Chapter 37: Dyspnea

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DYSPNEA

DEFINITION

The American Thoracic Society consensus statement defines *dyspnea* as a "subjective experience of breathing discomfort that consists 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, a symptom, can be perceived only by the person experiencing it and, therefore, must be self-reported. In contrast, signs of increased work of breathing, such as tachypnea, accessory muscle use, and intercostal retraction, can be measured and reported by clinicians.

EPIDEMIOLOGY

Dyspnea is common. It has been reported that up to one-half of inpatients and one-quarter of ambulatory patients experience dyspnea, with a prevalence of 9–13% in the community that increases to as high as 37% for adults aged ≥70 years. Dyspnea is a frequent cause for emergency room visits, accounting for as many as 3–4 million visits per year. Furthermore, it is increasingly appreciated that the degree of dyspnea may better predict outcomes in chronic obstructive pulmonary disease (COPD) than does the forced expiratory volume in 1 s (FEV_1), and formal measures of dyspnea have been incorporated into the Global Initiative for Chronic Obstructive Lung Disease (GOLD) COPD severity assessment guidelines. Dyspnea may also predict outcomes in other chronic heart and lung diseases as well. Dyspnea can arise from a diverse array of pulmonary, cardiac, and neurologic underlying causes, and elucidation of particular symptoms may point toward a specific etiology and/or mechanism driving dyspnea (although additional diagnostic testing is often required, as will be further discussed below).

MECHANISMS UNDERLYING DYSPNEA

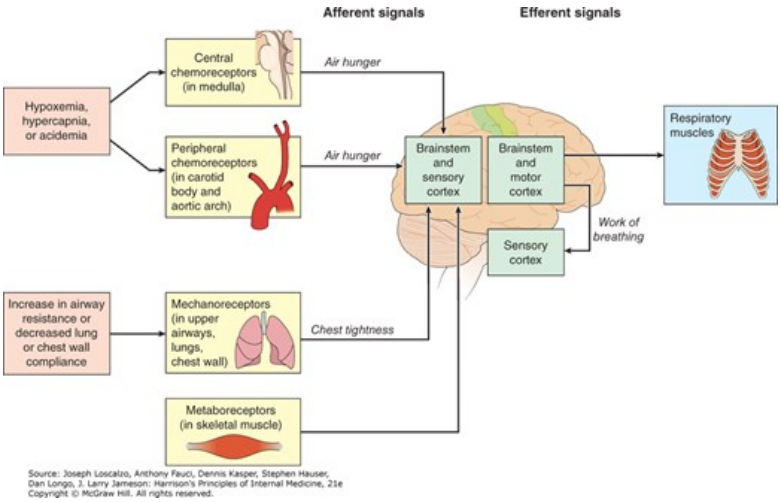
The mechanisms underlying dyspnea are complex, as it can arise from different contributory respiratory sensations. Although a large body of research has increased our understanding of mechanisms underlying particular respiratory sensations such as "chest tightness" or "air hunger," it is likely that a given disease state might produce the sensation of dyspnea via more than one underlying mechanism. Dyspnea can arise from a variety of pathways, including generation of *afferent* signals from the respiratory system to the central nervous system (CNS), *efferent* signals from the CNS to the respiratory muscles, and particularly when there is a mismatch in the integrative signaling between these two pathways, termed *efferent-reafferent mismatch* **(Fig. 37-1)**.

