CHAPTER 16

Dyspnea, Cough, and Terminal Secretions

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Key Points

- Dyspnea management incorporates both attention to correction of the physiological defect causing dyspnea and interventions aimed at the common neurological pathway for dyspnea.
- People living with chronic dyspnea or cough should be encouraged to notice what works well for them in managing those symptoms using "*N* of 1" trials and then implement those strategies whenever the symptom recurs.
- Terminal secretions do not seem to bother the patient but can be distressing for family, friends, and caregivers. Education that normalizes the condition and reassures observers that the terminal secretions do not cause discomfort for the patient is important for minimizing distress of those who observe the condition.

Introduction

Breathing is the one vital body function that can be controlled consciously or can continue without any awareness or thought, completely subconsciously, when conscious attention is placed elsewhere. The breath is the focus of many spiritual traditions and serves as a bridge between the conscious and subconscious mind.[1] Attention to the breath as a method to optimize well-being has been documented since ancient times.[2,3] Conscious breathing is used to release stress and tension, build energy, support emotions, manage symptoms, improve physical and mental performance, and facilitate spiritual transformation.[4] Breathing is an important component of many mind–body therapies including yoga, guided imagery, and somatic grounding.[5] The respiratory system is a topic of interest for both popular self-help authors and basic, translational, and clinical researchers who are searching for ways to optimize the health and minimize the symptoms of patients living with serious illness.

We take breath for granted, we rarely think about it, but when something goes awry, it is the cause of serious panic and fear. Difficulty breathing feels dangerous and like a sign of impending suffocation in the setting of chronic lung disease.[6] Patients tend to stop their activity if they perceive danger, which leads to deconditioning and increased dyspnea over time in the vicious cycle of inactivity.[7] Patients with chronic dyspnea related to severe cardiopulmonary disease may live with dyspnea for many years and experience the stigma of a debilitating invisible disability.[8] Dyspnea correlates with mortality more than other measures such as pulmonary function.[9] Given its impact on depression, mortality, and quality of life (QOL), the importance of dyspnea has been recognized with the description of dyspnea as "the first vital symptom."[10]

The metaphorical significance of dyspnea has been recognized by the Life of Breath project (https://lifeofbreath.org/), which explores breath at the intersection of medicine, art, and the humanities—a medical humanities approach. The disciplines of anesthesia and engineering may also supplement the traditional work of pulmonology and palliative care in offering a new perspective on dyspnea management.[11] The purpose of this chapter is to review the current understanding of the pathophysiology, assessment, and management options for people living with serious illness who experience dyspnea, cough, or terminal secretions.

Dyspnea

Terminology of Breathing

Breathlessness, shortness of breath, and dyspnea are often used interchangeably when talking about the difficulty of breathing experienced by patients living with serious illness. Other terms include labored breathing or breathing discomfort. Dyspnea can be categorized into three primary groups. "Work" or "effort" is often used to describe the sensation of patients with impaired or fatigued respiratory muscles.[2] "Chest tightness" is used to describe the dyspnea experienced in asthma.[12] "Unsatisfied inspiration" or "air hunger" describes the sensation at the end of exercise or when breathing high levels of carbon dioxide.[13] In addition, breathless patients report anxiety, distress, discomfort, fear, and other negative terms when describing their breathing experience.[14]

The nomenclature for dyspnea continues to develop. Dyspnea can be acute or chronic, continuous or episodic, with variation in the timing and coping response.[15] Evidence is beginning to accumulate that chronic breathlessness, previously called *refractory breathlessness*,[16] is a distinct syndrome with unique neural activity in the brain which persists after treatment of underlying disease.[17] *Dyspnea crisis* is a term used for patients whose dyspnea overwhelms their ability to cope, but who do not want to return to the emergency department and undergo intubation and mechanical ventilation.[18] These crises often happen in the context of a patient who is living with chronic breathlessness.[15] The pattern of dyspnea is unique with each individual and includes both continuous and breakthrough dyspnea.[14]

Patient Experience

Dyspnea is one of the most distressing symptoms at the end of life[19] and occurs in the majority of patients diagnosed with chronic obstructive pulmonary disease (COPD), lung cancer, or heart failure.[14] Dyspnea is frequently also present in community-dwelling older adults who do not have any of the diagnoses traditionally associated with dyspnea.[20] The trajectory of dyspnea is distinct according to diagnosis; patients with COPD often experience moderate to severe fluctuating dyspnea for months with little change as death approaches, while many patients with cancer experience increasing dyspnea as they approach death, even if the cancer is not in the lungs.[21]

When people are living with chronic lung disease, their life can begin to revolve around their breathing needs. The case study details the personal experience of a woman living with idiopathic pulmonary fibrosis (IPF). Along with the dyspnea, there are many logistical challenges to living with chronic lung disease and dyspnea—the need for oxygen and coordination with the medical equipment company, learning to use an oximeter, potential weight gain or loss. Self-care activities focus on managing the physical manifestations of the illness, coping with the psychological effects, minimizing the social burden of the illness, and developing the knowledge and skills necessary to interact wisely with the health-care team.[22] Patients often feel stigmatized and blamed for their disease because of the association between smoking and lung disease, and the insidious onset of the disease often interferes with early initial treatment.[8] The uncertainty of the symptom contributes to fear and difficulties with coping.[14] Chronic breathlessness is frightening and distressing for both patient and family,[14] but evidence-based multidimensional interventions can provide relief.[23,24]

Case Study: A Patient Living with Idiopathic Pulmonary Fibrosis

Robin was 54 years old when she first noticed that it was difficult to take a deep breath. She was on a ski vacation and attributed it to the elevation. She developed a dry cough that was not responsive to treatment, and 5 years later, some abnormalities ("honeycombing") showed up on her chest x-ray. After several false diagnoses, she was told that she had idiopathic pulmonary fibrosis and enrolled in a clinical trial of an antifibrotic medication.

At first, the persistent cough didn't change much. She felt more fatigue and decreased stamina rather than shortness of breath, but 5 years after diagnosis, she first noticed shortness of breath while showering. For the next 7 years, she experienced progressively increasing bouts of dry cough and shortness of breath triggered by less and less activity. The dry cough got longer, more frequent, and intense. She began to use supplemental oxygen, cut down on her volunteer activities, and carried an oximeter with her.

