

# AMERICAN THORACIC SOCIETY DOCUMENTS

## Respiratory Health after Military Service in Southwest Asia and Afghanistan

### An Official American Thoracic Society Workshop Report: Executive Summary

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#### Abstract

Since 2001, more than 2.7 million U.S. military personnel have been deployed in support of operations in Southwest Asia and Afghanistan. Land-based personnel experienced elevated exposures to particulate matter and other inhalational exposures from multiple sources, including desert dust, burn pit combustion, and other industrial, mobile, or military sources. A workshop conducted at the 2018 American Thoracic Society International Conference had the goals of: 1) identifying key studies assessing postdeployment respiratory health, 2) describing emerging research, and 3) highlighting knowledge gaps. The workshop reviewed epidemiologic studies that demonstrated more frequent encounters for respiratory symptoms postdeployment compared with nondeployers and for airway disease, predominantly asthma, as well as case series describing postdeployment dyspnea, asthma, and a range of other respiratory tract findings. On the basis of particulate matter effects in other populations, it also is possible that deployers experienced

reductions in pulmonary function from such exposure. The workshop also gave particular attention to constrictive bronchiolitis, which has been reported in lung biopsies of selected deployers. Workshop participants had heterogeneous views regarding the definition and frequency of constrictive bronchiolitis and other small airway pathologic findings in deployed populations. The workshop concluded that the relationship of airway disease, including constrictive bronchiolitis, to exposures experienced during deployment remains to be better defined. Future clinical and epidemiologic research efforts should address better characterization of deployment exposures; carry out longitudinal assessment of potentially related adverse health conditions, including lung function and other physiologic changes; and use rigorous histologic, exposure, and clinical characterization of patients with respiratory tract abnormalities.

**Keywords:** deployment; particulate matter; constrictive bronchiolitis

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## Overview

Land-based U.S. military personnel deployed to Afghanistan and Southwest Asia in support of military operations starting in 2001 experienced exposures to elevated levels of fine particulate matter (PM) as well as other, not well-characterized inhalational exposures, leading to concerns about potential adverse health effects arising from these exposures (1). Workshop goals were to 1) summarize and assess studies evaluating post deployment respiratory health, 2) update emerging research, and 3) identify conflicting findings and knowledge gaps.

Iraq, Afghanistan, and other deployment locations include large arid and semiarid regions where there is frequent exposure to geologic dust (2, 3). Additional sources of PM include various military operations such as burn pit emissions from open-air waste burning, vehicular exhaust, and poorly regulated industrial point sources. The workshop reviewed epidemiologic studies analyzing health

encounters during military service that have demonstrated increased deployment-associated encounters for respiratory symptoms and selected airway disease diagnoses (4–6). We also considered reports based on the Veterans Health Administration (VHA) encounters for health care, suggesting that former deployers may be more frequently diagnosed with obstructive lung disease, particularly asthma (7). In addition, we reviewed case series describing the clinical assessment of postdeployment dyspnea, and we considered Millennium Cohort Study data relevant to postdeployment asthma as well as other abnormalities (8–10). Of particular note, constrictive bronchiolitis and other small airway abnormalities have been reported in lung biopsies from case referral series (11). Based on a review of the established pathologic features of constrictive bronchiolitis (12–14), opinions among workshop participants differed regarding the interpretation of the prevalence of disease reported.

On the basis of a review of the adverse health effects of exposure to particulate matter with an aerodynamic diameter <2.5  $\mu\text{m}$  (PM<sub>2.5</sub>) in general population studies (15, 16), the workshop concluded that it was plausible that deployers could have experienced particulate exposure-associated decrements in pulmonary function. It was recognized, however, that there have been no findings to date assessing long-term health effects in cohorts of U.S. military personnel exposed to high ambient PM<sub>2.5</sub> concentrations. The workshop was updated on ongoing research projects. The Department of Veterans Affairs (VA) Cooperative Studies Program is using National Aeronautics and Space Administration (NASA) satellite data and airport visibility data (17, 18) to estimate historical PM<sub>2.5</sub> levels and assess associations with pulmonary function and current asthma in a national cohort of veteran deployers. The Department of Defense (DoD) Serum Repository, which includes 60 million samples, may serve as a supplemental means

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The study protocol in section 6.c. was approved by the Naval Health Research Center Institutional Review Board in compliance with all applicable Federal regulations governing the protection of human subjects. Research data were derived from an approved Naval Health Research Center Institutional Review Board protocol number NHRC.2000.0007.

