American Thoracic Society
MEDICAL SECTION OF THE AMERICAN LUNG ASSOCIATION

Dyspnea
Mechanisms, Assessment, and Management: A Consensus Statement

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INTRODUCTION

Respiration, the act of breathing, is unique in that, of all the vital functions, it alone is regulated not only by automatic centers located in the brainstem but also by voluntary signals initiated in the cortex. Insofar as individuals have some control over their breathing, sensations arising from respiratory activity affect the rate and pattern of breathing as well as the individual's functional status. Derangements in the respiratory controller, ventilatory pump, or gas exchanger may underlie uncomfortable breathing sensations, generally referred to as dyspnea by clinicians. While the initial goal of clinicians when treating a patient who is dyspneic is to remedy the physiologic derangement producing the sensation, there are many individuals with chronic cardiopulmonary disorders for which the underlying pathophysiology cannot be corrected. This, in turn, frequently results in long-term disability for the patient. A better understanding of the mechanisms, assessment, and treatment of dyspnea is necessary if clinicians are to improve their ability to monitor and treat patients with shortness of breath.

In the 1950s and 1960s much of the work on dyspnea focused on the impact of mechanical loads on respiratory symptoms (1). While there was an appreciation that there may be several different qualities of dyspnea, the general consensus was that the sense of effort was the primary element of breathing discomfort.

By 1984, when the National Heart, Lung, and Blood Institute sponsored a workshop on respiratory sensations and dyspnea, investigators were refining methodologies for assessment and quantification of respiratory sensations and examining more closely the neurophysiologic mechanisms producing these sensations (2). In the past decade great strides have been made in: (1) distinguishing among the sensations subsumed under the term dyspnea and in defining a glossary of terms to facilitate communication between patients and health care providers about these sensations (3–7); (2) developing a broader understanding of the role of pulmonary and chest wall receptors in producing respiratory discomfort (8); and (3) refining the causes of functional limitation in patients with chronic dyspnea (9, 10). Furthermore, new technological advances such as positron emission tomography (PET) scans have been employed by investigators to localize regions of the brain that may be responsible for processing respiratory sensations (11, 12).

We now have a greater appreciation for the differences between a respiratory "sensation," the neural activation resulting from stimulation of a peripheral receptor, and "percep-

tion," the reaction of the sentient individual to the sensation (13). Psychological and cultural factors may influence the reaction to a sensation, e.g., a stoic individual may deny respiratory discomfort and push beyond the limitations experienced by another person more sensitive to bodily messages. The context in which a sensation occurs can also impact the perception of the event. The sensation experienced by an individual during maximal exercise will evoke very different reactions than the same sensation occurring at rest. In the former instance, it may be perceived as a normal sensation, while in the latter it can provoke great anxiety if considered a sign of a pathologic condition. Understanding the physiological and emotional factors that impact sensations and perceptions, health care providers will be better armed to treat those with a faulty warning system. For example, failure to appreciate mechanical loads or gas exchange abnormalities may make individuals with asthma more vulnerable to near-fatal attacks (14). On the other hand, increased sensitivity to respiratory sensations may contribute to the hyperventilation syndrome (15) or to the disability associated with a sedentary existence (16).

Knowledge of factors contributing to dyspnea is critical to the development and selection of therapeutic interventions to alleviate breathing discomfort, and the interest in doing so is high (17, 18). There are approximately 14 million individuals in the United States with chronic obstructive pulmonary disease (emphysema and chronic bronchitis) (19). In addition, roughly 5% of the population, or another 10 million persons, suffer from asthma. These illnesses generate in excess of 17 million physician office visits a year at a cost of over 10.4 billion (20). When patients with interstitial disease, neuromuscular disorders, lung cancer, and cardiac disease are added to this figure, it is clear that there is a large segment of the population with chronic cardiopulmonary problems who are likely to suffer from dyspnea. Acute disorders such as pneumonia, pulmonary embolism, bronchitis, and myocardial ischemia add further to the prevalence of dyspnea around the world.

Patients with chronic pulmonary disease are often limited in their activities by respiratory discomfort. Reductions in functional status, quality of life, and disability are frequently consequences of this symptom. Diseases producing chronic dyspnea may leave the patient with significant breathlessness despite maximal therapy. Under these conditions, one should evaluate the specific mechanism(s) contributing to dyspnea in that particular patient since more than one process may frequently contribute to the patient's functional limitation, e.g., obstructive lung disease and cardiovascular deconditioning, or the emotional response to the patient's illness may exacerbate his/her response to the respiratory discomfort. Having identified these factors, appropriate additional treatment strategies might be devised. Pulmonary rehabilitation programs have been shown to relieve dyspnea, reduce hospitalizations, and improve quality of life (10, 21), yet the mechanisms by which they succeed remain controversial. A greater understanding of

the effects of specific components of pulmonary rehabilitation on dyspnea is necessary.

To examine the current state of our understanding of dyspnea, including its physiologic bases, methods of assessment, and management strategies for this often disabling symptom, the American Thoracic Society formed a multidisciplinary Dyspnea Work Group. The Work Group's goal is to provide an overview of dyspnea that is clinically relevant to physicians, nurses, and therapists engaged in the care of patients with shortness of breath.

Definitions

Dyspnea is the term generally applied to sensations experienced by individuals who complain of unpleasant or uncomfortable respiratory sensations. Many definitions of dyspnea have been offered, including: "difficult, labored, uncomfortable breathing" (22), an "awareness of respiratory distress" (23), "the sensation of feeling breathless or experiencing air hunger" (24), and "an uncomfortable sensation of breathing" (7). These definitions have sometimes mixed the true symptom (what patients say they are feeling) with physical signs (what the physician observes about the patient, e.g., "exhibits labored breathing"). In the final analysis, a symptom can only be described by the person who experiences it. In this context, recent investigations of the perception of breathlessness suggest that there are multiple types of dyspnea (3–7).

Given our greater understanding of the interplay between physiological and behavioral factors in producing respiratory discomfort as well as the spectrum of phrases used by patients to describe their sensations, we propose a broader definition of dyspnea. Specifically, we suggest that dyspnea is a term used to characterize 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. This broad definition of dyspnea will guide our discussion.

Goal

Having defined dyspnea to encompass not only physiologic mechanisms but also psychological, social, and environmental factors, we propose broadening the framework for discussion of respiratory discomfort. New strategies for treating dyspnea will expand our understanding of pathophysiologic mechanisms, which, in turn, will lead to refinement of our therapeutic approaches. Any assessment of dyspnea must take into consideration the question being asked. Are we trying to measure the intensity or quality of the sensation of respiratory discomfort or the emotional or behavioral response to the discomfort? Even assessment of the patient's overall functional status, a common outcome measure, is a complex undertaking. While one may be able to quantify a patient's activities, determining whether the individual's limitations are due to dyspnea, fatigue, or depression may be more difficult. Our goal in this statement is to review the current understanding of the pathophysiologic mechanisms of dyspnea, the tools used to assess this symptom and its impact on patients' lives, and therapeutic approaches that may be employed to ameliorate the discomfort. This approach assumes standard treatments for the underlying disease state have been exhausted.

MECHANISMS OF DYSPNEA

The sensation of dyspnea seems to originate with the activation of sensory systems involved with respiration. Sensory information is, in turn, relayed to higher brain centers where central processing of respiratory-related signals and contextual, cognitive, and behavioral influences shape the ultimate expression of the evoked sensation. The homeostatic systems involved in the regulation of respiration provide a framework for understanding the mechanisms of dyspnea.

Respiratory Control System

The respiratory control system functions to satisfy the metabolic requirements of the body. Respiratory motor activity emanates from clusters of neurons in the medulla. Efferent respiratory discharges activate the ventilatory muscles that expand the chest wall, inflate the lungs, and produce ventilation. The resulting breathing regulates the oxygen and carbon dioxide tensions and hydrogen ion concentration in the blood and body tissues. Chemoreceptors in the blood and brain as well as mechanoreceptors in the airways, lungs, and chest wall are involved in the automatic regulation of the level and pattern of breathing. Changes in P_{CO_2} and P_{O_2} are sensed by central chemoreceptors in the medulla (25) and peripheral chemoreceptors in the carotid and aortic bodies (26). Signals from these chemoreceptors are transmitted back to brainstem respiratory centers that adjust breathing to maintain blood-gas and acid-base homeostasis.

Afferent impulses from vagal receptors in the airways and lungs also exert important influences on the level and pattern of breathing. Pulmonary stretch receptors are stimulated as the lung expands; irritant receptors around the epithelial cells of the bronchial walls are activated by tactile stimulation in the bronchial mucosa, high rates of air flow, and increases in bronchial smooth muscle tone; and C fibers, found in the interstitium of the lung in proximity to the alveoli and pulmonary capillaries, respond to increases in pulmonary interstitial and capillary pressure (27).

The respiratory muscles are also innervated by a variety of sensory receptors. Muscle spindles are abundant in the intercostal muscles, and afferent activity from them are involved in both spinal and supraspinal reflexes (28, 29). The diaphragm contains tendon organs that signal muscle tension and exert inhibitory influences on central respiratory activity.

Feedback of afferent information from lung and chest wall mechanoreceptors provides respiratory motor and pre-motor neurons with important information regarding the mechanical status of the ventilatory pump as well as changes in length and force of contraction of the respiratory muscles. These signals allow adjustments to be made in the level and pattern of brainstem respiratory motor activity to compensate for changes in respiratory muscle function or ventilatory system impedance (30).

Chemoreceptor as well as lung and chest wall mechanoreceptor afferents may also project to higher brain centers to provide a direct appraisal of the chemical milieu of the body and of the mechanical status of the ventilatory apparatus. Additionally, and very importantly, corollary signals or efferent copies of brainstem respiratory center motor output appear to be transmitted to higher brain centers and result in a conscious awareness of the outgoing motor command (31). These may all play an important role in shaping the sensation of dyspnea.

Physiological Mechanisms

Our understanding of the physiologic mechanisms underlying the sensations of dyspnea is derived from studies employing a range of experimental conditions in animals, normal subjects, anesthetized subjects, and patients with cardiopulmonary and neurologic diseases. Conclusions from these findings, and ap-

parent contradictions among studies, must be viewed with an appreciation for the fact that those species differences and, in man, state differences, may have powerful effects on respiratory phenomena.