FIGURE 37-1

Signaling pathways underlying dyspnea. Dyspnea arises from a range of sensory inputs, many of which lead to distinct descriptive phrases used by patients (shown in italics in the figure). The sensation of respiratory effort (or work of breathing) likely arises from signals transmitted from the motor cortex to the sensory cortex when outgoing motor commands are sent to the respiratory muscles. Motor output from the brain stem may also be accompanied by signals transmitted to the sensory cortex and contribute to the sensation of work of breathing. The sensation of air hunger likely derives from stimuli that increase the drive to breathe (e.g., hypoxemia, hypercapnia, acidemia; mediated by signals from central and peripheral chemoreceptors), as well as airway and interstitial inflammation (mediated by pulmonary afferent signals) and pulmonary vascular receptors. Dyspnea arises, in part, from a perceived mismatch between the outgoing efferent messages to the respiratory muscles and incoming afferent signals from the lungs and chest wall. Chest tightness, often associated with bronchospasm, is largely mediated by simulation of vagal-irritant receptors. Afferent signals from airway, lung, and chest wall mechanoreceptors most likely pass through the brain stem before being transmitted to the sensory cortex,

although it is possible that some afferent information bypasses the brain stem and goes directly to the sensory cortex.

(Adapted from RM Schwartzstein: Approach to the patient with dyspnea. In: UpToDate, TW Post (Ed), UpToDate, Waltham, MA. (Accessed on 7 December 2021) 2018 UpToDate, Inc. For more information visit www.uptodate.com.)



Afferent signals trigger the CNS (brainstem and/or cortex) and include primarily: (1) peripheral chemoreceptors in the carotid body and aortic arch and central chemoreceptors in the medulla that are activated by hypoxemia, hypercapnia, or acidemia, and might produce a sense of "air hunger"; and (2) mechanoreceptors in the upper airways, lungs (including stretch receptors, irritant receptors, and J receptors), and chest wall (including muscle spindles as stretch receptors and tendon organs that monitor force generation) that are activated in the setting of an increased work load from a disease state producing an increase in airway resistance that may be associated with symptoms of chest tightness (e.g., asthma or COPD) or decreased lung or chest wall compliance (e.g., pulmonary fibrosis). Other afferent signals that trigger dyspnea within the respiratory system can arise from pulmonary vascular receptor responses to changes in pulmonary artery pressure and skeletal muscle (termed metaboreceptors) that are believed to sense changes in the biochemical environment.

Efferent signals are sent from the CNS (motor cortex and brainstem) to the respiratory muscles and are also transmitted by corollary discharge to the sensory cortex; they are believed to underlie sensations of respiratory effort (or "work of breathing") and perhaps contribute to sensations of "air hunger," especially in response to an increased ventilatory load in a disease state such as COPD. In addition, fear or anxiety may heighten the sense of dyspnea by exacerbating the underlying physiologic disturbance in response to an increased respiratory rate or disordered breathing pattern.

ASSESSING DYSPNEA

While it is well appreciated that dyspnea is a difficult quality to reliably measure due to multiple relevant possible domains that can be measured (e.g., sensory-perceptual experience, affective distress, and symptom impact or burden), and there exist no uniformly agreed upon tools for dyspnea assessment, consensus opinion is that dyspnea should be formally assessed in a context most relevant and beneficial for patient management and, furthermore, that the specific domains being measured are adequately described. There are a number of emerging tools that have been developed for formal dyspnea assessment. As an example, the GOLD criteria advocate use of a dyspnea assessment tool such as the Modified Medical Research Council Dyspnea Scale **(Table 37-1)** to assess symptom/impact burden in COPD.

TABLE 37-1

An Example of a Clinical Method for Rating Dyspnea: The Modified Medical Research Council Dyspnea Scale[a]

GRADE OF DYSPNEA	DESCRIPTION
0	Not troubled by breathlessness, except with strenuous exercise
1	Shortness of breath walking on level ground or with walking up a slight hill
2	Walks slower than people of similar age on level ground due to breathlessness, or has to stop to rest when walking at own pace on level ground
3	Stops to rest after walking 100 m or after walking a few minutes on level ground
4	Too breathless to leave the house, or breathless with activities of daily living (e.g., dressing/undressing)

[a]Which has been incorporated into the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines as a possible tool for rating dyspnea in chronic obstructive pulmonary disease.

