



## Evaluation of dyspnea in the elderly

Donald A. Mahler, MD\*, Gustavo Fierro-Carrion, MD,  
John C. Baird, Ph.D.

*Dartmouth Medical School, Pulmonary & Critical Care Medicine,  
Dartmouth-Hitchcock Medical Center, One Medical Center Drive, Lebanon, NH 03755-0001, USA*

### What is dyspnea?

The word “dyspnea” encompasses many different features. It can be considered to be a “sensation” (the neural activation resulting from stimulation of a peripheral receptor), a “symptom” (a subjective complaint most frequently due to cardiac or respiratory diseases), or an “illness” (the array of subjective states and behaviors that reflect the ways in which the disease disrupts an individual’s life) [1]. From a practical perspective many physicians and nurses use dyspnea to refer to “difficult or labored breathing” [1,2] or “an uncomfortable awareness of breathing” [3]. The American Thoracic Society recently defined dyspnea as “a subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity” [4].

Recent studies have examined the different qualities of dyspnea based on a particular disease [5,6]. For example, using cluster analysis a variety of different descriptors of dyspnea have been elucidated (Table 1). This information demonstrates that “work/effort” is common for all seven conditions studied, and that each disease has a unique set of descriptors. Furthermore, these data suggest that different mechanisms might contribute to dyspnea according to the underlying pathophysiology. This type of information might be helpful in evaluating the cause of dyspnea and in understanding the mechanism whereby a specific intervention can reduce or relieve the severity of dyspnea. For the purposes of this review the authors will use the words dyspnea and breathlessness interchangeably.

### Prevalence of dyspnea in the elderly

Dyspnea during exertion is a frequent complaint most commonly associated with a cardiac or respiratory disease, but it might also be due to obesity and

---

This manuscript was supported in part by NIH SBIR grant NHLBI #1R43HL68493-01.

\* Corresponding author.

*E-mail address:* donald.a.mahler@hitchcock.org (D.A. Mahler).

Table 1  
Descriptors of breathlessness by cluster and disease conditions

Cluster	COPD N = 56	Asthma N = 56	ILD N = 37	CHF N = 17	CF N = 9	DECOND N = 8	NM N = 6
Work/effort	*	*	*	*	*	*	*
Suffocating							
Exhalation				*			
Tight		*			*		
Inhalation				*			*
Shallow							
Rapid			*			*	*
Breathing more						*	
Heavy					*	*	
Air hunger							

Abbreviations: CF, cystic fibrosis; CHF, congestive heart failure; COPD = chronic obstructive pulmonary disease; DECOND = deconditioning; ILD = interstitial lung disease; NM = neuromuscular disease.

Specific clusters represent one or more of the three most common descriptors selected by patients with a particular diagnosis to describe their “uncomfortable awareness of breathing.” Most, but not all, patients reported the descriptors that were used to derive the clusters. “Suffocating,” “shallow,” and “air hunger” were not selected frequently enough by patients with any of the seven diseases and probably represent experiences in other conditions or situations.

deconditioning. As the prevalence of these conditions increases with advancing age, dyspnea becomes an important cause of morbidity in the elderly. Although extensive data do not exist on the prevalence of dyspnea in the elderly population, a review of the medical literature indicates prevalence in the range of 17% to 38% based on surveys of adults at different ages (Table 2) [7–10].

**Mechanisms of dyspnea**

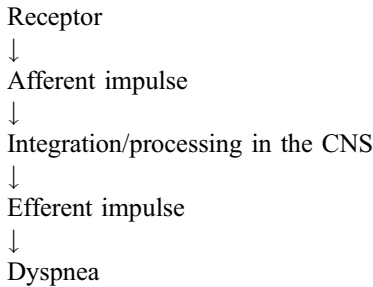
The mechanisms of dyspnea may be considered from a neurophysiological model.

Table 2  
Prevalance of breathlessness in the elderly

Author (year)	Age (yrs)	Number of subjects surveyed	Prevalence (%)	Definitions of breathlessness
Renwick (1999) <sup>a</sup>	≥ 45	508	17.4	“when walking on the level/walking in the house/ sitting at rest”
Boezen (1998) <sup>b</sup>	> 55	210	24.0	“at rest”
Dow (1991) <sup>a</sup>	≥ 65	2161	20.6	“at rest during the day at any time in the past 12 mo”
Horsley (1991) <sup>a</sup>	≥ 65	1803	38.0	“when hurrying on the level ground or a slight hill”

<sup>a</sup> Population survey from postal questionnaire using random sampling

<sup>b</sup> Random sample of subjects who performed a physical fitness test



## Receptors

The major receptor sites considered in the sensation of dyspnea include chemoreceptors, mechanoreceptors, and lung receptors [11].