Respiratory motor command corollary discharge. There is a conscious awareness of the outgoing respiratory motor command to the ventilatory muscles. This sense of respiratory motor output is distinct from sensations directly related to changes in muscle length or tension and is attributed to a corollary discharge from brainstem respiratory neurons to the sensory cortex during automatic reflex breathing or from cortical motor centers to the sensory cortex during voluntary respiratory efforts (32). Evidence for corollary discharges is functional rather than structural; specific receptors and pathways have not been identified. However, rostral projections from brainstem respiratory motor neurons to the midbrain and thalamus have recently been described in the cat, and these could represent the pathway of corollary discharges (33, 34). These corollary discharges are thought to be important in shaping the sense of respiratory effort. It is well established that factors that necessitate a greater motor command to achieve a given tension in the muscle, such as decreasing muscle length, muscle fatigue, or respiratory muscle weakness, cause a heightened sense of respiratory effort (32, 35, 36). The sense of respiratory effort intensifies with increases in central respiratory motor command and is proportional to the ratio of the pressures generated by the respiratory muscles to the maximum pressure–generating capacity of those muscles (37).

Chest wall receptors. Projections to the brain of afferent signals from mechanoreceptors in the joints, tendons, and muscles of the chest all appear to play a role in shaping respiratory sensations. Specifically, afferents from intercostal muscles have been shown to project to the cerebral cortex and contribute to proprioception and kinesthesia (38, 39).

Studies of the detection of just noticeable differences in added external ventilatory loads have suggested a primary role for muscle spindles in mediating the sensation of dyspnea (40). The sentience of chest wall muscles is further supported by the observations that vibration of the chest wall to activate muscle spindles produces an illusion of chest movement (41). Vibration of inspiratory muscles located in the upper rib cage in phase with inspiration produces a sensation of chest expansion and reduces the intensity of dyspnea in patients with chronic lung disease, both at rest and during exercise (42).

Voluntarily constraining ventilation ($\dot{V}E$) below the spontaneously adopted breathing level produces an intense sensation of air hunger, even when blood gases and the chemical drive to breathe are not allowed to change (43, 44). The increase in the intensity of dyspnea associated with reduced ventilation at a constant P_{CO_2} correlates closely with the degree to which tidal volume is reduced. This effect of constrained thoracic expansion on respiratory sensation is modified by chest wall vibration; with vibration of the upper rib cage during inspiration, the intensity of dyspnea associated with constrained breathing is reduced, suggesting a preeminent role for chest wall receptors (45).

Pulmonary vagal receptors. Afferent information from pulmonary vagal receptors project to the brain, and vagal inputs are important in shaping the pattern of breathing (46). There is some evidence that vagal influences, independent of any effect on the level and pattern of breathing, may also contribute to the sensation of dyspnea.

Patients with high cervical spinal cord transection, in whom feedback from chest wall receptors is blocked, are able to detect changes in tidal volume delivered by a mechanical ventilator, and experience a sensation of air hunger when their inspired volume is reduced (47, 48). This suggests that vagal receptors may contribute to the unpleasant sensations that result when thoracic expansion is limited and to the dyspnea that accompanies breathholding. Additionally, it has been shown that vagal blockade ameliorates dyspnea during exercise and alleviates the unpleasant sensations during breathholding (49–51). Dyspnea associated with bronchoconstriction is at least in part mediated by vagal afferents (52). This is suggested by the observation that the heightened sensation of difficulty in breathing resulting from airway obstruction induced by histamine inhalation is lessened following the inhalation of lidocaine to block airway receptors. Other studies have shown the intravenous injections of lobeline to stimulate pulmonary C fibers produces a sensation of choking and pressure in the chest (53).

Chemoreceptors. The dyspnea associated with hypercapnia and hypoxia is largely the result of the chemically induced increases in respiratory motor activity. There is some evidence that the sensation of dyspnea may also be directly affected by inputs from chemoreceptors. Both ventilator-dependent quadriplegics with high cervical spinal cord transection and normal subjects paralyzed with neuromuscular blocking agents experience sensations of air hunger when P_{CO_2} is increased (54, 55). Also, the sensation of dyspnea is more intense at given levels of ventilation produced by hypercapnia compared to the same level of ventilation achieved by exercise or by voluntary hyperventilation (56). It has also been shown that the relief of exercise-induced hypoxemia by the administration of oxygen results in a reduction of dyspnea out of proportion to the reduction in ventilation (57).

Pathophysiology of Dyspnea

An attractive unifying theory is that dyspnea results from a disassociation or a mismatch between central respiratory motor activity and incoming afferent information from receptors in the airways, lungs, and chest wall structures (44, 58). The afferent feedback from peripheral sensory receptors may allow the brain to assess the effectiveness of the motor commands issued to the ventilatory muscles, i.e., the appropriateness of the response in terms of flow and volume for the command. When changes in respiratory pressure, airflow, or movement of the lungs and chest wall are not appropriate for the outgoing motor command, the intensity of dyspnea is heightened. In other words, a dissociation between the motor command and the mechanical response of the respiratory system may produce a sensation of respiratory discomfort. This mechanism was first introduced by Campbell and Howell in the 1960s with the theory of "length-tension inappropriateness." The theory has been generalized to include not only information arising in the ventilatory muscles, but information emanating from receptors throughout the respiratory system and has been termed "neuro-mechanical" (59), or "efferent–reafferent dissociation" (55). Patients with a mechanical load on the respiratory system, either resistive or elastic, or respiratory muscle abnormalities will have a dissociation between the efferent and afferent information during breathing. The mismatch of neural activity and consequent mechanical or ventilatory outputs may contribute to the intensity of dyspnea under these conditions. This theory explains dyspnea associated with breathholding, the unpleasant sensation of air hunger experienced by patients receiving mechanical ventilation with small tidal volumes and low inspiratory flow rates, and the discomfort of subjects who voluntarily constrain the rate and depth of their breathing (43, 44, 48, 60).

Heightened ventilatory demand. It is regularly observed, both in normal individuals and in patients with lung disease,

that the intensity of the dyspnea increases progressively with the level of ventilation during exercise (61). This is attributable to the increase in respiratory motor output and a corresponding increase in the sense of effort. There are, however, important contextual influences on the interpretation of respiratory-related sensations. Thus, symptoms of shortness of breath are more likely to be reported when hyperpnea occurs at rest and cannot be accounted for by an increase in exertion or physical activity. Many conditions give rise to ventilation that is excessive for the level of physical activity, and consequently cause symptoms of dyspnea (62).

Increases in ventilation are required to compensate for the enlarged dead space that results from lung parenchymal and pulmonary vascular disease. Hypoxemia at altitude and in patients with respiratory disease stimulates arterial chemoreceptors and increases respiratory motor activity. This heightened motor command contributes to dyspnea. Patients with cardiorespiratory disease are often deconditioned because of prolonged inactivity. The state of physical conditioning is an important determinant of exercise capacity. Deconditioning is associated with an early and accelerated rise in blood lactate levels (63). Early lactic acid production by skeletal muscles during exercise imposes an additional respiratory stimulus, increases the ventilation at a given level of exercise, and heightens dyspnea (64). This and the additional burdens of advanced age, malnutrition, and hypoxemia impair respiratory and peripheral muscle function and lead to limitations in exercise capacity secondary to leg discomfort and dyspnea. The cycle of dyspnea, reduced activity, deconditioning, and more dyspnea is well recognized as a key contributor to the functional decline associated with both normal aging and cardiorespiratory illness (65, 66).

While the level of ventilation often correlates well with the intensity of dyspnea, increases in central inspiratory activity alone are unlikely to explain respiratory discomfort in all settings (67). As noted previously, for a given level of ventilation, different stimuli produce dyspnea of varying intensity (56), and supplemental oxygen reduces dyspnea associated with exercise in hypoxic subjects out of proportion to the reduction in ventilation (57). In addition, if all dyspnea were the consequence of heightened ventilatory demand, one might expect the quality of respiratory discomfort to be similar in all situations, a hypothesis that is unable to account for the findings of recent studies on the language of dyspnea, in which patients with different pathophysiologic conditions characterize their discomfort utilizing qualitatively distinct phrases (*see* QUALITIES OF DYSPNEA AND PHYSIOLOGIC MECHANISMS) (3, 4, 7).

Respiratory muscle abnormalities. Weakness or mechanical inefficiency of the respiratory muscles results in a mismatch between central respiratory motor output and achieved ventilation. This mismatch may explain the dyspnea experienced by patients with neuromuscular diseases affecting the respiratory musculature (68) and patients with respiratory muscle fatigue (69). As the pressure-generating capacity of the respiratory muscles fall and as the ratio of the pressures produced by the respiratory muscles to the maximum pressure that can be achieved increases, dyspnea progressively worsens (70).

Chronic obstructive pulmonary disease (COPD) is often characterized by overinflation of the lung and overexpansion of the thorax. This results in an enlarged FRC and foreshortening of the muscles of inspiration. Based on the length–tension properties of muscle, foreshortening of the inspiratory muscles in COPD may substantially reduce their force-generating capacity. This impairment in the mechanical advantage of the inspiratory muscles contributes importantly to symptoms of dyspnea (71). The relief of dyspnea following lung volume reduction surgery may be explained, at least in part, by the resulting changes in thoracic size and shape with increases in the resting length of the muscles of inspiration.

Airflow limitation in patients with COPD leads to dynamic hyperinflation, particularly during exercise. Several important consequences of dynamic hyperinflation serve to worsen dyspnea. The increase in lung volume causes breathing to take place on a stiffer portion of the pressure–volume curve, producing an added elastic load. The inward elastic recoil of the respiratory system at end-expiration imposes an added inspiratory threshold load. Finally, inspiratory muscle shortening with hyperinflation reduces muscle mechanical efficiency. The relief of dyspnea with inhaled bronchodilators has been attributed to reductions in exercise dynamic hyperinflation (72).

Abnormal ventilatory impedance. Respiratory diseases such as asthma and COPD which narrow airways and increase airway resistance, and diseases of the lung parenchyma, including interstitial pneumonitis and pulmonary fibrosis, which increase lung elastance, commonly cause dyspnea. When ventilatory impedance increases, the level of central respiratory motor output required to achieve a given ventilation rises. When the respiratory effort expended in breathing is out of proportion to the resulting level of ventilation, dyspnea results.

Changes in ventilatory impedance produced by diseases of the lungs can be simulated in normal subjects by the imposition of external ventilatory resistive and elastic loads. As the magnitude of the applied external ventilatory load is increased, there is a progressive rise in the intensity of dyspnea (73). Dyspnea intensity during external ventilatory loading corresponds primarily to the peak airway pressures developed by the contracting respiratory muscles, the duration of inspiration, and the breathing frequency (74).

