Airborne Hazards Exposure and Respiratory Health of Iraq and Afghanistan Veterans

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More than 2.6 million military personnel have been deployed to recent conflicts in Iraq and Afghanistan and were likely exposed to a variety of airborne hazards during deployment. Despite several epidemiologic reports of increased respiratory symptoms, whether or not these respiratory illnesses lead to reductions in lung function and/or specific pulmonary disease is unclear. We reviewed data published from 2001 to 2014 pertaining to respiratory health in military personnel deployed to Iraq and Afghanistan and found 19 unique studies. Study designs were primarily retrospective and observational in nature with patient symptom reporting and medical encounter data as primary outcome measures. Two case series reported on rare respiratory diseases, and one performed a standardized evaluation of new-onset respiratory symptoms. Respiratory outcomes in relation to proximity to a specific air pollution source (i.e., smoke from burning trash and sulfur mine fire) were described in 2 separate studies. Only 2 longitudinal investigations were identified comparing pre- and postdeployment measurement of exercise capacity. In summary, published data based on case reports and retrospective cohort studies suggest a higher prevalence of respiratory symptoms and respiratory illness consistent with airway obstruction. However, the association between chronic lung disease and airborne hazards exposure requires further longitudinal research studies with objective pulmonary assessments.

Abbreviations: ICD-9, International Classification of Diseases, Ninth Revision; PM2.5, fine particulate matter (i.e., particulate matter <2.5 μm in diameter); PM10, coarse or respirable particulate matter (i.e., particulate matter <10 μm in diameter).

INTRODUCTION

More than 2.6 million military personnel have served in Iraq and Afghanistan, with approximately 45% deploying multiple times (1). Veterans of these conflicts report concerns about exposure to poor air quality in Iraq and Afghanistan and the long-term health effects possibly associated with these exposures (2, 3). Military occupational health risks during deployment, such as respiratory toxicant exposure, extreme physical demands, and poor hygienic settings, may predispose service members to deployment-related lung disease (4). In fact, recent studies have implicated inhalational exposures during deployment in the etiology of new-onset asthma and constrictive bronchiolitis (5, 6). In response to these findings and other reports, attention and concern for the respiratory health of deployed service members are substantial (4, 7–15). Such concern has prompted the development of a national airborne hazards registry as part of recent legislation (16).

In this paper, we summarize the existing published data related to inhalational exposures and the respiratory health of service members deployed to Iraq and Afghanistan. To put this issue into context, we first provide a brief background of air pollution and then discuss how characteristics of military service and deployment may augment the risks of adverse health effects associated with airborne hazards exposure. We operationally define the term “deployment-related airborne hazards” as general and specific airborne pollutants characteristic of the deployment environment and use the more general term “air pollution” when referring to nonmilitary studies.
Air pollution

A temporal relationship between particulate air pollution exposure and adverse health effects has been recognized for over 80 years (17), and air pollution is currently the single largest environmental health risk globally (18). It should be noted that air pollution exposure is generally quantified as the mass of particles within a given volume of air (µg/m³). For example, World Health Organization air quality guidelines for fine particulate matter (i.e., particulate matter <2.5 µm in diameter (PM2.5)) suggest that 25 µg/m³ represents an allowable daily exposure level. However, PM2.5 levels in developing countries, including Iraq and Afghanistan, can routinely exceed 10,000 µg/m³ for prolonged periods (19). In other words, the intensity and duration of air pollution exposure in some deployments are far greater than those observed in more developed countries like the United States. Although important to health effects as well, the characteristics of PM2.5 and other airborne pollutants are beyond the scope of the present review as these have been comprehensively described elsewhere (20).

Whereas epidemiologic studies have focused primarily on the health effects of short-term and high-intensity or long-term and low-intensity exposures, the typical experience of a service member during a deployment may be characterized as a moderate-duration and high-intensity exposure. Pope et al. (21) suggested that the reviewed epidemiology identifies the acute-to-moderate-duration (hours to 1 year) time frame as the period of exposure most likely to induce cardiovascular events. These adverse events are thought to be achieved through vascular, hematological, and atherosclerotic changes that degrade cardiovascular and cardiopulmonary function in additive and synergistic ways (21). Derangement of the normal biological pathways may occur even at low levels of ambient pollution. In fact, recent data have demonstrated that the general population, and not just susceptible individuals, experiences respiratory effects from air pollution exposure even when levels are labeled safe according to existing US regulations (22). Given the growing understanding of air pollution and its potential impact on the health of the general US population, evaluation of the respiratory health of deployed service members is especially important because of their unusual degree of exposure.

In Figure 1, we summarize critical factors that underscore how military personnel may be uniquely vulnerable and susceptible to respiratory health effects during deployment. Vulnerability refers to when a cohort is at greater risk because of more frequent or higher levels of exposures, whereas susceptibility refers to an elevated risk of negative outcomes in comparison with a general population because of underlying conditions and/or personal characteristics (20). For example, deployment to a region with high ambient particulate matter increases the risk of exposure (or vulnerability) for military personnel. Factors specific to military service (e.g., physical activity, stress, and violence), tobacco use, and individual characteristics may further augment this risk and enhance susceptibility to adverse health effects from airborne hazards exposure. In the subsequent sections, we further describe how military personnel are at a greater risk of exposure to airborne hazards as well as a heightened risk for adverse health effects.

Vulnerability to airborne hazards

Ambient sampling was performed in 2006–2007 at 15 locations in the deployment environment, including 6 locations in Iraq and 2 locations in Afghanistan (19, 23). Over 3,000 filter samples and one-time bulk dust and soil samples were collected at each of these sites. The major findings from this surveillance indicated that fine (PM2.5) and coarse (particulate matter <10 µm in diameter (PM10)) levels exceeded occupational and military exposure guidelines at each of the 15 locations (19). In fact, levels of PM2.5 were approximately 10-fold greater than those observed at rural and urban monitoring sites in the United States (19). Geological dust, smoke from burning trash (i.e., “burn pits”), and industrial processing facilities were identified as the primary air pollution sources. Airborne dust can remain suspended for days to weeks, spread over hundreds of kilometers, and contribute to human disease (24). Dust and sand storms characteristic of the region were most responsible for elevated particulate matter levels, but trace metals (e.g., lead, arsenic, cadmium, and zinc) found within the PM2.5 fraction were the result of burn pits and industrial processing facilities (19).