### *Chemoreceptors*

Hypoxemia stimulates respiration through its effects on the peripheral chemoreceptors, and might thereby cause breathlessness in patients who have lung disease. For example, the oxygen desaturation that can occur in many patients with chronic obstructive pulmonary disease (COPD), interstitial lung disease (ILD), and pulmonary vascular disease can stimulate the peripheral chemoreceptors and contribute to dyspnea. On the other hand, many patients who have respiratory disease might experience dyspnea during exercise, but they might not develop hypoxemia.

Breathing carbon dioxide (CO<sub>2</sub>) stimulates the central chemoreceptors and increases ventilation. An increase in dead space ventilation can develop during exertion in patients who have severe respiratory impairment; alveolar ventilation might be therefore inadequate, resulting in hypercapnia. This enhances the central respiratory drive and can cause breathlessness. Interestingly, patients with respiratory disease, especially COPD, can have hypercapnia at rest, but describe little if any dyspnea despite the increase in PaCO<sub>2</sub>. This information suggests that chemoreceptors probably have limited contribution to the experience of exertional dyspnea.

### *Mechanoreceptors*

There are a number of receptors distributed throughout the respiratory system that respond to mechanical stimuli.

#### *Upper airway receptors*

Clinical observations are supported by clinical research studies showing that upper airway and facial receptors modify the sensation of dyspnea. Patients sometimes report a decrease in the intensity of their breathlessness when sitting by a fan or open window.

### *Chest wall receptors*

The brain receives projections from a variety of receptors in the joints, tendons, and muscles of the chest that influence ventilation. Mechanical stimuli such as vibration are known to activate these receptors, and might affect the sensation of breathlessness. For example, investigators have shown that in-phase chest wall vibration can reduce dyspnea in patients with COPD.

### *Pulmonary vascular receptors*

Receptors exist in the pulmonary arterial system that respond to increases in pressure or flow that result in increased ventilation. This process likely contributes to the sensation of dyspnea experienced by patients with pulmonary hypertension and acute pulmonary embolism.

### *Lung receptors*

The lung contains various types of receptors that transmit information to the CNS. Pulmonary stretch receptors in the airways respond to lung inflation, irritant receptors in the airway epithelium respond to a variety of mechanical and chemical stimuli and mediate bronchoconstriction, and C-fibers (unmyelinated nerve endings) located in the alveolar wall and blood vessels respond to interstitial congestion. Numerous studies suggest that afferent impulses from these vagal-mediated receptors might contribute to dyspnea. For example, stimulation of vagal irritant receptors appears to intensify the sensation of breathlessness and can impart a sense of chest tightness or constriction.

### *Afferent impulse*

Various nerve pathways can transmit the information after stimulation of the receptor sites to the CNS. As mentioned earlier, the vagal nerve transmits afferent information from the lung receptors.

### *Integration/processing in the CNS*

Although afferent signals associated with breathlessness are received, integrated, and processed in the CNS, little is actually known about these processes. It is believed that the motor cortex or brainstem respiratory neurons transmit a signal to the sensory cortex (ie, corollary discharge), which might contribute to a “sense of effort” to breathing [3,12]. This sensation increases whenever the central motor command is increased (eg, the load placed on the respiratory muscles is increased) or whenever the respiratory muscles become weak or fatigued (eg, prolonged increase in ventilation or dynamic hyperinflation which might occur with exercise).

## Efferent impulse

In response to afferent information, the CNS sends an efferent impulse by way of the phrenic nerve to the diaphragm and other respiratory muscles to increase respiration. How this impulse affects the level of ventilation, pattern of breathing, lung volume, flow rates, and so forth is not completely understood. The mechanisms of exertional dyspnea in patients who have cardiorespiratory diseases are multifactorial and complex. Stimulation of one or more of the aforementioned receptors could potentially contribute to dyspnea at rest and during exercise. In 1963 Campbell and Howell proposed the concept of “length–tension inappropriateness” as the cause of breathlessness [13]. According to their theory, dyspnea arises from a disturbance in the relationship between the force or tension generated by the respiratory muscles and the resulting change in muscle length and lung volume. A current hypothesis proposes that a “mismatch” occurs between afferent information to the CNS and the outgoing motor command to the respiratory muscles. In brief, this theory of “neuroventilatory dissociation” suggests that the brain anticipates or expects a certain ventilatory response based on the associated afferent information [3,14]. Any disconnect or deviation from this system can cause or intensify the perception of dyspnea.

## Aging and lung function

There are three distinct phases of pulmonary function over an individual’s lifetime. The lung grows progressively for the first 12 years of life; maturation accelerates until maximal function of the respiratory system is attained at age 20 for women and at 25 for men. Throughout the remainder of adult life the aging process causes a gradual deterioration of lung function, which appears to accelerate in the later years.