Abnormal breathing patterns. Dyspnea is common in diseases involving the lung parenchyma. It is possible that the rapid shallow breathing often noted in diseases of the lung parenchyma is a reflex response to the stimulation of pulmonary vagal receptors, but there is little direct evidence that pulmonary vagal receptors contribute directly to dyspnea. Pulmonary vagal receptors have been posited to play a role in the dyspnea of severe exercise (53), pulmonary congestion and pulmonary edema (51), and recurrent pulmonary embolism (75). Pursed lip breathing has been associated with reduced dyspnea intensity in patients with obstructive lung disease, an effect that may be due to a diminished respiratory frequency, changes in the pattern of ventilatory muscle recruitment, longer expiratory time, and larger tidal volumes (76).

Blood-gas abnormalities. Blood-gas abnormalities, while among the most serious consequences of cardiorespiratory disease, poorly correlate with dyspnea in individual patients. Hypoxemia causes respiratory motor activity to increase through chemoreceptor stimulation (77). Hypoxia may also have a direct dyspnogenic effect. This is suggested by the observation that supplemental oxygen administration relieves dyspnea in some patients with lung disease, even in the absence of any changes in ventilation (78, 79).

Similarly, the dyspnea produced by hypercapnia is largely the consequence of increases in respiratory motor output, but there also appears to be a direct effect of P_{CO_2} on the intensity of dyspnea (56). The effect of P_{CO_2} on ventilation depends primarily on changes in hydrogen ion concentration at the medullary chemoreceptors. In patients with chronic hypercapnia, metabolic compensation minimizes any changes in hydrogen ion concentration and consequently limits ventilatory responses and changes in respiratory sensation. On the other hand, the

responses to changes in hydrogen ion concentration may explain the dyspnea of diabetic ketoacidosis and renal insufficiency.

Qualities of Dyspnea and Physiologic Mechanisms

Utilizing dyspnea questionnaires in three studies involving more than 300 patients with a variety of cardiopulmonary disorders, both in the United States and the United Kingdom, investigators have demonstrated that individuals with presumed different physiologic causes for their breathing discomfort, as well as normal subjects made breathless by performing a variety of respiratory tasks, employ qualitatively distinct sensations to describe that discomfort (3–5, 24). While the sense of increased effort or work of breathing is a common feature for conditions characterized by abnormal mechanical loads (e.g., COPD, interstitial lung disease) and neuromuscular weakness, patients with congestive heart failure described a sensation of air hunger or suffocating, and the dyspnea of asthma is notable for a sensation of chest tightness. The consistency of these findings across a large number of patients in two different cultures suggests that these qualities of dyspnea reflect not merely variations in individual expectations or experiences, but inherent differences in the physiologic mechanisms underlying the sensations themselves.

Several studies have begun to provide additional direct information on the relationship between quality of dyspnea and the underlying mechanism producing discomfort. The sensation of air hunger has been shown to be associated with increases in respiratory drive, particularly in the presence of hypoxia or hypercapnia (5, 54, 55). While the intensity of this sensation may be modified by changes in tidal volume, changes that are likely to be sensed in part by transmission of afferent information from pulmonary stretch receptors to the central nervous system (48), the basic quality of the sensation persists. Furthermore, in an experimental model in which normal subjects were asked to breathe at a targeted level of hyperpnea while Pa_{CO_2} was modified by varying the concentration of inspired carbon dioxide, subjects were able to independently rate their sense of effort to breathe and sense of air hunger or unpleasant urge to breathe (80). As Pa_{CO_2} was raised, air hunger increased while the effort of breathing decreased. These data are consistent with the notion that the sensation of air hunger is associated with stimulation of chemoreceptors (54, 55) while the sense of effort to breathe may reflect central respiratory motor command (37).

In studies of methacholine-induced bronchoconstriction in subjects with mild asthma, several sensations of breathing discomfort appear in a sequential fashion (5). At very mild degrees of airway obstruction, the sensation of chest tightness predominates. As FEV_1 falls and the mechanical load on the system increases, the sensation of effort emerges while further declines in lung function are associated with a sensation of air hunger. These findings suggest that chest tightness may arise from bronchoconstriction-induced stimulation of pulmonary receptors, while the sensation of effort reflects the increased central motor command associated with the worsening mechanical load on the system. Air hunger may emerge in concert with even greater central motor activity. In patients with asthma presenting to an emergency department with acute flares of their disease, inhaled β-agonists reduce the sensation of chest tightness, while the effort and work of breathing, along with airways obstruction, persist (81). Thus, induction of bronchoconstriction produces chest tightness; alleviation of bronchoconstriction eliminates it. To the extent that airway inflammation, airways obstruction, and mechanical load persist, the sense of effort remains.

Psychologic Effects and Higher Brain Center Influences

Patients with chronic lung disease who suffer from dyspnea often exhibit anxiety and/or depressive symptoms (82–84). The exact cause-and-effect relationships, however, are unclear. On one hand, anxiety, anger, and depression can increase symptoms of breathlessness out of proportion to the impairment in cardiorespiratory function (62, 73, 85). But it has also been argued that the stress of a chronic respiratory illness and the associated physical disability may be the cause of mood disorders (86). In either event, it is clear that a variety of emotional changes can intensify dyspnea. Insofar as breathing is under considerable behavioral control by cortical and subcortical brain centers, anxiety, anger, and depression may lead to an increase in ventilation and a worsening of dyspnea. The quality and intensity of dyspnea at a given level of respiratory activity are also thought to be shaped by patient experience, expectation, behavioral style, and emotional state (87), which may explain in part why the relationship between dyspnea and the degree of impairment in lung function is not strong. Patients who tend to be adaptive and independent tolerate ventilatory loads with relatively few symptoms of dyspnea. Others who are more dependent, anxious, and focused inordinately on their health may experience severe dyspnea with relatively small increases in ventilatory impedance (63).

Summary

Dyspnea is a complex symptom. Sensations of difficult or labored breathing that accompany cardiorespiratory disease may vary in quality and may have different pathophysiologic bases. The predominant mechanisms involve corollary discharges of respiratory motor activity and feedback from chemoreceptors and mechanoreceptors in the lung and chest wall. Behavioral style and emotional state also exert important influences on the expression of respiratory sensations. Further research is necessary to better define and clarify the physiologic and psychologic factors underlying dyspnea to ensure a rational approach to the management of this pervasive symptom

DYSPNEA ASSESSMENT

Introduction

The assessment of dyspnea is a critical part of patient evaluation and management when cardiopulmonary disease is present. But dyspnea, like hunger or thirst, is largely a "synthetic sensation" in that it often arises from multiple sources of information rather than from stimulation of a single neural receptor. In addition, the severity of dyspnea as well as the qualitative aspects of unpleasant breathing experiences varies widely among patients. The variable nature of dyspnea reduces the likelihood that any single estimate of organic disease or illness will provide a ready index either to establish the intensity of dyspnea or to gauge the success of treatment. Therefore, dyspnea itself needs to be measured.

History and Physical Examination

Historically, the evaluation of dyspnea in patients has emphasized the search for corresponding pathophysiology. In most cases, the primary problem is heart, lung, or neuromuscular abnormalities, which can be identified largely by the history and physical examination. Diagnostic testing commonly follows to identify the specific nature of the disorder. This approach is the cornerstone of the assessment of dyspnea and leads to a correct diagnosis in many, but not all, cases. Correction or amelioration of the disorder follows and generally reduces the intensity of dyspnea, increases the comfort with which patients perform activities, and increases their capacity

to exercise. Discussion of specific diagnostic investigations and their associated criteria are beyond the scope of this statement.

Standard spirometry and lung volume measurements may be useful in the assessment of the dyspneic patient. These tests help distinguish patients with restrictive pulmonary disease from those with obstructive airway disease. There is a long-standing belief that the dyspnea associated with a given ventilatory index is greater in patients with restrictive compared with obstructive ventilatory impairments, but such a claim is not well substantiated. Measurement of lung volumes by plethysmography or by gas dilution techniques assesses increases in dead space, which lead to greater ventilatory requirements. Reassessment of lung function following administration of an inhaled bronchodilator can lead to the diagnosis of reversible airway obstruction. Hyperinflation, and the increase in hyperinflation that occurs with hyperpnea in patients with obstructive lung disease, can be inferred readily from flow–volume measurements.

Measurement of gas diffusion can be useful because a decreased diffusing capacity is associated with arterial desaturation during exercise. Such abnormalities are commonly found in patients with interstitial lung disease or emphysema and may result in hypoxia and hypercapnia, which can lead to a distressing urge to breathe that is independent of the exertional discomfort related to the inspiratory motor act. The measurement of arterial oxygen saturation is easily accomplished using pulse oximetry and is sufficiently accurate for most cases. Determination of hypercapnia requires arterial blood sampling. Mixed venous measurement is feasible, but the measurement is infrequently done and the factors contributing to mixed venous CO_2 pressure ($P\bar{v}_{CO_2}$), especially during exercise, are complex.

The clinician may incorporate comorbid conditions as well as psychologic status in the evaluation of the significance of symptoms. For example, in a study of six adults more intense dyspnea was associated with greater levels of anxiety (83). When dyspnea is severe, patients exhibit greater levels of distress from somatic complaints as well (82). Hypoxemia affects neurophysiologic functioning and, potentially, symptom reporting. Self-reported symptoms might also be viewed in light of medications that may influence the perception of breathing sensations.

Attempts to Standardize Symptom Reporting

The frequent discrepancy between severity of disease and intensity of breathing discomfort has been acknowledged for 40 years. This knowledge generated attempts to standardize the conditions under which these subjective symptoms are evaluated. Because the dyspneic patient is frequently unable to perform the daily activities of life due to discomfort associated with breathing, the first such noteworthy attempt involved the standardization of the reporting of the activities under which dyspnea occurred. In this context, Fletcher first published a five-point rating scale in 1952 that was employed by the Pneumoconiosis Research Unit to rate the impact of dyspnea on activities for patients relative to individuals of comparable age without lung disease (88). Subsequently, a revised version of the original five-point graded system, which focused on the patient's report of dyspnea while either walking distances or climbing stairs, was published (89). This questionnaire has also been referred to as the Medical Research Council (MRC) Scale (90). Patients are asked to indicate the level of activity that produces dyspnea and then, at subsequent visits, they are monitored to determine if dyspnea occurs with lower or greater levels of activity. It may be difficult with this scale to establish a change in dyspnea following a therapeutic intervention: a notable limit to the scale relates to the lack of clear limits between grades (91).

