

Combat zone exposure and respiratory tract disease

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Background: The impact of deployment to combat zones on the respiratory and sinonasal health of U.S. soldiers is an emerging public health concern. Retrospective studies have shown a correlation between deployment and development of post-deployment pathology, particularly of the aerodigestive system. Respiratory disease, including sinusitis, allergic rhinitis, and asthma, are commonly reported in soldiers deployed to the Middle East and Southwest Asia.

Methods: Current literature pertaining to combat zone exposure and development of respiratory disease was retrieved using PubMed, Embase, Web of Science, and Google Scholar.

Results: Several types of combat zone exposures exist that may play an influential role in the development of upper and lower respiratory tract diseases. Exposures including foreign dusts, harsh environments, particulate size, and close living quarters may play a causative role. The effect of combat zone exposures has been better examined for lower respiratory tract diseases; however, with the theory

of the unified airway, the upper respiratory tract may also be involved. There is evidence that the upper respiratory tract is susceptible, with an increased risk for development of sinusitis and sinonasal disease; however, the quality of evidence of the present literature is generally low.

Conclusion: More research is necessary to determine a pathophysiologic mechanism between combat zone exposure and the development of sinonasal disease. Practicing otolaryngologists should be aware of the possibility of combat zone exposures that could contribute to rhinologic symptomatology. © 2018 ARS-AAOA, LLC.

Key Words:

air pollution; asthma; paranasal sinus diseases; particulate matter; rhinosinusitis; sinusitis

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The impact of deployment to combat zones on the respiratory and sinonasal health of U.S. soldiers is an emerging public health concern. Anecdotal reports in the popular media suggest new or worsening respiratory disease after return from a tour of duty; however, prospective data are lacking to substantiate these claims. The U.S.

Armed Forces has over 1.3 million active duty servicemen and servicewomen with over 300,000 of these personnel deployed to regions outside of the United States. These individuals may be at risk for a variety of occupational exposures, which can be hazardous to their respiratory health. In addition to the direct threat of combat, soldiers often face difficult environmental conditions, including exposure to foreign particulate matter and close-quarters living conditions. Furthermore, there is the threat of toxic chemical agents either in the environment or when used as a weapon by opposing forces.

Retrospective studies have shown a correlation between deployment and development of post-deployment pathology, particularly of the aerodigestive system.^{1,2} A causative link is largely speculative and data are predominantly provided through subjective patient reports. However, respiratory disease, including sinusitis, allergic rhinitis, and asthma, have been reported as the most common nonpsychiatric clinical diagnoses among Iraq and Afghanistan veterans.³

Environmental and living conditions in foreign combat theaters can be drastically different from conditions in the

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TABLE 1. Summary of common symptoms and respiratory tract diagnoses in individuals with a history of combat zone exposures

Anatomic region	Symptoms	Respiratory tract pathology
Upper respiratory tract	Nasal congestion, postnasal drip, rhinorrhea, sore throat, hyposmia	Allergic rhinitis, nonallergic rhinitis, chronic sinusitis, recurrent acute sinusitis
Lower respiratory tract	Coughing, shortness of breath, wheezing	Asthma, acute bronchitis, chronic bronchitis, constrictive bronchiolitis

United States. Deployed soldiers are exposed to foreign dusts, harsh environments, and close living quarters. These conditions have been associated with the development of respiratory disease, including disease of the sinonasal tract.⁴ Despite anecdotal information and public media reports, the scientific literature is less clear as to how these exposures affect the health of deployed service members. Table 1 summarizes the most common symptoms and diagnoses of the respiratory tract associated with combat zone exposures.

In this review we summarize the available scientific knowledge about environmental and occupational exposures on respiratory health in U.S. soldiers stationed in the Middle East and Southwest Asia.

