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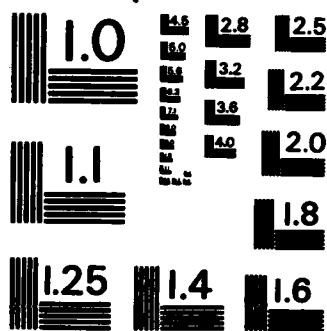
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HODGKIN'S DISEASE IN THE U. S. NAVY

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SUMMARY

Problem

The risk of the development of Hodgkin's disease has been shown to vary with social and occupational factors. Reports indicate Hodgkin's disease may have an infectious etiology, particularly in the young. Occupational exposures have also been implicated as risk factors. Active-duty enlisted naval personnel are often in crowded conditions and are involved in a wide variety of occupational specialties which may alter their risk of developing Hodgkin's disease.

Objective

The objective of this study was to assess occupational differences in risk for development of Hodgkin's disease in active-duty enlisted naval personnel compared to the U.S. population and total enlisted naval personnel incidence.

Approach

Average annual age-specific and age-adjusted incidence rates (first hospitalization rates) for Hodgkin's disease were calculated for active-duty personnel for the period 1974-79. Standardized incidence ratios were calculated for all Naval occupations in which at least one case occurred. Expected numbers of cases were calculated using U.S. rates provided by Surveillance, Epidemiology, and End Results (SEER), Incidence and Mortality Data, 1973-77, and total Navy age-specific incidence rates.

Results

Overall age-adjusted incidence rates of Hodgkin's disease among naval enlisted personnel did not differ significantly from the U. S. population. There was no evidence of increased age-adjusted rates with increase in length of service. However, the standardized incidence ratio for Hodgkin's disease in U.S. Navy machinist's mates was 1.8, compared to U.S. population (SEER) rates, and 2.3 compared to total Navy rates, revealing a statistically significant doubling of risk in this occupational group. This finding should be interpreted cautiously since multiple statistical comparisons may yield statistically significant results that may be due to chance alone.

Conclusions

Overall, the findings of the study do not provide evidence for short-term-latency-period Hodgkin's disease as a result of acute infections and multiple immunizations which characterize military service. The design of this study does not preclude the possibility that these exposures may have produced elevated rates of Hodgkin's disease after discharge from the Navy. The association between being a machinist's mate and developing Hodgkin's disease warrants further investigation.

Hodgkin's Disease in the U. S. Navy

A number of reports have suggested that Hodgkin's disease is a malignant neoplasm that may have an infectious etiology (1-7). This hypothesis is based on several observations. Hodgkin's disease has been reported to cluster in high schools, but these reports are inconclusive (8-11). An increased risk of Hodgkin's disease has been observed for those with a history of tonsillectomy or infectious mononucleosis (2,12-14). Risk factors similar to those identified for poliomyelitis, such as high socioeconomic status, having had few childhood infectious diseases, and being an only child or the sibling of a case, have led to the suggestion that a viral agent with a low clinical infection rate may be responsible (6,10,15). As for polio, Hodgkin's disease may be the uncommon result of a common infection with a clinical course dependent upon age at exposure and immunologic competence of the host (6,15,16).

Reports also indicate that immune stimulation through vaccination, exposure to B-lymphocyte mitogens, or to high levels of food antigens, may increase risk (16-20) or that Hodgkin's disease may be associated with autoimmune disorders (21,22).

Occupational exposures also have been implicated as risk factors (23-28), including exposure to benzene and other organic solvents among chemists, machinists, and workers involved in the manufacture of synthetic abrasives and rubber products (27-29). Less clear is the implication that exposure to wood and wood-products may be related to the development of Hodgkin's disease. This evidence is confounded by exposures to chemical wood preservatives, most notably pentachlorophenol, which can contain dioxin and has been found in the urine of wood-workers (30).

