Perceptions and Pathophysiology of Dyspnea and Exercise Intolerance

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KEYWORDS

• Dyspnea • Exercise • Exercise testing • Respiratory distress
• Ventilation

WHAT IS DYSPNEA?

Dsypnea is derived from the Latin *dyspnoea*, from Greek *dyspnoia* from dyspnoos, and is often described by patients as shortness of breath. It involves the perception of difficulty or painful breathing. It is a common symptom of numerous medical disorders, but psychologic factors can also contribute to the sensation of dyspnea. Dyspnea on exertion, or exertional dyspnea, indicates dyspnea that occurs or worsens during physical activity. This article discusses the physiology, etiologies, evaluative procedures, and treatment of dyspnea.

PATHOPHYSIOLOGY OF DYSPNEA

Dyspnea is a complex psycho-physiologic sensation that occurs in a variety of cardiopulmonary diseases (**Fig. 1**). Increased work of breathing occurs when there is an increase in mechanical loading of the respiratory system, both resistive and elastic.[1,2] The sensation of dyspnea requires intact afferent and efferent pathways for the full perception of the neuromechanical dissociation between the respiratory effort attempted and the work actually accomplished.[3] The sensation is triggered or accentuated by a variety of receptors located in the chest wall, respiratory muscles, lung parenchyma, carotid body, and brain stem.[4] The sensation of dyspnea is stronger in patients with higher scores for anxiety and has been reported in patients with anxiety disorders with no cardiopulmonary disease.[5–9] These observations demonstrate the importance of cerebral cognition in this complex symptom.

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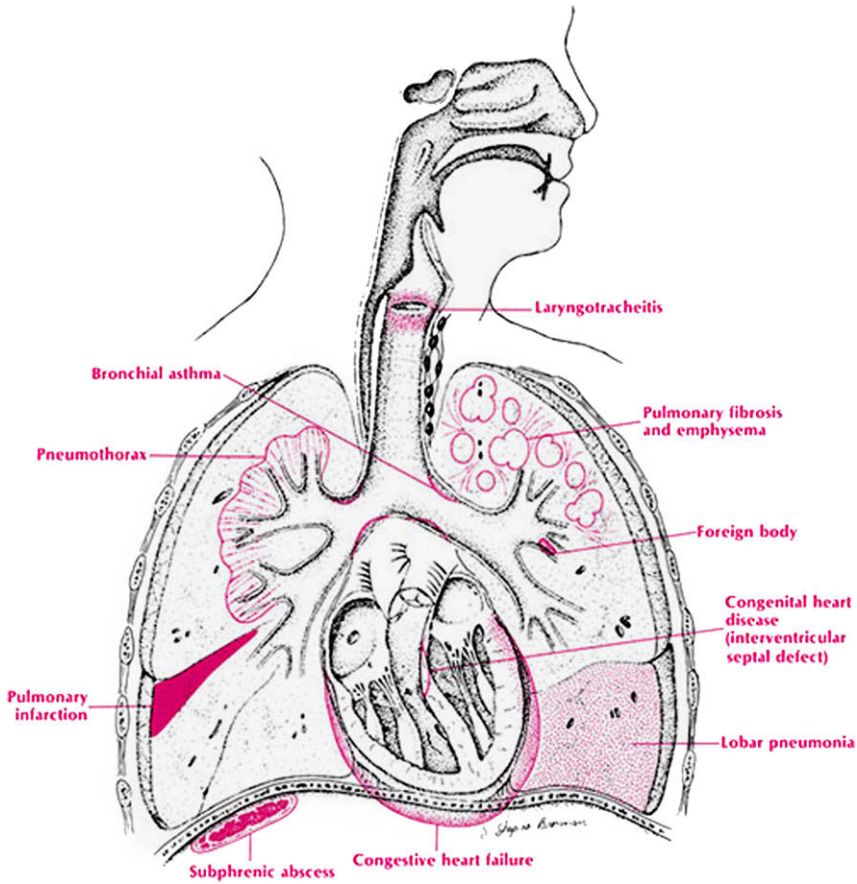

Fig.1. Cardiopulmonary sites that can cause dyspnea. (*From* Collins RD. Differential diagnosis in primary care. 4th edition. Philadelphia: Lippincott Williams & Wilkins; 2008. p. 141; with permission.)

CLINICAL MANIFESTATIONS OF DYSPNEA

People describe dyspnea in different ways. They certainly don't use the word dyspnea. Instead, people will say things such as, "I get tired easily," "I have trouble catching my breath," "I can't take a deep breath," "my throat gets tight," "my chest gets tight," "I can't keep up with the other kids," or simply "I get short of breath." Some of the differences appear to be cultural.[10] Complaints of dyspnea may occur spontaneously and unpredictably, in certain environments or during certain activities. They can be episodic or continuous.

