Appendix 2

CAUSES OF DYSPNEA IN MILITARY RECRUITS

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INTRODUCTION

Dyspnea is both a common and significant medical condition affecting military recruits. It has been described as the subjective awareness of difficult, labored, or uncomfortable breathing.[1] Dyspnea is a subjective manifestation of conditions ranging from acute, self-limited illnesses to chronic disorders resulting in significant limitations to job and exercise performance. The pathophysiology of dyspnea relates to the underlying etiology and often reflects complex interactions among the upper airways, lungs, chest wall, and heart. The differential diagnosis for dyspnea may be extensive. However, a limited number of conditions which are frequently provoked by the stressful conditions common to military training are usually responsible. Asthma is the most common respiratory disorder causing dyspnea in the recruit (see Chapter 22, Asthma and Its Implications for Military Recruits); other common causes are vocal cord dysfunction (VCD) and hyperventilation syndrome (HVS).

VOCAL CORD DYSFUNCTION

VCD is often diagnosed in soldiers referred to subspecialty care for the evaluation of dyspnea on exertion. This condition ranges widely, from the severe form frequently resulting in intubation and tracheostomy[2,3] to the more common and milder type manifesting as dyspnea on exertion.[4,5] VCD mimicking asthma is common in young adults with psychological disorders and in patients with chronic gastroesophageal reflux disease (GERD) or rhinitis. Patients with VCD, like those with asthma, often present with shortness of breath and wheezing, typically with an exertional component.[6,7] The association with GERD and rhinitis in asthma adds further confusion. The impact of VCD on military readiness may be substantial because these patients are frequent consumers of healthcare resources.[8] This section discusses the pathogenesis, diagnosis, management, and prognosis of VCD.

Reviewing the body of literature on VCD presents a number of problems. Authors apply a variety of different terms to VCD, such as laryngeal dysfunction, paroxysmal vocal cord movement, paroxysmal vocal cord dysfunction, episodic laryngeal dysfunction, irritable larynx syndrome, and extrathoracic airway dysfunction. A consensus on the appropriate diagnostic evaluation for VCD is needed for prospective studies of this disease. Presumably, the diagnosis would consist of some combination of symptoms and the results of pulmonary function testing and laryngoscopy.

Newer modalities such as impulse oscillometry may assist in determining whether obstruction occurs in the small or large airways. Analysis of expired nitric oxide may be used to determine if airway inflammation is present or absent.[9] These newer modalities are areas of possible research for physicians who diagnose and manage patients with VCD.

Pathophysiology

The pathophysiology of VCD is not fully understood, but several theories exist. A leading theory suggests that laryngeal hyperresponsiveness resulting from altered autonomic function, which develops following local inflammation, is an etiology for VCD.[10] This abnormality in autonomic function may be short-lived or persistent. Support for this concept comes from a series of investigations in Italy.[11,12] The investigators looked at the patterns of response to histamine challenge in patients with asthma-like symptoms and upper airway inflammation (sinusitis, postnasal drainage, and pharyngitis). Bronchial hyperreactivity (B-HR) was defined by a 20% fall in forced expiratory volume in 1 second (FEV1), and extrathoracic hyperreactivity (EA-HR) was defined as a 25% fall in maximal midinspiratory flow, both at values of 8 mg / mL or less. Patients could be characterized by one of four patterns: (1) B-HR only (11.1%); (2) EA-HR only (26.5%); (3) combined B-HR and EA-HR (40.6%); and (4) no response (21.8%). The EA-HR only and combined B-HR and EA-HR groups

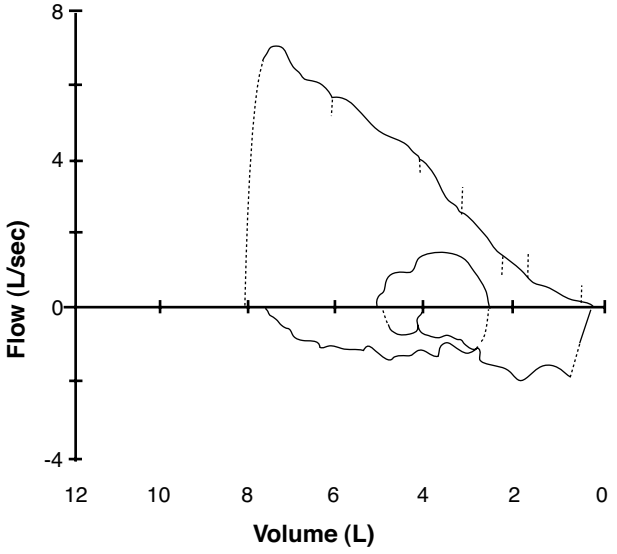

Fig. Appendix 2-1. Flow-volume loop with a variable extrathoracic obstruction.