Source: Reproduced with permission from DA Mahler, CK Wells: Evaluation of clinical methods for rating dyspnea. Chest 93:580, 1988.

DIFFERENTIAL DIAGNOSIS

This chapter focuses largely on chronic dyspnea, which is defined as symptoms lasting longer than 1 month and can arise from a broad array of different underlying conditions, most commonly attributable to pulmonary or cardiac conditions that account for as many as 85% of the underlying causes of dyspnea. However, as many as one-third of patients may have multifactorial reasons underlying dyspnea. Examples of a wide array of conditions that underlie dyspnea with possible mechanisms underlying the presenting symptoms are described in Table 37-2.

TABLE 37-2

Differential Diagnosis of Disease Processes Underlying Dyspnea

SYSTEM	TYPE OF PROCESS	EXAMPLE OF DISEASE PROCESS	POSSIBLE PRESENTING DYSPNEA SYMPTOMS	POSSIBLE PHYSICAL FINDINGS	POSSIBLE MECHANISMS UNDERLYING DYSPNEA	INITIAL DIAGNOSTIC STUDIES (AND POSSIBLE FINDINGS)
Pulmonary	Airways disease	Asthma, COPD, upper airway obstruction	Chest tightness, tachypnea, increased WOB, air hunger, inability to get a deep breath	Wheezing, accessory muscle use, exertional hypoxemia (especially with COPD)	Increased WOB, hypoxemia, hypercapnia, stimulation of pulmonary receptors	Peak flow (reduced); spirometry (OVD); CXR (hyperinflation; loss of lung parenchyma in COPD), chest CT and airway examination for upper airway obstruction
	Parenchymal disease	Interstitial lung disease[a]	Air hunger, inability to get	Dry end-inspiratory	Increased WOB, increased respiratory	Spirometry and lung volumes (RVD); CXR and chest CT (interstitial lung

			a deep breath	crackles, clubbing, exertional hypoxemia	drive, hypoxemia, hypercapnia, stimulation of pulmonary receptors	disease)
	Chest wall disease	Kyphoscoliosis, neuromuscular (NM) weakness	Increased WOB, inability to get a deep breath	Decreased diaphragm excursion; atelectasis	Increased WOB; stimulation of pulmonary receptors (if atelectasis is present)	Spirometry and lung volumes (RVD); MIP and MEPs (reduced in NM weakness)
Pulmonary and cardiac	Pulmonary vasculature	Pulmonary hypertension	Tachypnea	Elevated right heart pressures, exertional hypoxemia	Increased respiratory drive, hypoxemia, stimulation of vascular receptors	Diffusion capacity (reduced); ECG; ECHO (to evaluate pulmonary artery pressures)[b]
Cardiac	Left heart failure _____ Pericardial disease	Coronary artery disease, cardiomyopathy[c] _____ Constrictive pericarditis; cardiac tamponade	Chest tightness, air hunger	Elevated left heart pressures; wet crackles on lung examination; pulsus paradoxus (pericardial disease)	Increased WOB and drive, hypoxemia, stimulation of vascular and pulmonary receptors[d]	Consider BNP testing, especially in the acute setting; ECG, ECHO, may need stress testing and/or LHC
Other	Variable	Anemia Deconditioning Psychological Metabolic disturbances Gastrointestinal (e.g., gastroesophageal reflux disease [GERD], aspiration pneumonitis)	Exertional breathlessness Poor fitness Anxiety	Variable	Metaboreceptors (anemia, poor fitness); chemoreceptors (anaerobic metabolism from poor fitness); some subjects may have increased sensitivity to hypercapnia	Hematocrit for anemia; laboratory studies (e.g., metabolic panel, thyroid hormone testing for metabolic disturbances); consider upper gastrointestinal endoscopy and/or esophageal pH probe testing for GERD and concerns for aspiration; exclude other causes