The Oxygen Cost Diagram (OCD) is a scale designed to rate activities on a continuum according to the number of calories expended in the performance of the activity. This scale was developed in an effort to match a range of tasks with the occurrence of dyspnea. The OCD is a 100-mm vertical visual analog scale with 13 activities listed at various points along the line corresponding to increasing oxygen requirements for their completion, ranging from sleeping (at the bottom) to brisk walking uphill (at the top) (92). The patient is asked to indicate the level of activity that causes dyspnea by marking a point on the vertical line. The score for the OCD is obtained by measuring the distance from the bottom of the line to the mark, in millimeters. Unfortunately, not all patients engage in all the activities depicted along the continuum, and some need repeated instructions for marking the line at an appropriate level. Nonetheless, both the MRC and the OCD are easily used and have proven pragmatic utility.

One potential limitation of these scales is that they focus on a single dimension provoking dyspnea, i.e., magnitude of task. For example, effort exerted by the patient is not considered in the report of dyspnea. In an attempt to correct for this deficiency, Mahler developed the Baseline Dyspnea Index (BDI) to measure breathlessness at a single point in time. The BDI is administered during a brief interview and includes measurement of functional impairment (the degree to which activities of daily living are impaired) and magnitude of effort (the overall effort exerted to perform activities), in addition to magnitude of task (93). The BDI is used to rate the patient's dyspnea on each dimension on a scale ranging from 0 (no impairment) to 4 (extraordinary or severe). A kindred scale, the Transition Dyspnea Index (TDI), was devised to measure changes from an initial baseline state. An interviewer notes changes in dyspnea by comparing patient reports to the baseline state obtained with the BDI (94). The reliability and validity of the BDI and TDI have been documented, as well as its sensitivity to a range of clinical interventions (95, 96).

Most recently, the University of California at San Diego Shortness of Breath Questionnaire (UCSDQ) was developed. The UCSDQ is a 24-item questionnaire measuring dyspnea during the past week (97). In the modified version, patients are asked about the frequency of dyspnea when performing 21 different activities on a six-point rating scale (98). Three additional questions inquire about activity limitations due to shortness of breath, fear of harm from overexertion, and fear of shortness of breath. Reliability and validity for the instrument have been reported (98, 99).

Despite the advances implicit in these measures, there are recognized limits associated with the assessment process. Most importantly, because the intensity of dyspnea associated with ambulatory activity depends on the rate of work performance (power output), patients may reduce the rate of work performance and thereby minimize the intensity or distress of symptoms. For example, the patient who recognizes increasing shortness of breath on exertion can easily avoid the sensory experience and minimize symptoms by using the elevator to reach a third-floor office. Other residual problems also remain. The metabolic cost of ambulatory work increases with the patient's weight. Hence, modest ambulatory activity may be associated with dyspnea in obese subjects. Common degenerative diseases associated with aging decrease the efficiency of ambulation. Neural conditions associated with spasticity increase the metabolic cost of activity and thereby increase the ventilatory demands. Arthritis of the hip may also alter the efficiency of walking.

With all these approaches validity depends on the accuracy of patient reports. People may overestimate or underestimate their capacity to exercise. The established measures correct for some of these limitations but do not deal directly with the suspicion that patients may evaluate their work performance optimistically. To assess symptoms more directly, dyspnea has been evaluated during performance of supervised tasks (e.g., cycle ergometry, 6-min walk, methacholine challenge). In these instances, ratings of dyspnea are obtained from patients at the time of the intervention so breathlessness can be related directly to one or more cardiac or respiratory responses.

Exercise, Exertional Dyspnea, and Fatigue

In normal subjects, dyspnea intensifies as the oxygen uptake and carbon dioxide output increase with the muscular activities of everyday life. Although dyspnea under conditions of heavy exertion is considered normal, the metabolic demands at rest in patients with advanced cardiorespiratory and neuromuscular disorders is sufficient to result in dyspnea. Thus, the significance of dyspnea is inversely related to the intensity of exercise provoking the symptom; dyspnea at rest is considered more severe than dyspnea during intense exercise. The aim of assessment has broadened to include not only evidence of pathology but also identification of independent factors contributing to the intensity of dyspnea during physical activity. Accordingly, exercise testing becomes more explanatory than diagnostic. Diagnostic investigation is only sufficient to explain the intensity of dyspnea in general pathophysiologic categories. Explanatory investigation allows identification of the many independent physiologic factors contributing to uncomfortable awareness of breathing.

In the 1920s Means (100) recognized that dyspnea intensifies as the respiratory reserve declines. Meakins forwarded the idea that dyspnea was the perceived exertion or effort associated with respiratory muscle activity (101). The dyspnea index was devised as the maximal exercise ventilation to maximal voluntary ventilation ratio ($\dot{V}_{E_{max}}$/MVV); it was suggested that the percent of an individual's ventilatory capacity used during exercise indicated the severity of dyspnea. When the dyspnea index exceeded 50%, shortness of breath was invariably present. Analogously, Warring reported that if the walking ventilation/maximal breathing capacity ratio was less than 30%, the patient was not usually dyspneic. Today, maximal breathing capacity is seldom measured because it is inherent in the maximal flow volume loop, and the $\dot{V}_{E_{max}}$/MVV is predominantly used to evaluate the ventilatory reserve during exercise rather than as an estimate of dyspnea.

The intensity of dyspnea is considered appropriate when the ventilation is increased or when the ventilatory capacity is reduced. The measurement of breathlessness during exercise can be examined in relation to workload, power production, maximal oxygen uptake, or interactions among a range of respiratory-related variables. For example, the exertional activity of the inspiratory muscles depends on the neural activity responding to metabolic demand; the mechanical properties of the muscles, including length and strength of the inspiratory muscles; the endurance of the muscles, which depends on the ability of the heart and blood to supply oxygen to the tissue in combination with the nutritional and metabolic capacities of the muscles, and the load against which the muscles must contract. Respiratory muscle effort intensifies with ventilation as the load opposing inspiratory muscle contraction increases and when the inspiratory muscles are intrinsically weak or weakened by hyperinflation or fatigue. Maximal ventilation requires repetitive maximal inspiratory muscle contraction, and this results in fatigue. More effort is required to achieve the same ventilatory task if the activity is sustained. Fatigue contributes to the intensity of dyspnea experienced during sustained effort, but the measurement of the propensity to fatigue is currently inadequate.

The formal measurement of dyspnea during incremental exercise to symptom-limited capacity is becoming increasing popular in the explanatory assessment of dyspnea. Ventilatory capacity is measured prior to exercise, ventilation is measured during exercise, and these are related to the intensity of dyspnea rated using either the Borg Scale or Visual Analogue Scale. In 1970 Borg first described a scale ranging from 6 to 20 to measure perceived exertion during physical exercise (102). The scale was modified from its original form to a 10-point scale with verbal expressions of severity anchored to specific numbers (73, 103). Additional terms at the ends of the scale anchor the responses, thus facilitating more absolute responses to stimuli and enabling direct interindividual comparisons (104, 105). Care must be taken to provide consistent, specific instructions when using the scale. For example, different investigators have asked subjects to rate "severity of breathlessness," "need to breathe," and "effort of breathing." Extensive reports demonstrate the reliability and validity for Borg ratings of breathlessness (37, 106–110). Normative data are available for the Borg scale during incremental cycle ergometry.

The Visual Analogue Scale (VAS) consists of a line, usually 100 mm in length, placed either horizontally or vertically (111) on a page, with anchors to indicate extremes of a sensation. The anchors on the scale have not been standardized, but "not breathless at all" to "extremely breathless" (112) and "no shortness of breath" to "shortness of breath as bad as can be" (111) are frequently used. Scoring is accomplished by measuring the distance from the bottom of the scale (or left side if oriented horizontally) to the level indicated by the subject. The reliability and validity of the VAS as a measure of dyspnea has been reported (106, 109, 110). Common problems encountered in administering the VAS are difficulty seeing the line and anchors as well as forgetting how the scale is oriented.

The assessment of dyspnea using standardized protocols goes far beyond self-reported activity measures, but it is not without its limits. For example, in a recent study of factors limiting exercise, only 12% of patients stopped exercise solely because of breathing discomfort; 50% reported a combination of leg and breathing discomfort as the limiting factor (7). Clearly, the assessment of dyspnea during cycle ergometry or treadmill walking affords the opportunity to link symptoms to explanatory variables. But the process may not relate to a patient's dyspnea during the past week. In addition, the intensity of dyspnea during exercise does not reflect the frequency, distress, or quality of the experience encountered outside the clinic or laboratory. Frequency can be scored when the anchors on a VAS range from "none of the time" to "all of the time." Distress is the degree to which a patient is bothered by the symptom. Quality is evaluated through the choice of descriptors used by patients to characterize their breathing discomfort. Evaluation of the terms used by patients to describe their dyspnea is important in developing both a differential diagnosis of dyspnea and therapeutic strategies targeted at specific mechanisms contributing to the symptom. Currently, no single testing situation encompasses these attributes, or features, of dyspnea adequately.

Dyspnea and Quality of Life: Broadening Conceptions

In many instances symptoms appear excessive or highly variable in comparison to levels of pathophysiology (113, 114). In

addition, dyspneic patients describe a constellation of complaints that are influenced by demographic variables and sociocultural factors. These differences result not only from active processing of primary respiratory signals (e.g., ventilation achieved) but also multiple collateral physiologic signals (e.g., fatigue, muscular aching, air hunger). The perception of symptoms is an attribution process that incorporates the ways in which persons identify and evaluate symptoms and make interpretations about their causes and consequences. Increasingly, a comprehensive assessment of dyspnea includes evaluation of the cognitions, beliefs, and behaviors that reflect patients' understanding of and responses to disease.

Comroe (115) observed 40 years ago that dyspnea involved both the perception of and reaction to unpleasant stimuli. Quality-of-life measures are designed to measure how patients function physically, emotionally, socially, and occupationally in their day-to-day lives as a result of their cardiopulmonary disease. Improvements in these measures have been shown in some patients to be independent of changes in severity of disease. Questionnaires of this type usually appraise dyspnea within the context of a disease that interferes with the individual's life.

The Chronic Respiratory Disease Questionnaire (CRQ) developed by Guyatt and colleagues (116) is a 20-item questionnaire evaluating four dimensions of illness: dyspnea, fatigue, emotional function, and mastery. The CRQ is administered by an interviewer and requires 15–25 min to complete initially; less time is required for subsequent administrations. To evaluate dyspnea, each patient is asked to select the five most bothersome activities that elicited breathlessness during the last 2 wk. After the patient determines the five most important activities affecting daily life, the severity of breathlessness is determined on a seven-point scale. The activities identified are, naturally, unique to the patient and make comparisons of dyspnea scores with other patients difficult. Reliability and validity estimates for the CRQ have been reported (116).