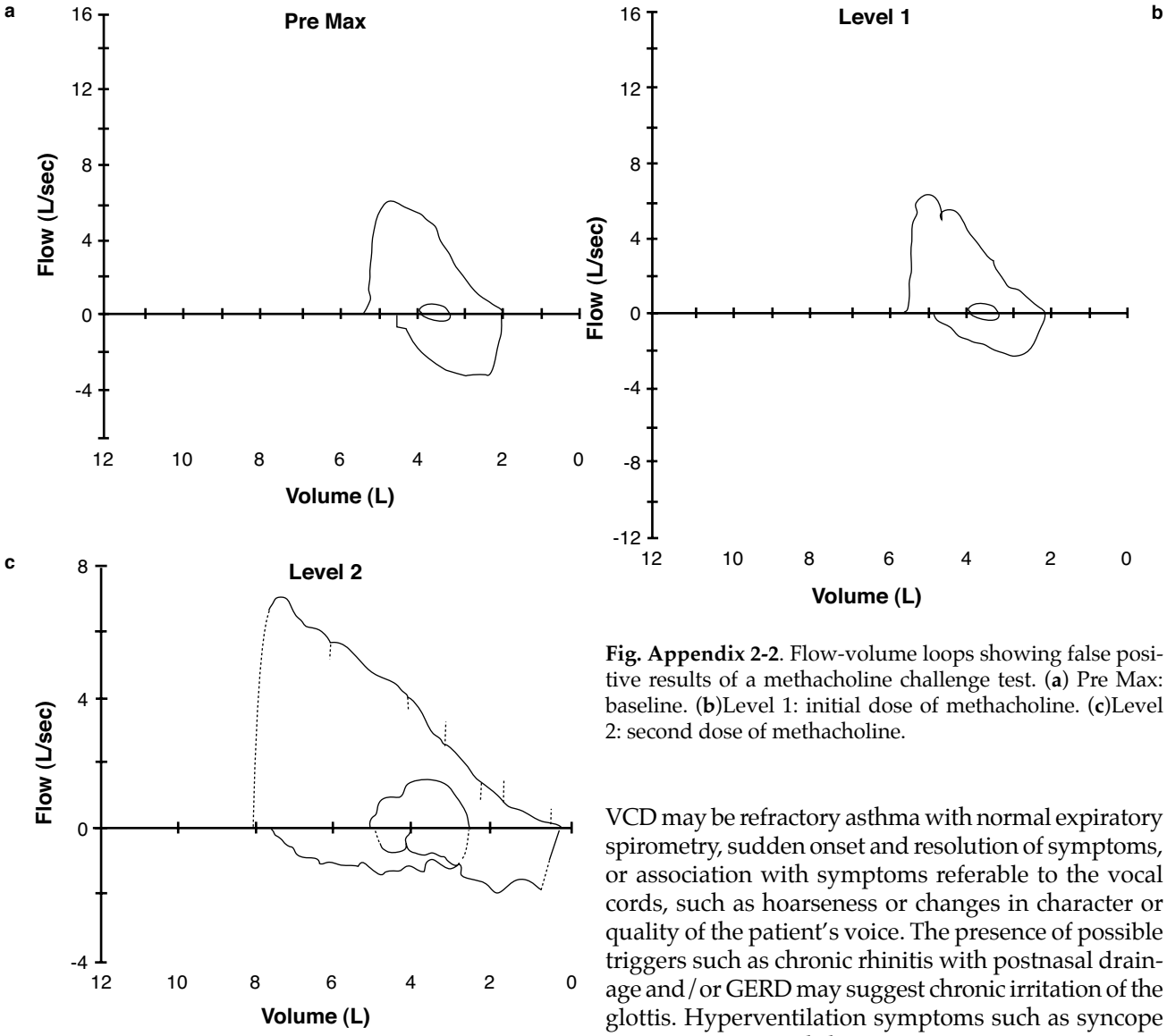

Fig. Appendix 2-2. Flow-volume loops showing false positive results of a methacholine challenge test. (**a**) Pre Max: baseline. (**b**)Level 1: initial dose of methacholine. (**c**)Level 2: second dose of methacholine.

