
Sarcoidosis Diagnoses Among U.S. Military Personnel: Trends and Ship Assignment Associations

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Background: Sarcoidosis is a granulomatous disorder of unknown cause that usually first involves the lungs.¹ After the diagnosis of a deck grinder was changed from sarcoidosis to dust-induced lung disease by the VA, the Navy asked the National Institute for Occupational Safety and Health (NIOSH) to determine if Navy work environments have been associated with lung diseases, some of which may have been reported as "sarcoidosis."

Methods: Sarcoidosis-related associations were measured using a case-control approach involving the modern personnel database of the Naval Health Research Center (NHRC). Sarcoidosis incidence rates were also computed using total Navy manpower data, and previously published military data from the 1940s and 1950s were juxtaposed with current findings to gain a broader historical perspective.

Results: When reported sarcoidosis incidence rates from 1943 to 1993 are examined, an unexplained peak of military sarcoidosis rates appears in the 1960s and 1970s along with a decline in the black/white ratio of these rates from about 17:1 to 6:1. The case-control analyses reveal a decreased risk for sarcoidosis diagnoses among men who worked only on "clean ships."

Conclusions: These findings suggest that sarcoidosis-like diseases in the military may be associated with environmental factors. To implement effective primary prevention, early detection, and treatment programs for sarcoidosis-like disease, these trends and work environment patterns need to be explained. Clinical studies of Vietnam-War-era veterans, which assess their work exposures and job activities in more detail, may identify preventable causes among this generation, which has a historically high rate of disease.

Medical Subject Headings (MeSH): sarcoidosis, pneumoconiosis, silicosis, military personnel, interstitial lung diseases, pulmonary tuberculosis, screening. (Am J Prev Med 1998;14: 176-183) © 1998 American Journal of Preventive Medicine

Sarcoidosis is a multisystem granulomatous disorder possibly caused by inhalation of airborne agents.² In young adults this syndrome usually presents with lung infiltrations and/or bilateral hilar lymphadenopathy detected by chest X-ray. The clinical course of sarcoidosis varies and is unpredictable.^{2,3} In whites this syndrome generally resolves spontaneously, while in blacks it often leads to fibrosis and sometimes death. Lung function impairment can persist even after X-ray abnormalities resolve.² Corticosteroid treatment is considered beneficial for preventing fibrosis and inhibiting granuloma formation when clinically indicated.^{2,4}

For diagnosis, "No tests are pathognomonic, not even pathology."⁵ Thus, sarcoidosis can be confused with work-related lung diseases with known causes, even silicosis.^{4,6} However, new imaging, immunologic, and mineralogic tests can help distinguish sarcoidosis from lung diseases with known causes. Patterns on high-resolution CT can help distinguish silicosis from sarcoidosis.⁷ Regarding groups of patients, resolution of chest X-ray abnormalities is common in sarcoidosis but is rare in chronic beryllium disease (and other dust-induced lung diseases).⁸

In practice, sarcoidosis is a diagnosis of exclusion, which is to be assigned only after known causes of sarcoidosis-like disease have been carefully eliminated. This is difficult when the typical clinical manifestations caused by a fibrogenic agent like silica are modified by the presence of other materials in mixed-dust expo-

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tures.⁹ Dusts of titanium, aluminum, zirconium, or mixtures of hard metals, can cause sarcoidosis-like granulomatous changes in the lung.¹⁰⁻¹³ In general, some sarcoidosis diagnoses may represent (1) new work-related diseases whose causes are yet to be identified or (2) diseases whose causes are already known but were not carefully ruled out or were never even considered.

Diagnoses of elimination are challenging for both surveillance and prevention. As a given population becomes exposed to new agents that cause sarcoidosis-like diseases, the pool of sarcoids can expand. And, as new causes of sarcoidosis-like disease are identified, the diagnoses of some sarcoids will be changed from "sarcoidosis" to this new disease category, shrinking the pool of sarcoids. When the lung disease of fluorescent light bulb workers was found to be caused by beryllium dusts, their "sarcoidosis" diagnoses were changed to "beryllium lung disease."⁸

For prevention, the confusion surrounding sarcoidosis poses two problems. First, it is difficult to prevent a disease of unknown cause. Second, when preventable diseases with known causes are mislabeled as "sarcoidosis" (or "cause unknown"), opportunities for disease prevention are lost unnecessarily.