It is important to recognize that the existing and robust literature on air pollution has focused primarily on particulate matter, ozone, sulfur dioxide, and carbon monoxide and less on the impact of dust storm events (25, 26) that are common in Iraq and Afghanistan. Dust storm particles include both fine and coarse fractions with a proposed greater concentration of fine particles during storm activity (27). Evidence of associations between dust-storm events and cardiopulmonary morbidity and mortality is mixed, with studies describing both increased (28–30) and no (31–33) association. These inconsistencies may be explained, in part, by regional variation in dust composition (26). Until recently, few studies
have examined the health effects of dust storms originating from the Middle East, which is surprising given the intensity and frequency of dust storm activity in this region (34). Investigators examined air pollution data (i.e., coarse particulate matter; PM10) from 6 monitoring sites in Kuwait over a 5-year period and found that dust storm events (PM10 >200 μg/m³) occurred 33.6% of the days (26). Dust storm events were found to be associated with increased risk of same-day asthma (relative risk = 1.07) and respiratory (relative risk = 1.06) admissions (26), but there was no association with same-day mortality (25). Data on the long-term health consequences of dust storm exposures in the regions of interest are lacking.

In light of ongoing reports of respiratory symptoms and activity limitations (35) and isolated cases of acute eosinophilic pneumonitis (36) in service members deployed to Iraq and Afghanistan, several investigators have focused on the toxicity of dust and sand particles from Iraq and Afghanistan (37–40). Wilfong et al. (40) were the first to evaluate the respiratory toxicity of 1-, 5-, or 10-mg sand particles obtained from Kuwait (Camp Beuhring) delivered via one-time intratracheal instillation in adult Sprague-Dawley rats. Particles from Kuwait were compared relative to positive (silica) and negative (titanium dioxide) controls. Investigators observed relatively low toxicity (e.g., inflammatory markers, pulmonary lesions) following exposure to Kuwaiti sand particles that were of similar magnitude to titanium dioxide and considerably lower in magnitude than silica (40). In a subsequent study, Dorman et al. (37) studied the respiratory toxicity of Iraqi sand (Camp Victory) but exposed animals through inhalation rather than intratracheal instillation. Investigators observed mild inflammation in the anterior nose and lung of rats exposed to Iraqi sand for 2 weeks (37). Rats in this study were also assigned a 4-week pretreatment period of either air or mainstream cigarette smoke prior to Iraqi sand exposure; cigarette smoke exposure did not amplify the effects in rats exposed to Iraqi sand.

Recently, Szema et al. (38) used an in vivo mouse model and performed airway instillations of surface grab samples of respirable particles obtained from Iraq (Camp Victory) during war time. Relative to the untreated controls, the dust-exposed mice demonstrated upregulation of inflammatory cytokines (i.e., interleukin-2) in bronchoalveolar lavage, and pathology reports showed polarizable crystals in lung tissue associated with septate inflammation. The investigators described the Camp Victory dust particles as angular, having sharp edges and containing trace metals including titanium. These findings of trace metals may corroborate descriptions of crystalline material (including iron and titanium) identified in biopsied lung tissue from some deployed soldiers (5, 41). These recent findings differ from those of earlier reports (19) that suggested that chemical and mineralogical compositions of dust from multiple sites in Iraq and Afghanistan were similar to those from other sites around the world. Future studies may consider more applied exposure paradigms (42) that have been implemented in related literature along with analysis of dust or sand particles from multiple regions in Iraq and Afghanistan.

Of the air pollution sources identified, burn pits have received increased scrutiny as this air pollution source is under US and coalition military control. An estimated 30–42 tons of solid waste are generated daily for an average military base in Iraq and Afghanistan and, for larger bases such as Joint Base Balad in Iraq with a population over 25,000, approximately 100–200 tons of waste could be burned in a single day (43). Given the logistical challenges of the combat environment, open-air waste burning was the primary method of waste disposal when other options were unavailable. Reports indicate that jet fuel was used as an accelerant for burning plastics, wood, metals, and other miscellaneous combustible and non-combustible materials (43). The US military conducted limited air sampling around the 10-acre (4.047-hectare) burn pit at Joint Base Balad and observed detectable levels of volatile organic compounds, polyaromatic hydrocarbons, polychlorinated dibenzo-p-dioxins and dibenzo-p-furans, and particulate matter. Depending on the intensity and magnitude, exposure to these known toxins may be associated with long-term health effects. Moreover, it is likely that the mixture of pollutants, rather than single pollutants, dictates possible health outcomes (20). General conclusions derived from limited air sampling data suggest that multiple sources of air pollution—and not solely burn pit emissions—contribute to poor air quality in the region (43). These conclusions are also supported by independent work from investigators outside of the United States (44–46). Notable limitations to ambient air sampling are discussed in greater detail in a 2011 report by the Institute of Medicine (43). Irrespective of the source, it appears that higher levels of air pollution than typically encountered in the United States are common in many deployment locations and could contribute to future pulmonary and cardiovascular health effects not yet identified (43). In addition to the frequent and proximate exposures to ambient airborne hazards, there are also factors unique to military service that may make military personnel more vulnerable to greater lung health risk.

Military personnel must train with and utilize small arms and heavy weapons as part of their duties. Hazardous airborne exposures to lead and silica dusts from indoor and outdoor firing ranges have been previously described (47) in addition to other chemicals and gases (e.g., carbon dioxide, carbon monoxide, hydrogen cyanide, ammonia, nitrous oxides, sulfur dioxide, and other compounds) (48, 49) from fire arms. Recently, lead ammunition has begun to be phased out by the US military with substitution with other materials such as tungsten, tin, zinc, and/or nylon, but emissions from lead-free ammunition have not been extensively studied. Wingfors et al. (50) recently characterized emissions from one type of lead-free ammunition and found that particulate material comprised both metal and organic compounds. In addition, approximately 90% of the particles produced after firing are in the very fine to ultrafine range (<30 nm) that may deposit deeply into the lung and may cause inflammatory changes or tissue damage. Given the potential toxicities of these novel compounds and their fine fraction, future studies in exposed military personnel are warranted.