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to identify chemical compounds associated with combustion product-related environmental exposures (19). Prospective cohort studies (the Millennium Cohort Study [20] and a planned Comparative Health Assessment Interview Research Study) and follow-up of participants enrolled in the Airborne Hazards and Open Burn Pit Registry also may provide additional information regarding the development of deployment-related health conditions. Another study, based at National Jewish Health (NJH), assessing molecular effects of desert dust exposure from Southwest Asia may provide information regarding biologic mechanisms.

#### Key Conclusions

- Deployed military personnel were exposed to ambient PM and other air pollutants, with contributions from a variety of sources, including geological dust; mobile and stationary sources; industrial sites; and various military operations, including burn pits.
- Studies of deployed military personnel reported to date have not included consistent assessment of self-reported or other estimated exposures potentially relevant to adverse respiratory effects.
- Findings derived from epidemiologic studies conducted in nonmilitary populations raise concern about the potential adverse effects of PM exposure on pulmonary function in deployers.
- On the basis of military health encounter data, returning military personnel had more frequent postdeployment health encounters than nondeployed personnel for respiratory symptoms and for airway disease, predominantly asthma.
- Postdeployment asthma has been described in case series and among deployers assessed in the Millennium Cohort Study (U.S. DoD).
- Other respiratory health conditions, including constrictive bronchiolitis and other small airway abnormalities, have been described in case series.
- Workshop participants had heterogeneous views regarding the interpretation of histologic changes of constrictive bronchiolitis and other small airway findings derived from case series of veterans undergoing lung biopsy for postdeployment dyspnea.
- There is a paucity of information regarding the long-term respiratory health status of postdeployment active military personnel and veterans.
- There is a need for further research better characterizing PM and other deployment-related exposures, to better characterize the respiratory health of postdeployment military personnel and veterans, and to identify associations between such exposures and adverse respiratory health outcomes.

## Introduction

Since October 2001, more than 2.7 million U.S. military personnel have been deployed to Central Asia (Afghanistan and Kyrgyzstan), Southwest Asia (Iraq, Kuwait, Qatar, and United Arab Emirates), and Africa (Djibouti) in support of Operation Enduring Freedom (OEF), Operation Iraqi Freedom (OIF), Operation New Dawn, and continuing operations (21). Land-based personnel experienced potential exposures to elevated levels of fine PM and other pollutants, leading to concerns about possibly associated adverse health effects.

The American Thoracic Society (ATS) sponsored a workshop, “Respiratory Health after Military Service in Southwest Asia and Afghanistan,” that took place at the 2018 ATS International Conference in San Diego, California. Workshop goals were to 1) summarize and critically assess published data relevant to postdeployment respiratory health, 2) provide an update on emerging research on this question, and 3) identify knowledge gaps that could be addressed by future research.

## Methods

A cross-disciplinary group of 25 experts participated. Sixteen oral presentations included the following:

1. A review of surveys and epidemiologic studies performed among previously deployed military personnel;
2. A summary of clinical data reported for previously deployed military personnel;
3. A review of lung pathologic findings in postdeployment personnel, including biopsies interpreted as showing constrictive bronchiolitis;
4. A review of airborne pollution exposures that might occur during deployment and their potential adverse respiratory health effects, including dust storms and other sources of PM such as burn pits and other military activities;
5. An update on novel approaches to exposure assessment; and
6. A description of other ongoing or planned studies.