Robin contracted influenza in January 2017, and she was left with a constant cough and sensation of sputum in her lower lobes. Her oxygen requirements increased considerably, she began to cough uncontrollably while walking, and she began to breathe through her mouth as she didn't feel like she could get enough air when breathing through her nose. She developed atrial tachycardia, which caused wide fluctuations in heart rate. During these episodes, she found that forcing herself to cough and laying on her bed with her head hanging over the side, below the level of the heart, would help her regain her equilibrium. She used large quantities of guaifenesin, nose blowing, water, and rest.

In the month before she died in November 2017, at the age of 68, she was very short of breath with minimal activities, and she required 10–15 L/min of oxygen to maintain an oxygen saturation of 90%. She was coughing at least hourly, and the coughing episodes lasted 2–5 minutes. She tried low-dose opioids for dyspnea management, but was concerned that her respiratory secretions became more difficult to expectorate. Up until the last week of her life, she was pleased with her QOL. She appreciated her scooter that gave her mobility (with her oxygen tanks) to attend her grandchildren's soccer games and dance recitals. She enjoyed the opportunity to move nearer her son for the last few years of her life, and she was satisfied with the "lasting good" she had done in this world.

Source: Excerpted from the writing of Robin Curley. Written October 31, 2017. Died November 15, 2017. Used with permission.

Pathophysiology of Dyspnea

Dyspnea is a complex phenomenon that includes the sensation of respiratory discomfort, an affective response to the sensation, and the impact on physical functioning and daily activities.[13] A beneficial model of breathlessness includes perception of both intensity and unpleasantness, emotional response, and functional consequences.[25] Many factors contribute to the sensation of dyspnea.[26] At its most basic level, the respiratory system is a pump that brings fresh oxygen to the tissues and removes carbon dioxide waste. The pump is activated by a neurological feedback system in communication with the musculature. The prevailing theory is that dyspnea results from a mismatch between respiratory demand and ventilatory mechanics,[27] an imbalance between the demand to breathe and the ability to breathe.[2] The automatic drive to breathe originates in the brainstem and communicates through a feedback system with the lungs and chest wall. When a mismatch occurs between the urge to breathe and actual ventilation, the brainstem communicates through a corollary discharge with the cortex and limbic regions of the brain, which triggers emotions, memories, abstract thoughts, and the evaluation and affective response to the dyspnea sensation.[9] A "final common pathway" of dyspnea, which is not linked to any specific etiology, may be explained by a central perception of breathlessness[27] triggered by the corollary discharge. The insular cortex, anterior cingulate cortex, and amygdala are areas in the brain that are active during breathlessness, as recognized by functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) scanning. These areas are also active in the fear response and influence the emotional reaction to dyspnea.[28]

Any factors that increase the demand to breathe or reduce the body's ventilatory capacity may trigger a sensation of dyspnea (see Figure 16.1). Physical deconditioning may do both and is therefore a primary reason for dyspnea, regardless of whether other causes of dyspnea are present.[29] Physical deconditioning contributes to dyspnea, even in otherwise healthy adults.[20] People with dyspnea learn to limit their activities to minimize their dyspnea, leading to reduced muscle bulk and increased deconditioning and thus contributing to a vicious cycle of inactivity.[7]

Increased Respiratory Demand

Increased respiratory demand can be triggered by multiple factors. Metabolism naturally increases in the setting of exercise or fever, and the built-in reserves of the ventilatory mechanics can easily accommodate those usual demands. Systemic illness such as

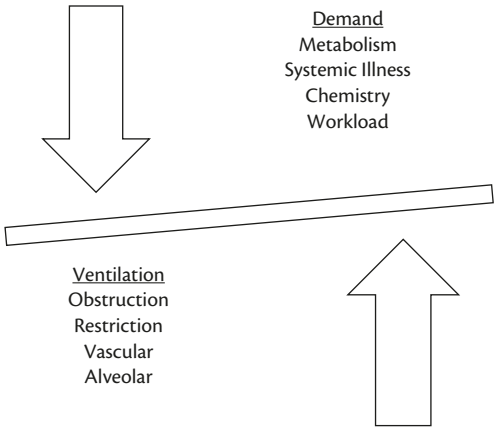

Figure 16.1 Imbalance between demand and ventilation.

hyperthyroid, sepsis, or cachexia also stimulate an increased demand on the respiratory system.[9] The muscle wasting of cachexia seen in COPD, heart failure, and cancer is linked to increased sympathetic drive, neurohumoral changes, and inflammation. The resulting skeletal muscle loss is independently associated with dyspnea, and exercise training possibly combined with nutritional supplementation may reverse breathlessness with the associated myopathy, exercise intolerance, and fatigue.[27]

A chemical imbalance between oxygen and carbon dioxide in the blood will also increase the respiratory demand. In anemia, the decreased hemoglobin available to carry oxygen prevents the cardiovascular system from supplying adequate oxygen to the tissues.[9] The healthy body can accommodate when traveling to altitude, but the lower oxygen concentration increases the respiratory demands on the body. In hypercapnic respiratory failure, the body's respiratory demand to expire carbon dioxide overwhelms its ventilatory capabilities and carbon dioxide builds up in the blood, leading to life-threatening respiratory acidosis.

Anything that increases the external workload on the respiratory system will increase respiratory demand and may fatigue the muscles beyond their ability to function. Obesity increases the body's requirements for respiration. Carrying heavy equipment or using the accessory respiratory muscles when they are needed for respiration may also overwhelm respiratory demand beyond its reserve capacity. Neuromuscular disorders increase the workload relative to the body's ability to move the respiratory pump, given reduced muscular strength and/or neurological input. Multiple sensory receptors throughout the respiratory system monitor lung mechanics, chemistry, and respiratory muscle function[2] and provide feedback to the brainstem respiratory centers when breathing adjustments are necessary to correct or maintain optimal respiratory function.

