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Recent news media articles have implied a direct relationship between environmental exposures such as burn pits during current deployments and the development of serious and debilitating chronic pulmonary disease. These articles suggest that the military is superficially investigating evidence that establishes a link between deployment and development of chronic lung disease. Anecdotal cases of military personnel with lung disease are detailed to suggest a systemic problem with undiagnosed and untreated pulmonary disease in deployed service members. Despite these contentions, the U.S. Army Medical Department and other agencies have been actively pursuing numerous scientific investigations into deployment-related lung disease to define the severity and prevalence of the issue. This article will review relevant research efforts by the U.S. military in the existing medical literature and address the current efforts planned by the services to systematically investigate the possibility of deployment-related pulmonary disease.

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Investigating the Respiratory Health of Deployed Military Personnel

COL Michael J. Morris, MC USA (Ret.); COL Lisa L. Zacher, MC USA*; David A. Jackson, PhD†*

ABSTRACT Recent news media articles have implied a direct relationship between environmental exposures such as burn pits during current deployments and the development of serious and debilitating chronic pulmonary disease. These articles suggest that the military is superficially investigating evidence that establishes a link between deployment and development of chronic lung disease. Anecdotal cases of military personnel with lung disease are detailed to suggest a systemic problem with undiagnosed and untreated pulmonary disease in deployed service members. Despite these contentions, the U.S. Army Medical Department and other agencies have been actively pursuing numerous scientific investigations into deployment-related lung disease to define the severity and prevalence of the issue. This article will review relevant research efforts by the U.S. military in the existing medical literature and address the current efforts planned by the services to systematically investigate the possibility of deployment-related pulmonary disease.

INTRODUCTION

Recent articles in the Army Times,[1,2] New York Times,[3] Stars and Stripes,[4] and other news media have implied there is a direct relationship between exposure to burn pit smoke and possible geological particulate matter (PM)[5–7] during deployments to Iraq and Afghanistan and the development of serious and debilitating chronic pulmonary disease. The undertone of these articles is that the military is at best superficially investigating evidence that establishes a link between deployment—in particular, exposure to combustion products from burn pits and other sources—and development of chronic lung disease. Several unsubstantiated, anecdotal cases of military personnel with lung disease are detailed in the articles suggesting there is a systemic problem with undiagnosed and untreated pulmonary disease in deployed service members. In fact, the U.S. Army Medical Department and other agencies have been pursuing numerous scientific investigations into deployment-related lung disease to define the severity and prevalence of the issue. However, there has been little opportunity for military researchers and physicians to adequately voice the relevant clinical issues that are currently being addressed. For example, military physicians were not called upon to testify about their experience with returning personnel at Congressional hearings on burn pit exposure conducted in November 2009.

Two important questions have been raised about various environmental exposures during deployment: (1) What is the current scientific evidence existing in the medical literature to support this implication of lung disease related to deployment and (2) What has the military done to investigate these contentions? This article will review relevant research efforts by the U.S. military in the existing medical literature and address the current efforts planned by the services to systematically investigate the possibility of deployment-related pulmonary disease.

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ENVIRONMENTAL SURVEILLANCE

It has been clear that service members in Southwest Asia (SWA) have been exposed to high levels of airborne PM since early in Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF). There has been ongoing environmental sampling in the Central Command Area of Operations since the onset of both conflicts. High levels of ambient PM are ubiquitous and exceed environmental, occupational, and military exposure guidelines.[8] Adverse health effects, including cardiovascular and pulmonary disease, are known consequences of exposure to high levels of PM with aerodynamic diameter of less than 10 μm (PM_{10}) and especially less than 2.5 μm ($PM_{2.5}$). The severity of the effect depends on the amount and duration of the exposure, the physical and chemical characteristics of the PM, and the underlying health of the exposed individuals.[9]

