Evaluating dyspnea: A practical approach -- When to consider cardiopulmonary exercise testing.

ABSTRACT: Shortness of breath is a common complaint associated with a number of conditions. Although the results of the history and physical examination, chest radiography, and spirometry frequently identify the diagnosis, dyspnea that remains unexplained after the initial evaluation can be problematic. A stepwise approach that focuses further testing on the most likely diagnoses is most effective in younger patients. Early bronchoprovocation challenge testing is warranted in younger patients because of the high prevalence of asthma in this population. Older patients require more complete evaluation because of their increased risk of multiple cardiopulmonary abnormalities. For patients who have multiple contributing factors or no clear diagnosis, cardiopulmonary exercise testing can help prioritize treatment and focus further evaluation. (J Respir Dis. 2006;27(1):10-24)

Dyspnea, the experience of breathing discomfort, is a common and complex problem that can be caused by multiple organic and psychosocial factors.1 Patients with chronic dyspnea have symptoms that last at least 3 weeks and are generally considered to have unexplained dyspnea if the cause cannot be identified after the initial history, physical examination, and screening tests.

In this article, we will provide a systematic, timely, and cost-effective approach to the assessment of dyspnea.

A STEPWISE APPROACH
A summary of the conditions associated with chronic dyspnea is displayed in Table 1.2-5 Multiple causes have been identified in up to one third of patients.6 The evaluation of dyspnea starts with a clinical assessment that guides the stepwise selection of tests that can accurately detect or exclude common associated conditions. An approach that combines strategies outlined by previous authors is summarized in Table 2.7-10

Step 1: Initial assessment

The initial clinical assessment includes a thorough history and physical examination. Although few would argue with this approach, it is important to recognize that history and physical examination findings alone have a limited predictive value in the diagnosis of chronic dyspnea.2 Isolated findings should therefore be interpreted with caution.

The addition of a chest radiograph to the initial clinical assessment has been shown to provide reasonable diagnostic accuracy for common conditions, including chronic obstructive pulmonary disease (COPD), interstitial lung disease (ILD), and congestive heart failure.2 Chest radiographic abnormalities are relatively uncommon in otherwise healthy young adults with dyspnea; sarcoidosis is the most common cause of abnormal findings in this setting.5 The diagnostic yield of a chest radiograph increases with age, as the prevalence of obstructive and interstitial lung diseases, cancer, and their complications increases.

If available, screening spirometry can rapidly identify the presence of obstructive lung disease in young adults in whom asthma is
clinically suspected and in older persons who have risk factors for 
COPD. Examination of the flow-volume loop for evidence of 
variable or fixed airway obstruction is an important part of this 
assessment, because conditions associated with these abnormalities 
can otherwise go undiagnosed despite extensive subsequent testing.

Pulse oximetry at rest or during ambulation can be included in the 
initial assessment to rapidly and noninvasively evaluate pulmonary 
gas exchange. Its major uses are to confirm normal oxygen 
saturation in patients at low risk for oxygen transport abnormalities 
and to identify a need for supplemental oxygen in patients with 
known cardiopulmonary disease.

Step 2: Focused testing

If the initial assessment fails to identify a clear diagnosis, further 
focused testing must be performed. Tests should be selected based 
on their ability to confirm or exclude common conditions and other 
possible diagnoses identified through the initial assessment. A 
focused approach is most effective in younger patients, in whom the 
possible causes of dyspnea are generally limited. As patients age, 
the differential diagnosis broadens, with cardiovascular disease 
becoming a more significant concern. Because of the increased risk, 
the approach to the older patient who has dyspnea must be more 
systematic and complete.

Dyspnea in young patients is commonly caused by asthma, vocal 
cord dysfunction, deconditioning, or psychiatric disorders.3,5 We 
favor bronchoprovocation challenge (BPC) testing as the next 
diagnostic step in young persons, because of the high prevalence of 
asthma in this
population. Methacholine is a cholinergic agent commonly used in this setting, and it has a well-established safety profile.11

BPC results must be carefully interpreted based on patient response—specifically, the dose of methacholine required to decrease the forced expiratory volume in 1 second by 20% or more, or PC20. The advantage of BPC using methacholine lies in its negative predictive value (over 90% with a PC20 greater than 8 to 25 mg/mL and a pretest probability of 30% to 70%) and its ability to diagnose asthma in a population in whom the prevalence of this disease is high. A low PC20 has a high post-test certainty (90% to 98% with a pretest probability of 20% to 80% and a PC20 less than 1 mg/mL). The clinical interpretation of borderline airway hyperreactivity (PC20 of 4 to 16 mg/mL), however, must be approached with caution because of the high frequency of false positives that occur in this range.11

