Approach to the patient with dyspnea

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Literature review current through: Feb 2021. | **This topic last updated:** May 27, 2020.

INTRODUCTION

Dyspnea, or breathing discomfort, is a common symptom that afflicts millions of patients with pulmonary disease and may be the primary manifestation of lung disease, myocardial ischemia or dysfunction, anemia, neuromuscular disorders, obesity, or deconditioning. Examination of the language of dyspnea suggests that this symptom represents a number of qualitatively distinct sensations, and that the words utilized by patients to describe their breathing discomfort may provide insight into the underlying pathophysiology of the disease.

The key elements in the evaluation of the patient with dyspnea will be reviewed here. The basic physiology of dyspnea, the evaluation of acute dyspnea, and dyspnea in pregnancy are discussed separately. (See "Physiology of dyspnea" and "Evaluation of the adult with dyspnea in the emergency department" and "Maternal adaptations to pregnancy: Dyspnea and other physiologic respiratory changes".)

DEFINITION OF DYSPNEA

A consensus statement of the American Thoracic Society defines dyspnea in the following way [1]:

"Dyspnea is a term used to characterize a subjective experience of breathing discomfort that is comprised of qualitatively distinct sensations that vary in intensity. The experience derives from interactions among multiple physiological, psychological, social, and environmental factors, and may induce secondary physiological and behavioral responses."

Dyspnea is considered acute when it develops over hours to days and chronic when it occurs for more than four to eight weeks. Some patients present with acute worsening of chronic breathlessness that may be caused by a new problem or a worsening of the underlying disease (eg, asthma, chronic obstructive pulmonary disease, heart failure).

The American Thoracic Society (ATS) statement on the mechanisms, assessment, and management of dyspnea, as well as other ATS guidelines, can be accessed through the ATS web site at www.thoracic.org/statements.

PATHOPHYSIOLOGY

Most patients with breathing discomfort can be categorized into one of two groups: respiratory system dyspnea or cardiovascular system dyspnea. Respiratory system dyspnea includes discomfort related to disorders of the central controller, the ventilatory pump, and the gas exchanger (table 1), while cardiovascular system dyspnea includes cardiac diseases (eg, acute ischemia, systolic dysfunction, valvular disorders, pericardial diseases), anemia, and deconditioning (figure 1). More than one process may be active in a given patient, and the basic physiology of dyspnea does not always adhere to this structure; for example, stimulation of pulmonary receptors can result from interstitial inflammation (respiratory system) or interstitial edema (cardiovascular system). Nevertheless, this construct offers an organized approach to the patient with dyspnea of unclear etiology. (See "Physiology of dyspnea".)

Respiratory — The respiratory system is designed to move air by bulk transport from the atmosphere to the alveoli, where oxygen uptake into the blood and elimination of carbon dioxide occurs by diffusion across the alveolar-capillary membrane. Carbon dioxide is then removed from the lungs by bulk transport to the atmosphere. Several components must be functioning smoothly for this process to occur; derangements in any of these elements can lead to dyspnea.

- **Controller** – The "respiratory controller" determines the rate and depth of breathing via efferent signals sent to the ventilatory muscles. Factors that stimulate the respiratory centers in the brainstem lead to increased ventilation and breathing discomfort in a variety of settings; these often are secondary to derangements in other parts of the system, such as hypoxia or hypercapnia due to ventilation/perfusion mismatching in the gas exchanger, or stimulation of pulmonary receptors as occurs with interstitial inflammation or edema. In addition, drugs such as aspirin (at a toxic dose) or progesterone and conditions such as pregnancy or diabetic ketoacidosis can produce dyspnea through central effects independent of problems in the ventilatory pump or gas exchanger. Typically, dyspnea associated with stimulation of the

respiratory controller is described as a sensation of "air hunger" or an "urge or need to breathe" [2-4]. (See "Control of ventilation" and "Physiology of dyspnea".)

To some degree, the breathing pattern may also reflect what are presumed to be attempts by the controller to reduce breathing discomfort. Thus, patients with severe airflow obstruction generally adapt a relatively slow, deep breathing pattern to minimize the pleural pressures needed to overcome airways resistance. Alternatively, patients with interstitial fibrosis or kyphoscoliosis and reduced lung or chest wall compliance have a characteristic rapid, shallow breathing pattern which minimizes the work needed to expand the thorax.

When the respiratory controller is stimulated (eg, by exercise), airflow obstruction may heighten the sensation of air hunger. The increase in respiratory rate during exercise in the setting of expiratory flow limitation can lead to exercise-induced air-trapping, a process known as dynamic hyperinflation. Dynamic hyperinflation is associated with a reduced inspiratory reserve and increased dyspnea. For those in whom hyperinflation is substantial, such that inspiratory capacity at rest or during exercise is limited by total lung capacity, dyspnea is further exacerbated, and patients may also complain of an inability to get a deep breath. (See "Dynamic hyperinflation in patients with COPD".)

For patients with restrictive lung disease, the adoption of breathing patterns with either an increase or decrease in tidal volume from their average resting tidal volume results in increased dyspnea [5]. Breathing with a rapid, shallow pattern, the patient experiences an increase in the ratio of dead space to tidal volume (since anatomic dead space is relatively fixed), which leads to a need for greater total ventilation (hence, the increase in respiratory rate); this adds to respiratory work-load and may contribute to the development of hypercapnia. In contrast, an increase in tidal volume requires a significant increase in respiratory work due to the stiffness of the lung. Since most patients with restrictive lung disease tend to use a rapid, shallow breathing pattern, we conclude that this pattern, relative to alternatives, must produce less dyspnea.

- **Ventilatory pump** – The "ventilatory pump" comprises the ventilatory muscles, the peripheral nerves which transmit signals to them from the controller, the bones of the chest wall to which the respiratory muscles are connected, the pleura which transforms movement of the chest wall to negative pressure inside the thorax, and the airways that serve as a conduit for the flow of gas from the atmosphere to the alveoli and back again. The most common derangements of the ventilatory pump result in a sense of increased "work of breathing" [6-10].

  Neuromuscular weakness (eg, myasthenia gravis, Guillain-Barré syndrome) leads to a condition in which the patient must exert near maximal inspiratory effort to produce a normal negative pleural pressure [11]. Patients with reduced compliance of the chest wall (eg, kyphoscoliosis) or

lungs (eg, interstitial fibrosis) must perform more work than normal to move air into the lungs. Obstructive lung disease is associated with increased resistance to flow and, in patients with significant hyperinflation, reduced compliance as breathing occurs on the stiff portion of the pressure-volume curve of the respiratory system. When hyperinflation results in an end-inspiratory volume that approximates total lung capacity, patients often complain of an inability to get a deeper satisfying breath [9]. A sensation of chest tightness may also be present in patients in whom acute bronchoconstriction is the cause of airflow obstruction [6,7,12,13].

- **Gas exchanger** – The "gas exchanger" consists of the alveoli and the pulmonary capillaries across which oxygen and carbon dioxide diffuse. Most of the common cardiopulmonary disorders leading to dyspnea are associated with some derangement of the gas exchanger due either to destruction of the diffusing membrane (eg, emphysema, pulmonary fibrosis) or the addition of fluid or inflammatory material into the lungs such that ventilation to alveoli is reduced regionally. To a lesser degree, the distance for diffusion may also contribute in these conditions or in the greatly dilated pulmonary capillaries seen in some patients with hepatopulmonary syndrome. Diseases affecting the gas exchanger are typically characterized by hypoxemia, either at rest or with exercise, and by chronic hypercapnia in more severe cases. These gas exchange abnormalities stimulate the respiratory centers in the brainstem and lead to a sensation of "air hunger" or an increased urge to breathe.

Cardiovascular — The cardiovascular system is designed to move oxygenated blood from the lungs to metabolically active tissues, and then transport carbon dioxide from the tissues back to the lungs. For this system to work optimally and avert breathing discomfort, one must have a pump that functions without generating high pulmonary capillary pressures. There must also be sufficient hemoglobin to carry oxygen and appropriate enzymes to utilize oxygen in the tissues.

- **Heart failure** – Heart failure is a clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle(s) to fill with or eject blood. Symptoms of heart failure fall into two major classes: those due to a reduction in cardiac output (fatigue, weakness, and dyspnea on exertion) and those due to increased pulmonary or systemic venous pressure and fluid accumulation (dyspnea at rest and exertion, edema, hepatic congestion, and ascites). When heart failure causes an increase in pulmonary venous pressure, it can lead to dyspnea either by producing hypoxemia or by stimulating pulmonary vascular and/or interstitial receptors (eg, unmyelinated J-receptors, also called C-fibers). Causes of heart failure include ventricular systolic dysfunction, ventricular diastolic dysfunction, and valvular disease. Cardiac tamponade may also lead to dyspnea by increasing pulmonary vascular pressures. (See "Physiology of dyspnea" and "Heart failure: Clinical manifestations and diagnosis in adults" and "Cardiac tamponade".)