These physiological changes in lung function are due mainly to three predominant factors: (1) a decrease in lung elasticity, (2) an increase in stiffness of the chest wall, and (3) a decrease in respiratory muscle strength [12,15,16]. The consequent changes in respiratory function with aging are summarized in Table 3. Furthermore, the decline in forced expiratory volume in one second (FEV<sub>1</sub>) might not be truly linear because the initial low rate of decline in FEV<sub>1</sub> accelerates with advancing years. Cigarette smoking increases the age-related decline in lung function. Aging of the lung also contributes to a decrease in the

Table 3  
Changes in lung function with aging

Increased	No change	Decreased
Functional residual capacity	Total lung capacity	Forced vital capacity
Residual volume		Expiratory flow rates
Alveolar-arterial oxygen difference (A-a) O <sub>2</sub> tension		Diffusing capacity
		Arterial oxygen
		Respiratory muscle strength

diffusing capacity for carbon monoxide, which results from a loss of lung tissue and alveolar–capillary surface area. In addition, there is a progressive reduction in arterial oxygen tension ( $\text{PaO}_2$ ) as represented by the equation [15]:

$$\text{PaO}_2 \text{ (mmHg)} = 100.1 - 0.325 \times \text{age (years)}$$

Aging does not influence arterial pH or arterial carbon dioxide tension ( $\text{PaCO}_2$ ), however.

Finally, the aging process produces morphologic and biochemical changes in skeletal muscles, including those of respiration. Inspiratory and expiratory mouth pressures remain relatively stable until 55 years of age, then begin to decline. These reductions in respiratory muscle strength might not only contribute to breathlessness, but might also limit the ability of elderly individuals to inspire fully and to expectorate mucous in the airway.

### **Ratings of dyspnea during exercise and the aging**

There is little, if any, published information about the effects of aging on ratings of breathlessness during exertion. In a preliminary cross-sectional study the authors compared the continuous ratings of breathlessness using a computerized system [17] during cycle ergometry in 16 healthy elderly individuals (age  $69 \pm 6$  years; 7 females, 9 males) and 26 healthy young subjects (age  $19 \pm 1$  years; 14 females, 12 males). Although the slope of work – dyspnea was similar between the two groups, the onset of breathlessness (dyspnea rating = 0.5, or “just noticeable,” on the Borg scale) occurred earlier in the elderly group than in the younger group (Figs. 1, 2).

A possible mechanism for the earlier onset of breathlessness in the older individuals might be related to a higher level of ventilation during exercise. For example, Brischetto et al [18] have shown that the slope of the ventilatory response relative to carbon dioxide production ( $\Delta\text{VE}/\Delta\text{VCO}_2$ ) during exercise was substantially higher in elderly subjects ( $\sim 30$ ) compared with young subjects ( $\sim 25$ ). Another possible mechanism contributing to the earlier onset of breathlessness is the diminished peripheral and respiratory muscle strength that occurs with advancing age.

### **Approach to the elderly patient with dyspnea**

The clinical approach to the individual who complains of exertional dyspnea includes a medical history, physical examination, and appropriate laboratory testing [12,19]. In evaluating the elderly patient with dyspnea it is important for the physician or nurse to consider that chronic dyspnea is generally due to one of five major etiologies: (1) cardiac disease, (2) respiratory disease, (3) deconditioning/obesity, (4) respiratory muscle dysfunction, or (5) psychological disorders (eg, hyperventilation syndrome, anxiety).