[a]Differential diagnosis of interstitial lung disease includes idiopathic pulmonary fibrosis, collagen vascular disease, drug- or occupation-induced pneumonitis, lymphangitic spread of malignancy; processes that are more alveolar rather than interstitial in nature can also less commonly contribute to parenchymal lung disease underlying chronic dyspnea and include entities such as hypersensitivity pneumonitis, bronchiolitis obliterans organizing pneumonia, etc. [b]Would additionally consider these patients for CT angiography to evaluate for presence of thromboemboli, ventilation/perfusion scanning to evaluate for the presence of chronic thromboembolic disease, and right heart catheterization to further evaluate for pulmonary hypertension. [c]Diastolic dysfunction in the setting of a stiff left ventricle is often seen and contributes significantly to insidious dyspnea that can be difficult to treat. [d]May stimulate metaboreceptors if cardiac output is sufficiently reduced to result in a lactic acidosis.

Abbreviations: BNP, brain natriuretic peptide; COPD, chronic obstructive pulmonary disease; CT, computed tomography; CXR, chest x-ray; ECG, electrocardiogram;

ECHO, echocardiogram; GERD, gastroesophageal reflux disease; LHC, left heart catheterization; MIP/MEP, maximal inspiratory and maximal expiratory pressures (obtained in the pulmonary function testing laboratory); OVD, obstructive ventilatory defect; RVD, restrictive ventilatory defect; WOB, work of breathing.

Respiratory system causes include diseases of the airways (e.g., asthma and COPD), diseases of the parenchyma (more commonly, interstitial lung diseases are seen in the setting of chronic dyspnea, but alveolar filling processes, such as hypersensitivity pneumonitis or bronchiolitis obliterans organizing pneumonia [BOOP], can also present with similar symptoms), diseases affecting the chest wall (e.g., bony abnormalities such as kyphoscoliosis, or neuromuscular weakness conditions such as amyotrophic lateral sclerosis), and diseases affecting the pulmonary vasculature (e.g., pulmonary hypertension that can arise from a variety of underlying causes, or chronic thromboemolic disease). Diseases affecting the cardiovascular system that can present with dyspnea include processes affecting left heart function, such as coronary artery disease and cardiomyopathy, as well as disease processes affecting the pericardium, including constrictive pericarditis and cardiac tamponade. Other conditions underyling dyspnea that might not directly emanate from the pulmonary or cardiovascular systems include anemia (thereby potentially affecting oxygen-carrying capacity), deconditioning, and psychological processes such as anxiety. Distinguishing between the myriad of underlying processes that might present with dyspnea can be challenging. A graded approach that begins with a history and physical examination, followed by selected laboratory testing that might then advance to additional diagnostics and potentially subspecialty referral, may help elucidate the underlying cause of dyspnea. However, a substantial proportion of patients may have persistent dyspnea despite treatment for an underlying process or may not have a specific underlying process identified that is driving the dyspnea.

