercise testing. Both allow qualitative visual assessment of overall systolic function and regional wall-motion. Echocardiography requires adequate visualization (windows), which may be problematic in a hyperventilating patient, especially if obesity or hyperinflation impair resting visualization. Radionuclide imaging is less subject to such problems, but tissue imaging with echo may narrow some of that advantage. Both methods allow for quantitative calculations of ejection fractions (the fraction of maximal end-diastolic volume that is ejected with each beat). The normal response is for both ventricular ejection fractions to increase with symptom-limited exercise (either supine or upright), so failure to increase suggests some cardiac (left, right, or both)

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contribution to exercise limitation. Abnormal exercise systolic responses can accrue from myocardial (e.g., hypertensive cardiomyopathy), valvular (e.g., AS), or regional ischemia. The development of regional wall-motion abnormalities of the left ventricle is strong evidence for regional ischemia and even suggests specific coronary distribution(s).

Exercise Hemodynamic Studies. For more difficult cases, it may occasionally be helpful to perform exercise testing with direct hemodynamic monitoring. Monitoring could include right heart catheterization, arterial cannulation, or both. As emphasized in the previous contribution on cardiac catheterization, the risk and cost of such an approach needs to be balanced against the potential to help the patient. For example, if a patient had both mitral stenosis and emphysema, the finding of a marked increase in exercise pulmonary wedge pressure (PWP) would suggest that the mitral stenosis is important in causing the patient's dyspnea, thereby warranting consideration of either mitral valvuloplasty or valve replacement.

Summary of Exercise Testing in Evaluating Severity and Etiology of Dyspnea. Using either a treadmill or supine or upright bicycle ergometry, it is possible to compare a patient's graded exercise with performance of normal subjects on a particular protocol and to infer severity of limitation. Observation of heart rate, BP, ventilatory rate, and respiratory pattern provide important clues as to mechanism of limitation. Recording of an ECG during exercise is an established way to assess whether either cardiac arrhythmias or ischemia or both contribute to the patient's limitation and dyspnea. The use of oximetry is another noninvasive adjunct; ILD and pulmonary vascular diseases are nearly always associated with a decline in exercise SaO₂. Exhaled gas measurements provide an even more objective measure of severity of limitation. Measurement of maximal exercise ventilation is

helpful in separating cardiac from pulmonary limitation. A high ratio of exercise ventilation to maximal voluntary ventilation suggests pulmonary limitation, but a low ratio of maximal O_2 consumption to peak exercise heart rate suggests cardiac limitation.

Images of the cardiac ventricles can be obtained with either radionuclide ventriculography or echocardiography. Either procedure allows assessment of ventricular systolic dysfunction (left, right, or both). Left ventricular wall-motion during exercise is a strong measure of the presence or absence of myocardial ischemia. Direct measurement of PWP and pulmonary artery pressure with right heart catheterization during exercise can distinguish the relative contributions of valvular, pericardial, or myocardial abnormalities to patient dyspnea. Direct measurement of exercise cardiac output can sometimes clarify the importance of anemia or fixed output conditions (AS of moderate severity) in patients with multifactorial dyspnea or with dyspnea that seems out of proportion to recognized pathology.

Stress Cardiac Imaging. Patients with coronary heart disease (CHD) frequently have episodes of painless or “silent” ischemia. In many patients the early symptom associated with myocardial ischemia is exertional dyspnea. Typically, when exertional dyspnea is an anginal equivalent, it will be relieved by rest and/or nitroglycerin. The symptom of dyspnea in this setting is thought to be related to alterations in diastolic relaxation and LV compliance occurring early during the course of myocardial ischemia. Additional symptoms of fatigue or exhaustion occur later in the course of myocardial ischemia because of decreased cardiac output secondary to decreased systolic LV, with or without mitral regurgitation due to ischemic papillary muscle dysfunction. Thus, dyspnea may be a very important early sign of CHD, because myocardial ischemia is first associated with diastolic dysfunction,

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followed by systolic dysfunction, then ECG changes, and finally symptoms of angina pectoris.

In the clinical setting, stress testing with cardiac imaging should be obtained when the standard exercise ECG is expected to be nondiagnostic, such as in patients with left bundle branch block, paced rhythms, LV hypertrophy with strain, and digitalis therapy. Pharmacologic perfusion cardiac imagery should be used in those with a physical limitation that prevents exercise testing (see below).

Stress Echocardiography. In patients with dyspnea, dobutamine stress echocardiography can be very useful in identifying CHD as the underlying etiology. Stress echocardiograms are obtained by combining exercise or pharmacologic infusion with standard echocardiography. Since many patients are unable to exercise and because at higher levels of exercise, body motion can introduce artifacts in echocardiographic images, pharmacologic infusion has gained in popularity. In the normally perfused myocardium, dobutamine infusion increases myocardial contractility and LV wall-motion. An abnormal test is defined as LV wall-motion abnormalities induced by dobutamine infusion, thus defining CHD. In general, the abnormalities detected by dobutamine infusion have higher sensitivity to identify CHD than changes seen with vasodilation (dipyridamole or adenosine) stress echocardiography.

The information provided by stress echocardiography can identify regional wall-motion abnormalities that may assist in choosing a revascularization strategy and/or to recognize the presence of stress-induced papillary muscle dysfunction. In particular, dobutamine stress echocardiography may be helpful in selecting optimal candidates for coronary bypass surgery among patients with poor LV function. Patients with multivessel CHD and depressed LV

function whose regional function improves during dobutamine stress echocardiography generally have improved LV function after revascularization.

Dobutamine stress echocardiography may also be useful in establishing prognosis. It is important to note that a negative stress dobutamine echocardiographic study among those with normal resting LV function is associated with a low cardiovascular event rate in follow-up. Finally, as a preoperative screening test, dobutamine stress echocardiography may be used to predict perioperative ischemic complications among patients having noncardiac surgery.

Stress Radionuclide Imaging. Stress radionuclide studies can yield important information regarding the relationship between symptoms of dyspnea and abnormalities on coronary perfusion. Myocardial ischemia may be induced by treadmill exercise or the pharmacologic methods described above in the section on “Stress Echocardiography.” The largest experience in radionuclide myocardial perfusion imaging is with thallium-201, although the more recently available tracer (technetium-99m sestamibi, which has similar diagnostic accuracy) has gained in usage. Generally, thallium-201 or technetium-99m sestamibi can be used interchangeably with comparable diagnostic accuracy to identify patients with CHD. Either planar or single-photon-emission computed tomographic (SPECT) techniques may be used to detect areas of reduced myocardial perfusion, suggesting CHD. Of the two techniques, SPECT imaging is more accurate than planar imaging in:

- Localizing underperfused regions of myocardium;
- Correctly predicting multivessel CHD; and
- Identifying the presence of ischemic heart disease.

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It should be noted that the sensitivity of thallium perfusion scans may be lower in women than men. Increased uptake of thallium-201 by the lungs is an important observation that denotes exercise-induced LV dysfunction, an important diagnostic finding pointing to cardiac pathology in patients with dyspnea of uncertain etiology.

In general, the indications for stress radionuclide imaging are the same as those for stress echocardiography. By definition, exercise-stress imaging either with echocardiography or radionuclide perfusion provides important information about exertional capacity that cannot be obtained with pharmacologic stress studies. The specificity and sensitivity of dobutamine stress echocardiography and thallium treadmill testing are comparable, but dobutamine stress echocardiography is generally less expensive. Both tests yield invaluable information in patients with dyspnea where an underlying ischemic etiology may be present. In addition to the previously mentioned indications, exercise thallium-201 perfusion studies may provide important information about the development of ischemic coronary vasculopathy as a cause of dyspnea in patients after cardiac transplantation, where angina as a symptom of myocardial ischemia is notably absent. In these patients, exertional dyspnea may be the only symptom of myocardial ischemia.

Special Blood Tests

A number of serum tests are occasionally helpful in the evaluation of dyspnea. These are briefly considered in this section.

Liver Function Tests. Pulmonary hypertension is sometimes associated with liver-function abnormalities, which are indicative of chronic active hepatitis or cirrhosis. Tests of hepatic synthetic function (e.g., albumin, serum glutamate-oxaloacetic transaminase, serum glutamate pyruvate transaminase, clotting factors) and secretory function (e.g., alkaline phosphatase) are appropriate in the evaluation of patients presenting with unexplained PH. The cause of hepatic-disease-related PH, known as *hepatopulmonary syndrome*, remains unknown. It may be due to failure of inactivation of pulmonary vasoconstricting substances or in the reduced production of vasodilator substances. The hepatopulmonary syndrome is also associated with (ABG) abnormalities, most commonly hypoxemia with postural changes (orthodeoxia) and an increased alveolar- PaO_2 difference.