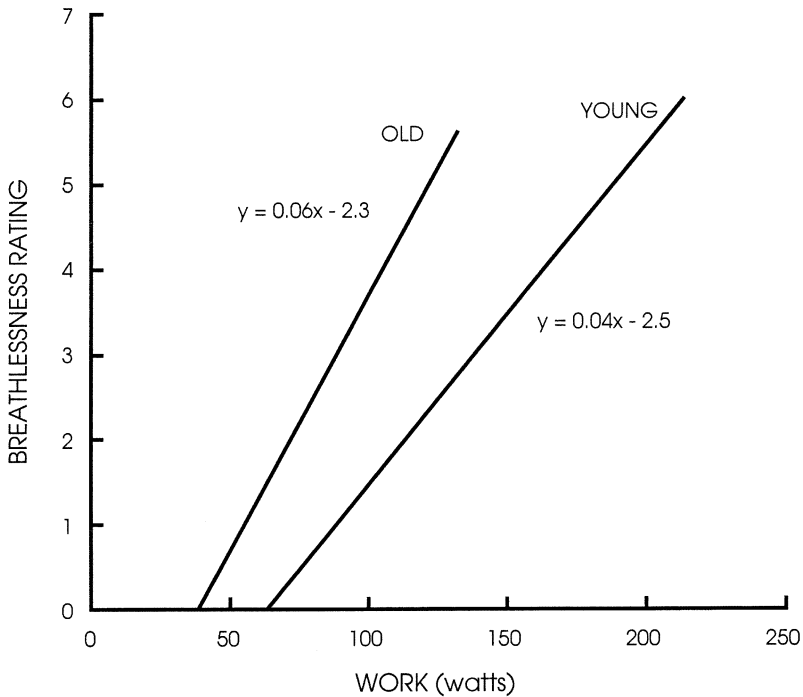


Fig. 1. Breathlessness ratings during incremental exercise on the cycle ergometer as a function of work (watts) in 26 healthy young subjects (age  $19 \pm 1$  years; 14 females, 12 males) and in 16 healthy older subjects (age  $69 \pm 6$  years; 7 females, 9 males). The functions represent the average parameters of the best fitting linear regression for individual subjects. Young subjects' data from Mahler DA, Mejia-Alfaro R, Ward J, et al. Continuous measurement of breathlessness during exercise: validity, reliability, and responsiveness. *J Appl Physiol* 2001;90:2188–96. Older subjects' data are unpublished.

A comprehensive patient history is the starting point for evaluating the problem of chronic dyspnea. It is imperative to decide whether or not “an awareness of breathing” is normal and appropriate, particularly with vigorous activities, or whether “unpleasant or labored” breathing is a manifestation of a disease process. This consideration should include the patient’s age, comparison with peers, daily or usual activities, overall fitness, and any other medical problems. The health care provider should inquire about various characteristics of dyspnea (Table 4). Because patients usually reduce activities to minimize breathing difficulty, it is important to ask the patient “What are your daily activities?” and “What activities have you stopped doing?” to assess the impact of the individual’s dyspnea on functional status. Additional information about social history (cigarette smoking, occupation, current or previous inhalational exposures, hobbies, etc) is essential.

The physical examination should include the neck, thorax, lungs, heart, and extremities. Selected abnormal findings are reported in Table 5. The neck area might reveal a shift of the trachea, jugular venous distention, an enlarged thyroid

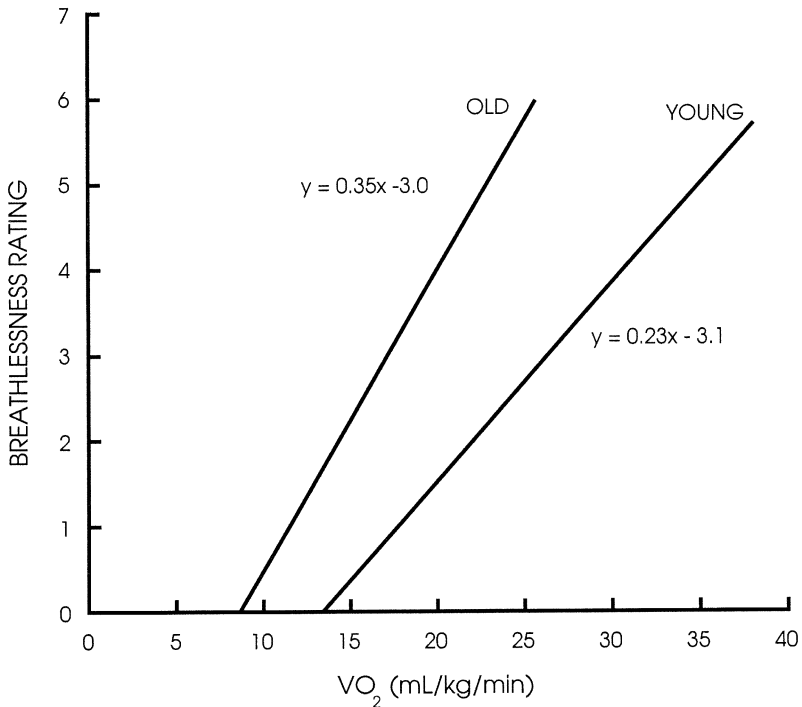


Fig. 2. Breathlessness ratings during incremental exercise on the cycle ergometer as a function of oxygen consumption (VO<sub>2</sub>) per kilogram of body weight (mL/kg/min) in the same groups of young and older healthy subjects as described in Fig. 1.

gland, or adenopathy. Use of accessory muscles of respiration (eg, sternocleidomastoid muscles) is associated with severe ventilatory impairment. Inspection of the thorax might show an increased anterior–posterior diameter or chest wall deformity. Auscultation of breath sounds should focus on intensity, timing of the respiratory phases, and any adventitious sounds. The lung examination is usually normal in patients who have COPD unless the FEV<sub>1</sub> is less than 50% of

