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Description Notes

Health Status of Vietnam Veterans

II. Physical Health

The Centers for Disease Control Vietnam Experience Study

The Vietnam Experience Study was a multidimensional assessment of the health of Vietnam veterans. From a random sample of enlisted men who entered the US Army from 1965 through 1971, 7924 Vietnam and 7364 non-Vietnam veterans participated in a telephone interview; a random subsample of 2490 Vietnam and 1972 non-Vietnam veterans also underwent a comprehensive medical examination. During the telephone interview, Vietnam veterans reported current and past health problems more frequently than did non-Vietnam veterans, although results of medical examinations showed few current objective differences in physical health between the two groups. The Vietnam veterans had more hearing loss. Also, among a subsample of 571 participants who had semen samples evaluated, Vietnam veterans had lower sperm concentrations and lower mean proportions of morphologically "normal" sperm cells. Despite differences in sperm characteristics, Vietnam and non-Vietnam veterans have fathered similar numbers of children.

(JAMA 1988;259:2706-2714)

THE CENTERS for Disease Control has undertaken a congressionally mandated health study of Vietnam veterans called the Vietnam Experience Study (VES). This is the second of three articles in this issue of THE JOURNAL about the health status of Vietnam veterans.

See also pp 2701 and 2715.

We herein describe the physical health status of a sample of US Army Vietnam veterans and a comparison group of other Vietnam-era US Army veterans. The first report focuses on current psychosocial characteristics of the veterans¹ and the third report focuses on reproductive outcomes.²

SUBJECTS AND METHODS

Participant Selection

The selection of participants and the methods used in locating and interviewing them have been described in detail elsewhere.^{1,3,4} After the vital status of a random sample of US Army Vietnam-era veterans had been ascertained, 9078 Vietnam and 8789 non-Vietnam veterans met study criteria and were thus eligible for telephone interview. Of these, 7924 Vietnam (87%) and 7364 non-Vietnam (84%) veterans completed telephone health interviews. Of the random subsample of veterans selected for further evaluation, 2490 Vietnam (75%)

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and 1972 non-Vietnam (63%) veterans underwent extensive physical and psychological health examinations.

Medical Examinations

All examinations were performed at one medical facility. Physicians, interviewers, and study technicians were unaware of which cohort the veterans were in. Board-certified internists, dermatologists, and neurologists performed complete general physical, dermatologic, and neurological examinations, respectively. Abnormal findings from these screening examinations were not evaluated further at the examination facility, but were reviewed with each veteran in an exit interview.

The peripheral arterial system was evaluated by using a Doppler instrument. Electrocardiograms were interpreted by board-certified cardiologists. Chest films were interpreted by radiologists. Pulmonary function was tested with a wedge spirometer, followed by computer analysis of spirometric results.

The nerve conduction velocity and amplitude of upper- and lower-extremity sensory and motor nerves were measured by standard techniques.⁵ Vibratory and thermal sensations were tested with specially designed instruments (Pflizer Vibrator⁶ and Thermal Tester⁷). Auditory acuity was tested with an audiometer that operated in automatic mode.

Trained technicians administered standard neuropsychological tests,^{8,9} including the general technical test section of the Army Classification Battery,

an aptitude test that participants took during their induction into the army. The neuropsychological test battery evaluated concept formation and problem-solving abilities, memory functioning, manual dexterity, verbal abilities, visual-perceptual-motor functioning, and mental control and attention.

Laboratory Methods

Standard hematologic assays were performed, and T and B lymphocytes were quantified using monoclonal antibodies.¹⁰ Delayed-type hypersensitivity was assessed with the Multitest CMI.¹¹ Immunoglobulin levels were measured by immunoprecipitin reaction.¹²

Most serum chemistry assays¹³ were performed on an autoanalyzer (Kodak Ektachem 700). Serum samples also were tested for various hormones and for markers of hepatitis B infection using commercial radioimmunoassays.¹⁴ A 12-hour overnight collection of urine was tested for levels of creatinine, D-glucuronic acid, and porphyrin. Porphyrin levels, measured by high-performance liquid chromatography,¹⁵ were classified by chronic hepatic porphyria pattern.¹⁶ Stool samples were tested for occult blood (Hemoccult, SmithKline Diagnostics, San Jose, Calif).