This study was prompted by a black serviceman (the "index case") who developed lung disease while grinding "non-skid" surface coatings from aircraft carrier decks. Deck-coating materials have included complex and variable mixtures of metal compounds, resins, pigments, and minerals (such as titanium and aluminum oxides and silica) while the deck-grinding tools used have contained hard metals. Although discharged with "sarcoidosis" in the 1970s, the diagnosis of this deck grinder (with a negative Kveim test) was changed to work-related, dust-induced lung disease by civilian and VA pulmonary specialists about 12 years later. In 1992, this deck grinder was referred to NIOSH's Health Hazard Evaluation team, which investigates reports of suspected work-related disease.

Historically, sarcoidosis studies have examined the tuberculosis (TB) link and patterns involving race and incidence rates in both military and civilian databases.¹⁴⁻¹⁹ The marked variation in sarcoidosis rates, the TB connection, and the declining black/white race ratio of incidence rates raised environmental concerns even prior to this study.^{2,15} Is the high black/white ratio of reported rates in the United States (which has declined from 17:1 to less than 4:1) due to genetic factors or disproportionate exposure to environmental toxins?¹⁴⁻¹⁶ As early as the 1950s scientists asked why reported rates of sarcoidosis were changing even though annual chest X-ray screening of Navy enlisteds was "generally practiced."¹⁵ Were variations due to changes in detection and reporting or changes in actual disease rates?

Methods

Navy Personnel Data

A database-examination approach was used to assess sarcoidosis trends and environmental associations, a strategy used during the past 50 years to detect the TB link, racial patterns, and rate trends. The NHRC computerized enlisted database was used because it contains demographic, medical, and personnel data for all the millions of Navy enlisteds who ever served on active duty since 1965. This database spans more decades and has more work-related codes than databases used in prior military studies. To determine if the sarcoidosis diagnoses reported have been associated with Navy work environments, modern work assignment codes were used that were first added to the NHRC database in 1973. Diagnoses of dust-related lung disease (the "pneumoconioses") were not analyzed because the numbers reported were too small.

This study was designed to look at reported diagnoses (as opposed to diagnoses that were reviewed and "confirmed" in some way) because only reported diagnoses can provide evidence of "real world" misclassification, as well as environmental links, as initially requested. Also, patterns of misclassification and environmental exposures can be closely related; and, historically, only by recognizing environmental links could some clusters of "misclassified" cases be reclassified (i.e., "sarcoidosis" in Salem, MA, among fluorescent light bulb workers). One initial hypothesis had been that the index case and others never had "true sarcoidosis" but really had known work-related lung diseases that had been misclassified. And so, as in the case of the NIH "ACCESS" sarcoidosis study proposal, resources were not allocated to scrutinize sarcoidosis cases to eliminate cases possibly misclassified because such cases are actually of key interest to the original request. That is, this study was designed to be able to detect patterns consistent with any of the following possibilities: (1) sarcoidosis cases reported in the NHRC database may include sarcoid-like lung diseases that could now be identified as known work-related diseases by modern methods ("misclassification"), (2) "true sarcoidosis" itself may have environmental causes not yet identified, and (3) environmental factors may predispose persons to sarcoidosis.

Trends and the black/white race ratio of rates were determined for recent decades and compared with findings from the 1940s and 1950s. Work assignment associations were measured as requested along with the TB association to check the NHRC data for consistency with other databases.

It had been proposed that if dust-induced lung diseases had been substantially misclassified as sarcoidosis, the sarcoidosis rates reported during the 1960s and 1970s should be higher than those of the 1980s and 1990s because industrial hygiene practices had

Table 1. The black and white enlisted males among all the cases and a random sample of controls downloaded from the NHRC personnel database