Reduced Ventilatory Capacity

Problems with airway obstruction, a restrictive defect, vascular problems, or fluid build-up in the air sacs can interfere with ventilation or gas exchange. In these situations, the body is not able to supply enough ventilation to meet the demand.[26] Obstruction occurs when something is preventing the movement of air, usually on exhalation. The obstruction can be caused by mucus build-up or constriction of smooth muscle surrounding the airways, which is often the case with asthma or chronic bronchitis. Obstruction also occurs when the air sacs/alveoli responsible for gas exchange are damaged and no longer able to function, such as what occurs with emphysema, or filled with fluid due to pneumonia or pulmonary edema. A mechanical obstruction can occur when a tumor or scar tissue blocks either the upper or lower airways. When obstruction continues over time, the lungs may become hyperinflated when exhalation does not match the volume of inhalation, thus reducing the space available in the lung for movement of air.

A restrictive pulmonary defect either prevents the lungs from expanding completely or requires additional effort to expand the lungs. The restriction can occur because of decreased compliance of the lung tissue where the lungs become stiff from a condition such as fibrosis or scarring. The pleural space and lining of the lung may be restricted due to plaque, or the restriction may be external due to obesity, kyphoscoliosis, or neuromuscular disease.

Common pulmonary vascular disorders include pulmonary emboli and pulmonary hypertension. Pulmonary emboli interrupt blood flow in a pulmonary artery. Small emboli may interrupt perfusion of blood into the capillaries surrounding the alveoli, causing a mismatch between ventilation and perfusion.[30] Large catastrophic pulmonary emboli may interrupt blood flow to an entire region of the lung and cause immediate death. Pulmonary hypertension may be idiopathic, genetic, drug-induced, or secondary to connective tissue or other cardiopulmonary diseases that increase blood flow to the lungs. Lymphadenopathy, superior vena cava obstruction, and ascites are complications of other serious illnesses that can also contribute to dyspnea.[9]

Pneumonia or pulmonary edema may interrupt ventilation when the alveoli fill with fluid or exudate, preventing the oxygen from entering the alveoli and reaching the capillaries. Pneumonia may be caused by bacteria, viruses, toxins, or aspiration. Pulmonary edema occurs when hydrostatic pressure from fluid overload moves fluid from the vascular space into the interstitial space and alveoli.

Final Common Pathway of Dyspnea

Breathlessness related to the physiology of the lungs, chest, airways, and blood vessels can be addressed by correcting the mismatch between respiratory demand and ventilatory mechanics. When breathlessness remains after the mismatch has been addressed, the breathlessness may be related to central neurological processing and perception, the "final common pathway," as confirmed by fMRI and PET imaging studies focused on the emotion-related areas of the insula, anterior cingulate cortex, and amygdala in the brain.[28]

The final common pathway of dyspnea may contribute to *symptom clusters*, the coexistence of two or more concurrent symptoms that may have a common cause.[31] Symptoms can occur because of the disease itself, treatment side effects, or comorbidities.[31] As serious illnesses progress, interventions may benefit the multiple symptoms in a symptom cluster simultaneously due to a shared common symptom pathway. Pain and dyspnea often coexist, frequently in the context of depression and functional impairments, and symptom-specific interventions may also relieve the other symptoms in the cluster.[20] A symptom cluster of cough, breathlessness, and fatigue has been identified in lung cancer.[32] Dyspnea has been correlated with anxiety, depression, fatigue, and cough.[33] Distress related to dyspnea is associated with symptom clusters that include fatigue and nausea.[34] Attention to both the mismatch between respiratory demand and ventilatory mechanics and the final common pathway of dyspnea provides keys to both measurement and interventions for dyspnea.

Measurement of Dyspnea

Patient-reported outcomes are the foundation of dyspnea measurement as no physiological correlate has been identified that accurately predicts dyspnea.[26] Dyspnea scales measure one or more of the sensation of respiratory discomfort, an affective response to the sensation, and the impact on physical functioning and daily activities (see Table 16.1).[13] When only one aspect of dyspnea is measured, unidimensional scales typically measure the intensity of the sensation. Scales such as the visual analogue scale (VAS), Borg scale, and numeric rating scale (NRS) can be used to measure intensity or distress related to the symptom. These scales are easy to implement in a clinical setting and familiar to patients who have often used similar scales for other purposes. Given the importance of the three domains of dyspnea, the Multidimensional Dyspnea Profile (MDP) was developed to measure sensory and affective dimensions of dyspnea.[35,36] It is easy to administer, acceptable to nurses for administration in the clinical setting,[37] and responsive to change over time. Identification of patients with a strong affective dimension to their dyspnea through the use of the MDP may provide a new target for interventions or optimize selection of interventions that are likely to benefit the affective component.[38]

With the modern development of psychometric theory, several short scales have been developed that provide additional information with minimal patient burden. The Dyspnea-12 (D-12) rates dyspnea using commonly used descriptive terms.[39] Both the MDP and D-12 provide a multidimensional assessment of dyspnea; the D-12 provides one single breathlessness severity score within the context of daily life while the MDP separates sensation and emotion.[40] The Shortness of Breath with Daily Activities Questionnaire (SOBDA) assesses dyspnea in COPD with 13 common activities.[41,42] The Dyspnea Management Questionnaire has a computer-adaptive test capability to measure intensity, anxiety, activity avoidance, and self-efficacy.[43] The Functional Assessment of Chronic Illness Therapy-Dyspnea (FACIT-Dyspnea) scale is a 10-item scale using interactive response technology methods to rate dyspnea with a variety of activities. The FACIT questionnaires are available free of charge on the FACIT website (www.facit.org).[44,45]

Early dyspnea research typically used psychometrically sound instruments that were not easily translated into the clinical setting because of their length and subject or provider burden. The Baseline/Transitional Dyspnea Index (BDI/TDI) assesses severity of dyspnea and change over time, taking functional impairment into account.[46] The UCSD Shortness of Breath Questionnaire rates dyspnea during a variety of common activities.[47,48] The dyspnea domain of the Chronic Respiratory Questionnaire quantifies dyspnea as a component of QOL.[49,50]