Early analyses of responses in the telephone interviews showed that Vietnam veterans were reporting more difficulty conceiving children²; therefore, analysis of semen samples was added to the examination for the last five months of the study. Of 705 veterans without vasectomy who were examined during this period, 571 participated (81%).¹ Participation rates were the same in the two cohorts. The Coilsoft system (Cryo Resources, New York),¹⁶ which employs computer analysis of digitized video images of sperm heads, was used to measure sperm concentration, movement characteristics, and shapes and dimensions of sperm heads. Morphology of sperm heads was classified according to World Health Organization criteria.¹⁶

Case Definitions

Chloracnelike lesions were defined as (1) comedones in a malar crescent or periauricular distribution, with nasal sparing, or (2) postinflammatory scars in chloracne-prone locations with a history of chloracne. Altered peripheral

Table 1.—Current Health Status and Postdischarge History of Selected Health Problems Reported During the Telephone Interview Among Vietnam and Non-Vietnam Veterans

Health Problems	Veterans, %					
	Interviewed			Examined		
	Vietnam (N=7924)	Non-Vietnam (N=7364)	Odds Ratio*	Vietnam (N=2490)	Non-Vietnam (N=1972)	Odds Ratio†
Current health status						
Perceived health status is "fair" or "poor"	19.6	11.1	1.8†	20.3	11.5	1.9†
Limitations in activities	28.6	21.5	1.3†	26.9	24.1	1.1
Prescribed medication use	19.1	16.0	1.1†	19.5	18.0	1.1
Somatic symptoms‡	9.6	5.7	1.7†	10.2	6.4	1.7†
Postdischarge health history						
Hospitalized	50.7	46.7	1.1†	51.8	49.5	1.0
Hypertension	25.4	20.3	1.3†	25.0	20.5	1.2†
Cancer	1.4	1.4	1.0	1.9	1.3	1.4
Benign growth	18.0	17.1	1.2†	20.1	18.5	1.1
Diabetes	1.9	1.4	1.2	1.7	1.5	1.1
Chloracne	1.4	0.3	3.9†	1.9	0.3	7.3†
Other skin conditions	31.2	19.7	1.9†	33.0	21.8	1.7†
Gastrointestinal tract ulcers	12.5	9.8	1.2†	12.6	10.2	1.1
Hepatitis	4.8	3.3	1.5†	4.8	4.0	1.3
Cirrhosis	0.7	0.5	1.3	0.7	0.6	1.1
Other liver conditions	2.7	1.8	1.4†	3.8	2.1	1.7†
Urinary tract problems	15.7	13.7	1.2†	16.8	15.2	1.1
Fertility difficulties§	20.0	15.6	1.3†	21.0	14.5	1.5†

*Odds ratio adjusted for the six entry characteristics. †95% confidence interval excludes 1.0.

‡Includes problems such as nervousness, fatigue, gastrointestinal tract ailments, dizziness, and headaches. §Tried to conceive a child over a period of a year or more without success.

arterial hemodynamic findings were defined as the presence of a femoral bruit, an absent posterior tibial pulse waveform (using a Doppler probe), or a resting brachial/ankle blood pressure ratio less than 1. Pulmonary function values of "never-smokers" without lung disease from the two combined cohorts were used to develop prediction equations of expected values based on race, age, and height.¹⁴ For all neuropsychological tests, scores were standardized (mean, 0; SD=1) to the two cohorts combined. For the current general technical test scores, the expected value of a standardized score was -1 or above. To adjust for effects of general ability, in other neuropsychological tests if the veteran's standardized general technical test score minus his standardized test score was greater than 1, the test score was lower than expected.¹⁴

Statistical Methods

The primary purpose of the analysis was to estimate the association between service in Vietnam and specific health conditions and measures. Dichotomous outcomes were analyzed by logistic regression¹⁵ to compute odds ratios (ORs) and 95% confidence intervals (CI). As a general approximation, if a 95% CI excludes 1.0, the OR estimate can be considered statistically significant (ie, $P < .05$). These analyses included the following six primary covariates, based on characteristics of the participants at entry into the US

Army: age at enlistment, race, year of enlistment, enlistment status (volunteer vs draftee), score on general technical test, and primary military occupational specialty. In certain analyses, additional covariates (eg, smoking status and alcohol use) also were included. In general, ORs changed little after these other covariates were added. Therefore, results presented herein are adjusted only for primary covariates, unless otherwise noted. When final models included significant interaction terms, ORs were standardized to the distribution of the interaction variable in both cohorts combined.^{15,20}

Similar analyses were conducted for continuously distributed measures by using multiple linear regression.²¹ Test results that were logarithmically normally distributed were transformed before analysis. Unadjusted means are presented in the tables for all measures. Differences that are statistically significant ($P < .05$) after adjustment for characteristics at entry into the army are noted in the tables.

RESULTS

Participant Characteristics

As described elsewhere,⁴ demographic and current socioeconomic characteristics of both groups were similar among both the telephone interview participants and the subsample of veterans who participated in the medical examinations. Among examinees, 46% of Vietnam and 43% of non-Vietnam

veterans were current smokers and 13% and 11%, respectively, reported heavy alcohol use (≥ 90 drinks per month).