Many activities of military service result in greater ventilation rates leading to inhalation of a greater proportion of particles and ultimately a greater pollutant dose exposure. The average adult breathes 10,000–20,000 liters of air in a day. At rest, the pulmonary ventilation rate is approximately 5–6 liters per minute and may exceed >100 L/minute during
exercise. Military service is physically active by nature that, like exercise, necessitates an increase in pulmonary ventilation. For example, carrying external loads (e.g., military rucksack) dramatically increases pulmonary ventilation even during light physical activity, such as walking. As exercise intensity increases from walking to jogging, there is also a shift from nasal to oral breathing, occurring at around 30–40 L/minute, which enables larger particles to bypass the protective filtering of the upper airways, further increasing the pulmonary exposure to pollutant dose. Controlled studies have been performed to evaluate particle entry into the lung as a function of exercise intensity. In comparison with rest, light exercise and high-intensity exercise result in increases of particle deposition into the lung of 3–4.5-fold and 6–10-fold, respectively. Further details regarding the health effects related to exercising in a polluted environment have recently been reviewed elsewhere.

Collectively, these studies suggest that the nature of airborne hazards exposure (i.e., high ambient levels of particulate matter from multiple sources and the physically active nature of military service) may substantially increase the cumulative exposure dose and thereby make military personnel more vulnerable to the adverse health effects associated with exposure.

Susceptibility to airborne hazards

There are many characteristics of deployed service members that may raise the risk of adverse health effects from exposure to airborne hazards. We describe the most prevalent of these here.

Active and passive cigarette smoking is associated with extraordinary morbidity and mortality, the pathomechanisms of which overlap considerably with ambient air pollution. Smoking also increases susceptibility to the health effects from airborne hazards. Approximately 40% of active duty military personnel smoke, and tobacco use is 2 times greater in deployed versus nondeployed military personnel. In comparison, approximately 18% of US adults above the age of 18 years smoke cigarettes. Sanders et al. found that 48% of military personnel deployed to Iraq and Afghanistan began or restarted smoking while deployed, and almost 40% smoked one-half pack of cigarettes or more per day. High rates of tobacco use are not restricted to US military personnel but are also elevated (40%–60%) in coalition forces. Although tobacco smoke constituents may differ in many respects from the ambient air pollution (e.g., dust storms) in deployed settings, the contribution of active and passive tobacco smoke exposure to soldiers’ cumulative exposures to airborne hazards in the deployment setting cannot be completely discounted, given the prevalence and intensity of tobacco use in stressful combat situations.

Combat exposure, military stressors, and post-traumatic stress disorder have all been identified as predictors for cigarette smoking. These psychological risk factors and mental health disorders have also been associated with respiratory symptoms and diseases such as asthma. In fact, moderate associations between probable post-traumatic stress disorder and respiratory symptoms have been described in first responders to the World Trade Center disaster.

However, associations between objective lung function and psychological stress and/or mental health disorders have been less consistent. Still, these potential relationships are concerning given the prevalence of mental health disorders in veterans returning from Afghanistan and Iraq, as well as the psychological stressors commonly experienced during military deployment. Further, growing epidemiologic evidence is emerging demonstrating that exposure to psychological stress enhances susceptibility to air pollution. Increased susceptibility has been observed following exposure to both violence and stress. Animal models have been utilized to better understand the mechanisms that may promote enhanced susceptibility to air pollution. For example, Clougherty et al. used a double-exposure paradigm where they subjected rats to social stress and concurrent exposure to particulate matter air pollution. Compared with nonstressed controls, exposed rats demonstrated altered breathing patterns (i.e., rapid and shallow) and a systemic inflammatory response (e.g., elevated C-reactive protein, tumor necrosis factor-α, white blood cells) consistent with airway disease. Additional studies are needed to further elucidate these psychogenically driven pathways, an inflammatory-mediated mechanism for enhanced susceptibility to air pollution is tenable.

Preexisting medical conditions, obesity, gender, and other personal characteristics (e.g., low education or socioeconomic status) have all been shown to modify the relationship between air pollution exposure and adverse outcomes; these have been reviewed in detail elsewhere. Although many medical conditions disqualify individuals for military service, respiratory conditions such as asthma are a common problem in military personnel even in the absence of symptoms. Further, medical standards were revised in 2002 to allow military personnel with controlled asthma to remain on active duty. In the context of airborne hazards exposure, the presence of asthma alone increases the risk of adverse health effects as total particle deposition in the lungs is 74% higher in adults with asthma compared with those without it. Furthermore, others have found particle deposition to vary as a function of age and gender, with particle deposition being greatest in adult men. Therefore, preexisting conditions and personal characteristics must be considered when determining an exposure risk profile for deployed military personnel. Individual susceptibility factors in deployed military personnel have not been thoroughly studied in the context of airborne hazards exposure, and they deserve further attention in larger epidemiologic studies.

METHODS

We conducted searches using PubMed and Google Scholar to identify articles pertaining to respiratory health and function of Iraq and Afghanistan service members using combinations (Boolean operators) of the following terms: Operation Enduring Freedom; Afghanistan; Iraq; Operation Iraqi Freedom; Iraq War, 2003; military personnel; military; veterans; deploy; burn pit; particulate matter; exposure; air pollution; respiratory symptoms; lung function; lung disease; asthma. Our search was performed in March 2014 and included English-language, peer-reviewed articles from 2002 to 2014. We also examined references from these articles to identify additional references.
studies. As our understanding of this issue remains in its early stages, all study designs were included in this review. Only articles pertaining to military personnel deployed to Iraq and Afghanistan (2001–present) were included in this review, and those pertaining to prior conflicts were omitted (86, 87). Also excluded from this review were case reports (41, 88), conference abstracts (89–94), and studies with nonrespiratory outcomes (95–97). Given the heterogeneity of outcome measures (e.g., self-report symptom, medical encounter, International Classification of Diseases, Ninth Revision (ICD-9), codes, and objectively assessed function), we conducted a descriptive review of the literature.