Impact on the lower respiratory tract

Disease of the lower respiratory tract (LRT) has been associated with service member deployment to Southwest Asia and the Middle East (Table 2). Up to 69% of soldiers have been affected to some degree by respiratory ailments,⁴ with asthma being the most commonly reported new respiratory diagnosis in the literature.⁵⁻⁷ Most reports have suggested a correlation exists between deployment and reversible obstructive disease, whereas others showed no increase in risk.^{8,9} Among veterans with recent deployment to Iraq and/or Afghanistan, Szema et al demonstrated a significantly increased rate of respiratory symptoms and changes in pulmonary function compared with soldiers stateside.¹⁰ In that cohort of 1,787 veterans, 14% presented with new-onset respiratory symptoms that required evaluation with spirometry upon returning home. Much of the literature has focused on patient-reported symptoms of respiratory disease as opposed to objective findings for diagnosis. Barth et al suggested an increase in reported respiratory disease with respiratory exposures (eg, exposure to dust, smoke, chemicals, and pollutants).¹¹ In studies supporting the development of respiratory disease after deployment, the most commonly cited risk factors were duration of deployment and number of deployments.¹²⁻¹⁴ Other associations include exposure to chemical fires, incineration of human and solid waste, dust storms, and combat smoke.¹⁵

Despite this suggested correlation, the development of true respiratory disease is controversial.¹⁶ In a recent prospective study of 46,077 deployed soldiers, an increased risk of asthma or chronic obstructive pulmonary disease

was not found. Despite this, there was a significantly increased number of deployed individuals complaining of new-onset respiratory symptoms (cough or shortness of breath) independent of smoking status. A new-onset cough was the most significant symptom, the risk of which was dependent on the duration of deployment. Notably, the increased risk of new symptoms was only significant in soldiers who underwent a land-based deployment.¹⁷ Chen et al. demonstrated an inverse relationship with spirometric findings and duration of deployment, suggesting that the longer duration increases the risk of objective changes in lung function.¹²

Impact on the upper respiratory tract

In contrast to the LRT, there is less evidence defining a causative role for combat zone exposure in developing pathology of the upper respiratory tract (URT). However, given the histologic similarities of the exposed tissue, it is plausible that environmental exposures leading to LRT pathology also affect the URT, including the paranasal sinuses. The phenomenon of the unified airway was proposed over a decade ago and there is mounting evidence supporting this process.^{18,19} These 2 regions of the airway share similar epithelium and studies have shown that inflammation in one location may lead to an inflammatory response in the other.²⁰ Table 3 summarizes the clinical studies addressing URT manifestations of combat zone exposures.

Sinus disease has been documented as one of the leading ailments in deployed soldiers to the Middle East.²¹ In a large-scale retrospective study using tissue obtained from Gulf War (1990-1999) veterans, Ladich et al demonstrated that chronic sinusitis and allergic rhinitis were the most common pathologies identified on histologic examination.²² Similarly, self-reported symptoms of soldiers deployed during Operation Desert Shield in Saudi Arabia (1990-1991) show increased complaints of persistent rhinorrhea after deployment.²³ These symptoms were also associated with exposure to outdoor conditions and living in tents. Multiple other upper respiratory complaints were demonstrated, supporting the hypothesis that environmental exposure increases mucosal inflammation. In a retrospective study of Australian soldiers in the Persian Gulf War, sinus symptoms were reported at higher frequency in the post-deployment cohort compared with controls.²⁴ Similar findings were demonstrated in a more recent study

TABLE 2. Summary of findings from clinical studies involving the lower respiratory tract

