Deployment-Related Respiratory Disease: Where Are We?

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Abstract

Military personnel and veterans who have deployed to Afghanistan, Iraq, and parts of Southwest Asia (SWA) since 1990 are at risk of developing a host of respiratory symptoms and deployment-related respiratory diseases (DRRDs). This review aims to summarize our current understanding of DRRD and inform pulmonary practitioners of recent updates to DRRD screening, diagnosis, evaluation, and management. The most common respiratory diseases in these patients include asthma, chronic sinonasal disease, laryngeal disease/dysfunction, and distal lung disease. Pulmonary function testing and chest imaging are the most commonly used diagnostic tools, but techniques such as lung clearance index testing via multiple breath washout, forced oscillation testing/impulse oscillometry, and quantitative chest computed tomography (CT) assessment appear promising as noninvasive modalities to aid in lung disease detection in this population. We also summarize guidance on conducting an occupational and deployment exposure history as well as recommendations for testing. Finally, we discuss the Sergeant First Class Heath Robinson Honoring our Promise to Address Comprehensive Toxics Act of 2022 (PACT Act) that includes a list of health conditions that are "presumptively" considered to be related to SWA military deployment toxic exposures, and provide resources for clinicians who evaluate and treat patients with DRRD.

Keywords
- deployment-related respiratory disease
- veterans
- bronchiolitis
- asthma
- burn pits
- PACT Act

The U.S. military has had a presence in the Middle East and surrounding countries, collectively referred to as Southwest Asia (SWA), for more than three decades, with nearly 3.5 million military personnel previously deployed to the region.[1] Military deployment to SWA has been linked to a spectrum of respiratory diseases affecting the upper and/or lower respiratory tract, as shown in ►**Fig. 1**.[2–5] Our understanding of deployment-related respiratory disease (DRRD) has been limited because of inadequate or absent exposure assessment, lack of systematic longitudinal occupational health surveillance with lung function testing, and absence of a gold standard noninvasive diagnostic test for SWA deployment-related distal lung abnormalities. Data on the prognosis and treatment are sparse. This review aims to

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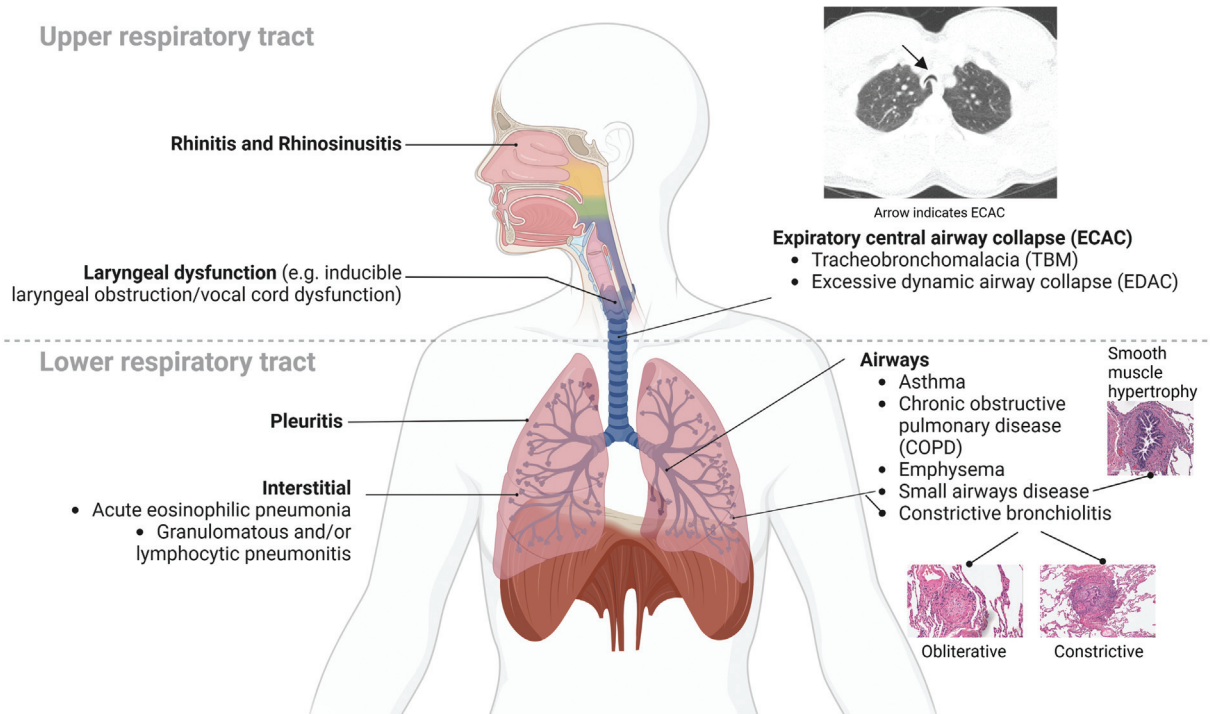