Naval personnel are involved in a wide variety of occupational specialties, some of which may involve exposure to the agents implicated in the development of Hodgkin's disease. Many other environmental factors associated with naval life-style, including crowding and aggregation of susceptibles, foster the spread of infectious diseases such as measles, rubella, and influenza (31, 32). These conditions and worldwide travel increase the need for frequent routine immunizations (33).

These occupational, social, and medical factors led us to hypothesize that there may be an increased risk of Hodgkin's disease in naval personnel compared to the general population, and that the risk may vary by occupation and length of service. To explore these hypotheses we ascertained first hospitalization rates for Hodgkin's disease among active duty naval personnel during a six-year period and compared these with incidence rates in the general population from the Surveillance, Epidemiology, and End Results (SEER) study of 10 areas combined of the U. S. in 1973-77 and with total Navy rates (34). Because Hodgkin's disease may sometimes be misclassified as lymphoma of another type, we also ascertained first hospitalization rates for all other lymphomas. These will be described in a separate report.

Methods

The Naval Health Research Center maintains an Inpatient Medical Data file which contains all hospitalizations, deaths, Medical Board, and Physical Evaluation Board findings for active-duty enlisted naval personnel for the period 1965-79. This file was searched for all first hospitalizations of white men diagnosed as having Hodgkin's disease (ICDA-8 code 201.0) for the period

1974-79 (95 incident cases). Naval occupational specialty, age, length of service, and educational level of cases were also identified from the file.

Cases chosen for inclusion in this study were defined as patients with a hospital diagnosis of Hodgkin's disease with corroborating Medical or Physical Evaluation Board findings, as determined from NHRC computer files (85 cases); or if these were not available (3 cases), pathological confirmation of Hodgkin's disease was done through the tumor registry in the admitting hospital. A Medical Board or Physical Evaluation Board diagnosis of a malignant disease such as Hodgkin's disease is routinely based on pathological confirmation.

Seven first hospitalization cases of Hodgkin's disease identified from the NHRC Medical file during the study period were excluded, 4 because Hodgkin's disease was not the primary diagnosis and the primary diagnosis was for a disease with clinical findings which may sometimes be difficult to distinguish with complete certainty from those of Hodgkin's disease. An additional 3 patients were excluded because of inconsistent (2 cases) or equivocal (1 case) Medical or Physical Evaluation Board findings. Among the seven incidence cases excluded, 4 occurred in machinists' mates.

An Enlisted Master Record file, also maintained by the Naval Health Research Center, provided average annual population estimates for all active duty personnel by age, race, sex, educational level, length of service, and approximately 95 occupational enlisted specialties during the period 1974-79. Age-specific and age-adjusted incidence rates were calculated for active-duty enlisted naval personnel (2,275,829 person-years). Standardized Incidence Ratios (SIRs) were calculated for all naval occupations having at least one case using rates provided by SEER and total Navy rates (34). Calculation of 95% confidence limits was performed assuming a Poisson distribution (35). Age-adjustment was done using the indirect method, a technique selected because the numbers of cases in some age categories were not large enough to provide the stability appropriate for direct adjustment.

Results

The age-adjusted incidence rate of Hodgkin's disease was lower in naval personnel (2.9 per 100,000 person-years) than in the U.S. population (3.7 per 100,000 person-years); however, this difference was not statistically significant (Table 1). Age-specific rates, also shown in Table 1, do not reveal any major deviations from rates expected based on the SEER population. Rates at ages 17-34 were lower in naval personnel than in the SEER population, but those at ages 35+ were 1.3 times higher.

Age-adjusted incidence rates increased from 2.3 to 4.0 per 100,000 after 11 years of service; however, this difference was not statistically significant (Table 2). Analysis of age-adjusted incidence rates by educational level revealed no significant differences (not shown).