Table 4  
Characteristics of dyspnea

- 
1. Onset
  2. Descriptive qualities
  3. Frequency
  4. Intensity
  5. Duration
  6. Triggers
  7. Provoking activities
  8. Associated respiratory symptoms (cough, sputum, wheezing, orthopnea, paroxysmal nocturnal dyspnea, chest pain)
  9. Strategies or actions that provide relief
-

Table 5  
Physical findings for evaluating chronic dyspnea

Findings	Condition
<b>HEENT</b>	
Pursed-lips breathing	COPD
<b>Neck</b>	
Shift in the position of the trachea	Unilateral lung or pleural disease
Jugular venous distension	Elevated right atrial pressure (right or left heart failure)
Enlarged thyroid gland	Hyper- or hypo-thyroidism
<b>Thorax</b>	
Increased anterior–posterior diameter	Hyperinflation (COPD)
Chest wall deformity	Kyphoscoliosis Thoracoplasty
<b>Lungs</b>	
Diminished intensity of breath sounds	Obstructive or restrictive disease
Prolonged expiration	Obstructive airway disease
Wheezing	Asthma; COPD; left heart failure
Mid–late inspiratory crackles	Interstitial lung disease Left heart failure
Pleural rub	Pleural effusion or pleuritis
<b>Heart</b>	
Diminished intensity of heart sounds	Hyperinflation; obesity; pericardial effusion
S <sub>3</sub> gallop	Ventricular dysfunction/failure
<b>Extremities</b>	
Clubbing	Lung cancer; chronic respiratory disease (not COPD)
Bilateral lower extremity edema	Right or left heart failure

predicted. In advanced COPD the usual physical findings are diminished intensity of breath sounds, a prolonged expiratory phase, and possibly early inspiratory crackles (due to airway secretions) at the posterior bases of the chest. Wheezing indicates turbulent airflow, which can be heard in asthma, COPD, and left ventricular failure; however, the absence of wheezing does not exclude airway disease. Crackles that occur at the beginning or the middle of inspiration and continue to the end of inspiration are expected in interstitial lung disease (except with sarcoidosis) and left heart failure. In most diffuse interstitial lung diseases, crackles first appear in the posterior basal areas of the lung and, as the disease progresses, might develop in the middle and upper lung zones. Key features of the cardiac examination are the point of maximal impulse, the presence of any heart murmur, and a possible gallop.

Using information obtained from the medical history and physical examination, the physician should be able to categorize chronic dyspnea into three possible categories: (1) suspected cardiac disease, (2) suspected respiratory disease, and (3) unexplained (ie, no real clues as to the cause).

For example, any two of the following are highly predictive of airflow limitation: 70 or more pack-years of cigarette smoking, decreased breath sounds, or history of COPD. The cognitive process whereby the physician integrates available data is based on knowledge and experience. The purpose of developing a “working hypothesis” is to identify the most likely cause of dyspnea and then

to focus diagnostic testing rather than use a “shotgun” approach (ie, order a myriad of tests at the initial evaluation).

### **Suspected cardiac disease**

The chest radiograph (CXR) is used to estimate heart size, configuration, and the status of the pulmonary vasculature. Cardiomegaly suggests a reduced ejection fraction, while vascular redistribution is effective for diagnosing increased left ventricular preload. A rest or exercise 12-lead ECG might diagnose an arrhythmia or ischemia. An echocardiogram has become an important diagnostic test to determine systolic function and to examine for valvular heart disease, chamber enlargement, wall motion abnormalities, and to estimate peak systolic pulmonary artery pressure.

These noninvasive tests can establish a specific cardiac cause for chronic dyspnea; however, additional testing (such as radionuclide imaging or cardiac catheterization) might be necessary along with consultation with a cardiologist.

### **Suspected respiratory disease**

Testing in the pulmonary function laboratory should be “targeted” in an attempt to answer specific questions. If asthma or COPD is suspected, spirometry should be ordered; a reduced FEV<sub>1</sub>/FVC ratio indicates obstructive airway disease. The additional measure of diffusing capacity (DLCO) might help to identify patients who have emphysema (ie, a reduced DLCO in the presence of obstructive airway disease). If a restrictive process is suspected, lung volumes should be measured. In a patient who has normal lung volumes and values for spirometry but a reduced diffusing capacity, the physician should consider anemia, interstitial lung disease, or pulmonary vascular disease as possible causes of dyspnea [19,20]. The measurement of inspiratory (P<sub>I</sub>max) and expiratory (P<sub>E</sub>max) mouth pressures is important in the evaluation of neuromuscular causes of chronic dyspnea, particularly if orthopnea is also present.