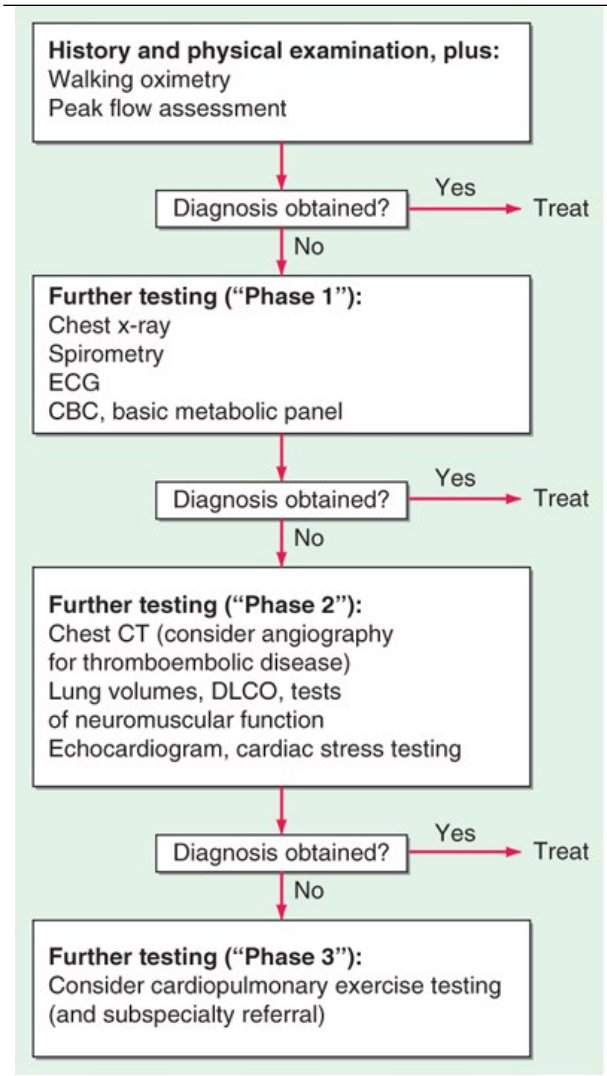
APPROACH TO THE PATIENT WITH DYSPNEA

Overall

For patients with a known prior pulmonary, cardiac, or neuromuscular condition and worsening dyspnea, the initial focus of the evaluation will usually address determining whether the known condition has progressed or whether a new process has developed that is causing dyspnea (See Fig. 37-2). For patients without a prior known potential cause of dyspnea, the initial evaluation will focus on determining an underlying etiology. Determining the underlying cause, if possible, is extremely important, as the treatment may vary dramatically based on the predisposing condition. An initial history and physical examination remain fundamental to the evaluation followed by initial diagnostic testing as indicated that might prompt subspecialty referral (e.g., pulmonary, cardiology, neurology, sleep, and/or specialized dyspnea clinic) if the cause of dyspnea remains elusive (Fig. 37-2). As many as two-thirds of patients will require diagnostic testing beyond the initial clinical presentation.

FIGURE 37-2

Possible algorithm for the evaluation of the patient with dyspnea. As described in the text, the approach should begin with a detailed history and physical examination, followed by progressive testing and ultimately more invasive testing and subspecialty referral as is indicated to determine the underlying cause of dyspnea. CBC, complete blood count; DLCO, diffusing capacity of the lungs for carbon monoxide; ECG, electrocardiogram. *(Adapted from NG Karnani et al: Am Fam Physician 71:1529, 2005.)*



History

The patient should be asked to describe in his or her own words what the discomfort feels like as well as the effect of position, infections, and environmental stimuli on the dyspnea, as descriptors may be helpful in pointing toward an etiology. For example, symptoms of chest tightness might suggest the possibility of bronchoconstriction, and the sensation of inability to take a deep breath may correlate with dynamic hyperinflation from COPD. Orthopnea is a common indicator of congestive heart failure (CHF), mechanical impairment of the diaphragm associated with obesity, or asthma triggered by esophageal reflux. Nocturnal dyspnea suggests CHF or asthma. Acute, intermittent episodes of dyspnea are more likely to reflect episodes of myocardial ischemia, bronchospasm, or pulmonary embolism, while chronic persistent dyspnea is more typical of COPD, interstitial lung disease, and chronic thromboembolic disease. Information on risk factors for drug-induced or occupational lung disease and for coronary artery disease should be elicited. Left atrial myxoma or hepatopulmonary syndrome should be considered when the patient complains of *platypnea*—i.e., dyspnea in the upright position with relief in the supine position.