Overall, active duty enlisted personnel had approximately the same risk of developing Hodgkin's disease as the general U.S. population (SIR = 0.8, 95% C.L. = 0.6-1.0) (Table 3). One entry level occupation, seaman, had a statistically significantly low risk for Hodgkin's disease, with one-tenth the risk of the U.S. general population (SIR = 0.1, 95% C.L. = 0.0-0.6), and one-fifth the risk of the total Navy (SIR = 0.2, 95% C.L. = 0.0-1.1). U.S. Navy machinist's mates had

about double the risk of Hodgkin's disease as the U.S. general population (SIR = 1.8, 95% C.L. = 0.9-3.2) and as the total Navy (SIR = 2.3 95% C.L. = 1.2-4.0), a statistically significant excess ($p = 0.004$). Machinist's mates were the only occupational group with a statistically significant excess. In this occupational group, no Hodgkin's disease cases occurred in less than one year of service, 3 cases in 1.0 to 1.9 years of service, 4 cases in 2.0 to 3.9 years of service and the remaining 5 cases in more than 4.0 years of service.

Hospital corpsmen who have higher incidence rates of infectious disease than other naval personnel (36), did not experience a significantly elevated rate of Hodgkin's disease. Seven cases were observed in this group, while 4.1 were expected based on U.S. Navy rates, yielding a nonsignificant SIR of 1.7. Occupational groups that had fewer than three cases of Hodgkin's disease are shown in Appendix A. All occupational groups were included in the computation of the standardized incidence ratios for "all occupations" shown at the bottom of Table 3.

Discussion

Studies of active-duty enlisted military personnel are most suitable for diseases with relatively short latency periods. Previous studies of Hodgkin's disease in persons with a history of mononucleosis observed median latency periods of 3-4 years (2,13,37). The latency period for Hodgkin's disease cases occupationally exposed to organic solvents in previously reported studies is in the range from 4 to 35 years with a median duration of 8 years (25). Diseases with extremely long latency periods, such as mesothelioma, cannot be readily studied with this method unless the data are supplemented with follow-up information on persons who retired or were otherwise separated from active service. This study is confined to enlisted personnel on active-duty, and it is possible that the incidence rates reported are underestimates, especially if Hodgkin's disease has a longer latency period than expected. Only data on active-duty personnel were available so it was not possible to determine first hospitalization rates of the disease after separation from the Navy.

Within these limitations, age-specific incidence rates of Hodgkin's disease in naval enlisted personnel were slightly lower than those in the U.S. population at ages 17-34 (Table 1), and the rate at age 35+ was higher in the Navy than in the U.S. population. This may be due to selection of recruits who are free of lymphadenopathy and other early signs of Hodgkin's disease. This is supported by the significantly reduced risk among seamen, an entry-level occupation.

A detailed examination of all Navy occupations with at least one Hodgkin's disease case identified only one occupation with a significantly elevated risk of Hodgkin's disease compared to the total Navy. This was machinist's mate (the Navy title corresponding roughly to the civilian occupation of stationary engineer), and its standardized incidence ratio was 2.3 ($p = 0.004$). A previous study has identified the occupation of machinist as having an increased risk of Hodgkin's disease (27), but the significant finding in the present study should be cautiously interpreted since it is not unusual in a statistical test involving multiple comparisons for a result to appear significant solely based on chance expectation. Machinist's mates use heavy machinery in enclosed settings and are exposed to a variety of volatile industrial solvents, cutting and lubricating oils, metal dusts and vapors, and freon. Agents associated with the development of

Hodgkin's disease include exposure to benzene and other solvents (23, 27, 29, 30). Some Navy machinist's mates may also be occupationally exposed to ionizing radiation, a known risk factor for lymphomas, although not necessarily Hodgkin's disease (38).

The lack of excess risk among naval personnel overall does not support the hypothesis that exposure to an infectious agent after age 17 plays a strong role in the etiology of Hodgkin's disease. However, analysis of rates among hospital corpsmen showed a non-significant excess when compared with both the U.S. population (SIR = 1.3) and the total Navy (SIR = 1.7). Hospital corpsmen have been observed to have higher hospitalization rates for infectious diseases than naval personnel in other occupations (36). The moderate increased risk for Hodgkin's disease in hospital corpsmen is consistent with an infectious disease hypothesis.