Fig. 1 Common deployment-related respiratory diseases.

summarize our current understanding of DRRD and inform pulmonary practitioners of recent updates to DRRD screening, diagnosis, evaluation, and management.

Epidemiology and Spectrum of Disease

The term DRRD defines the broad set of conditions observed in previously deployed individuals with respiratory symptoms.[6] The most common respiratory diseases in these patients include asthma, chronic sinonasal disease (e.g., rhinitis, sinusitis), laryngeal disease/dysfunction, and distal lung disease (including bronchiolitis, granulomatous inflammation, hyperinflation/emphysema, and pleuritis). A population-based survey of veterans that served between 2001 and 2008 found that 24% of respondents reported at least one respiratory disease including asthma (6.9%), bronchitis, and sinusitis.[7] For both deployed and nondeployed veterans, those reporting three or more hazardous exposures had greater prevalence of respiratory diseases, and exposure to smoke from oil fires significantly increased the risk of asthma in both groups.[7]

Sinusitis has been reported by 13 to 15% of deployed and nondeployed veterans.[7–9] In a population-based survey, deployed veterans were 29% more likely to be diagnosed with sinusitis compared with nondeployed veterans.[7,8]

Large epidemiologic studies show increased rates of new-onset asthma in returning deployers compared with military personnel who remain stationed in the United States, especially among those in combat positions or with burn pit exposure.[2,10,11] In 2004, the U.S. military relaxed its eligibility standards to allow those with mild asthma to deploy.[12] Not surprisingly, more frequent asthma exacerbations have subsequently been reported in military personnel returning from deployment, especially among those with poorly controlled asthma before deployment.[2,13,14] The clinical presentation of asthma overlaps with intermittent laryngeal obstruction/vocal cord dysfunction (ILO/VCD) and these conditions can co-occur.[15] Deployment exposures to burn pit combustion products, vehicle exhaust, and geologic dust along with comorbidities and personal risk factors such as gastroesophageal reflux disease (GERD), rhinosinusitis, cigarettes smoking, and higher body mass index are associated with higher rates of ILO/VCD.[4,16–18]

The term "distal lung disease" frequently has been used interchangeably with "constrictive bronchiolitis" (CB) or "small airways disease" but includes a larger spectrum of histopathologic features that may not be easily diagnosed without surgical lung biopsy. In a sentinel case series of deployed soldiers evaluated for exertional dyspnea, 49 had video-assisted thoracoscopic biopsies.[3] Thirty-eight of 49 were diagnosed with CB. There also were abnormal findings consistent with sarcoidosis, interstitial lung disease, respiratory bronchiolitis, and hypersensitivity pneumonitis. Twenty-eight of 38 diagnosed with CB reported exposure to hazardous ambient concentrations of sulfur dioxide at the Mishraq State Sulfur Mine Plant fire near Mosul, Iraq, in June 2003.[19] Most of those with CB had normal chest imaging findings (though some had air trapping). Findings on rest and exercise pulmonary function tests included isolated low diffusing capacity for carbon monoxide (DLCO) and lower maximal oxygen consumption and anaerobic threshold.[3] Among 29 participants that had repeat pulmonary function tests, the percent predicted total lung capacity (TLCpp) was significantly lower at follow-up; 45%

had >10PP decline in TLC.[20] In another case series of patients, those with deployment-related distal lung disease (DDLD) had longer deployment duration and had higher odds of decreased DLCO.[4]

A 2022 publication describes the pathologic features that distinguish DDLD from chronic hypersensitivity pneumonitis, smoking-related respiratory bronchiolitis, obliterative bronchiolitis, and normal lung tissue, as well as the features that overlap.[5] Another group of investigators used semiquantitative assessment of lung tissue to identify characteristic histologic features including increased lamina thickness of bronchioles, smooth muscle hypertrophy, and increased collagen density compared with normal controls.[20]

Other reported diseases among military personal returning from deployment to SWA include expiratory central airway collapse (ECAC), sleep apnea, chronic obstructive pulmonary disease (COPD)/emphysema, acute eosinophilic pneumonia and eosinophilic syndromes, and respiratory cancers.[1,21–25]

Clinical Approach to Diagnosis and Management

How Do I Determine if a Patient's Respiratory Disease Is Deployment-Related?