Telephone Interview

Although more than 80% of all veterans rated their current health status as "good" or "excellent," Vietnam veterans were almost twice as likely (19.6% vs 11.1%) to assess their health as "poor" or "fair" (Table 1). Most medical conditions were reported significantly more often by Vietnam veterans, including current limitations in activities, use of prescribed medications, various somatic symptoms, and having been hospitalized since discharge from active duty. When asked about the past occurrence of certain physician-diagnosed conditions, Vietnam veterans reported each condition more frequently than did other veterans, except for cancer (all sites combined). Odds ratios were greatest for chloracne and other types of skin conditions. Within each cohort, the prevalence of reported medical problems among those examined was similar to the prevalence in the total telephone interview group (Table 1). Odds ratios based on examination results were similar to those based on results of the telephone interview.

Medical Examinations

Among examination participants, dermatologic findings were similar in the two cohorts (Table 2). Chloracnelike skin lesions, hyperpigmentation, hirsutism, and skin cancer were rarely noted in either group. Infection-related conditions and postinflammatory scars were similarly prevalent in both cohorts of veterans.

About one third of Vietnam and non-Vietnam veterans were hypertensive (Table 3) and about 5% of veterans in each group reported current use of anti-hypertensive medication. Overall, the prevalence of any abnormal electrocardiographic finding was similar in the two groups. The largest relative difference was for left ventricular hypertrophy, although the 95% CI included 1.0. Altered peripheral arterial hemodynamic findings also were rare and were found at a similar prevalence among veterans in the two groups.

The proportion of veterans with abnormal findings on chest films was comparable in the two groups (Table 3). Calcified nodules were the most common specific pulmonary finding in each group. The proportions of veterans with diminished pulmonary function were the same in each group, and the ORs were unchanged after adjustment for current smoking status.

Few veterans in either cohort had any

evidence of peripheral neuropathy (Table 4). The largest relative difference between groups was for those veterans who had primarily subjective criteria (*symptoms*) of neuropathy (OR = 1.5), but the lower bound of the 95% CI included 1.0.

Vietnam veterans were 40% more likely to have high-frequency hearing loss than were non-Vietnam veterans (Table 4). Differences between the two groups in bilateral hearing loss were greatest among men with tactical military occupational specialties (infantrymen, armored vehicle crewmen, combat engineers, and artillery crewmen), for whom the OR (adjusted for preservice auditory acuity) was 2.5 (95% CI, 1.5 to 4.0); for men with nontactical specialties, it was 1.2 (95% CI, 0.9 to 1.6).

The current mean general technical test scores were significantly lower for the Vietnam veterans (Table 5), a finding that is consistent with differences noted at entry into the army. Adjustment for the six entry characteristics, including induction general technical test score, decreased this difference. The increase in general technical test scores since entry into service was similar for Vietnam and non-Vietnam veterans. There were small but statistically significant differences between cohorts in mean scores for three subtests—the RO Complex Figure Copy, the WAIS-R Block Design, and the Wisconsin Card Sorting Test (average number of cards per sort), but the proportions of veterans with test scores below expected values were similar in both groups. For other tests, there was little difference between cohorts after adjustment for the six entry characteristics.

Mean values of the results of immune function tests did not differ significantly between cohorts (Table 6). The proportions in each cohort with values above or below the reference range for all test measurements were similar; all ORs were less than 1.5 and their 95% CIs included 1.0. The percentages of participants who were anergic, defined as a less than 2-mm response to all seven recall antigens in the CMI test, were 3.5% for Vietnam and 3.9% for non-Vietnam veterans (OR = 1.0).

Results of most other laboratory tests were similar between cohorts (Table 7). For γ -glutamyl transferase, there were small but statistically significant differences in geometric means. After results were adjusted for current smoking status, alcohol use, illicit drug use, and body mass, these cohort differences virtually disappeared.

Total urinary porphyrin levels were practically the same in the two cohorts. One Vietnam veteran had a pattern of urinary porphyrin levels that was con-

Table 2.—Prevalence of Selected Skin Conditions Noted During Dermatologic Examination

Condition	Veterans, %		Odds Ratio*	95% Confidence Interval
	Vietnam (N = 2490)	Non-Vietnam (N = 1972)		
Chloroacne lesions	0.9	0.8	1.4	0.7-2.9
Acneiform lesions				
Comedones only	4.3	4.6	0.9	0.7-1.2
Any acne	15.6	16.8	0.9	0.8-1.1
Hyperpigmentation	4.0	3.2	1.2	0.9-1.7
Hirsutism	0.2	0.3		
Skin cancer	0.6	0.7	0.8	0.4-1.7
Infections				
Folliculitis	21.0	21.8	0.9	0.8-1.1
Tinea	37.6	38.0	1.0	0.8-1.1
Any infection	59.1	59.3	1.0	0.8-1.1
Postinflammatory scars	17.8	18.0	1.0	0.9-1.2

*Odds ratio adjusted for the six entry characteristics.