	Cases			Controls		
	Black	White	Total	Black	White	Total
Number of enlisted males	536	585	1,121	1,028	8,012	9,040
Mean age at entry in years	20.5	20.2	20.4	20.1	19.9	19.9
(Standard deviation)	(3.2)	(3.5)	(3.4)	(2.7)	(2.8)	(2.8)
Mean tenure in Navy in years	9.8	11.4	10.7	5.2	5.5	5.5
(Standard deviation)	(7.4)	(8.4)	(7.9)	(5.7)	(6.0)	(5.9)
Mean year of entry into Navy	1972	1969	1970	1979	1975	1976
(Standard deviation)	(10)	(9)	(9)	(9)	(10)	(10)
Enlisted with a ship assignment “Onboard Activity Code” (OBAC)	285	253	538	594	3,488	4,082

markedly improved. Also, ship assignments more likely to involve personnel with dusty, manual job skills (repair ships, tenders, carriers, and other industrial-like ships) should be positively associated with sarcoidosis diagnoses whereas cleaner assignments should be protective.

To address these issues using a case-control approach, data for all 1,220 enlisted given a diagnosis of sarcoidosis while on active duty (“cases”) and a random sample of 10,000 without a sarcoidosis diagnosis (“controls”) were downloaded from the same NHRC database that has been maintained since 1965. This database is complete in that all of the millions of Navy enlisteds who served since 1965 are included. NHRC scientists downloaded these samples since they have had decades of experience in the use of this personnel database for both research and administrative purposes. The NHRC used a random sampling method involving the last digit of the social security number. This randomization scheme was developed and validated years previously by a team of NHRC scientists including epidemiologists.

To further check the randomization scheme, the NHRC was asked to provide total manpower (“denominator”) data reported previously by year, race, and gender. These manpower data were used to directly compute incidence rates to duplicate the case-control trends found using the samples downloaded from the personnel data. The trends and associations were also duplicated using another random sample downloaded by the NHRC. The case-control results were also compared with findings previously published (the TB link and black/white ratio) as another check of consistency as well as to gain a broader historical perspective.

Demographic and environmental information used in the analyses included race (black or white), age at entry, year of entry, tenure (length of service), rate codes (“airman,” “seaman”), and type of ship assignment. Age at entry onto active duty (in years) is year of

entry minus year of birth. Year of entry refers to start of Navy service (date of first “event” in accessions file). Tenure, or length of service, represents the total number of years on active duty as of 1993. Rate codes were used to determine which enlisteds were in the “airman” and “seaman” career tracks (vs. medical or other tracks). The ship assignment indicator used was the new four-digit NHRC “on-board activity code” (OBAC) introduced in 1973.

In addition to the deck grinder assigned to a carrier, others on repair ships, tenders, and other “industrial-like” ships had also been hospitalized and diagnosed with sarcoidosis. To assess the importance of type of ship assignment, OBACs were grouped into “clean” and “industrial-like” categories. Repair ships, carriers, tenders, floating dry docks, and salvage ships were considered to have a higher proportion of enlisteds with dusty, manual job skills than hospital, troop transport, and environmental research ships. Overall, assignment only to “clean ships” should reflect personnel with “clean” job skills. The “clean ship” grouping used included hospital, research, cargo, store, tug, or escort ships, with OBAC numbers 125–134, 143–158, 160, 167–245, 302–386, 446–623, 629–660, and 868–894.

Analyses

Trends for sarcoidosis diagnoses were examined in two ways. First, case-control analyses were run. Second, sarcoidosis incidence rates for black and white men were computed directly using total manpower “denominator” data (published since 1975) to duplicate the case-control trends. Time period (years of entry), length of service (tenure), and age at entry were used in all models. Race was always taken into account either by looking at black and white males separately or by including race in those models with black and white men combined.

Table 2. Odds ratios for race (black vs. white), time period (“recent” vs. “earlier” years of entry), length of service (tenure in years), and age at entry (younger than 20 years of age vs. 20 or older) in a general sarcoidosis model of 10,161 black and white enlisted males as a function of basic personnel characteristics

Logistic model: sarcoidosis = function of race, time period, length of service, and age		
(Risk) Factors	Odds ratio	95% CI (LR)
Race (being black)	8.6	7.5–10.0
Time period (entered Navy before 1985)	4.7	3.6–6.3
Length of service (tenure in years)	1.1/year of service	1.1–1.1
Age at entry (age ≥20 years old)	1.4	1.3–1.7

Results

Table 1 describes the Navy enlisted personnel studied. Since the numbers of women and non-black and non-white personnel were relatively small, of the 1,220 enlisteds with a diagnosis of sarcoidosis only the 1,121 enlisted male cases who were black or white were used (92% of cases). Of the 10,000 controls in the random sample, the 9,040 black and white enlisted males were used (90% of controls).