The Saint George Respiratory Questionnaire (SGRQ) is a self-administered 76-item questionnaire measuring three areas: symptoms, activity, and impact of disease on daily life. Administration time is 20 min. Dyspnea is not evaluated specifically but rather included in the symptom category along with information about cough, sputum, and wheezing. The SGRQ has been translated into several languages, and reliability and validity estimates have been reported (117).

Dyspnea frequently affects many aspects of patient behavior, including functional status. Two scales have been developed specifically to gain information about the impact of respiratory distress on functional performance of day-to-day activities. The Pulmonary Functional Status and Dyspnea Questionnaire (PFSDQ) is a self-administered questionnaire that takes 10 to 15 min to complete, and measures both dyspnea and functional status independently. The patient assesses his/her ability to perform various activities as well as the amount of associated dyspnea. Dyspnea is also evaluated with three general appraisal questions that create global dyspnea scores that are separate from the score for dyspnea with activity. Reliability and validity estimates of the PFSDQ have been reported (118).

The Pulmonary Functional Status Scale (PFSS) is a self-administered questionnaire measuring the mental, physical, and social functioning of the patient with COPD (119). The PFSS requires 20 min to complete; dyspnea ratings are obtained in relation to several activities and reflected in a dyspnea subscale. Reliability and validity estimates for both scales have been reported (119, 120). The assessment of strat-egies employed by patients to cope with their symptoms reflects an additional dimension of quality of life (121, 122).

Summary

The assessment of dyspnea is a critical aspect of patient evaluation and management. While a sound history and physical examination remain the cornerstone of evaluation, significant strides have been made in the assessment of dyspnea. Standard inventories to determine the association between levels of activity associated with dyspnea are available. In addition, tools are available to relate the severity of symptoms with observed levels of cardiac and pulmonary responses during performance of supervised tasks. Inventories that embrace aspects of dyspnea related to quality of life are not yet a routine part of the history and physical examination, but have demonstrated a useful role in the clinic and in pulmonary rehabilitation. Measurement instruments may involve a cost for use, may be self-administered or require an interviewer, and will vary in the time required for completion and scoring. Which approach for measuring dyspnea should be used? The answer to this question depends entirely upon the purpose or intent of measurement.

TREATMENT OF DYSPNEA

The physiologic bases for the treatment of dyspnea is rooted in the discussion of the mechanisms underlying shortness of breath. In disease states associated with dyspnea, the amplitude of motor command output from the central controller is often increased and, depending on the degree of intrinsic mechanical loading (or impedance) that prevails, the relationship of motor output to the mechanical response of the ventilatory system (i.e., degree of neuromechanical dissociation, *see* PATHOPHYSIOLOGY OF DYSPNEA) is variably altered. It follows that any therapeutic intervention that reduces ventilatory demand (relative to capacity), reduces mechanical loading (which improves ventilatory capacity), or strengthens weakened inspiratory muscles should relieve dyspnea by reducing motor command output and/or by reducing neuromechanical dissociation. Further, approaches that target the central perception of dyspnea may also ease the breathing discomfort associated with these pathophysiologic alterations.

In this discussion, treatments for dyspnea are categorized and related to pathophysiologic mechanisms rather than to specific diseases. It is recognized that many of the therapeutic interventions currently available relieve dyspnea by addressing different mechanisms (Table 1). For a given intervention, some mechanisms may be more relevant than others. In addition, modest alterations in a number of physiologic and psychologic variables, as a result of a particular treatment, can culminate in clinically meaningful reduction in symptoms. Unfortunately, at this point in our understanding of mechanisms and treatment many unanswered questions remain. For example, how important are psychologic compared with physiologic treatments in alleviating or reducing dyspnea in any particular situation? Is there a drug that can reduce dyspnea without reducing ventilation? While there is much work to be done in this area, an approach to treatment that links mechanisms and treatments will assist in resolution of these questions as well as minimize the impact of this intractable symptom on the patient.

Reduce Ventilatory Demand

In many cardiopulmonary diseases, ventilation is elevated above normal values at rest and particularly during exercise

TABLE 1

THERAPEUTIC INTERVENTIONS AND THEIR TIE TO PATHOPHYSIOLOGIC MECHANISM

Pathophysiologic Mechanism	Therapeutic Intervention
Reduce ventilatory demand	
Reduce metabolic load	Exercise training: improve efficiency of CO_2 elimination
	Supplemental O_2 therapy
Decrease central drive	Supplemental O_2 therapy
	Pharmacologic therapy:
	Opiate therapy
	Anxiolytic therapy
	Alter pulmonary afferent information:
	Vibration
	Ventilator settings
	Inhaled pharmacologic therapy
	Fans
	Improve efficiency of CO_2 elimination:
	Altered breathing pattern
Reduce ventilatory impedance	
Reduce/counterbalance lung hyperinflation	Surgical volume reduction:
	Continuous positive airway pressure
Reduce resistive load	Pharmacologic therapy
Improve inspiratory muscle function	Nutrition
	Inspiratory muscle training
	Positioning
	Partial ventilatory support
	Minimizing use of steroids
Alter central perception	Education
	Cognitive–behavioral approaches
	Desensitization
	Pharmacologic therapy

(123–125). Increased $\dot{V}_E$ expressed either as an absolute value or as a fraction of the maximal ventilatory capacity (MVC), correlates strongly with ratings of exertional dyspnea (126, 127). Many patients with pulmonary disease have an accelerated ventilatory response to exercise that causes them to prematurely reach their low MVC, seriously curtailing their exercise capacity (128, 129). Interventions that reduce $\dot{V}_E$ or increase ventilatory capacity may translate into improved exertional dyspnea and increased exercise endurance by delaying encroachment on the MVC "ceiling." For practical purposes, any intervention that reduces CO_2 output ($\dot{V}_{CO_2}$), physiologic dead space (V_D/V_T), arterial hypoxemia, metabolic acidosis or alters the set point for arterial CO_2, will reduce $\dot{V}_E$ and dyspnea at a given work rate during exercise.

Reducing metabolic load.

Exercise training. Recent studies have shown that significant lactic acidemia may develop at low work rates during exercise in patients with COPD (63, 130). Targeted high-intensity exercise training has been shown to improve aerobic capacity and reduce the rate of rise in lactate levels with an attendant reduction in $\dot{V}_E$ in patients with moderate COPD (131). Controlled studies have shown that exertional dyspnea decreases and exercise tolerance improves in response to exercise training, even in patients with advanced disease (132, 133). Dyspnea improvement is multifactorial, but in a study that used regression analysis with multiple relevant independent physiologic variables, reduced $\dot{V}_E$ per work rate slopes emerged as the only significant predictor of change in Borg ratings following exercise training (133). Reduction in $\dot{V}_E$ was achieved primarily by a reduction in breathing frequency with little change in tidal volume (V_T) (133).

Supervised exercise training can achieve modest but consistent reductions in submaximal $\dot{V}_E$ (4 to 6 L/min) in the absence of reduced blood lactate levels. In this setting, reduced ventilatory demand is likely related to improved efficiency, seen as $\dot{V}_{CO_2}$ and oxygen consumption ($\dot{V}_{O_2}$) that are significantly reduced at a given work rate after training (133). Alternatively, altered central perception of the breathing discomfort, i.e., desensitization to dyspnea may account in part for these findings (*see below*). It is now well established that for patients with COPD who remain breathless despite optimal pharmacologic therapy, exercise training can confer significant additional symptomatic benefits.

Supplemental oxygen during exercise. Supplemental oxygen in patients with chronic lung disease can also result in reductions in blood lactate and $\dot{V}_E$ in patients with chronic lung disease. There is evidence from a number of studies that relief of dyspnea in patients receiving oxygen therapy occurs in proportion to the reduction in $\dot{V}_E$ (72, 134). One study of patients with COPD receiving oxygen found that improvement in exertional breathlessness ratings were almost completely explained by reduced $\dot{V}_E$ and related to reduced blood lactate levels (134). Similar findings were reported when oxygen was administered to patients with interstitial lung disease (135).

Decreasing central drive.

Oxygen therapy. Ventilation can be reduced in breathless patients with lung disease by directly reducing motor command output from the central controller, independent of peripheral metabolic alterations (i.e., reduced acidosis). For example, oxygen therapy can depress $\dot{V}_E$ by depressing the hypoxic drive that is mediated via peripheral chemoreceptors in the carotid body (136–142). Reduced chemoreceptor activation and attendant reduced $\dot{V}_E$, has been postulated to be the primary mechanism explaining dyspnea relief during supplemental oxygen use, either at rest or during exercise in patients with a variety of lung diseases (142, 143). Although dyspnea relief during oxygen therapy has been shown to be related to reduced $\dot{V}_E$ in some investigations, others have shown dyspnea diminishes either before or with small changes in $\dot{V}_E$ (78, 141), suggesting other factors such as altered perceptual response or nondirect depression of central drive. For example, oxygen may blunt the pulmonary artery pressure rise associ-

ated with exercise, that may decrease afferent input to the respiratory controller. Oxygen may improve ventilatory muscle function so that less efferent stimuli to breathe is required for any level of $\dot{V}E$. Air flow over the face and nasal mucosa during oxygen administration may itself ameliorate dyspnea through poorly understood mechanisms involving modulation of afferent information by input from cutaneous nerves (144, 145).

While oxygen therapy may acutely reduce exertional dyspnea, an individual's response to oxygen therapy cannot be predicted with precision. In responding patients, ambulatory oxygen may be used as an adjunct to exercise training programs or as a means of obviating skeletal muscle deconditioning by enabling patients to increase activities of daily living. In terminal patients supplemental oxygen may be useful in relieving severe dyspnea at rest, presumably by a combination of the mechanisms mentioned (146). Unfortunately, the effect of chronic oxygen therapy on chronic activity-related dyspnea and quality of life have not been systematically studied and the clinical appropriateness of this approach is uncertain. Reimbursement for supplemental oxygen is not available to patients whose condition does not meet specific physiologic criteria (Pa_{O_2}, 55 mm Hg or 56–59 mm Hg with polycythemia or cor pulmonale). Other dilemmas associated with the use of supplemental oxygen include the inconvenience, weight, and stigma of the delivery systems.

