

Chapter 14

VALUE OF LUNG BIOPSY IN WORKUP OF SYMPTOMATIC INDIVIDUALS

ROBERT MILLER, MD*

INTRODUCTION

THE MISHRAQ SULFUR MINE FIRE

CONSTRICTIVE BRONCHIOLITIS

CLINICAL PRESENTATIONS

EVALUATIONS

WHY NONINVASIVE STUDIES FAIL TO DETECT CONSTRICTIVE BRONCHIOLITIS

LONG-TERM FOLLOW-UP

RECOMMENDATIONS

SUMMARY

**Associate Professor of Medicine, Vanderbilt University School of Medicine, Division of Allergy, Pulmonary, and Critical Care Medicine, 6134 Medical Center East, Nashville, Tennessee 37232-8288*

INTRODUCTION

More than 2 million US service members have been deployed to the Middle East since 2001, including Operation Enduring Freedom (OEF) beginning in 2001 and Operation Iraqi Freedom (OIF) beginning in 2003. Service members participating in both conflicts experienced a variety of inhalational exposures. Some exposures, such as dust storms, were related to climate and location. Other inhalational exposures were associated with mission-oriented settings, including battlefield smoke, burning solid waste, burning oil, diesel exhaust, etc. There were still other exposures that were unique to specific countries, regions, and events. These unique exposures may have been limited in duration and scope, but frequently impacted large numbers of service members.

Inhalational exposures associated with service in Iraq and Afghanistan have received a lot of attention because of the number of troops involved and the high incidence of respiratory complaints linked to service. Reports of respiratory symptoms were common among service members deployed to Operation Desert Storm in the 1990s and more recently in soldiers returning from Iraq and Afghanistan. Epidemiological studies in the United States, England, and Australia have documented an increased incidence of respiratory disorders in soldiers who served in the Middle East versus soldiers deployed elsewhere. A 2009 study of 46,000 military personnel described increased respiratory symptoms among service members functioning in inland settings versus shore environments.¹⁻⁴

Deployments to Iraq and Afghanistan have been associated with a spectrum of respiratory complaints, including

- cough,
- bronchitis,

- shortness of breath,
- asthma,^{1,2,5-8}
- eosinophilic pneumonia,⁹ and
- small airway disease.¹⁰

Many soldiers became symptomatic during deployment. However, a larger number became symptomatic following deployment.^{2,10}

Surveys of soldiers returning from OEF/OIF estimate that 69% of personnel reported respiratory symptoms associated with deployment.⁷ Based on the *International Classification of Diseases, Ninth Revision, Clinical Modification* coding, Abraham et al¹¹ showed that a large number of these cases may be from obstructive lung disease (asthma and bronchitis). Their methods relied on coding and did not require supportive data, such as pulmonary function testing (PFT), X-ray films, or exercise testing that may offer more specific definition of the disorders. The Millennium Cohort Study (MCS) surveyed 46,000 soldiers and found an increased incidence of respiratory symptoms among soldiers who had been deployed versus those who had not been deployed. However, the differences that investigators initially noted between deployed versus nondeployed soldiers within the MCS could not be explained by an increased incidence of asthma, bronchitis, or emphysema.⁴ The MCS findings suggest that there may be other respiratory disorders contributing to the high incidence of respiratory complaints.

Clearly, there is a high incidence of respiratory disorders associated with Middle East deployment. Although many individuals returning from service in the Middle East have respiratory disorders that meet criteria for specific diagnoses, a significant number of service members returning with symptoms have been more difficult to characterize.

THE MISHRAQ SULFUR MINE FIRE

Approximately 20,000 soldiers from the 101st Airborne (Fort Campbell, KY) were deployed to Northern Iraq as part of OIF in early 2003. In July 2003, the Mishraq Sulfur Mine—located 25 km northeast of Camp Q West and 50 km south of Mosul Airfield—caught fire. Most of the Fort Campbell soldiers resided in the vicinity of the fire.