Vocal cord dysfunction is characterized by paradoxical adduction of the vocal cords during inspiration. This condition has been demonstrated in 10% to 15% of young patients evaluated for exertional dyspnea and in 40% of patients who sought evaluation for asthma that was unresponsive to aggressive therapy.5,12 In the largest published series to date, 56% of patients with vocal cord dysfunction were found to have objective evidence of asthma, underscoring the fact that these conditions are not mutually exclusive.13 Vocal cord dysfunction has been characterized as a form of conversion disorder and is commonly associated with a variety of psychiatric conditions, postnasal drip, and gastroesophageal reflux disease; it is most likely to occur in young, single women.13
Truncation of the inspiratory limb of the flow-volume loop is a characteristic finding in vocal cord dysfunction, but it is present in only 23% of patients who do not have acute symptoms. Flow-volume abnormalities can be precipitated by BPC testing in 60% of patients with vocal cord dysfunction or by exposure to inciting activities or triggers (such as perfumes, cold air, exercise). The gold standard for diagnosis is observation of anterior vocal cord adduction during inspiration alone or during both inspiration and expiration accompanied by a residual posterior glottic "chink" during laryngoscopy (Figure 1).

Since older patients are at increased risk for multiple cardiopulmonary abnormalities, they should undergo screening electrocardiography and more complete pulmonary function testing if the results of screening spirometry are abnormal. Resting ECG changes in patients with clinical risk factors for coronary artery disease have been shown to be of predictive value. A stress test or echocardiogram is a reasonable next step in this setting, especially if the patient's symptoms are out of proportion to pulmonary findings.

The aging process causes a gradual deterioration of lung function throughout adult life. Decreased lung elasticity, increased chest wall stiffness, and decreased respiratory muscle strength can result in significant changes in pulmonary function. These changes may be accelerated by tobacco use or other exposures.

Asthma remains an underdiagnosed and undertreated condition in patients older than 65 years, and it is important to consider this disease in older persons with suggestive symptoms. In one large cohort study, more than 15% of older persons reported symptoms of
possible or probable untreated asthma, resulting in reduced quality of life and increased morbidity.

Pulmonary function testing in older patients with dyspnea therefore must be more complete. In our pulmonary function laboratory, these patients undergo pre- and post-bronchodilator spirometry and measurement of lung volumes, carbon monoxide-diffusing capacity, and arterial blood gases (ABGs) as part of a standard dyspnea evaluation.

Maximum voluntary ventilation, maximum inspiratory pressure, and maximum expiratory pressure can be measured in patients with a clinical history or pulmonary function test results that suggest neuromuscular weakness. A recent comprehensive review of pulmonary function testing provides an excellent reference for a more detailed discussion on this topic.

Screening hemoglobin/hematocrit should be considered in high-risk populations. African Americans, Native Americans, immigrants from developing countries, pregnant women, and persons of low socioeconomic status are at highest risk for iron deficiency anemia in the United States. The risk of anemia in older persons is largely based on comorbid conditions, such as chronic kidney disease and occult colon cancer.

Although current guidelines do not support screening asymptomatic persons for thyroid disease, some authors continue to suggest that thyroid-stimulating hormone screening in persons at high risk for mild thyroid failure is cost-effective, based on computer decision models. Thyroid disease is most common in older and postpartum women; patients in geriatric units, acute hospital medical wards, and
psychiatric wards; and patients with autoimmune antibodies.22

A renal panel can identify metabolic acidosis and volume overload from chronic kidney disease, which are well-documented causes of chronic dyspnea. Hypertension, diabetes, and older age are major risk factors for chronic kidney disease; these risk factors are also more prevalent in the African American population.23

Step 3: Cardiopulmonary exercise testing

There are several limitations to the initial and focused evaluations outlined above. Resting cardiopulmonary measurements have been shown to correlate poorly with symptoms during exertion, and they cannot reliably predict exercise performance and functional capacity. Cardiopulmonary exercise testing (CPET) provides an objective and reproducible measurement of functional capacity (oxygen consumption, or V.O2max) and can identify the main cause(s) of symptoms in patients with multiple contributing conditions.

For patients whose dyspnea remains unexplained after Steps 1 and 2, incorporating CPET into the decision-making process can be a cost-effective and useful way to identify the exercise response pattern, focus further diagnostic testing, and provide objective measurements that can be used to assess clinical outcomes of therapy.24

A cycle ergometer is generally preferred for CPET, to minimize motion artifact and provide a direct measurement of work rate. Commercially available CPET systems process 4 primary signals—airflow, oxygen, carbon dioxide, and heart rate. These signals form
the basis for all measured and derived CPET variables, including V.O2, carbon dioxide output, and minute ventilation (Ve). Pulse oximetry, standard-interval 12-lead electrocardiography, and blood pressure are also monitored during a standard symptom-limited CPET. ABG measurements can be added to provide more accurate information on pulmonary gas exchange.