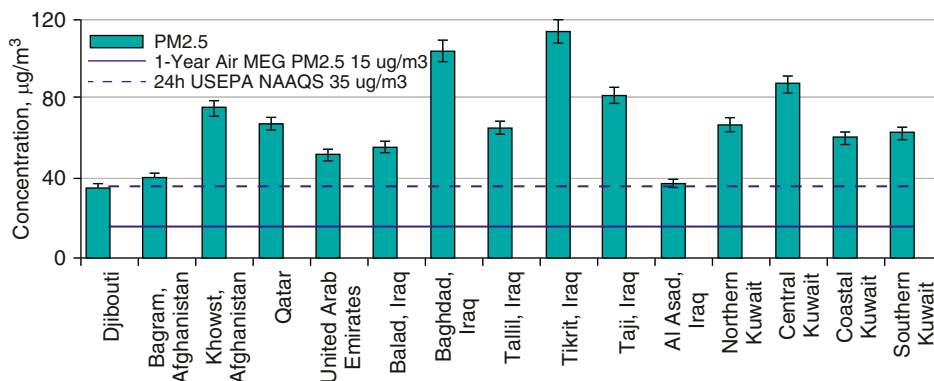
## Exposure Overview

### Exposure Assessment

Iraq, Afghanistan, and other deployment locations include large arid or semiarid regions where there is frequent exposure to desert dust and sand, including dust storms (22–24). In addition to mineral particles, dust storm particles include airborne bacteria, fungal spores, plant and grass pollens, and other agricultural pollen grains (25, 26). Additional sources of PM include: military operations, vehicle exhaust, and underregulated industrial sources. Open-air waste burning (burn pits) was the primary means of solid-waste management at military bases in Iraq, Afghanistan, and Djibouti (1). The DoD conducted the Enhanced Particulate Matter Surveillance Program (EPMSP) to characterize airborne exposures at 15 sites during 2006 and 2007 (3, 27). Mean 24-hour  $PM_{2.5}$  values were consistently high ( $\sim 40 \mu\text{g}/\text{m}^3$  to nearly  $120 \mu\text{g}/\text{m}^3$ ) (Figure 1), with concentrations that considerably exceeded the current U.S. annual  $PM_{2.5}$  exposure standard ( $12 \mu\text{g}/\text{m}^3$ ), the 1-year Military Exposure Guideline (solid blue line in Figure 1), and the 24-hour National Ambient Air Quality Standard ( $35 \mu\text{g}/\text{m}^3$ ; broken blue line in Figure 1).  $PM_{2.5}$  levels estimated based on military airport visibility data in Iraq, Afghanistan, Kuwait, and other countries in Southwest Asia (18) were also similar to the EPMSP levels (Figure 2).

### Institute of Medicine Report

In 2006, 2007, and 2009, air samples were collected by the U.S. Army at Joint Base Balad, the site of the largest burn pit in Iraq (28).  $PM_{2.5}$  levels indicated that off-base sources (representing ambient  $PM_{2.5}$ ) significantly contributed to on-base exposures. The 2011 Institute of Medicine report, “Long-Term Health Consequences of Exposure to Burn Pits in Iraq and Afghanistan,” noted that “a broader consideration of air pollution than exposure only to burn pit emissions—might be associated with long-term health effects, particularly in highly exposed populations (such as those who worked at the burn pit)



**Figure 1.** Mean particulate matter with an aerodynamic diameter less than or equal to 2.5 µm (PM<sub>2.5</sub>) concentrations at 15 sites in Iraq, Afghanistan, Kuwait, and other sites in 2006 and 2007 (27). MEG = military exposure guideline; NAAQS = National Ambient Air Quality Standards; USEPA = U.S. Environmental Protection Agency.

or susceptible populations (for example, those who have asthma), mainly because of the high ambient concentrations of PM from both natural and anthropogenic, including military, sources” (1). Findings from the EPMSF indicate that multiple sources contributed to PM exposures (3), but the major portion was of geologic origin from local soils (29). Analysis also identified the contribution of industrial sources to PM that varied by location, such as lead, zinc, and other metals from nearby smelters and battery manufacturing, and from transportation activities. At Joint Base Balad, polychlorinated dibenzo-*para*-

dioxin/furans, polycyclic aromatic hydrocarbons, and volatile organic compounds were detected in concentrations similar to those noted in polluted environments outside the United States (1).