Table 3.—Prevalence of Cardiorespiratory Conditions Among Examination Participants

Condition	Veterans, %		Odds Ratio*	95% Confidence Interval
	Vietnam (N = 2490)	Non-Vietnam (N = 1972)		
Hypertension†	33.5	31.4	1.1	0.9-1.2
Altered peripheral arterial hemodynamic findings‡	4.7	3.6	1.2	0.9-1.7
Electrocardiographic findings				
Ischemia§	1.9	1.8	1.1	0.7-1.7
Left ventricular hypertrophy	1.6	1.0	1.8	1.0-3.3
Any finding	14.3	13.9	1.1	0.9-1.3
Chest roentgenogram findings				
Pulmonary	18.0	14.1	1.1	1.0-1.4
Cardiac	1.0	0.9	1.3	0.7-2.5
Any finding	22.4	20.6	1.1	1.0-1.3
Pulmonary function parameters¶				
FEV ₁ , <80% of predicted	10.2	10.9	0.9	0.7-1.1
FVC, <80% of predicted	7.1	6.8	1.0	0.9-1.3
FEV ₁ /FVC%, <70%	6.1	6.1	1.0	0.8-1.3

*Odds ratio adjusted for the six entry characteristics.

†Systolic blood pressure greater than or equal to 140 mm Hg, diastolic blood pressure greater than or equal to 90 mm Hg, or current use of antihypertensive medications.

‡Resting index (brachial/ankle blood pressure) of less than 1.0, an absent posterior tibial pulse waveform, or a femoral bruit.

§Electrocardiographic changes of ischemia or infarction.

||Includes bradycardia, tachycardia, extrasystoles, nonspecific ST- and T-wave changes, and others.

¶FEV₁ indicates forced expiratory volume in 1 s; and FVC, forced vital capacity.

sistent with porphyria cutanea tarda. Nine other veterans, five Vietnam and four non-Vietnam, had porphyrin level patterns that were consistent with chronic hepatic porphyria.

With few exceptions, test results for endocrine function were similar in the two cohorts. A 1% higher mean serum glucose level in Vietnam veterans persisted after results were adjusted for entry characteristics and other covariates (current smoking status, alcohol use, body mass index, and medication use), but the proportions with values above 140 mg/dL were the same in both cohorts. After adjustment for entry characteristics, Vietnam veterans had about a 4% higher mean thyroid-stimulating hormone (TSH) level, a statistically significant difference. In addition, Vietnam veterans were twice as likely to have a TSH value above 10 mU/L (>10 μ U/mL). When hypothyroidism was defined either as a TSH of greater

than 10 mU/L (>10 μ U/mL) or as self-reported use of thyroid replacement medication, the OR was 1.3 (95% CI, 0.7 to 2.4).

The Vietnam and non-Vietnam veterans differed regarding two additional examination items, stool occult blood and hepatitis B serology. Occult blood was found in the stool samples of more Vietnam (1.3%) than non-Vietnam (0.5%) veterans (OR = 2.8; 95% CI, 1.3 to 6.0). Tests for few Vietnam (0.5%) and non-Vietnam (0.9%) veterans were positive for hepatitis B surface antigen (OR = 0.6). However, the prevalence of past hepatitis B infection (defined as having antibody to either surface or core antigens while being negative for hepatitis B surface antigen) was higher among Vietnam veterans (14.1%) than among non-Vietnam veterans (11.1%) (OR = 1.4; 95% CI, 1.1 to 1.6).

The 571 men who participated in semen sample analysis had demograph-

Table 4.—Prevalence of Neurological Conditions Among Examination Participants

Condition	Veterans, %		Odds Ratio ^a	95% Confidence Interval
	Vietnam (N=2490)	Non-Vietnam (N=1972)		
Peripheral neuropathy				
Symptoms only†	3.0	1.9	1.5	1.0-2.2
Signs only‡	8.2	8.5	1.2	1.0-1.6
Symptoms and signs	1.0	0.6	1.2	0.6-2.3
High-frequency hearing loss§				
Right ear	14.4	9.9	1.4	1.2-1.7
Left ear	18.4	12.9	1.4	1.2-1.6
Both ears	9.4	6.2	1.4	1.1-1.8

^aOdds ratio adjusted for the six entry characteristics.