The patient's symptoms during exercise coupled with objective measurements using a standardized dyspnea rating scale also provide vital information. Exercise flow-volume loop analysis is an evolving technology that can give important insight into breathing strategies when it is correlated with symptoms of dyspnea during exercise. A summary of important CPET variables is provided in Table 3.

CPET can be performed using a symptom-limited incremental or constant work protocol. An incremental exercise test consists of 3 minutes of rest, 3 minutes of unloaded pedaling, an 8- to 12-minute exercise phase in which work rate is continuously increased until peak exercise is reached, and 10 minutes of recovery.

The constant work protocol is commonly performed about 1 hour after incremental testing and consists of 6 to 10 minutes of continuous exercise using 70% to 80% of the previously achieved maximum work rate; ABGs are measured at rest and at 5 minutes. Constant work exercise can provide valuable information regarding gas exchange and has been demonstrated to be more sensitive than a 6-minute walk test in determining therapeutic efficacy of pharmacologic interventions.24

CPET interpretation requires a systematic approach that reviews the
reason(s) for and overall quality of the test, identifies key variables and graphic relationships to determine normal and abnormal exercise response patterns, and considers conditions that may be associated with these patterns.24,25

Step 4: Specialized testing based on exercise response patterns

CPET is a sensitive method of identifying the mechanisms and severity of the patient's exercise limitation. The observed exercise response pattern allows the interpreting clinician to focus on a limited differential diagnosis for further testing and treatment.9

-Normal exercise response: Normal CPET demonstrates a normal exercise capacity with normal cardiac and respiratory responses to exercise. At peak exercise, healthy persons approach their maximum predicted heart rate and oxygen pulse and have significant physiologic breathing reserve. Gas exchange tends to improve with exercise, and oxygen saturation remains stable throughout the test. A normal exercise response provides reassurance that no significant functional abnormalities exist and frequently obviates the need for further testing.

Patients who have psychogenic causes of dyspnea may have normal CPET findings; these findings should not discourage psychiatric referral if the patient provides a suggestive clinical history. Patients who have gastroesophageal reflux disease may also have a normal exercise response pattern. These patients may be treated with an empiric trial of acid suppression therapy, with referral for further gastroenterologic evaluation and endoscopy if symptoms persist.

-Hyperventilation/psychogenic disorders: As noted above, patients
with psychogenic causes of dyspnea often have normal or near-normal exercise tolerance. Abnormal breathing patterns at rest and during exercise should increase clinical suspicion and, in some circumstances, can be diagnostic. In contrast to the gradual increase in respiratory frequency during progressive exercise in healthy persons, patients who have hyperventilation syndrome may have an abrupt onset of regular, rapid, shallow breathing that is disproportionate to the level of metabolic stress (Figure 2).

Patients with hyperventilation syndrome can have a variety of psychogenic disorders. They commonly complain of "asthma-like" symptoms of dyspnea, chest pain, and light-headedness with exertion and may have a history of substance abuse or multiple somatic complaints. Anxiety and stress are among the several postulated mechanisms for hyperventilation, and both treatment of the underlying psychiatric disorder and behavioral modification techniques can be very successful in this otherwise challenging disorder.26,27

-Obesity: A spectrum of exercise responses can be seen in obese patients. Exercise capacity may be normal or low, and it will be even lower with significant obesity when expressed per kilogram of actual body weight (V.O2max/kg). The increased metabolic requirements of moving the excess weight during exercise results in a disproportionately increased V.O2, heart rate, and Ve at any given level of work. Coronary ischemia and diastolic dysfunction are commonly associated with obesity and must be carefully excluded during CPET evaluation. Once other causes of dyspnea are excluded, obese patients should be enrolled in a weight reduction/aerobic training program and monitored for symptom improvement.
Cardiac/ischemia: Patients with a cardiac/ischemia response pattern on CPET may have problems with the heart or the pulmonary or systemic circulation, or reduced oxygen delivery resulting from significant anemia. Exercise capacity is reduced, and anaerobic threshold is low as a result of the early onset of lactic acidosis. During exercise, heart rate is elevated and oxygen pulse is low, which is a surrogate marker of inadequate stroke volume augmentation during exercise.

An ECG may show evidence of cardiac ischemia if coronary artery disease is present. Ample ventilatory reserve is generally present, although gas exchange abnormalities may be observed if significant pulmonary hypertension is present.

Patients with suspected cardiac ischemia should be given empiric beta-blocker and aspirin therapy while further cardiac evaluation is performed. Monitoring response to therapy after risk stratification and coronary intervention is important, because continued symptoms may suggest additional diagnoses that require further evaluation.

Patients with a cardiac/ischemia response pattern and gas exchange abnormalities need to be assessed for pulmonary hypertension. Treatment of the underlying condition is generally the only management necessary for secondary...