not statistically significant. Testicular cancer has not been associated with exposure to TCDD or phenoxyherbicides. Moreover, testicular cancer is the most frequent malignancy among white males 30-34 years old and the second most frequent malignancy (after melanoma) among those 35-39 years old (Schottenfeld and Warshauer, 1982).

At physical examination, more Vietnam than non-Vietnam veterans had neck masses or soft tissue masses of the extremities. For the most part, these masses consisted of lipomas, cysts, and other benign and clinically inconsequential conditions. In the dermatology examination (see Chapter 5), the proportion of veterans in each cohort with lipomas was the same, 2.3%, but a slightly higher proportion of Vietnam veterans had epidermal inclusion cysts (9.4% versus 7.2%).

With regard to the head, eyes, ears, nose, and throat, the two groups were similar for most conditions, but findings for the physical examination differed slightly. Corneal scarring, which was increased among the Vietnam veterans, could be a sequela of combat-related trauma. Arteriolar spasm, also more prevalent among the Vietnam veterans (0.7% versus 0.4%), is usually associated with systemic hypertension. As noted in Chapter 9, however, the prevalence of hypertension is nearly equal in the two cohorts.

In our examination of the musculoskeletal system, we found the two groups similar in most respects. One unexpected finding was that the same proportion of veterans, about 1%, in each cohort had missing extremities and that, for the most part, these missing extremities were fingers. We expected the Vietnam veterans, with their greater likelihood of exposure to combat, to have more residual effects of previous trauma, such as missing limbs, than non-Vietnam veterans. Differential participation does not account for this finding since, as we show in Chapter 3, similar proportions of Vietnam (4%) and non-Vietnam (3%) veterans cited health-related reasons for not participating in the medical examinations. One possible explanation is that the number of servicemen who lost limbs in Vietnam is not as high as it is generally thought to be. Of the nearly 200,000 men wounded in Vietnam between 1965-1970, less than 0.5% required amputations (usually for treatment of significant vascular injuries) (Neel, 1973). When this percentage is applied to the number of Vietnam veterans in our study cohort (about 8% of whom were wounded while in the service), it becomes apparent that few service-related amputations should be detected among the Vietnam veterans who were examined. Furthermore, since limb loss can occur in nonmilitary settings after discharge (for example, in motor vehicle collisions or work with power tools), this similarity between cohorts in the prevalence of missing extremities becomes understandable.

On the basis of our review of published scientific reports, we expected the prevalence of genitourinary conditions to be greater among Vietnam veterans than among non-Vietnam veterans. Although Vietnam veterans were more likely to report having had various genitourinary symptoms in the year before the examination, we found few differences between the two groups at examination. The findings from physical examination and laboratory tests were similar for the two cohorts.

On the other hand, published reports contained little evidence to suggest that the general Vietnam experience or exposure to TCDD or phenoxyherbicides would adversely affect the hematologic system. In turn, we found no difference between the Vietnam and non-Vietnam veterans in the results of the hematologic tests. Further, even though we found that more Vietnam veterans had occult blood in their stool (see Chapter 6), only a small (<3%), and similar, proportion of veterans in each group were anemic at the time of the examination.

In conclusion, we found few differences between Vietnam and non-Vietnam veterans in the medical conditions evaluated in this chapter. The issue of cancer risk, for those cancers suggested as being associated with exposure to TCDD or phenoxyherbicides, will be further addressed in CDC's forthcoming report on the Selected Cancers Study. Vietnam veterans were more likely to have corneal scars and retinal arteriolar spasm, but these abnormalities were detected in only a small number of participants, and the percentages of other abnormal examination items relating to the head, eyes, ears, nose, and throat were similar for the two groups. Results for the other organ systems described in this chapter—musculoskeletal, genitourinary, and hematologic—did not differ between cohorts.

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CHAPTER 13

Semen Analysis

13. SEMEN ANALYSIS

13.1 INTRODUCTION

Vietnam veterans have expressed concern about adverse reproductive effects, including impotence, loss of libido, infertility, birth defects, and neonatal death, resulting from military service in Vietnam and possible exposure to Agent Orange (Bogen, 1979). Of these potential effects, the two that have received the greatest attention are adverse pregnancy outcomes and birth defects (Donovan *et al.*, 1983; Erickson *et al.*, 1984; Lathrop *et al.*, 1984). Until now, the unresolved issues of the effects of military service in Vietnam or of exposure to dioxin-containing phenoxyherbicides such as Agent Orange on male fertility have not been adequately studied (Lamb and Moore, 1984; Mattison *et al.*, 1984; Schrag and Dixon, 1985).

When we prepared the protocol for the Vietnam Experience Study (VES) (Centers for Disease Control, 1983), we decided that we would evaluate the veterans' fertility on the basis of the fertility histories they reported. However, we retained the option to add semen analysis, a key component in the evaluation of male fertility (Albertsen *et al.*, 1983), should circumstances justify it. After the study began, a preliminary evaluation of histories obtained from the telephone interview showed that Vietnam veterans were reporting more difficulties in conceiving pregnancies than were non-Vietnam veterans. This finding suggested that a more detailed and objective assessment of reproductive function was warranted in the VES medical examinations. In addition, recent technological advances in automated semen analysis made it feasible to perform objective, well-standardized, and quantitative tests of semen quality on a large scale. Consequently, during the last 5 months of the study, semen analysis was included in the medical examinations. In this chapter we present the results of the semen analysis for the subsample of 571 veterans who participated in this component of the VES.

No reports have been published on studies in which investigators have evaluated the fertility status, including semen characteristics, of U.S. Army ground troops who served in Vietnam. Most reported evaluations of the effects of exposure to dioxin or dioxin-containing herbicides on fertility have involved animals rather than humans. In animals 2,3,7,8-tetrachlorodibenzo-para-dioxin (TCDD) has been shown to lower testosterone levels, decrease the weight of the testes, cause pathological changes in the structure of the testes, and adversely affect spermatogenesis (Moore *et al.*, 1985). In certain animal species, including monkeys and chickens, spermatogenesis has decreased when the animals were exposed to high semichronic doses of TCDD (*i.e.*, doses that have generally caused death or systemic toxicity) (Lamb and Moore, 1984). To assess the effects of nonlethal doses of TCDD on male reproduction and fertility, Lamb *et al.* (1981) studied mice that were exposed continuously for 8 weeks to low-to-moderate doses of TCDD in their diet. Despite evidence of chemical toxicity (decreased weight gain, thymic involution, and liver enlargement), the animals' mating frequency and number of fertile matings were not affected. Neither were sperm counts per milligram of epididymis, sperm motility, and sperm morphology.

No results of human studies have been reported that show reduced male fertility following exposure to TCDD. Evaluations of the reproductive effects of TCDD among humans, including semen analysis, are limited. Fabro (1984) cited an unpublished report of railroad workers who, after cleaning up a TCDD-contaminated spill, had a 40% average decrease in sperm count and decreased plasma testosterone levels compared with unexposed workers. However, the report did not include data on which we could base an assessment of these workers' reproductive history. In the U.S. Air Force Ranch Hand Study, Lathrop *et al.* (1984) evaluated reproductive function in a group of men potentially exposed to dioxin during Agent Orange spraying in Vietnam. These investigators found that the distributions of sperm concentration and of the percentages of abnormally shaped sperm were similar for the Ranch Hand and comparison groups. The group exposed to herbicide did not have more fertility problems, nor did the two groups differ in the mean number of conceptions per veteran or in the proportion of men with childless marriages.

The problem of overcoming the many technical difficulties inherent in performing semen analyses is another reason why few investigators have evaluated the semen characteristics of Vietnam veterans or of other groups potentially exposed to dioxin or phenoxyherbicides. The traditional manual techniques are time-consuming and difficult to standardize. In addition, since the technician must often use subjective judgment (*e.g.*, in grading the quality of sperm motility or categorizing the shape of sperm heads) in these analyses, the interobserver variability is usually large.

Recent technological advances have led to the development of automated systems that have overcome many of the limitations of the traditional manual methods. These systems can perform standardized analyses rapidly and objectively by using computer image analysis. They also make it possible to measure a number of parameters that are impractical or difficult to measure manually. Thus, in addition to measuring sperm concentration, these systems have refined the previously subjective assessments of sperm motility and morphology by objectively measuring several characteristics of sperm motion, head shape, and size. Because of these advantages, several major fertility clinics and researchers throughout the world now use automated systems for semen analysis.

In the VES, we used an automated semen analysis system in two ways: (1) to measure sperm concentration, percentage of motile sperm, velocity (speed), linearity of motion (trajectory), amplitude and frequency of lateral head displacement, and (2) to measure sperm head dimensions (morphometry) and categorize sperm head size and shape (morphology). In this presentation, we focus on three measures of sperm quality: concentration, percentage of motile sperm, and percentage of sperm cells with "normal" morphology. These measures have been used the longest clinically, and more is known about their relationship to fertility potential than is known about other measures (Alexander, 1982; Belsey *et al.*, 1980; Chong *et al.*, 1983). Major reductions in these measures (a concentration of $\leq$20 million sperm per milliliter of semen, a percentage of motile sperm $<$40%, and a percentage of morphologically normal cells of $<$40%) have traditionally been used as indicators of reduced fertility potential. Little is known about the relationship between fertility and the newer quantitative measures of sperm motility and morphometry.

In addition to semen analysis, other evaluations related to male fertility were performed as part of the medical examinations. These evaluations, described elsewhere in this volume, involved all medical examination participants. Reproductive hormone measurements are presented in Chapter 11. In summary, the distributions of serum values of testosterone, luteinizing hormone (LH), and follicle-stimulating hormone (FSH) were similar in the Vietnam and non-Vietnam cohorts. In Chapter 12, we presented measurements of testes and other findings from physical examinations, results of urinalyses, and reports of medical conditions associated with the genitourinary system. In brief, the prevalence of missing or small testes was similar among Vietnam and non-Vietnam veterans, as were the other results of the physical examination and laboratory testing. Findings on reproductive outcomes, such as spontaneous abortions, stillbirths, and birth defects, are presented in Volume V (Reproductive Outcomes and Child Health) of the monograph. According to information on hospital birth records, Vietnam veterans were not at increased risk for fathering children with birth defects.

13.2 METHODS

13.2.1 Sample Design and Participation Rates

The sample design and participant selection procedures for the VES are described in Chapter 2. On May 18, 1986, after an initial pilot test, the semen analysis component of this study was put into full-scale operation, and during the rest of the study (through September 30, 1986), it was offered to all study participants examined. Study participants were given $50 as compensation for providing a semen specimen. Veterans who had vasectomies were given the opportunity to have their semen evaluated for the presence of sperm, but they were excluded from the statistical analyses. Excluding veterans with vasectomies, 705 study participants (399 Vietnam and 306 non-Vietnam veterans) were eligible for semen analysis. Of these, 81% in each cohort (324 Vietnam and 247 non-Vietnam veterans) provided a semen specimen.

Participation rates by cohort status and selected characteristics are shown in Table 13.1. In general, participation rates within selected military and sociodemographic strata were similar for Vietnam and non-Vietnam veterans. Relative to non-Vietnam veterans in the same strata, however, participation was increased for Vietnam veterans who were black, younger (30-34 years old at examination), less-educated (had completed <12 years of school), or nonsmokers. In each cohort, participation rates were higher for whites than for nonwhites. Participation was similar between cohorts for strata defined by reported psychological counseling, selected genitourinary conditions, gonorrhea, and reproductive history items. The veterans' reported fertility histories, in terms of number of live births conceived, had little influence on participation rates for either cohort. A history of difficulties conceiving a pregnancy or having a physician-diagnosed infertility condition, however, were associated with increased participation rates among non-Vietnam veterans, but not among Vietnam veterans. Few veterans in either cohort had a history of varicocele, epididymitis, or impotence.

In each cohort, the modest influence of most demographic, military service, medical history, and lifestyle characteristics on semen analysis participation rates is reflected in the similar distributions of these characteristics among those whose semen was analyzed compared with all those who had medical examinations (Table 13.2). The distribution of participants was similar for strata defined by selected military history items, sociodemographic factors, reported psychological counseling, genitourinary conditions, gonorrhea, and reproductive history items. The higher proportion of veterans in the semen analysis subsample who did not father any live births (compared with the proportion among all veterans who had medical examinations) can be attributed to our excluding study participants with vasectomies from the semen analysis subsample. In each cohort, the proportion of men who reported either problems conceiving pregnancies or physician-diagnosed infertility conditions was similar between semen analysis participants and all medical examination participants. In general, these similarities suggest that those who underwent semen analysis are representative of the larger group of veterans who had medical examinations.