Plasma Coagulation Profiles. Markedly elevated levels of plasminogen activator inhibitor may indicate impaired fibrinolysis, which may be involved in both thrombotic and primary pulmonary hypertension (PPH).

Immunological Indicators. Interstitial lung disease states, which are characterized by capillaritis and are within the spectrum of Wegener's granulomatosis, are commonly associated with serum abnormalities. Antinuclear antibody (ANA), antineutrophil cytoplasmic antibody (C-ANCA), and plasma ANA (P-ANCA) should be obtained when these immunologically mediated inflammatory pulmonary processes are suspected. A complete blood count indicating the presence of eosinophilia may be a clue to

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asthma and hypersensitivity (as in pneumonitis). Polycythemia may indicate the presence of occult hypoxemia.

Other Tests. Angiotensin-converting enzyme inhibitors and thermolysin-like metalloendopeptidase may be confirmative of active sarcoidosis. However, these tests are not specific and may be elevated in tuberculosis, fungal diseases, and other granulomatous disorders of the lungs. Reduced alpha₁-antitrypsin levels and characteristic phenotypes (e.g., ZZ, SZ) are associated with precocious and familial emphysema. Hypothyroidism is common in patients with PPH and may be the first clue to suggest this diagnosis. Often these tests are ordered as part of a “fishing expedition.” They should be used to confirm a clinical suspicion rather than for screening.

Right and Left Heart Catheterization

As discussed in Section A of this monograph, the evaluation of every patient with dyspnea should begin with a careful history and physical examination. Based upon impressions derived from the history and physical, decisions are made to go to simple diagnostic evaluations such as the 12-lead ECG and posteroanterior and lateral CXR. At that juncture, PFTs, echocardiography/Doppler studies, or radiographic imaging might be considered. The descriptor “invasive,” as applied to *catheterization*, serves to remind us that, in general, we should first seek to assess the patient noninvasively. We reserve both the risk and cost of invasive procedures for patients in whom: (1) a noninvasive evaluation has not been satisfactory; and (2) there is an indication that the diagnostic information to be obtained through such procedures will be of use.

Right Heart Catheterization. The types of measurements made during right heart catheterization include:

- Right atrial pressure;
- Pulmonary artery pressure;
- Pulmonary wedge pressure (PWP);
- Cardiac output and cardiac index;
- Systemic and pulmonary vascular resistance;
- Mixed venous O₂ tension and saturation;
and
- Oxygen saturations in various right heart locations (shunt run).

Imaging studies that can be obtained at the time of right heart catheterization include:

- Right ventriculography;
- Pulmonary angiography; and/or
- Wedge pulmonary angiography.

Table 7 lists some of the relevant measures and imaging studies, along with examples of clinical entities that can produce dyspnea and how these data may be diagnostically useful.

Left Heart Catheterization. The types of measurements made with left heart catheterization include LV/aortic systolic pressure gradient (LV/A-Syst P).

Imaging studies include left ventriculography, aortography, and selective coronary and graft angiography. Table 8 lists some of these measurements and imaging studies, along with examples of diseases and therapeutic options that might be clarified by obtaining these data. Coronary angiography will be considered separately.

Specific catheterization procedures allow for measurement of intracardiac pressures and flows and calculation of resistances. Measurement of O₂ saturations provides for calculation of intracardiac shunt fractions. Imaging with radiographic contrast

Table 7. Right Heart Diagnostic Data Referable to Diseases That May Produce Dyspnea and Therapeutic Options for Those Diseases

Right Heart Measurement or Image	Disease Examples	Therapy Examples
Right atrial pressure	Right ventricular heart failure Pericardial tamponade Pericardial constriction Cor pulmonale Right ventricular infarction	Diuretics Pericardiocentesis Pericardial surgery O ₂ therapy Reperfusion and volume therapy
Pulmonary artery pressure	PPH Acute PE Recurrent PE Cor pulmonale Passive hypertension Left heart failure Mitral valve disease	Vasodilators Heparin +/- lytics Thrombus surgery O ₂ ACE-I, diuretics Replacement or plasty
Pulmonary wedge pressure	"Active" PH Hypoxic lung PPH Recurrent emboli "Passive" PH Left heart systolic failure Mitral valve disease Left heart diastolic dysfunction	O ₂ Vasodilators Lytics or clot removal
Cardiac output	High-output failure Thyrotoxicosis A-V fistula Low output failure LV systolic	Treat thyroid Surgical closure ACE-I, beta-blockers
Shunt run (O ₂ sats)	Intracardiac shunt	Close ASD or VSD
Right ventriculography	Tricuspid regurgitation	Repair or replacement
Pulmonary angiography	Document PE	Embolectomy

ACE-I indicates angiotensin-converting enzyme inhibition drugs; ASD, atrial septal defect; A-V, arterial venous; LV, left ventricular; lytics, thrombolytic drugs; PE, pulmonary embolism; PH, pulmonary hypertension (i.e., mean pulmonary artery pressure >20 mm Hg; "active" pulmonary hypertension is also called *arteriolar* hypertension and is essentially vascular in origin; "passive" means secondary to elevated left-sided pressures); PPH, primary pulmonary hypertension; VSD, ventricular septal defect.

Table 8. Left Heart Catheterization Data Referable to Diseases That May Produce Dyspnea and Examples of Therapeutic Options for Those Diseases

Left Heart Measure or Image	Disease Examples	Therapy Examples
LV/A systP	Aortic stenosis Hypertrophic cardiomyopathy	Valve replacement Beta-blocker
LV/PWP	Mitral stenosis	Valvuloplasty
Left ventriculography	Mitral regurgitation	Valve repair
Aortography	Aortic regurgitation	Valve replacement

LV/A systP indicates left ventricular/aortic systolic pressure; LV/PWP, left ventricular/pulmonary wedge pressure.

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allows identification and quantification of regurgitant lesions. Measurement of pressure gradients with accompanying flow measurements provides for quantification of stenotic lesions. Imaging of chambers allows for both qualitative and quantitative assessment of systolic function of both ventricles. Measurement of pressures allows for quantitative assessment of both ventricles' diastolic performance. Imaging the coronary arteries with intravascular ultrasound and Doppler flow catheters enables operators to qualitatively and quantitatively assess coronary obstructions and to provide a road map for therapeutic catheter or surgical options.

All of these options come at a risk and a cost. Accordingly, they are second-line and “invasive.” The choice to perform them should involve careful weighing of benefits versus risks and costs. ■

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Wulfsberg EA, Hoffman DE, Cohen MM. Alpha₁-antitrypsin deficiency: impact of genetic discovery on medicine and society. *JAMA.* 1994;271:217-222. An excellent discussion of the many ramifications of the alpha₁-antitrypsin deficiency state.

E. Approaches to the Patient With Dyspnea

The following tables illustrate a stepwise approach to the patient with dyspnea, emphasizing cost, relative risk, and the need for consultation. The history and physical are of central importance in evaluating patients with dyspnea, both because they often lead to a specific diagnosis and because they are relatively inexpensive. Tables 9, 10, and 11 list important historical features and physical findings, along with primary diagnostic considerations. These findings direct the physician in selecting additional diagnostic studies. Tables 12 and 13 summarize these concepts and outline a stepwise approach to evaluation of the patient with dyspnea. Table 14 illustrates the relative costs incurred in the evaluation of patients with dyspnea. ■

History and Physical Findings in Relation to Most Common Diagnoses

Table 9. Historical Features and Primary Considerations in the Evaluation of Dyspnea

Historical Features	Primary Considerations
Sudden onset dyspnea	<ul style="list-style-type: none"> Pulmonary embolism Pneumothorax Acute myocardial infarction Acute cardiac tamponade Acute asthma
Subacute onset dyspnea	<ul style="list-style-type: none"> Pleurisy Pneumonia Asthma Anxiety Congestive heart failure (CHF)
Chronic dyspnea	<ul style="list-style-type: none"> Chronic obstructive pulmonary disease (COPD) CHF Interstitial lung disease Deconditioning Anxiety Asthma Pulmonary hypertension
Nocturnal onset dyspnea	<ul style="list-style-type: none"> CHF COPD Asthma Sleep disorders Mitral valve disease