Because patients often experience dyspnea only with activities, tools have been designed that quantify the impact of activity on dyspnea. The modified Medical Research Council Dyspnea Scale is a simple, classic, four-level tool that categorizes dyspnea according to activity level. This tool is not very sensitive to change over time so it is used to categorize patients according to symptom severity but not to document dyspnea improvement in intervention research.[51,52] The American Association of Cardiovascular and Pulmonary Rehabilitation has developed an outcomes toolkit to guide clinicians and researchers in selecting the best instruments for their projects. The AACVPR toolkit includes measures of functional status, exercise capacity, dyspnea, health-related QOL, and psychosocial tools with information about psychometric properties, clinically important differences, and brief description of each tool.[53] For patients who are not able to provide self-report, the validated Respiratory Distress Observation Scale provides an objective measure using respiratory and behavioral signs that have been correlated with dyspnea.[54,55]

When a brief overview of a variety of symptoms is needed for clinical practice or for the assessment of symptom clusters, dyspnea can be assessed as part of a symptom assessment survey. The Edmonton Symptom Assessment Survey (ESAS) is commonly used in palliative care and includes a 10-point NRS for nine symptoms including dyspnea.[56] ESAS has been validated in many languages other than English.[57–60] The Memorial Symptom Assessment Scale (MSAS) evaluates the intensity, frequency, and distress of 32 symptoms including dyspnea,[61,62] and validated translations of MSAS are also available in multiple languages.[63–66]

When measuring dyspnea, response shift,[67] the variety of available tools, and the effect of attention to the symptom are important factors to consider. Many patients subconsciously decrease their activity levels to cope with dyspnea, termed "response shift,"[67] so their actual dyspnea scores may not change but further inquiry into their current activity levels in comparison to several years prior may reveal dyspnea as the reason for reduced activity levels. The variety of available dyspnea tools provides the clinician or researcher with choices that can meet the needs of their individual project, but the variety also interferes with the ability to do meta-analyses or systematic reviews. There is a question on whether it is good to measure dyspnea or whether attention to a symptom causes increased distress from that symptom.[68] Increased suffering from the additional awareness of dyspnea may be an unintended consequence of measuring dyspnea.[27]

Interventions for Dyspnea

When considering management options for patients with dyspnea, the first consideration is to target specific mechanisms of dyspnea as correcting the physiological defect will often improve dyspnea.[27] After optimizing the pathophysiology of the symptom, dyspnea management strategies ultimately may provide relief through their effects on the central common pathway of dyspnea. With a focus on evaluating interventions where dyspnea was specified as an outcome, a task force of the Hospice and Palliative Nurses Association (HPNA) presented a review of the evidence available through December 2016 at the 2017 HPNA/American Academy of Hospice and Palliative Medicine Annual Assembly.[69] The strongest evidence supported long-acting beta agonist (LABA) combined with long-acting muscarinic antagonist (LAMA) inhaler therapy, immediate-release oral morphine, oxygen for patients with COPD or hypoxemia, pulmonary rehabilitation (PR), and specialist dyspnea service. Although the evidence is not as strong, short-acting beta agonist (SABA) and short-acting muscarinic antagonist (SAMA) inhalers, other forms of opioids, acupressure, fans, dyspnea self-management programs, and transcutaneous electrical nerve stimulation (TENS) of acupressure points are likely to be effective. Interventions that may be considered on an individual basis, balancing benefit with harm, include noninvasive ventilation, high-flow nasal oxygen, acupuncture, and co-enzyme Q10. The effectiveness of benzodiazepines, Heliox (a mix of helium and oxygen), and mindfulness for dyspnea management has not been established. Nebulized furosemide or morphine are unlikely to be effective for dyspnea relief. Many gaps in the literature exist, including populations beyond COPD and cancer, routes of delivery, alternate formulations, timing and dosage, safety profiles,

Table 16.1 Dyspnea measurement instruments

Name	Description	Considerations
Unidimensional Scales		
Borg-CR scale	Category ratio (CR) scale measures intensity of experience, using verbal anchors related to numbers	Requires permission from author for use (www.borgperception.se)
Numeric rating scale (NRS)	Eleven point scale from 0 to 10 for self-report of symptom experience	Commonly used for pain so many patients are familiar with NRS Can be used with any symptom or term
Visual analogue scale (VAS)	100 mm horizontal line with "none" on the left end of the line and "very severe" on the right end. Subjects select a place on the line to represent their subjective experience of the symptom.	Numbers are not placed along the line. VAS score is 0 to 100 but the subject is not aware of the numbers. Can be used with any symptom or term (distress, discomfort)
New Generation Dyspnea Measurement (since 2010)		
Dyspnea-12	Rating of breathlessness with 12 items	Extensive validity testing has been done
Dyspnea Management Questionnaire	Computer adaptive test with test bank of 71 items for multidimensional measurement; maximum of 20 items required to obtain subscale scores.	Questions are selected based on respondent's answers to previous questions Four subscales: dyspnea intensity, anxiety, activity avoidance, and activity self-efficacy.
Functional Assessment of Chronic Illness Therapy (FACIT)-Dyspnea	Seven-day recall developed using item response theory	Dyspnea is one scale in the FACIT measurement system. More information available at www.facit.org A 10- or 33-item version is available English version is free; multiple other languages available
Multidimensional Dyspnea Profile (MDP)	Measurement of the sensory and affective dimensions of dyspnea during a specific event or time.	Designed for both clinical and laboratory research Not disease specific Administration takes 1–3 minutes
Shortness of breath with daily activities questionnaire (SOBDA)	Evaluates dyspnea in patients with COPD in relation to 13 common physical activities, using e-diary	Developed as a patient-reported outcomes instrument for use in clinical research Development funded by GlaxoSmithKline
Classic Dyspnea Measurement (prior to 2000)		
Baseline/Transitional Dyspnea Index (BDI/TDI)	Interviewer-administered dyspnea rating according to functional impairment and magnitude of both task and effort. TDI assesses change from baseline. BDI range from 0 (severe) to 4 (unimpaired) and TDI ranges from −9 (deterioration) to +9 (improvement)	Request permission for use from donald.a.mahler@hitchcock.org Available in 73 languages More information available at http://mapi-trust.org/questionnaires/bdi-tdi/
Chronic Respiratory Disease Questionnaire (CRQ) –Dyspnea subscale	One of four subscales in a self-report or interviewer-led quality of life instrument.	Sensitive to change with interventions
Modified Medical Research Council (mMRC) dyspnea scale	Quantifies disability related to dyspnea on a 5-point scale with lower number indicating less dyspnea	Public domain May have low sensitivity to change In use for more than 50 years
UCSD Shortness of Breath Questionnaire	Rating of breathlessness on 6 point scale for 24 activities of daily living. Range from 0 to 12 with lower scores indicating greater breathlessness	Copyright by University of California Free to use with permission and acknowledgment for education and research
Dyspnea Proxy Measurement for Nonverbal Patients		
Respiratory Distress Observation Scale (RDOS)	Behavioral evaluation of 8 physical signs associated with respiratory distress when a patient is not paralyzed but unable to self report.	A 2-point change (out of 17 total points) indicates meaningful change in the patient's condition
Symptom Surveys		
Edmonton Symptom Assessment System (ESAS)	Quantitative assessment of 10 symptoms that allows for simple and rapid documentation of multiple patient-reported symptoms at the same time	Commonly used for screening and monitoring in palliative care Multiple permutations exist
Memorial Symptom Assessment Scale (MSAS)	Assessment of severity, frequency, and distress for 26 symptoms, and severity and distress for 6 symptoms when frequency is not important	Subscales include physical distress, psychological distress, and The Global Distress Index Short form includes 32 symptoms and one dimension Condensed version has 14 symptoms and one dimension