Other differences relate to perception.[11] Differences in perception influence the recognition of asthma. Children with asthma symptoms that have not been recognized by their parents have been shown to perceive dyspnea less readily than those whose asthma has been recognized by their parents.[12] Patients with chronic severe obstructive lung disease, such as asthma and chronic obstructive pulmonary disease, experience adaptation to the sensation of dyspnea. Such patients typically rate their feeling of breathlessness low for severe degrees of obstruction when compared with the acutely ill and with patients with mild chronic disease.[13] Of particular

importance is the demonstration that individuals who have experienced near-fatal episodes from asthma have a diminished perception of dyspnea.[14]

When taking a history, it is important to have the patient describe their perception of dyspnea in as much detail as possible. The level of function or dysfunction associated with the dyspnea is also important in assessing the clinical manifestations of dyspnea. In addition to the patient's perception, observations should be obtained from parents, teachers, coaches, or others who have the opportunity to observe the patient for signs of increased work of breathing.

Interestingly, there is a dissociation between dyspnea and actual respiratory effort.[3] Examples include observations in adults with pulmonary embolism or pulmonary hypertension who may report breathlessness out of proportion to respiratory effort, including changes in minute ventilation or pulmonary mechanics. Additionally, induced hypercapnia has been associated with dyspnea accompanied by actual reduction in respiratory effort.[3] Thus, the sensation of dyspnea can reflect either actual increased work of breathing, as in airway obstruction, or the perception of breathlessness, as occurs with acute hypoxemia or hypercapnia.

The feeling of dyspnea or breathlessness can also occur from panic and hyperventilation attacks, where the perception of difficulty breathing is not accompanied by any respiratory pathophysiologic abnormality other than the effects of the hyperventilation itself. Because dyspnea, from whatever cause, depends on perception, attempts have been made to standardize perception. The Borg and the Visual Analog Scales have been the most commonly used measures of dyspnea.[15–17]

PHYSICAL FINDINGS ASSOCIATED WITH DYSPNEA

Physical findings of dyspnea can range from none at all to obvious increased work of breathing manifested by retractions, tachypnea, nasal flaring, use of accessory muscles, and cyanosis. If the dyspnea occurs only during exercise, then reproduction of the exercise-induced dyspnea may require a formal exercise test to reproduce the symptom. This provides the opportunity to observe the patient during the dyspnea and measure cardiopulmonary physiology associated with the dyspnea.

Respiratory sounds may include inspiratory stridor, expiratory wheezing, crackles, or just normal air movement. Identifying respiratory sounds associated with the dyspnea can be helpful in identifying the physiologic abnormality. Inspiratory sounds indicate extrathoracic obstruction, while expiratory sounds indicate intrathoracic obstruction. The pitch of the sounds can also provide clues. Low-pitched inspiratory sounds are typically from supraglottic obstruction, while high-pitched inspiratory sounds are more likely to be from laryngeal or subglottic narrowing. Expiratory wheezing can be monophonic, representing obstruction of one intrathoracic airway, while polyphonic expiratory wheezing indicates more diffuse airway involvement. The extent of the obstruction influences the increased work of breathing to overcome the narrowing of the specific component of the airway.

PHYSIOLOGIC ABNORMALITIES ASSOCIATED WITH DYSPNEA

Both cardiac and pulmonary disease can be associated with dyspnea. Pulmonary edema affects lung compliance and gas exchange. Myocarditis affects cardiac output and limits oxygen delivery to tissues. Pulmonary function testing can differentiate between obstructive and restrictive causes of dyspnea. Obstructive causes are characterized by decreases in flow, while restrictive causes are characterized by decreased lung volumes. Gas exchange abnormalities can be assessed by measurement of oxygenation and pCO_2, while measurement of diffusing capacity can be used to determine

if there is a loss of the pulmonary capillary bed, as occurs in interstitial lung disease and pulmonary fibrosis. Exercise testing with cardiopulmonary monitoring can measure oxygen use, CO_2 production, cardiac function, and ventilatory abnormalities.

EXERCISE-INDUCED DYSPNEA

Exercise-induced dyspnea can be present when cardiac or pulmonary function is compromised at an earlier stage in the underlying disease than when dyspnea from those problems occurs at rest. Dyspnea during exercise in patients who otherwise have no known lung or heart disease is therefore a symptom that warrants investigation. It might represent a mild abnormality that is manifested only during exercise, in which increased ventilation and cardiac output are required, or it could be caused by a distinct pathophysiologic abnormality that is induced only by exercise.[18] Of the latter, exercise-induced bronchospasm as a manifestation of asthma is the most widely studied. Its prevalence is very high, but because of poor correlation between the degree of airway obstruction and the sensation of dyspnea, exercise-induced bronchospasm is subject to being unrecognized.[19–21] However, exercise-induced asthma is also subject to being over-reported.[22,23]

Following are selected cases representing common and uncommon examples of dyspnea, which demonstrate the diversity of clinical entities that can present with this symptom.