Table 10. Important Signs and Symptoms and Primary Diagnostic Considerations

Associated Symptoms and Signs	Primary Diagnostic Considerations
Wheezing	Asthma Congestive heart failure (CHF) Chronic obstructive pulmonary disease (COPD)
Cough	Pneumonia Asthma CHF COPD Interstitial lung disease
Chest pain: <ul style="list-style-type: none"> • Pleuritic • Angina • Relieved with exertion 	Pulmonary embolism (PE), pneumonia, pneumothorax Myocardial ischemia Anxiety
Syncope/pre-syncope	Pulmonary hypertension PE Idiopathic hypertrophic subaortic stenosis Aortic stenosis Dysrhythmia

Specific Findings and Common Diagnoses

Table 11. Physical Findings and Primary Diagnostic Considerations Used in Selecting Additional Diagnostic Studies

Specific Physical Findings	Examples of Diagnoses
General Observations	
Obesity	Deconditioning
Clubbing	Interstitial lung disease Bronchiectasis Neoplasm Cystic fibrosis Congenital heart disease
Kyphoscoliosis	Restrictive lung disease
Barrel chest	Chronic obstructive pulmonary disease (COPD)
Abnormal breathing	Congestive heart failure (CHF) Central nervous system disease
Use of accessory muscles for breathing	Asthma COPD
Pallor	Anemia
Edema/ascites	CHF Hepatic disease
Cardiovascular Observations	
Elevated jugular venous distension or hepatojugular reflux	CHF/pericardial disease/cor pulmonale
Delayed carotid upstroke	Aortic stenosis (AS)
Parasternal lift	Pulmonary hypertension (PH)
Diffuse apical impulse	Left ventricular (LV) enlargement, systolic dysfunction
Sustained apical impulse	LV hypertrophy, diastolic dysfunction
Increased S1	Mitral stenosis
Increased P2	PH
Fixed split S2	Atrial septal defect (ASD)
Single S2	AS
S3 gallop	Systolic dysfunction/CHF
S4 gallop	Diastolic dysfunction
Diastolic murmur	Valvular heart disease (pathologic)
<i>Pulsus alternans</i>	LV dysfunction
<i>Pulsus paradoxus</i>	Cardiac tamponade
Pulmonary Observations	
Increased tactile fremitus	Pneumonia (consolidation)
Decreased tactile fremitus	Pleural effusion Pneumothorax
Dullness to percussion	Atelectasis Pleural effusion Pneumonia
Hyperresonance	Emphysema
Bronchial or tubular breath sounds	Pneumonia
Crackles	CHF Idiopathic lung disease Pneumonia
Rhonchi	Bronchitis COPD
Egophony	Consolidation

(continued)

Stepwise Evaluation of Dyspnea

Table 12. Stepwise Approach to Evaluation of the Patient with Chronic Dyspnea

Complexity	Evaluation	Cost*	Risk	Need for Consultation
All patients with dyspnea	History and physical examination	\$	None	No
Diagnosis still not obvious	Spirometry, electrocardiogram (ECG), chest x-ray (CXR), and oximetry	\$	None	No
Diagnosis still not obvious	Arterial blood gases Full pulmonary function test Exercise testing Echocardiogram	\$ \$\$ \$\$\$ \$\$\$\$	Minimal	No
Diagnosis still not obvious	Ventilation-perfusion (V/Q) scan	\$\$	None	No
Diagnosis still not obvious	Chest computed tomography (CT) scan, Stress echo, Stress perfusion studies	\$\$\$ or \$\$\$\$	Minimal	Yes
Diagnosis still not obvious	Right and left heart catheterizations	\$\$\$\$\$	Low	Yes

*These are approximate costs, based on Medicare relative values. Regional and institutional differences can be expected.

\$ = \$0 to 200; \$\$ = \$201 to 500; \$\$\$ = \$501 to 1,000; \$\$\$\$ = \$1,001 to 5,000; \$\$\$\$\$ = >\$5,000.

Table 13. Stepwise Approach to Evaluation of the Patient with Acute Dyspnea

Diagnosis*	Tests
Acute myocardial infarction	ECG, cardiac enzymes
Pulmonary embolism	V/Q scan or spiral CT
Airflow obstruction	Spirometry
Tension pneumothorax	CXR

*In severe acute dyspnea, the physician must first evaluate these diagnostic imperatives.

Relative Costs of Patient Evaluation Tests

Table 14. Relative Costs Incurred in the Evaluation of Patients With Dyspnea

Test	Cost*
History and physical examination	\$
Consultation (e.g., cardiology, pulmonary)	\$
Routine blood test	\$ (per test)
Electrocardiography	\$
Chest x-ray	\$
Spirometry	\$
O ₂ saturation	\$
Blood gas analysis	\$
Conventional computed tomography (CT)	\$\$\$
High-resolution CT	\$\$\$
Spiral CT	\$\$\$\$
Ventilation-perfusion \dot{V}/\dot{Q} scan	\$\$
Complete pulmonary function tests	\$\$
Treadmill test	\$\$
Cardiopulmonary exercise testing	\$\$\$
Echocardiography	\$\$\$
Transesophageal echocardiography	\$\$\$\$
Stress echocardiography	\$\$\$
Thallium echocardiography	\$\$\$\$
Right heart catheterization	\$\$\$\$
Left heart catheterization	\$\$\$\$\$
Special blood tests	\$\$

*These are approximate costs, based on Medicare relative values. Regional and institutional differences can be expected.

\$ = \$0 to 200; \$\$ = \$201 to 500; \$\$\$ = \$501 to 1,000; \$\$\$\$ = \$1,001 to 5,000; \$\$\$\$\$ = >\$5,000.

F. Case Studies

1. Diastolic Dysfunction

Case 1.1 Occult Congestive Heart Failure (CHF), Including Diastolic Dysfunction

A 78-year-old, retired African-American male with a history of hypertension, diabetes mellitus, and peripheral vascular disease presented with symptoms of fatigue and shortness of breath. The past medical history is pertinent in that the patient is a nonsmoker with no symptoms of chest pain but with a history of progressive exertional dyspnea over the past several months, without orthopnea or paroxysmal nocturnal dyspnea (PND). There is no prior history of heart disease, including a heart murmur or myocardial infarction.

Physical examination found the blood pressure (BP) to be 189/91 mm Hg and pulse 68 beats/min. There was no jugular venous distension, and the chest was clear on auscultation. The first and second heart sounds were normal, with no third or fourth heart sounds. No systolic or diastolic murmurs were present. Trace pedal edema was noted, and the peripheral pulses were diminished in the lower extremities. The resting electrocardiogram (ECG) revealed voltage criteria for left ventricular hyper-trophy (LVH), with ST-T abnormalities secondary to LVH. Chest x-ray (CXR) revealed the cardiac size to be at the upper limits of normal, with no evidence for congestive heart failure (CHF). An echo-cardiogram revealed normal LV function with LVH. An exercise thallium myocardial perfusion study revealed a large perfusion defect in the lateral wall. The result of a pulmonary evaluation, which included spirometry, was normal.

In view of these findings, cardiac catheterization was performed, revealing normal LV systolic function with an ejection fraction of 0.55 and mild lateral hypokinesis. The LV end-diastolic pressure was 22 mm Hg. Coronary arteriography identified a 95% left circumflex stenosis; therefore, percutaneous coronary intervention was performed with successful stent placement at the site of the stenosis, with no residual coronary narrowing.

Comment. This patient demonstrates myocardial ischemia presenting with predominant symptoms of dyspnea. In addition, the associated risk factor of hypertension is a known cause of diastolic dysfunction, which in this case may have exacerbated the patient's symptoms of dyspnea. Thus, the combined effects of myocardial ischemia and diastolic dysfunction were significant contributors to the pathophysiology demonstrated by this patient. This case study emphasizes the importance of understanding the relationship of symptoms of dyspnea to myocardial ischemia and diastolic dysfunction in patients with significant cardiovascular risk factors.

Case 1.2 Diastolic Dysfunction, Left Ventricular Hypertrophy (LVH), and Chronic Obstructive Pulmonary Disease (COPD)

A 68-year-old African-American male presented with progressive dyspnea on exertion and recent intermittent dyspnea at rest. He is an ex-smoker and has a known diagnosis of chronic obstructive pulmonary disease (COPD) that is partly responsive to inhaled bronchodilators. He has no known heart disease. His medical history is negative for chest pain, cough, fever, orthopnea, PND, or edema.