†Numbness, tingling, burning sensation, or weakness of arms or legs.

‡Findings from neurological physical examination or out-of-reference-range values for nerve conduction velocity or amplitude tests or vibration and thermal thresholds.

§Average hearing threshold greater than or equal to 51 dB at three combined frequencies: 3000, 4000, and 6000 Hz.

Table 5.—Selected Results of Neuropsychological Tests

Measure ^a	Arithmetic Mean		% Below Expected Value			
	Vietnam Veterans (N=2490)	Non-Vietnam Veterans (N=1972)	Vietnam Veterans	Non-Vietnam Veterans	Odds Ratio†	95% Confidence Interval
ACB general technical test score at examination	109.4	111.9‡	17.4	15.8	1.1	0.9-1.3
CVLT, total correct						
Trials 1-5	45.7	47.0	17.2	16.4	1.1	1.0-1.4
Short-delay free recall	9.5	9.7	18.7	19.0	1.1	0.9-1.3
Long-delay free recall	9.7	10.1	17.7	18.8	1.0	0.9-1.2
Grooved pegboard, s						
Dominant hand	73.7	73.0	24.1	21.9	1.0	0.9-1.2
Nondominant hand	76.2	77.0	23.7	21.0	1.0	0.9-1.2
PASAT, total correct in trial 1	38.8	39.1	12.0	12.9	0.9	0.8-1.1
RO complex figure						
Copy	32.8	32.9‡	14.6	15.1	1.0	0.8-1.2
Short-delay recall	19.9	20.4	17.4	18.0	1.0	0.9-1.2
Long-delay recall	20.1	20.5	18.9	17.6	1.0	0.9-1.2
WAIS-R						
Information subtest	9.0	10.3	8.0	7.2	1.1	0.9-1.3
Block design subtest	10.4	10.7‡	14.8	15.8	0.9	0.8-1.1
Wisconsin Card Sorting Test, average No. of cards per sort	21.4	20.2‡	24.4	21.6	1.1	1.0-1.4
Word list generation, F, A, S total	34.7	35.7	16.8	18.3	1.0	0.8-1.2

^aACB indicates Army Classification Battery; CVLT, California Verbal Learning Test; PASAT, Paired Auditory Serial Addition Test; RO, Rey-Osterrieth Test; and WAIS-R, Wechsler Adult Intelligence Scale Revised.

†Odds ratio adjusted for the six entry characteristics.

‡P<.05 (after adjustment for the six entry characteristics).

ic and medical history characteristics that were nearly identical to those of all the veterans who took part in the medical examination,⁴ suggesting that these veterans were representative of the entire examination sample. Some differences were found in semen characteristics (Table 8), with Vietnam veterans having significantly lower mean sperm concentrations than non-Vietnam veterans and twice the proportion with values below the clinical reference value of 20 million cells per milliliter. Five Vietnam and three non-Vietnam veterans had sperm concentrations below 5 million cells per milliliter. The mean percentage of morphologically "normal" cells also was significantly lower in the Vietnam group than in the non-Vietnam group (57.9% vs 60.8%). This difference was reflected in a higher prevalence of men with low levels (<40%) of morphologically normal cells

among the Vietnam veterans (OR = 1.6), although the 95% CI of the OR included 1.0. These differences persisted, even after adjustment for the six entry characteristics and six additional covariates (current smoking status, alcohol use, illicit drug use, medication use, time since previous ejaculation, and time between sample collection and video recording). Measurements of sperm head dimensions indicated that the Vietnam veterans' lower proportion of normal cells was due to their having larger and more tapered sperm heads. The percentage of motile cells was similar in the two cohorts, as were other measures of sperm movement characteristics, such as velocity, lateral head motion, and linearity of motion.

Several hundred other conditions were evaluated during the examinations, particularly during the dermatologic, neurological, and general physical

examinations. For the most part, these conditions were found with similar frequency in the two cohorts.

COMMENT

Although most of the veterans who participated in this study considered their health to be good or excellent, Vietnam veterans tended not to perceive their current health status as being as good as that of non-Vietnam veterans. In the telephone interview, Vietnam veterans reported many health conditions and symptoms more frequently than did other veterans. In the medical examination, however, we found few cohort differences.