Extinguishing the Mishraq Sulfur Mine fire presented risks to both civilians and military personnel. The fire burned for 1 month and reportedly released 21 million pounds of sulfur dioxide (SO₂) a day.¹² Sulfur fires, like the Mishraq fire, release both hydrogen sulfide (H₂S) and SO₂. H₂S is a noxious gas with an odor compared to rotten eggs; it causes neuromuscular weakness and, in severe cases, respiratory failure. The effects of H₂S are believed to be reversible once

exposure to H₂S has ended. SO₂ has an odor compared to burning matches and is a potent pulmonary toxin. It is associated with upper airway irritation, irritant asthma, and constrictive bronchiolitis (CB).¹³

The US Army collected a limited number of random air samples during the fire. More than 50% of the 32 samples were above the Army's maximal standard of 13 parts per million (ppm). Some of the concentrations were as high as 120 parts per million.¹⁴

The health effects of SO₂ exposure can manifest at the time of exposure or long afterward. Acute effects include airway irritation, cough, bronchoconstriction, and wheezing. Asthmatics are particularly sensitive to SO₂. Chronic effects of SO₂ exposure include reactive airways dysfunction

syndrome, chronic obstructive pulmonary disease, CB, and increased frequencies of acute asthma exacerbations.^{10,15}

Most of the soldiers deployed with the 101st Airborne in early 2003 returned in early 2004. Many deployers returned to Fort Campbell complaining of increased dyspnea

on exertion and an inability to complete their 2-mile runs within regulation time. Standard pulmonary evaluations at Fort Campbell's Blanchfield Army Community Hospital failed to reveal a specific cause for the soldier's exercise limitations.

CONSTRICTIVE BRONCHIOLITIS

Fort Campbell's Blanchfield Army Community Hospital began referring patients with exercise limitations to Vanderbilt University Medical Center in 2004. Vanderbilt providers were aware of the increase in respiratory complaints associated with Operation Desert Storm in 2001^{1,2,5} and reports of eosinophilic pneumonia associated with OIF in 2003 to 2004.⁹ Patients referred to Vanderbilt, however, did not seem to have asthma and did not fit the pattern of eosinophilic pneumonia.

Vanderbilt and Blanchfield providers created a protocol to evaluate soldiers returning with unexplained shortness of breath. The protocols included chest X-ray radiographs, high-resolution computerized tomography (HRCT), full PFT, and cardiopulmonary exercise testing (CPET). For most patients, these studies were normal or near normal and did not identify the cause for their exercise limitation.

Approximately one-half of the soldiers referred underwent thoracoscopic lung biopsy to better understand the cause for their limitation. Performing surgical lung biopsy in the setting of normal chest imaging, normal PFT, and CPET is unusual. However, at the time of deployment, the majority of the soldiers exhibited high levels of physical fitness, and, on return, these deployers were incapable of completing a

2-mile run within regulation time. Exercise limitations persisted, and service members were declared nondeployable and were facing discharge without a compensable diagnosis.

Lung biopsies appeared to provide an explanation for the soldiers' exercise limitations. In the majority of cases, the small airways had features of CB. Several of the biopsies had other small airway and/or parenchymal abnormalities, including respiratory bronchiolitis, respiratory bronchiolitis with interstitial lung disease, nonspecific small airway scarring, and sarcoidosis (Table 14-1).

The pathological characteristics of CB consist of extrinsic narrowing of the luminal wall from subepithelial fibrin or smooth-muscle deposition in membranous bronchioles. In most cases, the remaining portions of the lung parenchyma appear normal. All soldiers diagnosed with CB met this case definition, but individual variations were noted. There were varying degrees of smooth muscle versus fibrin deposition. Most, but not all, biopsies had accompanying arteriopathy. Many biopsies had associated inflammation noted as inflammatory luminal granulation, bronchial-associated lymphoid tissue, or respiratory bronchiolitis. Almost all cases had peribronchial pigment deposition, the composition of which is currently being investigated (Figure 14-1).