In patients with low cardiac output, oxygen delivery to the tissues is reduced, which may lead to changes in tissue metabolism with associated accumulation of products of anaerobic energy generation leading to stimulation of metabo- or ergoreceptors [14,15], which can lead to dyspnea.

- **Anemia** – Anemia can severely impair oxygen delivery because the bulk of oxygen carried in the blood is hemoglobin-bound (see "Structure and function of normal hemoglobins"). Nevertheless, the exact mechanism by which anemia produces dyspnea is not known. As described above for low cardiac output heart failure, the inability to sustain aerobic metabolism may lead to stimulation of "ergoreceptors" [14,15]. Anemia also leads to increased cardiac output, which may necessitate elevated left ventricular volume and pulmonary vascular pressures. However, the quality of dyspnea is usually quite different in these two clinical situations.

- **Deconditioning** – Individuals usually complain of respiratory discomfort when they engage in vigorous physical activity, even in the presence of a normal cardiovascular and respiratory system and normal hematocrit. More fit individuals experience less discomfort for any given workload; cardiovascular fitness is determined by the ability of the heart to increase maximal cardiac output and by the ability of the peripheral muscles to utilize oxygen efficiently for aerobic metabolism.

  In contrast, a sedentary existence reduces fitness and leads to dyspnea, often with seemingly trivial tasks. It is common for patients with chronic cardiopulmonary disease to assume a sedentary lifestyle in an effort to avoid breathing discomfort. However, the end result over a span of months to years is that the individual becomes progressively deconditioned (ie, reduced maximal cardiac output, reduced capillary density in the muscles, and reduced mitochondrial capacity to sustain aerobic metabolism) and ultimately may be limited more by poor cardiovascular fitness than by the underlying disease [16]. Dyspnea due to deconditioning is typically described as "heavy breathing" or a sense of "breathing more" [8], and with careful questioning, one can determine that the patient is actually limited by fatigue or leg discomfort rather than breathing discomfort.

CLINICAL ASSESSMENT

While clinical history is often insufficient to make a secure diagnosis, it provides guidance in narrowing the diagnostic possibilities and selecting diagnostic tests. In one study of 85 patients presenting to a pulmonary unit with a complaint of chronic dyspnea, the initial impression of the etiology of dyspnea based upon the patient history alone was correct in only 66 percent of cases [17]. Thus, a systematic diagnostic approach to these patients is necessary.

Temporal pattern and triggers — The temporal pattern of breathlessness and association with certain triggers can provide important clues. Breathing discomfort arising over the course of minutes to hours is due to a relatively limited number of conditions (table 2). These entities typically have associated symptoms and signs that provide clues to the appropriate diagnosis, eg, substernal chest pain with cardiac ischemia; fever, cough, and sputum with respiratory infections; urticaria with anaphylaxis; and wheezing with acute bronchospasm. However, dyspnea may be the sole complaint. In these cases, attention to historical information and a review of this limited differential diagnosis are important. The approach to acute dyspnea is described separately. (See "Evaluation of the adult with dyspnea in the emergency department".)

- **Exertional, positional, and nocturnal dyspnea** – Chronic exertional dyspnea and paroxysmal nocturnal dyspnea (PND) are both associated with heart failure, although nocturnal dyspnea is more specific to heart failure. Asthma is also associated with exertional and nocturnal dyspnea, but unlike PND does not usually improve with sitting or standing.

  Orthopnea, the development of or worsening of dyspnea in the supine position, is also associated with heart failure and increased pulmonary capillary pressure due to the increased venous return to the heart in this position. Central obesity, however, with a large protuberant abdomen, may also lead to orthopnea; increased intra-abdominal pressure associated with large abdominal girth impairs movement of the diaphragm during inhalation. Finally, patients with inspiratory muscle weakness may also complain of orthopnea due to the increased work of breathing associated with moving the diaphragm against high intra-abdominal pressure.

  Bendopnea, the worsening of dyspnea when leaning forward, is described in patients with decompensated heart failure [18].

  Dyspnea that is not exacerbated by exertion is more often due to a functional or perceptual problem than to cardiopulmonary disease.

- **Intermittent dyspnea** – Intermittent dyspnea associated with cold air or animal dander exposure suggests asthma; work-related dyspnea may suggest occupational asthma; and dyspnea following upper respiratory infections may be due to asthma or chronic obstructive pulmonary disease (COPD).

  In addition to asthma, intermittent symptoms that resolve completely between episodes can be seen with recurrent aspiration; recurrent pulmonary emboli and heart failure can also wax and wane, but generally are characterized by a baseline level of dysfunction. The presence of specific, reproducible inciting events such as exercise or cold air exposure is common with airways hyperreactivity.

- **Rapidity of symptom onset and progression** – The rapidity with which symptoms develop during exercise can also provide useful diagnostic information. For example, patients who develop shortness of breath and wheezing after walking 50 to 100 feet often have acute elevations in pulmonary capillary wedge pressure (usually due to cardiac diastolic dysfunction) or pulmonary hypertension. In contrast, symptoms of exercise-induced asthma usually are precipitated by more intense activity, beginning three minutes into exercise, peaking within 10 to 15 minutes, and resolving by 60 minutes. (See "Exercise-induced bronchoconstriction".)

  Respiratory muscle weakness generally leads to gradually progressive dyspnea, sometimes with an acute worsening at a time of illness, particularly a respiratory infection.

Severity of dyspnea — For patients with chronic dyspnea, formal assessment of the severity of dyspnea can help create a baseline for future comparisons [19]. A number of instruments are available to help assess the severity of dyspnea, such as the Baseline Dyspnea Index, the Modified Medical Research Council (mMRC) dyspnea scale (table 3), and the Borg scale (table 4) [20-24]. It is important to note that scales like the mMRC do not measure dyspnea directly; rather, they assess the intensity of exercise that provokes dyspnea and, indirectly, the degree of disability resulting from dyspnea.

Associated symptoms — Associated symptoms such as cough, sputum production, nasal congestion, chest pain, peripheral edema, Raynaud phenomenon, joint swelling, and muscle weakness can help identify areas for further investigation. As examples, asymmetric lower extremity edema might suggest venous thromboembolic disease; Raynaud phenomenon is seen in a number of rheumatic diseases that are associated with interstitial lung disease or pulmonary hypertension; and symmetric swelling of the metacarpophalangeal joints may be a clue to rheumatoid lung disease.

Descriptors of breathing discomfort — Attention to the quality or descriptor that a patient associates with the breathing discomfort often provides clues to the underlying diagnosis [25]. This observation comes from studies in which dyspnea questionnaires (table 5) were presented to patients with breathing discomfort from a variety of cardiopulmonary disorders [6-8,26]. Subjects were asked to select the phrases that best described their breathing discomfort, and distinct clusters emerged. While some clusters of phrases were common to a number of disease categories (eg, increased work or effort of breathing was found with COPD, asthma, and neuromuscular disease), each disease had a relatively unique set of clusters associated with it.

The combined data from studies that were performed in patients with known cardiopulmonary disorders or in normal subjects made breathless under experimental conditions indicate the following (table 6) [2,6-8,25,26]:

- The sensation of "air hunger" has been associated with acute bronchoconstriction and hyperinflation in asthma and COPD, heart failure, pulmonary embolism, and restricted thoracic motion, as well as acute hypercapnia from any cause [3,4,27].

- Acute bronchoconstriction leads to a series of sensations as the degree of obstruction worsens, from "chest tightness" to an increased "effort to breathe" to a sensation of "air hunger" [6-9,12,13]. The sensation of "tightness" appears to be independent of the work of breathing [28]. Attention to the use of verbal descriptors of dyspnea may help the clinician avoid underestimation of the severity of airflow limitation when objective measurements of lung function are not possible.

- Report of "increased work of breathing" is associated with COPD, moderate to severe asthma, myopathy, and pulmonary fibrosis.

- Patients with COPD and dynamic hyperinflation sometimes complain of a sensation of "unsatisfying breaths" or a sense that they "cannot get a deep breath" [9].

- A sensation of rapid, shallow breathing may correspond to interstitial lung disease or reduced chest wall compliance.

- Heart failure is also associated with a sensation of "suffocation" [6].

- A sense of heavy breathing is typical of deconditioning.

Patient questionnaires have been developed for use in research and clinical settings, and allow the doctor to assess symptom intensity, quality, and associated affective responses as part of the medical history (eg, anxiety, fear) [29,30]. However, it is important to remember that an individual's language, sex, ethnicity, and culture can influence the wording used to describe dyspnea [31-36]. Further research in this area is underway. (See 'Perceptual and psychological factors' below.)