had significantly greater probability of having upper airway inflammation. Interestingly, female sex was a significant factor affecting the presence of both EA-HR and B-HR.[12] An earlier study by this same group also found that EA-HR was much more frequent in women than men.[13] Inflammation of the upper airway may also explain the association of VCD and GERD, but this area remains open to research.

Diagnosis

Patients with VCD usually present with one or more of the cardinal symptoms of asthma: dyspnea, wheezing, cough, and chest tightness.[14] They are frequently misdiagnosed with asthma and overtreated with asthma medications. Clues to the presence of VCD may be refractory asthma with normal expiratory spirometry, sudden onset and resolution of symptoms, or association with symptoms referable to the vocal cords, such as hoarseness or changes in character or quality of the patient's voice. The presence of possible triggers such as chronic rhinitis with postnasal drainage and/or GERD may suggest chronic irritation of the glottis. Hyperventilation symptoms such as syncope or presyncope, lightheadedness, or numbness and tingling may occur.[15] An association with sexual abuse has been reported in the literature.[16] VCD should be suspected when physical examination reveals an inspiratory wheeze over the glottis.

The role of pulmonary function testing to include or exclude coexistent asthma has not been well defined. It is well known that patients with VCD may produce striking cutoff of the inspiratory portion of the flow-volume loop consistent with a variable extrathoracic obstruction (Figure Appendix 2-1), although this may not always be present in asymptomatic patients. During severe episodes, both the inspiratory and the expiratory portions of the flow-volume loop may be truncated. Additionally, VCD may interfere with the interpretation of airway challenge testing, producing a false positive test when airway inflammation is not present (Figure Appendix 2-2). A positive methacholine

challenge without the development of obstruction and with abnormal inspiratory loops may be a clue that obstruction in the upper, rather than lower, airway may be the cause. For those patients with transient exertional symptoms, exercise tidal flow-volume loops may hold some promise as a diagnostic entity.[17] Spirometry is typically normal, but may show a mild restrictive pattern. Flow-volume loops often reveal inspiratory flow limitation and truncation.

Definitive diagnosis requires direct visualization of the vocal cords and is made by demonstration of paradoxical movement.[18] There are no accepted diagnostic standards for VCD, although there have been attempts to define VCD and what constitutes an appropriate evaluation.[18] Demonstration of inappropriate adduction of the vocal cords by direct visualization of the vocal cords in symptomatic patients remains the gold standard. Apposition of the anterior portion of the true vocal cords with a posterior "chink" is the classic appearance of VCD (Figure Appendix 2-3). Upper-airway obstruction that produces symptoms may also occur with incomplete adduction of the vocal cords and/or hyperadduction of the arytenoid cartilages. However, normal laryngoscopy in the absence of symptoms does not exclude the diagnosis and has a reported false negative rate of 40%.[14] Therefore, it may be necessary to provoke symptoms. Exercise or methacholine challenge testing are most commonly used. Hyperventilation maneuvers, forced vital capacity maneuvers, and pressured speech may be used during the laryngoscopy.[18] Tobacco smoke, ammonium nitrate, perfume, or other exposures known to trigger an attack may also be used. An experienced laryngoscopist familiar with this disorder is also important, because those who are inexperienced may mistake gagging, laryngospasm, or other laryngeal disorders for VCD.