TABLE 14-1

HISTOPATHOLOGY OF 65 SERVICE MEMBERS UNDERGOING SURGICAL LUNG BIOPSY AT VANDERBILT UNIVERSITY MEDICAL CENTER BETWEEN 2005–2012

No.	Pathological Diagnosis
52	Constrictive bronchiolitis
4	Respiratory bronchiolitis
2	Respiratory bronchiolitis with interstitial lung disease
2	Hypersensitivity pneumonitis
3	Sarcoidosis
2	Other

Note: Between 2004–2010, 80 soldiers were evaluated with unexplained shortness of breath; 49 of them were referred for video-assisted thoracoscopic surgery. The majority of them met the criteria for constrictive bronchiolitis. Although all of the diagnoses are consistent with inhalational causes, the focus is on those soldiers who were diagnosed with constrictive bronchiolitis.

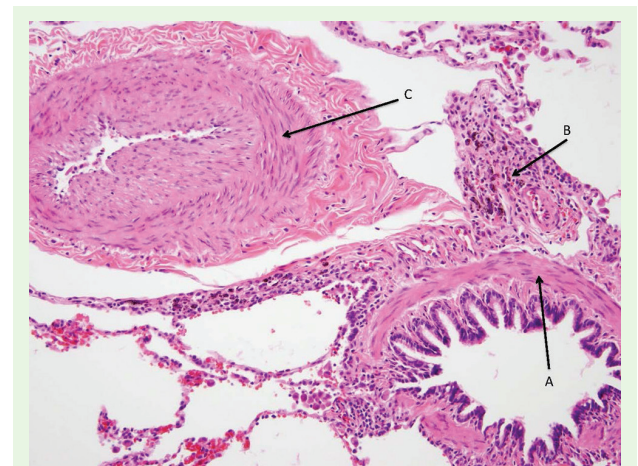


Figure 14-1. Peribronchial pigment deposition. (A) Intra-luminal deposition of fibrin and smooth muscle resulting in airway narrowing. (B) Peribronchial pigment deposition. (C) Arteriopathy associated with bronchiolar changes.

The initial suspicion was that the sulfur mine fire was the only cause for constrictive bronchiolitis. Over time, however, more soldiers presented with exercise limitations who had not been exposed to the Mishraq Sulfur Mine fire. Twenty-five percent of the original 38 soldiers with CB had only the usual exposures and were not exposed to the sulfur fire. Vanderbilt investigators have now biopsied 65 soldiers, with 52 having CB. More than 50% of those examined had the usual exposures associated with deployment and no exposure to the sulfur mine fire.¹⁰

The diagnosis of CB did not lead to significant changes in therapy, but did provide an explanation for symptoms. More importantly, soldiers diagnosed with the disorder were able to receive disability benefits that would not have been available without biopsy. Soldiers who have unexplained exercise limitation and who do not undergo biopsy typically do not receive a rating for their disorder unless another label such as asthma is assigned.

Surgical biopsies of the lung have always been controversial. The controversy for returning service members and their providers involves doing biopsies for those with symptoms who happen to have normal preoperative studies. The procedure is invasive and is associated with a small, but real, risk of complications. There is always a question of how a positive biopsy will affect clinical management or benefit

the patient. Clinicians often wonder if there is enough of a benefit to justify the risk. They will also consider the possibility of less invasive approaches for either diagnosis or to direct therapy.

Fort Campbell and Vanderbilt providers felt that biopsies were appropriate and in the best interest of the soldiers. Biopsies provided an explanation for the patients' exercise limitations. Biopsies also confirmed inhalational injury and helped characterize a disorder that had not been previously described in service members. Biopsy results did not usually affect treatment as there are no known treatment options for patients with constrictive bronchiolitis. Many soldiers were spared treatment with potentially high-risk therapy, such as systemic corticosteroids that are not effective in this disorder.