The discrepancy between the telephone interview findings and the results of the medical examinations has several possible explanations. One is that the conditions had resolved by the time of the examinations. Alternatively, Vietnam veterans may have reported more symptoms and past medical conditions because they experienced more stress than did non-Vietnam veterans. In the VES psychological evaluations, we found that a greater proportion of Vietnam veterans currently were anxious and depressed.^{1,22} Stress can produce anxiety, depression, and a variety of somatic symptoms.²³ The VES also has found that perceived exposure to herbicides (a perception that in itself may lead to additional stress) is associated both with psychological problems and with self-reported adverse health conditions,^{3,4,24} but is not associated with objective measures of exposure.²⁵

Among the few differences found between cohorts at examination, two of note were stool occult blood and left ventricular hypertrophy on electrocardiogram. The association between military service in Vietnam and these two health measures cannot be easily explained. Furthermore, the large number of tests we performed increased the probability of spurious associations. In any event, these two abnormalities were rare, affecting less than 2% of the veterans in either group, and, for both findings, the absolute difference between cohorts was less than 1%.

Two of the cohort differences can be explained on the basis of prior military experiences. Increased hearing loss in Vietnam veterans, particularly among those who had tactical military occupational specialties, is consistent with results of several studies of army troops that show that exposure to military noise results in irreversible hearing impairment.^{26,27} Similarly, the higher prevalence of past hepatitis B infection among Vietnam veterans may be

Table 6.—Results of Hematologic and Immune Tests

Variable	Mean*		% Below Reference Range†			% Above Reference Range†		
	Vietnam Veterans (N=2490)	Non-Vietnam Veterans (N=1972)	Vietnam Veterans	Non-Vietnam Veterans	Odds Ratio‡	Vietnam Veterans	Non-Vietnam Veterans	Odds Ratio‡
	Hemoglobin level, g/L (g/dL)	160 (16.2)	160 (16.1)	2.4	2.3	1.1	4.5	4.2
Total white blood cell count, × 10 ⁹ /L (/mm ³)	6.7 (6705)	6.5 (6548)	6.7	7.6	1.0	3.3	2.6	1.2
Total lymphocyte count, /mm ³	1973	1836	4.8	5.3	1.0	5.2	4.6	1.2
Lymphocyte subset populations								
B-cell count, /mm ³	240	230	4.4	4.2	1.1	5.2	4.1	1.2
T-cell count, /mm ³	1460	1460	4.8	5.1	1.0	5.2	4.7	1.1
T-cell subset populations								
T4, /mm ³	1020	990	4.5	5.0	1.0	5.5	3.9	1.4
T8, /mm ³	560	550	4.2	4.4	1.0	4.5	6.3	0.9
T4/T8 ratio	1.8	1.8	4.7	5.3	0.9	5.1	4.7	1.1
Serum immunoglobulin levels, g/L (mg/dL)								
IgG	10.78 (1078)	10.77 (1077)	5.0	5.0	1.0	4.8	5.1	1.0
IgM	1.21 (121)	1.21 (121)	4.7	4.7	1.0	4.6	5.1	0.9
IgA	2.07 (207)	2.03 (203)	4.4	5.6	0.8	5.0	4.8	1.0

*Means are arithmetic for hemoglobin level, total white blood cell count, and total lymphocyte count; all other means are geometric.

†Reference ranges were defined as values between the fifth and 95th percentiles for both cohorts combined, except for hemoglobin level (140 to 180 g/L [14 to 18 g/dL]).

‡Odds ratio adjusted for the six entry characteristics.

Table 7.—Results of Selected Laboratory Tests

Tests	Geometric Mean		% Out of Reference Range*			
	Vietnam Veterans (N=2490)	Non-Vietnam Veterans (N=1972)	Vietnam Veterans	Non-Vietnam Veterans	Odds Ratio†	95% Confidence Interval
Serum analyte levels						
Alanine aminotransferase, U/L	26.4	25.6	5.3	4.4	1.2	0.9-1.5
Aspartate aminotransferase, U/L	26.0	26.0	5.4	4.4	1.2	0.9-1.8
γ-Glutamyl transferase, U/L	43.2	41.1‡	5.5	4.4	1.3	1.0-1.8
Total bilirubin, μmol/L (mg/dL)	13.7 (0.8)	13.7 (0.8)	5.1	4.9	1.0	0.7-1.4
Triglycerides, mmol/L (mg/dL)	1.06 (94.1)	1.05 (92.6)	4.7	5.3	0.9	0.7-1.2
Total cholesterol, mmol/L (mg/dL)	5.43 (209.8)	5.36 (207.2)	5.1	4.7	1.1	0.8-1.5
HDL cholesterol, mmol/L (mg/dL)	1.11 (42.6)	1.12 (43.3)	5.3	4.3	1.2	0.9-1.5
Fasting glucose, mmol/L (mg/dL)	5.2 (93.4)	5.1 (92.4)‡	0.8	0.6	1.0	0.4-2.2
Thyroid-stimulating hormone, mIU/L (μU/mL)	1.6 (1.6)	1.6 (1.6)‡	1.0	0.6	2.0	0.9-4.3
Free thyroxine index	2.2	2.2	5.4	4.6	1.2	0.9-1.5
Testosterone, nmol/L (ng/mL)	22.1 (8.37)	22.3 (8.44)	5.0	5.0	1.0	0.8-1.3
Follicle-stimulating hormone, IU/L (mIU/mL)	6.6 (6.6)	6.5 (6.5)	4.7	5.2	0.9	0.7-1.2
Luteinizing hormone, IU/L (mIU/mL)	13.3 (13.3)	13.1 (13.1)	5.2	5.2	1.0	0.8-1.3
Urine analyte levels						
o-glucuronid acid, mg/g of creatinine	10.6	10.2	5.1	4.9	1.0	0.8-1.4
Total porphyrin, μg/g of creatinine	43.0	42.2	5.2	4.5	1.2	0.8-1.8