RESULTS

Using our predefined search criteria, we identified 19 articles in which data were collected on military personnel deployed to Iraq and Afghanistan after 2001. Studies were categorized by the following outcomes: 1) respiratory symptoms, illnesses, and conditions; 2) clinical diagnoses of respiratory disease; and 3) outcomes from specific exposures.

Respiratory symptoms, illnesses, and conditions

As in the general population, respiratory illnesses are very common among service members and rank as the second highest cause of non–combat-related diagnoses in troops serving in the US military theater of operations in the last 20–25 years. In the earlier period of the 2003–2004 conflicts, approximately 70% of those deployed to Iraq and Afghanistan reported at least 1 episode of an acute respiratory illness during their deployment, and almost 15% reported 3 or more episodes of respiratory illnesses in the course of their deployment (60). Approximately 1 of 5 (∼17%) of those with respiratory illnesses indicated that the illness was severe enough that they sought medical attention. The authors found no observed relationship between cigarette smoking and self-reported respiratory illnesses during deployment in this cross-sectional study, suggesting that factors other than tobacco use are likely contributory to respiratory symptomatology and morbidity in the deployed setting (60).

Among the 15,463 troops surveyed, the incidence rate of acute respiratory illness was shown to decline to approximately 40% later during the operations in 2005–2006, yet 33.8% of these individuals reported that respiratory illness adversely impacted their work activities and job performance (98). Factors associated with increased risk of acute respiratory illness included female sex, military service in the US Navy, lack of hygienic toilet facilities, increasing age, higher occupational rank, and deployment to Iraq relative to Afghanistan (98). The underlying etiology of the increased rates of acute respiratory illnesses during deployment is yet to be fully elucidated, and it appears that the incidence and prevalence of acute respiratory illness are not restricted to US military personnel but affect coalition forces as well (99). Specifically, retrospective analysis of medical records of Polish military in Iraq and Afghanistan found acute respiratory illness to be one of the most common health problems in outpatient medical facilities (99). Additionally, there is indication that exposure to combustion-derived particles such as diesel exhaust in civilians may enhance an inflammatory response in the respiratory tract and increase susceptibility to viral respiratory infections, resulting in the increased frequency and severity of respiratory symptoms (97). Findings of increased acute respiratory symptoms and respiratory-related medical encounters secondary to short-term air pollution exposure are consistent with a well-recognized body of literature in civilians (100–102) and are therefore an expected finding in deployed military personnel.

One of the first studies to evaluate the chronic respiratory impacts of deployment was by Szema et al. (6), who conducted a retrospective review of medical diagnoses of more than 6,000 military personnel who were deployed, discharged from military active duty, and evaluated at the Northport, New York, Veterans Affairs Medical Center from 2004 to 2007. This study showed that deployment to Iraq was associated with a higher risk of having a new ICD-9 code diagnosis of asthma postdeployment relative to military service stateside (6.6% vs. 4.3%; crude odds ratio = 1.58, 95% confidence interval: 1.18, 2.11). The higher risk of asthma in those deployed persisted when the data were stratified for sex and gender. This study did not account for confounders, such as personal history of smoking, and did not have data on patient reports of exposures to airborne hazards in the course of their deployment or military duties. Despite these limitations, the higher rates of new diagnoses of asthma in Iraq-deployed veterans (6) raise a clinical concern that warrants further consideration, particularly as similar findings are well documented in occupationally exposed first responders to the World Trade Center disaster (103, 104). The data on new-onset asthma in Iraq-deployed military personnel are inconsistent with medical encounter data from the Department of Defense, which demonstrated a decreasing incidence of asthma diagnoses in active duty US service members from 1999 to 2008 (105). These differences may lie in the fact that data from the Department of Defense come from active duty personnel with varied deployment locations rather than from a veteran population deployed only to Iraq during 2004–2007 (6).

The Millennium Cohort Study was launched prior to the start of combat operations in Iraq and Afghanistan and is designed to evaluate exposures and long-term health outcomes in 150,000 participants from all branches of the US military (35, 106). In a study that analyzed the data on approximately 46,000 Millennium Cohort Study participants who completed baseline surveys in 2001–2003 and follow-up surveys in 2004–2006, and after control for smoking status, self-reports of new-onset respiratory symptoms (persistent cough, shortness of breath) were higher in those deployed to Iraq and Afghanistan compared with those not deployed (14% vs. 10%) (35). Land-based deployment was independently associated with an increased reporting of respiratory symptoms among service members deployed to Iraq and Afghanistan in the cohort, suggesting that experiences or exposures associated with ground combat may be an important factor in symptom reporting (35). However, the rates of specific diagnoses of chronic bronchitis, emphysema, or asthma did not differ between the 2 groups. Recent data from a separate population-based health survey (i.e., the National Health Survey for a New Generation of US Veterans) on over 20,000 veterans who served from 2001 to 2008 observed similar
rates of obstructive lung disease in those deployed and not deployed (107). However, in this study, those deployed were 29% more likely to have a sinusitis diagnosis than were those not deployed. To date, the Millennium Cohort Study (35) and the National Health Survey for a New Generation of US Veterans (107) are the only 2 longitudinal prospective epidemiologic studies available on the respiratory health of veterans of Iraq and Afghanistan.

Abraham et al. (108) conducted a case-control study that evaluated the relationship between Iraq and Afghanistan deployment and respiratory conditions by linking deployment history with postdeployment Department of Defense medical records in active duty US military personnel. Medical utilization data demonstrated increased rates of respiratory symptoms and medical encounters for obstructive pulmonary diseases postdeployment relative to predeployment, particularly in service members who had a single deployment versus those who had multiple deployments. For those with multiple deployments, the rates of encounters for respiratory symptoms increased significantly only after their fourth deployment relative to baseline. One might expect to see an increase in respiratory symptoms or encounters observed with greater cumulative number of deployments, reflecting a dose-response relationship. This was not observed in the study by Abraham et al. (108), perhaps because persons who have substantial respiratory symptoms or impairments from their first deployment were less likely to deploy again to Iraq and Afghanistan, resulting in a healthy worker effect. It is also plausible that those who had multiple deployments may have unidentified protective factors or may have been assigned to locations or job tasks that did not have significant levels of exposures to airborne hazards. The lack of individual data on specific exposures in the theater of operations is a significant limitation of this study.