and variations across the disease trajectory. The search strategy did not yield literature related to nonpharmacologic therapies such as breathing strategies,[70] energy conservation,[71] cognitive behavioral therapy,[72] or yoga.[73]

The concept of "total dyspnea,"[74] which acknowledges the multiple components of distress related to dyspnea and incorporates the meaning of the symptom within a context of whole-person care, provides a rationale for the value of pharmacological, mechanical, and behavioral dyspnea management strategies that address patient suffering in the psychological, social, and existential as well as physical realms. Quality of care for patients with dyspnea includes attention to dyspnea intensity, distress, functional impact, and qualitative descriptors that may distinguish causes of dyspnea.[75]

Pharmacological Strategies

Beta agonist and muscarinic antagonist inhaler therapies are the mainstay of treatment for many patients with chronic lung disease, especially COPD. Inhaled medications can be administered by nebulizer, metered-dose inhalers, dry powder inhalers, or soft mist inhalers. Characteristics of the device, patient capabilities, and optimal technique are all important considerations when selecting inhaled medications.[76] Although oral steroids may be beneficial for dyspnea relief near end of life,[77] the systemic side effects may not be worth it for people who are not imminently dying. Opioids are a mainstay of pain management in palliative care, and low doses of oral or parenteral opioids are also beneficial for dyspnea management.[54] The beneficial effects on dyspnea of opioids and oral steroids may be synergistic when used in combination.[78]

Oxygen therapy may be beneficial for dyspnea and even prolong life in patients with hypoxemia,[79] but the mortality benefit is not present in patients with mild hypoxemia at rest (SpO_2 89–93%) or during exercise (SpO_2 80–89% for no more than 5 minutes during a 6-minute walk).[80] Nasal high-flow oxygen therapy may be useful for improving lung mechanics and for short-term emergency treatment of dyspnea.[81,82] As end of life approaches and comfort becomes the primary focus, maintaining oxygen saturation is no longer the goal, and a fan or pursed lip breathing may be more advantageous.[83]

Opioids have become an important foundation for treatment of chronic dyspnea after medical therapy focused on the underlying pathophysiology has been optimized. Concerns arising from the opioid epidemic have encouraged the search for other medications that can be used for dyspnea management.[84] The increasing focus on the central neural pathway of dyspnea has renewed interest in alternative and repurposed medications that can reduce chronic dyspnea through effects on the dyspnea pathway. Several classifications of medications including anxiolytics, antidepressants, antihistamines, cannabinoids, and herbal-based treatments have been studied but evidence is insufficient to recommend them for dyspnea treatment.[84] The question has been raised whether opioids might improve exertional dyspnea if taken prior to exercise,[7] and further research is required to answer that question. Recent evaluation of patient-controlled therapy for breathlessness resulted in less administration of total opioid dose over time and better control of breathlessness.[85] Another innovative possibility that might prove beneficial for the palliative relief of dyspnea may be very-low-dose ketamine, which has been shown to decrease the body's response to hypercapnia.[86]

Mechanical

Patients with serious life-threatening illness increasingly seek palliative care concurrently with pursuing surgical interventions for their lung disease. In addition to mechanical ventilation that is used to relieve respiratory distress,[87] surgical and bronchoscopic procedures may be appropriate for some patients with dyspnea. Lung volume reduction surgery has been shown to improve dyspnea, exercise tolerance, and survival in patients with predominantly upper lobe emphysema and low exercise capacity.[88] A variety of noninvasive endoscopic options for lung volume reduction are now available, including the use of bronchial valves, coil implants, and thermal vapor ablation.[89] These therapies may be appropriate considerations for patients with dyspnea primarily related to lung hyperinflation.[90] Patients with emphysema, pulmonary fibrosis, cystic fibrosis, pulmonary hypertension, bronchiectasis, and other diagnoses[91] experience improvement in dyspnea after lung transplantation.[92]

When the lung is not able to expand because of a malignant pleural effusion or a trapped lung due to pleural fibrosis or inflammation, relief from dyspnea may occur with the placement of a tunneled pleural catheter to drain excess fluid into the abdominal cavity, pleurodesis to adhere the lung to the chest wall and prevent future build-up of fluid, or decortication (removal of restricting tissue) by video-assisted thoracoscopy.[93,94] Patients may experience obstruction of the central airways due to tumors or stenosis. Airway stents, balloon dilatation, laser ablation, cryotherapy, or radioactive brachytherapy may provide symptomatic relief in those situations.[95]

