

# You're the Flight Surgeon

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You are an Air Force flight surgeon assigned to an overseas clinic that supports two airlift squadrons. You are seeing morning sick call and your first patient is a previously healthy 32-yr-old African-American C-21 (Learjet 35) pilot who presents with a chief complaint of nonproductive cough and fever for the past 5 d. He also complains of anorexia and fatigue. He denies dyspnea, wheezing, night sweats, dizziness, significant travel history, sick contacts, smoking history, nasal congestion, heartburn, or seasonal allergies. He has no significant past medical history and takes no medications. On physical exam his vital signs include the following: temperature 100.6°F (38.1°C), blood pressure 116/76, heart rate 82, respiratory rate 16, and pulse oximetry 95% on room air. In general he appears tired but healthy. His head, eyes, ears, nose, and throat exam shows a clear oropharynx without pharyngeal injection or cobblestoning, normal tympanic membranes that demonstrate normal mobility, patent nares without erythema or discharge, and supple neck without cervical lymphadenopathy. His lungs are clear to auscultation without wheezes or rhonchi and his heart demonstrates regular rate and rhythm without murmurs, rubs, or gallops. The abdomen is soft, nontender, and without appreciable organomegaly. His extremities have no edema and strong peripheral pulses. His skin exam reveals no lesions.

## 1. What is the most likely diagnosis at this point?

- A. Upper respiratory tract infection.
- B. Bacterial pneumonia.
- C. Asthma.
- D. Gastroesophageal reflux.

## ANSWER/DISCUSSION

**1. A.** An upper respiratory infection of viral etiology would be the most common cause for these symptoms. Pneumonia is possible, but his pulmonary exam is unremarkable and his cough is nonproductive. Asthma seems unlikely, as it classically presents with shortness of breath or wheezing and would not cause a fever. Gastroesophageal reflux is possible, as heartburn symptoms need not be present, but symptoms would not be associated with fever.

You prescribe a codeine-containing cough suppressant to help the pilot sleep and place him on duties not to include flying status with

instructions to follow up in the next 48 to 72 h or sooner if worsening or new symptoms arise. He follows up with you in 3 d and is concerned regarding the duration of symptoms. He reports that his cough has improved only when he takes the prescribed medication but is still present. He also admits to some shortness of breath associated with the cough that he had previously been reluctant to admit due to concern regarding his continued flying status. He denies new symptoms and the physical exam remains unchanged.

## 2. Which of the following would be the best next step?

- A. Chest x-ray (CXR), complete blood count, and complete metabolic panel.
- B. Chest computed tomography (CT).
- C. Spirometry.
- D. No testing indicated at this point.

## ANSWER/DISCUSSION

**2. A.** Shortness of breath requires further investigation. You order a CXR, which is remarkable only for bilateral hilar adenopathy. Laboratory evaluation reveals normal blood cell lines and serum electrolytes. A chest radiograph is preferred over CT for initial evaluation of cough. Spirometry indications include differentiating restrictive lung disease from obstructive lung disease, differentiating cardiac-induced versus pulmonary-induced shortness of breath, along with diagnosing asthma. Spirometry is most often used as a means to track the course of a disease rather than as a diagnostic tool. In this case, ordering spirometry is a reasonable option but not the best next step.

## 3. Based on this information, which diagnosis tops your differential diagnosis list?

- A. Pneumonia.
- B. Bronchitis.
- C. Berylliosis.
- D. Sarcoidosis.

DOI: 10.3357/AMHP.3945.2015

## ANSWER/DISCUSSION

**3. D.** Sarcoidosis is the most likely diagnosis given the radiograph result. Bilateral hilar adenopathy is not characteristic of either pneumonia or bronchitis. Radiographic findings of pneumonia usually involve evidence of infiltrate or opacities consistent with lung consolidation. Bronchitis is a clinical diagnosis and may have nonspecific changes on CXR such as increased lung markings, bronchial wall thickening, or tubular opacities. Environmental exposures to aluminum, beryllium, and zirconium can produce a granulomatous reaction similar to sarcoidosis. Berylliosis is a consideration based on these CXR findings, but the diagnosis would require an occupational or recreational exposure to beryllium. The patient's occupation as a pilot makes this unlikely and specific questioning confirms a lack of exposure.