CASE STUDIES OF DYSPNEA

Case 1

A 10-year-old boy with known asthma comes home from school complaining of difficulty breathing. His mother observes that he has suprasternal retractions. He is taken to the local emergency room, where diffuse polyphonic wheezing is heard and oximetry indicates an O_2 saturation of 93%. Albuterol aerosol is given, his retractions decrease, his O_2 is now 92%, but he states that he feels better and that it is now easier to breath. So what was the mechanism for his dyspnea? Central receptors for hypoxemia? Was he also hypercapneic? Or was it the increased airway resistence from bronchospasm?

It is unlikely that the modest degree of hypoxemia would have been sufficient to make him complain of difficulty breathing. The rapid response to albuterol is consistent with decreasing the resistence to air flow, with consequent lessor effort resulting in chest wall receptors no longer sending signals of increased respiratory effort. Hypoxemia can be from ventilation-perfusion mismatching and commonly occurs early in acute asthma. Because albuterol relaxes pulmonary arteriol smooth muscle in addition to bronchial smooth muscle, ventilation-perfusion mismatching may actually worsen from use of a bronchodilator, even though symptomatic relief results from the decrease in airway resistance from the bronchodilatation. Alternatively, a severe increase in airway resistance greater than can be maintained by the patient results in hypoventilation, with a consequent increase in pCO_2. The rapid relief of dyspnea, despite the continued mild degree of hypoxemia, makes that scenario unlikely in this patient. His dyspnea was therefore a manifestation of the increased work of breathing perceived through receptors in the chest wall.

The presence of continued mild hypoxemia is from the ventilation-perfusion mismatching, resulting from the shunting of pulmonary arterial blood from poorly ventilated areas of the lung to better-ventilated areas. If the same degree of hypoxemia was accompanied by continued increased work of breathing manifested by continued retractions and discomfort, then obtaining a pCO_2 would be critical to identify the potential for early signs of respiratory failure.

Treatment requires a short course of oral corticosteroid to reverse the obstruction from inflammation that results in differential ventilation and the consequent ventilation-perfusion mismatching. Inhaled corticosteroids may then be indicated as long-term maintenance medication if this episode is more than a manifestation of intermittent viral respiratory-induced asthma.[24]

Case 2

A 15-year-old girl takes a typical teenage summer-time job in Iowa, called detasseling. (Detasseling is done to cross-breed, or hybridize, two different varieties of corn. Fields of corn that will be detasseled are planted with two varieties of corn. By removing the tassels from all plants of one variety, all the grain growing on those plants will be fertilized by the other variety's tassels.) She developed severe dyspnea with respiratory sounds that were described as wheezing, and was taken to the local emergency room, where an injection of epinephrine relieved her symptoms. The next day, she again attempted detasseling, with the same result. She then abandoned her goal of detasseling but continued for the next 3 weeks to have similar episodes of dyspnea, described by the patient, emergency room care givers, and her primary care pediatrician as ''wheezing.'' These episodes would occur both spontaneously and with exertion, and would not respond to epinephrine as they did on the first 2 days. Trials by her primary care pediatrician of antiasthmatic medications, including inhaled albuterol, oral corticosteroids, and inhaled corticosteroids, failed to either prevent or relieve acute symptoms when they occurred. Symptoms would last up to several hours, considerably limiting activity of this normally very active adolescent.

After 3 weeks of these daily symptoms, she was referred to the authors' pediatric allergy and pulmonary clinic. She was initially asymptomatic. However, a treadmill exercise reproduced her dyspnea and the respiratory sound previously described as wheezing. The sound precipitated during exercise testing was high-pitched and limited to inspiration. Spirometry before and after the onset of dyspnea demonstrated inspiratory airway obstruction (**Fig. 2**).[25] Flexible laryngoscopy during the episode demonstrated paradoxical vocal cord movement (video with audio can be seen and heard as Video 3 at the following site: http://pediatrics.aappublications.org/cgi/content/full/120/4/855).

This demonstrated that her dyspnea was from the vocal cord dysfunction syndrome. While the evaluation included a large positive skin prick test to corn pollen, which explained the initial episodes as being consistent with laryngeal edema from intense exposure to the corn pollen during the detasseling procedure, the subsequent episodes were from the functional disorder of vocal cord dysfunction with paradoxical motion, whereby the vocal cords paradoxically closed on inspiration with relaxation and consequent opening on expiration.[26]

Instructions by a speech pathologist provided this girl with the ability to stop the paradoxical movement when it would start, but it continued to occur during vigorous activity, interfering with her activities as a cheerleader. Suspecting a vagal mechanism for this, a trial of pre-exercise treatment with an anti-cholinergic inhaler, ipratropium, reliably prevented the exercise-induced vocal cord dysfunction.[27] This regimen allowed her to resume her usual athletic activities, including cheerleading.