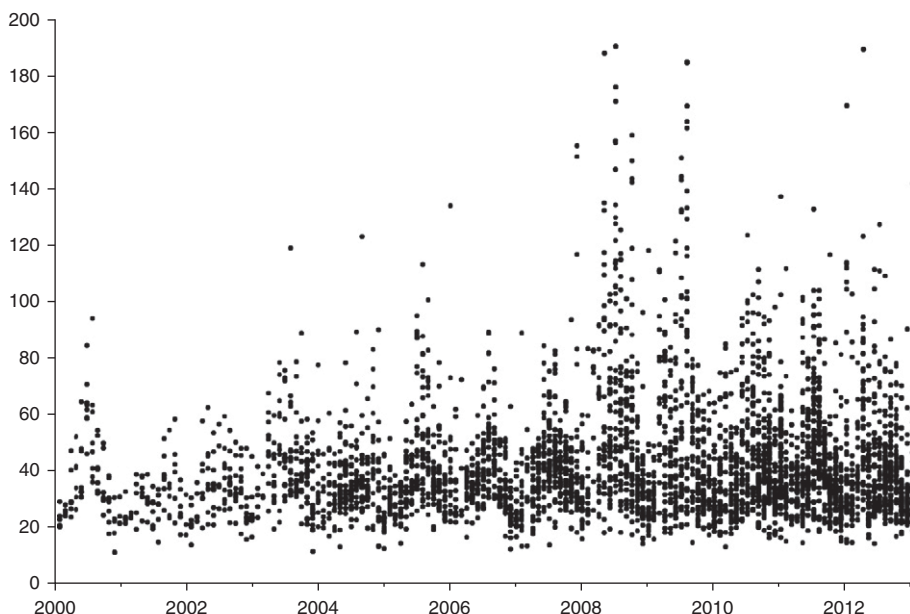
### Effects of Desert Dust on Respiratory Illness

Despite the significant contribution of desert dust to ambient PM in the deployment region, a review of existing health studies presented at the workshop identified no large-scale epidemiological studies assessing

the cumulative effect of PM on pulmonary function or on risk of asthma or other chronic pulmonary diseases among exposed populations, although a few observational reports were available for review (30–32) (P. Yiallourous, workshop presentation). Reports of adverse effects of dust storms on health have focused primarily on the description of short-term adverse respiratory effects. These include care for asthma and other respiratory illnesses (33–35) and respiratory infections, including hospital admissions for pneumonia (36–38) and chronic obstructive pulmonary disease (COPD) exacerbations (39, 40). Surveys of military personnel conducted immediately after leaving deployment suggest that personnel could have experienced acute respiratory effects while deployed similar to the findings reported in the desert dust-exposed cohorts (41, 42).

### PM<sub>2.5</sub> and Long-Term Pulmonary Health Effects in Nonmilitary Cohorts

Population-based epidemiological studies assessing exposure to ambient PM<sub>2.5</sub> have demonstrated that chronic exposure (10–14 yr in duration) at levels lower than those experienced during deployment results in reduced pulmonary function assessed by spirometry (15, 16). Other cohort studies also suggest an association between ambient air pollution and the development of COPD (43–45). Small airway structural changes have also been described in association with ambient pollution (46). There is no comparable literature assessing pulmonary function in populations similar to previously deployed veterans who experienced high



**Figure 2.** Monthly predictions of particulate matter with an aerodynamic diameter less than or equal to 2.5 µm in µg/m<sup>3</sup> (y-axis) by year (2000–2012) for sites in Afghanistan, Iraq, Kuwait, Kyrgyzstan, United Arab Emirates, Djibouti, and Qatar, based on military airport visibility data. Reprinted from Reference 18 by permission of Air & Waste Management Association, www.awma.org.



PM exposures over a relatively short duration (on the basis of total deployment time, estimated mean [standard deviation], 10.6 [6.6] mo) (E. Garshick, workshop presentation of unpublished data).