Sarcoidosis is a granulomatous process that can affect any organ system, with the pulmonary system most commonly involved. The diagnosis may be delayed due to nonspecific signs and symptoms or because the individual is asymptomatic. Asymptomatic patients are typically identified on routine chest radiograph and account for 30–50% of patients newly diagnosed with sarcoidosis.<sup>4</sup> Sarcoidosis is also complicated by ethnic differences. African-Americans have a tripled risk compared to the Caucasian population. The rate of sarcoidosis in the male and female population is 5.9 and 6.3 per 100,000 person-years, respectively.<sup>8</sup> Clinical presentation is typically prior to the age of 40, most commonly in the third decade of life.<sup>12</sup> The etiology remains unclear, with evidence suggesting an infectious cause along with a genetic predisposition for sarcoidosis. Proposed infectious causes include mycobacteria, viruses, and bacteria such as *Borrelia burgdorferi* and *Propionibacterium acnes*.<sup>8</sup>

Symptoms are variable based on ethnicity, racial background, and severity of organ involvement. Acute sarcoidosis is more common in the Caucasian population and typically has a spontaneous remission within 2 yr. Of patients presenting with Lofgren's syndrome (fever, weight loss, ankle arthritis, erythema nodosum, myalgias, and bilateral hilar adenopathy), 90% also typically experience spontaneous remission within 2 yr.<sup>12</sup> Nonspecific symptoms such as fatigue, weight loss, malaise, and low-grade fever are reported by one-third of sarcoidosis patients. These symptoms are more common in African-Americans and Asian Indians.<sup>8</sup> Chronic sarcoidosis typically has a gradual onset and is classified as to whether or not there is pulmonary involvement. Common pulmonary symptoms are dry cough, dyspnea, and chest pain. Of patients with pulmonary sarcoidosis, 85 to 95% will have abnormal chest radiographs. Pulmonary sarcoidosis can be staged according to the chest radiograph findings. Stage I is characterized by bilateral hilar adenopathy. Stage II has bilateral hilar adenopathy with reticular opacities. Stage III is defined by reticular opacities with shrinking hilar nodes. Stage IV disease manifests with significant parenchymal involvement, including reticular opacities, volume loss, traction bronchiectasis, calcification, cavitation, and/or cyst formation.<sup>8</sup>

Extrapulmonary manifestations can involve multiple organ systems. Erythema nodosum, although nonspecific, is a common cutaneous finding in sarcoidosis. Firm papular lesions, usually 2 to 5 mm in size, are another common skin complaint. Lupus pernio involving the nose, cheeks, and lips portends a poor prognosis, as it is often associated with severe pulmonary sarcoidosis. Sarcoidosis may also affect any part of the eye; a common manifestation is anterior uveitis, which often presents with a red, painful eye, photophobia, and blurred vision. Other associated eye disorders include conjunctivitis, posterior uveitis, and optic

neuropathy. Hepatic sarcoidosis is typically asymptomatic; however, patients may present with abdominal pain and pruritus.<sup>4</sup> Renal involvement may cause membranous nephropathy, glomerulonephritis, polyuria, hypertension, and tubular defects. Calcium metabolism may be abnormal due to production of extrarenal calcitriol.<sup>8</sup> One-quarter of patients may have splenic enlargement, which can lead to anemia, leukopenia, and thrombocytopenia. Cardiac and central nervous system (CNS) involvement is of particular concern and will be further elaborated.

The diagnosis of sarcoidosis is dependent on the presence of non-caseating granulomas. If no skin or lymph node involvement is available for biopsy, flexible bronchoscopy is a commonly used method to obtain bronchial and transbronchial samples. If this method is inconclusive, then other procedures such as mediastinoscopy, video-assisted thoracoscopy, or lung biopsy can be performed.<sup>6</sup> Biologic markers can also be used in the diagnosis. Of untreated patients, 75% will have an elevated angiotensin-converting enzyme level with a low false positive rate. A bronchoalveolar lavage CD4 to CD8 ratio greater than 3.5 also provides valuable diagnostic information.<sup>12</sup> Spirometry may be normal or may show a restrictive pattern depending on the location of pulmonary granulomas and establishes a baseline for serial testing.<sup>8</sup>

#### 4. What is the most appropriate treatment for our patient at this point?

- A. Inhaled corticosteroids.
- B. Systemic corticosteroids.
- C. Methotrexate.
- D. Observation.