Cigarette smoking and exposures to dusts and fumes — The absence of cigarette smoking argues strongly against a diagnosis of COPD, unless the patient has a history of tuberculosis or use of biomass cooking fuels. In one study, a history of smoking cigarettes had a positive predictive value for COPD of 0.4; COPD is uncommon among patients who have never smoked or have smoked less than 10 pack years [37]. The occupational history may lead to diagnosis of diseases such as asbestosis, chronic beryllium disease, silicosis, or another pneumoconiosis. (See "Asbestos-related pleuropulmonary disease" and "Chronic beryllium disease (berylliosis)" and "Silicosis".)

Physical examination — A complete physical examination is essential. In particular, attention should be directed at the presence or absence of stridor, wheezing, crackles, tachycardia, arrhythmia, heart murmurs, gallop, peripheral edema, muscle weakness, dysphonia, and evidence of rheumatic

disease. However, the absence of physical findings tends to have a greater negative predictive value, than the positive predictive value of any identified signs [17].

- Clubbing is associated with a number of causes of dyspnea, including bronchiectasis, idiopathic pulmonary fibrosis, lung cancer, and cyanotic heart disease, but not asthma or COPD.
- Jugular venous distention may suggest left sided heart failure or cor pulmonale.
- Decreased or distant heart sounds may suggest a pericardial effusion, but may also be due to obesity or hyperinflation from emphysema.
- Abdominal rounding, the protruding of the central abdomen with diminished transverse diameter during exhalation, has been associated with acute heart failure [38].

EVALUATION OF ACUTE DYSPNEA

Breathing discomfort arising over the course of minutes to hours is generally due to a limited number of conditions (table 2) and generally involves processes that require prompt evaluation and treatment. Clues to the need for an urgent evaluation include heart rate >120 beats/minute, respiratory rate >30 breaths/minute, pulse oxygen saturation (SpO_2) <90 percent, use of accessory respiratory muscles, difficulty speaking in full sentences, stridor, asymmetric breath sounds or percussion, diffuse crackles, diaphoresis, and cyanosis. The evaluation of dyspnea in the emergency department is described separately. (See "Evaluation of the adult with dyspnea in the emergency department".)

INITIAL TESTING IN CHRONIC DYSPNEA

When evaluating chronic dyspnea, we follow a step-wise diagnostic approach of initial testing, follow-up testing, and advanced testing, starting with the tests that are the least invasive and most likely to yield a diagnosis.

Most common causes — The majority of patients with chronic dyspnea of unclear etiology have one of five diagnoses, although the spectrum of potential causes is broad and more than one etiology may be present (table 7) [17,37,39]. It is also important to remember that the presence of a known chronic cardiopulmonary disease does not guarantee that the patient's symptoms or the etiology of their exercise limitation are due to that condition, particularly in patients with coexisting conditions [16].

The five most common causes of chronic dyspnea are the following:

- Asthma (see 'Respiratory' above)
- Chronic obstructive pulmonary disease (COPD) (see 'Respiratory' above)
- Interstitial lung disease (see 'Respiratory' above)
- Myocardial dysfunction (see 'Cardiovascular' above)
- Obesity/deconditioning (see 'Cardiovascular' above)

Pace of testing — For patients with chronic dyspnea, the severity of dyspnea and rate of worsening are important determinants of the pace and location of diagnostic testing [19]. The optimal sequence of diagnostic testing for chronic dyspnea has not been determined. We typically follow an algorithm that utilizes three tiers of testing: initial testing (table 8), follow-up testing based on results of initial tests (table 9A and table 9B and table 9C), and advanced testing if the diagnosis remains uncertain (table 10). Within each tier, we select tests based on the patient's clinical features, results of prior tests, and likelihood of a diagnostic result. One study found that the most informative tests for adults (age 45 to 84) with dyspnea and no known cardiopulmonary disease were the forced expiratory volume in one second (FEV_1) obtained by spirometry, the N-terminal pro-brain natriuretic peptide (NT-proBNP), and percent emphysema on chest computed tomography [40].

Specific tests — After reviewing the clinical findings for patterns that appear suggestive of one or two of the above five most common processes, the narrowed differential diagnosis is used to select tests that focus on these possibilities. As an example, if the patient is age 20 to 40 and has a clinical picture of allergic rhinitis and intermittent dyspnea, the initial testing might be limited to spirometry pre and post bronchodilator. Similarly, a 70 year old patient with known coronary artery disease, peripheral edema, and no smoking history might be evaluated for heart failure with an electrocardiogram, a serum NT-proBNP, and echocardiogram before considering spirometry.

If the clinical evaluation doesn't allow narrowing of the differential we usually obtain the following "initial tests" (table 8):

- Complete blood count (to exclude anemia): The degree of dyspnea associated with anemia may depend on the rapidity of blood loss and the degree of exertion that the patient undertakes. (See 'Cardiovascular' above.)
- Glucose, blood urea nitrogen, creatinine, electrolytes.
- Thyroid stimulating hormone (TSH).
- Spirometry pre and post inhaled bronchodilator OR full pulmonary function tests (PFTs) if the clinical evaluation does not suggest asthma or COPD.
- Pulse oximetry during ambulation at a normal pace over approximately 200 meters and/or up two to three flights of stairs.
- Chest radiograph.
- Electrocardiogram.

- Plasma BNP or NT-pro BNP

Spirometry can identify the presence and severity of airflow obstruction, and when both FEV_1 and forced vital capacity (FVC) are reduced proportionately (ie, the FEV_1/FVC ratio is normal or high), restrictive disease is suggested. When intrathoracic airflow limitation is noted or when a diagnosis of asthma is suspected, postbronchodilator spirometry determines whether there is reversibility of airflow limitation. Typically in asthma, airflow limitation is reversible, although a large component of airways edema and inflammation may need a course of inhaled or oral glucocorticoid therapy to achieve complete reversibility. Patients with a clinical suspicion of asthma and reversible airflow limitation on spirometry would be managed with a trial of specific therapy for asthma. Patients with a smoking history longer than 20 years and irreversible airflow limitation on spirometry are usually managed with a presumptive diagnosis of chronic obstructive pulmonary disease (COPD). However, other causes of irreversible airflow limitation (eg, bronchiectasis, bronchiolitis, central airway obstruction) should be considered if the patient does not respond to empiric therapy for asthma or COPD. (See "Asthma in adolescents and adults: Evaluation and diagnosis", section on 'Diagnosis' and "Chronic obstructive pulmonary disease: Definition, clinical manifestations, diagnosis, and staging", section on 'Diagnosis' and "Overview of bronchiolar disorders in adults", section on 'Diagnosis'.)

The chest radiograph may identify a pleural effusion, kyphoscoliosis, cardiomegaly, interstitial lung disease, or pulmonary vascular redistribution, as potential causes of dyspnea. A pleural effusion will need a directed evaluation as to the cause (eg, benign asbestos effusion, malignancy, trapped lung, rheumatoid effusion, infection, heart failure), usually including thoracentesis. Kyphoscoliosis identified on chest radiograph (and physical examination) is typically evaluated with full pulmonary function tests to determine the likelihood of hypercapnia. Interstitial lung disease is often evaluated further with measurement of lung volumes and diffusing capacity for carbon monoxide (DLCO) and by CT scan of the lungs to help characterize the underlying process. Heart failure suggested by the NT-pro BNP and chest radiograph will need further evaluation with an echocardiogram to determine the cause. The evaluation of these processes is discussed separately. (See "Diagnostic evaluation of a pleural effusion in adults: Initial testing" and "Chest wall diseases and restrictive physiology", section on 'Kyphosis and scoliosis' and "Determining the etiology and severity of heart failure or cardiomyopathy".)

FOLLOW-UP TESTING IN CHRONIC DYSPNEA

The second phase of the evaluation of dyspnea is aimed at clarifying abnormalities that were noted on initial testing, but were not diagnostic (table 9A and table 9C and table 9B). In addition,

some patients will have had normal results on initial testing, but have persistent symptoms that require further evaluation.

Pulmonary function tests — Patients with findings suggestive of interstitial lung disease (eg, crackles, reduced forced vital capacity without airflow limitation, desaturation with exertional pulse oximetry) and those without a clear diagnosis will need pulmonary function testing (PFT) beyond spirometry, guided by the results of the above tests (table 9A). Alternatively, these tests may be obtained at the time of initial spirometry. (See 'Initial testing in chronic dyspnea' above and "Overview of pulmonary function testing in adults" and "Diffusing capacity for carbon monoxide".)

As described above, spirometry before and after inhaled bronchodilator can secure a diagnosis in the case of asthma and chronic obstructive pulmonary disease (COPD). Other PFT findings may provide clues regarding which follow-up tests are likely to be helpful (table 9A).