The prescription of oxygen itself is problematic. Ideally, flow rates should be adjusted to correct severe hypoxemia at all times and to decrease dyspnea maximally with activity. While high flow rates (e.g., 4–6 L/min) may be optimal for correction of hypoxemia and relief of dyspnea with activity, they may be impractical for use outside the home. Oxygen administered by the transtracheal route may provide greater relief of dyspnea than when similar correction of hypoxemia is achieved by nasal oxygen. In this case the greater relief of dyspnea may be related to manipulation of additional mechanisms, including reduced $\dot{V}E$ (147), decreased work of breathing, and possibly stimulation of flow receptors in large airways (148).

Pharmacologic therapy. Medications have been explored as a means of alleviating dyspnea, presumably by altering perceptual sensitivity or because of known respiratory depressive effects. Two types of medication have been examined for this purpose: opiates and anxiolytics.

Opiates are known respiratory depressants that reduce the central processing of neural signals within the central nervous system, and have been shown to decrease $\dot{V}E$, both at rest and during submaximal levels of exercise (often with attendant increase in arterial P_{CO_2}) (149). Endogenous opioids have been shown to modulate dyspnea in acute bronchoconstriction (150). In addition, opiates may alleviate dyspnea by blunting perceptual responses so that for a given stimulus, the intensity of respiratory sensation is less. A number of studies have shown that opiates acutely relieve dyspnea and improve exercise performance in patients with COPD (151–153). Despite the beneficial effects of opiates, for acute dyspnea there is insufficient evidence to recommend their regular use in the long-term management of dyspneic patients (152). Given the well-documented side effects of opiates, including hypercapneic respiratory failure, altered mental status, constipation, nausea, vomiting, drowsiness, increased tolerance, and possibly sleep-related oxygen desaturation, one should use caution when administering these drugs. Despite safety concerns, these drugs do have a place in the management of patients in the terminal phase of their illness.

Interest in inhalation of opiates has been stimulated by the finding of opioid receptors on sensory nerves in the respiratory tract. Inhaled morphine has been postulated to modify respiratory sensation by binding to these receptors. However, limited data to date demonstrated that local administration of opioids such as low-dose nebulized morphine does not relieve dyspnea during exercise in patients with COPD or interstitial lung disease (154).

Anxiolytics have the potential to relieve dyspnea by depressing hypoxic or hypercapnic ventilatory responses (152, 155–157) as well as by altering the emotional response to dyspnea. However, several controlled studies with various benzodiazepines (155–157) have failed to demonstrate consistent improvement in dyspnea over placebo, and the active drug tended to be poorly tolerated (155–157). The limitations of these studies include small sample sizes and uncertainty as to whether the patients studied suffered from excessive anxiety in addition to breathing difficulty. However, given the prevalence of severe anxiety in breathless patients with pulmonary disease, it is reasonable to recommend a trial of anxiolytic therapy on an individual basis, particularly in those with morbid anxiety or respiratory panic attacks, with careful monitoring of the symptomatic response and vigilance for adverse effects.

Alter pulmonary afferent information. One strategy proposed for the treatment of dyspnea has been to alter transmittal of afferent information to the central controller. During inspiration, a variety of sensory receptors are stimulated in the central airways (flow receptors), the lung parenchyma (stretch receptors), and the chest wall (muscle spindles, joint receptors, tendon organs), and afferent information is transmitted back to the central nervous system. Potentially, a dissociation between the efferent or outgoing neural impulses from the brain to the ventilatory muscles and afferent pathways intensifies breathing discomfort. Interventions that increase stimulation of receptors throughout the respiratory system and alter transmittal of afferent information to the central controller potentially reduce dyspnea.

Currently there is little evidence to implicate peripheral mechanoreceptors in the airways or lungs in the causation of dyspnea in pulmonary disease (49, 158–160). Studies have shown that juxtacapillary (J) receptors, supplied by unmyelineated C fibers, are activated in response to vascular congestion or mechanical distortion from interstitial fluid accumulation, and can result in tachypnea, at least in animals (157, 158). However, the role of vagal afferents in mediating hyperventilation has been questioned, particularly in view of the findings of an intact ventilatory response to exercise in vagally denervated (post-transplantation) subjects (159). Also, vagal blockade has highly variable effects on dyspnea (49), and inhalation of aerosolized topical anesthesia has inconsistent effects on dyspnea in patients with restrictive lung disease (160) and in normal subjects (161).

It has recently been postulated that activation of peripheral mechanoreceptors (ergoreceptors) in response to increased metabolite accumulation in abnormal peripheral skeletal muscles may be instrumental in stimulating the sympathetic system and producing the excessive ventilatory response to exercise seen in patients with stable, chronic, congestive heart failure (162–164). An altered metabolic milieu in deconditioned peripheral muscle and consequent ergoreceptor stimulation may, in the sensory domain, give rise to symptoms of both increased leg discomfort and dyspnea via ventilatory stimulation. There is preliminary information that ergoreceptor activation can be favorably modified by exercise training with resultant diminished ventilation, at least in patients with chronic congestive heart failure (164). However, the role of ergoreceptors in the causation of excessive $\dot{V}E$ and exertional symptoms in chronic pulmonary disease has not been studied.

Despite the limited evidence for peripheral mechanical receptor involvement in dyspnea, several strategies endeavor to improve dyspnea through manipulation of afferent information. The evidence varies, however, regarding the effectiveness of these strategies to reduce dyspnea. Several methods to alter stimulation of mechanoreceptors have been suggested, including use of chest wall vibration, altering ventilatory flow rates or modes of ventilation, use of inhaled lidocaine, bupivacaine, and opiates, and use of fans.

Vibration. The mechanism by which chest wall vibration improves dyspnea is unclear, but the effect is proposed to be from direct influence of afferents from the intercostal muscle spindles on higher brain centers (42), reflex suppression of brainstem respiratory output, or a decrease in the sense of effort. Studies have demonstrated that application of vibration to intercostal muscles reduced dyspnea in normal control subjects made breathless with an inspiratory resistive load, hypercapneic COPD patients who were dyspneic at rest, and patients with COPD who were made acutely hypercapneic (42, 165, 166). Sibuya and colleagues (42) demonstrated that application of chest wall vibration in phase with respiration, so that contracting respiratory muscles are vibrated, decreased dyspnea and changed breathing to a slower and deeper pattern in patients with severe chronic respiratory disease who were dyspneic at rest. But phased chest wall vibration had little benefit for those with less severe COPD who have little or no dyspnea at rest. In addition, there may be a therapeutic window for this effect, since application of vibration to intercostal muscles out of phase with inspiration increases dyspnea (42) and chest wall vibration during the rapidly accelerating dyspnea associated with exercise had little impact on breathing discomfort (166).

Ventilator settings. Patients with respiratory failure who are placed on mechanical ventilators often complain of respiratory discomfort despite a significant reduction in the work of breathing. Ventilator settings historically have been set to achieve a particular $\dot{V}E$ with attention to the VT and airway pressures necessary for adequate gas exchange. Modes of mechanical ventilation and flow rates potentially influence dyspnea. Use of pressure support ventilation has been suggested by some investigators to be more comfortable for patients and result in less dyspnea compared with volume ventilation (167–169). There is, however, little empirical evidence to support this notion, and further investigation is needed (170). Manning and colleagues (60) have demonstrated that inspiratory flow rates, and presumably stimulation of flow receptors in the central airways, may be an important determinant of patient comfort, i.e., that dyspnea may be alleviated on a mechanical ventilator by increasing the afferent feedback from the large airways. Kollef and Johnson (171) demonstrated that dyspnea induced by administration of 4 L/min of transtracheal oxygen was significantly reduced with tracheal anesthesia, suggesting that the effect of flow-sensitive tracheal receptors can be altered.

Inhaled pharmacologic therapy. Use of inhaled pharmacologic agents may contribute to the relief of dyspnea in selected populations of patients with lung disease. Inhaled lidocaine or bupivicaine may alter afferent information arising from pulmonary receptors. Studies have not documented a dyspnea treatment effect of inhaled "caines" in patients with COPD and interstitial lung disease (161, 162, 172), but beneficial effects have been demonstrated in patients with asthma. Similarly, experimental studies on administration of low-dose opiates via nebulizers have not resulted in a significant decrease in dyspnea during exercise in patients with COPD or interstitial lung disease (173). The findings from the few studies available vary because of differences in research methodologies. Furthermore, the majority of case reports on use of nebulized opiates are for palliative care in end-stage lung disease (174–178), and the effect in these cases may result from systemic absorption of the drug rather than stimulation of local pulmonary receptors. Although there is theoretical and case support for use of inhaled and nebulized opiates and lidocaines, little empirical or experimental evidence exists to guide practice.

Fans. The movement of cool air with a fan has been observed clinically to reduce dyspnea in pulmonary patients. Stimulation of mechanoreceptors on the face or a decrease in the temperature of the facial skin, both of which are mediated through the trigeminal nerve, may alter afferent feedback to the brain and modify the perception of dyspnea. Cool air has been shown to reduce dyspnea in normal volunteers in response to hypercapnia and inspiratory resistive loads (144). In related work the contribution of receptors in the oral and nasal mucosa to dyspnea has been examined in normal subjects and patients with COPD. The oral inhalation of warm, humidified air, as well as the application of topical anesthesia to the oral mucosa, both of which may reduce stimulation of flow or temperature receptors, has been shown to reduce dyspnea in normal subjects (179). Further, the air flow over the face and nasal mucosa during oxygen administration may improve dyspnea (140, 141). Although facial cooling has not been studied in patients with COPD, the clinical reports of relief of dyspnea from patients with COPD, combined with the work in normal volunteers, suggest there may be a role for the use of facial cooling as a treatment for dyspnea.

Improve efficiency of CO_2 elimination. Physiologic dead space (VD/VT) is increased both at rest and during exercise in patients with a variety of pulmonary diseases (interstitial lung disease, COPD, peripheral vascular disease) because of ventilation–perfusion ($\dot{V}/\dot{Q}$) abnormalities. In contrast to healthy individuals, where VD/VT declines from rest to peak exercise because of improved $\dot{V}/\dot{Q}$ relationships, the VD/VT often does not decline in pulmonary disease, in part because of the reduced (or restricted) VT response. Theoretically, any intervention that will reduce the mechanical constraints on lung volume expansion (i.e., improve inspiratory capacity or vital capacity) can result in a deeper, slower breathing pattern during exercise, which will reduce the relative dead space and improve the efficiency of CO_2 elimination.

Altered breathing pattern. In COPD, the reduction of dynamic lung hyperinflation with bronchodilators (180) or volume reduction surgery, including bullectomy (181), can improve inspiratory capacity and breathing pattern and may in turn reduce ventilatory demand (182). Similarly, steroid therapy in patients with interstitial lung disease can increase vital capacity and potentially result in a slower, deeper breathing pattern during exercise (182).