At some point, it may be possible to identify this disorder without a biopsy. An example is the use of surgical lung biopsies for interstitial lung disease. Lung biopsies for interstitial lung disease are less common than they were in the past. Noninvasive studies, including better serological studies and recognizable patterns on HRCT, have allowed clinicians to identify disorders such as idiopathic pulmonary fibrosis without biopsy. For now, however, the only way for soldiers to obtain appropriate compensation for this war-related injury is histological confirmation.

CLINICAL PRESENTATIONS

Soldiers serving in Iraq and Afghanistan appear to experience a wide spectrum of respiratory symptoms. Service members deployed to Operation Desert Storm had a higher incidence of respiratory complaints and asthma-like symptoms¹⁻⁴ that manifested more frequently in postdeployment settings.^{2,10} Service members in both OEF and OIF commonly complained of cough upon arrival in the Middle East.¹¹ There have been reports of acute respiratory failure from eosinophilic pneumonia,⁹ as well as an increased incidence of asthma among OEF/OIF deployers.⁸

All of the soldiers diagnosed with CB had exercise limita-

tions, and most of them also had cough or chest tightness. Unexplained exercise limitations and, specifically, an inability to complete a 2-mile run within regulation time strongly correlated with the presence of CB (in the absence of other explanations for such limitations).

Service members typically became symptomatic post-deployment, with a unique association to restarting their training regimens. Two of the Vanderbilt patients diagnosed with CB, however, developed acute respiratory distress during deployment and later ended up with exercise and PFT impairments more severe than other patients.

EVALUATIONS

Providers caring for soldiers with shortness of breath or other respiratory symptoms postdeployment should obtain a formal occupational exposure history for each deployment. Most patients will need standard chest X-ray radiographs and full PFT. Methacholine challenge may be helpful in screening for asthma, but was usually negative for patients diagnosed with CB.¹⁰

CPET appears to be a less-sensitive screening tool for small airways disease. Patients with CB appear to have mean levels of maximal oxygen consumption and anaerobic thresh-

olds at lower limits of normal; however, many CB patients are clearly within normal range (maximal oxygen consumption: 80% of the predicted value; anaerobic threshold: 40% of the predicted maximal oxygen consumption). PFT and CPET measurements in this cohort were lower than those reported for soldiers who had not been deployed (Tables 14-2 and 14-3).^{16,17} CPET will be difficult to use as a diagnostic screen until better baseline data exist for CPET studies of healthy soldiers who have never been deployed. CPET may be valuable to monitor for progression in those diagnosed

TABLE 14-2

PULMONARY FUNCTION TESTING IN THE INITIAL 38 SOLDIERS DIAGNOSED WITH CONSTRICTIVE BRONCHIOLITIS*

	Comparison Group ^{1,2}	Patient [†]	p Value
FEV ₁ (%pred)	99.1 ± 9.2	86.7 ± 13.3	<0.001
FVC (%pred)	101.6 ± 10.7	90.3 ± 13.2	<0.001
FEV ₁ /FVC (%)	97.4 ± 5.0	79.1 ± 7.6	<0.001
TLC (%pred)	99.6 ± 12.0	96.1 ± 15.5	0.230
DLCO (%pred)	90.6 ± 12.6	73.4 ± 15.4	<0.001

* Not matched for age and body mass index.

[†] Only one of our patients had pulmonary function testing prior to deployment.

DLCO: diffusing capacity of the lungs for carbon monoxide; FEV₁: forced expiratory volume in 1 second; FVC: forced vital capacity; pred: predicted; TLC: total lung capacity

Data sources: (1) Morris MJ, Grbach VX, Deal LE, Boyd SY, Morgan JA, Johnson JE. Evaluation of exertional dyspnea in the active duty patient: the diagnostic approach and the utility of clinical testing. *Mil Med.* 2002;167:281–288. (2) Still JM, Morris MJ, Johnson JE, Allan PF, Grbach VX. Cardiopulmonary exercise test interpretation using age-matched controls to evaluate exertional dyspnea. *Mil Med.* 2009;174:1177–1182.

with CB or suspected of having CB.