On physical examination, the vital signs were remarkable for a BP of 170/100, a pulse of 82 beats/min, and a respiratory rate (RR) of 18 breaths/min. The lungs were clear to auscultation and percussion. There was no wheeze on forced expiration. The heart examination revealed a normal jugular venous waveform at approximately 5 cm H₂O, but hepatjugular reflux was present. The apical impulse was sustained and a palpable S₄ noted. Auscultation revealed a regular rate and rhythm, normal S₁ and S₂, an S₄ at the apex, and a short grade 2/6 systolic outflow murmur along the left sternal border, without further radiation. The remainder of the physical examination was normal. The ECG showed normal sinus rhythm and increased LV voltage in the limb leads only. The CXR was remarkable for mild cardiomegaly and hyperinflated lungs, without

infiltrate. On spirometry, there was no change in the patient's forced expiratory volume in 1 second (FEV_1) measurement, which at 1.5 L/min. was not improved with an inhaled bronchodilator. An echocardiogram revealed mild LVH with normal LV systolic function and no valvular abnormalities, but the LV inflow Doppler study was compatible with diastolic dysfunction.

Comment. This patient has mixed heart and lung disease, with each contributing to his dyspnea. The previously undiagnosed hypertension had led to the development of LV hypertrophy and subsequent diastolic dysfunction. The abnormal diastolic function remained well-compensated at rest; but, with exertion and transient increases in left atrial pressures, dyspnea was provoked and then accentuated by aggravation of the bronchospastic component of the patient's COPD (cardiac asthma). In the early stages of diastolic dysfunction, the resting cardiac pressures were still within the normal range and therefore explain the paucity of physical findings at presentation.

2. Dyspnea With Asthma and COPD

A common cause of dyspnea is airflow obstruction, which is the physiologic hallmark of asthma and COPD. Asthma is generally an acute and intermittent cause of airflow obstruction. By contrast, COPD is characterized as a chronic, progressive process with inexorable progression of airflow obstruction. However, overlaps occur. Chronic unrelenting asthma may also progress to a stage of chronic irreversible airflow obstruction, if not effectively managed, due to remodeling and fibrosis of the conducting airways. Two cases in which unrelenting dyspnea was the main symptom serve to illustrate how asthma may be mislabeled COPD.

Case 2.1 Dyspnea With Occult Asthma

A 41-year-old white male then working as a lawyer and field geologist was referred several years ago due to cough and dyspnea. These symptoms had been insidious and progressive, leading to a reduction in the patient's activities of daily living. He was limited in playing golf and gardening. He had been a smoker for 20 years but had stopped smoking 1 year before this evaluation. His family history revealed a brother with asthma.

On examination, he was dyspneic at rest with a pulse of 110 and respirations of 24. Use of accessory muscles was noted. He had a hyperinflated, nearly silent chest and a normal cardiac examination. The abdominal and extremities examinations were normal. Clubbing was absent, but there was a mild tremor. The patient's spirometry results are presented in Table 15.

This patient was already receiving theophylline and used an inhaled beta-agonist bronchodilator. His serum theophylline level was 18 (normal is 8 to 20 mg/mL).

Following a 7-day course of corticosteroids, the patient's forced vital capacity (FVC) was 5.26 and FEV₁ 4.49 (see Table 16). Thus, this patient demonstrated complete reversibility with the use of corticosteroid drugs. This is a classic example of the "hidden asthmatic." Sometimes these patients present simply with cough and at other times with unexplained airflow obstruction.

On follow-up, this patient remained asymptomatic. By the time he returned for study, he was receiving corticosteroids and cromolyn, along with inhaled beta-agonists. Thus, his management was conducted entirely by the inhaled route. His repeat ventilatory spirometric functions are shown in Table 17. Although a mild abnormality is present, possibly from some airways remodeling, the patient's degree of impairment

Table 15. Dyspnea Due to Occult Asthma Case: Spirometry

	Baseline	Post-inhaled Bronchodilator	Predicted
FVC	1.45	1.86	4.67
FEV ₁	0.57	0.66	3.62

FEV₁ indicates forced expiratory volume in 1 second; FVC, forced vital capacity.

Table 16. Dyspnea Due to Occult Asthma Case: Follow-up Spirometry

	Baseline	7-day Corticosteroids	Predicted Value
FVC	1.45	5.26	4.67
FEV ₁	0.57	4.49	3.63

Table 17. Dyspnea Due to Occult Asthma Case:
Further Follow-up Spirometry

	Baseline	7-day Corticosteroids	11 Years Later
FVC	1.45	5.26	3.81 (90%)
FEV ₁	0.57	4.49	2.45 (77%)

Table 18. Dyspnea Due to Occult Asthma Case: Full Pulmonary Function Studies
Follow-up 24 Years After Initial Examination

	Pre-bronchodilator	Post-bronchodilator
FVC	3.85	3.91 (100%)
FEV ₁	1.72	1.74 (63%)
Total lung capacity (TLC)	7.53	6.54 (115%) (-14%)
Residual volume (RV)	3.68	2.60 (120%) (-29%)
DLCO (mL/min/mm Hg)	22.3 (115%)	
DLCO/VA	3.65 (98%)	

DLCO indicates diffusing capacity for carbon monoxide; VA, alveolar volume.

is only minimal. It is important that this patient continue to receive anti-inflammatory preventive therapy and bronchodilators for symptomatic episodes for the rest of his life (see Table 18). These complete pulmonary function tests were done 24 years after the initial examination.

Comment. This is an interesting patient whose case suggests that there is loss of elastic recoil along with airway remodeling, but no emphysema, in terms of damage to the air-blood interface. Thus, this patient's course and prognosis were dramatically improved by smoking cessation and aggressive treatment of the underlying disease, which proved to be bronchial asthma.

Case 2.2 Dyspnea With Emphysema

A 32-year-old woman saw her physician for chronic progressive dyspnea on exertion. She had episodes of wheeze, but no cough or mucus. She had been given beta-agonistic bronchodilators for exertional dyspnea, but these were not effective. The patient had smoked cigarettes, approximately one package per day, for 12 years. She had been otherwise healthy.

Her family history revealed a father who died of emphysema at age 52 and an aunt living with emphysema at age 55. Both were heavy cigarette smokers. An older brother was reported to have asthma but had never had any spirometric tests.

The patient's physical examination revealed marked hyperinflation and decreased breath sounds. The patient's ventilatory function tests are presented in Table 19. Note that marked airflow obstruction is present, with an insignificant degree of improvement following inhalation of a beta-agonistic aerosol.

The patient's α_1 -antitrypsin level was 22 (normal is 180 to 220 mg/dL). The α_1 -antitrypsin phenotype was ZZ.

Table 19. Dyspnea Due to Emphysema Case: Ventilatory Function Tests

	Baseline	30 Minutes After Inhalation of Albuterol
FVC	3.05	3.10 (78%)
FEV ₁	1.05	1.10 (33%)

FVC = forced vital capacity

FEV₁ = forced expiratory volume in 1 second

Comment. This patient has emphysema, not asthma, associated with the α_1 -antitrypsin deficiency state. A considerable number of patients with α_1 -antitrypsin present with wheezing dyspnea and are commonly “labeled” asthmatic. Such patients with precocious emphysema often have rapid declines in FEV₁. Smoking cessation, of course, is key to management. Replacement antiprotease therapy is under study.

Case 2.3 Dyspnea With Vocal Cord Dysfunction

A 30-year-old woman consulted a pulmonologist for “steroid-dependent asthma” and reported the abrupt onset of asthma during nursing training. It was characterized by sudden tightness in the chest and inability to breathe. The patient felt that she was suffocating. She denied cough but had a very loud wheezing sound during each attack. She had visited the emergency room on numerous occasions and had been hospitalized twice, where she exhibited poor symptomatic responses to inhaled beta-agonist bronchodilators. Her managing doctors had resorted to using escalating doses of corticosteroids to control her asthma. Her most recent maintenance dose of prednisone was 60 mg each morning. She was found in extremis in the hospital and was intubated and mechanically ventilated overnight. Immediately following intubation, the patient was observed to have normal airflow and air entry. Ventilator inflation pressures were only 10 cm H₂O. She was cushingoid due to long-term use of corticosteroids, and was obese. She was receiving oral hypoglycemic agents for diabetes mellitus.