Reference (first author)	Design	Location of deployment/conflict (year)	Significant findings
Abraham ⁵	Case-control	OEF/OIF (2001-2005)	Increased rate of respiratory symptoms after deployment; deployment duration not associated with development of obstructive respiratory disease
Abraham ⁷	Retrospective cohort	OIF (2005-2007)	25% increase in rates of respiratory symptoms; 54% increase in rates of asthma
Barth ¹¹	Retrospective survey	OEF/OIF (2001-2008)	Exposure linked to respiratory disease regardless of deployment
DelVecchio ¹⁶	Retrospective cohort	OEF/OIF (2005-2009)	No significant difference in incidence of asthma or PFTs based on deployment status; asthma severity classification did not differ between groups
Falvo ¹⁴	Cross-sectional analysis	Iraq/Afghanistan (2012-2015)	Longer deployment duration associated with increased FEV1/FVC
Holley ¹³	Retrospective review	OEF/OIF (2012-2013)	Increased rate of spirometric abnormalities in those with respiratory complaints
King ¹⁵	Case series	Iraq/Afghanistan (2004-2009)	Constrictive bronchiolitis found in lung biopsies of those exposed to particulate matter leading to dyspnea
Matthews ⁹	Retrospective cohort	Southwest Asia (2005-2009)	Deployment status did not affect COPD diagnosis
Morris ⁶	Prospective cohort	Iraq/Afghanistan (2010)	Airway hyperreactivity was the most common cause of abnormal PFTs
Sanders ⁴	Cross-sectional survey	Afghanistan (2003-2004)	Respiratory illness reported by 69.1% of deployed respondents; 22.5% developed allergy attack; 3.6% had asthma attack
Sharkey ⁸	Retrospective cohort	OEF/OIF (2002-2011)	62% increased incidence of asthma compared with U.S.-stationed service members
Smith ¹⁷	Prospective cohort	Iraq/Afghanistan (2001-2003)	Land-based veterans had higher rates of respiratory symptoms than offshore veterans
Szema ¹⁰	Retrospective cohort	Iraq/Afghanistan (2004-2010)	New-onset asthma was 6 times higher in deployed group; no difference in FEV1/FVC values between groups

COPD = chronic obstructive pulmonary disease; FEV₁ = forced expiratory volume in 1 second; FVC = forced vital capacity; OEF = Operation Enduring Freedom; OIF = Operation Iraqi Freedom; PFT = pulmonary function test.

with U.S. soldiers deployed to Afghanistan and Iraq during Operations Enduring Freedom and Iraqi Freedom (2001 to present). Patients in that study showed a significantly increased risk for sinusitis after deployment, but not LRT disorders such as asthma or bronchitis.²⁵ This trend of increased sinonasal inflammation has been reported in other countries as well.²⁴

An increased incidence of allergic rhinitis has been reported in soldiers deployed in the Persian Gulf War.²⁶ Due to the presence of indigenous grass, weed, tree pollens, as well as mold in Middle Eastern countries, there is a risk for development of allergic rhinitis in previously unsensitized individuals. Allergic rhinitis, in turn, may predispose a deployed soldier to development of other URT disease such as sinusitis.²⁷ These exposures increase morbidity while abroad and may lead to increased health burden upon returning home. According to a large systematic

review addressing the international prevalence of allergic rhinitis, the most commonly reported aeroallergens in the Middle East were *Salsola* species and other weed pollens.²⁸ Other allergens were dust mites, cockroaches, and other grass and weed pollens. A similar spectrum of allergens are present in North America; however, the particular species vary, suggesting the potential for unsensitized individuals to develop new atopic symptoms after foreign exposures.²⁹

Chemical exposures

An area of particular concern for deployed soldiers is the risk for exposure to environmental chemicals as well as chemical weapons, which may have an effect on the respiratory mucosa. Acute rhinologic symptoms are commonly associated with occupational exposures to a variety of

TABLE 3. Summary of findings from clinical studies involving the upper respiratory tract