When standard PFT and chest X-ray radiographs fail to yield a diagnosis or to help guide therapy, additional testing should include HRCT. The HRCT test was usually normal or near-normal in patients who were ultimately diagnosed with CB. However, HRCT did show changes with other diagnoses, such as hypersensitivity pneumonitis, sarcoidosis, and bronchiectasis.¹⁰

WHY NONINVASIVE STUDIES FAIL TO DETECT CONSTRICTIVE BRONCHIOLITIS

Noninvasive studies, such as PFT, CPET, and HRCT do not appear to provide adequate screening for CB in soldiers following deployment. Many reasons for this have been considered. The small airways of the lungs represent the largest cross-sectional area of the tracheobronchial tree. As a result, symptoms may not occur until a large cross-section has been affected.^{20–22}

Those soldiers diagnosed with CB were highly trained, elite athletes prior to becoming symptomatic. Most patients presented because they could no longer exercise at high capacity. The PFT and CPET were within normal limits for most patients diagnosed with CB. The question became this: Were CB patients' PFT/CPET results lower than what they would have been prior to deployment? Only one of the soldiers had predeployment PFT, and his predeployment study appeared to be much better than his PFTs prior to biopsy.

TABLE 14-3

CARDIOPULMONARY EXERCISE TESTING IN THE INITIAL 38 SOLDIERS DIAGNOSED WITH CONSTRICTIVE BRONCHIOLITIS*

	Comparison Group ^{1,2}	Patient	p Value
VO _{2max} (%pred)	105.4 ± 14.3	85.1 ± 15.2	<0.001
VATS (%VO _{2max})	78.2 ± 15.3	45.0 ± 9.5	<0.001
Max HR (%pred)	95.2 ± 5.7	87.2 ± 9.5	<0.001
RR (breaths/min)	44.5 ± 6.7	34.2 ± 7.7	<0.001
V _E /VCO ₂ (%pred)	31.9 ± 4.0	28.3 ± 3.5	<0.001

*Not matched for age and body mass index.

Max HR: maximal heart rate; pred: predicted; RR: respiratory rate; VATS: video-assisted thoracoscopic surgery; V_E: minute ventilation; VCO₂: carbon dioxide production; VO_{2max}: maximal oxygen consumption

Data sources: (1) Morris MJ, Grbach VX, Deal LE, Boyd SY, Morgan JA, Johnson JE. Evaluation of exertional dyspnea in the active duty patient: the diagnostic approach and the utility of clinical testing. *Mil Med.* 2002;167:281–288. (2) Still JM, Morris MJ, Johnson JE, Allan PF, Grbach VX. Cardiopulmonary exercise test interpretation using age-matched controls to evaluate exertional dyspnea. *Mil Med.* 2009;174:1177–1182.

Some clinicians have recommended screening all soldiers with unexplained respiratory problems for vocal cord dysfunction (VCD).^{18,19} Although this may be a simple maneuver, the cohort with CB did not have symptoms typical for VCD (eg, wheezing, stridor, or throat clearing). Patients evaluated at Vanderbilt did not have any upper airway symptoms to suggest VCD. Vanderbilt patients had CB, a diagnosis that seemed to explain their respiratory complaints.

The possibility exists that this cohort suffered significant loss of function, but still tested in a range of normal. This possibility was supported when the Vanderbilt cohort was compared with historical controls.^{16,17} An analogous cohort would include firefighters who worked at the World Trade Center site in 2011 to 2012. Each firefighter had annual spirometry prior to the World Trade Center attacks. Mean forced expiratory volume in 1 second measurements several months after working at the World Trade Center site were 439 cc lower than pre-September 2011 studies.²³

Vanderbilt biopsies showed that 64% (95% confidence interval, 57.6–71 on nonparametric bootstrap analysis) of the small airways were affected in the 38 soldiers diagnosed with CB.¹⁰ Findings of CB appear to be correlated with a reduced exercise capacity, but not severe changes in PFT and CPET; these disparities need to be examined. Could CB possibly be

associated with exercise-induced air-trapping not evident at rest? Pathology examination shows significant arteriopathy associated with small airway changes. Is pulmonary hypertension with exertion a possibility? Both of these prospects need to be considered as we evaluate this population.