*Reference ranges were defined as less than or equal to the 95th percentile for both cohorts combined, except for the following values: HDL cholesterol, free thyroxine index, testosterone, follicle-stimulating hormone, and luteinizing hormone, greater than or equal to the fifth percentile for the combined cohorts; fasting glucose, less than 7.8 mmol/L (<140 mg/dL); and thyroid-stimulating hormone, less than or equal to 10 mIU/L (>10 μU/mL).

†Odds ratio adjusted for the six entry characteristics.

‡P<.05 (after adjustment for the six entry characteristics).

related to service in a country where this viral infection is endemic.²⁹

The purpose of the VES was to evaluate health effects that may have resulted from the "general experience" of having served in Vietnam. In designing the telephone interview and the physical examinations, we used a broad approach but emphasized health conditions that have been suggested as being related to prior exposure to herbicides or dioxin.^{30,31} On examination, we found no differences between cohorts in these health effects, such as skin conditions, peripheral neuropathy, hepatic dysfunction, porphyria, lipid abnormalities, and impaired immune function.

The observed similarity between cohorts regarding herbicide or dioxin-

related conditions has several possible explanations. Examinations were performed 15 to 20 years after the veterans had been in the army, and most of the conditions of interest may have resolved in that time. Alternatively, the two groups may not differ in such conditions at present because few of the study participants were heavily exposed to dioxin-containing herbicides. An objective measure of herbicide exposure, such as a serum dioxin level, was not available at the time of the VES.³² However, in a recent study of enlisted Vietnam veterans, we found that few US Army ground troops had been heavily exposed to dioxin-containing herbicides.³³

Although we found no overall in-

crease in cancers reported by Vietnam veterans, the VES was not designed to assess adequately the risk of rare cancers. The Centers for Disease Control is conducting a separate study³⁴ designed to evaluate Vietnam veterans' risks for six specific cancers that have been suggested as being associated with herbicide or dioxin exposure.

Among the subsample of 571 men whose semen characteristics were evaluated, Vietnam veterans were found to have lower sperm concentrations and a significantly lower average proportion of "normal" sperm heads. Low sperm concentrations, low levels of morphologically normal sperm, and low percentages of motile sperm have traditionally been used as indicators of

Table 8.—Selected Results of Semen Sample Analysis

Sperm Characteristic	Mean*		% Below Reference Range†			
	Vietnam Veterans (N=324)	Non-Vietnam Veterans (N=247)	Vietnam Veterans	Non-Vietnam Veterans	Odds Ratio‡	95% Confidence Interval
Concentration	64.6§	79.0§	15.9	8.1	2.3	1.2-4.3
Motile cells, %	56.9	60.4	28.0	23.4	1.2	0.6-1.8
Morphologically "normal" cells, %	57.9	60.8	15.9	11.4	1.8	0.9-2.8

*The mean for sperm concentration is geometric; all other means are arithmetic.

†Reference ranges were defined as concentration, greater than 20 million cells per milliliter; proportion motile, greater than or equal to 40%; and proportion normal cells, greater than or equal to 40%.

‡Odds ratio adjusted for the six entry characteristics.

§Million cells per milliliter.

||P<.05 (after adjustment for the six entry characteristics).

reduced fertility potential.^{16,26-40} The Vietnam veterans were twice as likely to have low sperm concentrations (<20 million/mL) and about 1½ times more likely to have low levels (<40%) of normal sperm heads compared with the non-Vietnam group. Although this latter finding was not statistically significant, it is consistent with the statistically significant decrease in the mean proportion of normal sperm heads. The two cohorts had about the same proportion of men whose semen samples were judged to have low motile sperm counts (<40% motile cells).