The Assistant Secretary of Defense for Health Affairs chartered the Joint Particulate Matter Working Group in 2005 to investigate potential health issues related to this ongoing PM exposure. A symposium was held at the National Institute of Occupational Safety and identified knowledge gaps that included enhanced physical and chemical characterization of the PM and assessment of its toxicity. In response to this recommendation, the U.S. Army Center for Health Promotion and Preventive Medicine (now the Public Health Command) commenced the Enhanced Particulate Matter Surveillance Program. This program collected ambient PM from 15 locations throughout the Central Command Area of Operations over approximately a year and extensively characterized the physical, chemical, and mineralogical properties of the PM.[10]

Although other thorough characterizations of PM from single location in SWA have been performed, [11] only the Enhanced Particulate Matter Surveillance Program has evaluated materials from a broad range of locations.

SOUTHWEST ASIA PM

In addition to recommending increased environmental surveillance in theater, the Particulate Matter Working Group also recommended that the pathogenicity and toxicity of SWA dusts be evaluated. Naval researchers in collaboration with U.S. Army Corps of Engineers are engaged in continuing efforts to characterize the soil and PM microbiota in theater to address potential health risks from novel pathogens.[11] Laboratory work conducted with PM dust from Camp Buehring by the Navy Environmental Health Effects Laboratory showed no long-term toxicity in exposed rats,[12] and 2-week inhalational exposures of rats to Camp Victory surface soil fines also by the Navy Environmental Health Effects Laboratory did not induce notable adverse responses in the animals (LT V. Mokashi, USN, personal communication). These studies are also consistent with independent rat studies using intratracheally instilled PM_{10} from Camp Victory by the U.S. Army Center for Environmental Health Research and National Institute for Occupational Safety and Health. Although there was evidence of acute inflammation shortly after instillation, it rapidly resolved, and at most limited effects were observed 150 days after exposure. (D.A. Jackson, unpublished data). Although the material tested causes irritation and inflammation in the short term like other dusts,[13] there is no evidence that it is toxic in the long term. However, the studies in hand use PM from a limited number of locations and are either single instillations or short-term inhalational exposures. It is of some concern that PM from other locations or that longer or multiple exposures might be more pathogenic.[14]

RESPIRATORY SYMPTOMS

In general, there are reported increases in respiratory symptoms such as cough and dyspnea during deployment. Reporting on the health effects of the Kuwait oil fires of 1991 among U.S. troops, survey research by Army investigators found an increase in reported symptoms of upper respiratory tract irritation, shortness of breath, and cough associated with proximity to the Kuwaiti oil fires. The effects were generally short-lived and resolved after leaving Kuwait.[15] Further survey research 5 years after the conclusion of the First Gulf War noted a modest correlation in self-reported symptoms of asthma and bronchitis in a cohort of 1,560 veterans based on oil fire proximity, but the findings were not correlated with modeled exposures. The authors concluded that oil fire smoke exposure was not the cause of increased respiratory symptoms.[16] A review of hospitalization data did not demonstrate an increase in theater or any military treatment facility admissions related to oil fire exposure or respiratory disease.[17,18] Researchers from the U.S. Naval Medical Research Center conducted a survey of 15,000 redeploying military personnel from Iraq and Afghanistan and estimated that 69.1% reported experiencing respiratory illnesses, of which 17% required medical care.[19] Further survey data from the Millennium Cohort Study conducted by the Naval Health Research Center on respiratory symptoms found that deployed personnel had a higher rate of newly reported respiratory symptoms than nondeployed personnel (14% vs. 10%), with similar rates of chronic bronchitis/emphysema (1% vs. 1%) and asthma (1% vs. 1%) observed. The authors suggested that specific exposures rather than deployment may be a determinant of postdeployment respiratory illness.[20]