Case 3

The 15-year-old girl in Case 3 had a 1.5-year history of recurrent, extremely severe dyspnea. Episodes were sufficiently impressive to observers that paramedics were repeatedly called for urgent transportation to a local hospital emergency room. Symptoms would last for variable periods of time and occurred with sporadic frequency,

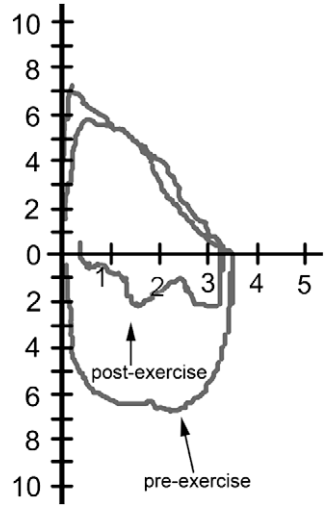

Fig. 2. Spirometry before and after exercise in the girl described in Case 2, showing the marked decrease in the inspiratory portion of the flow-volume loop in association with dyspnea, and an inspiratory wheeze-like sound (technically a high-pitched stridor). (*From* Weinberger M, Abu-Hasan M. Pseudo-asthma: when cough, wheezing, and dyspnea are not asthma. Pediatrics 2007;120(4):860; with permission.)

without apparent inciting factors. She had been treated with various antiasthmatic medications, including inhaled and oral corticosteroids, with no benefit. She had been hospitalized several times, where she received intravenous corticosteroids and vigorous use of inhaled bronchodilators, also without benefit.

The first time this girl was seen at the authors' pediatric allergy and pulmonary clinic, she was free of any symptoms of dyspnea and her physical examination was normal. Initial spirometry was completely normal. To further assess the cause of the dyspnea, a bronchoprovocation with histamine was planned. While preparing the vials of the various concentrations of histamine needed for the progressive inhalational provocation, and before any had been administered, she began having severe respiratory distress, with both inspiratory and expiratory wheezing-like sounds. Her spirometry changed from showing normal inspiratory and expiratory flow to severe obstruction in both phases of respiration (**Fig. 3**). Flexible laryngoscopy during the episode demonstrated virtually complete closure of the vocal cords, leaving only a small aperture for air movement with no abduction, except briefly during speech (video with audio can be seen and heard as Video 4 at the following site: http://pediatrics.aappublications.org/cgi/content/full/120/4/855).[25]

Treatment focused on speech pathology, to teach the patient control over her vocal cords when symptoms occurred. Response to treatment was only partially effective. She was able to control some episodes but not others. Lack of continuity for her care hampered progress. She and her single mother subsequently moved to Texas, and she was lost to follow-up.

Case 4

A 9-year-old girl was transferred from a local hospital to the authors' pediatric intensive care unit (PICU) because of progressive dyspnea and hypoxemia. She had a prior history of intermittent asthma, with appropriate responses to conventional measures,

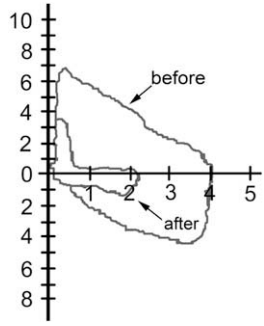

Fig. 3. Spirometry before and after the onset of dyspnea in the girl described in Case 3, showing the marked decrease in the inspiratory and expiratory portion of the flow-volume loop in association with an inspiratory wheeze-like sound (technically a high-pitched stridor on inspiration and a monophonic wheeze on expiration). (*From* Weinberger M, Abu-Hasan M. Pseudo-asthma: when cough, wheezing, and dyspnea are not asthma. Pediatrics 2007;120(4):860; with permission.)

although the authors did not have the medical records for those ambulatory care episodes. On this occasion, progressively greater need for oxygen had been needed to keep O_2 saturations above 90%, despite frequent β_2 agonist (albuterol) aerosol and intravenous corticosteroids. Transfer was arranged when that level of O_2 saturation could not be maintained, even with 100% O_2 by mask. When seen in the PICU, she was severely dyspneic, with rapid respirations and mild intercostal retractions. Despite continuous albuterol aerosol and an intravenous β_2 agonist, her O_2 saturations fell below 70%. She was intubated and ventilated with 100% O_2, but her saturation stayed at 70%. She required only 15-cm H_2O pressure to provide adequate ventilation at an appropriate volume setting for her size. A blood gas demonstrated a pCO_2 of 28 mm Hg at that ventilator setting.

Because there was no evidence of airway obstruction based on the modest pressure requirements for ventilation, it appeared likely that the vigorous use of β_2 agonists was increasing ventilation-perfusion mismatching in a lung disease other than asthma. Stopping all bronchodilator use resulted in oxygen requirements to maintain saturations greater than 90%, rapidly decreasing from 100% to an FiO_2 of 70%. After permitting her to rest overnight on the ventilator with progressively decreasing O_2 requirement, she was extubated the following morning with only 40% O_2 required. The need for oxygen gradually decreased over the ensuing days.