## Epidemiologic and Observational Studies in Previously Deployed Military Personnel

### DoD Healthcare Encounters

Investigators from the U.S. Army Public Health Command reviewed clinical encounters using *International Classification of Disease, Ninth Revision (ICD-9)* codes to categorize respiratory health-related conditions before and after deployment. Analyses indicate a postdeployment increase in encounters for respiratory symptoms and obstructive lung diseases, predominantly asthma (4–6).

### VHA Healthcare Encounters

In an assessment of asthma prevalence among returning troops at the Northport VA Medical Center, Szema and colleagues found higher asthma rates among deployers than nondeployers (47, 48). Among deployers receiving VHA health care nationally from October 2002 through September 2011, the prevalence of encounters for chronic lung disease (mainly asthma) increased (7).

### Prospective Cohort Studies

The Millennium Cohort Study was established by the U.S. DoD to prospectively study the short- and long-term self-reported health effects of military service (20). Compared with predeployment surveys, deployed persons more frequently reported respiratory symptoms (surveyed 2004–2006) than nondeployers (49). Through 2013, there was an increased risk of self-reported new onset of health professional–diagnosed asthma (9).

### European Studies

A retrospective questionnaire-based study of Swedish military personnel who served primarily in Afghanistan (2008–2009) and who were surveyed 36 months to 5 years later, found an increased prevalence of wheeze, wheeze without a cold, nocturnal coughing, and chronic bronchitis among soldiers compared with a referent group of civilians (50). A statistically significant relationship was found between months spent in a desert environment and wheeze, wheeze with breathlessness, and wheeze without a cold.

## Findings in Clinical Assessments of Previously Deployed Military Personnel and Veterans

Four centers that regularly evaluate veterans and military personnel postdeployment have published their clinical findings. These centers are the VA War Related Illness and Injury Study Center (WRIISC), National Jewish Health (NJH), Brooke Army Medical Center and other military medical facilities, and Vanderbilt University Medical Center.

### Asthma and Airway Diseases

Assessment of active duty personnel and veterans demonstrated that postdeployment spirometry was usually normal, and the most common specific diagnoses are asthma and nonspecific airway hyperresponsiveness. Among 124 veterans referred for evaluation to the New Jersey WRIISC (both with and without respiratory symptoms), 26% had a positive bronchodilator response measured in spirometry. This was positively associated with deployment length, adjusted for smoking history (51). In a subsequent description of 138 veterans evaluated at the New Jersey WRIISC, 74.6% had normal pulmonary function, 19.6% had an obstructive deficit, and 5.8% had a restrictive deficit (52).

At NJH, among 127 consecutive symptomatic military deployers referred for clinical evaluation, asthma was diagnosed in 31.5%, rhinitis/rhinosinusitis in 15%, and inducible laryngeal obstruction in 14.2% (S. Krefft, workshop presentation of unpublished data). Among 113 previously deployed, spirometry was normal in 70.8%, suggested restriction in 19.5%, obstruction in 5.3%, and a mixed pattern in 4.4%.

Brooke Army Medical Center investigators assessed Army personnel undergoing medical discharge with asthma. Of 194 previously deployed with asthma, 52% had been diagnosed with asthma after deployment, whereas 48% had been previously diagnosed (10). The STAMPEDE (Study of Active Duty Military for Pulmonary Disease Related to Environmental Deployment Exposures) was conducted by the same investigators and evaluated 50 active duty military with new-onset dyspnea during deployment (8). The primary findings were that 42% had a nondiagnostic evaluation, whereas asthma and nonspecific bronchial hyperreactivity were the most common diagnoses, being present in 40%.

## Reduction in Diffusing Capacity of the Lung for Carbon Monoxide

Among the four centers, the prevalence of a reduction in diffusing capacity of the lung for carbon monoxide varied considerably depending on center, referral population, and choice of predicted values (11, 52–54).