### **Unexplained chronic dyspnea**

If the cause of dyspnea is unclear, the authors recommend measurement of spirometry and diffusing capacity, a CXR, a resting 12-lead ECG, and oximetry as initial screening tests. If the results of these tests are normal, then anxiety/hyperventilation, deconditioning, and respiratory muscle weakness are the likely etiologies. As previously suggested, P<sub>I</sub>max and P<sub>E</sub>max should be measured to evaluate respiratory muscle strength. Muscle weakness can be isolated to the respiratory system or can be part of a systemic process. Flaherty and colleagues [21] described 28 patients referred for unexplained dyspnea who had normal spirometry, lung volumes, and gas exchange, but had reduced values for P<sub>I</sub>max

and PEmax. Based on biopsies of the limb muscles, these patients were diagnosed with mitochondrial myopathy that presumably also affected their muscles of respiration. The severity of breathlessness was statistically related to indices of respiratory muscle impairment.

If the cause of chronic dyspnea remains unexplained, then a cardiopulmonary exercise test should be performed [19,22]. This test will hopefully simulate the patient's experience of breathlessness and identify psychogenic dyspnea (inconsistent and fluctuating levels of ventilation, an irregular pattern of breathing, and elevated levels of ventilation relative to metabolism) or deconditioning (decreased maximal oxygen consumption but normal cardiorespiratory exercise responses).

### **Treatment of dyspnea**

Therapy for the relief of dyspnea should focus on the underlying pathophysiology of the specific disease. Various bronchodilator medications have been shown to reduce breathlessness in patients who have COPD [23–26]. For example, the improvement in dyspnea with inhaled albuterol [23] and with ipratropium bromide [25] was correlated with reduced dynamic hyperinflation during exercise as opposed to spirometric measures. These studies emphasize that reliance on FEV<sub>1</sub> as the sole objective measure of change with bronchodilator therapy can be misleading [27]. Moreover, even with optimal medical therapy many patients still experience breathlessness with daily activities. Weight gain or deconditioning should be considered as frequent contributing causes for exertional dyspnea in patients who have any chronic disease.

#### *Breathing training*

Pursed-lips breathing (PLB) is a common technique that is used by many patients who have obstructive airway disease, especially those with COPD. PLB is thought to relieve the sense of dyspnea by decreasing the respiratory rate and increasing the tidal volume. Furthermore, this breathing pattern might provide a “sense of control” for the patient and a strategy to implement when breathing distress develops. Diaphragmatic breathing might also be beneficial.

#### *Coping strategies*

A cognitive–behavioral approach might be helpful to “manage” dyspnea [28]. The processes include the interactive factors of cognition, behavior, emotion, environment, and physiology. The cognitive–behavioral perspective is based on the belief that individuals can be taught new patterns of thinking, feeling, and behaving, and that self-management is an essential feature. Specific strategies include attention (monitoring the intensity of dyspnea, increasing knowledge about illness management, and graduated levels of dyspnea to achieve “desensitization”) and distraction (relaxation, biofeedback, music, hypnosis, guided imagery, and self-talk). These techniques are usually taught by nurses

or respiratory therapists at individual sessions, support groups, or as part of a comprehensive pulmonary rehabilitation program.

### *Exercise training/reconditioning*

An exercise program can reverse deconditioning and improve fitness in almost any elderly patient who has exertional dyspnea. Several randomized, controlled studies have demonstrated reductions in dyspnea based on activities of daily living and during exercise testing after physical training [29,30]. The mechanisms for improvement of dyspnea include physiological training responses, enhanced mechanical efficiency, improvement in respiratory muscle strength, or psychological benefits, such as desensitization or improved tolerance.

Various modes (walking, cycle ergometry, swimming, rowing) are appropriate. Low-impact activities are encouraged to minimize musculoskeletal injury in elderly individuals. An indoor mode of exercise is essential as an alternative to outdoor exertion when there is inclement weather. The major question or controversy concerning exercise prescription for elderly patients is the intensity of training. Because intensity and duration are interrelated, a practical approach for elderly individuals is to start with a modest intensity (eg, ~50% of peak  $\text{VO}_2$ ) and gradually increase duration until the patient can exercise continuously for at least 20 to 30 minutes. Although heart rate is the traditional method of monitoring the intensity of exercise training, Horowitz et al [31] and Mejia et al [32] have shown that dyspnea ratings obtained from an incremental exercise test can be used as a target for patients who have COPD to regulate/monitor the intensity of exercise training. For many patients who have a chronic disease, it can take months of training to achieve the recommended goals of an exercise training program. Thus, the individual's motivation and the availability of a supervised training program might be important in enabling the patient to achieve a reduction in exertional breathlessness.