Case-Control Findings

A general logistic model for all 10,161 black and white male cases and controls, showing the relative importance of basic personnel factors in terms of odds ratios (ORs), is shown in Table 2. Being of black race and the earlier years of entry (earlier “time period”) are two risk factors (ORs > 1) strongly associated with a Navy diagnosis of sarcoidosis. Case-control trend analyses comparing more than two time periods revealed a progressively greater risk of sarcoidosis in earlier years. Race is in this model because blacks in the U.S. military have had higher rates of sarcoidosis since this was first reported in the 1940s. Time period is included because industrial hygiene practices have improved over time and have reduced toxic exposures. Length of service (tenure) is in the model because some causes of sarcoidosis-like disease are environmental (silica, metal dusts, etc.), and tenure can reflect cumulative exposure. Age at entry is included since disease rates can be higher in the third and fourth decades of life.⁴

Of note, the OR relating black race to sarcoidosis diagnoses has declined over time. As shown in Table 3, the black race OR for Navy enlisted men has declined to about six.

Ship Assignment Associations

Four different models in Table 4 show that for both black and white airmen and seamen who ever had a ship assignment OBAC (aside from basic “sea school” training, OBAC = 7,000), having “only had clean ship assignments” is associated with a decreased risk of being diagnosed with sarcoidosis (ORs < 1, a “protective effect”). This protective effect is stronger (ORs much smaller than 1) among black servicemen than white. “Airmen” and “seamen” were used because they are more likely to engage in substantial dusty, manual labor than those in medical or other career tracks. In these four models, four categories of time period were used (entry years: ≤ 1974, 1975–1981, 1982–1987, 1988–1993). As shown in the last two models in Table 4, this protective effect was also found when considering only the subgroups that entered the Navy after 1973 or after 1979. By 1974 OBACs were in universal use. The impact of type of ship assignment and tenure on the OR for black race is shown in each of the last two models in Table 4 by comparing the race ORs for the full models to the “crude” race ORs for models in which the tenure and ship assignment variables have been removed. When ship assignments (or tenure plus ship assignments) are included in these models, the importance of race is reduced. The impact of ship assignments (both in terms of the magnitude of the protective effect of clean ships and the reduction in the race OR) is less during more recent years when both the sarcoidosis rates and the black/white race ratio are lower.

Trends

The black/white race ratios of rates (computed using the total manpower data available since 1975) are

Table 3. The odds ratios for being of black race in the general sarcoidosis model for two different time periods (showing the decline in the race OR over time)

Logistic model: sarcoidosis = function of race, length of service, and age		
2 time periods	Odds ratio for black race	95% CI (LR)
“Earlier” years (entered before 1985)	8.8	7.6–10.3
“Recent” (entered in 1985 or later)	6.1	3.6–10.5

Table 4. Odds ratios showing protective effect of “only had clean ship assignments” for the black and white airmen and seamen (enlisted males) who ever served on ships

A. 745 blacks

Model: sarcoidosis = function of time period, length of service (tenure), age, ship assignment

(Protective) Factor	Odds ratio	95% CI (LR)
“Only had clean ship assignments”	0.06	0.00–0.27

B. 3,008 whites

Model: sarcoidosis = function of time period, length of service (tenure), age, ship assignment

(Protective) Factor	Odds ratio	95% CI (LR)
“Only had clean ship assignments”	0.37	0.13–0.84

C. 2,903 blacks and whites combined who entered after 1973 (OBAC data complete)

Sarcoidosis = function of race, time period, length of service (tenure), age, ship type

Factors	Odds ratio	95% CI (LR)
“Only had clean ship assignments” (in full model)	0.19	0.06–0.47
“Adjusted race” (being black, in full model above)	9.4	7.0–12.7
“Crude race” (tenure and ship variables removed)	10.1	7.6–13.5