## Constrictive Bronchiolitis and Other Lung Biopsy Findings

**Pathologic criteria for constrictive bronchiolitis.** The workshop reviewed the standard pathologic criteria for assessing bronchiolitis in lung tissue samples (K. Jones, workshop presentation). The broad category of bronchiolitis refers to a range of disorders characterized by combinations of inflammation and fibrosis involving the small airways. Constrictive bronchiolitis (which has also been called obliterative bronchiolitis) is a pattern of injury characterized by subepithelial scarring resulting in narrowing or obliteration of the bronchioles, without the presence of luminal plugs. This pathology is observed in chronic rejection among lung transplant recipients or in chronic graft-versus-host disease after bone marrow transplantation, autoimmune connective tissue, other systemic disorders (e.g., inflammatory bowel disease), drug reactions (e.g., due to penicillamine), ingested toxins (e.g., *Sauropus androgynus*), and infection (e.g., adenovirus) (12–14, 55). Constrictive bronchiolitis has also been reported after inhalation injury, including after sulfur mustard (gas) used in the Iraq–Iran war (56), and in food-flavoring workers exposed to the ketone butter flavoring diacetyl (13, 57–59).

As noted by Epler (13, 14) the characteristic histopathological finding of constrictive bronchiolitis is subepithelial scarring that leads to narrowing of the airway. It was noted during the workshop that in some references (60), smooth muscle hypertrophy has been included in the description of constrictive bronchiolitis. Most recent descriptions, however, emphasize that constrictive bronchiolitis is a fibrotic airway disorder (14, 61) (K. Jones, workshop presentation).

**Results of lung biopsy in symptomatic deployers.** Investigators from Vanderbilt University Medical Center investigated 80 postdeployment military personnel referred from Ft. Campbell, Kentucky, with unexplained shortness of breath and exercise limitation, cough, or chest tightness after deployment (11). Forty-nine

underwent video-assisted thorascopic surgery (VATS) lung biopsy and 38 had pathology interpreted as finding constrictive bronchiolitis. The predominant bronchiolar tissue changes were reported to include smooth muscle in seven cases, fibrous tissue in three cases, and mixed smooth muscle and fibrous tissue in 28 cases. Other small airway biopsy findings included: respiratory bronchiolitis (71.0% of biopsies), peribronchiolar inflammation (89.5%), pigment deposition (97.4%), polarizable material within pigment (94.7%), and bronchiolar-associated lymphoid tissue (50%). The 11 soldiers who underwent lung biopsy without findings of constrictive bronchiolitis did have other pathologic findings, including hypersensitivity pneumonitis, respiratory bronchiolitis, respiratory bronchiolitis-associated interstitial lung disease, and sarcoidosis.

In 127 symptomatic military postdeployment personnel assessed at NJH, VATS lung biopsies from 52 were reported as having a range of overlapping abnormalities, including bronchiolitis (including constrictive bronchiolitis), emphysema with hyperinflation, and granulomatous pneumonitis (C. Rose, workshop presentation of unpublished data). There were differing views among workshop participants regarding the interpretation of the histologic changes interpreted as showing constrictive bronchiolitis.

### Eosinophilic Pneumonia

One of the earliest reported pulmonary diseases associated with deployment in Southwest Asia was acute eosinophilic pneumonia in 18 patients (62). An additional retrospective review of 43 patients with acute eosinophilic pneumonia (all deployed to Iraq, Afghanistan, Kuwait, or other locations, including the previous cases) from 2003 to 2010 was subsequently published. In that series, 91% were men, with a mean age of 25.5 years, and cigarette smoking was reported in 91% (63).

### Other Pulmonary Abnormalities

Diagnostic computed tomography scans obtained in symptomatic postdeployers have generally been reported as normal or only subtly abnormal, showing mosaic attenuation consistent with air trapping and/or centrilobular nodules, consistent with small airway disease (Reference 64 and S. Krefft, workshop presentation of unpublished data).

## Airborne Hazards and Open Burn Pit Registry

Public Law 112-260 Section 201, enacted in 2013, requires the VA to implement the Airborne Hazards and Open Burn Pit Registry to maintain a registry for those individuals who may have been exposed to burn pit emissions during their military service. As of May 2018, 140,691 have participated. A benefit of the registry may be to track the incidence of various pulmonary conditions (D. Helmer, workshop presentation).

