You're the Flight Surgeon

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You're the flight surgeon at a military aviation medicine clinic. Your patient is a 22-yr-old man who was recently commissioned as an officer on active duty military service and accepted into initial flight training. He presents with complaints of dyspnea upon exertion, especially a feeling of not being able to "fill his lungs" with air when running. The service member minimally passed the physical fitness requirements for commissioning a few months previously and recently failed a physical fitness examination by exceeding the maximum allowable time for the run event by 2 min. His current condition has kept him from completing his preliminary aviation officer leadership training. He states that as a member of the Reserve Officer Training Corps 1-2 yr ago, he had no difficulties with passing his physical fitness tests, but now he cannot run beyond a mile and a half without stopping to rest. He reports that as an adolescent he did not have difficulty with sprinting, but always had difficulty with long distance running. Furthermore, the service member reports that he has only a few weeks to pass a physical fitness test and expresses his concern that failure to do so will lead to his removal from military service. He tells you that he has hired the services of a personal trainer to help him improve his scores on this test.

The service member does not appear to be in any distress at this meeting. He is asymptomatic and reports no other current health concerns. The patient's vital signs are stable and within normal limits, but you notice that his body mass index (BMI) has been steadily increasing over the last 7 yr from a low of 19.5 to a current high of 26.3. Besides having occasional lower back pain that the service member ascribes to having played high school football, his past medical history is benign and noncontributory with no previous cardiac or pulmonary issues. The patient denies using tobacco products and endorses occasional consumption of alcohol. He is not using any medications or over-the-counter supplements. He has not traveled recently and denies any significant occupational exposures. The physical examination is unremarkable with no adventitious lung sounds.

1. What is your next decision?

A. With his BMI > 25 (overweight) he is probably deconditioned. You prescribe a "walk-to-run" and weight loss program with follow-up in 2 mo.
B. You suspect malingering and a loss of motivation to fly. You refer to the behavioral health clinic for evaluation.
C. Issue a grounding slip and place on physical activity restrictions to include no running.
D. Prescribe an albuterol metered dose inhaler for pre-exercise use. Refer for pulmonary function tests (PFTs) within the week with immediate follow-up posttest for review of results.

ANSWER/DICUSSION

1. D. Although his BMI of 26.3 is an indicator that he may be slightly overweight and that weight loss may be prudent, answer A does not address the short time that the service member has to remedy the situation of passing a physical fitness examination. Also, a walk-to-run program is for beginners, not those with an athletic background with a progressive declination in performance. Answer B is not the best answer because the patient has expressed concerns that his military career is at stake and has not only come to the flight surgeon for assistance but has hired a personal trainer to help address his conditioning issues. Answer C is not warranted as the service member is not currently flying and physical activity restrictions could further degrade his physical conditioning. It is reasonable to begin a trial of an albuterol inhaler with the possibility of exercise-induced bronchoconstriction in this patient while obtaining PFTs as an initial work-up. Exercise-induced bronchoconstriction responds well to β2-agonists, like albuterol, and in combination with PFTs could add to the diagnostic findings.[1]

The service member returns in a week and reports that the albuterol inhaler has not helped his aerobic exercise capacity. Results of his PFTs show prealbuterol treatment values as follows: forced expiratory volume at 1 s (FEV1) of 4.45 L (92% predicted), a forced vital capacity (FVC) of 3.56 L (84% predicted), and an FEV1/FVC of 80% predicted. The use of inhaled albuterol did not improve his FEV1 and only improved his FVC by less than 5%. The electrocardiogram results are within normal limits.

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2. Using the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria,[6] which of the following interpretations of his PFT results is most accurate?

A. His FEV1/FVC ratio of < 85% is worrisome for his age group and signals an obstructive defect.
B. FVC < 84% in this otherwise healthy man is indicative of a restrictive defect.
C. Some studies show the GOLD criteria can underdiagnose up to 50% of young adults with obstructive lung disease, and it may be better to use the American Thoracic Society guidelines for this patient.
D. An FEV1 > 90% by itself indicates no lung pathology.

ANSWER/DICUSSION

2. C. Concerns have been raised about the accuracy of the GOLD criteria in young adults, including the aforementioned potential for false negatives as well as the potential for false positives in healthy nonsmokers.[4,5] A, B, and D are not accurate uses of the PFT values as described in the GOLD criteria. According to these criteria, a 22-yr-old man would have a worrisome result if his FEV1/FVC ratio was < 70%, FVC was less than the lower limits of normal (LLN) of 4.24 L, and his FEV was less than the LLN of 3.55 L. The FEV1 is not used in isolation to make clinical decisions using the GOLD criteria.

The FEV1/FVC ratio LLN for this service member is 73.8%. His FEV1/FVC ratio of 80% is interpreted as "normal" by both American Thoracic Society criteria and GOLD criteria.[6] In addition, as he had no improvement in FEV1 following β2-agonist use, he does not meet the 12% FEV1 improvement criterion necessary for the obstruction reversibility needed for an asthma diagnosis.[8] With his window for passing a physical fitness test closing soon, and the patient having concerns for possible environmental allergen exposure, you decide to place him on an oral, nonsedating antihistamine. You also give him an intramuscular injection of methylprednisolone to mitigate any possible respiratory inflammation that he may have and you place a referral to pulmonology.