- **Reduced forced vital capacity (FVC)** – If a decrease in the FVC is noted on spirometry, but without airflow limitation, the next step is to determine the cause of the decrease in FVC. The possibility of an underlying "restrictive" abnormality is assessed with measurement of lung volumes, looking for a similar decrease in total lung capacity and functional residual capacity. A restrictive pattern may be caused by interstitial lung disease, pleural disease (eg, trapped lung), chest wall disease (eg, kyphoscoliosis), or ventilatory muscle weakness (eg, diffuse or due to diaphragmatic paralysis). Respiratory muscle weakness can be evaluated further with maximal inspiratory and expiratory pressures at the mouth, maximal voluntary ventilation in one minute, and supine spirometry that is compared with sitting spirometry results. (See "Respiratory muscle weakness due to neuromuscular disease: Clinical manifestations and evaluation", section on 'Diagnostic evaluation' and "Tests of respiratory muscle strength".)

  Alternatively, if total lung capacity and residual volume are normal or increased, the decrease in vital capacity may be an indicator of reduced elastic recoil or air trapping and the patient may have emphysema or bronchiolitis without airflow limitation that is measurable on spirometry. (See "Office spirometry" and "Pulmonary function testing in asthma".)

- **Suspicion for asthma with normal baseline spirometry** – Bronchoprovocation testing (eg, with methacholine, histamine, or mannitol) is typically obtained in patients with recurrent, episodic dyspnea suggestive of asthma who have normal or near normal spirometry. A trial of therapy for asthma is an alternative, but bronchoprovocation is preferred to enable a precise determination of asthma. Studies have shown that up to 30 percent of patients with a clinical diagnosis of asthma do not have airway reactivity on formal testing [41,42]. Empiric therapy can lead to gradual acceleration of treatment, including use of systemic glucocorticoids, with attendant side effects if the patient does not have asthma. (See "Bronchoprovocation testing"

and "Asthma in adolescents and adults: Evaluation and diagnosis", section on 'Initial spirometry is normal'.)

If a flow-volume loop was not obtained during the initial spirometry, we use that test to evaluate the upper airway for obstruction, particularly variable upper airway obstruction that may not be apparent on expiratory spirometry. However, pulmonary function testing is relatively insensitive for upper airway obstruction, so direct visualization of the upper airway following bronchoprovocation or exercise challenge may be necessary. (See "Evaluation of wheezing illnesses other than asthma in adults", section on 'Evaluation of stable patients with wheeze'.)

- **Evaluation of gas transfer** – A diffusing capacity for carbon monoxide (DLCO) is helpful in the evaluation of dyspnea, particularly in the identification of interstitial lung disease (suggested by reduced lung volumes), emphysema or bronchiolitis (suggested by an obstructive pattern), and pulmonary vascular disease. Pulmonary vascular disease (eg, pulmonary hypertension, chronic thromboembolic disease, pulmonary veno-occlusive disease) is suggested by the combination of normal spirometry and lung volumes, but abnormal gas transfer manifest by a decrease in DLCO and pulse oxygen saturation on exertion (eg, ≥5 percent). (See "Diffusing capacity for carbon monoxide".)

- **Low oxygen saturation** – A low resting oxygen saturation (eg, ≤95 percent) or a significant decline in oxygen saturation during exercise (≥5 percent) warrants further evaluation. The differential diagnosis includes COPD, interstitial lung disease, pulmonary vascular disease, bronchiolitis obliterans, intrapulmonary or intracardiac shunt, and heart failure. Thus, such patients typically need high resolution computed tomography (HRCT) and a transthoracic echocardiogram, possibly with a bubble study.

- **Reduced lung volumes and obesity** – Obesity is associated with reductions in expiratory reserve volume and function residual capacity and, in some patients, a decrease in total lung capacity (restrictive ventilatory defect) [43]. However, the changes in lung volumes do not necessarily correlate with dyspnea and it can be difficult to know whether this pattern of reduced lung volumes is due to obesity or another respiratory disease. In a population study (NHANES III), subjects in the highest quintile of body mass index (BMI), had the lowest risk for significant airflow obstruction, so obesity by itself is less commonly a cause of classical airflow obstruction [44]. (See "Chest wall diseases and restrictive physiology", section on 'Obesity'.)

Chest computed tomography — Chest computed tomography (CT) is helpful in the evaluation of dyspnea in the following settings (table 9B):

- **Abnormalities on the chest radiograph that need further characterization** – Suspected interstitial lung disease is evaluated by HRCT, and central masses and suspected large airway

obstruction (eg, tumor) are best evaluated by CT with contrast and direct visualization. On the other hand, vascular redistribution and abnormal heart size are best evaluated by measurement of a serum N-terminal pro-brain natriuretic peptide (NT-pro BNP) or transthoracic echocardiography.

- **When HRCT is helpful despite a normal chest radiograph** – A small percentage of patients with interstitial lung disease may have a normal chest radiograph on presentation; HRCT scan clearly is more sensitive for detecting subtle ground glass or reticular opacities [45,46]. Thus, patients with crackles on physical examination, reduced lung volumes on pulmonary function testing, or a decreased DLCO should have HRCT scans even if the chest radiograph is normal. (See "High resolution computed tomography of the lungs".)

  A minority of patients with a history of cigarette smoking, normal spirometry, and normal chest radiographs have extensive emphysema on high-resolution CT scan [47]. These patients generally demonstrate oxygen desaturation with exercise and have a low diffusing capacity.

- **Evaluation for suspected thromboembolic disease** – For patients with suspected thromboembolic disease based on risk factors, lower extremity edema, or a low DLCO with normal lung volumes, a computed tomographic pulmonary angiogram (CTPA) is usually the next step unless the patient has a contraindication to intravenous contrast. Alternative tests that are helpful in the evaluation of possible thromboembolic disease include a ventilation-perfusion lung scan, lower extremity proximal vein compressive ultrasound, and magnetic resonance pulmonary angiography. (See "Clinical presentation, evaluation, and diagnosis of the nonpregnant adult with suspected acute pulmonary embolism" and "Epidemiology, pathogenesis, clinical manifestations and diagnosis of chronic thromboembolic pulmonary hypertension".)

Echocardiography — Echocardiography is generally performed when heart failure (HF) or pulmonary hypertension are suspected on the basis of clinical findings, brain natriuretic peptide (BNP) or NT pro-BNP levels, cardiomegaly on chest radiograph, oxygen desaturation with exertion, or when the cause of dyspnea remains unclear after the initial evaluation described above (table 9C). Transthoracic echocardiogram with color flow Doppler is typically ordered (to evaluate left ventricular systolic and diastolic function, occult valvular abnormalities, and also pulmonary artery and right-sided pressures).

- **Suspected left ventricular dysfunction** – Echocardiography may confirm HF due to reduced left ventricular (LV) systolic function (HF-REF). (See "Determining the etiology and severity of heart failure or cardiomyopathy".)

- **Suspected diastolic dysfunction** – If LV ejection fraction and end-diastolic volume are normal, echocardiography can identify features of diastolic dysfunction (heart failure with preserved

ejection fraction [HF-PEF]), such as LV hypertrophy (LVH), concentric remodeling, and left atrial enlargement. Additional Doppler features of diastolic dysfunction include elevated pulmonary artery systolic pressure, and impaired ventricular relaxation (eg, early/late [E/A] filling <1). HF-PEF due to diastolic dysfunction can be a cause of exertional dyspnea; further support for the diagnosis comes from an elevated BNP and a trial of therapy. (See "Echocardiographic evaluation of left ventricular diastolic function" and "Heart failure with preserved ejection fraction: Clinical manifestations and diagnosis", section on 'Echocardiography' and "Treatment and prognosis of heart failure with preserved ejection fraction", section on 'Treatment'.)

Among older adults with unexplained chronic dyspnea after an initial evaluation (eg, history, physical examination, pulmonary function tests, and a chest radiograph), nearly two-thirds have evidence of diastolic dysfunction [48], which can manifest as dyspnea with relatively minimal exertion.

- **Suspected pericardial disease** – Constrictive pericarditis can be difficult to diagnose in patients who present with chronic dyspnea, although patients generally have peripheral edema. Findings on echocardiography that may suggest constrictive pericarditis include increased pericardial thickness, dilation of the inferior vena cava with absent or diminished inspiratory collapse, abnormal filling of the ventricles in diastole, and pronounced respiratory variation in ventricular filling. When occult constrictive pericarditis is suspected, right heart catheterization is performed with measurement of hemodynamics before and after infusion of a liter of warm saline. (See "Constrictive pericarditis", section on 'Two-dimensional and M-mode' and "Variants of constrictive pericarditis".)

- **Suspected pulmonary hypertension** – Elevated pulmonary artery (PA) pressures by Doppler echocardiography may indicate pulmonary hypertension, but need confirmation by pulmonary artery catheterization to confirm the elevated PA pressures and exclude left ventricular dysfunction. (See 'Advanced testing in chronic dyspnea' below.)