The recommended approach to assessing a patient for exposure-related respiratory disease is to first obtain diagnostic clarity and then address causation. For previously deployed patients, details should be obtained on exposure to occupational hazards including, but not limited to, desert dust particulate matter, burn pit or trash-burning emissions, and diesel exhaust. Diagnoses of chronic rhinitis/rhinosinusitis, asthma, COPD/emphysema, bronchiolitis, and respiratory cancers should raise concern for a DRRD. The Department of Veterans Affairs (VA) has determined that if a veteran is diagnosed with one of these respiratory conditions and has a history of deployment to SWA from August 1990 to present, the respiratory condition is considered to be deployment-related based on a VA presumption.[26]

What Symptoms Are Common in These Patients?

New-onset dyspnea, wheeze, cough, sputum production, and decreased exercise tolerance have frequently been reported during and after deployment.[11,12,27–32] The National Academies of Sciences, Engineering, and Medicine noted in their 2020 report on health effects of airborne hazards that "respiratory symptoms are arguably the most commonly studied health outcomes in association with deployment in the SWA Theater of Military Operations."[1] Frequency of self-reported respiratory symptoms was significantly higher following deployment than in the predeployment period, with exertional dyspnea (75.1%) and decreased exercise tolerance (72.6%) the most commonly reported presenting symptoms.[30] In another study, the incidence rate for respiratory symptoms was between 7 and 39% higher among those who deployed compared with military personnel stationed in the United States.[11,32]

Taking an Exposure History

Deployment to SWA is associated with particulate matter exposure from sandstorms, combat dust, local polluting industries, burn pit combustion products, diesel exhaust, and other fuels including jet propellant 8.[1,33–37] Additionally, some deployed military personnel referred to as "deployers" were exposed to poor ambient air quality following a sulfur plant fire at Al-Mishraq near Mosul, Iraq, in 2003.[38] In addition to these hazards, military personnel may also have occupational exposures to vapors, gases, dusts, and fumes, including paints and solvents during regular job tasks while deployed that confer risk for lung injury.[1,37,39] For example, vehicle maintenance workers using chemical agent resistant coating paints may be exposed to toxic compounds including isocyanates, which are known respiratory sensitizers linked to asthma.[40] See ►**Table 1** for examples of questions recommended for obtaining a deployment exposure history.

While specific air monitoring data during deployment are limited, some clinicians at the VA may have access to a tool called the Individual Longitudinal Exposure Record (ILER) that can be used to develop a record of service-related exposures for individual patients or locations.[41] Although not anticipated to be fully operational until September 2023, the information collected over a service member's military career may make ILER a useful supplement for exposure information in the future.[42]

What Diagnostic Tests Are Recommended for Clinical Evaluation?

At a minimum, patients with persistent chest symptoms should have full pulmonary function testing (PFT) with pre- and postbronchodilator spirometry, lung volumes, and single-breath DLCO testing as well as a high-resolution chest computed tomography (CT) with expiratory imaging to assess for air trapping. Diffusion impairment, when present, may be indicative of DDLD, but is not required for the diagnosis.[4] In cases where PFTs are normal or abnormalities are subtle, cardiopulmonary exercise testing can be useful to assess for cardiac, ventilatory, or gas exchange abnormalities. When asthma is suspected but not established with spirometry, bronchial challenge testing is indicated. Although high-resolution chest CT scans often are normal or have nonspecific abnormalities, in combination with other clinical findings, the presence of air trapping/mosaicism may suggest bronchiolitis, while centrilobular nodules may reflect a cellular/inflammatory bronchiolitis.[43] More than 50% collapse of the trachea or proximal bronchi on dynamic expiration may point to a diagnosis of ECAC.[44] Additional testing to assess for upper airway disease includes sinus imaging with a noncontrast CT scan or rhinolaryngoscopy to assess for sinonasal disease and/or laryngeal dysfunction. Additional testing and consultation to identify comorbid conditions that may aggravate respiratory conditions also may be helpful, as outlined in ►**Table 2**.[45,46]

What Are Some of the Emerging Ways to Diagnose Deployment-Related Lung Disease?