## New Approaches to Assessment of Deployment-related Exposures and Health Effects

### Assessment of Deployment PM<sub>2.5</sub> Exposures

A new study, VA Cooperative Studies Program #595, Pulmonary Health and Deployment to Southwest Asia and Afghanistan (NCT02825654; also called SHADE [Service and Health among Deployed Veterans]) has been designed to assess the respiratory health of previously deployed veterans. SHADE, which commenced recruitment in June 2018, is being conducted at six VA Medical Centers to enroll approximately 5,000 veterans with land-based deployments in Afghanistan and Southwest Asia. The primary objectives are to study whether greater cumulative exposure to PM<sub>2.5</sub> experienced during deployment is associated with lower lung function assessed by pre- and post-bronchodilator spirometry and to examine associations with healthcare provider-diagnosed asthma. Historical NASA satellite aerosol optical depth (AOD) and military airport visibility (visual range assessment) records will be used to reconstruct deployment-related PM<sub>2.5</sub> at each Veteran's deployment locations (17, 18). On the basis of historical airport visibility data between 2000 and 2012 from 104 military sites in Iraq, Afghanistan, Kuwait, Kyrgyzstan, United Arab Emirates, Djibouti, and Qatar, estimated monthly average PM<sub>2.5</sub> concentrations at these sites were mainly between 50  $\mu\text{g}/\text{m}^3$  to nearly 200  $\mu\text{g}/\text{m}^3$  (Figure 2) (18).

### DoD Serum Repository and Metabolomics

The DoD serum repository started in the mid-1980s to store serum samples

remaining after required human immunodeficiency virus testing. Serum samples are obtained from active military personnel during periodic medical examinations, before overseas assignments, and before and after major deployments (19, 65). Serum samples collected from 200 persons pre- and postdeployment were compared with nondeployed control subjects. Naphthalene was found to be elevated postdeployment, and four dioxin/furan compounds were measurable in 38% of the samples and elevated postdeployment (66, 67). Other exploratory analyses have found microRNAs differentially expressed in previous deployers (68, 69). These analyses suggest that high-resolution metabolomic, gene expression, and other approaches may be used to identify associations between deployment, specific chemical compounds, and/or altered gene expression, and eventually adverse health outcomes

### Mechanisms of Lung Epithelial Injury

A 5-year DoD-funded study newly underway at NJH "Mechanisms and Treatment of Deployment-Related Lung Injury: Repair of the Injured Epithelium," will focus on understanding mechanisms by which exposure to PM may predispose the lung epithelium to injury after a second stimulus. This investigation will test the hypothesis that exposure to respirable PM from Southwest Asia triggers inflammatory signaling pathways in respiratory epithelial cells, which, after a second stimulus, leads to dysregulated production of proinflammatory mediators that drive lung epithelial cell injury.

## Summary and Key Questions

### Deployment-associated Exposures

As described in the 2011 IOM report (1), military personnel deployed to Afghanistan and Southwest Asia (including Kuwait and Iraq) experienced a complex mixture of exposures. Most notable and widespread have been the ambient PM<sub>2.5</sub> exposures known to be greater than U.S. levels. Sources contributing to PM<sub>2.5</sub> included desert dust with a mix of organic and inorganic constituents, waste incineration from burn pits, and poorly regulated or unregulated local industrial and vehicular pollution. The quantitative assessment of PM<sub>2.5</sub> over each deployment using airport visibility and

NASA satellite AOD data, as proposed in the new SHADE study, represents an advance in exposure assessment that should reduce misclassification compared with self-reported exposure intensities. Future studies should include efforts to characterize more specific exposures on the basis of job duties or deployment location (using estimates of PM<sub>2.5</sub> or other pollutants) rather than simply considering deployment status as a single exposure, because exposure may vary based on job duties, location, and time in theater. The use of banked serum samples to characterize exposures using selected biomarkers related to burn pit or other military exposures may be feasible in the future to better characterize exposure status.