Because of this interesting observation of low inflation pressures following intubation, the patient was directed to rapidly taper the corticosteroid drugs and use inhaled beta-agonists as sparingly as possible. She was asked to return to the office during her next attack, however mild it might be. She returned 1 week later, with wheeze and shortness of breath. It was

obvious that the patient had inspiratory stridor on examination. To prove the diagnosis, a flow-volume loop with the inspiratory curve was obtained (see Figure 11).

Comment. Vocal cord dysfunction was the cause of this woman's "asthma." This is one of the common masqueraders for asthma. Vocal cord dysfunction is believed to be a somatization disorder, due to psychic trauma. It is most common in women who are healthcare workers or children of healthcare workers. Other causes of upper airways obstruction are tracheal stenosis following intubation for mechanical ventilation, congenital tracheal webs in children, and tracheal tumors. Management of vocal cord dysfunction is quite different from asthma and focuses upon breathing training and voice control. Asthmatic medications are not useful in vocal cord dysfunction. Of course, steroid side effects can be devastating.

Case 2.4 Dyspnea From Airflow Obstruction

A 19-year-old female Olympic rower complained of increasing dyspnea with exercise. Her performance had decreased by 15% to 20%, and she was concerned that she would not qualify for the U.S. Olympic team. She admitted to chest tightness with exercise but denied cough, wheeze, nocturnal symptoms, allergies, and a family or personal history of asthma.

Her examination revealed a 6-foot, 2-inch female who appeared to be extremely fit with no abnormalities. Room air saturation was 98% at rest and with exercise. The CXR was normal. Spirometry revealed an FEV₁ of 125% of predicted value and a FVC of 130% of predicted value. There was no fall in the FEV₁ after 10 minutes of stair running. The patient started on regularly inhaled corticosteroids and beta-agonist therapy. When the patient returned in 6 weeks, she was asymptomatic and both her FEV₁ and FVC were measured at 140% of predicted.

Comment. Predicted values with spirometry are extremely helpful in most situations. In this case, however, because of the patient's unique genetic ability and superb fitness, the predicted values were misleading. Because of dyspnea on exertion, chest tightness, and no baseline spirometry, the patient was given a therapeutic trial rather than ordering more complex studies. Her response to therapy documented significant reversible airflow obstruction.

3. Idiopathic Pulmonary Fibrosis (IPF)

An 81-year-old male, who retired from dentistry at age 69, presented with a chief complaint of worsening shortness of breath while playing tennis. Approximately 6 years earlier, the patient first noted mild shortness of breath while playing tennis. His past medical history and review of systems were entirely negative. He was a lifelong nonsmoker and was on no medications at the time he presented.

On physical examination his temperature was 96.7°F; BP 150/80 mm Hg; pulse 59; and RR 16. At 6 feet 2 inches in height, his weight had been stable. Auscultation of the chest revealed diffuse, bilateral, dry Velcro-type crackles. Cardiac examination was normal without an increased P2. There was no clubbing, cyanosis, or edema, and the patient looked healthy and well.

Pulmonary function testing (PFT), including spirometry, lung volumes, diffusing capacity for carbon monoxide (DLCO), and resting and exercise SaO₂, were completed. There was a moderately severe restrictive ventilatory defect, with a concomitant mild obstructive ventilatory defect and a severe reduction in DLCO (see Table 20).

The resting SaO₂ breathing ambient air was 94%. After the patient walked on the flat for a few minutes, the exercise SaO₂ was 82%. With the patient utilizing

**Table 20. Idiopathic Pulmonary Fibrosis Case:
Pulmonary Function Studies**

	Baseline	Post-Inhaled Bronchodilator
Forced vital capacity (FVC)	2.60 (59%)	No change
Forced expiratory volume in 1 second (FEV ₁)	1.81 (65%)	No change
FEV ₁ / FVC	69%	No change
Total lung capacity	4.43 (61%)	
Residual volume	1.67 (58%)	
Diffusing capacity for carbon monoxide (mL/min/mm Hg)	5.3 (22%)	

4 liters of oxygen, the resting SaO₂ rose to 98% and the exercise SaO₂ was 90%.

A chest radiograph revealed diffuse, coarse reticular markings involving both lungs to a greater extent in the bases than in the upper lung zones (see Figure 12). A high-resolution computed tomography (CT) scan showed extensive peripheral interstitial fibrosis with honeycombing, particularly at the lung bases, bilaterally (see Figure 13). There was no evidence of focal air-space disease or pleural effusion. Angiotensin-converting enzyme results were normal. Additional test results included a negative tuberculin skin test with a positive mumps control.

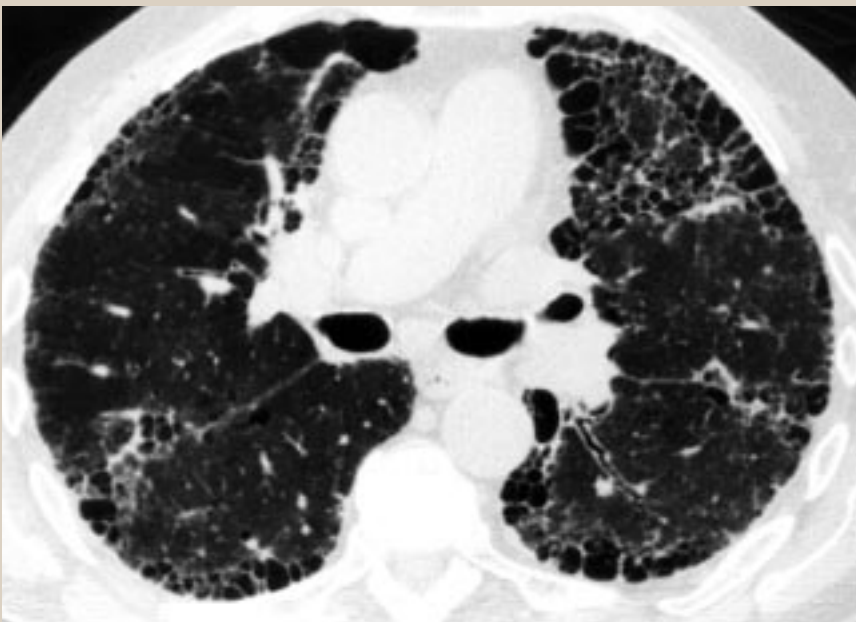
The patient was treated for several weeks with methylprednisolone, 40 mg/day (0.5 mg/kg), and did not experience either symptomatic or objective improvement in chest radiograph or lung function tests. Accordingly, corticosteroids were discontinued. Over the ensuing 5 years, the patient remained stable in terms of lung function testing and chest radiographs. However, his shortness of breath gradually increased, and he was no longer able to play tennis.

Comment. This patient's clinical presentation, radiographic findings, and lung function tests were classic for idiopathic pulmonary fibrosis of the "usual interstitial pneumonitis" (UIP) type. A history of several years of progressively worsening shortness of breath in patients of advanced age is common. The benign clinical course of the patient over 5 years following presentation is testimony to the fact that this disease is sometimes slowly progressive. In other patients, however, respiratory symptoms and pulmonary dysfunction worsen steadily and often rapidly. Neither corticosteroids nor cytotoxic agents have been shown in large, controlled randomized trials

Figure 12. Case Study: Chest Radiograph Showing Diffuse, Coarse Reticular Markings



Figure 13. Case Study: High-Resolution Computed Tomography Scan Showing Extensive Peripheral Interstitial Fibrosis With Honeycombing



to significantly improve survivorship in this disease. Patients die an average of 4 years following diagnosis. Other classifications of “idiopathic interstitial pneumonitis with fibrosis” as determined by biopsy, such as desquaminate interstitial pneumonitis (DIP) and nonspecific interstitial pneumonitis (NSIP), are frequently steroid-responsive.

4. Chronic Recurrent Pulmonary Emboli (PE)

A 67-year-old man with a 4-year history of exertional dyspnea presented for preoperative evaluation prior to surgery for prostate cancer. When he first developed dyspnea, he was found to have mild arterial O₂ desaturation. Pulmonary function tests done at that time demonstrated a mild obstructive deficit, no evidence of restrictive disease, and a normal DLCO. He also underwent a cardiac evaluation that included a normal ECG and exercise study. Treatment with bronchodilators was ineffective, but he adapted to his symptoms by decreasing his activities.