13.2.2 Laboratory Methods

Standardized protocols were followed for the collection and processing of semen samples. After voluntarily abstaining for at least 48 hours from any sexual activity that involved ejaculation, each participant collected a semen specimen in his hotel room by masturbating (without using lubricants or condoms) into a plastic container. The participant

Table 13.1 Semen Analysis Participation Rates Among Vietnam and Non-Vietnam Veterans, by Selected Characteristics

	Vietnam		Non-Vietnam	
Characteristic	**Rate (%)[a]**	**No.[b]**	**Rate (%)[a]**	**No.[b]**
Total Sample	81	324	81	247
Age at Entry (Years)				
16-19	80	164	80	106
20-33	82	160	81	141
Type of Enlistment				
Drafted	82	215	81	166
Volunteered	80	109	80	81
Primary MOS				
Tactical	85	120	75	54
Other	79	204	82	193
Race				
White	84	262	83	200
Black	74	45	69	29
Other	65	17	75	18
Year of Entry				
1965-66	76	106	77	36
1967-69	83	184	83	187
1970-71	89	34	83	24
Enlistment GT Score				
40-89	76	69	81	58
90-109	83	118	77	64
110-129	85	97	78	84
130-160	76	32	95	38
Age at Examination (Years)				
30-34	93	14	78	25
35-39	82	217	84	150
≥40	79	93	75	72
Current Smoking Status				
Nonsmoker	86	85	78	64
Ex-smoker	79	89	82	71
Current smoker	80	150	82	112
Illicit Drug Use (Past Year)				
None	81	257	81	188
Marijuana only	84	36	81	35
Other	79	31	80	24
Alcohol Consumption (Avg. Drinks/Mo.)				
≤29	80	202	79	153
30-89	88	84	85	74
≥90	74	37	79	19
Marital Status				
Never married	80	33	77	20
Ever married	81	291	81	227
Education (Years)				
1-11	77	43	64	16
12-15	82	216	83	180
≥16	81	65	78	50

Table 13.1 Semen Analysis Participation Rates Among Vietnam and Non-Vietnam Veterans, by Selected Characteristics — Continued

	Vietnam		Non-Vietnam	
Characteristic	Rate (%)[a]	No.[b]	Rate (%)[a]	No.[b]
Income (Dollars)				
≤20,000	79	89	76	68
20,001-40,000	83	161	84	122
>40,000	83	65	79	50
No. Hospitalizations in Army				
0	82	178	80	164
1	80	93	80	59
≥2	83	52	85	23
Psychological Counseling				
None	82	292	82	226
Health professional	81	25	68	17
Other	64	7	100	4
Urinary Tract Infection				
No	81	282	79	212
Yes	85	39	94	33
Prostatitis				
No	81	307	81	226
Yes	89	16	75	21
Varicocele				
No	81	319	81	245
Yes	100	3	50	2
Epididymitis				
No	81	320	81	244
Yes	80	4	100	3
Gonorrhea				
No	82	267	82	217
Yes	76	54	73	30
Total Number of Live Births Conceived After Assignment to Primary Tour of Duty				
0	82	101	81	61
1	86	78	82	62
2	78	85	81	73
≥3	80	60	78	50
Infertility Condition Diagnosed by a Doctor				
No	82	306	80	241
Yes	78	18	100	5
Failure to Conceive With 1 Partner, ≥1 Year				
No	82	262	79	211
Yes	78	62	92	35
Difficulty Getting a Satisfactory Erection				
No	82	319	81	242
Yes	50	5	71	5
Difficulty Getting a Satisfactory Ejaculation				
No	82	321	81	243
Yes	25	2	67	4

[a] Percentage of eligible veterans who underwent semen analysis.

[b] Number of veterans with a particular characteristic who participated in the semen analysis. Numbers may not sum to the total sample size because of missing values.

Table 13.2 Comparison of Selected Characteristics of All Medical Examination Participants With Those of Veterans Undergoing Semen Analysis, by Cohort

	Vietnam				Non-Vietnam			
	All Med Exam		Semen Analysis		All Med Exam		Semen Analysis	
	Participants (N=2490)		Participants (N=324)		Participants (N=1972)		Participants (N=247)	
Characteristic	%	No.[a]	%	No.[a]	%	No.[a]	%	No.[a]
Age at Entry (Years)								
16-19	52	1301	51	164	45	896	43	106
20-33	48	1189	49	160	55	1076	57	141
Type of Enlistment								
Drafted	62	1537	66	215	65	1280	67	166
Volunteered	38	953	34	109	35	692	33	81
Primary MOS								
Tactical	34	847	37	120	25	499	22	54
Other	66	1643	63	204	75	1473	78	193
Race								
White	82	2054	81	262	81	1600	81	200
Black	11	286	14	45	12	239	12	29
Other	6	150	5	17	7	133	7	18
Year of Entry								
1965-66	33	830	33	106	37	726	35	86
1967-69	56	1399	57	184	38	744	35	87
1970-71	10	261	10	34	25	502	30	74
Enlistment GT Score								
40-89	24	578	22	69	21	419	24	58
90-109	33	806	37	118	29	565	26	64
110-129	33	807	31	97	34	675	34	84
130-160	11	257	10	32	15	301	16	38
Age at Examination (Years)								
30-34	6	161	4	14	13	259	10	25
35-39	72	1803	67	217	59	1171	61	150
≥40	21	526	29	93	27	542	29	72
Current Smoking Status								
Nonsmoker	25	619	26	85	28	543	26	64
Ex-smoker	29	715	27	89	29	577	29	71
Current smoker	46	1156	46	150	43	852	45	112
Illicit Drug Use (Past Year)								
None	74	1843	79	257	73	1438	76	188
Marijuana only	14	351	11	36	16	324	14	35
Other	12	292	10	31	11	207	10	24
Alcohol Consumption (Avg. Drinks/Mo.)								
≤29	61	1516	63	202	63	1235	62	153
30-89	26	634	26	84	26	514	30	74
≥90	13	328	11	37	11	207	8	19
Marital Status								
Never married	9	215	10	33	9	168	8	20
Ever married	91	2275	90	291	91	1804	92	227
Education (Years)								
0-11	14	341	13	43	10	199	7	16
12-15	67	1679	67	216	65	1279	73	180
≥16	19	470	20	65	25	492	20	50
Age at Entry (Years)								
Income (Dollars)								
≤20,000	29	704	28	89	28	540	28	63
20,001-40,000	51	1236	51	161	49	950	51	122
>40,000	21	502	21	65	23	444	21	50

Table 13.2 Comparison of Selected Characteristics of All Medical Examination Participants With Those of Veterans Undergoing Semen Analysis, by Cohort — Continued

	Vietnam				Non-Vietnam			
	All Med Exam Participants (N=2490)		Semen Analysis Participants (N=324)		All Med Exam Participants (N=1972)		Semen Analysis Participants (N=247)	
Characteristic	%	No.[a]	%	No.[a]	%	No.[a]	%	No.[a]
No. Hospitalizations in Army								
0	55	1362	55	178	66	1302	67	164
1	29	710	29	93	25	497	24	59
≥2	16	403	16	52	9	168	9	23
Psychological Counseling								
None	87	2155	90	292	90	1777	92	226
Health professional	10	248	8	25	8	153	7	17
Other	3	85	2	7	2	40	2	4
Urinary Tract Infection								
No	87	2166	88	282	88	1727	87	212
Yes	13	311	12	39	12	235	13	33
Prostatitis								
No	94	2342	95	307	93	1841	92	226
Yes	6	142	5	16	7	129	9	21
Varicocele								
No	99	2454	99	319	98	1937	99	245
Yes	1	29	1	3	2	33	1	2
Epididymitis								
No	99	2457	99	320	99	1949	99	244
Yes	1	28	1	4	1	22	1	3
Gonorrhea								
No	83	2053	83	267	87	1710	88	217
Yes	17	431	17	54	13	262	12	30
Total Number of Live Births Conceived After Assignment to Primary Tour of Duty								
0	24	595	31	101	22	432	25	61
1	22	544	24	78	23	457	25	62
2	33	824	26	85	33	642	30	73
≥3	21	524	19	60	22	437	20	50
Infertility Condition Diagnosed by a Doctor								
No	95	2352	94	306	96	1897	98	241
Yes	5	135	6	18	4	71	2	5
Failure to Conceive With 1 Partner, ≥1 Year								
No	78	1940	81	262	84	1657	86	211
Yes	22	544	19	62	16	309	14	35
Difficulty Getting a Satisfactory Erection								
No	97	2404	98	319	98	1931	98	242
Yes	3	84	2	5	2	41	2	5
Difficulty Getting a Satisfactory Ejaculation								
No	98	2437	99	321	99	1946	98	243
Yes	2	49	1	2	1	26	2	4

[a] Numbers may not sum to the total sample size because of missing values.

then placed the container in an insulated cup and, within 30 minutes of the collection, delivered the cup to a sample processing room located in the hotel. To allow time for the samples to liquify, technicians stored them in an incubator at 30 °C. All samples were video recorded within 2 hours and 20 minutes after they were collected. For video recording, 5 microliters of the specimen was added to a Makler chamber and placed on a microscope viewing stage that had been warmed to 37 °C. Then, 30-second recordings were made of 8 different fields from preassigned areas of the chamber.

Semen analysis was performed with the Cellsoft computer-assisted semen analyzer system (Ast *et al.*, 1986). This system has two major software components, a motility module and a morphology module. For the motility analysis, the videotaped images were analyzed by using a personal computer with specialized hardware installed for the processing of digitized images. Data were recorded for sperm concentration and movement characteristics (percentage of motile sperm cells, linear velocity, straight-line velocity, linearity of motion or trajectory, amplitude of lateral head displacement, and beat/cross frequency). The lateral head displacement and beat/cross frequency are measures of the magnitude and frequency of lateral sperm head movement, respectively. On the basis of their size, luminosity and motion characteristics, mature sperm cells were distinguished from immature sperm cells and other cells occasionally found in semen, such as leukocytes, lymphocytes, and epithelial cells.

For morphology and morphometry analysis, a drop of semen was placed onto a microslide, fixed in 95% ethanol, and stained with Papanicolaou (Pap) stain. The microslide was placed under a microscope, and each sperm head image was individually computer-analyzed for quantitative measurements and for classification of sperm head shape. Before the study began, an expert in andrology set the Cellsoft morphology analysis parameters on the single instrument used for semen analysis. These parameters, which remained the same throughout the study, were used to identify and classify individual sperm cells into morphologic cell types. This classification was based on quantitative (morphometric) measurements of sperm head area, perimeter, length/width ratio, and major axis length. The five morphologic cell categories, based on World Health Organization criteria (Belsey *et al.*, 1980), were normal, large, small, tapered, and amorphous. Amorphous types included sperm with cytoplasmic droplets, abnormally shaped single heads, or double heads. This computer system could not analyze immature sperm, or sperm with midpiece or tail abnormalities, so these types of sperm were not analyzed morphologically. Additional details on semen specimen collection and processing are in Supplement A (Laboratory Methods and Quality Control) of the monograph.

Some of the 571 participant specimens could not be analyzed for all of the semen characteristics. Three of the veterans' specimens contained no sperm. Several samples were lost because of technical difficulties during the processing procedures. Thus, microslide preparations from 566 specimens were analyzed for sperm morphology and morphometry, and 546 samples were video recorded for sperm concentration and motility analysis.

A majority of specimens were inadvertently videotaped at a higher magnification (X 1.5 versus X 1.0 for the ocular lens setting) than the computer software manufacturer recommended. This fact was noted during a software update on August 7, 1986. Subsequently, samples were videotaped at the recommended magnification of X 1.0. As a result, the parameter settings for motility measurements were adjusted to account for differences in magnification. The settings used to analyze videotapes made at the two microscope magnifications are shown in Table 13.3.

We implemented several quality control procedures to ensure that all technicians used similar analytical methods throughout the study. For quality control of concentration and motility measurements, three videotapes (recorded at the X 1.0-ocular lens setting) were made of specimens with high, medium, and low-normal concentrations of sperm, respectively. These tapes were played at the beginning of each analytical run. Before the participants' specimens could be analyzed, the results from all three quality control tapes had to be within predetermined acceptable performance limits for sperm concentration, percentage of motile sperm, and mean linear velocity. For quality control of morphologic and morphometric measurements, a set of 20 microslides, prepared from a single specimen, was used. At the beginning of the study, all 20 slides were analyzed to determine acceptable performance limits for measurements of mean cell area, mean cell perimeter, mean length/width ratio, and mean major axis length. During the study, one slide (randomly chosen by the quality control supervisor) was analyzed at the start of each analytical run. Before participants' specimens could be analyzed, the quality control results had to be within the performance limits for each measure. Further details on quality control methods, acceptable performance limits, and quality control measurements are in Supplement A of the monograph. In general, laboratory performance was good. The coefficients of variation (CVs), as measures of reliability, were ≤10% for all but one measure—the CV for the percentage of morphologically normal cells was 11.1%.