Exposures to ambient particulate matter are purported to be etiological factors for increased reporting of respiratory ailments in those deployed to Iraq and Afghanistan. Abraham et al. (109) in a case-crossover analysis examined the relationship between particulate matter data collected between December 2005 and June 2007 and medical data from health encounters at military bases in the corresponding locations of deployment. The authors reported that there was no observed relationship between elevated levels of particulate matter (PM_{2.5} and PM_{10}) and acute respiratory outcomes in deployed military personnel. The limitation of this study includes the use of medical encounter data, which captures only illnesses severe enough to warrant medical attention, and is therefore subject to underreporting, particularly in light of the prevailing military culture where service members are unlikely to seek medical attention until their ability to function on the job is significantly and adversely impacted. Further, the environmental sampling comprised only 15 sites in the course of 1–6 days without direct correlation to individual exposures and related health outcomes.

In summary, the available observational data on short-term respiratory outcomes in those deployed to Iraq and Afghanistan are consistent for higher incidence and prevalence of acute respiratory illness. (Refer to Table 1 for a review of these studies). As a whole, these studies provide important information but vary in terms of quality. For example, conclusions from studies utilizing questionnaires administered only following (60, 81) deployment to Iraq and Afghanistan are more likely compromised by recall bias. Medical record reviews common to many of the aforementioned studies (6, 99, 108–110) may have more limited internal and external validity because of the inherent biases reflected in documentation and health-care seeking. At this point, longitudinal prospective studies (pre- and postdeployment) with standardized instruments, such as the Millennium Cohort Study (35) and the National Health Survey for a New Generation of US Veterans (107), are few.

With respect to long-term health effects and specific chronic respiratory disease, the available data are mixed. Although preliminary hospital-based clinical data suggest that new asthma diagnoses and/or evaluations with spirometry are higher in those deployed to Iraq and Afghanistan relative to their nondeployed counterparts, the fact that this is a care-seeking population precludes generalization, more so that the population-based studies to date do not show such an association. However, the research is still evolving and, given the fact that high exposures to airborne irritants are well known to cause new-onset asthma and/or to aggravate preexisting asthma in other settings, a high index of clinical suspicion for asthma is recommended for Iraq and Afghanistan military personnel who present with persistent respiratory symptoms.

Objective evidence of respiratory disease and dysfunction

Presently, the majority of studies describing a relationship between chronic lung disease and deployment contain limited objective data and rely predominately on retrospective analysis of health-care utilization data (e.g., ICD-9 codes and medical encounters). There are a few exceptions in which objective data are available to support a clinical diagnosis; these include cases of acute eosinophilic pneumonia (36), constrictive bronchiolitis (5), and vocal cord dysfunction (111). Refer to Table 2 for a description of these studies.

Acute eosinophilic pneumonia is a type of interstitial lung disease characterized by an increase in eosinophils in the lungs with or without peripheral eosinophilia. This disease has been associated with Churg-Strauss syndrome, parasitic infections, and drug reactions. In 2004, Shorr et al. (36) described 18 cases of acute eosinophilic pneumonia in military personnel deployed in or near Iraq during March 2003–March 2004. The authors used the criteria of Philit et al. (112), including febrile illness, cough, dyspnea, and infiltrates on chest radiographs for less than 1 month, to identify the cases. Unlike Philit et al. (112), however, the authors included personnel who did and did not have respiratory failure. The authors divided these cases into definite (n = 7) and probable (n = 11) acute eosinophilic pneumonias as defined by bronchoalveolar lavage or bronchoscopy-confirmed pulmonary eosinophilia or elevated peripheral eosinophils. All patients underwent extensive workup to exclude other causes of acute eosinophilic pneumonia, but no common source exposure was identified despite a peak incidence between the months of July and August. Cigarette smoking was common to each case, and 78% reported new-onset smoking, which was considered a risk factor for acute eosinophilic
<table>
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<td>Sanders, 2005 (60)</td>
<td>Cross-sectional</td>
<td>Acute respiratory illness</td>
<td>15,459</td>
<td>Health survey questionnaire on return from deployment</td>
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<td>Cross-sectional</td>
<td>Respiratory symptomsa (asthmatics vs. nonasthmatics)</td>
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<td>Cross-sectional self-report data only, recall bias</td>
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<tr>
<td>Soltis, 2009 (98)</td>
<td>Cross-sectional</td>
<td>Acute respiratory illness</td>
<td>15,463</td>
<td>Health survey questionnaire during deployment</td>
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<td>Retrospective cohort</td>
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<td>Medical encounter for pulmonary disease (ICD-9 codes 490–496)</td>
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<td>Abraham, 2012 (109)</td>
<td>Case-crossover</td>
<td>Medical encounter for cardiovascular and respiratory outcomes</td>
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<td>Associations between short-term particulate matter exposure and cardiorespiratory encounters not observed</td>
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<td>Smith, 2012 (121)</td>
<td>Retrospective cohort</td>
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<td>22,297 (3,585 within 3 miles⁵ of burn pit)</td>
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<td>Baird, 2012 (123)</td>
<td>Retrospective cohort</td>
<td>Respiratory symptoms, medical encounter</td>
<td>6,352 potentially exposed to Al-Mishraq sulfur fire; 4,153 nonexposed</td>
<td>Health survey questionnaire and ICD-9 codes at pre- and postdeployment</td>
<td>Health concerns and symptoms common in exposed; no difference in medical encounters between exposed and nonexposed</td>
<td>Individual-level exposure not available, retrospective design, self-report symptoms, long-latency diseases unknown</td>
</tr>
</tbody>
</table>