Breathing retraining, including diaphragmatic breathing and pursed lip breathing, has been advocated to relieve dyspnea in patients with obstructive lung disease. Although early studies show that these techniques reduce breathing frequency, increase VT, and improve $\dot{V}/\dot{Q}$ relationships (183–185), their efficacy in relieving dyspnea is highly variable among patients. Many patients adopt slower, deeper breathing techniques during the breathing retraining period but quickly resort to their spontaneous fast, shallow breathing pattern when unobserved. Moreover, the rapid, shallow breathing pattern characteristically adopted by patients with obstructive or restrictive lung disease likely represents an optimal compensatory strategy for intrinsic mechanical loading (i.e., elastic load).

Reducing Ventilatory Impedance

Just as strategies to reduce ventilatory demand can improve dyspnea, reduction of ventilatory impedance can ameliorate

breathing discomfort in patients with chronic pulmonary disease. Strategies to minimize ventilatory impedance, whether by mechanical, surgical, or pharmacologic approaches, all have as a goal maximizing breathing mechanics by reducing lung hyperinflation and resistance to air flow.

Reduce lung hyperinflation. The FRC is dynamically and not statically determined in patients with significant obstructive lung disease. In the setting of expiratory flow limitation and increased ventilatory demand (e.g., during exercise or hyperventilation), the interval between successive breaths is insufficient to re-establish the equilibrium point of the respiratory system. Consequently, end-expiratory lung volume is increased above the volume normally dictated by the balance between the recoil forces of the chest wall and lung (i.e., passive FRC). This condition is termed dynamic lung hyperinflation, which has been shown to have serious mechanical and sensory consequences.

Dynamic hyperinflation results in the operating V_T being positioned at the upper nonlinear extreme of the respiratory system's pressure–volume relationship, where there is a substantial elastic load. Furthermore, the presence of positive pressure in the airways at the end of exhalation, so called auto–positive end-expiratory pressure (auto-PEEP) or intrinsic PEEP, imposes an additional threshold inspiratory load on the ventilatory muscles which must be overcome at the initiation of each breath. Dynamic hyperinflation also results in severe mechanical constraints on volume expansion as manifest by the high V_T to inspiratory capacity ratio at rest and at low levels of exercise in patients with severe expiratory flow limitation. Dynamic hyperinflation has been shown to be an important independent contributor to dyspnea in COPD (76), most likely as a result of the increased inspiratory effort requirements and attendant neuromechanical dissociation of the ventilatory pump. It follows that any intervention that will reduce dynamic hyperinflation or counterbalance (e.g., continuous positive airway pressure) its adverse mechanical effect will unload the ventilatory muscles and enhance neuro-mechanical coupling (76), thereby ameliorating dyspnea.

Surgical volume reduction. Dyspnea relief after surgical volume reduction in selective patients with massive bullae ($>$ 1/3 of hemithorax) by a combination of unilateral bullectomy and volume reduction surgery has been attributed to the beneficial effects of the reduction in operational lung volumes (186). Similarly, dyspnea relief following bilateral volume reduction surgery in selected patients with severe hyperinflation due to emphysema has been shown to be strongly correlated with reduced dynamic hyperinflation and improved ventilatory muscle performance (187). Symptom alleviation and improved exercise tolerance following surgical reduction procedures may reflect improved chest wall mechanics, increased lung recoil with attendant reduced expiratory flow limitation, and, in some patients, reduced ventilatory demand as a result of improved arterial oxygen saturations following surgery (188, 189). Surgical intervention is considered for severely hyperinflated patients who remain incapacitated by dyspnea despite optimal pharmacologic therapy and pulmonary rehabilitation. However, despite favorable short-term results, increasing refinement of selection criteria, and improvements in surgical technique, the eventual role of volume reduction surgery in the management of patients with COPD remains to be determined.

Continuous positive airway pressure. Low levels of continuous positive airway pressure (CPAP) have been shown to relieve dyspnea during acute bronchoconstriction in asthma (190), in patients weaning from mechanical ventilation (191), and during exercise in patients with advanced COPD (192–

194). CPAP likely relieves dyspnea by counterbalancing the effects of the inspiratory threshold load (secondary to dynamic hyperinflation) on the inspiratory muscles (193), and reducing neuromechanical dissociation of the ventilatory pump. In patients with obstructive lung disease with increased auto-PEEP or intrinsic PEEP, CPAP levels should be carefully titrated to maximal subjective benefit. In practice, maximal benefit is usually seen with levels just below the patient's measured auto-PEEP. Prescribing CPAP levels that exceed the inspiratory threshold load will only result in further hyperinflation, symptomatic deterioration, and an increased risk of barotrauma.

Reduce resistive load. The resistive load on the ventilatory muscles is increased in obstructive lung diseases because of airway narrowing from intrinsic airway disease or reduced static lung recoil with diminished airway tethering and compressible airways, as in emphysema. This increased load is perceived as respiratory discomfort. Interventions that decrease the resistive load by reversing bronchoconstriction or by decreasing airway inflammation and edema potentially relieve dyspnea. Pharmacologic therapies have been examined for their effects on airway resistance.

Pharmacological therapy. In theory, use of steroids will relieve dyspnea by decreasing airway inflamation and edema. Bronchodilators can reduce the resistive load in asthma or in patients with COPD who have reversible bronchoconstriction. These improvements in dyspnea following bronchodilator therapy correlate weakly with improved spirometric indices. Thus, the relationship between change in acute dyspnea ratings and change in FEV_1 is not linear, with some patients having significant relief of dyspnea with only trivial improvement in expiratory flow rates (126, 195–198). Therefore, acute spirometric changes following inhaled bronchodilators in the pulmonary function laboratory may not accurately predict the long-term clinical effect of the drug.

Inhaled β_2-adrenergic agonists, inhaled anticholinergics, and sustained release theophylline have all been shown in randomized controlled trials to improve dyspnea in patients with stable COPD. For example, theophylline therapy has a dose–response association with improved exercise tolerance (as measured by the 6-min walking distance) and reduced thoracic gas volume (199). Similarly, dyspnea relief following β_2-agonist therapy (albuterol) correlates with reduced operational lung volumes and improved neuromechanical coupling (72). Improved respiratory symptoms, following β-agonist that increases FEV_1, by approximately 300 ml, may be mediated primarily by the associated decrease in lung volumes.

Improving Inspiratory Muscle Function: Strength and Endurance

Dyspnea has been related to weakness and fatigue of respiratory muscles (200). As previously mentioned, COPD is characterized by hyperinflation, a condition in which the respiratory muscles must function at a mechanical disadvantage. Thus, their ability to generate pressure can fall. If the pressure generated by the inspiratory muscles per breath approaches the maximum pressure that can be achieved, dyspnea worsens. Reduction of ventilatory demand and impedance will ultimately enhance respiratory muscle function, but specific strategies to maintain or improve respiratory muscle function can add to overall dyspnea abatement.

Nutrition. Alterations in respiratory muscle energy balance, either secondary to a reduction in energy supply to the muscle or an increase in respiratory muscle energy demand (depletion of muscle energy stores) (201, 202) can lead to respiratory muscles weakness, fatigue (203), and worsening dys-

pnea. Decreased body weight is associated with decreased diaphragm mass (204, 205), intercostal muscle fiber size (205), and sternomastoid thickness (206) and fatigability (207). Approximately 30 to 50% of patients with COPD are underweight (208, 209) and demonstrate reductions in respiratory muscles mass, strength, and endurance (210, 211). Markedly diminished subcutaneous fat stores and lean body mass have been observed in patients with a weight loss of more than 10% of ideal body weight (212).

Several investigators have shown improvement in respiratory muscle function in response to nutritional repletion with short-term use of enteral or parenteral nutrition (213–215) and in outpatient (214) and inpatient controlled trials of oral supplementation (215, 216). Others have shown the benefits of outpatient programs directed at patient education (217) and distribution of nutritional supplements (218, 219). The choice of outcome measures to assess the impact of nutritional supplementation is controversial. Few investigators of nutrition repletion in COPD evaluated its effects on dyspnea. One randomized clinical trial that examined the effects of a 4-mo nutrition supplementation program on dyspnea, measured with the VAS and the OCD, showed no significant improvement (213).

Inspiratory muscle training. Because of the association between respiratory muscle dysfunction and dyspnea, an improvement in respiratory muscle function with inspiratory muscle training (IMT) could lead to a reduction in dyspnea. A meta-analysis of IMT in 17 clinical trials found limited support for its use in terms of pulmonary function, respiratory muscle strength and endurance, exercise capacity, and functional status in patients with COPD (220). However, there is some evidence that IMT with resistance breathing leads to a decrease in the intensity of dyspnea. Harver and colleagues (221) showed a consistent improvement in clinical baseline and transition dyspnea indices with IMT. Kim and colleagues (222) demonstrated that patients who used IMT with a threshold load device at 30% maximal inspiratory pressure reported fewer symptoms of dyspnea; nevertheless, those who used either a very light load or sham treatments also reported less dyspnea. Systematic evaluation of this intervention with attention to subgroups within the COPD population of patients is necessary to determine the effect of IMT on dyspnea.

Positioning. It is a well-accepted clinical axiom that patients with COPD change body position to improve dyspnea. Body positions that increase abdominal pressure may improve intrinsic characteristics of the respiratory muscles and their function. The leaning forward position has been reported to improve overall inspiratory muscle strength (223), increase diaphragm recruitment, reduce participation of neck and upper costal muscles in respiration, and decrease abdominal paradoxical breathing, as well as reduce dyspnea in COPD (224–226).

Partial ventilatory support. Use of noninvasive forms of ventilation have been suggested as a means of resting the respiratory muscles of individuals whose ventilatory demand consumes a large portion of their ventilatory capacity (e.g., patients with neuromuscular weakness or severe COPD). Partial ventilatory support can be delivered by negative or positive pressure ventilation. Negative pressure ventilation delivered by a pneumosuit for 5 h per day, 5 d per week for 4 wk improved respiratory muscle function and dyspnea (227). However, dyspnea in the control group receiving pulmonary rehabilitation also improved. Other investigations of negative pressure ventilation have demonstrated inconclusive results (228, 229). Thus, although it is possible that partial ventilatory support with negative pressure ventilation has some beneficial

effects on dyspnea perception, its role in the treatment of dyspnea remains unclear.