13.2.3 Statistical Methods

We used the analytical methods described in detail in Chapter 2. Regression analyses were conducted for the measures of sperm concentration, movement characteristics, morphology, and morphometry listed in Table 13.4. The distribution of values for each sperm measurement was evaluated before the values were statistically analyzed. Values for sperm concentration, sperm cells per ejaculate, mean cell area, mean cell perimeter, mean length/width ratio, and mean major axis length were approximately log-normally distributed; thus, they were logarithmically transformed before the analysis. The other sperm motility measures and the percentages of sperm cell heads in each of five morphologic categories (normal, large, small, tapered, and amorphous) were approximately normally distributed. In testing for differences between cohorts, we used categorical data analysis to examine the mean proportion of cells within each morphologic category. The statistical program, SAS

Table 13.3 Software Parameter Settings for Measurement of Sperm Motility on Videotapes, by Microscope Magnification

	Ocular Magnification	
	X 1.0	X 1.5
No. of Frames To Analyze	15	15
No. of Frames per Second	30	30
Video Standard (A/E)	A	A
Minimum Sampling		
Motile	1	1
Velocity	4	4
Maximum Velocity, μm/sec	140	140
Threshold Velocity, μm/sec	10	10
Threshold Grey Level[a]		
Cell Color	White	White
Pixel Scale, μm/pixel	0.688	0.459
Dilution Factor	1.000	1.000
Cell Size Range, pixels	5-25	11-56
Lateral Head Displacement		
Minimum number of points	7	7
Minimum velocity, μm/sec	18	18
Minimum linearity	3.50	3.50

[a] Set at the beginning of each analytical run.

Table 13.4 Measurements of Sperm Motility, Morphology, and Morphometry

Measurement	Reference Range[a]
Motility	
Sperm concentration in semen, million cells/mL	>20
No. of sperm cells per ejaculate, million	
Motile cells, %	≥40
Mean linear velocity, μm/sec	
Mean straight line velocity, μm/sec	
Mean linearity, trajectory index	
Mean beat/cross frequency, Hz	
Mean amplitude lateral head displacement, μm	
Sperm Head Morphology Categories, % cells	
Normal	≥40
Large	
Small	
Tapered	
Amorphous	
Sperm Head Morphometry	
Mean area, μm^2	
Mean perimeter, μm	
Mean length/width ratio	
Mean major axis length, μm	

[a] Reference ranges are based on commonly used clinical criteria. Values falling below these reference ranges have been shown to be correlated with reduced fertility potential (Alexander, 1982; Belsey *et al.*, 198[illegible]; Chong *et al.*, 1983).

PROC CATMOD (SAS Institute, 1985), makes it possible to simultaneously test multiple logit response functions with a multinomial outcome variable. This statistical test has the advantage of accounting for the intercorrelation of different response functions (Grizzle *et al.*, 1969; Landis, 1985; Stanish, 1985).

Before analyzing the data, we made several additional adjustments for technical factors associated with semen collection and processing. We excluded the motility data on the 18 specimens (from 14 Vietnam and 4 non-Vietnam veterans) for which the time lapse between collection and videotaping was greater than 2 hours and 20 minutes (or for which the time lapse could not be determined). For 63 specimens (from 37 Vietnam and 26 non-Vietnam veterans), the participants indicated that they had spilled some of the specimen as they were collecting it. These specimens were excluded from analyses of sperm concentration, number of cells per ejaculate, and semen volume. Within each specimen, individual sperm initially classified by the software program as "motile" but having a linearity ≤1.[illegible] or a straight-line velocity ≤5.0 micrometers per second were reclassified as "nonmotile" and were excluded from computations of mean linear velocity, mean straight-line velocity, mean linearity, mean amplitude lateral-head displacement, and mean beat/cross frequency. These types of cells accounted for <2% of all motile cells with velocity measurements. Sperm cells classified as motile but not followed for four frames (required for the software program to calculate velocity measurements) were excluded from calculations of the specimen's mean sperm velocity.

In the Model 2 regression analyses, we used three of the covariates that were defined in Chapter 2: current smoking status, current alcohol consumption, and current illicit drug use. In addition, for all sperm measurements, the number of days from the last previous ejaculation until the day the semen was collected was also included as a covariate. For sperm counts and movement characteristics, the time (in minutes) between semen collection and videotaping was also included as a covariate. An indicator variable for ocular magnification (X 1.5 versus X 1.0) during videotaping was included as a covariate for analyzing concentration, number of sperm cells per ejaculate, and sperm motility measures. Additional categorical variables were included in regression analyses, but because they had little or no effect upon the comparison of cohorts, these covariates, unless otherwise indicated, were not included in final regression models. These variables were income; education; drug use while in the Army; use of antimalarial drugs in the Army; age at examination; region of birth; marital status; fathering no live births since assignment to the primary tour of duty; body mass index; depression or anxiety in the past year; post-traumatic stress disorder (PTSD) in the past year; low and high levels of testosterone of follicle-stimulating hormone, and of luteinizing hormone; urinary tract infection; prostatitis; epididymitis; varicocele; gonorrhea; syphilis; genital herpes; malaria; month of semen collection; and current medication use (of those drugs that influence sperm production).

Results of analyses of the potential effect of three factors—intertechnician variability, month of specimen collection, and ocular magnification—upon relative cohort differences are presented in Supplement B (Medical and Psychological Data Quality). These results indicate that, for the first two factors, there was no confounding or effect-modification. The ocular magnification setting did not appear to alter the effect of Vietnam service on the various sperm measures; nonetheless, a higher proportion of the Vietnam veterans' specimens were videotaped at the X 1.5 setting than were non-Vietnam veterans' specimens. Because of the potential confounding, ocular magnification was included as a covariate for the regression analyses of sperm measures derived from the videotapes.

13.3 RESULTS

Mean sperm concentration was 20% lower for Vietnam veterans than for non-Vietnam veterans (64.8 versus 79.8 million cells per milliliter of semen) (Table 13.5). This difference was mainly attributable to a higher proportion of specimens from Vietnam veterans having sperm concentrations ≤20 million per milliliter (Figure 13.1). A similar 20% decrease was seen in the mean number of sperm cells per ejaculate, but this difference diminished and was not statistically significant after adjustment for the entry characteristics. The mean proportion of motile sperm and other sperm motility measures were, on the average, similar for Vietnam and non-Vietnam veterans. The distribution of the percent of motile sperm was similar between cohorts (Figure 13.2).

Specimens from Vietnam veterans had a lower mean proportion of morphologically "normal" sperm than did specimens from non-Vietnam veterans (57.9% versus 60.8%) (Table 13.6). This 2.9% difference in mean values reflects a slight shift in the Vietnam veterans' distribution towards a lower percentage of normal sperm cells (Figure 13.3). After race was accounted for, results of categorical data analysis suggest that the Vietnam veterans' lower percentage of normal cells was due to their having slightly higher proportions of large, tapered, and amorphous sperm cells (Table 13.7). Results of our analysis of morphometric data also indicated that specimens from Vietnam veterans were more likely to contain larger and more tapered sperm (Table 13.6). Both the mean cell perimeter and the mean length of the major axis of the sperm cells were significantly larger for Vietnam than for non-Vietnam veterans. Regression analyses suggested that these cohort differences in morphometric measures were primarily attributable to differences among those who entered military service between 1970-71. However, the association between mean percentage of

Table 13.5 Means[a] and Differences Between Means for Measures of Sperm Counts and Sperm Movement Characteristics Among Vietnam and Non-Vietnam Veterans

					Multivariate Results			
	Crude Mean		Crude Results		Model 1[b]		Model 2[c]	
Measure	Vietnam	Non-Vietnam	Mean Diff	95% CI	Mean Diff	95% CI	Mean Diff	95% CI
Sperm Counts								
Concentration, million cells/mL	64.8	79.8	-18.8	-32.7,-2.1	-20.2	-34.5,-2.8	-20.7	-33.4,-5.4
Sperm cells, million/ejaculate	146.7	184.7	-20.6	-36.3,-1.1	-16.8	-33.9, 4.7	-16.7	-31.8, 1.8
Movement Characteristics								
Motile cells, %	56.9	60.4	-3.4	-7.5, 0.6	-3.3	-7.6, 1.1	-2.1	-6.4, 2.2
Mean linear velocity, μm/sec	49.9	50.6	-0.7	-2.5, 1.0	-0.6[d]	-2.5, 1.3	-0.1[d]	-2.0, 1.8
Mean straight line velocity, μm/sec	35.6	36.3	-0.7	-2.3, 0.9	-0.5	-2.3, 1.2	-0.1	-1.9, 1.6
Mean linearity	6.9	6.9	-0.0	-0.2, 0.1	-0.0	-0.2, 0.1	-0.0	-0.2, 0.2
Mean amplitude lateral head displacement, μm	2.1	2.1	-0.0	-0.1, 0.1	0.0	-0.1, 0.1	0.0	-0.1, 0.1
Mean beat/cross frequency, Hz	14.9	14.9	-0.0	-0.4, 0.3	-0.0	-0.4, 0.3	-0.0	-0.4, 0.3

[a] Means and differences are arithmetic for all measures except concentration and sperm cells/ejaculate; for these two measures, means are geometric, and mean difference refers to the percent difference in geometric means.

[b] Model 1 contains the six entry characteristics.

[c] Model 2 contains the six entry characteristics and smoking status, illicit drug use, alcohol consumption, abstinence from sexual activity (no. of days before sample collection), time between sample collection and analysis (in minutes), and videotaping magnification.

[d] Standardized for type of enlistment.

Table 13.6 Means and Differences Between Means for Morphologic and Morphometric Sperm Measures Among Vietnam and Non-Vietnam Veterans

					Multivariate Results			
	Crude Mean[a]		Crude Results		Model 1[b]		Model 2[c]	
Measure	Vietnam	Non-Vietnam	Mean Diff[d]	95% CI	Mean Diff[d]	95% CI	Mean Diff[d]	95% CI
Morphology								
Normal cells, %	57.9	60.8	-2.9	-5.6,-0.2	-3.8	-6.6,-0.9	-3.4[e]	-6.3,-0.5
Morphometry								
Mean cell area, μm^2	9.0	8.8	1.8	0.0, 3.8	1.4[f]	-0.6, 3.5	1.4[f]	-0.6, 3.4
Mean cell perimeter, μm	12.4	12.2	1.5	0.4, 2.6	1.3[f]	0.2, 2.5	1.3[f]	0.2, 2.5
Mean cell length/width ratio	1.7	1.6	1.6	-0.2, 3.5	1.6	-0.4, 3.6	1.6	-0.4, 3.5
Mean cell major axis length, μm	4.4	4.3	1.7	0.4, 3.1	1.5[f]	0.1, 3.0	1.5[f]	0.1, 2.9

[a] The mean for the percentage of normal cells is arithmetic; all other means are geometric.
[b] Model 1 contains the six entry characteristics.
[c] Model 2 contains the six entry characteristics and smoking status, illicit drug use, alcohol consumption, and abstinence from sexual activity (no. of days before sample collection).
[d] For the percentage of normal cells, the mean difference is arithmetic; for all other measures it is the percent difference in geometric means.
[e] Standardized for income.
[f] Standardized for year of entry.

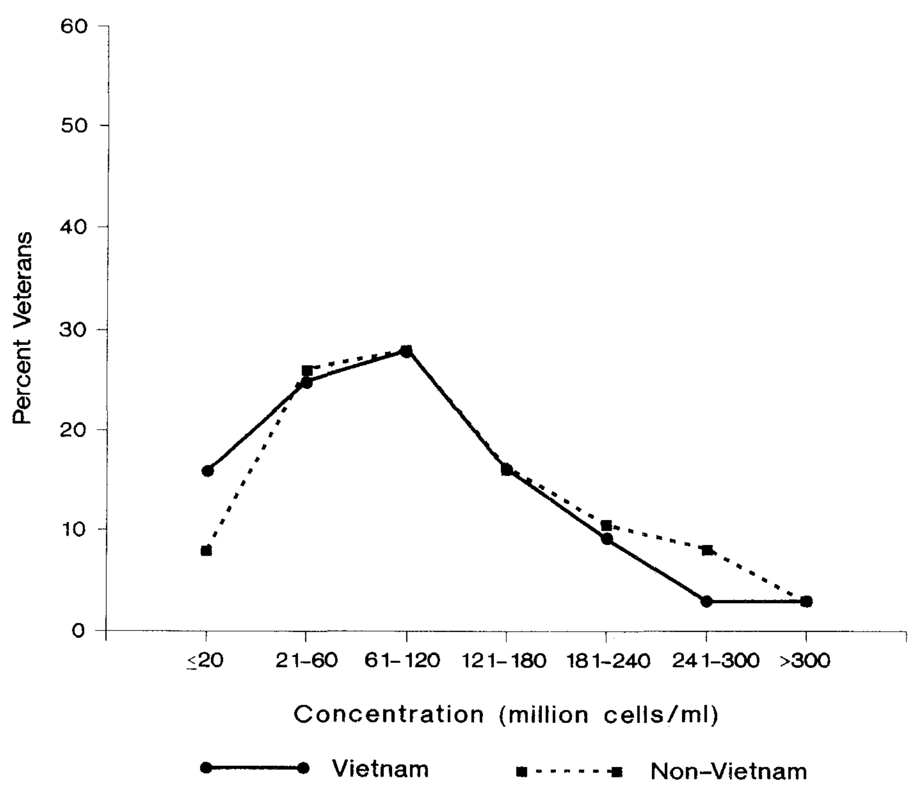
Table 13.7 Mean Proportions of Sperm Cells in Each Morphologic Category Among Vietnam and Non-Vietnam Veterans, by Race, and Odds Ratios for Different Sperm Categories

Morphologic Category	Race[a]	Mean Proportion of Cells		Categorical Data Analysis[b]	
		Vietnam	Non-Vietnam	OR	95% C.I.
Normal	White/Other	.586	.617	1.0	Referent
	Black	.531	.523		
Large	White/Other	.104	.093	1.2	0.7-2.2
	Black	.134	.088		
Small	White/Other	.113	.123	1.0	0.6-1.6
	Black	.106	.117		
Tapered	White/Other	.186	.156	1.2	0.7-1.8
	Black	.217	.265		
Amorphous	White/Other	.012	.011	1.2	0.2-6.0
	Black	.013	.008		

[a] White/Other: Vietnam, N=276; non-Vietnam, N=217. Black: Vietnam, N=45; non-Vietnam, N=28.