Table continues
Table 1. Continued

<table>
<thead>
<tr>
<th>First Author, Year (Reference No.)</th>
<th>Study Design</th>
<th>Symptom, Illness, Condition</th>
<th>Sample Population</th>
<th>Data Source</th>
<th>Key Findings</th>
<th>Limitations</th>
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<tr>
<td>Korzeniewski, 2013 (99)</td>
<td>Retrospective design; reliance on ICD-9 codes 490 to 496, 786–796 for cases of burn pit exposure</td>
<td>Respiratory tract diseases most common ailments with a prevalence ranging from 45 to 62 cases per 100 persons</td>
<td>Medical record review for respiratory encounters; no increased risk if deployed with burn pit exposure</td>
<td>Retrospective design; diagnoses were made by self-report</td>
<td>Respiratory tract diseases, most common ailments with a prevalence ranging from 45 to 62 cases per 100 persons.</td>
<td>产值更加bad，long-latency diseases unknown.</td>
</tr>
<tr>
<td>Barth, 2014 (107)</td>
<td>Retrospective cohort</td>
<td>Asthma, sinusitis, and bronchitis</td>
<td>18,430 deployed with burn pit exposure; 6,337 deployed without burn pit exposure; 157,053 nondeployed</td>
<td>Health survey questionnaire for respiratory outcomes</td>
<td>Medical encounters increased postdeployment; no increased risk if deployed with burn pit exposure</td>
<td>Respiratory encounters increased postdeployment; no increased risk if deployed with burn pit exposure.</td>
</tr>
<tr>
<td>Abraham, 2014 (122)</td>
<td>Retrospective cohort</td>
<td>Medical encounters for respiratory outcomes</td>
<td>157,053 nondeployed</td>
<td>Medical record review for respiratory encounters, including diagnoses with ICD-9 codes 490–496, 786–796</td>
<td>ICD-9 codes 490-496 indicate medical encounter for obstructive pulmonary disease.</td>
<td>Respiratory encounters increased postdeployment; no increased risk if deployed with burn pit exposure.</td>
</tr>
</tbody>
</table>

Abbreviations: FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; ICD-9, International Classification of Diseases, Ninth Revision; OEF, Operation Enduring Freedom; OIF, Operation Iraqi Freedom.

Respiratory symptoms include cough, wheezing, sputum production, and chest pain or tightness. 
Obstructive diagnosis includes asthma, bronchitis, or emphysema. 
ICD-9 codes 490–496 indicate medical encounter for obstructive pulmonary disease.

pneumonia in these patients. Shorr et al. (36) have recommended that military personnel presenting with unexplained respiratory complaints during or after a recent deployment exclude acute eosinophilic pneumonia.

In 2011, King et al. (5) described 38 cases of constrictive bronchiolitis in deployed military personnel who endorsed exercise limitations and reported exposures to airborne hazards during their deployment to Iraq or Afghanistan. Constrictive bronchiolitis was defined as the presence of extrinsic narrowing of the luminal wall caused by subepithelial fibrosis, smooth-muscle hypertrophy in membranous bronchioles, or both with an increase in wall thickness of more than 20% of normal. Typically, individuals with constrictive bronchiolitis will present with dyspnea on exertion and nonproductive cough and demonstrate abnormalities on pulmonary function and imaging. However, pulmonary function and cardiopulmonary exercise testing were mostly within normal limits along with limited findings on computed tomography scans in these 38 cases. One of the few exceptions to mostly normal findings was mild-to-moderate reduction in lung diffusing capacity of carbon monoxide (73% of predicted values), which is similar to findings in nontransplant cases of constrictive bronchiolitis (113). The majority of cases reported exposures to airborne hazards during their deployment (e.g., dust storms, burn pits, combat smoke), including 28 of 38 individuals reporting exposure to the Mosul sulfur mine fire in northeastern Iraq in 2003. These 38 cases were identified out of a total of 49 symptomatic military personnel who underwent lung biopsy. However, it should be noted that the other 11 biopsy samples not diagnosed as constrictive bronchiolitis did reveal other diagnoses including sarcoidosis, respiratory bronchiolitis interstitial lung disease, respiratory bronchiolitis, hypersensitivity pneumonitis, and other diagnoses. In conclusion, King et al. (5) recommended considering constrictive bronchiolitis in veterans of Iraq and Afghanistan with exercise limitations and mostly normal findings on imaging and physiological studies.

The case series of deployed US service members with constrictive bronchiolitis (5) has been met with controversy (114, 115), including criticism about the limited battery of testing to rule out exertional dyspnea in symptomatic military personnel (115). For example, vocal cord dysfunction has been described in active duty military personnel with complaints of exertional dyspnea (116). Assessment of vocal cord dysfunction is not commonly performed in an evaluation of exertional dyspnea despite its increased prevalence in military populations (117). Recently, a retrospective review of vocal cord dysfunction diagnoses obtained at the primary medical evacuation center for military patients from Iraq and Afghanistan identified 48 cases of vocal cord dysfunction on the basis of laryngoscopy (111). Spirometry was within normal limits for all cases, but 2 of 48 had a positive bronchodilator response, and 8 of 48 had a positive methacholine challenge test. All cases reported exertional dyspnea, 46% were being treated for gastroesophageal reflux disease, 60% were receiving treatment for rhinitis, and 63% had a formal psychiatric diagnosis. These comorbid conditions are common in individuals with vocal cord dysfunction and are consistent with irritant-induced, exercise-induced, and/or psychogenic etiologies. In light of these findings and prior reports, military
<table>
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<tr>
<th>First Author, Year (Reference No.)</th>
<th>Study Design</th>
<th>Clinical Diagnoses</th>
<th>Sample Population Size, No.</th>
<th>Outcome Measure(s)</th>
<th>Key Findings</th>
<th>Limitations</th>
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<tr>
<td>Shorr, 2004 (36)</td>
<td>Descriptive case series</td>
<td>Acute eosinophilic pneumonia</td>
<td>18</td>
<td>Morbidity, mortality</td>
<td>2 of 18 died; 78% with new-onset smoking during deployment</td>
<td>Only 7 cases met definitive criteria for acute eosinophilic pneumonia.</td>
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<tr>
<td>Sharp, 2008 (120)</td>
<td>Prospective cohort</td>
<td>N/A</td>
<td>110</td>
<td>Fitness and body composition pre- and postdeployment</td>
<td>−4.5% VO$_2$ peak, −4.9% upper body power, −3.5% fat-free mass</td>
<td>Study not designed to specifically assess pulmonary symptoms or function; only 9-month deployment to Afghanistan studied.</td>
</tr>
<tr>
<td>Lester, 2010 (119)</td>
<td>Prospective cohort</td>
<td>N/A</td>
<td>73</td>
<td>Fitness and body composition pre- and postdeployment</td>
<td>12.6% increase in 2-mile$^a$ run time; 9% increase in body fat</td>
<td>Study not designed to specifically assess pulmonary symptoms or function; only 13-month deployment to Iraq studied.</td>
</tr>
<tr>
<td>King, 2011 (5)</td>
<td>Descriptive case series</td>
<td>Constrictive bronchiolitis</td>
<td>49</td>
<td>Pathology testing, pulmonary function testing, cardiopulmonary exercise testing, and high-resolution computed tomography imaging</td>
<td>38 of 49 (76%) diagnosed with constrictive bronchiolitis; 68% had normal high-resolution computed tomography imaging, 34% had normal results from pulmonary function testing, and cardiopulmonary exercise testing was within normal limits; 36 of 37 biopsy samples showed polarizable material.</td>
<td>28 of 38 exposed to sulfur fire, unblinded pathology review.</td>
</tr>
<tr>
<td>Morris, 2013 (111)</td>
<td>Descriptive case series</td>
<td>Vocal cord dysfunction</td>
<td>48</td>
<td>Laryngoscopy, spirometry, and methacholine challenge test</td>
<td>All dyspnea; 48% had a truncated flow-volume loop, 83% had a negative methacholine challenge test, and 3 of 48 had abnormal spirometry test results.</td>
<td>Retrospective design, missing data on some cases</td>
</tr>
<tr>
<td>Morris, 2014 (118)</td>
<td>Descriptive case series</td>
<td>New-onset pulmonary symptoms</td>
<td>50</td>
<td>Pulmonary function testing, cardiopulmonary exercise testing, methacholine challenge test, bronchoalveolar lavage, impulse oscillometry system testing, and high-resolution computed tomography imaging</td>
<td>42% had nondiagnostic evaluation; 20% had airway hyperreactivity; and 66% had mental health and sleep disorders.</td>
<td>Potential sampling bias; no lung biopsy</td>
</tr>
</tbody>
</table>