### *Upper extremity resistance training*

Because arm activities (eg, carrying objects or lifting) commonly provoke breathlessness in patients who have cardiac or respiratory disease, it is important to incorporate upper extremity resistance training as part of the reconditioning program [29,30]. For example, Simpson et al [33] demonstrated that weight lifting exercises of the arms and legs reduced dyspnea and improved health status in patients who had COPD compared with a control group. Several range of motion exercises (8–12 repetitions) with light weights can be used to improve performance for task-specific arm activities.

### *Ventilatory muscle training*

The rationale for ventilatory muscle training (VMT) is that respiratory muscle weakness might contribute to the experience of breathlessness. By augmenting respiratory muscle strength, VMT might improve functional status and reduce

dyspnea. Selected studies of targeted VMT in patients who have COPD show both increased respiratory muscle strength and a corresponding improvement in dyspnea [34,35]. Although the best method of VMT has not been established, training regimens aimed at enhancing strength might be more efficacious than an endurance program. One approach is to train with an inspiratory resistance such as the commercially available threshold loading device (Healthscan Products, Cedar Grove, NJ). VMT should involve target pressures of approximately 30% to 40% of P<sub>I</sub>max with a slow breathing frequency of 12 to 15 breaths/minute. Although the exact duration of training is unclear, most studies have required that subjects train 15 to 30 minutes/day. This type of program incorporates an endurance component in addition to the resistive load. Whether or not VMT will be beneficial for patients with mitochondrial myopathy remains to be determined.

### *Psychotropic medications*

Several randomized, controlled trials have evaluated anxiolytic and antidepressant medications for relief of dyspnea in patients with COPD. Although the results show no proven benefit for these types of drugs, anecdotal experience clearly shows that some patients with severe anxiety or depression experience relief of dyspnea with the appropriate type and dose of medication. A trial of an anxiolytic or antidepressant medication should be considered in selected individuals who exhibit anxiety or depressive symptoms.

Narcotic medications such as codeine or morphine can also provide relief of dyspnea [36,37]. Although oral agents might cause side effects such as drowsiness and constipation if used for a sustained time period, nebulized therapy can be an alternative method of delivery. A trial of a narcotic medication for relief of dyspnea might be particularly suited in two situations: severe breathlessness (despite optimal medical therapy) that substantially interferes with a patient's quality of life, and terminal care of a patient who is experiencing distressing breathlessness. Subcutaneous and intravenous routes can be used to administer the opioid.

## **References**

- [1] Harver A, Mahler DA. Dyspnea: sensation, symptom, and illness. In: Mahler DA, editor. Dyspnea (Lung biology in health and disease, Vol. 111). New York: Marcel Dekker; 1998. p. 1–35.
- [2] Wright GW, Branscomb BV. Origin of the sensations of dyspnea. *Trans Am Clin Climatol Assoc* 1954;1966:116–25.
- [3] Schwartzstein RM, Manning HL, Weiss JW, et al. Dyspnea: a sensory experience. *Lung* 1990; 168:185–99.
- [4] American Thoracic Society. Dyspnea—mechanisms, assessment, and management. A consensus statement. *Am J Respir Crit Care Med* 1999;159:321–40.
- [5] Mahler DA, Harver A, Lentine T, et al. Descriptors of breathlessness in patients with cardiorespiratory diseases. *Am J Respir Crit Care Med* 1996;154:1357–61.
- [6] Simon PM, Schwartzstein RM, Weiss JW, et al. Distinguishable types of dyspnea in patients with shortness of breath. *Am Rev Respir Dis* 1990;142:1009–14.
- [7] Boezen HM, Rijcken B, Schouten JP, et al. Breathlessness in elderly individuals is related to low lung function and reversibility of airway obstruction. *Eur Respir J* 1998;12:805–10.

