



Sarcoidosis in U.S. Military Veterans

Can Lessons from Those Who Have Served Shape the Future of Sarcoidosis?

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Sarcoidosis was first described in military populations in 1949 (1). It remains a disease of multisystemic nonnecrotizing granulomatous inflammation without a known cause or cure (2). Sarcoidosis most frequently affects the lungs but can impact nearly any other organ depending on the site of granulomatous infiltration. It more frequently afflicts underserved populations, including women and Black Americans (3). Sarcoidosis also associates with patients who report occupational exposures, including insecticides, molds, bioaerosols, and exposures associated with agricultural employment (4). Although studies have previously examined sarcoidosis in the veteran population (5–7), a comprehensive assessment of the epidemiology, risk factors, and geographic distribution of sarcoidosis in veterans remained overdue. The Veterans Health Administration (VHA) is the largest integrated healthcare system in the United States with associated electronic health records (EHRs). In this issue of *AnnalsATS*, Seedahmed and colleagues (pp. 797–806) use

the VHA to report on the epidemiology of sarcoidosis within a population of more than 13 million U.S. veterans served by the VHA system during the past two decades (8).

An association between occupational exposures and sarcoidosis has long been debated. Military service and its environmental exposures are complex and vary by service branch, role, era of service, and region of deployment (9). Two large historical cohorts of U.S. Navy personnel (10, 11) demonstrate the complexities of tracking sarcoidosis in the military over time and that environmental exposures and specific military occupational duties associate with increased incidences of sarcoidosis. First, it was demonstrated that, among 1,120 sailors, those assigned to “clean ships” with limited or no industrial activity had a decreased risk of sarcoidosis (10). A subsequent Naval study of 674 hospitalized patients with sarcoidosis identified a decrease in sarcoidosis over time, particularly after 1989. Ship repair or structural mechanic roles were identified as significant risk factors for incident sarcoidosis (11). Recent military conflicts in Iraq, Afghanistan, and other portions of Southwest Asia resulted in new and unique exposures, including high exposure to airborne particulate matter such as geological dust, smoke from burn pits, and heavy metal condensates (12). Increased measurements of metal elements have subsequently been found in the plasma of veterans with pulmonary sarcoidosis compared with controls (5). In veterans registered in the Airborne Hazards and Open Burn Pit Registry who were deployed to Afghanistan or Southwest Asia, self-reported cumulative exposure to convoy activities involving vehicle operations was the only exposure that reached significance for increased sarcoidosis risk in adjusted analysis (6). In 2022, the association of burn pit exposure and sarcoidosis was recognized on a

legislative level with the passage of the Honoring Our PACT (Promise to Address Comprehensive Toxics) Act through the U.S. Congress. Title 4, Section 406 of the PACT Act, expands health care coverage to veterans with sarcoidosis and burn pit exposure (13).

Seedahmed and colleagues sought to expand this knowledge base by analyzing the VHA EHR data of all veterans who received care at a VA facility or at a non-VA facility that was paid for by VA. The diagnosis of sarcoidosis was established with the presence of either a single inpatient *International Classification of Diseases (ICD)* code or two outpatient *ICD* codes for sarcoidosis. Patients with alternative diagnosis codes were excluded if the alternative diagnosis was coded two years before or one year after the index sarcoidosis code. The incidence of sarcoidosis in any organ system after the 1999 first international consensus Statement on Sarcoidosis and between January 1, 2004, and December 31, 2019, was then calculated. Of 13,320,196 veterans screened, 23,747 veterans with sarcoidosis were identified. Propensity-score matching was used to select three control cases for each sarcoidosis case, further strengthening the study.

Overall, the veteran population was noted to have twice the annual prevalence and a four to five times higher annual incidence of sarcoidosis compared with the nonveteran population. Incidence and prevalence increased over time. Multivariate analysis by logistic regression was performed to examine factors that influenced incidence. Risk factors significantly associated with a new diagnosis of sarcoidosis included Black race, female sex, living in any continental region of the United States outside the west, history of tobacco use, and having served in the Army, Air Force, or multiple service branches. The greatest regional prevalence

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of sarcoidosis in 2019 was in the South Atlantic states.

Study limitations include the inability to detect persons with sarcoidosis who do not seek care, thus underestimating the true annual prevalence inclusive of patients with quiescent disease. Persons seeking care outside of VHA remain unmeasured. There is also the potential to underestimate peak incidence and prevalence due to disease latency periods extending past the data collection dates. Additionally, as the writers discuss, regional prevalence patterns intersect with regional race demographics.

A relative strength of the study is its inclusion of veterans receiving care for their sarcoidosis in community care programs as well as VA facilities. This is more likely to approximate true health care use in veterans with sarcoidosis. The increased numbers of veterans seeking care for sarcoidosis may certainly be affected by their universal access to health care compared with U.S. civilian populations, affording veterans better access to diagnosis and longitudinal follow-up. Nevertheless, Seedahmed and colleagues' estimates of the incidence and prevalence of sarcoidosis in U.S. veterans exceeds those in nonveteran populations who have universal health care (3), suggesting that military service itself may be a risk factor for

increasing the incidence and prevalence of sarcoidosis.

Seedahmed and colleagues find increased risk for sarcoidosis in multiple service branches in which duties and deployment are highly varied. Risk factors other than the deployed environment may play a role. One study conducted in active-duty Army soldiers failed to detect a difference in rates of sarcoidosis diagnosis in deployed versus nondeployed personnel (14). Follow-up studies that drill down to the specific external environmental exposures, internal atmosphere of work areas, and associated duties are needed to shed light on actionable risk-factor modification for military service members. In addition, data on the specific clinical phenotype of sarcoidosis may provide further insights. Recent retrospective research on exposure histories associates differing prediagnosis exposures with sarcoidosis organ manifestations, such as exposure to inorganic dusts correlating with pulmonary sarcoidosis and reactive chemical exposure correlating with cardiac sarcoidosis (15).

Finally, a key methodology that impacts future research is in defining sarcoidosis via *ICD, 10th Revision* coding independent of biopsy data while also setting exclusion criteria for alternative competing diagnoses.

This method differs from a previously published cohort of veterans with sarcoidosis (7). The diagnosis of sarcoidosis is frequently supported by biopsy data but also must integrate clinical expertise, particularly because many granulomatous and nongranulomatous mimics occur (16). Similar to implementation of coding-based definitions for a complex disease such as sepsis, further validation of the complex diagnosis of sarcoidosis may need to be conducted in future EHR-based research to ensure that sarcoidosis diagnoses are captured with fidelity.

In summary, Seedahmed and colleagues have made a landmark contribution to the epidemiology of sarcoidosis in U.S. veterans. An association between sarcoidosis and military occupational exposure to burn pits was recently recognized by the U.S. Congress via the Honoring Our PACT Act burn-pit legislation, which was signed into federal law on August 10, 2022 by the President of the United States. The mechanisms of these environmental exposure and the increased incidence and prevalence of sarcoidosis in U.S. veterans demand further study. ■

Author disclosures are available with the text of this article at www.atsjournals.org.

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