Two years later, after a CXR showed an abnormality, the patient had a chest CT scan and was found to have a small pleural-based density in the right lower lobe consistent with plaque. Six months prior to presenting, a sleep study demonstrated a moderate sleep breathing disorder, including evidence of increased upper airway resistance, hypoventilation, and prolonged periods of arterial desaturation.

The patient’s condition progressed to the point where he was symptomatic with limited activities despite the use of bronchodilators and nocturnal oxygen. At the time of this latest evaluation, he had had a chronic nonproductive cough and occasional episodes of purulent bronchitis. He also had a history of prior pneumonias, gastroesophageal reflux disease, varicose veins, superficial thrombophlebitis, and left-ankle fracture. There was no history of deep vein thrombophlebitis (DVT), major leg or pelvic trauma, or smoking. He had had some exertional subscapular

pain previously, but there was no history of typical angina, pleuritic chest pain, hemoptysis, or syncope. A brother had DVT.

On physical examination, vital signs were normal. There was slight cyanosis of the nail beds and lips. The lungs were clear. There was a palpable left parasternal impulse. The second heart sound was loud and narrowly split, with no third sound. The jugular venous pressure was elevated with hepatojugular reflux. There was trace edema.

A complete blood count (CBC) and chemistries were normal. A CXR was unremarkable except for a hiatal hernia. An ECG demonstrated sinus rhythm, right bundle branch block, right-axis deviation, and prominent r' voltage in V1 suggestive of right ventricular hypertrophy. Repeat PFTs demonstrated moderate restrictive and mild obstructive disease and a reduction in DLCO to 60% of predicted. A repeat echocardiogram demonstrated right ventricular enlargement, moderate tricuspid regurgitation, and significant pulmonary hypertension (PH), with an estimated pulmonary artery systolic pressure of 70 mm Hg. The O₂ saturation was 88% at rest supine, 90% standing, and 82% during limited exercise.

A ventilation-perfusion (\dot{V}/\dot{Q}) lung scan subsequently demonstrated multiple segmental and large subsegmental perfusion defects with \dot{V}/\dot{Q} mismatch, indicating a high probability of pulmonary embolism (PE). This was confirmed by pulmonary angiography, which demonstrated surgically accessible pulmonary thromboembolic disease. The patient subsequently underwent successful bilateral pulmonary thromboendarterectomy. Pulmonary arterial pressure fell from 62/21 mm Hg by preoperative catheterization to 47/23 mm Hg by bedside monitoring postoperatively. He also had an inferior vena caval filter inserted despite normal bilateral venous

ultrasound studies and was placed on warfarin. The patient improved symptomatically but continued to have exertional O₂ desaturation. His prostate cancer was treated nonsurgically.

Comment. This is a case of chronic PE presenting as unexplained dyspnea. Although the patient had several appropriate tests during his initial evaluation 4 years earlier, his arterial desaturation remained unexplained and should have prompted further testing (including a V/Q scan) at that time.

5. Dyspnea and Angina Secondary to Pulmonary Hypertension*

A 64-year-old man underwent evaluation for limiting dyspnea accompanied by chest tightness. Three years prior, he had documented DVT and PE, but while taking warfarin he had no clinical recurrence. The patient had progressive limiting dyspnea and chest pain over a period of 2 months. Rest and sublingual nitroglycerin provided relief, but his symptoms were occurring with increasing frequency and required less activity to be provoked. Diltiazem and isosorbide dinitrate had been prescribed with some improvement. An outpatient Holter monitor, obtained in the evaluation of episodic dizziness, had revealed multiform premature ventricular beats and episodes of >2.5 mm ST segment depression.

Physical examination revealed a BP of 116/70 mm Hg, regular pulse at 92 beats/min, RR 15/min, jugular venous pulse ~5 cm above right-atrial level, parasternal lift, S4 gallop without a murmur, and clear lung fields to auscultation. An ECG demonstrated normal sinus rhythm, normal axis, nonspecific ST-T wave changes, and poor R-wave progression across the precordial leads. The patient's CXR demonstrated mild cardiomegaly and clear lung fields. Spirometry was reportedly normal. Resting room air blood gases were as follows: PaO₂ = 66 mm Hg; PaCO₂ = 22 mm Hg;

*Previously reported in and reprinted here with permission from Chest. 1991;100:534-539.

pH = 7.52; SaO₂ = 94%. A perfusion lung scan, found to be unchanged from a study done 1 year prior to admission, was interpreted as indicating low probability for acute embolism.

The patient underwent treadmill exercise testing on a Bruce protocol. During Stage I, he experienced his typical dyspnea and chest tightness. When his systolic BP fell from 140 mm Hg to 110 mm Hg, the exercise was stopped. His ECG demonstrated 1-mm flat ST depression in leads II, III, AVF, and V6 and, in retrospect, it also demonstrated transient S1, S2, S3, RS in V1, and deep S in V6.

Cardiac catheterization demonstrated normal coronary anatomy on angiography and normal LV wall -motion with a calculated LV ejection fraction of 0.58. Right heart catheterization revealed a right atrial pressure of 3 mm Hg and pulmonary artery pressure of 50/26, with a mean value of 35 mm Hg. The patient's pulmonary wedge pressure (PWP) was 13 mm Hg, yielding a pulmonary artery diastolic to wedge pressure gradient of 13 mm Hg. Contrast right ventriculography demonstrated a dilated, hypocontractile right ventricle. No PE was seen on pulmonary angiography.

On a separate occasion, and after informed consent, the patient underwent a symptom-limited, supine bicycle ergometry study with simultaneous hemodynamic monitoring and radionuclide ventriculography to assess the mechanism of his dyspnea. At a low level of activity (100 KPM/min), his pulmonary artery pressure increased from a mean of 50 mm Hg at rest to 75 mm Hg. This was accompanied by an elevation of right atrial pressure from 6 mm to 20 mm Hg and a decline in right ventricular ejection fraction from 0.33 to 0.25. In contrast, LV ejection fraction was 0.61 at rest and 0.57 with exercise. His PWP was 9 at rest and not accurately obtained with exercise. During room air breathing, the patient

experienced chest tightness, as well as dyspnea. An ECG demonstrated ST depression. After a 30-min. rest, the exercise test was repeated while the patient was given oxygen at 2 L/min. Similar pulmonary pressure and right ventricular ejection fraction levels were obtained, but there were neither ECG changes nor the experience of chest tightness. Low-flow chronic oxygen was added to the patient's regimen and isosorbide dinitrate discontinued. Warfarin was continued. Over a period of 8 months, the patient experienced dramatic improvement in his exercise capacity and, on repeat exercise testing, he doubled his workload.

Comment. This unusual case demonstrates dyspnea and angina of predominantly right ventricular origin secondary to PH. Although acute PE was not documented with either perfusion scintigraphy or pulmonary angiography, the clinical decision was made to continue long-term anticoagulation. Chronic home oxygen treatment provided improvement in symptomatic status.

6. Other Causes of Cardiac Dyspnea

A 34-year-old woman presented with increasing dyspnea on exertion. She denied any history of cardiac or pulmonary disease, including cough, sputum production, chest pain, or wheezing. Physical examination revealed an anxious patient, with a resting heart rate of 100 beats/min. On first examination, faint expiratory wheezes were heard. Cardiac auscultation revealed an II/VI systolic murmur. The remainder of the examination was normal.

The patient was started on a long-acting theophylline preparation. Two days later, she returned with a marked increase in her dyspnea. Auscultation revealed an increase in systolic murmur with additional accentuation, with a Valsalva maneuver. An echocardiogram showed asymmetric hypertrophy

of the midventricular septum and systolic anterior motion of the mitral valve, with a dynamic gradient of 80 mm Hg.

Comment. An initial clinical diagnosis of asthma was made when, in fact, the wheezing was cardiac in origin. Administration of theophylline resulted in increased contractility under decreased left and diastolic ventricular volume, which resulted in increased dynamic outflow obstruction. The echocardiogram confirmed the diagnosis of hypertrophic obstructive cardiomyopathy.

7. Psychogenic Dyspnea

A 32-year-old woman was seen in the emergency room because of sudden shortness of breath, reporting, “I just can’t breathe, I just can’t get my breath.” On examination, tachycardia of 110, RR of 26 breaths/min., BP of 118/78 mm Hg, and sighing respirations were observed. Echomoses were present in the right arm and left buttock.