[b] Results of a categorical data analysis of multiple logit response functions using CATMOD (Stanish, 1985). The results show the ratio of odds of having certain abnormal sperm classifications compared with normal for Vietnam versus non-Vietnam cohorts, accounting for race.

Figure 13.1 Distribution of Sperm Concentration by Place of Service



normal cells (a proportion that is based on a combination of these morphometric measures) and place of service was not restricted to these 2 years of entry.

Specimens from Vietnam veterans were twice as likely as specimens from non-Vietnam veterans (15.9% versus 8.1%) to have sperm concentrations less than or equal to the clinical reference value of 20 million cells per milliliter of semen (Table 13.8). Specimens from five Vietnam and three non-Vietnam veterans had sperm concentrations below 5 million cells per milliliter. More semen specimens from Vietnam than non-Vietnam veterans contained less than 40% motile cells and less than 40% morphologically normal cells, but these differences were not statistically significant. However, specimens from more Vietnam (5.1%) veterans had all three of these abnormalities (crude OR=3.2, 95% CI 1.1-9.6) (Table 13.9).

In Table 13.10, the two cohorts are compared on the basis of these three abnormal sperm characteristics across strata defined by eight selected characteristics of military service. Low sperm concentration was consistently more prevalent among Vietnam veterans than among non-Vietnam veterans across strata, except among blacks, for whom the numbers were small. These results suggest that no single characteristic of Army service can account for the Vietnam cohort's higher percentage of veterans with low sperm counts. Neither can it be explained by psychological factors (Table 13.11). Among those with certain psychological problems (alcohol abuse or dependence, anxiety, depression, or post-traumatic stress disorder (PTSD)) during the year preceding the examination, the proportion with low sperm counts was higher for Vietnam than for non-Vietnam veterans—except among those with PTSD (Table 13.11). In general, having a lower proportion of normal sperm cells was more common among the Vietnam veterans within each stratum defined by an Army service or psychological characteristic (Tables 13.10 and 13.11). There were no consistent trends or significant associations between having a low percentage of motile sperm cells and serving in Vietnam.

Among Vietnam veterans, there were no trends in the percentage of veterans with semen abnormalities by level of self-reported combat or herbicide exposure (Table 13.12). The percentage of veterans with sperm abnormalities was less for those who reported taking antimalarial drugs during Vietnam service than for those who reported not taking these drugs.

The volumes of the semen specimens from about 7% of the veterans in each cohort were <1 milliliter. The semen of about 6% of Vietnam and non-Vietnam veterans had a pH <7.5 or >8.5. Results for the other semen characteristics measured were generally similar for the two cohorts. These measurements are presented in Appendix H.

13.4 DISCUSSION

Semen analysis was added to the medical examination because of a preliminary analysis of responses in the first half of the telephone interviews. Vietnam veterans reported more difficulties in conceiving pregnancies than did non-Vietnam veterans. For the subsample of 571 men whose semen characteristics were evaluated in the medical examinations, there were cohort differences in semen quality. In particular, results for Vietnam veterans showed about a 20% decrease in average sperm concentration, and twice the proportion with values for sperm concentration at or below the clinical reference value of 20 million cells per milliliter of semen. These cohort differences in sperm concentration were also reflected in similar decreases in the total number of sperm cells per ejaculate. In addition, results for Vietnam

Figure 13.2 Distribution of Percent Motile Sperm Cells by Place of Service

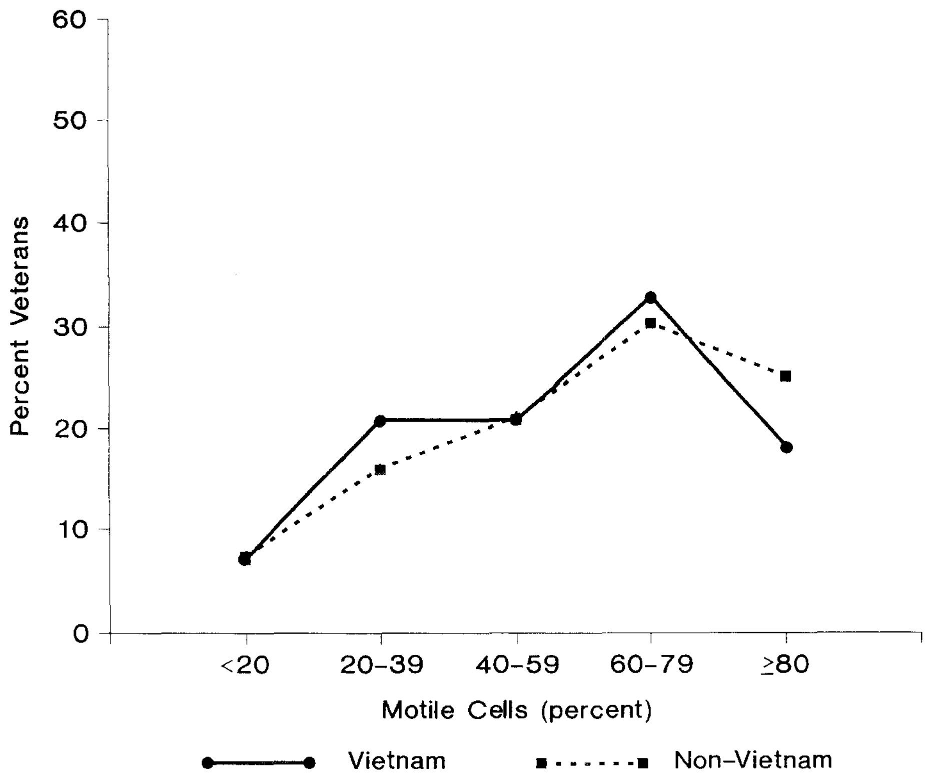


Table 13.8 Percent and Number of Vietnam and Non-Vietnam Veterans With Semen Abnormalities and Odds Ratios, by Semen Abnormality

Semen Abnormality	Vietnam		Non-Vietnam		Crude Results		Multivariate Results Model 1[a]		Multivariate Results Model 2[b]	
	%	No.	%	No.	OR	95% CI	OR	95% CI	OR	95% CI
Concentration ≤20 million cells/mL	15.9	42	8.1	17	2.1	1.2-3.9	2.3	1.2-4.3	2.7	1.3-5.7
Motile cells <40%	28.0	83	23.4	54	1.3	0.9-1.9	1.2	0.8-1.8	1.1	0.7-1.7
Normal cells <40%	15.9	51	11.4	28	1.5	0.9-2.4	1.6	0.9-2.8	1.6	0.9-2.9

[a] Model 1 contains the six entry characteristics.
[b] Model 2 contains the six entry characteristics and smoking status, illicit drug use, alcohol consumption, abstinence from sexual activity (no. of days before sample collection), time between sample collection and analysis (in minutes), and taping magnification. The time and magnification variables were not included in the analysis of normal cells.

veterans showed a significantly lower average proportion of morphologically "normal" sperm heads. Measurements of the dimensions of sperm heads indicated that sperm from Vietnam veterans tended to have larger and more tapered heads than sperm from non-Vietnam veterans.

Figure 13.3 Distribution of Percent Morphologically Normal Sperm Cells by Place of Service

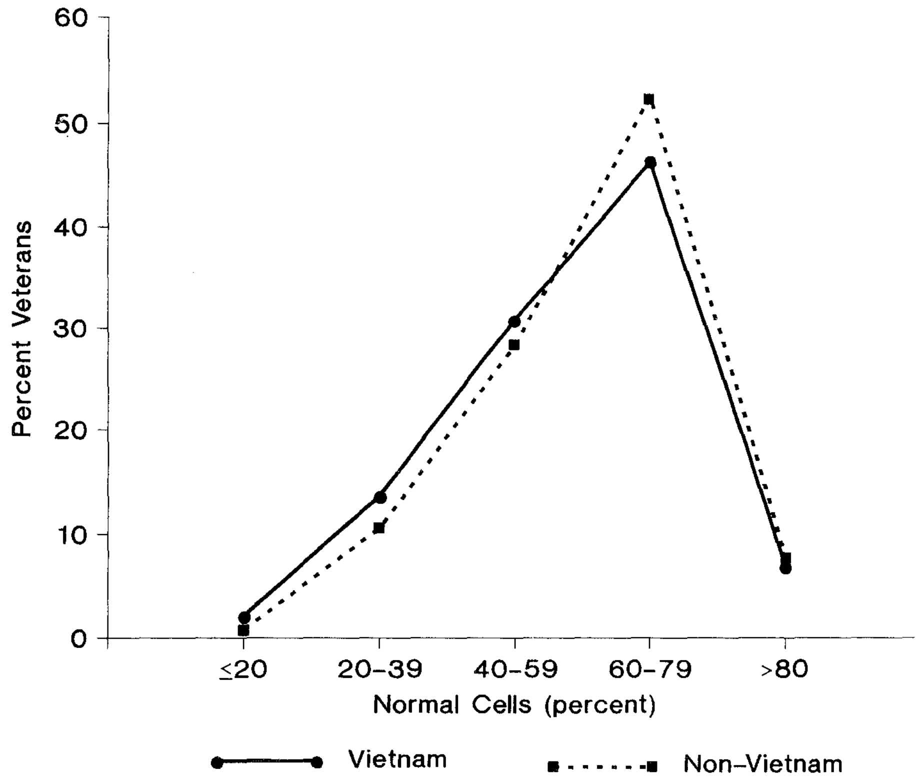


Table 13.9 Percent and Number of Vietnam and Non-Vietnam Veterans With Single and Multiple Types of Semen Abnormalities

	Vietnam		Non-Vietnam	
Semen Abnormality	%	No.	%	No.
Concentration ≤20 million cells/mL only	2.3	6	0.5	1
Motile cells <40% only	13.6	35	13.7	28
Normal class cells <40% only	6.2	16	5.4	11
Concentration ≤20 million cells/mL and motile cells <40% only	3.9	11	4.0	9
Concentration ≤20 million cells/mL and normal cells <40% only	1.3	4	0.0	0
Motile cells <40% and normal cells <40% only	1.9	6	2.1	5
Concentration ≤20 million cells/mL and normal cells <40% and motile cells <40%	5.1	16	1.7	4

Table 13.10 **Percent and Number of Vietnam and Non-Vietnam Veterans With Semen Abnormalities, by Selected Army Service Characteristics and Type of Abnormality**

	Type of Abnormality											
	Concentration ≤20 Million Cells/mL				Normal Cells <40%				Motile Cells <40%			
	Vietnam		Non-Vietnam		Vietnam		Non-Vietnam		Vietnam		Non-Vietnam	
Characteristic	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.
Age at Entry												
16-19	15.3	20	11.4	10	17.3	28	10.5	11	25.8	39	26.8	26
20-33	16.5	22	5.7	7[a]	14.5	23	12.1	17	30.1	44	20.9	28
Race												
White	16.9	37	7.4	13[a]	13.5	35	9.1	18	28.0	68	21.4	40
Black	12.5	4	16.0	3	28.9	13	25.0	7	31.6	12	34.6	9
Other	7.7	1	6.7	1	17.7	3	16.7	3	18.8	3	27.8	5
Primary MOS												
Tactical	17.8	16	11.1	5	15.1	18	13.0	7	26.9	29	30.6	15
Other	14.9	26	7.3	12[a]	16.3	33	11.0	21	28.6	54	21.4	39
Enlistment GT Score												
40-89	26.4	14	14.9	7	26.9	18	13.8	8	47.6	30	32.7	17
90-109	9.5	9	5.6	3	11.9	14	11.3	7	21.9	23	21.1	12
110-129	17.1	14	5.3	4[a]	15.6	15	8.3	7	24.7	23	22.0	18
130-160	19.2	5	9.4	3	12.5	4	15.8	6	14.3	4	18.9	7
Type of Enlistment												
Drafted	16.6	28	9.7	14	15.4	33	9.2	15	29.4	57	22.6	35
Volunteered	14.7	14	4.6	3	16.8	18	16.1	13	25.2	26	25.0	19
Year of Entry												
1965-66	12.0	11	12.3	9	18.1	19	9.4	8	23.6	23	29.6	24
1967-69	18.6	27	5.5	4[a]	13.2	24	12.8	11	32.1	53	19.8	16
1970-71	14.8	4	6.3	4	23.5	8	12.2	9	23.3	7	20.3	14
Drug Use in Army												
None	16.3	33	8.5	14[a]	15.3	37	10.9	21	27.1	61	23.9	43
Marijuana only	15.6	7	12.0	3	16.4	9	17.2	5	33.3	17	23.3	7
Other	13.3	2	0.0	0	21.7	5	9.1	2	25.0	5	15.8	3
Heroin Use in Army												
No	15.7	40	8.3	17	15.2	47	11.8	28	28.3	81	24.1	54
Yes	12.5	1	0.0	0	[illegible]	4	0.0	0	[illegible]	1	0.0	0

[a] Confidence limits for the crude odds ratio comparing Vietnam and non-Vietnam veterans do not include 1.0.