D. 1,755 blacks and whites combined who entered after 1979 (only more recent years)

Sarcoidosis = function of race, time period, length of service (tenure), age, ship type

Factors	Odds ratio	95% CI (LR)
“Only had clean ship assignments” (in full model)	0.33	0.10–0.84
“Adjusted race” (being black, in full model above)	7.7	5.1–11.5
“Crude race” (tenure and ship variables removed)	8.1	5.4–12.4

displayed as the right three bars in Figure 1 and support the case-control findings (and previously published data) that being black is a major risk factor. Similarly, the average annual sarcoidosis incidence rates are shown as the six right bars for blacks and whites in Figure 2. The declines in the incidence rates from 1975 to 1993 using manpower data (the right six bars in Figure 2) duplicate the declining case-control trends found using the personnel data.

To view these trends in a broader historical context, data from three prior studies are included as the left three bars in Figure 1 and the left six bars in Figure 2. Since the 1940s the black/white ratio of the reported sarcoidosis rates has declined as shown in Figure 1. Using these same studies for the left six bars in Figure 2, a peak in sarcoidosis incidence rates appears during the Vietnam years. Although the 1965–1974 bar could not be calculated (manpower data unavailable), case-control trend analyses using the personnel data indicate higher rates before 1975. That is, according to NHRC personnel data, which includes all enlisteds who served since 1965, a peak in sarcoidosis rates occurred during the Vietnam War years.

Pulmonary TB Association

In the NHRC database, as in other databases examined historically, a small proportion of sarcoids have both pulmonary TB and sarcoidosis diagnoses. Using NHRC data, TB is found to be associated with sarcoidosis when

pulmonary TB is added to all models (all ORs >20 with *P* values <0.01), an association consistently reported previously.²

Discussion

For more than 100 years sarcoidosis has remained a mystery.⁴ “The predilection of sarcoidosis for young black adults in the U.S. and young white adults elsewhere has resisted all proposed explanations.”¹⁰ The high (but declining) black/white ratio of reported rates over the past 50 years may reflect disproportionately high black exposure to causative agents or changing patterns of detection or misclassification.^{14,16}

This study is the first to address environmental factors and recent trends using modern NHRC sarcoidosis data that describe more cases spanning more decades than military data used previously. Measurement of work assignment associations was possible because OBACs were added in 1973. The unexplained peak in the reported rates during the Vietnam era, the declining black/white ratio of these rates, and the protective effect of “clean ship” assignments are consistent with the environmental links originally proposed. That is, reported sarcoidosis diagnoses may include known work-related lung diseases (misclassification), or “true sarcoidosis” may have environmental causes yet to be identified (and may not be entirely, or even partially, genetic). Also, the declining importance of type of ship