Pulmonology orders a computerized tomography scan of the service member's chest that reveals diffuse ground-glass opacities of the lungs bilaterally. The pulmonologist performs a transbronchial biopsy and a subsequent minimally invasive open biopsy of the left lung that rules out interstitial lung disease. However, the biopsies uncover evidence of pulmonary arterial hypertension (PAH), including focal bronchial fibrosis and arterial medial hypertrophy. A referral to cardiology is placed that produces essentially normal two-dimensional and bubble echocardiograms. As part of this work-up, a right heart catheterization shows normal right and left filling pressures at rest with mild elevation of his pulmonary artery pressures (average of 30 mmHg) with exercise. A pressure of 30 mmHg is generally considered the upper limit of normal, but is more in line with values for healthy individuals 50 yr or older.[7] The patient is placed on convalescent leave to heal from the procedures and is sent to a pulmonary vasculature specialty clinic for further evaluation.

3. Which one of the following answers is true concerning risk factors for PAH?

A. Heritable PAH is associated with a detection of germline mutations in the bone morphogenetic protein receptor type 2 (*BMPR2*) gene in 40% of cases.
B. Selective serotonin reuptake inhibitors, fenfluramine, cocaine, and St. John's wort have been associated with increased risk of developing PAH.
C. Systemic sclerosis and other connective tissue diseases have no known association with increased risk of PAH.
D. PAH is a relatively common complication of human immunodeficiency virus infection.

ANSWER/DICUSSION

3. B. The use of all of these compounds is associated with PAH. However, only the compounds aminorex, fenfluramine derivatives, and toxic rapeseed oil have been identified as "definite" risk factors. For answer A, *BMPR2* mutations were detected in 70% of heritable PAH cases. It appears that PAH patients with *BMPR2* mutations are less likely to display vasoreactivity than those without the mutation. There is a prevalence of PAH in systemic sclerosis patients of 7–12%, with infrequent reports of PAH in other connective tissue diseases. PAH is a rare, but well-established, complication of human immunodeficiency virus infection at a prevalence of 0.46%.[11]

The pulmonary vasculature specialty clinic performs arterial oxygenation studies that show that the service member has an oxygen saturation of 97% at rest. However, his oxygen saturation drops to 87% within 3 min of performing moderate exercise at a heart rate of 112 bpm. The vascular specialists support the initial diagnosis of PAH, stating that the service member is early in the development of the disease and that he would benefit from the use of a phosphodiesterase type 5 inhibitor. He is prescribed oral tadalafil and scheduled for further work-up at the specialty clinic to discern underlying pathology.

4. Which one of the following answers is correct concerning tadalafil therapy and PAH?

A. It is a disease-modifying pharmaceutical that reverses PAH in approximately 35% of cases.
B. The goal of this therapy is to improve exercise tolerance and delay clinical worsening.
C. Effectiveness is highest in patients rated as World Health Organization (WHO) Functional Class IV.
D. The recommended oral dose is 20 mg once daily.

ANSWER/DICUSSION

4. B. Tadalafil can improve overall exercise tolerance and delay decline but does not reverse the course of the disease. Effectiveness of this therapy is best for WHO Functional Classes II-III (slight to marked limitation). Tadalafil does not have as significant an effect in WHO Functional Class IV (severe limitation). The recommended oral dose is 40 mg (20 mg twice a day).[10]

Follow-up in your clinic finds that the patient has refused treatment with tadalafil. It has been 6 mo since your first encounter with this patient for dyspnea upon exertion and he is still having difficulty with running and cannot pass his physical fitness examination. At this time, you broach the topic of his ability to complete aviation training and sustain a career in military aviation.

AEROMEDICAL DISPOSITION

Although the prevalence of PAH in the general population is not known, no longer is it thought of as a disease exclusively of childbearing-age females. It is a disease that affects all age groups, genders, and ethnicities,[12] and the flight surgeon should be aware of its presence in the military population. PAH is not compatible with aviation military service, as it prevents service members from performing their functional duties. Aeromedical concerns are centered on PAH's highly variable prognosis that is often progressive and fatal. Furthermore, hypoxia as found at altitude induces pulmonary vasoconstriction, worsening the symptoms of PAH. PAH can, in turn, lead to interventricular septal deviation toward the left ventricle that may delay filling and cause diastolic dysfunction.[2] PAH is not detailed in its own section in military aeromedical guides. However, PAH is a disqualifying condition in the U.S. Army Aeromedical Policy Letters, the U.S. Navy Aeromedical Reference and Waiver Guide, and the U.S. Air Force Waiver Guide as part of the waiver considerations for conditions such as obstructive sleep apnea, atrial septal defects, cardiomyopathy, and venous thrombosis. In addition, the daily use of tadalafil is not authorized by the U.S. Army, Navy, or Air Force while on flight status.[9,13,14] The Federal Aviation Administration's Guide for Aviation Medical Examiners also does not explicitly address PAH, but includes PAH in its list of signs that suggest that an airman may have an increased risk for obstructive sleep apnea.[3]

Although the exact etiology of this service member's PAH is unknown, it was determined that his inability to perform his minimum physical requirements and the likely progressive nature of his disease disqualified him from aviation service. The service member was removed from aviation training and is currently awaiting the results of a medical evaluation board, where he will most likely not meet retention standards for his branch of service.

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