Table 13.11 Percent and Number of Vietnam and Non-Vietnam Veterans With Semen Abnormalities, by Selected Psychological Conditions and Type of Abnormality

	Type of Abnormality											
	Concentration ≤20 Million Cells/mL				Normal Cells <40%				Motile Cells <40%			
	Vietnam		Non-Vietnam		Vietnam		Non-Vietnam		Vietnam		Non-Vietnam	
Psychological Condition[a]	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.
Anxiety												
No	16.6	40	8.2	16[b]	15.9	47	12.4	28	29.6	81	22.4	48
Yes	8.7	2	6.7	1	16.0	4	0.0	0	8.7	2	35.3	6
Depression												
No	15.6	39	7.9	16[b]	16.1	49	11.5	27	29.0	82	22.4	50
Yes	21.4	3	12.5	1	12.5	2	10.0	1	7.1	1	50.0	4
PTSD												
No	15.7	38	7.7	16[b]	16.1	48	11.5	28	27.4	75	23.1	53
Yes	18.2	4	50.0	1	13.0	3	0.0	0	34.8	8	50.0	1
Alcohol Abuse or Dependence												
No	17.2	37	9.0	16[b]	16.4	43	11.5	24	27.9	68	23.6	47
Yes	8.8	3	3.9	1	15.0	6	7.1	2	19.4	7	25.0	6

[a] Met DSM-III criteria for the condition during the year preceding examination.

[b] Confidence limits for the crude odds ratio comparing Vietnam and non-Vietnam veterans do not include 1.0.

Table 13.12 Percent and Number of Vietnam Veterans With Semen Abnormalities, Overall and by Reported Army Service Experience and Type of Abnormality

	Type of Abnormality					
	Concentration ≤20 Million Cells/mL		Normal Cells <40%		Motile Cells <40%	
Experience	**%**	**No.**	**%**	**No.**	**%**	**No.**
Overall	15.9	42	15.9	51	27.9	83
Combat Exposure Index[a]						
1 (Lowest)	15.3	9	12.5	9	30.8	21
2	15.9	10	17.6	13	27.1	19
3	15.0	12	17.9	17	27.6	24
4 (Highest)	18.0	11	15.2	12	25.4	18
Herbicide Exposure						
None	15.5	19	16.1	26	31.3	45
Low	15.3	13	15.6	15	21.7	20
Mid-High	18.2	10	16.1	10	28.3	17
Antimalarial Drug Use						
No	20.5	9	17.3	9	32.0	16
Yes	13.9	28	14.8	36	25.3	57

[a] From combat exposure questionnaire administered during psychological evaluation.

Other measures of semen characteristics and reproductive function were similar between the two cohorts. Measures of sperm movement, including the percentage of motile cells, velocity, linearity of motion, and lateral head motion, were alike in the two cohorts, and the volume and the pH of semen samples were about the same for both groups. As we reported in Chapters 11 and 12, respectively, the reproductive hormone levels and the prevalences of genital abnormalities (noted on physical examination) were similar for the two cohorts.

We do not believe that the differences between cohorts in sperm concentration and sperm head size and shape (morphology) are due to biases in study design or execution. Participation bias is unlikely, since both cohorts had similarly high (over 80%) participation rates in the semen analysis component.

Neither do we believe that the differences are due to information bias. The semen measurements were almost totally automated, with a computer making the measurements. In addition, the technicians who prepared the videotapes and slides of the semen specimens and who ran the computer analyses were not aware of the participants' cohort status.

Confounding by other factors that could influence semen characteristics is also unlikely. For most of the important factors that could affect semen characteristics, such as race, age, and alcohol use, the two cohorts were similar. In addition, we performed multivariate analyses that adjusted for all of these relevant personal variables—and for technical factors related to specimen collection and processing—that could have affected semen characteristics.

Since semen analysis was performed for only a subsample of the VES participants, questions may arise about how representative the subsample is of all the VES participants and whether the findings may relate only to this particular subsample. The characteristics of the men who participated in the semen analysis were nearly identical to those of the entire group that participated in the medical examination. This suggests that the semen analysis participants were representative of the medical examination participants. The possibility that the findings in the semen analysis may have been spurious (or caused by chance) cannot be ruled out, but the level of significance of the statistical tests and the consistency in the differences between cohorts indicate that this explanation is unlikely.

The effects of the lower concentration of sperm and the fewer normal sperm cells upon reproductive function are difficult to determine. The exact correspondence between particular deficiencies in semen quality and fertility potential is not well established. Though major reductions in sperm quantity and quality are generally agreed to be associated with reduced fertility (Meistrich and Brown, 1983; Smith *et al.*, 1977; Wickings *et al.*, 1983; Zukerman *et al.*, 1977), the effects of subtle sperm changes on fertility remain uncertain (Wyrobek *et al.*, 1982, 1984). Various investigators have found that different aspects of semen quality may be best correlated with fertility. Some have found that two measures, sperm concentration and the percentage of normal sperm, correlate best with fertility (Sherins and Howards, 1986). Others claim that motility measures correlate better (Aitken *et al.*, 1982a, 1982b, 1985; Collins, 1987; Wyrobek *et al.*, 1982, 1984). Male infertility, however, has many causes, and all of the factors that contribute to this condition are not likely to be reflected in a single test result or measure (Albertsen *et al.*, 1983).

Another reason why it is difficult to relate semen characteristics to fertility is that, in the past, the measurements of semen quality have been subject to variability and subjectivity. Only recently, with the technical development of computer-assisted semen analysis systems, has it become possible to obtain standardized, objective, and reproducible measures of semen characteristics (Katz and Davis, 1987). This new technology has also permitted investigators to measure certain semen characteristics, such as head dimensions, velocity, and lateral head motion, that previously could not be measured on a large scale. Because the technical developments are so recent, relatively little information is available on the relationship between these newer measures and fertility potential.

In clinical evaluations and epidemiologic studies, the measures that have been in use the longest include sperm concentration, sperm morphology, and the percentage of motile sperm (Wyrobek *et al.*, 1983). Major reductions in these measures have traditionally been used as indicators of reduced fertility potential (Alexander, 1982; Belsey *et al.*, 1980; MacLeod and Gold, 1951a, 1951b; Wyrobek *et al.*, 1983). On the basis of these clinical criteria (Alexander, 1982; Belsey *et al.*, 1980; Chong *et al.*, 1983), the Vietnam veterans had double the proportion of men with low sperm concentration (≤20 million per milliliter) and about a 50% increase in the proportion of men with low levels (<40%) of normal sperm heads. This latter finding, although not statistically significant, is consistent with the finding of a significant decrease in the mean percentage of normal sperm heads for the Vietnam group. The two cohorts differed only slightly in the proportion of men with semen samples of low motility (<40% motile sperm cells). The proportion of men who had low values on all three measures was significantly higher for Vietnam veterans than for non-Vietnam veterans (5.1% versus 1.7%).

Another difficulty in trying to draw definitive conclusions from the semen differences noted in this study is that we evaluated current semen characteristics, whereas the participants had served in the Army 10 to 20 years before the study. We do not know how the semen characteristics for these men may have changed in the intervening years. For example, the differences noted for the Vietnam veterans may have been stable over time or greater during and immediately after active duty, with a lessening over the years between that duty and this study. Results of studies of men exposed to dibromochloropropane (Eaton *et al.*, 1986; Potashnik, 1983) and radiation (Meistrich, 1986) have shown that, after exposure, semen quality initially decreases but then improves with increased time, provided the stem cells (type A spermatogonia) have not been destroyed.

The fertility histories of Vietnam and non-Vietnam veterans suggest that cohort differences in semen characteristics have not increased the number of Vietnam veterans unable to father children (Table 13.13). Among the semen analysis participants, there were no significant differences between Vietnam and non-Vietnam veterans in the average number of children fathered after the men were assigned to their primary tour of duty (1.4 versus 1.5) or in the proportion who have not fathered any children (31% versus 25%). Among all telephone interview participants and all medical examination participants, the fertility histories of Vietnam and non-Vietnam veterans were even more similar.

These results—that Vietnam veterans reported more difficulties conceiving pregnancies and were more likely to have certain deficiencies in semen quality—are not necessarilyin-compatible with our finding that men in both cohorts fathered similar numbers of children. Of those veterans in each cohort who reported past difficulties conceiving a pregnancy (after trying for 1 or more years with one partner), about three-quarters have fathered children (Table 13.13). Even among those who had been told by a physician that they had a particular condition that would impair their fertility, about half have fathered children. In a study in which investigators evaluated fertility over a 20-year period, low sperm counts were found to be related to the time interval to pregnancy, but pregnancy rates were not significantly affected unless the sperm count was below 5 million cells per milliliter of semen (Bostofte *et al.*, 1982). Thus, Vietnam veterans may have had a more difficult time conceiving pregnancies, perhaps resulting in delays in conceiving pregnancies, but, overall, Vietnam and non-Vietnam veterans have been able to father similar numbers of children.

Less clear are the implications of the observed differences in semen characteristics for pregnancy outcomes. Results of some investigations in animals, mainly mice, suggest a relationship between induced sperm changes and heritable genetic damage. However, no results of studies among humans have clearly shown that sperm head changes are related to adverse reproductive outcomes (Wyrobek *et al.*, 1982) or to birth defects. Results of early studies and case reports suggested that poor semen quality was associated with spontaneous abortions and other adverse pregnancy outcomes (Joel, 1966; MacLeod and Gold, 1957). In a more recent study, however, investigators found no evidence that diminished semen quality is responsible for spontaneous abortions (Homonnai *et al.*, 1980). For the semen analysis participants in the VES, children of Vietnam veterans and non-Vietnam veterans had similar rates of documented birth defects (5.9% versus 5.7%).

We could not determine the reasons for the differences in sperm characteristics between Vietnam and non-Vietnam veterans. The VES was designed to evaluate health effects resulting from the general experience of military service in Vietnam. Little information, mostly from the participants' recollections, was available regarding the specific components that may have made up the Vietnam service experience.

Possible explanations for the semen findings in the Vietnam cohort include exposure to infectious agents (Wyrobek *et al.*, 1983), illicit drug use (Singer *et al.*, 1986), alcohol use(Brzek, 1987; Gallant, 1986; Kucheria *et al.*, 1985), and the general stress (Poland *et al.*, 1986) of serving in a combat situation. We evaluated the influence of reported current use of alcohol, marijuana, other illicit drugs, cigarettes, and certain medications and found that they did not account for the differences in sperm characteristics between Vietnam and non-Vietnam veterans. Neither did we find that the more prevalent psychological disturbances

Table 13.13 Comparison of Fertility Histories Among Vietnam and Non-Vietnam Veterans Who Completed Telephone Interviews, Participated in Medical Examinations, and Had Semen Samples Analyzed

	Vietnam			Non-Vietnam		
Fertility History	**Interviewed (N=7924)**	**Examined (N=2490)**	**Analyzed[a] (N=324)**	**Interviewed (N=7364)**	**Examined (N=1972)**	**Analyzed[a] (N=247)**
Proportion (%) Who Fathered One or More Live Births[b]						
Overall	77.1	76.1	68.8	77.0	78.0	75.2
Self-reported fertility problem[c]						
Yes	72.7	76.5	71.0	73.1	71.5	74.3
No	78.3	76.0	68.3	77.9	79.4	75.4
Physician-diagnosed infertility condition[d]						
Yes	57.1	57.8	50.0	60.7	57.8	40.0
No	78.2	77.2	69.9	77.7	78.8	75.9
Average Number of Live Births Fathered[a]	1.6	1.6	1.4	1.6	1.6	1.5

[a] Restricted to those without vasectomy.
[b] Restricted to live births conceived after assignment to primary tour of duty.
[c] Failure to conceive with 1 partner after trying for ≥1 year.
[d] Reported during telephone interview having physician-diagnosed infertility condition.

experienced by Vietnam veterans, including anxiety, depression, alcohol abuse or dependence, and post-traumatic stress disorder, accounted for the differences. Neither were past sexually transmitted diseases, as reported by the veterans, related to the sperm differences between cohorts, nor were the differences accounted for by technical factors, such as time between last ejaculation and specimen collection or time between specimen collection and analysis.