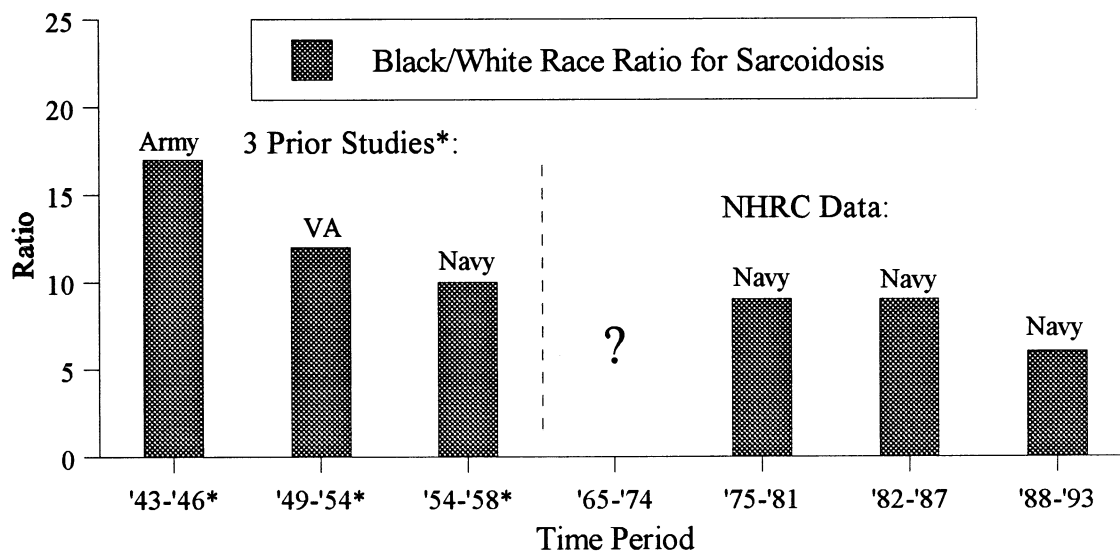


Figure 1. Black/white race ratios of the sarcoidosis incidence rates reported during different (and unequal) time periods showing both NHRC and previously published data. The “?” indicates that total manpower data were not available for this time period. *Reproduced from Teirstein and Lesser¹⁹ with permission of the publisher.

assignment over time parallels the declines in both the sarcoidosis rates and the black/white race ratio.

Overall, it is difficult to postulate plausible explanations for these findings unrelated to environmental factors such as less effective disease detection after 1965 (which somehow affected blacks differently than whites and was related to type of ship assignment). Even changes in medical care over time can be related to environmental issues such as increased awareness and detection of known work-related diseases (resulting in less misclassification). Also, even with time period included in all models to take secular trends into account, the ship associations persist. Certainly screening is important since, historically, Navy sarcoidosis diagnoses usually have resulted from chest X-ray screening.¹⁵ However, even when sarcoidosis rates were noted to be changing in the 1950s, regular annual chest X-ray screening of enlisteds was already “generally practiced.”¹⁵ However, if the marked decline in rates after 1965 actually reflects missed diagnoses, then the high rates reported during the peak years may persist but are unrecognized. Of note, if a substantial number of diagnoses were missed in recent years, one would have expected these to have included mostly the milder cases among whites with a corresponding return of very high black/white ratios. Under-reporting, if any, can delay prevention efforts, treatment, and appropriate career planning. Steroid treatment for sarcoidosis is considered beneficial in preventing progressive fibrosis. Early recognition of sarcoid-like diseases with known causes is needed to detect and control hazardous exposures to silica, metal dusts, or sensitizers.

Effective screening, detection, and reporting are also needed to identify new outbreaks and new causes of sarcoidosis-like disease, as successfully achieved in the fluorescent light bulb industry.

Of note, the work environment links to sarcoidosis diagnoses found were predicted by Navy personnel. The Vietnam War era was described as a period of increased activity (more missions, repairs, flights, and deck resurfacing on aircraft carriers), dustier working conditions, and less than optimal industrial hygiene practices in a wartime setting. Navy personnel described examples of activities that generated dusts and fumes containing silica, aluminum, hard metals, isocyanates, beryllium, and other materials capable of causing sarcoid-like lung disease. The physicians who changed the deck grinder’s diagnosis to dust-induced lung disease suggested that the high rate of sarcoidosis-like disease in blacks might simply reflect increased exposure to airborne toxins.

The association found between pulmonary TB and sarcoidosis in the NHRC data has been reported previously, and this consistency is reassuring.² Three major explanations for the TB-sarcoidosis link are possible. First, some silicotics, who are prone to TB, may have been misclassified as “sarcoids,” and this TB association may represent the well-established link between pulmonary TB and silica exposure.²⁰ Of note, high rates of TB have been found in coal workers at mines with a high silica content.⁹ Second, those with both diagnoses may actually have only one of these conditions. Third, TB and sarcoidosis may be linked through biological mechanisms independent of the TB-silica connection.