The ideal role for noninvasive ventilation for the palliation of dyspnea is still being explored.[96,97] High-intensity positive pressures, using the highest inspiratory pressures that the patient can tolerate, may provide more dyspnea relief, improvement in hypercapnia, and improved mortality above that experienced with the usual low-intensity noninvasive ventilation.[98] Other noninvasive mechanical interventions to consider for airway clearance and optimal breathing are oscillatory positive pressure devices such as the Acapella, Flutter, or Aerobika[99]; autogenic drainage[100]; active cycle of breathing[101]; and high-frequency chest wall oscillation.[102] Although the evidence is not strong for any of these noninvasive options, an "*N* of 1" trial with careful consideration of the risk–benefit analysis may be beneficial for people living with breathlessness.[103]

Behavioral

Dyspnea is a complex multifactorial symptom, and therefore complex interventions are often necessary to adequately address the multiple causes of the symptom. Pulmonary rehabilitation (PR) is an interdisciplinary program that combines exercise training, patient education, and psychosocial support in a comprehensive evidence-based intervention for patients with lung disease.[104] PR classes typically meet 2–3 times per week for several hours per session over a 6- to 12-week interval. Some PR programs also provide maintenance exercise indefinitely after the completion of the initial program. PR shares many similarities with palliative care in its focus on symptom management and QOL. The foundation of PR is exercise training, whereas palliative care integrates more of a focus on advance care planning and the spiritual dimension of health.[105] Now that palliative care is recognized as a valuable treatment for patients across the spectrum of serious illness, it makes sense to get palliative care involved earlier, soon after PR and as soon as

Table 16.2 Nonpharmacological interventions for dyspnea

Professional	Self-management	Complementary
Pulmonary rehabilitation	Posture: braced forward lean	Relaxation/Mindfulness-based Stress Reduction (MBSR)
Breathlessness intervention	Pursed lip breathing	Biofeedback
Pacing/Energy conservation	Abdominal breathing	Spinal movement
Cognitive Behavior Therapy (CBT)	Fan/Air movement	Acupuncture/acupressure
Music/Distractive auditory stimuli	Exercise	Yoga/Tai Chi/Qigong
Chest wall vibration	Acceptance	Branch-chain amino acids
Noninvasive ventilation	Socialize	
Education		
Walking aid: rollator/cane		
Dyspnea plan		
Neuromuscular electrical stimulation		

patients are symptomatic. The beneficial outcomes following PR decline over time, and perhaps palliative care follow-up after PR would support maintenance of PR outcomes over time.

Despite the attention that dyspnea management has received in the literature, patients and their families spend many hours on their own between medical appointments coping with dyspnea to the best of their abilities. Self-management is still the primary mainstay of dyspnea treatment.[22] Activated patients who embrace their own personal initiative and engagement can increase their independence and QOL in the presence of their dyspnea.[6] Patients report many strategies for managing their symptoms, and very few of those strategies include evidence-based or medically prescribed interventions. Patients find themselves strategically planning their daily activities, using creative thinking and assistive devices to accomplish their daily tasks.[22] Integrating exacerbation action plans in self-management interventions improves health-related QOL and decreases the probability of hospitalization.[106]

Several excellent models and treatment algorithms for dyspnea management have been published.[6,9,103] Principles of high-quality dyspnea management can be applied in all settings, and the treatment algorithms are similar even in the emergency department.[107] Many interventions have minimal effect on their own but contribute to a cumulative benefit when used in combination.[26] Nonpharmacological and complementary therapies are recommended if they have research evidence to support them[108] or if the safety profile merits an "*N* of 1" trial with minimal concern.[103] (See Table 16.2 for a list of nonpharmacological professional, self-management, and complementary therapies to consider.) Most of the nonpharmacological and complementary therapies that patients use or providers recommend for dyspnea management are focused on the central pathway of dyspnea. Interventions focused on anxiety, depression, and other symptoms commonly found with dyspnea in symptom clusters can be beneficial for improving dyspnea as well.[30]

When patients living with chronic dyspnea experience a dyspnea crisis, the sense of helplessness experienced by family caregivers contributes to the distress caused by dyspnea.[14] Patients at risk for dyspnea crisis can plan in advance with their families so that when a dyspnea crisis occurs, each family member will have a practiced response that will normalize the experience, decrease the panic, and quickly institute predetermined strategies that will mitigate the breathing crisis.[18] A "dyspnea plan" can include both pharmacological and nonpharmacological measures and rituals to enact when dyspnea crisis occurs.[6]

Several outpatient dyspnea clinic models have been tested with promising results.[23,24] Complex interventions for breathlessness assess both the sensory and affective components and focus on modulating the central perception of breathlessness regardless of the original pathophysiology of the symptom. The interprofessional team assists patients to manage their affective response to the symptom while still addressing the original pathophysiology of the illness that caused the symptom. The "softer skills" such as empathic listening in the context of new service models may provide relief for dyspnea.[11]

The interprofessional team offers unique perspectives related to dyspnea management interventions. From a physical therapy perspective, physical conditioning, reassurance, positioning, and explanations of the anatomy and physiology related to breathing strategies are effective means to support patients in managing their dyspnea.[109] Occupational therapists use energy conservation and supervised practice to support patients in maintaining their everyday activities.[110–112] Although respiratory therapists have traditionally practiced in hospital settings, their experience in leading PR programs demonstrates their expertise in supporting dyspnea management within a whole-person context.[113–115] Given the ubiquity of dyspnea within the healthcare system, it makes sense to educate allied health providers and health coaches on strategies specific to dyspnea management.[116,117] Successful interventions for dyspnea benefit from multiple perspectives.

Cough Physiology, Measurement, and Interventions

Despite cough being a very distressing symptom that interrupts social situations and is physically exhausting,[118] no interventions are consistently effective in treating cough. Over time, cough can affect

physical, mental, and social health. It interferes with sleep, fatigues the muscles, interferes with vocal quality, and contributes to urinary incontinence.[119] Cough is one of the most common symptoms that spur medical visits.