When her hand was held in a calming manner and the doctor looked into her anxious face, her respiration was reduced and her sighing ceased. She started to cry and told the physician of abuse by her live-in boyfriend. Her childhood was also marred by abuse. At a follow-up appointment 1 week later, she was calm but depressed. A series of follow-up visits were arranged.

Comment. Psychogenic dyspnea is common. It eases with exercise. The history and physical examination make the diagnosis. Laboratory tests and imaging studies are not required. ■

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The Snowdrift Pulmonary Conference

This is the latest monograph developed by the Snowdrift Pulmonary Conference, a not-for-profit corporation that is dedicated to the dissemination of knowledge about the lungs and lung diseases and now also cardiopulmonary diseases. Bringing together both private-practice pulmonologists and academicians, the conference organizers have launched a program for primary care practitioners and the patients they serve. This is a consumer-oriented program. The following concise and authoritative monographs for the frontline practitioner have been published:

Frontline Treatment of COPD 2nd ed (1996 and 2000)

Frontline Treatment of Asthma (1997)

Frontline Treatment of Common Respiratory Infections (1998)

Frontline Treatment of Venous Thromboembolism (1999)

Frontline Assessment of Common Pulmonary Presentations (2000)

Frontline Assessment of Lung Cancer and Occupational Pulmonary Diseases (2001)

Frontline Pulmonary Procedures and Interventions (2001)

All of the monographs in the *Frontline* series will be periodically updated. They will be available in hard copy or in a CD-ROM format. They can be viewed on the Internet at:

www.FrontlinePulmonology.org

Lung cancer, the most common fatal malignancy of men and women, presents the most challenging frontier. To help disseminate the new knowledge about the role of early identification and intervention in lung cancer, the Snowdrift Pulmonary Conference has produced, as a major new initiative, a quarterly

newsletter, *Lung Cancer Frontiers (LCF)*. Now reaching the nearly 9,000 board-certified pulmonologists in North America, *LCF* is available on the Internet at:

www.LungCancerFrontiers.org

We believe that an enlightened and informed public working with their personal physician and consultants can help guide the future of medicine as we aim to prevent, cure, and diminish the number and severity of lung diseases that impact the health of our nation. ■

Postscript

It was a daunting task to attempt to write a brief, yet comprehensive monograph on the complex symptom of dyspnea. Full-length textbooks have been devoted to this topic, yet none have been practical enough for easy use by clinicians. We have done our utmost to provide a concise, instructive, and interesting explanation of dyspnea and how patients who suffer from this common symptom can be evaluated, with implications for treatment.

Respiration is fundamental to life in all aerobic creatures. Breathing with comfort is critical to a good quality of life. Naturally, altered sensations of breathing cause emotional highs and lows. Some profound comments about breathing have been captured by many authors. A few citations are in order:

The first breath is the beginning of death.

English proverb

This truism recognizes that we are dependent on breathing throughout our life and reminds us of our mortality. The following two quotations are self-explanatory.

Some folk seem glad even to draw their breath.

William Morris (1834-1896)

More would I, but my lungs are wasted so that strength of speech is utterly denied me.

William Shakespeare, *Henry IV*

(continued)

A reasonable understanding of lung mechanics is reflected in the following two citations:

When man grows old . . . there is much gas within his thorax, resulting in panting and troubled breathing.

Huang Ti, The Yellow Emperor(2697-2597 B.C.)

These muscles have a voluntary and an involuntary movement seeing that they are those which open and shut the lung. When they open they suspend their function which is to contract, for the ribs which at first were drawn up and compressed by the contracting of these muscles then remain at liberty and resume their natural distance as the breast expands. And since there is no vacuum in nature the lung which touches the ribs from within must necessarily follow their expansion; and the lung therefore opening like a pair of bellows draws in the air in order to fill the space to formed.

Leonardo da Vinci (1452-1519)

A favorite of one of the editors (TLP) is from John Keats, who died of tuberculosis at age 26:

*A thing of beauty is a joy forever:
Its loveliness increases; it will never
Pass into nothingness; but still will keep
A bower quiet for us, and a sleep
Full of sweet dreams, and health, and quiet
breathing.*

John Keats (1795-1821)

Today, the joys of comfortable breathing are embodied in the mastheads of publications aimed at a lay audience, such as:

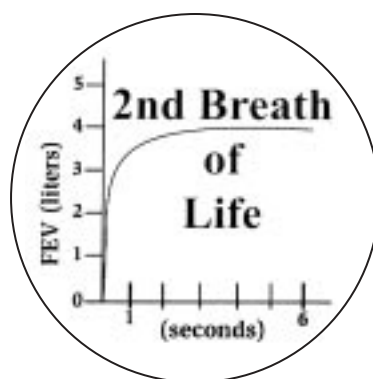
Breathe Well,
Boehringer Ingelheim Pharmaceuticals, Inc.,
P.O. Box 1164, West Caldwell, NJ 07007-9472

and these produced by patient care organizations:

Second Wind,
Pulmonary Education and Research Foundation,
P.O. Box 1133 Lomita, CA 90717-5133

Breathe Easy,
Moore Medical Service, 115 Grand Avenue,
Spencer, IA 51301

The new healthcare initiative in the United States known as the National Lung Health Education Program (NLHEP) uses the concept of the second breath of life on its web site, www.NLHEP.org:



The point of this is to get spirometry on the frontline and into the office of all primary care physicians and specialists such as cardiologists, for the purpose of advancing the cause of diagnosing and treating DYSPNEA. ■

**Thomas L. Petty, MD, Co-Editor**

Dr Petty received his MD degree at the University of Colorado in Denver in 1958. He interned at Philadelphia General Hospital and began his residency training at the University of Michigan in Ann Arbor before returning to Denver to complete it at the University of Colorado. A board-certified internist and pulmonologist, Dr Petty is Professor of Medicine both at the University of Colorado Health Sciences Center and at Rush University in Chicago. He was previously head of the Division of Pulmonary Sciences at the University of Colorado and, from 1964 to 1989, Director of the fellowship training program there. Having served most recently as Director of the HealthONE Center for Health Sciences Education, he is now a consultant to HealthONE and other medical institutions throughout the United States.

Dr Petty was the organizer and founding president of the Association of Pulmonary Program Directors. He has served as president of the American College of Chest Physicians (ACCP) and is a former member of the Board of Governors of the American Board of Internal Medicine. He is currently Chairman of the National Lung Health Education Program (NLHEP)

In 1995 Dr Petty received the distinguished service award of the American Thoracic Society, was elected to the Colorado Physicians' "Hall of Fame," received the annual award for excellence of the American Association for Respiratory and Cardiovascular Rehabilitation, and was elected master fellow of the ACCP. In 1996 he received the master award of the American College of Physicians. He remains active in teaching, patient care, and research.



Sidney C. Smith, Jr, MD, Co-Editor

Dr Smith is Professor of Medicine, Chief of Cardiology, and Director of the Center for Cardiovascular Science and Medicine at the University of North Carolina at Chapel Hill. He received his MD degree from Yale University in New Haven, Connecticut, and completed a residency in internal medicine and a fellowship in cardiology at Harvard Medical School/Peter Bent Brigham Hospital in Boston, Massachusetts.

Prior to joining the faculty of the University of North Carolina, Dr Smith was Clinical Professor of Medicine at the University of California, San Diego, and Director of the San Diego Cardiac Center at Sharp Healthcare. He also served as Director of the Cardiovascular Laboratories at the University of Colorado.

Dr Smith served as national President of the American Heart Association (AHA) from 1995 to 1996. His service with the AHA spans 2 decades and includes work at all levels of the organization and with three different AHA affiliates. He has been a member of a number of national committees with the American College of Cardiology (ACC) and has been active in the development of ACC/AHA Practice Guidelines. Currently, he serves as Chair of the ACC/AHA Committee to Revise PTCI (percutaneous coronary intervention) Guidelines. Dr Smith is a member of the editorial boards for such entities as the *Journal of Interventional Cardiology*, the *American Heart Journal*, and the American College of Cardiology Education and Learning Program. He also serves on the medical advisory board for the *Time-Life Medical Series* of books. The author of more than 150 articles and book chapters, Dr Smith presents regularly at scientific meetings and guest lectures. He has spoken

about heart disease and stroke in interviews with CNN, CBS, NBC, and many national newspapers.