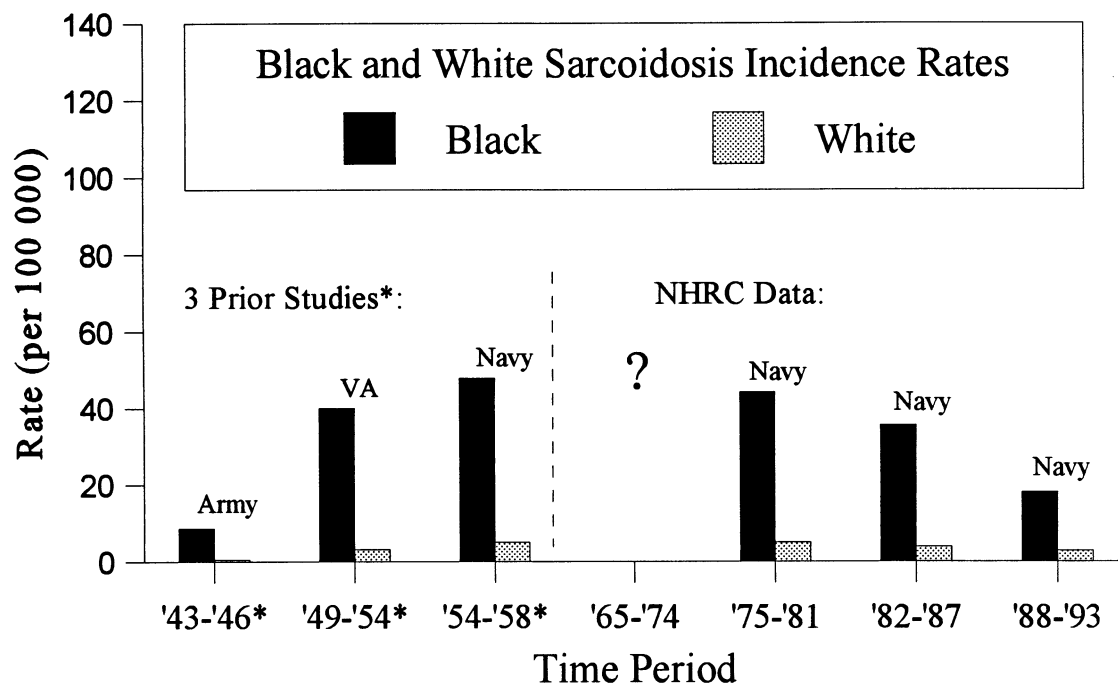


Figure 2. Black and white average annual sarcoidosis incidence rates reported for different (and unequal) time periods using both NHRC and previously published data. The “?” indicates that total manpower data were not available for this time period. *Reproduced from Teirstein and Lesser¹⁹ with permission of the publisher.

Conclusions

These findings are consistent with the original hypothesis that preventable, environmental exposures may cause (or increase one’s susceptibility to) sarcoidosis-like disease in naval settings. Sarcoidosis rates during the past 50 years reveal a declining black/white race ratio and an unexplained peak in the Vietnam War era. Enlisted men assigned only to “clean ships” have been less likely to be diagnosed with sarcoidosis. The magnitude of this Navy work environment association has declined in recent years and parallels the declines in both the importance of race and the sarcoidosis rates.

These findings are particularly striking because (1) they were predicted by Navy personnel, (2) ship assignments are only crude indicators of underlying job activities and airborne exposures, and (3) the work environment associations are strong even though the critical Vietnam War era (with its high rate of disease and wartime exposures) was not included since OBACs had not yet been in use.

This study, the first to find work environment associations for sarcoidosis in a military setting, highlights opportunities relevant for prevention. Clinical studies that assess the medical status and work histories of “sarcoids” and dust-exposed personnel in detail may identify specific, preventable hazards not possible using crude database codes. Vietnam-War-era veterans represent a special opportunity for

medical study because they have historically high sarcoidosis rates. Also, the size of the work environment associations for this key generation remains unknown because OBACs had not yet been introduced. The historical progression from descriptive sarcoidosis studies to detection of military work environment associations should be extended to include clinical studies of those veterans still living who are at high risk for lung disease, particularly generations of veterans with high rates of sarcoidosis.

Finally, these findings warrant serious consideration of the following recommendations made by those Navy personnel who predicted these patterns: (1) workers with pulmonary sarcoidosis (or other lung diseases of unknown cause) should not be returned to jobs with dust or fume exposures, (2) more detailed job activity and exposure information should be included in military databases, (3) being of black race may reflect increased exposure to causative factors as opposed to a genetic predisposition, (4) workers with firsthand experience are well suited to identify work-related hazards and propose disease-related research hypotheses, and (5) Navy “sarcoids” and dust-exposed personnel should be studied clinically to identify preventable causes for lung disease, particularly Vietnam-War-era and black personnel who have high rates of sarcoidosis-like lung disease.

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