Reference (first author)	Design	Location of deployment/conflict (year)	Significant findings
Barth ¹¹	Retrospective survey	OEF/OIF (2001-2008)	80% risk for sinusitis after exposure
Barth ²⁵	Retrospective cohort	OEF/OIF (2001-2008)	Prevalence of sinusitis higher in deployed group; no significant increase in rates of asthma
Brennan ²¹	Retrospective cohort	OIF (2004-2005)	15% of all otolaryngology visits were due to sinusitis
Kelsall ²⁴	Cross-sectional survey	PGW (1990-1991)	Higher rates of sinus complaints in deployed vs nondeployed respondents (aOR = 1.5)
Ladich ²²	Cohort study	PGW (not specified)	Most common histology of deployed soldiers was chronic sinusitis and allergic rhinitis
Richards ²³	Retrospective survey	ODS (1990-1991)	Chronic rhinorrhea found in 15.4% of respondents, higher than in nondeployed; rhinorrhea associated with outdoor living; cough and sore throat also common findings
Sanders ⁴	Retrospective survey	Iraq/Afghanistan (2003-2004)	22.5% of deployed soldiers reported allergy attacks during deployment
Szema ²⁶	Retrospective cohort	Persian Gulf region (2004-2007)	Association with deployment and development of allergic rhinitis (9.9% vs 5.1%)

aOR = adjusted odds ratio; ODS = Operation Desert Shield; OEF = Operation Enduring Freedom; OIF = Operation Iraqi Freedom; PGW = Persian Gulf War.

chemical agents.³⁰ In general, little is known about the specific long-term respiratory health effects of single, repeated, or chronic exposures to chemical agents encountered in combat zones.

One chemical class with a reported correlation between exposure and development of URT symptoms and disease are sulfur mustards (SMs). SMs are alkylating agents that induce the formation of reactive oxygen species after depletion of glutathione, exposure to which directly affects skin and mucous membranes and leads to inflammation.³¹ Acute toxicity from SM may be due to depletion of nicotinamide adenine dinucleotide, eventually leading to coagulation necrosis of cells and disruption of the dermal-epidermal junction. All mucosal membranes of the respiratory tract, including the sinonasal tract, are at risk for damage with exposure.³² Symptomatology may not necessarily align with objective evidence, such as in a case-control series assessing computed tomography imaging of the sinuses of returning combatants, which found no difference between exposed and nonexposed individuals.³³ In contrast, veterans of the Iran-Iraq War (1980-1988) with a history of SM exposure have been shown in a retrospective observational study to have increased chronic sinusitis as well as laryngeal inflammation, postnasal drip, and dysphonia.³⁴ In that study, analysis of biochemical markers, flexible fiber-optic laryngoscopy, and computed tomography of the sinuses revealed a high incidence of chronic sinusitis as well as partial vocal fold immobility and inflammation.

Other classes of chemical weaponry have been the subject of limited study with regard to URT health. Organophosphates (OPs) are compounds that inhibit acetylcholinesterase, resulting in augmented parasympathetic nervous system activity and symptoms, including

rhinorrhea, lacrimation, and gastrointestinal motility. These agents have been used as weapons throughout modern history beginning in the 1930s and in World War II (1939-1945).³⁵ Military exposure in reference to URT pathology is not well documented in the literature and has predominantly focused on neurologic symptoms and effects.³⁶ One case report from Nigeria described irreversible anosmia in a military officer exposed to OP pesticide in close quarters.³⁷ The long-term effects on the URT with regard to combat exposure is not known; however, there is some evidence suggesting that long-term occupational exposure does increase the risk for development of asthma and other respiratory-related symptoms.³⁸

Dioxin herbicides, notably Agent Orange, which gained notoriety for use in the Vietnam War (1961-1971), may also be associated with URT disease; however, there is very limited evidence in the literature to support or refute this observation. One report on the long-term effects of dioxin exposure assessed a cohort of men exposed to 2,3,7,8-tetrachlorodibenzo-*p*-dioxin and compared them to those without exposure.³⁹ The authors found a statistically significant increase in the incidence of upper respiratory infections compared with an unexposed cohort. A paucity of evidence persists despite claims in popular media outlets and anecdotal patient reports.

Etiologic considerations

Although a direct mechanism has not yet been established, there is evidence to suggest a variety of factors that increase the risk of URT and LRT pathology. There are more data supporting etiology in LRT disease processes such as asthma; however, extension of these mechanisms to the

URT is likely when considering the concept of a unified airway.