A confounding factor in evaluating respiratory symptoms in deployed service members is the higher rate of tobacco use in the military and its increased use during deployment. The 2006 National Health Interview Survey estimated that 23.5% of males and 18.1% of females in the United States were smokers. A recent survey of soldiers deployed to Iraq reported that 51.9% of males and 41.7% of females were using tobacco products before deployment; 58.3% of males and 52.1% of females were using tobacco during deployment, and 25.4% of males and 48% of females increased the use of tobacco during deployment. Effect on health and performance associated with tobacco use should not be underestimated. Furthermore, smoking prevention and smoking cessation programs need to be markedly improved.[21]

Asthma

Very limited data exists on the effects of deployment on asthma. The current guidelines for accession of new military personnel are service specific, but in general, an established diagnosis of asthma after the age of 12 has been an exclusion criterion. Despite these restrictions, asthma remains a significant problem in active duty military that may mirror the incidence in the general population. Nish and Schwietz evaluated 192 Air Force recruits for symptoms of exertional dyspnea and found that 45% of these patients had a previous diagnosis of asthma. The majority of these patients had mild or exercise-induced disease but had clinically significant symptoms to be referred for a formal evaluation.[22] Morris et al[23] found that nearly half of their active duty patients with exertional dyspnea had either asthma or exercise-induced bronchospasm. The extreme climate conditions in SWA along with high PM exposures because of environmental dust exposure could potentially contribute to poor asthma control with increased exacerbations. Roop et al[24] surveyed deploying Army personnel and found that 5% of troops deployed to SWA reported a previous diagnosis of asthma. In this study, there were no differences between asthmatics and nonasthmatics as both groups reported significantly increased respiratory symptoms during deployment compared with symptoms preceding deployment. A retrospective chart review of over 6,000 Veterans Administration medical records (based solely on ICD-9 diagnostic codes) found higher rates of new-onset asthma in deployed U.S. military personnel between 2004 and 2007 compared with nondeployed military personnel

stationed in the United States (6.6% vs. 4.3%).[25] There is no data currently available to suggest that deployment is a definitive cause of new-onset asthma.

Constrictive Bronchiolitis

Constrictive bronchiolitis (also known as bronchiolitis obliterans) is a lung disease characterized by fixed airways obstruction and fibrosis of the distal airways or bronchioles, with extrinsic narrowing or obliteration of the bronchiolar lumen.[26] It is associated with environmental and occupational inhalation exposures, classically following exposure to nitrogen and sulfur dioxides, and may cause permanent respiratory impairment. Constrictive bronchiolitis usually presents with subtle onset of exertional shortness of breath and nonproductive cough. Spirometry will typically show airflow obstruction without postbronchodilator increase, and high-resolution computed tomography (CT) scanning of the chest often shows heterogeneous air trapping most prominent on expiratory imaging, sometimes with areas of patchy ground-glass opacities and scattered cylindrical bronchiectasis.[27] In an abstract presented at the 2008 American Thoracic Society meeting, the evaluation of 47 soldiers from Fort Campbell, Kentucky, was reported.[28] Thirty-five of the soldiers reported exposure to a sulfur fire during a 2-week period in 2003 in Iraq. Symptoms were primarily exertional dyspnea with running, and most patients had normal spirometry and high-resolution CT scans of the chest. Many of the patients underwent open lung biopsy, and 24 of these soldiers had pathologic findings consistent with constrictive bronchiolitis. However, these patients were never evaluated by military pulmonologists, and there has been no independent confirmation of the findings. It remains highly controversial if these patients actually have constrictive bronchiolitis related to sulfur dioxide exposure as the majority lack evidence of airway obstruction on spirometry or chest imaging. The epidemiologic report by the Army concluded: "This exploratory analysis did not show a definite link between sulfur fire exposure in Iraq and either chronic or recurring respiratory diseases. However, the results do not rule out the possibility of such an association. Apart from the possible net effects of the sulfur fire on specific subpopulations, it is significant that a sample of all returning OIF and OEF veterans experienced more respiratory problems after their deployment compared to before deployment."[29]. Further review of the Department of Defense (DoD) electronic medical records failed to identify any further cases of constrictive bronchiolitis apart from the Fort Campbell soldiers.