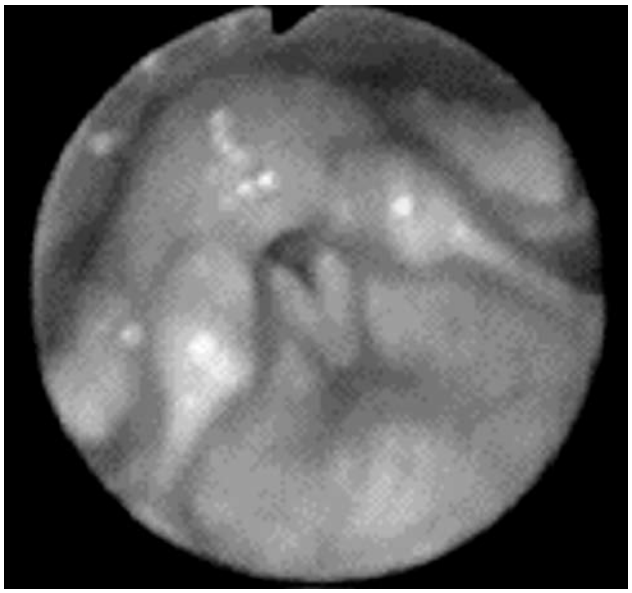

Fig. Appendix 2-3. Vocal cord adduction during inspiration with posterior "chink."

Earlier studies looking at the various etiologies associated with dyspnea and exercise limitations must be considered in context of the more recent understanding of the significant impact that VCD plays in this patient population. Many of these studies did not assess for this disorder. As stated previously, the prevalence of VCD was likely underestimated in the study conducted by Morris et al. A study that prospectively assessed 40 military patients with exertional dyspnea found a 15% incidence of VCD.[5] Interestingly, patients with VCD are often found to have bronchial hyperreactivity in methacholine challenge tests, but with a lesser reduction in the ratio of FEV1 to forced vital capacity compared to those with asthma. These abnormal tests result from a decreased inspiratory volume leading to decrease in FEV1 versus concomitant obstructive lung disease, which has been reported previously as high as 56% in a group of patients hospitalized for severe VCD.[14] Exercise challenge testing may also be useful in establishing a diagnosis of VCD. In a study by Morris and colleagues,[5] VCD was diagnosed only after exercise in 8 of the 10 patients with this disorder.

Management and Prognosis

The management of VCD includes education, medical management of triggers and coexistent diseases, speech therapy, and sometimes the management of stress or other psychiatric problems. Management begins with education and reassurance of the patient. Allowing the patient to visualize the abnormal vocal cord motion during laryngoscopy is helpful for understanding and cooperating with speech therapy. An educational handout or referral to appropriate Internet sites with accurate VCD information is important in validating the diagnosis and obtaining acceptance of the management plan. Medical management of coexistent asthma, if present, should be based on published guidelines, with care taken not to overtreat the patient. Chronic rhinitis with postnasal drainage and/or GERD should be treated aggressively. Referral to a speech pathologist trained in the management of VCD has been the mainstay of therapy for these patients. Speech therapy in the appropriate patient has a significant probability of success.[19] Patients with significant stress, emotional or psychiatric problems, or a history of sexual abuse may benefit from a referral

to an interested psychologist or psychiatrist.

In summary, VCD is a common mimic of asthma that occurs in approximately 15% of patients referred to a subspecialist for dyspnea. Although the medical literature is flawed, VCD appears to occur much more commonly in women than men. Soldiers with VCD frequently have a good response to treatment and, unlike asthmatic service members, can often be retained.

HYPERVENTILATION SYNDROME

HVS is also a common disorder among recruits with dyspnea. This condition was described as "soldier's heart" during the Civil War.[20] It can present as an acute or chronic form. Hyperventilation is defined as breathing in excess of metabolic demands and is associated with a reduction in $PaCO_2$, respiratory alkalosis, and a wide range of symptoms. It may be primary and referred to as HVS, or may be secondary to organic disease. Therefore, HVS, like VCD, is a diagnosis of exclusion.