ADVANCED TESTING IN CHRONIC DYSPNEA

Referral to a specialist is usually needed for patients who do not respond to treatment for the diagnosis deemed most likely by the initial evaluation and when diagnostic procedures such as a bronchoscopy, lung biopsy, cardiopulmonary exercise test, or pulmonary artery catheterization may be needed. The use of these tests to evaluate dyspnea is described in the table (table 10).

Suspected interstitial lung disease — The evaluation of interstitial lung disease that is suspected on the basis of pulmonary function testing and high resolution computed tomography (HRCT) may

include additional laboratory testing, bronchoscopy with bronchoalveolar lavage, and lung or mediastinal lymph node biopsy, as described separately. (See "Approach to the adult with interstitial lung disease: Clinical evaluation" and "Approach to the adult with interstitial lung disease: Diagnostic testing" and "Interpretation of lung biopsy results in interstitial lung disease".)

Pulmonary hypertension suggested by echocardiography — When elevated pulmonary artery pressures are suggested by Doppler echocardiography and are supported by an elevated brain natriuretic peptide (BNP) and oxygen desaturation on exertion, the next step in the evaluation of suspected pulmonary hypertension is pulmonary artery catheterization to confirm an elevated mean pulmonary artery pressure (mPAP >20 mmHg at rest) and exclude diastolic dysfunction (unlikely with pulmonary artery wedge pressure [PAWP] <15 mmHg). The evaluation of pulmonary hypertension is described separately. (See "Echocardiographic evaluation of the pulmonic valve and pulmonary artery", section on 'Pulmonary hemodynamics' and "Clinical features and diagnosis of pulmonary hypertension of unclear etiology in adults", section on 'Diagnosis'.)

If the diagnosis of pulmonary hypertension is confirmed, the patient will need further evaluation for treatable causes of pulmonary hypertension. (See "Clinical features and diagnosis of pulmonary hypertension of unclear etiology in adults", section on 'Post-diagnostic testing and classification'.)

Exercise echocardiography has been proposed as a method to screen patients for early pulmonary hypertension. However, exercise-induced increases in Doppler estimates of pulmonary artery systolic pressure (PASP) are multifactorial and not specific for pulmonary hypertension. (See "Overview of stress echocardiography".)

Unclear cause of dyspnea on exertion — For patients who have dyspnea that is persistent and unexplained by the results of the above studies, additional testing may be warranted. At this point it may be reasonable for the patient to engage in a conditioning program for two to three months to see whether dyspnea improves before proceeding with more invasive testing. For patients in whom deconditioning is not believed to be contributing to symptoms, proceeding directly to additional testing is reasonable.

Cardiopulmonary exercise testing — A cardiopulmonary exercise test (CPET) can be helpful when the etiology of a patient's dyspnea remains unclear after the evaluation described above or when dyspnea seems out of proportion to the severity of the patient's known cardiac or pulmonary disease [1,49,50]. A CPET can assess the workload that the patient can achieve, the degree of dyspnea experienced (eg, Borg or other visual scale), the peak oxygen uptake, cardiac output (calculated from carbon dioxide production and oxygen uptake), and relationship of minute ventilation to carbon dioxide production. (See "Cardiopulmonary exercise testing in cardiovascular disease" and "Exercise physiology".)

In particular, CPET may help identify patients with mitochondrial disorders (eg, McArdle's myophosphorylase deficiency, isolated mitochondrial myopathy) by demonstrating a reduction in maximum oxygen uptake (VO_2 max), reduced peripheral oxygen extraction (increased mixed venous oxygen), and an increase in blood lactate after exercise. (See "Mitochondrial myopathies: Clinical features and diagnosis", section on 'Exercise testing'.)

A CPET may be helpful in providing support for the presence of deconditioning or in detecting a low threshold for respiratory discomfort. Patients with a low threshold for respiratory discomfort typically terminate the test at mild workloads because of dyspnea, but have no evidence of cardiopulmonary abnormality. In patients with both pulmonary and cardiac disease, either of which could cause the patient to have dyspnea limiting their exercise capacity, CPET may assist in the determination of the actual cause of the limitation. (See 'Chronic dyspnea with a normal evaluation' below.)

Cardiopulmonary exercise testing with pulmonary artery catheterization — Cardiopulmonary exercise testing with pulmonary artery catheterization, also known as an invasive CPET or iCPET, is performed at specialized centers [51]. The role of iCPET in the evaluation of dyspnea has not been clearly defined. Typically, it is used in the evaluation of exercise-induced pulmonary arterial hypertension, exercise-induced heart failure with preserved left ventricular ejection fraction (HFpEF), and preload dependent limitations to cardiac output.

CHRONIC DYSPNEA WITH A NORMAL EVALUATION

Occasional patients with chronic dyspnea will go through a complete evaluation without identification of a cause. Others may have near normal testing, such that a slight decrease in peak oxygen uptake, anaerobic threshold, and peak heart rate are thought to be most consistent with deconditioning or obesity. While obese patients frequently report dyspnea [52], in a given individual it can be difficult to know how much dyspnea is attributable to obesity. For patients who report dyspnea but have normal or near normal testing, we explain the reassuring nature of testing in detail, advise a conditioning program, and ask the patient to return in 6 to 12 months for re-evaluation. The re-evaluation is important due to the infrequent situation in which a treatable cause of dyspnea is missed initially, but becomes apparent on subsequent testing.

Dyspnea due to obesity per se is commonly associated with a sense of increased effort to breathe or work of breathing, likely due to the weight of the chest wall [53]. Hypoxemia, either at rest or with exertion, may be caused by ventilation/perfusion mismatching at the bases of the lungs, a consequence of narrowing of airways in these regions due to the increased pleural pressure resulting from the weight of the chest wall.

Other chest symptoms (eg, heartburn) and psychological factors can lead to the perception of dyspnea, as described below. Use of a Borg scale during cardiopulmonary exercise testing will sometimes identify dyspnea associated with a low work load and normal cardiorespiratory function (table 4). (See "Cardiopulmonary exercise testing in cardiovascular disease".)

PERCEPTUAL AND PSYCHOLOGICAL FACTORS

The global rating that a patient gives for dyspnea may reflect both sensory and emotional (ie, affective) elements. In a study of laboratory-induced dyspnea, air hunger was associated with greater unpleasantness for a given level of sensory intensity than was the sense of respiratory work or effort [54]. The context in which a sensation occurs may alter the affective component of the intensity and needs to be considered when assessing the patient.

For a given physiologic derangement that may cause dyspnea, perceptual responses vary widely among individuals. Anxiety, anger, pain, and depression may be associated with dyspnea intensity out of proportion to the physiologic impairment [55-58]. Increased ventilation associated with anxiety, anger, or pain may push an individual with a limited pulmonary reserve at baseline closer to his or her ventilatory limits and increase the perceived respiratory discomfort for any given activity.

To the extent that dyspnea occurs unexpectedly or cannot be quickly relieved, it may give rise to a range of emotional reactions, which can then lead to further physiological derangements (eg, tachypnea, hyperinflation). For any given gas exchange or mechanical problem with the cardiopulmonary system, the emotional or affective response may contribute to the intensity or discomfort of the sensation [54]; questionnaires have been developed that incorporate both qualitative and affective descriptors [29,30,54].

Patients with hyperventilation syndrome typically experience a sensation of air hunger or an inability to take a deep breath in the absence of cardiopulmonary disease. These individuals may have panic and/or anxiety disorders, and on examination are often observed to breathe with very large tidal volumes despite the complaint that they cannot take a deep enough breath. (See "Hyperventilation syndrome in adults".)

Sex, ethnicity, and cultural context appear to influence an individual's description of dyspnea, but further research is needed to understand the exact differences and their effects on the experience and description of dyspnea [6,8,31,59-62].

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Chronic obstructive pulmonary disease" and "Society guideline links: Dyspnea".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Shortness of breath (dyspnea) (The Basics)")
- Beyond the Basics topics (see "Patient education: Shortness of breath (dyspnea) (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- Dyspnea is a term used to characterize a subjective experience of breathing discomfort that comprises qualitatively distinct sensations that vary in intensity. Dyspnea is considered acute when it develops over hours to days and chronic when it has been present for more than four to eight weeks. (See 'Definition of dyspnea' above.)
- Dyspnea can be the first manifestation of a variety of cardiopulmonary disorders. It is not uncommon for a patient to have more than one problem contributing to breathing discomfort. (See 'Pathophysiology' above.)
- The history and physical examination lead to accurate diagnoses in patients with dyspnea in approximately two-thirds of cases. Important components of the history include the characteristics of dyspnea (ie, timing, severity, and triggers), exposures that may contribute to the

lung disease (eg, allergens, cold air, occupational agents, cigarette smoke), and interventions or medications that reduce dyspnea. (See 'Clinical assessment' above.)