Overall, the findings of the study do not provide evidence for short-term causation of Hodgkin's disease as a result of the multiple immunizations and acute infections which characterize military service. The design of this study, however, does not preclude the possibility that these exposures may have produced elevated rates of Hodgkin's disease after discharge from the Navy. The association between the Navy occupation of machinist's mate and development of Hodgkin's disease warrants further investigation.

Table 1
Age-Specific and Age-Adjusted Incidence Rates of Hodgkin's Disease per
100,000 Person-Years for Active Duty Enlisted Naval Personnel and
United States Population, White Males, 1974-79

Age	Naval personnel			
	Person-years at risk	Hodgkin's disease		SEER In- cidence rate†
		No. of cases	Average annual incidence rate*	
17-19	449,890	11	2.4	3.5
20-24	964,189	39	4.0	5.7
25-34	597,022	25	4.2	5.1
35+	257,840	13	5.0	3.9
Unknown	6,888	0	0.0	0.0
Total	2,275,829	88	-	-
Crude rate			3.9	3.7
Age-adjusted rate‡			2.9	-

*Navy incidence rate based on first hospitalization rate for Hodgkin's disease, International Classification of Diseases, Eighth Revision, Code 201.

†United States population rates are provided by the Surveillance, Epidemiology and End Results, (SEER) Incidence and Mortality Data: 1973-77 (34).

‡Adjusted by the indirect method using age-specific incidence rates provided by SEER applied to the Navy study population and should be compared with the SEER crude rate.

Table 2
Age-Adjusted Incidence Rates of Hodgkin's Disease per 100,000
Person-Years, by Duration of Service, Active
Duty Enlisted Naval Personnel, White Males, 1974-79

Duration of service (yrs)	Person-years at risk	No. of cases	Crude average annual rate	Age-adjusted incidence*	
				Average annual rate	95% Confidence limits†
0.0 - 1.9	764,783	21	2.7	2.3	(1.6, 3.5)
2.0 - 3.9	559,990	21	3.8	2.5	(1.7, 3.8)
4.0 - 6.9	297,990	15	5.0	3.4	(1.9, 5.6)
7.0 - 10.9	209,373	11	5.2	3.7	(1.8, 6.6)
11.0+	436,775	20	4.6	4.0	(2.4, 6.2)
Unknown	6,918	0	0.0	0.0	(--, --)
Total	2,275,829	88	3.9	2.9	2.3 3.6

*Incidence rates based on first hospitalizations. Duration of service specific age-adjusted rates obtained by the indirect method using SEER incidence rates applied to the Navy study population.

†Based on the Poisson distribution.

Table 3
Standardized Incidence Ratios (SIR) and 95% Confidence
Limits for Hodgkin's Disease, by Occupation,
Active Duty Enlisted Naval Personnel, White Males, 1974-79