Acute Eosinophilic Pneumonia

Eighteen cases of acute eosinophilic pneumonia occurred from March 2003 to March 2004 among 183,000 military personnel deployed in or near Iraq. There were two deaths reported from this cohort and was first reported in the medical literature in 2004 by Shorr et al.[30] Acute eosinophilic pneumonia is an unusual disease of unknown etiology, characterized by acute illness (<2 weeks of symptoms), respiratory failure, bilateral pulmonary infiltrates, hypoxia, and predominant eosinophilia on bronchoalveolar lavage.[31] Extensive evaluation failed to demonstrate an infectious etiology or association with known causes, and no geographic clustering was evident. Most individuals reported exposure to fine airborne dust, and all used tobacco, with 78% reporting that they had started smoking recently. New-onset smoking was considered a risk factor in these patients.[30] Current data being collected from Landstuhl Regional Medical Center in Germany now shows there are 45 diagnosed cases.

CLINICAL DEPLOYMENT LUNG STUDIES

Physicians at Brooke Army Medical Center have developed and instituted numerous clinical protocols aimed at exploring postdeployment lung disease in military personnel.

(1) "A Database Registry of Military Personnel Diagnosed with Post-Deployment Chronic Pulmonary Disease" is a retrospective database study of all active duty military with a variety of chronic pulmonary diagnoses to include asthma, emphysema, chronic bronchitis, chronic obstructive pulmonary disease, bronchiectasis, sarcoidosis, pulmonary fibrosis, constrictive bronchiolitis, and other pulmonary interstitial/infiltrative disorders. This is a preliminary research study examining the relationship between onset of chronic pulmonary disease and deployment history and is presently under way at Brooke Army Medical Center.

(2) "The STAMPEDE Registry of Deployment Related Lung Disease" is a study that establishes a prospective database registry throughout the DoD military treatment facilities enrolling all military personnel with diagnosed chronic lung disease (as listed earlier) related to deployment. This study will collect clinical data on these patients for 10 years postdiagnosis and allow development of centralized database to examine for short-term and long-term pulmonary effects of deployment.

(3) "Pre- and Post-Deployment Spirometry to Detect Airways Disease Related to Environmental Dust Exposure" is a prospective study of deploying soldiers from Fort Hood, Texas, using standard spirometry and impulse oscillometry pre and postdeployment. The purpose of this study is to compare military personnel who have recently returned from the OIF/OEF for evidence of spirometric changes related to prolonged environmental exposure in the current theaters of operation.

(4) "STudy of Active Duty Military for Pulmonary Disease related to Environmental Dust Exposure (STAMPEDE)" is a prospective clinical evaluation of active duty military with new complaints of dyspnea postdeployment that began in the fall of 2010. Participants enrolled in this study will undergo a complete pulmonary evaluation to include chest radiograph, high-resolution CT of the chest, full pulmonary function testing, impulse oscillometry, methacholine challenge testing, and bronchoscopy

with bronchoalveolar lavage (and transbronchial biopsy if indicated). This study will allow for a complete evaluation to determine diagnoses and establish any chronic inflammatory findings in the lung.

(5) "Pre- and Post-Deployment Evaluation of Military Personnel for Pulmonary Disease Related to Environmental Dust Exposure (STAMPEDE II)" is designed as a prospective evaluation of health active duty military pre and postdeployment to detect if acute or chronic lung disease develops in these military personnel specifically because of dust exposure. Participants will have baseline radiographic and pulmonary function testing before deployment with a complete pulmonary evaluation postdeployment.

(6) Baseline Spirometry Values for Iraqi National Military: The impact of chronic dust exposure will evaluate Iraqi military personnel with a pulmonary questionnaire and baseline spirometry to ascertain baseline pulmonary function in a sample of the native population.