Pathophysiology of Cough

The cough reflex in the brainstem protects the airways from mechanical or chemical irritants mediated by sensory nerves in the large and peripheral airways. Voluntary cough and the urge to cough are centered in the cerebral cortex.[119] Early brain imaging evidence suggests that the conscious regulation of cough occurs in brain regions and neural pathways that are separate from the urge to cough. Both the voluntary and the reflex pathways are involved in cough control.[120] Overlap with the descending inhibitory pathways related to other stimuli may explain why cough is suppressed in the presence of other stimuli.[121] Cough is stimulated by mechanical (airway size), biochemical (capsaicin), and neurosensory changes.[119] Irritation can be caused by the presence of pathology in the airways, parenchymal inflammation from treatment, heightened cough reflex sensitivity, or comorbidities such as gastroesophageal reflux disease (GERD) or sinusitis.[121] With hypersensitivity, even minimal irritation such as laughing, talking, or temperature changes can lead to cough.[121] Other irritants include smoking and perfume. Central processing may occur in several brain regions.[119]

The most common causes of cough are smoking, lung pathology such as asthma, postnasal drainage (PND), GERD, and medications.[120] New pathologies have been identified for cough. Obstructive sleep apnea can manifest with cough, possibly because of pressure buildup in the upper airway which may increase diaphragmatic pressure and contribute to GERD; treatment with continuous positive airway pressure (CPAP) can alleviate the cough. Cough from enlarged tonsils can be treated with tonsillectomy. Other unusual sources of cough might be protracted bacterial bronchitis; basidiomycetes fungus, treated with antifungal medications; cervical spondylosis; and abnormal salivary glands at the base of the tongue.[122] *Cough hypersensitivity syndrome* (CHS) signifies neuronal activation, sensitization, and/or dysfunction which leads to excessive coughing.[123] Chronic dry cough is very common in IPF, possibly due to traction of the parenchyma related to fibrosis.[119] GERD may cause microaspiration of acid and reflux of gastric contents into the airways. Medications such as angiotensin converting enzyme (ACE) inhibitors and beta blockers have been associated with cough.[119] Chronic lung disease such as COPD/emphysema or infection can also contribute to chronic cough. Chronic sinusitis and postnasal drip (PND) syndrome may be asymptomatic, or patients may not notice PND which can contribute to chronic cough.[119] Cough can also be the first sign of lung cancer. The recognition of laryngeal irritability and chronic hypersensitivity has led to the idea that cough is a sensory neuropathy.[120] Other triggers include foods, smells, laughing, and laryngeal dysesthesia or "tickle" in the throat.[120] Sensory neuropathic cough may present with chronic cough, laryngospasm, or paradoxical vocal cord dysfunction.[120]

Cough can be completely voluntary and under conscious control, completely reflexive in response to a stimulus, or a combination of reflexive and voluntary. Reflexive coughing can become more pronounced as a person becomes sensitized to a given stimulus. Sensitization is triggered by inflammatory mediators that may be released after exposure to viruses, antigens, or inhaled toxins like cigarette smoke.[123]

Measurement of Cough

Intensity, frequency, and disruptiveness are components of cough that should be measured.[124] VAS subjective scales are easy to use for each component. Several instruments including the Leicester Cough Questionnaire[125] and the Cough Specific Quality of Life Questionnaire[126] measure the global impact of cough. A seven-item Cough Severity Diary has been tested in patients with chronic and subacute cough.[127] Objective measurement of cough has been attempted with ambulatory cough monitoring (ACM) such as the Leicester Cough Monitor and the VitaloJAK (Vitalograph, Inc., Lenexa, KS).[128] Although objective measurement is intuitively attractive, many threats to validity exist including the difficulty in distinguishing cough from other sounds, determining the marker of severity, and objective quantification. Perhaps both subjective and objective measures need to be assessed together.[121]

Cough can be divided into acute, subacute, and chronic cough.[122] Cough hypersensitivity syndrome encompasses chronic idiopathic cough, chronic refractory cough, and sensory neuropathic cough.[120] Recent guidelines for the evaluation and treatment of unexplained chronic cough provide an assessment algorithm.[129] Sputum eosinophils or exhaled nitric oxide should be evaluated to identify patients with bronchial hyperresponsiveness who might respond to inhaled corticosteroids.[129]

Interventions for Cough

The goal for cough treatment is to allow normal cough while blocking pathological cough.[123] Many therapies have been suggested for cough, seemingly because none of them work very well. It may be that cough appears to be one entity but actually has multiple causes that have not yet been identified or linked to an effective intervention. Behavioral cough control techniques and vocal hygiene strategies taught by a speech therapist may reduce cough symptoms.[130,131] Additional strategies may include pursed lip breathing, swallowing to diminish the urge to cough, avoiding smoking and mouth breathing, minimizing alcohol and caffeine, increasing water intake, or using steam inhalation.[130]

The CHEST Expert Cough Panel is developing clinical practice guidelines as living documents that are continually updated as new evidence, technologies, and recommendations become available.[132] For cough in adult patients with lung cancer, they recommend a stepped approach starting with the identification and treatment of coexisting causes of cough, nonpharmacological cough suppression exercises, endobronchial brachytherapy, and graduated trials of various cough suppressants.[133] Although many substances including glaucine, Chinese herbs, Duopect, moguisteine, pipazethate, guaifenesin, N-acetylcysteine, diphenhydramine, loratadine, erythromycin, ipratropium, and inhaled corticosteroids have been tested as antitussives, codeine and dextromethorphan are the only two agents that have been shown to reduce frequency and severity of chronic cough.[134] Slow-release morphine and dextromethorphan, which is a codeine analog, both act centrally to inhibit the cough reflex. Thalidomide has been tested for cough because of its anti-inflammatory properties, but the side effects are severe, including birth defects and sensorimotor peripheral neuropathy. With the recognition that cough may be triggered by sensory neuropathic cough or laryngeal irritability, neuromodulators used to treat

neuropathic pain, such as gabapentin, pregabalin or amitriptyline, may be helpful.[120]