- [8] Dow L, Coggon D, Osmond C, et al. A population survey of respiratory symptoms in the elderly. *Eur Respir J* 1991;4:267–72.
- [9] Horsley JR, Sterling IJ, Waters WE, Howell JB. Respiratory symptoms among elderly people in the New Forest area as assessed by postal questionnaire. *Age Ageing* 1991;20:325–31.
- [10] Renwick DS, Connolly MJ. Do respiratory symptoms predict chronic airflow obstruction and bronchial hyperresponsiveness in older adults? *J Gerontol* 1999;54A:M136–9.
- [11] Manning HL, Schwartzstein RM. Pathophysiology of dyspnea. *N Engl J Med* 1995;333:1547–53.
- [12] Manning HL, Mahler DA, Harver A. Dyspnea in the elderly. In: Mahler DA, editor. *Pulmonary disease in the elderly patient (Lung biology in health and disease, Vol. 63)*. New York: Marcel Dekker; 1993. p. 81–112.
- [13] Campbell EJM, Howell JBL. The sensation of breathlessness. *Br Med Bull* 1963;19:36–40.
- [14] O'Donnell DE. Exertional breathlessness in chronic respiratory disease. In: Mahler DA, editor. *Dyspnea (Lung biology in health and disease, Vol. 111)*. New York: Marcel Dekker; 1998. p. 97–148.
- [15] Knudson RJ. How aging affects the normal adult lung. *J Respir Dis* 1981;2:74–84.
- [16] Mahler DA, Rosiello RA, Loke J. The aging lung. *Clin Geriatr Med* 1986;2:215–25.
- [17] Mahler DA, Mejia-Alfaro R, Ward J, et al. Continuous measurement of breathlessness during exercise: validity, reliability, and responsiveness. *J Appl Physiol* 2001;90:2188–96.
- [18] Brischetto MJ, Millman RP, Peterson DD, et al. Effect of aging on ventilatory response to exercise and CO<sub>2</sub>. *J Appl Physiol* 1984;56:1143–50.
- [19] Mahler DA. Diagnosis of dyspnea. In: Mahler DA, editor. *Dyspnea (Lung biology in health and disease, Vol. 111)*. New York: Marcel Dekker, 1998. p. 221–60.
- [20] Masotti L, Ceccarelli E, Cappelli R, et al. Pulmonary embolism in the elderly: clinical, instrumental and laboratory aspects. *Gerontology* 2000;46:205–11.
- [21] Flaherty KR, Wald J, Weisman IM, et al. Unexplained exertional limitation: characterization of patients with a mitochondrial myopathy. *Am J Respir Crit Care Med* 2001;164:425–32.
- [22] Weisman IM, Zeballos RJ. Clinical evaluation of unexplained dyspnea. *Cardiologia* 1996;41: 621–34.
- [23] Belman MJ, Botnick WC, Shin JW. Inhaled bronchodilators reduce dynamic hyperinflation during exercise in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1996;153:967–75.
- [24] Casaburi R, Mahler DA, Jones PW, et al. A long-term evaluation of once-daily inhaled tiotropium in chronic obstructive pulmonary disease. *Eur Respir J* 2002;19:217–24.
- [25] O'Donnell DE, Lam M, Webb KA. Spirometric correlates of improvement in exercise performance after anticholinergic therapy in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1999;160:542–9.
- [26] ZuWallack RL, Mahler DA, Reilly D, et al. Salmeterol plus theophylline combination therapy in the treatment of COPD. *Chest* 2001;119:1661–70.
- [27] Tantucci C, Duguet A, Similowski T, et al. Effect of salbutamol on dynamic hyperinflation in chronic obstructive pulmonary disease patients. *Eur Respir J* 1998;12:799–804.
- [28] Carrieri-Kohlman V, Gormley JM. Coping strategies for dyspnea. In: Mahler DA, editor. *Dyspnea (Lung biology in health and disease vol. 111)*. New York: Marcel Dekker; 1998. p. 287–313.
- [29] ACCP/AACVPR Pulmonary Rehabilitation Guidelines Panel. Pulmonary rehabilitation: joint ACCP/AACVPR evidence-based guidelines. *Chest* 1997;112:1363–96.
- [30] American Thoracic Society. Pulmonary rehabilitation—1999. *Am J Respir Crit Care Med* 1999; 159:1666–82.
- [31] Horowitz MB, Littenberg B, Mahler DA. Dyspnea ratings for prescribing exercise intensity in patients with chronic obstructive pulmonary disease. *Chest* 1996;109:1169–75.
- [32] Mejia R, Ward J, Lentine T, et al. Target dyspnea ratings predict expected oxygen consumption as well as target heart rate values. *Am J Respir Crit Care Med* 1999;159:1485–9.
- [33] Simpson K, Killian K, McCartney N, et al. Randomised controlled trial of weight lifting exercise in patients with chronic airflow limitation. *Thorax* 1992;47:70–5.
- [34] Harver A, Mahler DA, Daubenspeck JA. Targeted inspiratory muscle training improves respi-

- ratory muscle function and reduces dyspnea in patients with chronic obstructive pulmonary disease. *Ann Intern Med* 1989;111:117–24.
- [35] Lisboa C, Munoz V, Beroiza T. Inspiratory muscle training in chronic airflow limitation: comparison of two different training loads with a threshold device. *Eur Respir J* 1994;7:1266–74.
- [36] Luce JM, Luce JA. Management of dyspnea in patients with far-advanced lung disease. *JAMA* 2001;285:1331–7.
- [37] Mazzacato C, Buclin T, Rapin C-H. The effects of morphine on dyspnea and ventilatory function in elderly patients with advanced cancer: a randomized double-blind controlled trial. *Ann Oncol* 1999;10:1511–4.