Less clear are the implications of the observed differences in semen characteristics for pregnancy outcomes. No studies among humans have clearly shown that poor semen quality is related to adverse reproductive outcomes^{41,42} or birth defects. In the VES, although there were differences in sperm characteristics between Vietnam and non-Vietnam veterans, rates of most adverse pregnancy outcomes were similar.^{4,43} Specifically, among those who participated in semen sample analysis, the rates of birth defects (as determined by birth record information) were 5.9% for Vietnam and 5.7% for non-Vietnam veterans' children.

The fertility histories of those who had semen samples analyzed suggest that cohort differences in semen characteristics have not resulted in an increase in the number of men unable to father children.⁴ In each cohort, the average number of children fathered per veteran after assignment to primary tour of duty was similar (1.4 for Vietnam vs 1.5 for non-Vietnam veterans), as was the proportion who have not fathered any children (31% vs 25%). Among all VES participants, the fertility histories of Vietnam and non-Vietnam veterans were identical (average number of children, 1.6; proportion who fathered no children, 23%). These results are consistent with the results of a 20-year follow-up study⁴⁴ that found that lower sperm concentration correlated with the time interval to pregnancy but that pregnancy rates were not affected

unless the sperm concentration was below 5 million cells per milliliter.

We were not able to determine the reasons for the differences in sperm characteristics between Vietnam and non-Vietnam veterans. We evaluated several factors that are known or suspected to affect sperm characteristics, including race, age, reported history of sexually transmitted diseases, and current use of alcohol, marijuana, other drugs, cigarettes, and certain medications. None of these accounted for the differences in sperm characteristics. We also did not find that the more prevalent psychological disturbances experienced by Vietnam veterans, including anxiety, depression, and posttraumatic stress disorder, accounted for the differences in semen characteristics.

The differences in sperm characteristics between the Vietnam and non-Vietnam cohorts did not seem to be specific to a particular subgroup of veterans. There were no consistent variations in the findings of semen sample analysis in the two cohorts according to the army entry and service characteristics, including year of entry and military occupational specialty category. The findings also do not seem to be accounted for by reported use of heroin or other drugs while in the army. Level of combat experienced in Vietnam seems not to be related to findings from semen sample analysis, as there was no relationship between semen characteristics and military occupational specialty (tactical vs nontactical) or self-reported combat experiences. The possibility that exposure to dioxin-containing herbicides may have affected the sperm of Vietnam veterans is a potential concern. However, this explanation seems unlikely since in a recent study we found that few army ground troops were heavily exposed to dioxin-containing herbicides⁴⁵; also, in the VES there was no difference in semen characteristics according to different levels of self-reported herbicide exposure.

In this epidemiologic study, the possibility that biases in design or conduct may have affected the findings, includ-

ing those from semen sample analysis, needs to be considered. Some of the increased prevalence of self-reported conditions among Vietnam veterans could have been due either to their enhanced recall of these conditions compared with non-Vietnam veterans or to their different health care-seeking practices. Such biases, however, should have had little effect on the examination findings. The examiners and technicians did not know the participants' cohort status, nor were they allowed to take any "history" from the participants as they conducted the examinations.

Another concern is the possibility of selection or participation bias. Participation bias should have been minimal for the telephone interview component, since participation rates were high in that phase of the study. For the medical examinations, however, the participation rates were lower, and the Vietnam group had a higher participation rate than did the non-Vietnam group. Yet, detailed analyses of the factors that influenced participation showed that those examined were similar to those interviewed by telephone.⁴

The findings are also not likely to be explained on the basis of confounding by other factors. The two cohorts were similar on most important characteristics—eg, age, race, and certain personal habits—known to influence health. Further, additional analyses, adjusted for the effects of several important characteristics that influence health, did not change the study results.

In conclusion, most Vietnam veterans who participated in this study felt they were in good current health 15 to 20 years after service. However, Vietnam veterans more frequently reported current somatic symptoms and physician-diagnosed diseases than did non-Vietnam veterans. Most of these conditions were not currently detectable by the comprehensive physical and laboratory screening examinations used in this study. One physical difference that is still detectable is that Vietnam veterans, particularly those who served in tactical military occupational specialties, have greater hearing loss. Further, among the subsample of participants who had semen samples evaluated, there were certain differences in semen characteristics between Vietnam and non-Vietnam veterans. These included a decrease in the Vietnam veterans' sperm concentrations and a significant decrease in the average proportion of "normal" sperm cells. Despite these differences, Vietnam and non-Vietnam veterans have fathered similar numbers of children.

Use of trade names is for identification only and does not constitute endorsement by the Public

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