The differences in sperm characteristics between the Vietnam and non-Vietnam cohorts did not appear to be specific to a particular subgroup of veterans. For the two cohorts, the semen findings did not consistently vary according to the Army entry and service characteristics, including year of entry and military occupational specialty (MOS). Although some of the morphometry results (measures of sperm head dimensions) suggested that the findings of larger and more tapered sperm heads for the Vietnam group may have been restricted to those Vietnam veterans who entered the service in 1970-71, the analysis of sperm morphology classifications did not substantiate this conclusion—that is, having fewer normal sperm heads was not restricted to Vietnam veterans who entered the Army in 1970-71. Neither were the concentration differences limited to these 2 years of enlistment. In addition, the findings do not appear to be accounted for by reported use of heroin or other drugs (including illicit and antimalarial drugs) while in the Army. The level of combat experienced in Vietnam was not related to the semen findings, because there were no associations between abnormal semen characteristics and having either a tactical MOS or higher levels of self-reported combat experience.

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 herbicides (Centers for Disease Control, 1987). In addition, in the VES, we found that semen characteristics did not differ according to levels of self-reported herbicide exposure.

In conclusion, 10 to 20 years after military service in Vietnam, certain differences in semen characteristics are evident in the Vietnam group relative to a comparable group of veterans who did not serve in Vietnam. The largest difference is a decrease in the concentration of sperm; another significant difference is a decrease in the average proportion of normal sperm cells. These differences in sperm quality may have caused some difficulties in Vietnam veterans' ability to conceive pregnancies, but they do not appear to have increased the proportion of Vietnam veterans who have been unable to father children.

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CHAPTER 14

Synthesis

14. SYNTHESIS

14.1 INTRODUCTION

The Vietnam Experience Study (VES) was a historical cohort study designed to ascertain whether adverse health effects are associated with service in the U.S. Army in Vietnam. This volume (III) has focused on the results of a comprehensive series of examinations of the veterans' current physical health. In this chapter we highlight the important similarities and differences found between Vietnam and non-Vietnam veterans during the medical and psychological examinations and discuss the strengths and limitations of this study. Furthermore, using information from elsewhere in the monograph, we examine several major issues of concern to veterans and others, including herbicide exposure, the association between combat experience and physical health, and the relationship between psychological status and the reporting of somatic symptoms.

14.2 SUMMARY OF PHYSICAL HEALTH FINDINGS

As originally conceived, the VES was intended to be a companion study to two other related studies, the Agent Orange Study and the Selected Cancers Study, both of which were designed to focus more on the possible health effects of exposure to herbicides containing dioxin. As such, the VES was designed to evaluate health effects that may have resulted from the general experience of military service in Vietnam. From the outset, in designing a study to examine the current health of a group of men 15 to 20 years after their Army service, we recognized a major difficulty—namely, that the Vietnam experience comprised numerous factors, many of which are unknown, poorly defined, or not quantifiable (Centers for Disease Control, 1983). Nonetheless, most current adverse health effects should fall within four broad etiologic categories: those related to prior infections, consequences of previous trauma, ill effects attributable to environmental toxins, and medical sequelae of psychological stress. Selected results from the medical examinations related to each category are presented in Table 14.1. Additional details on each outcome are in the respective organ-specific chapters (Chapters 5-13).

The hypothesis that Vietnam veterans, who served in a country where exotic tropical diseases abound, are more likely than other veteran to have current problems from these prior infections is attractive, but not well supported by available evidence (Genta *et al.*, 1987). Without a doubt gastrointestinal and dermatologic infections were a major cause of severe manpower loss during the conflict (Greenberg, 1969; Wells, 1982). For diarrheal diseases, the average annual rate of hospitalization during 1965-69 ranged from 35 to 69 per 1,000 men; for skin conditions, the corresponding rates ranged from 19 to 33 hospitalizations per 1,000 men (Neel, 1973). Except for recurrent minor skin infections caused by *Trichophyton mentagrophytes*, however, most of these gastrointestinal and dermatologic infections had short incubation periods and were self-limited, so we would not expect to find residual health effects.

Several diseases endemic to Southeast Asia are, however, characterized by long latent periods or chronicity, and men who served there might be at increased risk for these diseases, which include hepatitis B, syphilis, tuberculosis, melioidosis, and malaria (Barrett-Conner, 1978). In general, we found little evidence that these infections are more of a problem among Vietnam veterans than among non-Vietnam veterans.

Table 14.1 Percent and Number of Vietnam and Non-Vietnam Veterans With Selected Health Outcomes and Odds Ratios Adjusted for Entry Characteristics, by Etiologic Category

	Vietnam		Non-Vietnam		Model 1[a]	
Etiologic Category and Outcome	**%**	**No.**	**%**	**No.**	**OR**	**95% CI**
Infectious						
Hepatitis B surface antigen	0.5	13	0.9	18	0.6	0.3-1.2
Past hepatitis B infection[b]	14.1	350	11.1	217	1.4	1.[illegible]-1.6
Rapid plasma reagin test positive	0.5	13	0.9	18	0.6	0.3-1.3
Tuberculosis on chest roentgenogram	0.4	9	0.3	6	1.2	0.4-3.3
Traumatic						
Missing extremity	1.1	28	1.3	26	0.8	0.5-1.4
Bilateral mid-to-high-frequency hearing loss[c]	9.4	235	6.2	123	1.4	1.1-1.8
Toxin-Related[d]						
Chloracne-like skin lesions	0.9	22	0.8	15	1.2	0.5-2.5
Peripheral neuropathy[e]	8.2	204	6.5	128	1.2	1.0-1.6
Chronic hepatic porphyria	0.3	6	0.2	4	–	–
δ-Glutamyl transferase, >140 IU/L	5.5	136	4.4	87	1.3	1.0-1.8
D-glucaric acid, >29.1 mg/g creatinine	5.1	127	4.9	96	1.0	0.8-1.4
Total triglycerides, >273 mg/dL	4.7	116	5.3	105	0.9	0.7-1.2
Total cholesterol, >282 mg/dL	5.1	126	4.7	93	1.1	0.8-1.5
Serum IgG, <734.2 mg/dL	5.0	125	5.0	98	1.0	0.8-1.4
Absolute T4 lymphocytes, <560 cells/mm^3	4.5	111	5.0	99	1.0	0.7-1.3
Absolute T8 lymphocytes, <280 cells/mm^3	4.2	105	4.4	87	1.0	0.8-1.4
Anergy[f]	3.5	88	3.9	76	1.0	0.7-1.4
Stress-Related						
Hypertension[g]	33.5	835	31.4	619	1.1	0.9-1.2
Ischemia or infarction on electrocardiogram	1.9	48	1.8	35	1.1	0.7-1.7
Miscellaneous						
Stool occult blood	1.3	29	0.5	9	2.8	1.3-6.0
ECG left ventricular hypertrophy	1.6	41	1.0	20	1.8	1.0-3.3
Semen concentration, ≤20 million cells/mL[h]	15.9	42	8.1	17	2.3	1.2-4.3
Morphologically "normal" sperm cells, <40%[h]	15.9	51	11.4	28	1.6	0.9-2.8

[a] For all modeled outcomes except tuberculosis (which has an unadjusted OR), Model 1 contains the six entry characteristics.
[b] Positive for antibody to hepatitis B core or surface antigens and negative for hepatitis B surface antigen.
[c] Average hearing threshold ≥51 dB at three combined frequencies: 3000, 4000, and 6000 Hz.
[d] Reference values for g-glutamyl transferase, D-glucaric acid, triglycerides, and cholesterol were the 95th percentile for both cohorts combined. For IgG, T4 lymphocytes, and T8 lymphocytes, the reference values were the 5th percentile for the combined cohorts.
[e] ≥2 findings from neurological physical examination or out-of-reference-range values for neurodiagnostic tests (nerve conduction and amplitude, thermal and vibratory sensation).
[f] <2-mm response to all seven antigens in CMI test.
[g] Systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, or current use of antihypertensive medication.
[h] 324 Vietnam and 247 non-Vietnam veterans had semen samples analyzed.

At the time of the examination, only a few (<1%) veterans were infected with hepatitis B, although serum tests for Vietnam veterans were more likely than those for non-Vietnam veterans to show evidence of past hepatitis B infection. A similarly, small (<1%) proportion of veterans in each group reported having had a diagnosis of syphilis since being discharged, and for a simlar proportion, responses to the rapid plasma reagin (RPR) test were positive. For tuberculosis, only a few veterans in each group had been diagnosed, since their discharge, as having the disease; the current chest roentgenogram findings were comparable; and the distributions of skin-test reactions to the old tuberculin antigen in the cell-mediated immunity (CMI) test were similar. Few veterans reported hospitalizations for melioidosis or other conditions that might have been unrecognized *Pseudomonas pseudo-*

mallei infections. Finally, although relapsing malaria was once a problem among returning Vietnam veterans (Centers for Disease Control, 1986), it should not be a problem now because, even if a person is not treated, vivax malaria (the most common cause of relapses) lasts, at the most, 8 years (Coatney *et al.*, 1971).

Regarding the consequences of previous trauma, we found that, at the time of the examination, a similar proportion, about 1%, of Vietnam and non-Vietnam veterans had missing extremities. This may be surprising, since about half of the wounds sustained during the Vietnam conflict involved the upper and lower extremities (Neel, 1973). One possible explanation is that veterans with missing limbs were less likely to participate in the medical examinations. Yet, as noted in Chapter 3, similar proportions of Vietnam (4%) and non-Vietnam (3%) veterans cited health-related reasons for not participating. Another possible explanation is that the number of wounded servicemen who lost limbs in Vietnam is not as high as it is generally thought to be. For example, less than 0.5% of the nearly 200,000 men wounded in Vietnam between 1965 and 1970 required amputations (usually for treatment of significant vascular injuries) (Neel, 1973). About 8% of the Vietnam veterans in our study reported being wounded while in the Army. Given our study size and the likelihood that limbs might be lost in other nonmilitary settings after discharge (for example, in motor vehicle collisions or work with power tools), this similarity of proportions is less surprising.

Another health effect of trauma that might be expected after wartime service is hearing loss. Modern military weapons can produce levels of sound that permanently damage hearing. Vietnam veterans were more likely to have mid-to-high-frequency hearing loss than non-Vietnam veterans. Differences between the two groups were greater among men with a tactical military occupational specialty (MOS), which included infantryman, armored vehicle crewman, artillery crewman, and combat engineer. These findings are consistent with results of several studies of Army troops which show that exposure to military noise results in irreversible hearing impairment (Brown, 1985; Man *et al.*, 1975; Walden *et al.*, 1975).

Although the VES was intended to evaluate health effects that may have resulted from the general experience of having served in Vietnam, we emphasized the evaluation of conditions that have been suggested as being related to prior exposure to herbicides or dioxin (Webb *et al.*, 1986). Upon examination, the Vietnam and non-Vietnam veterans were similar with regard to these conditions, which include chloracne and other skin disorders, peripheral neuropathy, hepatic dysfunction, porphyria, lipid abnormalities, and impaired immune function.

Psychological stress has been considered a contributing factor for a variety of somatic diseases, including hypertension and ischemic heart disease (Jenkins, 1976; Syme and Torfs, 1978), peptic ulcer disease (Lam, 1984), immune dysfunction, and cancer (Kasl, 1984). Service in Vietnam was, undoubtedly, a stressful event. Yet, we found little difference between cohorts in the prevalence of any of these medical conditions.

We focused our analysis on health outcomes thought to be related to previous infections, to trauma, to herbicide exposure, and to stress, but we found several unexpected differences between Vietnam and non-Vietnam veterans. The tests for more Vietnam (1.3%) than non-Vietnam veterans (0.5%) were positive for stool occult blood. We could not determine the site of blood loss among those whose tests were positive, but in both groups veterans with this finding had a variety of conditions that can be associated with stool occult blood. Left ventricular hypertrophy (LVH), as shown by electrocardiogram, was also more prevalent among Vietnam veterans (1.6% versus 1.0% for non-Vietnam veterans). This finding is also difficult to explain, but it does not appear to be related to differences between the two groups in either body mass or prevalence of hypertension, two important determinants of LVH in men of this age. For these two findings – stool occult blood and LVH – the association with previous military service cannot be easily explained. In any event, the proportion of Vietnam veterans that we found with each of these abnormalities is about what would be expected on the basis of results of previous studies of men of simlar ages (Kannel *et al.*, 1969; Winawer *et al.*, 1980).