Physical Examination

Initial vital signs might be helpful in pointing toward an underlying etiology in the context of the remainder of the evaluation. For example, the presence of fever might point toward an underlying infectious or inflammatory process; the presence of hypertension in the setting of a heart failure might point toward diastolic dysfunction; the presence of tachycardia might be associated with many different underlying processes including fever,

cardiac dysfunction, and deconditioning; and the presence of resting hypoxemia suggests processes involving hypercapnia, ventilation-perfusion mismatch, shunt, or impairment in diffusion capacity might be involved. An exertional oxygen saturation should also be obtained as described below. The physical examination should begin during the interview of the patient. Inability of the patient to speak in full sentences before stopping to get a deep breath suggests a condition that leads to stimulation of the controller or impairment of the ventilatory pump with reduced vital capacity. Evidence of increased work of breathing (supraclavicular retractions; use of accessory muscles of ventilation; and the tripod position, characterized by sitting with the hands braced on the knees) is indicative of increased airway resistance or stiffness of the lungs and the chest wall. When measuring the vital signs, the physician should accurately assess the respiratory rate and measure the pulsus paradoxus **(Chap. 270)**; if the systolic pressure decreases by >10 mmHg on inspiration, the presence of COPD, acute asthma, or pericardial disease should be considered. During the general examination, signs of anemia (pale conjunctivae), cyanosis, and cirrhosis (spider angiomata, gynecomastia) should be sought. Examination of the chest should focus on symmetry of movement; percussion (dullness is indicative of pleural effusion; hyperresonance is a sign of pneumothorax and emphysema); and auscultation (wheezes, rhonchi, prolonged expiratory phase, and diminished breath sounds are clues to disorders of the airways; rales suggest interstitial edema or fibrosis). The cardiac examination should focus on signs of elevated right heart pressures (jugular venous distention, edema, accentuated pulmonic component to the second heart sound); left ventricular dysfunction (S3 and S4 gallops); and valvular disease (murmurs). When examining the abdomen with the patient in the supine position, the physician should note whether there is paradoxical movement of the abdomen as well as the presence of increased respiratory distress in the supine position: inward motion during inspiration is a sign of diaphragmatic weakness, and rounding of the abdomen during exhalation is suggestive of pulmonary edema. Clubbing of the digits may be an indication of interstitial pulmonary fibrosis or bronchiectasis, and joint swelling or deformation as well as changes consistent with Raynaud's disease may be indicative of a collagen-vascular process that can be associated with pulmonary disease.

Patients should be asked to walk under observation with oximetry in order to reproduce the symptoms. The patient should be examined during and at the end of exercise for new findings that were not present at rest (e.g., presence of wheezing) and for changes in oxygen saturation.

Chest Imaging

After the history elicitation and the physical examination, a chest radiograph should be obtained if the diagnosis remains elusive. The lung volumes should be assessed: hyperinflation is consistent with obstructive lung disease, whereas low lung volumes suggest interstitial edema or fibrosis, diaphragmatic dysfunction, or impaired chest wall motion. The pulmonary parenchyma should be examined for evidence of interstitial disease, infiltrates, and emphysema. Prominent pulmonary vasculature in the upper zones indicates pulmonary venous hypertension, while enlarged central pulmonary arteries may suggest pulmonary arterial hypertension. An enlarged cardiac silhouette can point toward dilated cardiomyopathy or valvular disease. Bilateral pleural effusions are typical of CHF and some forms of collagen-vascular disease. Unilateral effusions raise the specter of carcinoma and pulmonary embolism but may also occur in heart failure or in the case of a parapneumonic effusion. CT of the chest is generally reserved for further evaluation of the lung parenchyma (interstitial lung disease) and possible pulmonary embolism if there remains diagnostic uncertainty.