Abbreviations: N/A, not applicable; VO$_2$, oxygen uptake.

$^a$ Two miles (3.2 km).
personnel with exertional dyspnea and normal objective findings on imaging and lung function studies may benefit from an evaluation for vocal cord dysfunction before proceeding to more invasive diagnostic evaluations. 

Recently, Morris et al. (118) from Brooke Army Medical Center reported on the first prospective evaluation of new-onset respiratory symptoms in active duty military personnel deployed to Iraq or Afghanistan called the Study of Active Duty Military for Pulmonary Disease Related to Environmental Deployment Exposures (STAMPEDE). In this study, 50 consecutive military personnel with new-onset pulmonary symptoms and within 6 months of returning from Iraq or Afghanistan were studied. A comprehensive and standardized assessment was performed that included deployment and symptom questionnaires, full pulmonary function tests, chest radiographs, high-resolution chest computed tomography, methacholine challenge testing, fiberoptic bronchoscopy, and bronchoalveolar lavage. Despite the battery of testing, 42% of this sample had nondiagnostic evaluations, and the authors did not pursue open lung biopsy in these cases. In those receiving a diagnosis (n = 29), 36% were diagnosed with airway hyperreactivity as detected by obstruction on baseline spirometry, bronchodilator response, and/or a positive methacholine challenge test. No additional patterns emerged with the exception of isolated reductions in diffusing capacity in 8% of cases. Additionally, high rates of sleep (52%–62%) and mental health (67%–69%) disorders were present irrespective of a definitive pulmonary diagnosis. Although the sample size is limited, the Study of Active Duty Military for Pulmonary Disease Related to Environmental Deployment Exposures (118) provides important objective data on the evaluation of deployed military personnel with new-onset symptoms. Findings of airway hyperreactivity are consistent with those from prior reports of obstruction and new-onset asthma (108–110, 122).

Two additional prospective studies have been published characterizing fitness pre- and postdeployment to Iraq (119) and Afghanistan (120). The focus of these studies was to evaluate changes in physical fitness and body composition during deployment, and it did not consider airborne hazards exposure or respiratory symptoms. Lester et al. (119) evaluated 2-mile (3.2-km) run time before and after a 13-month deployment to Iraq in 73 US Army soldiers. Following deployment, 2-mile run times were 13% slower, and peak oxygen consumption estimated from run times worsened by approximately 12%. Investigators observed that all deployed soldiers had significant decreases in cardiorespiratory performance (i.e., longer 2-mile run time) irrespective of predeployment performance (119). In a separate study, Sharp et al. (120) directly measured oxygen consumption before and after a 9-month deployment to Afghanistan in 110 US Army soldiers. In comparison with predeployment, postdeployment peak oxygen consumption (mL/kg/minute) significantly declined 6.6% on average (range, −1.0% to −8.8%). Investigators from both studies attribute these modest declines in performance to a reduced training volume during deployment. For example, Sharp et al. (120) reported that 80% of the sample performed aerobic training 3 days per week or more predeployment, whereas that proportion declined to 35.2% during deployment. Although job-related aerobic activity was not considered during deployment, Lester et al. (119) found that 71% of their sample reported no job-related aerobic activity. Although these 2 studies suffer from small samples and the absence of appropriate control groups, they increase the possibility that relative deconditioning due to diminished training and physical activity contributes to reports of increased dyspnea after deployment.

Outcomes from specific exposures

Although both natural and anthropogenic sources contribute to the elevated particulate matter (PM$_{2.5}$ and PM$_{10}$) and poor air quality that are ubiquitous to the deployment environment of Iraq and Afghanistan, the greatest attention has been paid to specific exposures, such as open-air burn pits. To address this issue, Smith et al. (121) examined the relationship between proximity to burn pits and respiratory outcomes (i.e., newly reported chronic bronchitis or emphysema, asthma, and respiratory symptoms) among Millennium Cohort participants (n = 22,844) who deployed to Iraq or Afghanistan. Other than a marginally significant increased rate of reporting of respiratory symptoms in Air Force personnel who were located within 2 miles of Joint Base Balad during their deployment to Iraq, there was no relationship between location within 3 or 5 miles of known open air burn pit operations and newly reported respiratory symptoms, asthma, bronchitis, and emphysema. Limitations to this study include lack of objective cardiopulmonary function data and the use of distance from burn pits as a proxy for exposure. However, this longitudinal design does offer some considerable advantages including the ability to account for the potential confounding factors of smoking status and physical activity.