In 1993 Dr Smith was honored as the AHA's Physician of the Year and in 1996 received the association's Distinguished National Leadership Award. In 1998 he was elected to "Best Doctors in America." In 2000 he was awarded the prestigious Gold Heart Award by the AHA.

The focus of Dr Smith's research has been on lipoprotein abnormalities, reperfusion therapies for acute myocardial infarction, and medical management of unstable angina pectoris. He is currently evaluating the role of primary and secondary prevention efforts in the treatment of cardiovascular disease.



J. Kern Buckner, MD

Dr Buckner received his MD degree from Duke University in 1980. He completed his medical internship, residency, chief medical residency, and cardiology fellowship at the University of Colorado Health Sciences Center in Denver. He is a diplomat of the Boards of Internal Medicine and Cardiovascular Diseases with added qualification in Interventional Cardiology.

In addition to being in private practice, Dr Buckner is Chief of Cardiology at Swedish Medical Center in Englewood, Colorado, and Clinical Assistant Professor of Medicine at the University of Colorado Health Sciences Center. He remains active in clinical research and teaching.

**Roy V. Ditchey, MD**

Dr Ditchey received an undergraduate degree in biology from Stanford University in Palo Alto, California, and his medical degree from the University of California, Irvine. He trained as an intern and resident in internal medicine at the Johns Hopkins Hospital in Baltimore, Maryland, before continuing his postdoctoral studies as a cardiology fellow at the University of California, San Diego. Appointed Assistant and then Associate Professor of Medicine at the University of Colorado Health Sciences Center in Denver (1980-1985), Dr Ditchey served as Associate Professor of Medicine at the University of Vermont from 1985 to 1995. He is currently in private practice in Redding, California.

**James T. Good, Jr, MD**

Dr Good received his MD degree from the University of Kansas in Kansas City, where he completed a medical internship, residency, and chief medical residency. He then undertook a 3-year pulmonary and critical care fellowship at the University of Colorado in Denver, where he remained for the next 4 years as Assistant Professor of Medicine and medical director of both the Respiratory Therapy Department and the Critical Care Unit of Denver General Hospital. Dr Good is currently in private practice in pulmonary and critical care medicine in south Denver and is medical director of the Swedish Medical Center Critical Care Unit.

A fellow of the American College of Physicians and the American College of Chest Physicians (ACCP), Dr Good served as the governor of the ACCP's Colorado and Wyoming divisions from 1988 to 1994. His scientific interests include management of critical patients with acute respiratory failure, pleural

diseases, and asthma. He remains actively involved in clinical research, teaching medical students and residents, and contributing to continuing medical education programs.



Richard A. Matthay, MD

Dr Matthay received his AB degree from Stanford University in Palo Alto, California, in 1963. For the next 2 years, he served as an officer in the Army Medical Service Corps in Texas, Louisiana, and Korea. He received his MD degree from Tufts University School of Medicine in Boston, Massachusetts, in 1970 and by 1975 had completed his internship and residency and a pulmonary and critical care medicine fellowship at the University of Colorado Medical Center in Denver. Dr Matthay has served as Associate Director and Training Director of the Pulmonary and Critical Care Section at Yale University School of Medicine in New Haven, Connecticut, since 1975. In 1984 he was appointed Professor of Medicine. He was awarded the Boehringer Ingelheim Chair of Medicine at Yale in 1994, and in 2000 he received the Connecticut Thoracic Society Humanitarian Award.

Dr Matthay receives enormous gratification from teaching and mentoring medical students, residents, and fellows. He has written more than 350 publications. His primary research interests are the application of biomarkers in the early diagnosis of lung cancer, right ventricular function in lung disease, and pulmonary manifestations of the systematic autoimmune diseases.

Douglass Morrison, MD

Dr Morrison received a BA degree in Biochemistry from Harvard University in 1969 and his MD degree from the University of Pittsburgh in 1973. He completed his internship and residency and a pulmonary fellowship at the University of South Florida in Tampa, followed by a cardiology fellowship and 1 year of a nuclear medicine residency at the University of Washington in Seattle. For 4 years, Dr Morrison was Director of the Coronary Care Unit at the Tucson Veterans Administration (VA) Hospital and Assistant Professor of Medicine and Radiology at the University of Arizona. For the next 15 years, he was Director of the Cardiac Catheterization Laboratory at the Denver VA Hospital and on the faculty of the University of Colorado College of Medicine. He was named Professor of Medicine in 1995. In 1999 he returned to the Tucson VA Hospital as Director of the Cardiac Catheterization Laboratory, while also simultaneously serving as Professor of Medicine and Radiology and attending graduate school in epidemiology at the University of Arizona.

Dr. Morrison is board-certified in internal medicine, pulmonary disease, cardiovascular disease, and interventional cardiology and a Fellow of the American College of Physicians, the American College of Cardiology, and the Society for Cardiac Angiography and Interventions. He was the Principal Investigator of the Veterans Affairs Cooperative 385 study, and the Angina With Extremely Serious Operative Mortality Evaluation (AWESOME) study, a 5-year nationwide randomized trial comparing coronary artery by-pass graft (CABG) to percutaneous intervention for patients with medically refractory myocardial ischemia and high risk of adverse outcomes with CABG.

Glossary of Abbreviated Terms

ABG	Arterial blood gas
ACE-I	Angiotensin-converting enzyme inhibition drugs
ANA	Antinuclear antibody
AS	Aortic stenosis
ASD	Atrial septal defect
A-V	Arterial venous
BP	Blood pressure
C-ANCA	Antineutrophil cytoplasmic antibody
CBC	Complete blood count
CHD	Coronary heart disease
CHF	Congestive heart failure
CO	Carbon monoxide
COPD	Chronic obstructive pulmonary disease
CT	Computed tomography
CXR	Chest x-ray
DIP	Desquamitative interstitial pneumonitis
DLCO	Diffusing capacity for carbon monoxide
DVT	Deep venous thrombophlebitis
ECG	Electrocardiogram
FEF	Forced expiratory flow
FEV ₁	Forced expiratory volume in 1 second
FEV ₆	Forced expiratory volume in 6 seconds
FVC	Forced vital capacity
HRCT	High-resolution computed tomography
ILD	Idiopathic lung disease
IPF	Idiopathic pulmonary fibrosis
IV	Intravenous

LLN	Lower limits of normal
LV	Left ventricular
LV/A systP	Left ventricular/aortic systolic pressure
LVEDP	Left ventricular end-diastolic pressure
LVH	Left ventricular hypertrophy
LV/PWP	Left ventricular/pulmonary wedge pressure
Lytics	Thrombolytic drugs
NHANES III	The third National Health and Nutrition Examination Survey
NIVA	Noninvasive vascular assessment
NLHEP	National Lung Health Education Program
NSIP	Nonspecific interstitial pneumonitis
O ₂	Oxygen
PaCO ₂	Arterial carbon dioxide tension
PaO ₂	Arterial oxygen tension
PCO ₂	Carbon dioxide partial pressure
PD ₂₀	Provocative dose to reduce FEV ₁ by 20% (methacholine challenge)
Pdi	Transdiaphragmatic pressure
Pdi _{max}	Maximum transdiaphragmatic pressure
PE	Pulmonary embolism
Pe _{max}	Maximum expiratory pressure
PFT	Pulmonary function test
pH	Expression of acidity or alkalinity
PH	Pulmonary hypertension
Pi _{max}	Maximum inspiratory pressure
PIOPED	Prospective Investigation of Pulmonary Embolism Diagnosis
PND	Paroxysmal nocturnal dyspnea
PO ₂	Arterial oxygen partial pressure
PPH	Primary pulmonary hypertension
PWP	Pulmonary wedge pressure

(continued)

RR	Respiratory rate
RV	Residual volume
SI, Q3, T3	Suggest pulmonary embolism
SaO ₂	Arterial oxygen saturation
SPECT	Single-photon-emission computed tomography
SZ	One phenotype of alpha ₁ -antitrypsin deficiency
TLC	Total lung capacity
UIP	Usual interstitial pneumonitis
VA	Alveolar volume
VC	Vital capacity (of lung)
\dot{V}/\dot{Q}	Ventilation-perfusion
VSD	Ventricular septal defect
VTE	Venous thromboembolism
ZZ	One phenotype of alpha ₁ -antitrypsin deficiency

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