Pulmonary function testing the following day showed no evidence for airway obstruction, but decreased lung volumes and diffusing capacity were observed. This subsequently normalized over several weeks. Recurrences of this restrictive lung disease were observed over subsequent years, but with gradually decreasing frequency. Decreased lung volumes and diffusion capacity for carbon monoxide (DLCO) without airway obstruction was observed with each of these, all of which were self-limited without treatment after a trial of corticosteroids was not found to alter the course. Bronchodilators were avoided and hospitalization was rarely required, and then only with no need for assisted ventilation or intensive care. By the time she started college, these episodes stopped reoccurring.

While the etiology of this apparently interstitial lung disease was never identified, this patient's clinical course shows the potential danger of assuming asthma in all cases of acute respiratory distress in children. Use of β_2 agonists for dyspnea with hypoxemia in the absence of airway obstruction risks substantial worsening of

hypoxemia by pulmonary arteriolar dilatation, thereby overcoming the normal protective reflexive pulmonary arteriolar constriction that shunts blood from poorly ventilated to better ventilated areas of the lung. The improvement in ventilation that occurs from the bronchodilatation of a β_2 agonist in asthma generally results in greater overall benefit, whereas the absence a bronchospastic component to the clinical situation results in only worsening of hypoxemia, as occurred in this patient.

Case 5

This 3-year-old boy was admitted to the University of Iowa Children's Hospital because of progressive dyspnea on exertion and recent onset of cyanosis. His mother described him as becoming very short of breath when going up stairs. One month earlier, he had similar symptoms, was hospitalized locally, given antibiotics, and recovered completely within a few days. When seen by the authors, he had rapid respirations with only minimal intercostal retractions. He appeared definitely cyanotic but other than the tachypnea, he did not appear distressed at rest. He was afebrile. An arterial blood gas showed a pO_2 of 50 with a pCO_2 of 32 mm Hg. A chest X-ray showed perihilar and right lower lobe infiltrates (**Fig. 4**).

In investigating the potential etiology, a history of raising doves in the front room of the house was obtained (**Fig. 5**). Examination of the boy's serum identified precipitins to pigeon serum and pigeon droppings (**Fig. 6**). The common precipitin to pigeon droppings and serum in this boy confirm that the lung disease is a manifestation of pigeon breeder's lung disease, an allergic alveolitis.[28] It was the impressive degree of hypoxemia without a major degree of increased work of breathing that suggested an interstitial or alveolar process and not an airway cause for his dyspnea.

Within a few days in the hospital, spontaneous recovery was apparent, with normalization of his blood gases. He was kept in the hospital until his parents could remove

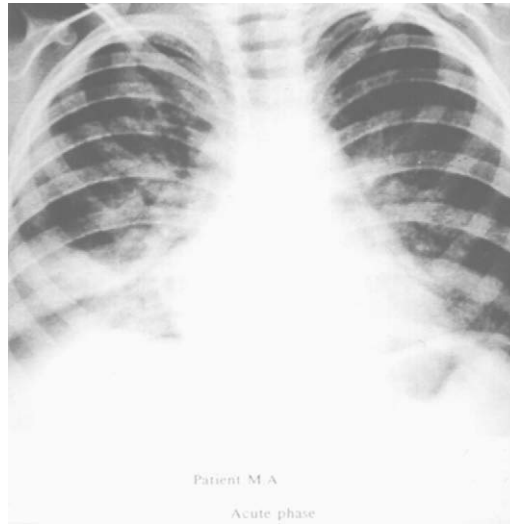

Fig. 4. Chest film of 3-year-old boy described in Case 5, with dyspnea on exertion, tachypnea, cyanosis; he was afebrile, had minimal intercostal retractions, and did not appear to be distressed while at rest. (*From* Wolf SJ, Stillerman A, Weinberger M, et al. Chronic interstitial pneumonitis in a 3-year-old from hypersensitivity to dove antigens. Pediatrics 1987;79(6): 1027; with permission.)

Fig. 5. One of the doves (a pink pigeon) raised in the front room of the home of the child described in Case 5.

the pigeons and clean the front room of the house. He subsequently remained well. In contrast to his complete recovery, repeated exposure over prolonged periods can be associated with irreversible pulmonary fibrosis in someone with allergic alveolitis, also called hypersensitivity pneumonitis.

Case 6

A 16-year-old high school basketball player judged competitive for college scholarships was seen in the Pediatric Allergy & Pulmonary Clinic for exercise-induced dyspnea. Although an excellent and aggressive player, he could not last a quarter without complaining of shortness of breath. The coach would pull him out, and after a few minutes rest he was able to re-enter the game. A previous diagnosis of asthma led to the use of albuterol, without any response.