Early analyses of responses in the telephone interviews showed that Vietnam veterans were reporting more difficulties in conceiving children, so, for the last 5 months of the study, we added semen analysis to the examination. For a subsample of 571 participants who had their semen evaluated, Vietnam veterans had lower concentrations of sperm and a lower mean proportion of morphologically normal sperm cells. We could not determine the reasons for these differences, although we examined numerous factors that may affect the characteristics of sperm. Further, the differences did not appear to be specific to a particular subgroup of veterans. Despite these differences in sperm characteristics, however, the Vietnam and non-Vietnam veterans have similar fertility histories. The rates for most adverse pregnancy outcomes were similar for women who conceived with Vietnam-era veterans, regardless of which cohort the veterans were in. Among all Vietnam and non-Vietnam participants in the VES, the average number of children fathered after discharge from the service was the same, 1.6, as was the proportion who fathered no children, 23%.

14.3 STUDY STRENGTHS AND LIMITATIONS

The validity of the VES findings should be considered in the light of the study's recognized strengths and limitations. One of its greatest strengths is the design. An important factor in the design was the method used to select participants. They were identified from a random sample of Vietnam-era Army veterans. Eligibility criteria were chosen to identify two cohorts that would be as similar as possible at the time of enlistment with regard to major health-influencing factors. All indications were that misclassification of cohort status was minimal. Comparability of the two cohorts at the time of entry into the Army was considered a crucial objective, in order to increase the likelihood that any subsequently observed health differences between cohorts would be the result of service in Vietnam rather than the result of differences in preservice health factors. This objective was met, insofar as the two groups were similar with regard to most relevant risk factors or other characteristics that might be expected to influence physical and psychological health.

Another strength is the method used to conduct the study. In both cohorts, identical techniques were used to obtain information. All examinations were performed at one medical facility. Outside experts assisted in selecting and designing the tests for the examination. All data were collected and processed according to standardized protocols. Only board-certified physicians and trained technicians conducted the examinations and tests, and they were unaware of which cohorts the veterans were in. Throughout the study, we closely monitored the performance of the examiners and technicians and the quality of the data they collected.

One of the main potential limitations of this study is that, for Vietnam and non-Vietnam veterans, rates for participating in the examinations differed. Results of detailed analyses of the factors that affected participation indicate, however, that those examined were similar to those selected for examination but not examined, particularly with regard to health-influencing characteristics.

Another potential limitation is that participants underwent so many tests. The large numbers of tests increased the probability of our finding spurious or chance associations. We tried to minimize the likelihood of this problem by specifying before analysis those conditions or outcomes that we expected to be more prevalent among the Vietnam veterans. In addition, when possible, we developed case definitions and used them to summarize cohort differences on the basis of composite information related to an organ system or function.

From the outset we recognized an additional limitation—namely, that service in Vietnam was not a single, homogeneous experience for each of the soldiers assigned there. Rather, it was a collection of heterogeneous experiences that, in all likelihood, varied from individual to individual, from campaign to campaign, and from year to year. Components of this experience that might have influenced subsequent health include exposure to combat and hostilities, use of illicit drugs, life under harsh environmental or culturally unfamiliar conditions, infectious diseases, and contact with herbicides and other chemicals. One other limitation was that since these experiences occurred 15 to 20 years earlier, some ill effects from exposures might have resolved during the years between the exposures and the examination. In the VES we had little objective information on the components that made up each serviceman's tour of duty. Because of this lack of information, we could not always identify the reasons for the observed differences in current physical health. The effects of herbicide and combat exposure upon health are two of the issues of greatest concern to veterans and others. The difficulties in accurately measuring these two components of the Vietnam experience will be discussed in subsequent sections. Despite these shortcomings, the VES has provided a panoramic assessment of the current physical and psychological health of a sample of Vietnam-era veterans who served their country during a difficult period.

14.4 THE ISSUE OF HERBICIDE EXPOSURE

Many of the concerns voiced by Vietnam veterans and the public have focused on possible health effects resulting from exposure to herbicides such as Agent Orange. The VES was not designed to address this issue, but we examined a number of the health conditions suggested as being associated with exposure to phenoxyherbicide or dioxin in detail and found no differences between cohorts.

An objective measure of herbicide exposure, such as the level of dioxin in the blood serum, was not available at the time of the VES (Centers for Disease Control, 1988). In the telephone interview, however, the veterans were asked a series of questions about possible exposure to herbicides while in Vietnam. Responses were grouped to calculate a herbicide exposure index.

This subjective measure of herbicide exposure presents several problems. First, it is based on the veterans' recollections of circumstances that may have been of no particular concern to them at the time and which occurred some 15 to 20 years earlier. Thus, the information on which the measure is based is subject to differential recall. This potential for recall bias could result in an overestimate of the association between self-perceived herbicide exposure and a particular health outcome. We called attention to this overestimation in our discussion of the results of the telephone interview (Volume II). We found an association between self-perceived herbicide exposure and almost all reported medical conditions, many of which researchers have never suggested as being related to phenoxyherbicides. The nonspecificity of these associations suggests the possibility that differential recall may be biasing these results.

Second, in a recently completed companion study, we could not validate self-perceived exposure as an index of herbicide exposure by using more objective measures (Centers for Disease Control Veterans Health Studies, in press). In that study of enlisted Vietnam veterans, in which we measured dioxin levels in serum as an indicator of past exposure to herbicides containing dioxin, we found no association between self-reported exposure to herbicides and dioxin levels. Furthermore, the results of that study indicated that few Army ground troops had been heavily exposed to dioxin-containing herbicides while in Vietnam.

In the VES we further evaluated the hypothesis that self-perceived exposure to herbicides was associated with differential recall. We examined the four conditions from the medical examination—(1) peripheral neuropathy, (2) pulmonary dysfunction, (3) peripheral vascular disease, and (4) cardiac ischemia—for which we had both objective information (test results) and subjective information (symptoms). We reasoned that if self-perceived herbicide exposure was a valid proxy for actual exposure, then there should be an association between reported herbicide exposure and reported symptoms, as well as with subclinical signs of disease (abnormal test results without symptoms). In contrast, if self-perceived herbicide exposure was influenced by differential recall, then there should be an association between reported exposure and reported symptoms, but not with subclinical signs of disease.

For this analysis, we used the herbicide exposure index, with its four ordered categories that reflect an increasing likelihood of exposure, as described in detail in Volume II (Telephone Interview). In brief, for an index of 1, the veteran reported no herbicide exposure; for 2, he reported passing through a defoliated area; for 3, he reported being present during spraying or getting herbicide on his skin or clothing; and for 4, he reported handling spray equipment or spraying herbicides.

Signs and symptoms used in this analysis (and later in the analysis of combat exposure) were selected for each of the four conditions. A veteran was considered to have signs of peripheral neuropathy if he had ≥2 positive findings for the neurological physical examination or out-of-reference values for neurodiagnostic tests (nerve conduction velocity and amplitude, vibration and thermal thresholds). To have neurological symptoms the veteran needed to report ≥2 of the following: numbness, tingling, burning sensation, or weakness of the arms or legs. A sign of pulmonary dysfunction was having any of the following values for pulmonary function tests (PFTs): forced expiratory volume in 1 second (FEV1) ≤80% of predicted volume; forced vital capacity (FVC) ≤80% of predicted capacity; or, a FEV1/FVC percent ratio <70%. Pulmonary symptoms were a persistent cough, coughing up blood, shortness-of-breath at rest, difficulty breathing at night, and wheezing. For peripheral vascular disease, signs were defined as findings of altered peripheral arterial hemodynamics (APAH). These findings were a resting ankle-to-brachial blood pressure ratio <1, an absent posterior tibial pulse waveform, or a femoral bruit. Claudication was considered a symptom of peripheral vascular disease. For cardiac ischemia, patterns of ischemia or infarction shown on electrocardiogram (ECG) were considered signs, whereas symptoms included exertional chest pain, rapid heart beating, fainting, or difficulty breathing at night.

Results are shown in Table 14.2. For each of the four health conditions, the proportions of veterans with only subclinical signs of disease were the same, regardless of the level of

Table 14.2 Percent of Vietnam Veterans With Physical Health Findings and Symptoms, by Self-Perceived Herbicide Exposure Index

Findings and Symptoms[b]	Herbicide Exposure Index[a] 1 (N=1051) %	2 (N=762) %	3 (N=561) %	4 (N=109) %
Peripheral Neuropathy				
Signs without symptoms	8.4	7.6	8.6	6.4
Symptoms regardless of signs	2.0	5.6	11.8	11.9
Pulmonary Dysfunction				
Abnormal PFT without symptoms	10.7	9.2	11.8	7.3
Any symptoms regardless of PFT results	14.9	26.6	30.8	45.9
Peripheral Vascular Disease				
APAH without symptoms	3.8	5.0	4.6	4.6
Claudication regardless of APAH findings	1.2	2.9	4.3	9.2
Cardiac Ischemia				
ECG signs without symptoms	1.7	1.2	0.5	0.9
Any symptoms regardless of ECG signs	14.1	21.0	28.0	34.9

[a] See text for explanation.
[b] See text for definitions of signs and symptoms. PFT = pulmonary function test; ECG = electrocardiogram; APAH = altered peripheral arterial hemodynamics

self-perceived exposure to herbicide. For example, among those with no prior herbicide exposure, 10.7% have PFT abnormalities (but no symptoms), but among those who report the heaviest level of previous exposure, 7.3% have PFT abnormalities. In contrast, the proportions of veterans with symptoms (regardless of whether they also have objective signs) increase with each higher level of self-perceived exposure. These relationships between self-perceived exposure and subjective and objective disease criteria are shown in Figures 14.1-14.4.

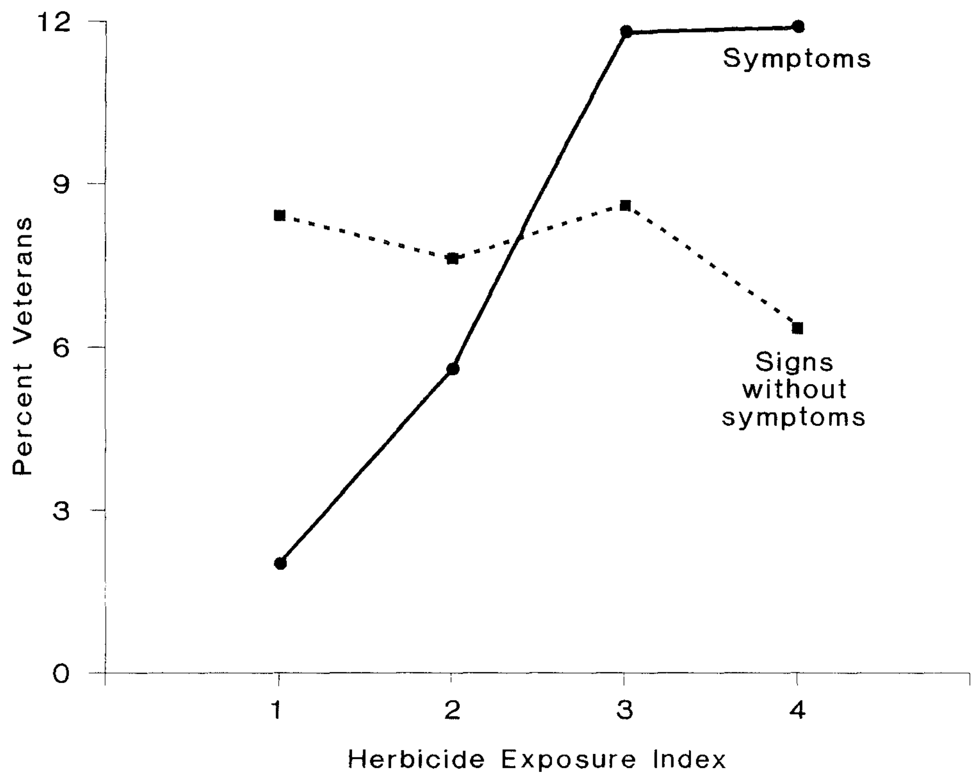
These findings indicate that the associations between reported health outcomes and perceived herbicide exposure are probably due to differential reporting between those who are symptomatic and those who are not. We do not know the reason for this differential reporting, but a likely explanation is that those with symptoms may need to attribute them to a "cause." Considering the attention the possible ill effects from contact with Agent Orange have received in the news media, the veterans' perceptions of herbicide exposure could be a cause of, or an explanation for, some of their symptoms.

14.5 COMBAT EXPERIENCE AND CURRENT PHYSICAL HEALTH

For the past two decades veterans and the public have also been deeply concerned about the effect of the Vietnam combat experience on veterans' health. Researchers have devoted much effort to describing and understanding the psychological sequelae of military service in Vietnam. Considerably less is known about the relationship between exposure to combat and physical health. In the VES we had no objective information on the amount of combat experienced by individual veterans. We did, however, have two indicators or measures, both less than perfect, of previous combat experience.