### Adverse Respiratory Health Effects

**Previous deployers with respiratory symptoms.** Studies conducted by DoD analyzing military encounter data suggest that more encounters occur for respiratory symptoms and for obstructive lung disease, predominantly asthma, after deployment (4–6). A study in Swedish troops deployed to Afghanistan also documented the persistence of symptoms several years after deployment (50). Case series describing the evaluation of symptomatic military personnel do not note any single etiology, emphasizing the importance of a comprehensive clinical assessment, but asthma has been a common finding (References 8 and 47, and S. Krefft, workshop presentation of unpublished data). This is consistent with epidemiologic findings from the Millennium Cohort Study that demonstrate an increased risk of new-onset asthma (by self-report) related to combat exposure during deployment (9) and the observational findings where approximately half of the deployed persons discharged with asthma after deployment did not have a previous known diagnosis (10). Nonetheless, a number of questions remain as to the drivers of increased health care utilization for respiratory conditions and potential under- and overdiagnosis of specific conditions. The relationship of asthma postdeployment to specific exposures, such as burn pit work, is not known, nor is the relationship to previous pulmonary function test abnormality or previous asthma diagnosis. A study underway at NJH designed to elucidate the molecular effects of desert dust PM exposures on airway epithelial cells may

provide insights into the mechanisms and the potential for airway damage.

**Constrictive bronchiolitis.** Centers performing VATS lung biopsies in a selected group of previously deployed service members undergoing evaluation for dyspnea have reported constrictive bronchiolitis, other small airway abnormalities, and granulomas (Reference 11 and presentation of unpublished data, S. Krefft and C. Rose). A review of histologic criteria defining constrictive bronchiolitis indicated that these criteria have not been applied consistently across case series. Because the histologic criteria for diagnosis of constrictive bronchiolitis have varied, in particular the presence of bronchiolar subepithelial scarring, it has been difficult to compare results across centers. There was a heterogeneity of views among workshop participants regarding the interpretation of the findings of constrictive bronchiolitis and its potential relationship to dyspnea and related respiratory symptoms postdeployment.

**Future lung disease.** The findings summarized in this workshop regarding estimated PM<sub>2.5</sub> levels during deployment raise concerns about the future respiratory health of previously deployed military personnel (active duty and veterans), especially given that adverse respiratory health effects have been observed at PM levels much lower than those experienced during deployment (15, 16). Although multiple sources contributed to PM during deployment, the predominant contribution was desert dust. Epidemiologic studies have demonstrated an association between acute desert dust exposure and increased hospitalization for asthma, pneumonia, and other respiratory causes (33–40). Desert dust exposure may also have contributed to the acute respiratory illness experienced during deployment as reported retrospectively in postdeployment surveys (41, 42). There are few currently available data, however, to guide the assessment of long-term effects of repeated PM or other air pollutant exposures during deployment, nor is there prior literature quantifying chronic pulmonary health effects attributable to the substantially higher but much shorter (usually months to up to several years) exposures.

### Key Questions

Suggestions to further understand the health effects of PM and other potential exposures during deployment include:

1. Better characterization of respiratory symptoms and clinical respiratory disease postdeployment, including airway diseases in previous deployers presenting for health care and the potential exposures they experienced during deployment;
2. Improved assessment of long-term clinical consequences and outcomes of former deployers with respiratory symptoms and with respiratory disease, as there is a lack published information regarding follow-up among such persons. Many do not receive a conclusive respiratory diagnosis when symptomatic. Population-based nonmilitary studies have demonstrated that chronic respiratory symptoms are associated with reduced pulmonary function and an increased risk of future pulmonary disease (70–72).
3. More consistent characterization of specific histologic abnormalities, including the prevalence of constrictive bronchiolitis and other small airway abnormalities, established through review of biopsy material using standardized criteria comparable across studies and delineating the relationship of such pathologic abnormalities with PM and other exposures.
4. Determination of the cross-sectional associations among cumulative exposures (in particular PM) and respiratory conditions (in particular asthma), and pulmonary function deficits, adjusted for smoking and other covariates.
5. Evaluation of the long-term longitudinal effects of deployment-related exposures (such as self-reported exposures as in the Airborne Hazards and Open Burn Pit Registry, externally estimated cumulative PM exposures in the SHADE study, or biomarkers as in the DoD serum repository) on the incidence of adverse respiratory health conditions or pulmonary function decline over time. ■

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