More diagnostic clarity may be obtained by measuring the lung clearance index (LCI) score via multiple breath washout

Table 1 Occupational and military deployment history questions

• Have you been deployed to Southwest Asia since August 1990 or to Afghanistan, Djibouti, Jordan, Syria, and Uzbekistan since September 2001?
• During your deployment(s), how often, if at all, were you exposed to:
– Smoke and fumes from open burn pits?
– Smoke from other types of trash or waste burning (e.g., burn barrels)?
– Smoke from oil well fires?
– Fires?
– Explosions?
– Sandstorms?
– Diesel exhaust?
– Aircraft exhaust?
• What other hazards, if any, were you exposed to or do you have concerns about?
• Did you have any respiratory symptoms (e.g., shortness of breath, cough, chest tightness, wheezing) before deploying? If yes, did your symptoms develop while deployed or after returning from deployment?
• Did you seek medical attention for shortness of breath, cough, chest tightness, wheezing, or other respiratory problem?
• Did you take a physical fitness test before deployment? If yes, did you pass the test? What was your approximate run-time for the physical fitness test (1.5 miles for Navy or Air Force/2 miles for Army/3 miles for Marine Corps)?
• Did you take a physical fitness test after deployment? If yes, did you pass the test?

Table 2 Recommended diagnostic evaluation for deployment-related respiratory diseases (DRRDs)

Evaluation on all patients	Additional studies considered based on clinical findings
• Comprehensive medical and occupational/deployment history and physical exam • PFTs (pre- and post-BD spirometry, lung volumes, diffusion capacity) • High-resolution chest CT scan (unless done within 12 mo)	• Cardiopulmonary exercise testing • Methacholine challenge • Respiratory force measurements (maximal inspiratory pressure, maximal expiratory pressure) • Direct laryngoscopy • Sinus CT without contrast ± ENT consultation • Allergy/immunology consultation • Laboratory studies (serum IgE, blood eosinophils) • Cardiology studies/consultation • Sleep studies/consultation • GI studies/consultation • Surgical lung biopsy

Abbreviations: BD, bronchodilator; CT, computed tomography; ENT, ear, nose, and throat; GI, gastrointestinal; IgE, immunoglobulin E; PFT, pulmonary function test.

(MBW) testing, which has demonstrated utility in measuring differences in ventilation inhomogeneity between deployers with clinically confirmed distal lung disease and asthma from healthy controls.[47,48] Normative data in over 100 healthy controls have been published for comparison. The Global Lung Initiative's efforts to establish more robust reference values for LCI via MBW may facilitate the identification of a DDLD such as bronchiolitis based on measurement of an LCI score above the upper limit of normal.[49,50] Another diagnostic tool that has been evaluated among military deployers is impulse oscillometry (iOS), which is commercially available and may be especially useful for patients that have trouble performing forced maneuvers.[51] Quantitative imaging parameters of emphysema, air trapping, and airway wall thickening can identify subtle abnormalities that may be useful in noninvasive diagnosis of DRRD[52] and are available commercially.[53,54] Davis et al used a technique called parametric response mapping (PRM) to assess degrees of functional small airways disease (fSAD) in military personnel with constrictive bronchiolitis (MPCB), a second group with COPD, and a control group of asymptomatic smokers.[54] PRM is a computational technique that compares differences in lung density between inspiratory and expiratory CT scans. The MPCB group had a higher (and more abnormal) fSAD score than the control group and those with Global Initiative for Chronic Obstructive Lung Disease (GOLD) stages 0, 1, and 2 COPD.

When Could a Lung Biopsy Be Helpful?

Fewer veterans have required lung biopsy due to increased knowledge of the case definitions of DDLD and frank discussion of risks and benefits of invasive testing.[6] When

noninvasive techniques are unavailable and further diagnostic clarity is needed or if symptoms worsen and lung function declines, a lung biopsy may be warranted.[6] Results may inform treatment strategies.[46]

What Treatment Options Are Helpful?

Treatment of DRRD focuses on removing a veteran from ongoing exposures to respiratory hazards that can aggravate the disease. Apart from addressing potential aggravating exposures, DRRD treatment does not differ from treatment of nondeployment-related rhinitis/rhinosinusitis, laryngeal dysfunction (VCD/ILO), ECAC, asthma, COPD, pleuritis, distal lung diseases, or respiratory cancers. Patients may find otolaryngology consultation beneficial for management of severe sinonasal disease or laryngeal dysfunction refractory to speech therapy and treatment of aggravating factors (e.g., GERD).