## ANSWER/DISCUSSION

**4. A.** Treatment of symptomatic pulmonary sarcoidosis typically uses inhaled corticosteroids, but may involve systemic corticosteroids if more severe. Pulmonary sarcoidosis may not require treatment, as many patients are without symptoms and may follow a course of non-progression or remission. Because our patient has stage I pulmonary sarcoidosis with only mild respiratory symptoms, a trial of inhaled corticosteroids is indicated. Methotrexate is a second-line therapy and is typically used in the setting of steroid-refractory disease or in the presence of significant steroid-associated adverse effects.<sup>3</sup>

From an aeromedical standpoint, the three most concerning areas of involvement include the pulmonary, cardiac, and neurologic systems. Restrictive pulmonary disease can present an aeromedical concern if gas exchange is altered. Patients with stage II or III pulmonary disease are at risk for developing hypoxic symptoms earlier due to decreased oxygen diffusion. Cardiac sarcoidosis can present as sudden death, accounting for between 23–66% of sarcoidosis-related deaths. Granulomas and cardiac tissue fibrosis lead to myocardial dysfunction, and infiltration of the electrical system can lead to arrhythmias. Commonly seen cardiac rhythm abnormalities are supraventricular arrhythmias such as tachycardia and atrial fibrillation, along with right bundle branch block and ectopic beats. Cardiac sarcoidosis can be present without clinical symptoms or electrical signs. An electrocardiogram (ECG), although routinely obtained, may not detect sarcoidosis involving the heart. If the ECG is abnormal, an echocardiogram is obtained; if the

echocardiogram is abnormal, further imaging is warranted. Magnetic resonance imaging allows visualization of areas of sarcoid involvement.<sup>2</sup> Neurological involvement is also of concern to the flight surgeon. Manifestations of CNS involvement include hypothalamic hypopituitarism, central diabetes insipidus, hydrocephalus, lymphocytic meningitis, cranial nerve palsies, and seizures. CT and magnetic resonance imaging can aid in the diagnosis if neurological symptoms are present.

According to Air Force standards, sarcoidosis is disqualifying for all flying classes. For air traffic controllers, ground-based controllers, and space and missile operations duty personnel, sarcoidosis is disqualifying if progressive, with severe or multiple organ involvement not responsive to therapy. A history of cardiac or CNS involvement is not waivable. No aviator should fly while undergoing systemic steroid treatment due to the unpredictability of side effects, especially involving the CNS. Air Force pilots may be considered for aeromedical waiver if asymptomatic, stable, and without functional impairment, and it has been at least 6 mo since any systemic steroid treatment. An aeromedical waiver requires a thorough history, including occupational and environmental exposures, symptoms, activity level, and medications, along with a complete physical exam with emphasis on pulmonary, cardiac, neurologic, ocular, hepatic, and dermatologic systems. Testing should include CXR, biopsy results, spirometry, tuberculosis skin test, ECG, and 24-h Holter monitor. Laboratory evaluation includes complete blood count, calcium, liver function tests, creatinine, blood urea nitrogen, urinalysis, and 24-h urine calcium.<sup>10</sup> Navy aviators with sarcoidosis are disqualified for flying duties until they are asymptomatic without medications at least 2 yr.<sup>7</sup> Army aviators diagnosed with sarcoidosis are also disqualified. However, a waiver may be granted if in remission for at least 1 yr with a normal systemic work-up.<sup>9</sup> Therefore, once the aviator of any military service branch has stabilized, it is possible to obtain a waiver to permit flying duties. According to the Federal Aviation Administration, a special issuance is required if symptoms are present. The focus will be the involved organ system(s) with stable pulmonary function tests. CNS or cardiac sarcoidosis, even with pacemaker placement, is unlikely to be waived.<sup>5</sup> There have been no published aircraft fatalities attributed to sarcoidosis.<sup>1,11</sup>

Our patient with early stage pulmonary sarcoidosis was treated with inhaled corticosteroids with resolution of his cough and shortness of breath. His work-up was otherwise normal and he received an aeromedical waiver to continue flying duties.

**Andrus DE. *You're the flight surgeon: sarcoidosis.* *Aerosp Med Hum Perform.* 2015; 86(1):67–69.**

## ACKNOWLEDGMENT

The author would like to thank Maj. Christopher Keirns, USAF, MC, FS, of the Air Force Aeromedical Consult Service, for his invaluable review and clinical expertise as it pertains to sarcoidosis. The views expressed in this article are those of the author and do not necessarily reflect the official policy or position of the Air Force, the Department of Defense, or the U.S. Government.

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This article was prepared by Niraj Govil, M.D., M.P.H., M.S.

It's a busy Monday morning with patients. You have an inordinate amount of return to flying status patients as well as flying physical health assessments to perform. Suddenly, the phone rings on your direct line. It's the operations group commander; he is very concerned about one of his pilots.

This is one of the more stellar pilots in the squadron. He is a 35-yr-old male instructor pilot with over 1800 total military flying hours. To add to his flying responsibilities, he has many other stressors, including taking extra classes to complete his master's degree before meeting the lieutenant colonel board, having a 12-mo-old son, and suffering from a loss of sleep due to helping his wife with the kids and housework.

DOI: 10.3357/AMHP.4025.2015