Disease-directed treatment for cancer-related cough may include drainage of pleural effusions, brachytherapy (radiation in direct contact with tissue), or photodynamic therapy.[130] A Cochrane review of randomized controlled trials (RCTs) for cancer-related cough treatment found minimal evidence but suggested that pharmacologic treatments like butamirate linctus, codeine 60 mg, morphine, dihydrocodeine, cromoglycate, and hydropropizine or levodropropizine may be beneficial for cough.[130] Given the low level of evidence and the age of the research, proposed recommendations for palliative cough management balance risk with benefit. The first step is to consider disease-directed treatment and review medications to see if any might be exacerbating the cough. Evaluate and treat any comorbidities that may be contributing to cough. Then consider sodium cromoglycate, which is relatively safe but supported only by minimal evidence. If still not responsive, consider opioid derivatives such as morphine, codeine, or dextromethorphan.[118]

In patients with unexplained cough that has not responded to a trial of inhaled corticosteroids, speech therapy and gabapentin trials are recommended.[129] A recent systematic review of treatments for cough related to the common cold found many treatment options available, but the evidence was not compelling for any of the options. The evidence was not strong enough to support recommendations for decongestants, antihistamines, acetylcysteine, nonsteroidal anti-inflammatory drugs (NSAIDs), honey, zinc lozenges, over-the-counter (OTC) antitussives, expectorants, mucolytics, or combination products.[135] The evidence base has not changed since previous guidelines were published in 2006, and the majority of the research on cough interventions was published before 2000.[134]

Terminal Secretions: Physiology, Measurement, and Interventions

Many terms are used to describe terminal secretions, usually including phrases such as "movement of bronchial secretions," "noisy breathing," or "sound in relation to respiration."[136] These secretions occur in the terminal phase of illness and are distressing for professional and family caregivers. The study of terminal secretions is inhibited by ethical concerns about randomizing dying patients who may not be able to give consent or share their perspective.[137] Does anyone know what it feels like to have terminal secretions? We have strong opinions on how to manage it, but we don't really know for sure because no one can tell us that the interventions were helpful or not.

Pathophysiology of Terminal Secretions

Terminal secretions, also called "death rattle," are caused by breathing through secretions in the upper airways as a patient approaches death and is no longer able to clear the secretions through swallowing or coughing.[137] The tongue may also cause obstruction and contribute to noisy breathing in patients who are nearing end of life.[137] Most patients die within 48 hours after developing terminal secretions.[138]

Hipp and Letizia propose that brain hypoxia causes ongoing release of acetylcholine from the parasympathetic nervous system, which activates the salivary and bronchial glands, leading to excessive secretions. Inability to swallow, weakened gag and cough reflexes, and decreased level of consciousness all contribute to the development of noisy breathing.[139] Dehydration may make secretions more tenacious and difficult to clear, especially in the setting of dysphagia and decreased mental status.[140] Noise during respirations occurs when the movement of air disturbs the oropharyngeal secretions, and the sound is amplified through the mouth and nasal passages.

Measurement of Terminal Secretions

Terminal secretions can be caused by excessive oral and salivary secretions, also termed type 1 or "real" death rattle. It occurs when the patient's level of consciousness has decreased and seems to be amenable to anticholinergic treatment. Type 2 or "pseudo" death rattle is caused by bronchial secretions that are formed due to pulmonary pathology such as infection, aspiration, or edema. Type 2 secretions are not as amenable to anticholinergic treatment and can be very distressing as the patient may be conscious when experiencing these secretions.[141] A combination of both types of terminal secretions may occur. The Victoria Respiratory Congestion Scale (VRCS) has been developed to quantify terminal secretions and noisy breathing using a 0–3 scale depending on the distance at which noisy congestion is audible.[141]

Interventions for Terminal Secretions

Antimuscarinic (most anticholinergic agents act on muscarinic acetylcholine receptors) medications are typically used to decrease secretions, but their efficacy is questionable. Perhaps they would be better used as preventive measures and started early, prior to the development of terminal secretions, since anticholinergic drugs do not remove existing secretions but prevent the formation and accumulation of secretions after the medication has been initiated.[142] Another option to maximize treatment might be to gently suction the secretions prior to beginning anticholinergic treatment.[143] Side effects such as urinary retention and dry mouth are problematic for patients near the end of life.[137] Withholding hydration is another management technique that was the focus of an observational study. No difference in terminal secretions was found after withholding hydration, although those in the nonhydration group experienced less frequent peripheral edema, pleural effusion, and ascites.[144] Guideline-based hydration improved family satisfaction and may decrease terminal secretions at end of life.[145]

Although the evidence in favor of anticholinergic therapy is weak,[136,146] such therapies are regularly used in clinical practice so Bennett and colleagues developed an evidence-based guideline that outlines the characteristics and considerations of each of the available anticholinergic options.[140] Specific information regarding dosage and cost were published by Brock and colleagues.[147] Nonpharmacological interventions to reduce terminal secretions and noisy breathing include repositioning, suctioning, and restricting medically administered hydration, although these interventions have not been scientifically studied. Educating the family about behavioral indicators that affirm the absence of distress can be very helpful. The phrase "death rattle" can be distressing, and other terms are preferable in discussions with families.[148] Although nurses often worry about the meaning of terminal secretions for family members, many families actually express relief that the terminal secretions indicate that the patient will soon be done with suffering.[149] Staff education can lead to higher quality care of patients with terminal secretions and also preserve scarce resources with

lower cost options.[147] Both families and staff can find terminal secretions to be distressing, although the distress can be relieved with careful education that the patient is not uncomfortable, it is a normal part of the dying process for many people, and it won't last long. Many times, families get their cues from the staff on whether or not to be distressed by situations such as terminal secretions.[147]

Conclusion

When faced with patients experiencing dyspnea, cough, terminal secretions, and associated distress caused by cardiopulmonary, neuromuscular, or metastatic disease, the goal often becomes eradicating or managing the symptom. In the context of the bothersome respiratory conditions that are often present in patients receiving palliative care, it is possible to achieve a positive sensation of breathing, relief from cough, and an absence of excessive secretions at the end of life. Nurses must use all available resources to provide relief and optimize breathing status for patients with serious illness.

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