Deployment-related asthma (DRA) may be endotyped as T-helper cell type 2 (Th2)–high inflammation or Th2-low inflammation, in which case Th2-high asthmatics that have abnormally increased blood immunoglobulin E and/or eosinophil concentrations may benefit from treatment with biologics (e.g., omalizumab, benralizumab, and mepolizumab) for poorly controlled asthma.[55] As both Th2-high and Th-2-low asthma endotypes are present in DRA, future drug development targeting Th2-low inflammation may benefit the DRA population.[56]

Currently, there is no evidence-based treatment for DDLD.[6] Future recommendations will depend on results from larger observational and prospective trials.[6] There may be utility in periodic monitoring of symptoms and lung function to identify those subjects at risk of progressive respiratory disease.

What Is the Long-term Prognosis of Deployment-Related Respiratory Disease?

The natural history of DRRD and more specifically DDLD is unknown. Recent histopathologic studies indicate that some DDLD patients may have ongoing inflammation and progressive disease, while others may have evidence of injury without progression.[5,20]

Practical Information and Resources for Clinicians Serving Veterans

Presumptive Service Conditions

Since 2021, the Congress and the VA have put forth and enacted legislation related to military service–connected medical conditions and benefits for those who have been exposed to occupational hazards during military deployments abroad in SWA and nearby regions.[26,57] The VA has added several burn pit and other toxic exposure presumptive illnesses and cancers based on the Sergeant First Class Heath Robinson Honoring our Promise to Address Comprehensive Toxics Act of 2022 (PACT Act). This change expands benefits for Gulf War era and post-9/11 era veterans who have deployed to Bahrain, Iraq, Kuwait, Oman, Qatar, Saudi Arabia, Somalia, or the United Arab Emirates (UAE) after August 2, 1990, or to Afghanistan, Djibouti, Egypt, Jordan, Lebanon, Syria, Uzbekistan, or Yemen after September 11, 2001. For a list of these presumptive respiratory conditions, see ►**Table 3**.

Table 3 Presumptive deployment-related respiratory diseases (DRRDs)

• Asthma that was diagnosed after service
• Chronic bronchitis
• Chronic obstructive pulmonary disease (COPD)
• Chronic rhinitis
• Chronic sinusitis
• Constrictive bronchiolitis or obliterative bronchiolitis
• Emphysema
• Granulomatous disease
• Interstitial lung disease (ILD)
• Pleuritis
• Pulmonary fibrosis
• Sarcoidosis
• Respiratory (breathing-related) cancer of any type

What Do I Do if My Patient Requests a "Burn Pit" Evaluation?

As awareness grows about airborne hazards associated with SWA deployment and the PACT Act, medical providers will likely encounter questions related to how a veteran may request and complete a VA Airborne Hazards and Open Burn Pit Registry (AHOBPR) evaluation, file a claim for service connection and disability, or obtain a nexus letter.

VA Airborne Hazards and Open Burn Pit Registry

Veterans, Reservists, National Guard members, and Active Duty military personnel are eligible to complete an AHOBPR questionnaire and request a medical evaluation to document military deployment exposures and health concerns, which may prompt referral for further testing (e.g., chest X-ray and PFT). Although not considered a part of the Veterans Benefits Administration or claims process, a veteran may submit the diagnostic test results from a Registry examination in support of a VA claim for service connection and disability.[58]

VET-HOME

The VA has made plans to launch a network of specialized providers linked to a centralized call center known as the Veterans Exposure Team-Health Outcomes of Military Exposures (VET-HOME).[59] Veterans and medical providers will be able to call for guidance on registry exams that are available for veterans seeking further information and evaluation related to toxic exposures including burn pits and other hazards of concern related to SWA deployment.[58,60] In addition to providing guidance to service members with SWA exposures, VET-HOME will also be a resource about other toxic exposures from different military locations and combat eras (e.g., water contamination at Camp Lejeune,

Agent Orange related to Vietnam era, ionizing radiation exposure).[61]

How to File a Claim

Veterans can find information about filing a claim or appeal by accessing information from va.gov/disability or asking for assistance from a claims agent, a Veterans Service Officer (VSO), or an attorney.