Clearly, CB is one of the conditions contributing to a rising incidence of respiratory disorders following deployment. The relative contribution of CB to the rising incidence of respiratory complaints has not been quantified

because as many clinicians fail to consider the disorder. The fact that CB requires surgical biopsy for diagnosis has hampered efforts to identify the association between CB and deployment-related respiratory complaints. Experts from a number of fields agree that exposures in Iraq and Afghanistan place deployers at risk for respiratory symptoms and disease. Evaluations of deployed populations would be easier if we had both pre- and postdeployment data from service members.

LONG-TERM FOLLOW-UP

The majority of service members diagnosed with CB left military service with a disability rating or retirement. A few continued to serve in noncombat capacities, and others continued to serve with further exposure to Middle East environments. Those who have followed up at Vanderbilt complain of persistent exercise limitations and, in some cases, progressive exercise limitations. Most service members have gained weight from being more sedentary and not being able to exercise. Follow-up chest X-ray radiographs,

HRCT, and PFTs have been performed on several of those diagnosed with CB and have generally remained stable. Many service members undergoing follow-up CPET have demonstrated reduced exercise capacities compatible with deconditioning, but also consistent with disease progression. The US Department of Veterans Affairs has recognized CB as being associated with service in the Middle East. They will inherit the responsibility for following this population over time and monitoring disease progression.

RECOMMENDATIONS

In February 2010, a working group of pulmonologists, occupational and preventive specialists, industrial hygienists and exposure scientists, the US Department of Defense, and the Department of Veterans Affairs convened at National Jewish Health (Denver, CO) to discuss inhalational exposures and the risk of respiratory disease associated with deployment to the Middle East.²⁴ This group recommended

- pre- and postdeployment respiratory questionnaires, as well as pre- and postdeployment spirometry;
- formal pulmonary evaluations for soldiers experiencing persistent cough, shortness of breath, or an unexplained drop in physical readiness testing; and
- surgical lung biopsies, when appropriate.

SUMMARY

Respiratory symptoms and a number of respiratory disorders have been linked to service in the Middle East. Some service members become symptomatic during deployment, but many will become symptomatic only after returning home. Disorders such as asthma may be easy to diagnose with PFT and may respond to standard treatment. Some patient complaints may be nonspecific in nature and appropriate to follow or treat empirically. Disorders affecting small airways may be more difficult to diagnose and even

more disabling. Providers need to be aware that there is a group of patients who served in the Middle East who may have advanced airways disease in the absence of normal noninvasive testing. Individuals with this presentation should be evaluated by providers with expertise in the area of interstitial lung disease or postdeployment respiratory disorders. Lung biopsies may be necessary to complete the evaluation of some individuals presenting with unexplained shortness of breath.

REFERENCES

1. Haley RW, Kurt TL. Self-reported exposure to neurotoxic chemical combinations in the Gulf War: a cross-sectional epidemiologic study. *JAMA*. 1997;277:231-237.
2. Coker WJ, Bhatt BM, Blatchley NF, Graham JT. Clinical findings for the first 1000 Gulf war veterans in the Ministry of Defence's Medical Assessment Programme. *BMJ*. 1999;318:290.