Physical examination revealed an extremely fit-looking tall adolescent. Baseline pulmonary function was normal. Treadmill running with cardiopulmonary monitoring

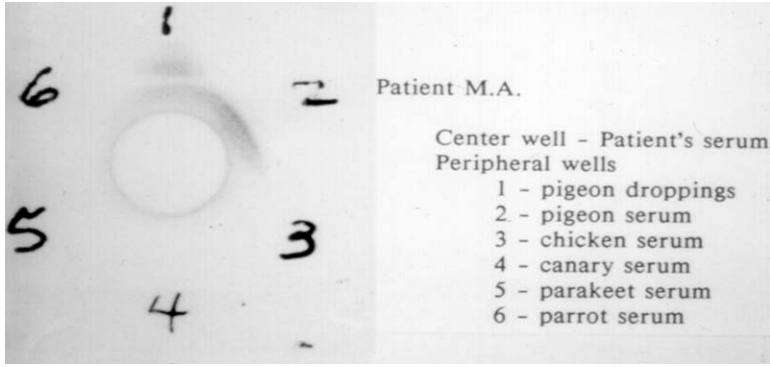

Fig. 6. Ouchterlony double-gel diffusion with the serum of the patient described in Case 5; his serum is in the center well and the indicated antigens are in six surrounding wells on an agar plate. The common precipitin to pigeon droppings and serum in this boy confirm that the lung disease is a manifestation of allergic alveolitis from pigeon breeder's lung disease. (*From* Wolf SJ, Stillerman A, Weinberger M, et al. Chronic interstitial pneumonitis in a 3-year-old from hypersensitivity to dove antigens. Pediatrics 1987;79(6):1027–9; with permission.)

was performed with increasing ramp until his typical symptom of dyspnea was reproduced (**Fig. 7**).

Although the initial monitoring of cardiac and pulmonary gas exchange was consistent with that of a well-conditioned athlete, the onset of his reproduced dyspnea was associated with a sudden increase in the heart rate to 220 beats per minute. Upon cessation of exercise, the heart rate stayed at 220 for up to 10 minutes, when it abruptly dropped to 90. A consult from a cardiac electrophysiologist interpreted the ECG as demonstrating supra-ventricular tachycardia. Electophysiologic studies subsequently identified an alternate conductive pathway to the atrioventricular bundle. A radio-frequency ablation procedure was then performed, after which he was then able to complete quarters in basketball without the previously experienced dyspnea.

The relevance of presenting this patient is the presence of the symptoms, shortness of breath, in the absence of any pulmonary abnormality. At no time did this boy complain of palpitations. In the absence of reproducing his symptoms during appropriate physiologic monitoring, his treatable problem would not have been identified.

Case 7

A 16-year-old girl was referred to the Pediatric Allergy & Pulmonary Clinic because of exercise-induced dyspnea. She was captain of her basketball team, but continued to

Fig. 7. Treadmill testing with cardiopulmonary monitoring. Oxygen use and carbon dioxide production with breath-by-breath analysis combined with ECG cardiac monitoring permit assessment of physiologic function and physical conditioning. A pressure transducer permits measurement of flow-volume loops during exercise to assess upper or lower airway obstruction during exercise. (*From* Weinberger M, Abu-Hasan M. Pseudo-asthma: when cough, wheezing, and dyspnea are not asthma. Pediatrics 2007;120(4):862; with permission.)

experience exercise-induced symptoms that limited her activity and required her to frequently sit out of the game for a period of time because of dyspnea. These symptoms had been present for at least the two previous years. She had been diagnosed at age 14 with exercise-induced asthma and placed on an inhaled corticosteroid. The dose had been progressively increased because of continued exercise-induced dyspnea. She also used albuterol before exercise. Despite consistent adherence to the prescribed regimen, no benefit was apparent from any of this.

Treadmill exercise testing with cardiopulmonary monitoring was performed while running during a progressively increasing ramp. Based on the heart rate and oxygen use, she demonstrated a high level of cardiovascular function consistent with being a well-conditioned athlete. Her exercise-induced dyspnea was not reproduced until well beyond her anaerobic threshold. Her capillary pH at the end of exercise was 7.18, and a pCO_2 of 42 mm Hg with no apparent cardiac or pulmonary pathophysiology.

The diagnosis of her exercise-induced dyspnea was thus because of reaching normal physiologic limitation. As exercise progressively increases, maximum oxygen use is eventually reached and anaerobic metabolism becomes the eventual source of energy. That produces lactic acid, and the resultant metabolic acidosis is translated by receptors into a demand for greater minute ventilation to create compensatory respiratory alkalosis by decreasing pCO_2. However, increased carbon dioxide is being simultaneously produced and the neurologic demand for increased ventilation encounters the physical limits of ventilation. The continued respiratory drive beyond the capability of the body to meet the demand results in dyspnea, which is interpreted by some as abnormal shortness of breath.