Occupation*	No. of cases	Person-years at risk	SIR (95% Confidence limits)†	
			U.S. controls	Navy controls
Torpedoman's mate	3	21,644	2.7 (0.6, 7.9)	3.4 (0.7, 9.9)
Gunner's mate	4	39,245	2.0 (0.5, 5.1)	2.5 (0.7, 6.4)
Interior communications technician	3	30,572	1.8 (0.4, 5.3)	2.4 (0.5, 7.0)
Machinist's mate	12	133,247	1.8 (0.9, 3.2)	2.3‡ (1.2, 4.0)
Electronics technician	3	35,370	1.8 (0.4, 5.3)	1.9 (0.4, 5.5)
Yeoman	4	47,135	1.7 (0.5, 4.4)	2.0 (0.5, 5.1)
Engineman	3	45,436	1.3 (0.3, 3.8)	1.7 (0.3, 5.0)
Hospital corpsmen	7	103,655	1.3 (0.5, 2.7)	1.7 (0.7, 3.5)
Fire control technician	3	47,349	1.2 (0.2, 3.5)	1.6 (0.3, 4.7)
Aviation structural mechanic	5	80,654	1.2 (0.4, 2.8)	1.5 (0.5, 3.5)
Fireman	5	100,766	1.0 (0.3, 2.3)	1.7 (0.6, 4.0)
Airman	4	87,627	0.9 (0.2, 2.3)	1.5 (0.4, 3.8)
Aviation machinist's mate	3	68,230	0.9 (0.2, 2.6)	1.1 (0.2, 3.2)
Radioman	3	80,690	0.7 (0.1, 2.0)	0.9 (0.2, 2.6)
Seaman	1	288,155	0.1 (0.0, 0.6)	0.2 (0.0, 1.1)
All occupations	88	2,275,829	0.8 (0.6, 1.0)	1.0 (0.8, 1.2)

*Only occupations with three or more cases are shown with the exception of Seaman, all others are listed in Appendix A. The "All occupations" category is based on the occupations in this table and those in Appendix A.

†Based on the Poisson distribution.

‡Significant at the $p = 0.004$ level, two-tailed.

Appendix A

Naval occupational groups with 1-2 cases of Hodgkin's disease.

Numbers of cases and standardized incidence ratios for U.S. population and Navy population, respectively, are shown in parentheses.

Dental technician (2, 2.9, 3.8); Storekeeper (2, 1.1, 1.3); Mess management specialist (2, 1.0, 1.3); Boiler technician (2, 0.7, 0.9); Electrician's mate (2, 0.6, 0.8); Hull Technicians (2, 0.6, .8); Musician (1, 4.0, 4.5); Utilities man (1, 2.6, 3.2); Tradesman (1, 2.2, 2.6); Photographer's mate (1, 1.9, 2.3); Aviation antisubmarine warfare operator (1, 1.2, 1.6); Ship's serviceman (1, 1.2, 1.6); Aviation fire control technician (1, 1.0, 1.3); Personnel man (1, 0.6, 0.8); Aviation electrician's mate (1, 0.5, 0.6); Boatswain's mate (1, 0.5, 0.5); Sonar technician (1, 0.5, 0.5); Cryptologic technician (1, 0.4, 0.5); Aviation electronics technician (1, 0.3, 0.4).

Naval occupational groups with no cases of Hodgkin's disease.

Aerographer's mate; Air controlman; Aircraft maintenance technician; Aircraft survival equipment man; Antisubmarine warfare technician; Aviation boatswain's mate; Aviation maintenance administration man; Aviation storekeeper; Aviation support equipment technician; Aviation ordnance man; Avionics technician; Boilermaker; Builder; Construction electrician; Construction man; Constructionman*; Construction mechanic; Data processing technician; Data systems technician; Disbursing clerk; Electronic warfare technician; Engineering aid; Equipment man; Equipment operator; Gas turbine systems technician; Illustrator-Draftsman; Instrument man; Intelligence specialist; Journalist; legalman; Lithographer; Machinery repairman; Master-at-Arms; Mineman; Missile technician; Molder; Navy Counselor; Ocean systems technician; Operations specialist; Opticalman; Patternmaker; Photographer's mate; Postal clerk; Precision instrument man; Quartermaster; Religious person; Signalman; Sonar technician; Steelworker.

*Construction man and constructionman are two different occupational categories in the U.S. Navy.

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20. cont.

First hospitalization rates for Hodgkin's disease among Active Duty naval personnel and compared them with incidence rates in the U.S. population. We found no significant differences in age-adjusted naval and U.S. population rates, although the rate in the Navy at ages 35+ was 1.8 times the U.S. population rate. Navy machinist mates had double the rates of Hodgkin's disease of the U.S. population, a statistically significant excess.



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