- The patient's description of breathing discomfort can help narrow down diagnostic possibilities. In addition, the presence of more than one type of breathing discomfort can lead to recognition that more than one disease process is contributing to dyspnea. (See 'Descriptors of breathing discomfort' above.)

- Breathing discomfort arising over the course of minutes to hours (acute dyspnea) generally requires prompt evaluation and treatment. The evaluation of acute dyspnea is described separately. (See 'Evaluation of acute dyspnea' above and "Evaluation of the adult with dyspnea in the emergency department".)

- Among the many causes of chronic dyspnea (table 7), the most common are asthma, chronic obstructive pulmonary disease (COPD), interstitial lung disease, cardiomyopathy, and obesity/deconditioning. In addition, deconditioning is often a contributing factor in patients with chronic lung disease. (See 'Initial testing in chronic dyspnea' above.)

- When evaluating chronic dyspnea, we follow a step-wise diagnostic approach of initial testing (table 8), follow-up testing (table 9A-C), and advanced testing (table 10), starting with the tests that are the least invasive and most likely to yield a diagnosis. Within each tier, the individual tests are selected based on the patient's clinical features, results of prior tests, and response to therapy. (See 'Initial testing in chronic dyspnea' above.)

- The initial tests are selected based on a review of the clinical findings for patterns suggestive of one or two of the above five most common causes of dyspnea (table 8). When asthma or COPD is suspected, the initial testing might be limited to spirometry pre and post bronchodilator, while an older patient with coronary artery disease and peripheral edema should be evaluated for heart failure before considering spirometry. (See 'Initial testing in chronic dyspnea' above.)

- Follow-up testing in the evaluation of dyspnea should clarify abnormalities that were noted on initial testing, but were not diagnostic (table 9A and table 9B and table 9C). In addition, some patients with normal results on initial testing, but persistent symptoms, require further evaluation. Thoracic computed tomography (CT) is generally reserved for patients in whom there is a suspicion of interstitial lung disease, occult emphysema, or chronic thromboembolic disease. Echocardiography is useful for evaluating suspected left ventricular dysfunction, pulmonary hypertension, and diastolic dysfunction. (See 'Follow-up testing in chronic dyspnea' above.)

- Advanced testing includes procedures such as right heart catheterization, stress echocardiography, cardiopulmonary exercise testing (CPET), and invasive CPET (table 10).

Cardiopulmonary exercise testing is a useful study in patients in whom the cause of their breathing discomfort remains elusive after standard testing, in patients in whom deconditioning is a serious consideration, and in patients who appear to have breathing discomfort out of proportion to their physiologic derangements. (See 'Unclear cause of dyspnea on exertion' above.)

Topic 1436 Version 21.0

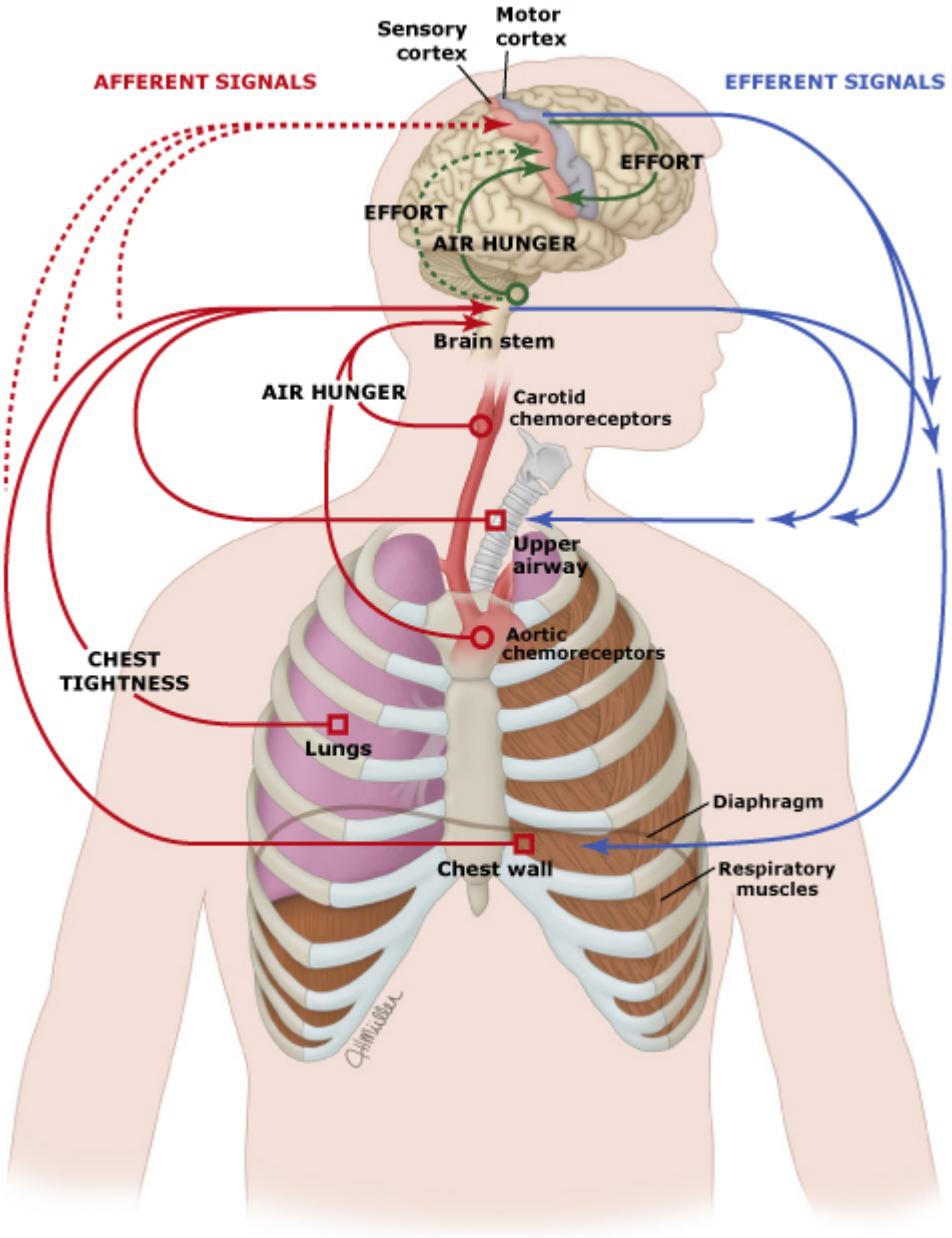
GRAPHICS

Components of the respiratory system

Controller
Brain stem
Cortical-volitional
Cortical-behavior
Ventilatory pump
Ventilatory muscles
Bones; joints of the thorax
Airways
Peripheral nerves
Pleura
Gas exchanger
Alveoli
Pulmonary circulation

Graphic 118505 Version 1.0

Efferent and afferent signals that contribute to the sensation of dyspnea



The symptom of dyspnea likely arises from a range of sensory inputs, many of which lead to qualitatively distinct descriptive phrases used by patients. The sensation of respiratory effort arises from signals transmitted from the motor cortex to the sensory cortex (green arrow) when outgoing motor commands are sent to the ventilatory muscles (blue arrow). Motor output from the brain stem (blue arrow) may also be accompanied by signals transmitted to the sensory cortex, contributing to the sensation of effort (dotted green arrow).

The sensation of air hunger probably derives from a combination of stimuli that increase the drive to breathe such as insufficient oxygen or excess carbon dioxide (mediated by signals from chemoreceptors in the carotid body and aortic arch), acute hypercapnia or acidemia (mediated by signals from the peripheral and central chemoreceptors), airway and interstitial inflammation (mediated by pulmonary afferents), and vascular receptors. The intensity of air hunger is increased when there is a perceived mismatch between the outgoing efferent messages to the ventilatory muscles and incoming afferent signals from the lungs and chest wall.

Chest tightness, commonly associated with bronchospasm, is mediated by stimulation of vagal-irritant receptors. Afferent signals (red arrows) from airway, lung, and chest wall receptors most likely pass through the brain stem before being transmitted to sensory cortex, although it is also possible that some afferent information bypasses the brain stem and goes directly to sensory cortex (dotted arrow).

Red arrows: afferent signals; Blue arrows: efferent signals; Green arrows: signals within the central nervous system; Dotted lines: hypothetical pathways; Circles: chemoreceptors; Squares: mechanoreceptors.

Graphic 69322 Version 5.0

Causes of acute dyspnea

Cardiovascular system
Acute myocardial ischemia
Heart failure
Cardiac tamponade
Respiratory system
Bronchospasm
Pulmonary embolism
Pneumothorax
Pulmonary infection - bronchitis, pneumonia
Upper airway obstruction - aspiration, anaphylaxis

Graphic 82700 Version 1.0

Modified Medical Research Council (mMRC) dyspnea scale

Grade	Description of breathlessness
0	I only get breathless with strenuous exercise
1	I get short of breath when hurrying on level ground or walking up a slight hill
2	On level ground, I walk slower than people of the same age because of breathlessness, or have to stop for breath when walking at my own pace
3	I stop for breath after walking about 100 yards or after a few minutes on level ground
4	I am too breathless to leave the house or I am breathless when dressing

Adapted from: Fletcher CM, Elmes PC, Fairbairn MB, et al. The significance of respiratory symptoms and the diagnosis of chronic bronchitis in a working population. British Medical Journal 1959; 2:257.