Numerous possible causes have been cited such as particulate matter, close living quarters, exposure to oil and burn pit smoke, microbes, and the presence of ambient particulate matter. Most studies have failed to show a correlation between open pit burning and fires and the development of respiratory pathology.^{7,40-42} This finding may be due in part to short durations of exposure. In contrast, there is compelling evidence to suggest that close living quarters is linked to spread of respiratory infectious disease, which inevitably could lead to URT and LRT symptoms.⁴³⁻⁴⁵ Despite this, there are no studies assessing the long-term respiratory complications of close-quarters living in combat zone populations, as much of the literature in that area is focused on pre-deployment military recruits.

Environmental factors, notably the presence of inhaled ambient particulate matter (PM), are believed to contribute significantly to the development of many respiratory tract disorders. Reports suggest PM as well as heavy metals may be the cause of respiratory symptoms,⁴⁶ and the size and composition of the particulate play an important role in determining which site of the respiratory system is affected. Types of PM can range from sand and dust to exhaust, fumes, and chemicals; the composition of which determines the effect and the symptoms experienced by a patient.⁴⁷ Furthermore, the size of the PM dictates the deposition within the respiratory tract, as smaller particles have the ability to travel more distally due to size. Fine PM is defined as any particle <2.5 μm, and the maximum daily exposure as suggested by the World Health Organization is 25 μg/m³. In the Middle East the levels of fine PM can exceed the recommended level and have been shown to be as high as 111 μg/m³, suggesting an increased exposure risk for troops in the region.⁴⁸

The diversity of PM portends a wide array of aeroantigens that can lead to sensitization and subsequent development of allergic-type symptoms affecting the sinonasal tract as well as the lower respiratory mucosa.²⁷ Szema et al developed an in vivo model to determine the pathogenesis of the respiratory disease by exposing mice to dust collected from Iraq. The dust from Iraq was found to induce higher levels of lower airway inflammation when compared with control dust from San Joaquin, California and Montana. Furthermore, the dust samples from Iraq displayed particle

sizes as small as 2.5 μm and exhibited sharp edges, similar to asbestos fibers, which have been found to lead to robust lymphocytic airway inflammation in murine models.⁴⁹ This airway hyperresponsiveness to PM has been established in other environments as well. A murine model assessing inflammatory response to urban particulate matter in Baltimore, Maryland, showed marked activation of the complement cascade, specifically complement factor 3, within the airway.⁵⁰

In addition to ambient PM, soldiers are at increased risk for exposure to other aerosolized chemicals and matter. Discharge of munitions leads to release of a wide array of chemicals and hard metals, which may also have an effect on the respiratory tract. Specifically, the discharge of firearms leads to release of aerosolized lead particles that can be inhaled, although the exact role of this material on respiratory mucosa has not been evaluated.⁵¹ Despite the plausible correlation with munitions exposures, this remains as an area requiring further investigation.

Conclusion

Battlefield exposure has garnered increasing attention in the past decade due to a large and important cohort of soldiers in combat zones around the world. These servicemen and servicewomen return home from duty with complaints involving the upper and lower respiratory tract, and may have important albeit uncommon clinical histories that make their diagnosis complicated and their treatment plans unique. The majority of the literature examining this relationship is retrospective in nature and often limited by self-reported symptoms without objective diagnoses. Moreover, the effect of combat exposure on URT disease has been the subject of comparatively little study, with the result being that the clinician must base evaluation and management recommendations on the same principles used in the care of individuals in the general population. Prospective and large retrospective cohort studies are needed to establish the association between soldiers returning from the battlefield and the development of URT disease. This, in turn, may have utility for physicians who treat combat veterans with respiratory ailments. Until additional study has been completed, it is important that practicing otolaryngologists and other specialists remain aware of the possibility of combat zone exposures that could contribute to rhinologic symptomatology. 🌐

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