3. Kelsall HL, Sim MR, Forbes AB, et al. Respiratory health status of Australian veterans of the 1991 Gulf War and the effects of exposure to oil fire smoke and dust storms *Thorax*. 2004;59:897–903.
4. Smith B, Wong CA, Smith TC, et al. Newly reported respiratory symptoms and conditions among military personnel deployed to Iraq and Afghanistan: a prospective population-based study. *Am J Epidemiol*. 2009;170:1433–1442.
5. Petruccelli BP, Goldenbaum M, Scott B, et al. Health effects of the 1991 Kuwait oil fires: a survey of US Army troops. *J Occup Environ Med*. 1999;41:433–439.
6. Roop SA, Niven AS, Calvin BE, et al. The prevalence and impact of respiratory symptoms in asthmatics and nonasthmatics during deployment. *Mil Med*. 2007;172:1264–1269.
7. Sanders JW, Putnam SD, Frankart C, et al. Impact of illness and non-combat injury during Operations Iraqi Freedom and Enduring Freedom (Afghanistan). *Am J Trop Med Hyg*. 2005;73:713–719.
8. Szema AM, Peters MC, Weissinger KM, et al. New-onset asthma among soldiers serving in Iraq and Afghanistan. *Allergy Asthma Proc*. 2010;31:67–71.
9. Shorr A, Scoville S, Cersovsky S, et al. Acute eosinophilic pneumonia among US military personnel deployed in or near Iraq. *JAMA*. 2004;292:2997–3005.
10. King MS, Eisenberg R, Newman JH, et al. Constrictive bronchiolitis in soldiers returning from Iraq and Afghanistan. *N Engl J Med*. 2011;365:222–230.
11. Abraham JH, DeBakey SF, Reid L, Zhou J, Baird CP. Does deployment to Iraq and Afghanistan affect respiratory health of US military personnel? *J Occup Environ Med*. 2012;54:740–745.
12. Defend America. US Department of Defense News About the War on Terrorism. <http://www.defendamerica.mil/iraq/update/june2003/iu063003.html>. Accessed September 17, 2013.
13. Charan NB, Myers CG, Lakshminarayanan S, Spencer TM. Pulmonary injuries associated with acute sulfur dioxide inhalation. *Am Rev Respir Dis*. 1979;119:555–560.
14. Department of the Army, Headquarters, 61st Medical Detachment (Sanitation). *Executive Summary: Sulfur Mine Fire, Mishraq Sulfur State Company, Objective Cheetah*. Washington, DC: DOA; July 8–14, 2003.
15. The National Academies. *Health Effects of Project Shad Chemical Agent: Sulfur Dioxide [CAS 7446-09-5]*. Silver Spring, MD: The Center for Research Information, Inc; 2004.
16. Morris MJ, Grbach VX, Deal LE, Boyd SY, Morgan JA, Johnson JE. Evaluation of exertional dyspnea in the active duty patient: the diagnostic approach and the utility of clinical testing. *Mil Med*. 2002;167:281–288.
17. Still JM, Morris MJ, Johnson JE, Allan PF, Grbach VX. Cardiopulmonary exercise test interpretation using age-matched controls to evaluate exertional dyspnea. *Mil Med*. 2009;174:1177–1182.
18. King M, Newman J, Miller R. Constrictive bronchiolitis in soldiers. *N Engl J Med*. 2011;365:1743–1744.
19. Chang AB, Masel JP, Masters B. Post-infectious bronchiolitis obliterans: clinical, radiological and pulmonary function sequelae. *Pediatr Radiol*. 1998;28:23–29.
20. Devakonda A, Raoof S, Sung A, Travis WD, Naidich D. Bronchiolar disorders: a clinical-radiological diagnostic algorithm. *Chest*. 2010;137:938–951.
21. Visscher DW, Myers JL. Bronchiolitis: the pathologist’s perspective. *Proc Am Thorac Soc*. 2006;3:41–47.
22. Schwarz MI, King TE. *Interstitial Lung Disease*. 4th ed. Hamilton, Ontario, Canada: B. C. Decker; 2003: 796.

23. Aldrich TK, Gustave J, Hall CB, et al. Lung function in rescue workers at the World Trade Center after 7 years. *N Engl J Med.* 2010;362:1263–1272.
24. Rose C, Abraham J, Harkins D, et al. Overview and recommendations for medical screening and diagnostic evaluation for post-deployment lung disease in returning US warfighters. *J Occup Environ Med.* 2012;54:1–6.