Laboratory Studies

Initial laboratory testing should include a hematocrit to exclude occult anemia as an underlying cause of reduced oxygen-carrying capacity contributing to dyspnea, and a basic metabolic panel may be helpful to exclude a significant underlying metabolic acidosis (and conversely, an elevated bicarbonate might point toward the possibility of carbon dioxide retention that might be seen in chronic respiratory failure—in such a setting, an arterial blood gas may provide useful additional information). Additional laboratory studies should include electrocardiography to seek evidence of ventricular hypertrophy and prior myocardial infarction and spirometry, which can be diagnostic of the presence of an obstructive ventilatory defect and suggest the possibility of a restrictive ventilatory defect (that then might prompt additional pulmonary function laboratory testing, including lung volumes, diffusion capacity, and possible tests of neuromuscular function). Echocardiography is indicated when systolic dysfunction, pulmonary hypertension, or valvular heart disease is suspected. Bronchoprovocation testing and/or home peak-flow monitoring may be useful in patients with intermittent symptoms suggestive of asthma who have a normal physical examination and spirometry; up to one-third of patients with the clinical diagnosis of asthma do not have reactive airways disease when formally tested. Measurement of brain natriuretic peptide levels in serum is increasingly used to assess for CHF in patients presenting with acute dyspnea but may be elevated in the presence of right ventricular strain as well.

Distinguishing Cardiovascular from Respiratory System Dyspnea

If a patient has evidence of both pulmonary and cardiac disease that is not responsive to treatment or it remains unclear what factors are primarily driving the dyspnea, a cardiopulmonary exercise test (CPET) can be carried out to determine which system is responsible for the exercise limitation.

CPET includes incremental symptom-limited exercise (cycling or treadmill) with measurements of ventilation and pulmonary gas exchange and, in some cases, includes noninvasive and invasive measures of pulmonary vascular pressures and cardiac output. If, at peak exercise, the patient achieves predicted maximal ventilation, demonstrates an increase in dead space or hypoxemia, or develops bronchospasm, the respiratory system may be the cause of the problem. Alternatively, if the heart rate is >85% of the predicted maximum, if the anaerobic threshold occurs early, if the blood pressure becomes excessively high or decreases during exercise, if the O_2 pulse (O_2 consumption/heart rate, an indicator of stroke volume) falls, or if there are ischemic changes on the electrocardiogram, an abnormality of the cardiovascular system is likely the explanation for the breathing discomfort. Additionally, a CPET may also help point toward a peripheral extraction deficit or metabolic/neuromuscular disease as potential underlying processes driving dyspnea.

TREATMENT OF DYSPNEA

The first goal is to correct the underlying condition(s) driving dyspnea and address potentially reversible causes with appropriate treatment for the particular condition. Multiple different interventions may be necessary, given that dyspnea often arises from multifactorial causes. If relief of dyspnea with treatment of the underlying condition(s) is not fully possible, an effort is made to lessen the intensity of the symptom and its effect on the patient's quality of life. More recent work at the consensus conference level has sought to define an identifiable entity of persistent dyspnea in order to develop an approach to improving efforts to address symptom management for this condition. In 2017, an international group of experts defined "chronic breathlessness syndrome" as "the experience of breathlessness that persists despite optimal treatment of the underlying pathophysiology and results in disability for the patient." Despite an increased understanding of the mechanisms underlying dyspnea, there has been limited progress in treatment strategies for dyspnea. Supplemental O_2 should be administered if the resting O_2 saturation is ≤88% or if the patient's saturation drops to these levels with activity or sleep. In particular, for patients with COPD, supplemental oxygen for those with hypoxemia has been shown to improve mortality, and pulmonary rehabilitation programs (including some community-based exercise programs such as yoga and Tai Chi) have demonstrated positive effects on dyspnea, exercise capacity, and rates of hospitalization. Opioids have been shown to reduce symptoms of dyspnea, largely through reducing air hunger, thus likely suppressing respiratory drive and influencing cortical activity. However, opioids should be considered for each patient individually based on the risk-benefit profile in regard to the effects of respiratory depression. Studies of anxiolytics for dyspnea have not demonstrated consistent benefit. Additional approaches are under study for dyspnea, including inhaled furosemide that might alter afferent sensory information.

FURTHER READING

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