In a study of children and adolescents referred to the authors for exercise-induced dyspnea, most had been previously diagnosed and treated for asthma. The most common cause of exercise-induced dyspnea in these patients, occurring in over half of those tested, was physiologic limitation. It was the perception of these individuals that the dyspnea they were experiencing represented an abnormal physical problem. These patients included the full range of cardiovascular conditioning from highly conditioned competitive athletes to those attempting vigorous exercise with little prior conditioning and consequent below-average cardiovascular conditioning. In the absence of cardiopulmonary monitoring during exercise that reproduced their symptoms, the etiology of the exercise-induced dyspnea would have continued to be inappropriately treated in many of these patients (**Fig. 8**).[22]

Case 8

A 26-year-old pediatric cardiology fellow with a long history of severe chronic asthma entered the authors' care program. She had a documented history of at least one episode of respiratory failure requiring intubation and ventilatory assistance. With appropriate maintenance medication, her asthma had become well controlled until she developed symptoms of a viral respiratory infection associated with disturbing cough. As the cough increased, she became increasingly dyspneic, and came to the University of Iowa Emergency Treatment Center. Because of impressive dyspnea and tachypnea, she was admitted immediately to the medical intensive care unit. A blood gas there showed a pO_2 of 220 on oxygen, a pH of 7.54, and a pCO_2 of 18 mm Hg. The presence of excellent oxygenation with respiratory alkalosis was consistent with hyperventilation, a diagnosis that was as apparent to this medically sophisticated patient as it was to the physicians caring for her.

While the cough was probably a manifestation of her asthma, her experience in the recent past of requiring intubation and assisted ventilation from respiratory failure was

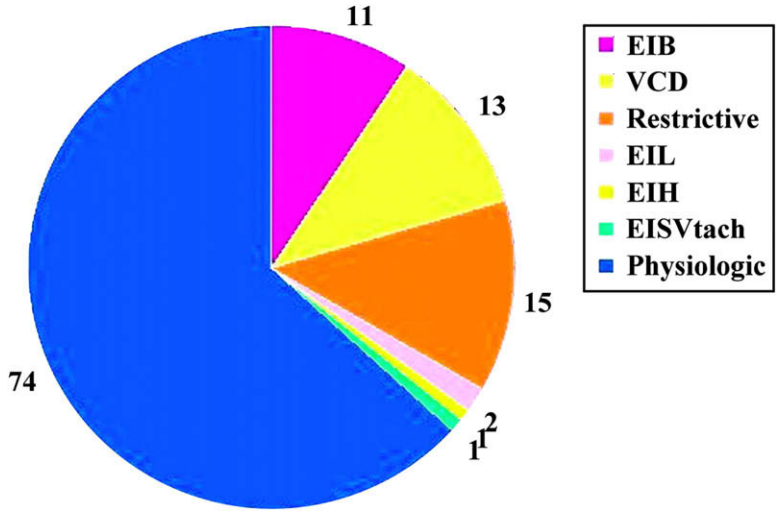

Fig. 8. Diagnoses determined by treadmill exercise testing with physiologic monitoring. *Abbreviations*: EIB, exercise-induced bronchospasm; EIH, exercise-induced hyperventilation; EIL, exercise-induced laryngomalacia; EIVTach, exercise-induced supraventricular tachycardia; Physiologic, normal physiologic limitation without other abnormality; Restrictive, apparent restriction of chest wall movement; VCD, vocal cord dysfunction. (*From* Weinberger M, Abu-Hasan M. Pseudo-asthma: when cough, wheezing, and dyspnea are not asthma. Pediatrics 2007;120(4):862; with permission.)

the likely explanation for the anxiety-induced hyperventilation in this case. The authors present this young adult because this medically sophisticated pediatric cardiology fellow was asked if she could tell the difference between the dyspnea she experienced in this case and dyspnea when she experienced asthma leading to respiratory failure. Her response was that both felt the same. This emphasizes that dyspnea is perceived as dyspnea, whatever the etiology.

The authors have had several children and adolescents with similar histories of life-threatening episodes from acute asthma who subsequently experienced similar symptoms of dyspnea associated with hyperventilation. Unless emergency treatment center physicians are alert to this possibility, inappropriate treatment for asthma will be given that will not relieve the dyspnea and will continue to result in repeated such care requirements. Such patients should be suspected if initial pulse oximetry in a dyspneic asthmatic is in the high 90s while breathing room air. When a blood gas, capillary, or venous is adequate, it can then be determined if the pH is high and the pCO_2 is low, consistent with respiratory alkalosis from hyperventilation. Provision for a means of assessing lung function at home permits the patient to distinguish dyspnea from the airway obstruction of acute asthma from that of anxiety and hyperventilation, thereby preventing unnecessary episodes of urgent medical care.

Case 9

A 16-year-old girl with cystic fibrosis had been admitted to the hospital with an exacerbation of her lung disease. Despite increased cough and decreased spirometric values indicating worsening airway obstruction, she was not initially dyspneic. She was treated with intravenous tobramycin and piperacillin. Three days into treatment, she began to experience increasingly severe dyspnea associated with neither hypoxemia nor hypocapnia. She was transferred to the PICU. Her hemoglobin was found to

have dropped to less than 4 mg/dL, in association with severe hemolysis mediated by antibodies to the pipericillin.

This patient illustrates that increased airway obstruction in chronic lung disease, such as cystic fibrosis, is often not associated with dyspnea, despite levels of airway obstruction that would cause dyspnea when occurring acutely in someone with asthma. This patient also demonstrates the potential for dyspnea from the decreased oxygen-carrying capacity of severe anemia, even while blood gases themselves remain normal.