In support of these findings, Abraham et al. (122) recently performed a retrospective cohort study to examine associations between Operation Iraqi Freedom deployment and postdeployment medical encounters for respiratory symptoms and conditions. Incidence rate ratios were calculated for personnel deployed to locations in Iraq and Kuwait with (Joint Base Balad, Camp Taji) and without (Camp Arifjan, Camp Buehring) active burn pits during the time of investigation, as well as to nondeployed reference locations (Korea, United States). This included a total sample of over 180,000 personnel across locations. Relative to nondeployed personnel, incidence rate ratios of 1.25 for respiratory symptoms and 1.54 for asthma were significantly elevated in deployed personnel (122). However, respiratory symptoms and conditions were similar in personnel deployed to locations with or without burn pits. Future studies are warranted to determine if these risks are present at other bases with burn pits, including sites in support of Operation Enduring Freedom (Afghanistan).

For approximately 1 month in 2003, a large fire burned continuously at the Al-Mishraq sulfur plant in Mosul, Iraq. Baird et al. (123) compared respiratory outcomes in a small group of fire fighter responders (n = 191) who were present at the sulfur plant fires with those from a larger, more dispersed, but potentially exposed population (n = 6,341) and 2 unexposed groups (n = 4,153). The authors concluded that, although there was a positive association between self-reported symptoms and health concerns in those potentially exposed to the sulfur fires, there was no significant difference.
in the clinical encounters for chronic respiratory disease between the exposed and control populations. Limitations of this study are similar to those described previously (121), such as proximity to the sulfur fire was used as a surrogate for exposure and the reliance on self-report measures.

**DISCUSSION**

In this review, we have summarized the existing knowledge on the relationship between airborne hazards exposure and respiratory health in Iraq and Afghanistan veterans. On the basis of the available peer-reviewed published data, military personnel deployed to Iraq and Afghanistan appear to experience elevated rates of acute respiratory symptoms during deployment and may be at greater risk for postdeployment respiratory symptoms and illnesses. However, the limited data presently available preclude any definitive conclusions on the possible long-term negative impacts of airborne hazards exposure, such as the development of chronic lung disease. Current emphasis should be placed on the comprehensive clinical evaluation of symptomatic military personnel, as well as on longitudinal research studies to objectively evaluate the respiratory health of deployed veterans. Refer to the Web Appendix available at [http://aje.oxfordjournals.org/](http://aje.oxfordjournals.org/) for a description of some of these recent efforts, including a web-based self-assessment for veterans that covers 6 unique domains (Web Table 1).

Despite the lack of available data, we believe concern for potential long-term health effects related to airborne hazards exposure is justified. With respect to the types of exposures of concern, approximately 120,000 military personnel returning from Iraq who completed the postdeployment health reassessment survey between September 2005 and August 2006 listed their top 5 exposures of concern as sand and dust storms, loud noises, smoke from burning trash, vehicle exhaust, and petrochemical fuel (124). Work from our tertiary care center has also found that veterans of Iraq and Afghanistan are significantly concerned about the long-term health effects associated with these airborne hazards exposures (2, 3). A retrospective analysis of exposure and health concerns in more than 450 military personnel deployed to Iraq and Afghanistan showed that almost all (94%) reported exposures to airborne hazards during their deployment, and virtually all (93%) expressed some degree of concern about exposures to specific air pollutants, such as smoke from open burn pits. This concern about deployment exposures was also shown to be associated with a greater somatic symptom burden in these veterans (3).

From our review of the literature, we identified several important knowledge gaps. Foremost, our understanding of the health effects related to airborne hazards exposure in military personnel is almost exclusively derived from short- and long-term air pollution exposure studies in nonmilitary populations. Although these studies support biological plausibility, the health outcomes and endpoints related to an exposure profile that is characteristic of deployed military personnel (i.e., intermediate duration (months to year) and high levels of particulate matter) are poorly understood. First responders to the World Trade Center disaster have been suggested as an appropriate comparison cohort given similarities in exposure to combustion-derived particulates and other respiratory toxicants (110). Although the exposure profiles for deployed military personnel and World Trade Center first responders are not identical, findings from the World Trade Center cohort do provide relevant data in terms of respiratory symptoms and impaired pulmonary function that persist months to years postexposure (103, 125, 126). Recently, Glaser et al. (104) have further investigated the time interval between World Trade Center exposure and incident diagnoses of obstructive airway disease and found that the relative rates (high vs. low exposure) of diagnoses persist throughout the 5-year period following exposure. Although the magnitude of this risk declined beyond the acute (<15 months after 9/11) period, the elevated risk of obstructive airway disease diagnoses persisted. Similar temporal trends have been reported in respiratory symptoms as well, such that significant declines in symptom prevalence are observed in the 12–24 months after exposure but fail to return to preexposure levels up to 5 years postexposure (127).

In conclusion, the current literature supports a clear increase in respiratory symptoms and illnesses in military personnel during and following deployment to Iraq and Afghanistan, with the predominant clinical phenotype being airway obstruction and hyperreactivity. The literature has also documented 2 notable clusters of rare diseases, constrictive bronchiolitis and acute eosinophilic pneumonia, yet their etiology and prevalence remain to be fully understood. Beyond these case series, limited other objective data are available to evaluate lung function, structure, and pathology in deployed personnel. During deployment, military personnel were exposed to airborne hazards that exceeded exposure guidelines from a variety of sources. Although the characteristics of military service and deployment may predispose individuals to greater risk of adverse health effects associated with exposure (Figure 1), direct evidence of an association between exposure and other chronic respiratory diseases is lacking at the present time. Future longitudinal research studies with comprehensive and objective assessments are necessary to better understand the potential long-term health consequences associated with deployment to Iraq and Afghanistan.

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