Graphic 86426 Version 2.0

The modified Borg Scale for assessing the intensity of dyspnea or fatigue

0	Nothing at all
0.5	Very, very slight (just noticeable)
1	Very slight
2	Slight (light)
3	Moderate
4	Somewhat severe
5	Severe (heavy)
6	
7	Very severe
8	
9	
10	Very, very severe (maximal)

This Borg scale should be printed on heavy paper (11 inches high and perhaps laminated) in 20-point type size. At the beginning of the 6-minute exercise, show the scale to the patient and ask the patient this: "Please rate the intensity of your 'breathing discomfort' using this scale." Then ask this: "Please rate your level of fatigue using this scale." At the end of the exercise, remind the patient of the breathing number that they chose before the exercise and ask the patient to grade their breathing level again. Then ask the patient to grade their level of fatigue, after reminding them of their grade before the exercise.

Sources:

1. *Reproduced with permission from: Borg GA. Psychophysical bases of perceived exertion. Med Sci Sports Exerc 1982; 14:377. Copyright © 1982 Lippincott Williams & Wilkins.*
2. *Reproduced with permission from: the American Thoracic Society. ATS statement: Guidelines for the six-minute walk test. Am J Respir Crit Care Med 2002; 166:111.*

Graphic 63981 Version 4.0

Dyspnea questionnaire

Please select up to three phrases that best describe your breathing discomfort. If you choose more than one phrase, please also note the phrase that most closely describes the sensation you feel. If none of these phrases applies, please write in your own description of your breathing discomfort.
My breathing is shallow.
I feel an urge to breathe more.
My chest is constricted.
My breathing requires effort.
I feel a hunger for more air.
I feel out of breath.
I cannot get enough air.
My breath does not go in all the way.
My chest feels tight.
My breathing requires work.
I feel that I am smothering/suffocating.
I feel that I cannot get a deep breath.
I feel that I am breathing more.
My breath does not go out all the way.
My breathing is heavy.
Other descriptions:

Graphic 76579 Version 1.0

Qualities of dyspnea and associated disease states

Descriptor	Pathophysiologic mechanism	Disease state
Chest tightness or constriction	Bronchochonstriction, interstitial edema	Asthma
		Myocardial ischemia
Increased work or effort of breathing	Airways obstruction, neuromuscular disease, reduced chest wall or pulmonary compliance	COPD, moderate to severe asthma, myopathy, pulmonary fibrosis
Air hunger, need to breathe, urge to breathe	Increased drive to breathe	HF, pulmonary embolism, moderate to severe asthma or COPD
Rapid, shallow breathing	Reduced chest wall or pulmonary compliance	Interstitial fibrosis
Suffocating, smothering	Alveolar edema	Pulmonary edema
Heavy breathing, breathing more	Inadequate oxygen delivery to the muscles	Deconditioning

Graphic 69244 Version 1.0

Conditions associated with chronic or recurrent dyspnea

Upper airway
Laryngeal mass
Vocal fold paralysis
Inducible laryngeal obstruction (also known as paradoxical vocal fold motion)
Goiter
Neck mass compressing airway
Chest/abdominal wall
Diaphragmatic paralysis
Kyphoscoliosis
Late pregnancy
Massive obesity
Ventral hernia
Ascites
Intra-abdominal process
Pulmonary
Asthma
Bronchiectasis
Bronchiolitis
COPD/emphysema
Interstitial lung disease
Mass compressing or occluding airway
Pleural effusion
Previous major lung resection (eg, lobectomy, pneumonectomy)
Pulmonary right-to-left shunt
Pulmonary hypertension
Trapped lung
Venous thromboembolism (VTE)
Cardiac
Arrhythmia
Constrictive pericarditis, pericardial effusion
Coronary heart disease
Deconditioning
Heart failure (systolic or diastolic dysfunction)
Intracardiac shunt
Restrictive cardiomyopathy
Valvular dysfunction
Neuromuscular disease
Amyotrophic lateral sclerosis
Phrenic nerve disease/dysfunction

Glycolytic enzyme defects (eg, McArdle)
Mitochondrial diseases
Polymyositis/dermatomyositis
Toxic/metabolic/systemic
Anemia
Metabolic acidosis
Renal failure
Thyroid disease
Miscellaneous
Anxiety
Early pregnancy (effect of progesterone)

COPD: chronic obstructive pulmonary disease.

Graphic 104817 Version 4.0

Evaluation of dyspnea: Initial testing

Tests are selected based on clinical likelihood. As examples, a patient under age 40 with suspected asthma might just need spirometry pre/post bronchodilator; a young patient without suspicion for heart failure or pulmonary hypertension might not need an ECG or plasma BNP; and a patient with suspected heart failure might not need spirometry. However, some patients will need all tests in this section.

Test	Rationale/indications
Hemoglobin/hematocrit	Anemia can present as dyspnea or reduced exercise tolerance.
Glucose, blood urea nitrogen, creatinine, electrolytes, phosphate, calcium	For adults with other comorbidities or over age 40, screen for metabolic causes of dyspnea.
Thyroid stimulating hormone (TSH)	Hyper and hypothyroidism can present as dyspnea or reduced exercise tolerance.
Spirometry pre/post bronchodilator with or without lung volumes and DLCO	Depending on the likelihood of asthma or COPD and difficulties of travel and scheduling, spirometry pre/post bronchodilator may be ordered initially without full PFTs. Alternatively, full testing (spirometry pre and post bronchodilator, lung volumes, DLCO, ambulatory oximetry) may be more expeditious. Refer to UpToDate table on follow-up testing based on initial results.
Assess SpO_2 (eg, walking ≥200 feet and two flights of stairs)*	Hypoxemia at rest or desaturation with exertion indicates the need to pursue definitive diagnosis. Obtain full PFTs, CXR, BNP, ECG, and possibly echocardiogram. Refer to UpToDate table on follow-up testing based on initial results.
Chest radiograph	Indicated for most dyspneic patients, particularly those who are over age 40, have suspected heart failure or interstitial disease, or abnormal PFTs. Not needed in routine evaluation of asthma.
ECG	Indicated for most dyspneic patients over age 40. Not needed in young patients with clear diagnosis of asthma and response to treatment. Refer to UpToDate table on follow-up testing based on initial results.
Plasma BNP or NT-pro BNP	Useful screening test for HF although not entirely specific; dyspnea due to HF is associated with plasma BNP >400 pg/mL; high negative predictive value for BNP <100 pg/mL, although BNP increases with age.

ECG: electrocardiogram; BNP: brain natriuretic peptide; DLCO: diffusing capacity of the lungs for carbon monoxide; COPD: chronic obstructive pulmonary disease; PFTs: pulmonary function tests; SpO_2: pulse oxygen saturation; CXR: chest radiograph; NT-pro BNP: N-terminal pro BNP; HF: heart failure.
* Stop exertion if SpO_2 decreases to 90 percent or patient becomes symptomatic.