Case 10

A 14-year-old boy with a diagnosis of systemic lupus erythematosis (SLE) made 3 years earlier, with no prior history of respiratory complaints, was admitted to the PICU with a history of progressive fatigue, dyspnea, and chest pain. He had no fever or cough. He was tachypneic and had an O_2 saturation by pulse oximetry of 91%, which increased readily to 99% with supplemental O_2. He appeared to be experiencing increased respiratory effort, but there was minimal inspiratory movement with each breath. He was started on 250 mg of intravenous methylprednisolone every 8 hours.

By the second day of admission, his O_2 saturation normalized although he was still dyspneic. Pulmonary function at that time demonstrated no airway obstruction, but his vital capacity was only 20% of predicted, and his total lung capacity was 34% of predicted. By day five he was no longer dyspneic; his vital capacity and total lung capacity had increased to 31% and 44% of predicted, respectively. His single breath DLCO normalized for alveolar volume (DLCO/Va) was only mildly reduced at 78% of predicted. Continued treatment by the pediatric rheumatologist further improved his vital capacity and total lung capacity to 45% and 57% of predicted, respectively, by 23 days after admission; his DLCO/Va had increased somewhat to 87% of predicted by that time.

While the physiologic mechanism of this uncommon complication of SLE, known as shrinking lung syndrome, is only speculative, it appears to be associated with restricted diaphragmatic movement, which was in fact demonstrated fluoroscopically in this patient.[29] This case illustrates that restrictive changes are well tolerated until a critically low level of ventilation is reached. This patient also demonstrates the value of lung volumes and DLCO in addition to just spirometry in identifying the physiologic abnormality associated with dyspnea. While there is the potential for interstitial lung disease to be associated with collagen-vascular diseases, the modest decrease in the DLCO for this patient did not provide support for that type of physiologic abnormality.

SUMMARY

Dyspnea is a complex psycho-physiologic sensation that has many causes that can be anatomic, physiologic, or psychologic. The entities causing dyspnea include commonly occurring problems, such as asthma, and uncommon but clinically important problems to identify, such as allergic alveolitis and the shrinking lung syndrome of systemic lupus erythematosis. Functional disorders, such as the variations of vocal cord dysfunction and hyperventilation, require identification so those patients can be treated behaviorally and not subjected to inappropriate medication. Exercise-induced dyspnea, while a characteristic of asthma, should not be assumed to be asthma in the absence of other symptoms of asthma and a convincing response to prevention by pretreatment with an albuterol aerosol. Treadmill exercise testing that reproduces symptoms with cardiopulmonary monitoring can identify the physiologic

Table 1
Intervention for dyspnea

Intervention	Recommendation	Grading of Recommendation (Based on Evidence of Benefit)	Quality of Supporting Evidence
Albuterol (salbutamol) aerosol	Only for asthma	Strong	Strong
Corticosteroids, inhaled	Only for chronic asthma	Strong	Strong
Corticosteroids, oral, short course of high dose	For exacerbations of asthma	Strong	Strong
Corticosteroids, oral, short course of high dose	For assessment of response to support the diagnosis of asthma as the cause of dyspnea	Moderate	Moderate
Long acting β_2 agonists	As additive agent to inhaled corticosteroids for chronic asthma	Moderate	Strong
Montelukast	For chronic asthma	Low	Moderate
Epinephrine (adrenalin) injection	For acute laryngeal edema of systemic anaphylactic reaction	High	High
Speech therapy	For recurring spontaneous episodes of vocal cord dysfunction	Moderate	Low
Ipratropium aerosol	For prevention of exercise-induced vocal cord dysfunction	Moderate	Low
Ipratropium aerosol	For severe acute asthma not responding to albuterol	Moderate	Moderate
Environmental adjustment	For allergic asthma	Moderate	Low
Environmental adjustment	For allergic alveolitis	High	Moderate

abnormality, whether exercise-induced bronchospasm, vocal cord abnormalities, or the various other physiologic causes demonstrated to be associated with exercise-induced dyspnea. The following outline (see also **Table 1**) lists the steps health care professionals should follow when a patient presents with dyspnea:

I. A complete medical examination with particular attention to cardiorespiratory systems and a focus on:
   A. Determining its clinical pattern
      1. Present all of the time
      2. Present only during exercise
      3. Present only with specific environmental exposures
   B. Level of respiratory dysfunction (ie, degree of disability)
   C. Observation of level of dysfunction from others
   D. Presence of airway noises
II. Evaluation should include:
   A. Chest X-ray
   B. Baseline oximetry
   C. Blood pH and pCO2 when oximetry below normal or if dyspnea presents with normal oximetry
   D. Spirometry with considerations for lung volumes and diffusing capacity if patient is able to perform
   E. Cardiorespiratory exercise test to reproduce exercise-induced symptoms if patient is able to do this
III. Referral for further evaluation and management if:
   A. Dyspneic at rest and diagnosis not apparent
   B. Hypoxemic and diagnosis not apparent

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