DEVELOPMENT OF FUTURE PULMONARY HEALTH RESEARCH PROGRAM

Prompted by the concerns raised in these articles, anecdotal and case report data about deficits in pulmonary health of returning service members, a working group convened in February 2010 at National Jewish Health in Denver. The group included pulmonologists, occupational and preventive medicine specialists, industrial hygienists, and exposure scientists from several academic medical centers, the DoD, and the Department of Veterans Affairs. These physicians and scientists reviewed the available data on known and potential respiratory health outcomes and possible risk factors. This working group explored the exposure parameters that might confer increased risk of postdeployment lung disease such as type, severity, and duration of exposure, extended deployments, proximity and duration of exposure to burn pits or fires, reported frequency of exposure to ambient PM and desert dust storms, and particular job duties. Given the potential adverse pulmonary outcomes, the working group made some general recommendations including: (1) standardized pre and postdeployment medical surveillance; (2) criteria for medical referral and diagnosis; and (3) case definitions for key deployment-related lung diseases. The outcomes from this conference are scheduled to be published in 2011.

In the wake of the National Jewish Health Working Group, it became clear that a coordinated effort to resolve issues related to deployment-related respiratory disease would be required because available data was limited and drawn from sundry sources. In response to this problem, a new Pulmonary Health Task Area was proposed by the Military Operational Medicine Research Program (MOMRP) of the U.S. Army Medical Research and Materiel Command (MRMC) with the support of the MRMC commander. In June 2010, the MOMRP brought together a diverse group of experts to examine current medical evidence and gaps and to formulate a multidisciplinary research plan to address the issue of deployment-related respiratory disease. The working group included representatives of all four services, Veterans Affairs, and academic experts in pulmonary medicine, toxicology, pulmonary pathology, occupational and preventive medicine, computer science, and epidemiology. The Pulmonary Health Task Area Working Group proposed priorities for research for the new Task in four specific focus areas, clinical research, animal models of toxicity, biomarkers, and exposure assessment/epidemiology, and identified four major data gaps, prevalence and severity of deployment-related disease, methods for diagnosis and screening, intervention and treatment, and toxicity and pathogenicity of SWA PM.

The proposed clinical studies include the STAMPEDE studies described previously and pathological evaluations of autopsy samples from deployed vs. nondeployed service members, and assessments of pulmonary disease in native Iraq populations. Animal studies were directed at determining whether there are differences in the toxicity/pathogenicity of PM from different locations in SWA and in attempting to use working dogs which are exposed to the same environment as service members as surrogates for clinical studies. The working group also proposed to apply advanced data extraction and computational tools to identifying novel biochemical and physiological biomarkers from biosamples and physiological measurements collected in the clinical and animal studies. Finally, several approaches to identifying potential associations between medical encounters and health outcomes in military medical records and environmental surveillance data were proposed. Linking the DoD and Veterans' Affairs records could provide prospective data useful for understanding the chronicity of deployment-related pulmonary disease. Although the Task Area has not yet been funded, several studies that align with it have been initiated, and linkages among different agencies, commands, and services have already been forged.

CONCLUSION

There is no presently adequate toxicological, epidemiological, or clinical data to reliably evaluate either the prevalence or severity of adverse effects of inhalational exposures to PM or burn pit combustion products in military personnel deployed to SWA. Moreover, the current clinical evidence on the effect of deployment on respiratory health is primarily retrospective in nature and does not provide any clear information on specific causative factors or the effect on the deployed population as a whole. Without prospective pulmonary data on patients before deployment, identification of specific environmental exposures during deployment, and thorough evaluations postdeployment, identifying causal relationships between events during deployment and pulmonary disease will not be possible. The DoD has and is continuing to respond to service members' health and wellness needs by evaluating the possibility of deployment-related pulmonary disease in SWA in a comprehensive and scientific manner by acquiring objective

evidence for risk factors, guiding disease mitigation, and ensuring correct diagnosis and treatment.

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