Partial ventilatory support has also been instituted noninvasively using a nasal or face mask interface to deliver positive pressure. In nonintubated patients with COPD who were receiving nasal pressure support ventilation (BiPAP) for 2 h per day for five consecutive days, there was a significant decline in baseline dyspnea at rest (230). Other positive pressure modes, such as proportional assist ventilation or CPAP (which was previously described), reduce exertional dyspnea and improve exercise endurance in patients with COPD (194, 231–233). Currently, it remains uncertain if the benefits of partial ventilatory support are sustained beyond the immediate period of the intervention.

Minimizing the use of steroids. As mentioned earlier, steroid use can be beneficial to pulmonary patients by reducing ventilatory impedance from airway inflammation and increasing the vital capacity in interstitial lung disease. On the other hand, the adverse effects of steroids on muscles are well known and may offset the gains in lung function (234–237). Much of what is known about steroid myopathy has been derived from studies on animal models (238, 239), often with steroid treatment exceeding usual clinical doses for patients. In humans, it is still not clear if short courses of steroids (240) or long-term, low doses (< 12 mg daily) in patients with asthma (241) have a negative effect on respiratory muscles. Recent work suggests that steroid-dependent patients with asthma demonstrate reductions in inspiratory muscle endurance compared with both non–steroid-dependent patients with asthma and patients with COPD (242). However, correlations could not be made between the cumulative dose of steroids taken by the steroid-dependent group and changes in decline in muscle strength reported by others (243). Until more consistent findings are available on the effects of steroids on respiratory muscles, the use of steroids for the express purpose of reducing dyspnea must still be weighed against the deleterious effects on muscle wasting and weakness.

Altered Central Perception

Variation in the perception of dyspnea results in part from the effects of cognitive, emotional, and behavioral factors on the conscious awareness of the demand to breathe (e.g., in response to exercise, hypoxia) and on the affective response to the symptom. Cognitive–behavioral strategies have been designed to modulate these factors as well as the affective response to the sensation. Interventions to alter central perception include education about the disease process and the teaching of coping strategies, such as relaxation, distraction, guided imagery, symptom monitoring, and goal setting.

Cognitive–behavioral strategies are used clinically in the management of dyspnea and may increase an individual's confidence in his or her ability to manage the symptom (244, 245). Although there is a dearth of hard data about the benefits of these cognitive–behavioral approaches specifically for the treatment of dyspnea, their success in modulating other symptoms suggests they should be useful for dyspnea. Choice of specific management strategies depends on the suspected mechanism(s) and the patient's ability and motivation to learn and carry out the intervention. When behavioral interventions are included in a comprehensive pulmonary rehabilitation program, dyspnea is decreased in the short term. At this point the individual contribution of specific cognitive–behavioral approaches or self-care strategies to overall improvements in dyspnea is not known.

Education. Practitioners of pulmonary rehabilitation generally believe that education about disease and its treatment

provide patients with tools for understanding and controlling their symptoms, especially dyspnea. The benefit of education *per se* for the treatment of dyspnea has been established only for patients with asthma (246). In patients with COPD, the benefits of education have not been studied systematically apart from the rest of the pulmonary rehabilitation program. One exception was the study by Sassi-Dambron and coworkers (247), which compared education about dyspnea management strategies with general health education lectures. General education resulted in no added improvement in dyspnea; however, the investigators did not control for knowledge level or application of the dyspnea management strategies (247). Education about self-care strategies (e.g., avoiding triggers, symptom monitoring, medication adjustment, recognizing problems as they arise) is thought to increase the patients' confidence so that they can control their symptoms while doing more. This knowledge may alter the perception of, and thus tolerance for, dyspnea.

Cognitive–behavioral approaches. Some approaches to dyspnea focus on modifying the affective response, e.g., anxiety or distress, to the symptom. In patients with pain syndromes, distraction, relaxation, and education about the symptom have been shown to modify the intensity of the symptom, increase tolerance, and decrease distress. Improvements in dyspnea and anxiety have been shown following distraction interventions such as music during exercise (248). Relaxation training may also improve dyspnea in the short term but has not been shown to have long-term effects (249, 250).

Monitoring symptoms helps patients and clinicians understand the pattern of symptom intensity, the factors that trigger the symptoms, and the impact of interventions on discomfort (251). The inability of some patients to accurately assess changes in airway resistance indicates that there is a range of perceptual sensitivity to altered lung function. Monitoring of dyspnea can be combined with objective physiologic measures, such as peak expiratory flow rate, to improve self-assessment and management (252).

Desensitization. Desensitization, or exposure to greater than usual sensations of dyspnea in a safe environment, has been theorized to increase a patient's self-efficacy for coping with a symptom and potentially heighten the perceptual threshold (253). The precise mechanism behind these changes in dyspnea, independent of changes in $\dot{V}_E$, is unknown. It is possible that exercise in a monitored and supportive environment may enable patients to overcome apprehension, anxiety, and/or fear associated with exertional dyspnea. Exercise training has been proposed as the most powerful means of desensitization to dyspnea (254).

Pharmacologic therapy. Opiates and anxiolytics can alter perceptual sensitivity to sensations. As previously described, this change in perception can blunt the patient's response to the dyspnea stimuli. Because of safety concerns, the use of these medications should be individualized to the patient.

Approach to the patient. Given the multiple factors that can contribute to dyspnea and the varied mechanisms by which pathophysiologic states produce respiratory discomfort, the most reasonable approach to the patient presenting with dyspnea is to determine the specific cause(s) of dyspnea and develop an individualized treatment plan. For patients with chronic dyspnea there is a need for ongoing evaluation, since the plan of care will require frequent adjustments over time.

The evaluation of the patient with dyspnea must begin with a thorough history of the symptom. The history must examine the key characteristics of the symptom, including quality, intensity, duration, frequency, and distress. The quality of the discomfort should be examined by soliciting descriptions in the patient's words and, if necessary, by inquiring about characteristics using phrases found in dyspnea questionnaires (3–6). The interviewer should be aware that a patient may have more than one type of breathlessness and that different circumstances may result in a different combination of sensations. These qualitative features may provide insight into the underlying pathophysiology leading to the discomfort and have been shown to be relatively reliable (8).

Having defined the quality of the respiratory discomfort, the interviewer attempts to quantify the intensity of the sensation, frequency with which it occurs, duration with which it lasts, and its associated distress. Also, it is important to determine the usual context of specific activities that precipitate dyspnea. Category scales are perhaps easiest to use to quantify intensity in the clinical arena, although the VAS is acceptable, particularly if one is making comparisons of different sensations or the same sensation under varying conditions. Having measured the intensity of the sensation, the interviewer should ascertain the impact the discomfort has had on the patient's life, i.e., does it prevent him or her from engaging in any activities? Measures that link dyspnea with activities and/or evaluate quality of life can assist the clinician in standardizing this line of inquiry and may provide insight into the patient's emotional response to the symptom as well.

With the clues provided in the history, a physical examination and laboratory evaluation can be pursued with the intent of defining the major pathophysiologic derangement contributing to the respiratory discomfort (255). One must first distinguish between two broad categories: cardiovascular dyspnea, i.e., conditions associated with increased cardiac filling pressures or inadequate oxygen delivery to the tissues; and pulmonary dyspnea, i.e., conditions associated with heightened respiratory drive, altered chest wall or pulmonary mechanics, muscle weakness, or gas exchange abnormalities. Simultaneous occurrence of more than one problem is not uncommon, e.g., a patient with COPD and congestive heart failure or COPD and cardiovascular deconditioning.

Initial therapy is dictated by the underlying pathophysiology. Attempts are made to reduce mechanical impedance, improve gas exchange, enhance cardiac output, or reduce intracardiac pressures. Despite these efforts, however, the patient often continues to experience significant breathlessness. Treatment options are then directed to specific elements of the pathophysiology of the patient's dyspnea: reducing the threshold inspiratory load associated with COPD, alleviating respi-
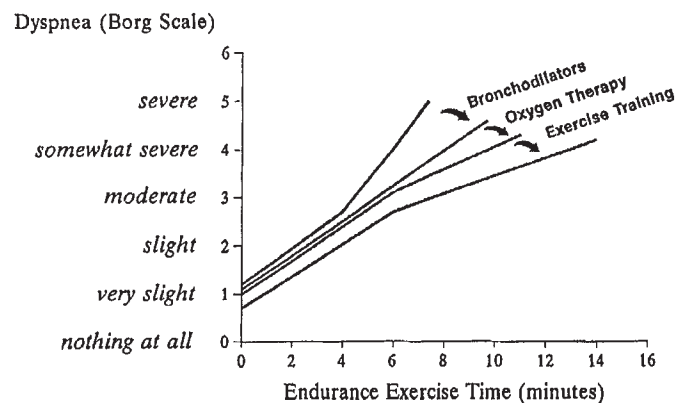

Figure 1. Graphic depiction of a hypothetical case that illustrates the cumulative benefit of interventions targeting pathophysiologic mechanisms of dyspnea.

ratory muscle fatigue or reducing hyperinflation, minimizing neuromechanical disassociation, and improving physical conditioning. For example, if a patient with severe COPD (FEV_1 = 34% predicted and RV = 220% predicted) is referred due to significant distressing breathlessness, the following approach could be taken. Initial workup reveals that there is marginal oxygenation that worsens with exercise (Pa_{O_2} = 64 mm Hg at rest; Sa_{O_2} = 83% with exercise), 6-min walk test distance is a mere 110 m, exercise endurance measures at 75% of peak V_{O_2} are poor (peak time, 7 min; dyspnea = Borg 5; leg discomfort = Borg 4), and the BDI is 9, indicating moderate to severe dyspnea. Initial interventions to optimize bronchodilators demonstrate a minimal although important decrease in dyspnea and increase in exercise time, and additional improvement is seen when oxygen therapy (3 L/min) is added during exercise (Figure 1). With the completion of pulmonary rehabilitation (exercise reconditioning), the exercise endurance time reaches its peak of nearly 14 min with a maximum dyspnea of 4 on the Borg Scale, and the TDI shows a +3 (moderate) improvement. This example demonstrates both a general approach to treatment of significant breathlessness and the characteristic cumulative impact of a treatment plan that targets several elements of the pathophysiology.

A complete therapeutic plan must also consider behavioral and emotional response of the patient and his or her family to the symptom and any attendant disability. As therapeutic interventions are implemented, one must assess the impact of treatment on the characteristics of the sensations and any resulting change in the individual's functional status. Finally, for patients in the terminal stages of cardiopulmonary disease who are suffering from intractable dyspnea, judicious use of opiates can provide substantial comfort.

This Statement was prepared by an ad hoc Committee of the Nursing Assembly. Members of the Committee were:

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