Graphic 104818 Version 3.0

Pulmonary function testing in the evaluation of chronic dyspnea

Pulmonary function tests

Abnormality	Interpretation	Further testing
Airflow obstruction with complete reversibility following inhaled bronchodilator	Likely asthma: Institute therapy based on severity of obstruction according to current guidelines.	Reassess dyspnea and spirometry after treatment trial.
Airflow obstruction that is irreversible or incompletely reversible following bronchodilator	Likely COPD, especially in smokers. Chronic/severe asthma can cause airflow limitation that is incompletely reversible with bronchodilator, but may improve over time with inhaled or oral glucocorticoid therapy. Less commonly bronchiolitis or bronchiectasis.	Reassess dyspnea and spirometry after treatment trial/pulmonary rehabilitation/smoking cessation/removal of allergen exposure.
		Bronchiolitis should be suspected in patients with poor response to therapy for asthma/COPD or with the combination of airflow limitation and impaired gas transfer, may need HRCT to look for radiographic evidence of bronchiolitis or bronchiectasis.
Normal (expiratory) spirometry	Normal spirometry does not exclude asthma or upper airway obstruction. Depending on clinical suspicion: ▪ Review inspiratory and expiratory flow volume loop for upper airway flow limitation ▪ Obtain bronchoprovocation challenge (eg, methacholine, mannitol, exercise) ▪ Obtain lung volumes, DLCO, SpO_2 with exercise (if not already done)	Positive bronchoprovocation: Asthma is likely cause of dyspnea. Reassess after treatment trial.
		Bronchoprovocation negative but flow volume loop has slowing on inspiratory phase suggesting possible upper airway obstruction; direct visualization needed to confirm.
		Refer to "Lung volumes normal but DLCO reduced and/or SpO_2 <95% or decreases by >4% with exertion" below.
Reduced FVC with normal FEV_1/FVC	Evaluate for restrictive process (pleural, chest wall, or neuromuscular), interstitial lung disease, or air trapping. ▪ Obtain/review lung volumes and DLCO ▪ Examine CXR re: pleural effusion, kyphoscoliosis, or hemidiaphragm elevation	Lung volumes (FVC and TLC) confirm restrictive pattern, DLCO normal or slightly low: Consider pleural, chest wall, and neuromuscular disease. ▪ Obtain MEP, MIP, MVV ▪ Review imaging ▪ Consider fluoroscopy for diaphragm dysfunction
		Reduced DLCO and lung volumes suggest interstitial lung disease or emphysema: Consider HRCT.
		Increased RV or FRC suggests airtrapping (eg, due to emphysema, LAM, bronchiolitis) as a cause of low FVC. HRCT can identify emphysema, cystic changes of LAM, mosaic pattern suggestive of bronchiolitis.
Lung volumes normal but DLCO reduced and/or SpO_2 <95% or decreases by >4% with exertion	Possibilities include early ILD and pulmonary vascular disease: Obtain HRCT, BNP, and echocardiogram with Doppler assessment of PA pressures.	If no ILD on HRCT and BNP and echocardiogram suggest pulmonary hypertension, may need PA catheterization.
Normal flow volume loop, lung	Increasing likelihood of nonrespiratory	Obtain/review CXR, echocardiogram.

volumes, DLCO, ambulatory SpO_2, and bronchoprovocation	cause of dyspnea.	May need CPET.

COPD: chronic obstructive pulmonary disease; HRCT: high resolution computed tomography; DLCO: diffusing capacity of the lungs for carbon monoxide; SpO_2: pulse oxygen saturation; FVC: forced vital capacity; FEV_1: forced expiratory volume in one second; CXR: chest radiograph; TLC: total lung capacity; MEP: maximal expiratory pressure; MIP: maximal inspiratory pressure; MVV: maximal voluntary ventilation; RV: right ventricular; FRC: functional residual capacity; LAM: lymphangioleiomyomatosis; ILD: interstitial lung disease; BNP: brain natriuretic peptide; PA: pulmonary artery; CPET: cardiopulmonary exercise test.

Graphic 104821 Version 3.0

Imaging in the evaluation of chronic dyspnea

Imaging		
Abnormality	**Interpretation**	**Further testing**
Normal or increased reticular markings on chest radiograph	Review PFTs re: evidence of restriction, abnormal DLCO, or low SpO_2 at rest or with exertion. If abnormalities suggest ILD, obtain HRCT.	Review HRCT pattern to differentiate types of ILD; obtain appropriate tests for rheumatic diseases, HP, pneumoconiosis. Refer to UpToDate topics on evaluation of interstitial lung disease.
Hyperinflation	DDx includes COPD/emphysema, asthma, normal variant, bronchiolitis, lymphangioleiomyomatosis, Marfan syndrome, Birt-Hogg-Dube.	Correlate with PFTs. If airflow limitation, empiric bronchodilator therapy. Consider HRCT.
Pleural effusion or thickening on chest radiograph	Pleural effusion, trapped lung, and fibrothorax can lead to dyspnea through altered pleural mechanics and compressive atelectasis.	Evaluation usually requires thoracentesis of pleural effusion, sometimes with measurement of pleural pressures. In addition, chest computed tomography with contrast is frequently part of the evaluation.
Abnormal spine, rib cage, or diaphragm	Review PFTs to assess degree of functional impairment.	For patients with chest wall disease and an FVC <1 L, consider assessment for hypercapnia.
Enlarged or abnormal heart contour on chest radiograph	Obtain BNP and echocardiogram with Doppler assessment of PA pressures: Review pericardium, systolic/diastolic function, valvular function.	If echocardiogram normal, consider MRI or CT scan to evaluate abnormal heart size/contour.

PFTs: pulmonary function tests; DLCO: diffusion capacity of the lungs for carbon monoxide; SpO_2: pulse oxygen saturation; ILD: interstitial lung disease; HRCT: high resolution computed tomography; HP: hypersensitivity pneumonitis; DDx: differential diagnosis; COPD: chronic obstructive pulmonary disease; FVC: forced vital capacity; BNP: brain natriuretic peptide; PA: pulmonary artery; MRI: magnetic resonance imaging; CT: computed tomography.

Graphic 111477 Version 1.0

Cardiac testing in the evaluation of chronic dyspnea

Cardiac evaluation		
Test	**Interpretation**	**Follow-up**
ECG shows arrhythmia, conduction disturbance, or myocardial injury	ECG abnormalities may be a clue to underlying coronary artery or myocardial disease. Obtain treadmill/other stress test and echocardiogram.	
Treadmill or nuclear stress test can be helpful even in absence of chest pain	Some patients are more aware of dyspnea than chest pressure. Patients with COPD may report dyspnea that is due to comorbid cardiac disease.	Testing suggests CAD; evaluate and treat.
Transthoracic echocardiogram: Useful in the identification of systolic and diastolic ventricular dysfunction, hypertrophic cardiomyopathy, valvular disease, pericardial disease, and pulmonary hypertension	Echocardiogram shows reduced left ventricular systolic function (HFrEF): Likely cardiomyopathy or CAD.	Evaluate for risk factors. Initiate treatment.
	Echocardiogram shows preserved ejection fraction (HFpEF). Assess severity and potential risk factors; initiate treatment.	Depending on response to treatment, may need right and/or left heart catheterization to confirm.
	Echocardiogram shows elevated PA pressure with normal systolic LV function. DDx includes pulmonary hypertension, CTEPH, HFpEF, others. Check BNP, assess for risk factors.	Consider right heart catheterization to confirm diagnosis of PH (mean PAP ≥25 and PAWP <15). Consider V/Q scan re: CTEPH. Obtain appropriate tests for secondary PH (eg, rheumatic diseases, HBV, HCV, HIV, PSG).

ECG: electrocardiogram; COPD: chronic obstructive pulmonary disease; CAD: coronary artery disease; PA: pulmonary artery; LV: left ventricular; DDx: differential diagnosis; CTEPH: chronic thromboembolic pulmonary hypertension; BNP: brain natriuretic peptide; PH: pulmonary hypertension; PAP: pulmonary artery pressure; PAWP: pulmonary artery wedge pressure; V/Q: ventilation perfusion; HBV: hepatitis B virus; HCV: hepatitis C virus; HIV: human immunodeficiency virus; PSG: polysomnography.

Graphic 111478 Version 1.0

Evaluation of dyspnea: Advanced testing

Patients who require this level of testing for undiagnosed dyspnea may benefit from referral to a pulmonary or cardiology specialist		
Test	**Rationale**	**Further testing**
Revisit description of dyspnea; Consider upper airway contribution (including nasal obstruction), muscle weakness, or fatigue being interpreted as dyspnea	Conditioning program with reassessment of symptoms and PFTs at 6 to 12 month intervals.	Further testing as described below if no response to conditioning program or patient prefers more immediate answers.
Exercise echocardiography	Wall motion and Doppler parameters are monitored during treadmill or cycle exercise to elicit exercise related PH, identify segmental wall motion abnormalities suggestive of CAD, or unmask mitral or aortic valvular disease that is hemodynamically significant during exercise.	Exercise-related pulmonary hypertension may need further evaluation with invasive CPET, if clinically significant dyspnea. CAD and valvular disease will need appropriate evaluation and treatment.
Obtain CPET	CPET can help identify nonrespiratory causes of exercise limitation, mitochondrial disease, and can help distinguish whether cardiac or respiratory problems are causing the patient's limitation in cases in which more than one disease is present.	Patients with normal testing including a normal CPET are likely to have deconditioning or a perceptual or psychological cause for dyspnea.
Serum lactate (rest and exercise)	Plasma lactate level at rest and fasting >2.5 mmol/L may suggest mitochondrial disease.	Further correlation needed with CPET, creatine kinase, and possibly muscle biopsy.
Invasive CPET (with arterial line and/or pulmonary artery catheter in place)	Depending on the level of suspicion and availability of testing, iCPET may be performed directly or based on exercise echocardiogram findings.	iCPET is largely used to identify or exclude exercise-related PH, HFpEF, and preload dependent limitations to cardiac output.

PFTs: pulmonary function tests; CPET: cardiopulmonary exercise test; PH: pulmonary hypertension; CAD: coronary artery disease; iCPET: invasive CPET; HFpEF: heart failure with preserved ejection fraction.

Graphic 104824 Version 1.0