Patients are diagnosed with HVS if they meet five of the following criteria: episodic dyspnea that is sudden in onset, brief in duration, and unrelated to exercise; palpitations; circumoral or peripheral paresthesias; inability to fill the lungs to take a satisfying breath; severe anxiety or fear associated with dyspnea; lightheadedness or dizziness; frequent sighing or yawning; and trembling of the hands.[21]

Most patients with HVS have multiple somatic symptoms and anxiety. Symptoms often include painful tingling in the hands and feet; numbness and sweating in the hands; dizziness and tingling leading to tetany and paresthesias of the hands, face, and trunk; giddiness; headache; ataxia; tinnitus; syncope; chest pain; and frequent sighing. Evaluation should include a chest radiograph and an arterial blood gas measurement for evaluating the appropriate PaO_2 in response to hypocapnea. A widened alveolar-arterial oxygen gradient (A-a gradient) at rest should direct attention towards pulmonary parenchymal or vasculature disease, while a normal A-a gradient makes these diagnoses unlikely.[22] See the following formulas (FIO_2: fraction of inspired oxygen):

$$\text{A-a gradient} = [(FIO_2 \times 713) - (PaCO_2/0.8)] - PaO_2$$

$$\text{Expected A-a gradient} = 2.5 + 0.21 \times \text{age in years}$$

If the diagnosis is in doubt, a ventilation-perfusion scan can help rule out pulmonary embolism. Also, mild asthma may precipitate hyperventilation. Diagnosis of HVS is often difficult, but when clear symptoms of hyperventilation—documented by a reduced $PaCO_2$ in an arterial blood gas analysis, in the absence of organic disease—is found, a diagnosis can be made with confidence.

Treatment includes reviewing the inciting history and providing the patient with an explanation for the condition as well as support, usually over a period of months. The acute or subacute form of HVS is most amenable to treatment. Service members with this condition may frequently be retained on active duty.

MISCELLANEOUS CAUSES OF DSYPNEA

Other causes of dyspnea that frequently mimic asthma include postviral and postinflammatory airway hyperreactivity, as well as anatomic abnormalities such as obstruction with a foreign body, vascular rings, laryngeal webs, tracheal stenosis or bronchostenosis, and enlarged lymph nodes or tumors (benign or malignant) causing compression or mechanical obstruction of the airways. Postinflammatory or postinfectious airway hyperactivity has similar spirometric criteria for diagnosis, but follows an episode of infection and is self-limited, usually resolving within 6 months. Reactive airways dysfunction syndrome is the onset of an asthma syndrome that occurs after a heavy exposure to chemical fumes. Deconditioning is a diagnosis of exclusion that is occasionally diagnosed in recruits. After full evaluation by spirometry, bronchoprovocation testing, and laryngoscopy, a cardiopulmonary exercise test is performed, which may suggest deconditioning and exclude other causes of exercise intolerance. Malingering is also a diagnosis of exclusion.

SUMMARY

Dyspnea, a common and significant medical condition affecting military recruits, is a subjective manifestation of conditions ranging from acute, self-limited illnesses to chronic disorders resulting in significant limitations to job and exercise performance. The pathophysiology of dyspnea relates to the underlying etiology and often reflects complex interaction among the upper airways, lungs, chest, wall and heart. A thorough evaluation, including history, physical examination, chest radiograph, and spirometry will usually result

in a diagnosis. Causes of chronic dyspnea in a military population include deconditioning as well as cardiac and respiratory disorders; respiratory disorders are by far the most likely.

VCD, found in up to 15% of patients complaining of dyspnea in a military population, is the inappropriate adduction of the vocal cords during respiration. The etiology of VCD is not well understood, but the condition frequently occurs in association with poorly controlled postnasal drainage or GERD. VCD should be suspected in patients with a history suggestive of asthma that cannot be confirmed with physiologic testing, or who have been diagnosed with asthma but respond poorly to treatment. The diagnosis of VCD is suggested by truncation of the inspiratory portion of the flow-volume loop. The diagnosis is confirmed with direct visualization of the vocal cords with a fiberoptic laryngoscope by an experienced clinician.

HVS is another common respiratory disorder found in patients presenting with dyspnea or dyspnea on exertion. The etiology of HVS is also poorly understood. Patients are diagnosed with HVS if they meet five conditions in a list of criteria. Serious disorders such as asthma or pulmonary embolism may cause hyperventilation; therefore, HVS is a diagnosis of exclusion. The diagnosis is established by arterial blood gas testing.

The impact of exertional dyspnea on a recruit's military career depends on the etiology of the disease, the ability to perform assigned duties, and the regulations of the recruit's branch of service. After orthopedic problems, respiratory disorders resulting in the inability to perform strenuous physical activity are the most frequent reason for recruits failing to meet the requirements of military service and resulting in separation from the service.

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