Nexus Letter

Some medical conditions are thought to have been either caused or aggravated by occupational hazards during military service. While establishing the causal nature of a musculoskeletal injury may be straightforward and immediately recognized as service-related (e.g., knee injury while in boot camp), there are other chronic illnesses with gradual onset or latency in which assessing causation may be more challenging. However, with the recent passage of the PACT Act, certain cancers and respiratory diseases, if present in a military service member or veteran who deployed to SWA from August 1990 to present, are considered to be service connected by "presumption." While the PACT Act includes an extensive list of respiratory diseases related to SWA deployment by presumption, there are some gaps that have left out conditions that have also been reported in the SWA-deployed population. Two such conditions include laryngeal dysfunction (VCD/ILO) and ECAC.[4,17,21] Veterans who file claims for these conditions may have to provide evidence of a probable causal connection between SWA deployment hazards and laryngeal dysfunction and/or ECAC. In such cases, it is not uncommon for a veteran to ask a primary care provider or specialty physician to provide a letter that describes the link or "nexus" between military service or deployment exposures and the medical condition(s).[62]

If the clinician believes that a particular medical condition is likely related to military service/SWA deployment that is not on the list of presumptive SWA-connected medical conditions, the medical provider can author a brief nexus letter that includes the following components:

- The rationale for the causal association. A provider does not need to be certain of a link but should describe the likelihood that the medical condition is related to previous military service and more specifically SWA deployment.
- The likelihood of a link between deployment and respiratory disease as either "not likely," "at least as likely as not," "more likely than not," or "highly likely."[63]
- A brief description of clinician's credentials and medical expertise, treatment relationship with patient (if one exists vs a one-time evaluation).
- A statement indicating review of the veteran's relevant medical records, summary of deployment history and deployment exposures, medical diagnosis, and a statement assessing the likelihood that the medical condition is related to SWA deployment.
- Relevant references from scientific literature may help support the rationale for the medical opinion about whether or not a connection is likely between SWA deployment/exposures and respiratory disease.

Unanticipated Consequences of the PACT Act

The nomenclature used for certain presumptive conditions may lead to some unexpected confusion for medical providers and patients. Clinicians should be aware of and prepared to discuss the difference between radiologic findings of SWA deployment–related granulomatous lung disease and "prior granulomatous disease." For example, under the PACT Act, there is no distinction made between granulomatous lung disease (e.g., sarcoidosis, hypersensitivity pneumonitis, DDLD with granulomatous inflammation) and benign conditions such as past granulomatous disease from prior *Histoplasma* exposure that commonly occurs in endemic regions and that typically requires no clinical evaluation or treatment.

The Future of Prevention, Diagnosis, and Management of DRRD

After more than three decades of a U.S. military presence in SWA, the public health community still faces challenges associated with DRRD prevention efforts. Currently, the Department of Defense does not perform routine pre- and postdeployment lung function testing on all military personnel as conducted regularly in other occupational cohorts such as the New York Fire Department. Identification of excessive declines in spirometric lung function aided in identifying respiratory impairment and lung disease in World Trade Center first responders, and similar medical surveillance could be beneficial in the SWA-deployed population or perhaps military personnel exposed to other respiratory hazards or locations that may share similar inhalational hazards to those encountered in SWA.[64] While well-established algorithms for diagnosis of sinonasal disease and laryngeal dysfunction exist and often are familiar to specialty providers, diagnostic confirmation of DDLD may still be challenging without lung biopsy when conventional noninvasive testing is normal or nondiagnostic. As we learn more about promising markers of noninvasive testing, such as iOS/forced oscillation testing, MBW/LCI, and quantitative imaging, expansion of these testing modalities to assessment of longitudinal lung function and long-term respiratory health outcomes can improve our understanding of the natural history of DRRD. Treatment recommendations for distal lung disease await further research. Establishing diagnostic clarity and using consistent case definitions and terminology for DDLD may inform future research collaborations and clinical trials assessing pharmacotherapy or treatment options of varying endotypes and phenotypes of DDLD.

While recent legislation has focused on expanding research and benefits for SWA-deployed military veterans, fewer resources are available to civilian contractors who deployed to SWA in support roles of military operations. Thus, clinicians evaluating nonmilitary patients with history of SWA deployments should familiarize themselves with the

spectrum of SWA DRRDs to assist in diagnostic evaluation and management of new-onset or aggravated respiratory symptoms and disease. Finally, recent insights about pathogenesis and disease detection of SWA DRRDs may help the public health community mitigate risk of occupational diseases in new exposure settings related to military and wartime exposures.

Conflict of Interest
None declared.

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