One indicator was the veteran's primary military occupational specialty (MOS), a designation given to each serviceman shortly after he completed basic training and before he was assigned a tour of duty. A tactical MOS, which includes infantryman, armored vehicle crewman, artillery crewman, and combat engineer, indirectly indicates that a veteran was likely to have participated in direct combat. Vietnam, however, has been described as "a war

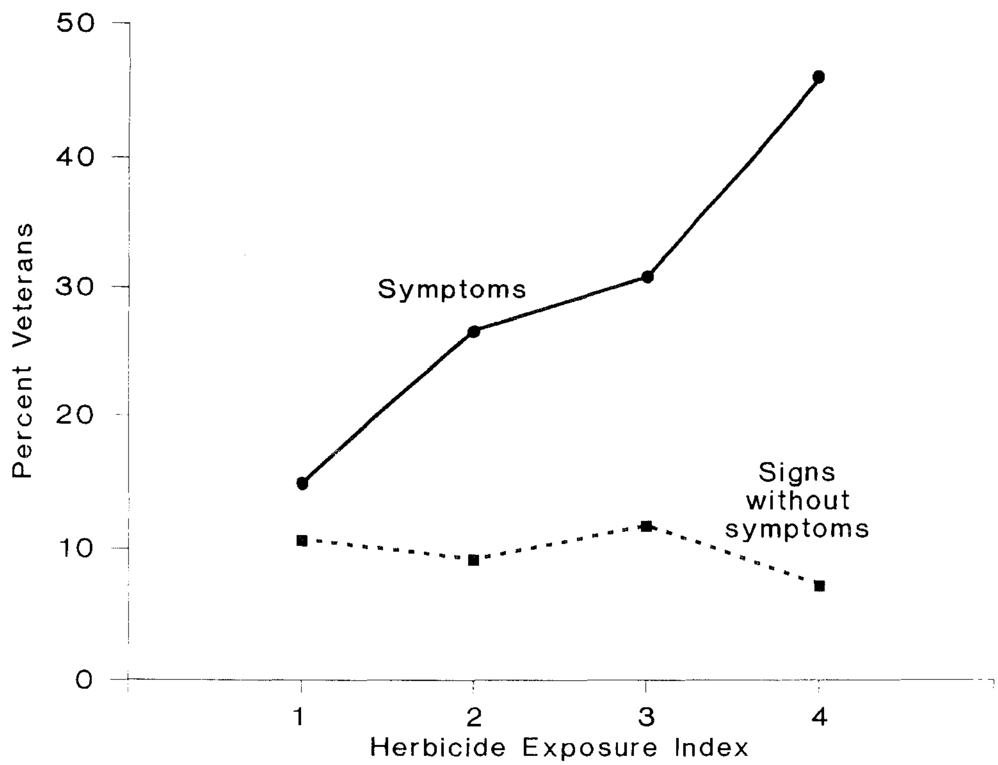
Figure 14.1 Vietnam Veterans With Signs and Symptoms of Peripheral Neuropathy by Herbicide Exposure Index



of no frontlines" or strategic boundaries (Palmer, 1978), one in which rear echelon troops were also subjected to terrorist attacks and hostile fire. As such, we realize that some men with a nontactical MOS would have experienced heavy combat, and vice versa. Because of this potential misclassification, when the MOS is used to indicate combat experience, the association between combat exposure and a particular health outcome tends to be underestimated.

The other indicator was derived from the veterans' responses to the questionnaire on exposure to combat. This questionnaire was completed near the end of the psychological evaluations on the second day of the medical examination. As with the assessment of herbicide exposure, this assessment relies on participants' recollections of events that occurred some 15 to 20 years earlier. Therefore, the information elicited in the questionnaire may be subject to differential recall. This recall bias could cause the association between combat exposure and a self-reported health outcome to be overestimated. Although both of these indicators (military occupational specialty and self-reported combat exposure scores) are imperfect measures, they nonetheless are probably related to some extent to the actual level of combat experienced. For example, Vietnam veterans with a tactical MOS had higher self-reported combat exposure scores (mean = 34, out of a possible maximum score of 72) than Vietnam veterans with a nontactical MOS (mean = 18).

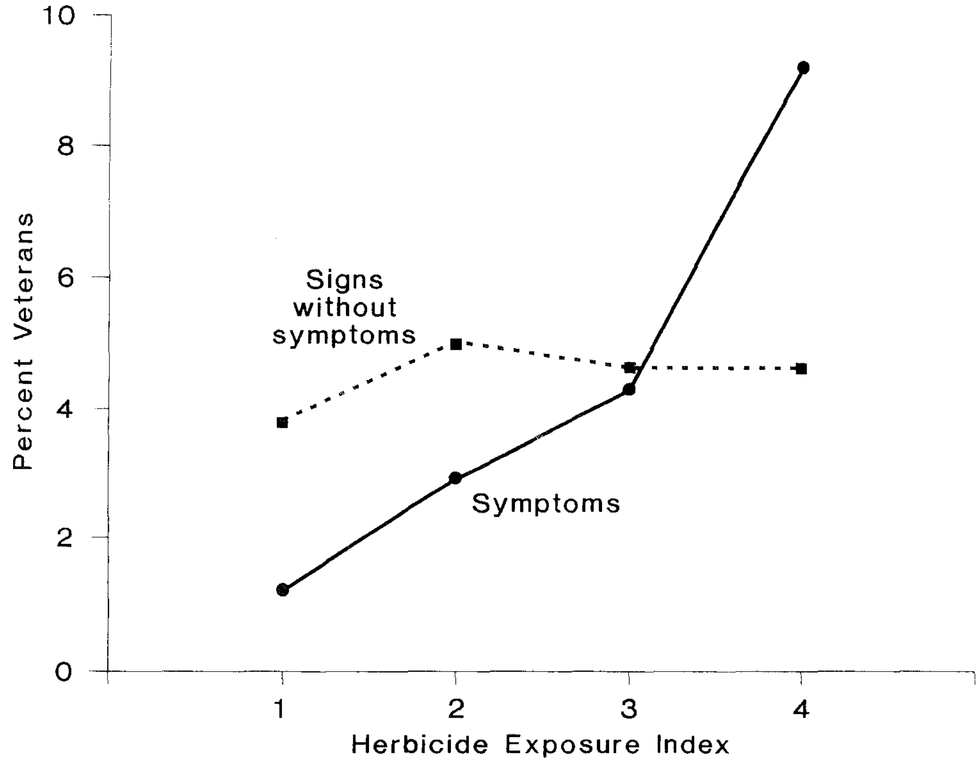
Figure 14.2 Vietnam Veterans With Pulmonary Signs and Symptoms, by Herbicide Exposure Index



In general, men who served in Vietnam with a tactical MOS do not have a higher relative risk for current ill health than do men who served in Vietnam with a nontactical specialty. We used multivariate statistical techniques to evaluate several hundred health outcomes—findings from the physical examination and results from laboratory assays and other tests. We included MOS as a covariate in each of the primary (Model 1) analyses and found it to be a meaningful interaction term in only one instance. In our analysis of mid-to-high-frequency hearing loss, we found that Vietnam veterans with a tactical MOS were at increased risk for this outcome compared with those with a nontactical MOS.

In Table 14.3, results for several health outcomes are stratified by MOS. In addition tohearing loss, two of these outcomes—hypertension and peptic ulcer disease—have been suggested as being associated with combat experience (Brown, 1985; Gill and Bell, 1981; Goulston *et al.*, 1985; Graham, 1945). Among veterans with a tactical MOS, the OR for hearing loss is 2.2, whereas among those with a nontactical MOS, the OR is 1.4. For two health outcomes, peripheral vascular disease and peptic ulcer disease, results are opposite from what might be expected: the relative differences between Vietnam and non-Vietnam veterans are greater among those with nontactical specialties. This implies that with the exception of hearing loss, there is no association between combat exposure (as reflected by a tactical MOS) and these particular health outcomes.

Figure 14.3 Vietnam Veterans With Signs and Symptoms of Peripheral Vascular Disease, by Herbicide Exposure Index

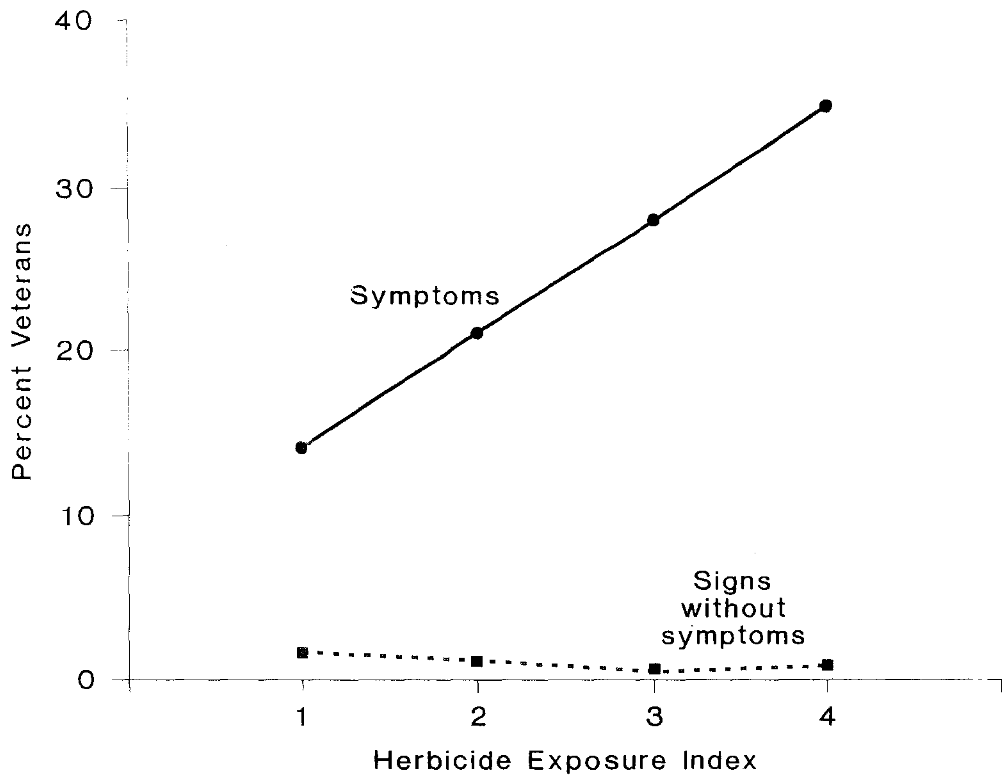


The association between self-reported combat exposure and ill health needs to be evaluated in light of possible differential reporting of combat experience by study participants with physical symtpoms. To evaluate the hypothesis that self-reported combat exposure was associated with differential recall, we examined the relationship between self-reported combat exposure and the four health outcomes for which we had both objective (test results) and subjective (symptoms) information: peripheral neuropathy, pulmonary dysfunction, peripheral vascular disease, and cardiac ischemia.

We reasoned that if self-reported exposure to combat was a valid proxy for actual exposure, then there should be an association between reported combat exposure and reported symptoms, as well as with subclinical signs of disease (abnormal test results without symptoms). In contrast, if self-reported combat exposure was influenced by differential recall, then there should be an association between reported exposure and reported symptoms, but not with subclinical signs of disease. For this analysis, we used the combat exposure index, with its four ordered categories that reflect an increasing likelihood of exposure, as described in Volume IV.

For each of these four conditions (Table 14.4), trends with the combat exposure index are seen for those veterans with the self-reported symptoms, but not for those who have only abnormal test results, but no symptoms. These trends suggest that much of the association between self-reported combat exposure and certain health outcomes may be explained by differential reporting among those veterans who are symptomatic.

Figure 14.4 Vietnam Veterans With Signs and Symptoms of Cardiac Ischemia, by Herbicide Exposure Index



14.6 PSYCHOLOGICAL STATUS AND SYMPTOM REPORTING

Stress may play a role in the development of several behavioral and emotional problems, including drug and alcohol abuse, anxiety, depression, and somatization (Kellner, 1987; Yager *et al.*, 1984). As noted in Volume IV (Psychological and Neuropsychological Evaluation), we found that, according to the Diagnostic Interview Schedule (DIS), Vietnam veterans were more likely than non-Vietnam veterans to meet criteria for current depression (4.5% versus 2.3%), anxiety (4.9% versus 3.2%), and alcohol abuse or dependence (13.7% versus 9.2%). Few veterans met criteria for drug abuse or dependence. About 15% of Vietnam veterans had experienced combat-related post-traumatic stress disorder (PTSD) sometime during or after military service, and 2.2% had the disorder during the month before the examination. In addition, using combined results from the DIS and the Minnesota Multiphasic Personality Inventory (MMPI), we found that current "poor psychological status" (see below) was twice as common among Vietnam veterans who entered the Army from 1965-1967 than among other veterans who entered during the same period.

In the telephone interview (Volume II) Vietnam veterans reported many health conditions and symptoms more frequently than did other veterans. As described in Chapters 5-13 of this volume, results for the subsample of veterans who participated in the medical examinations showed a similar trend.

Table 14.3 **Percent and Number of Vietnam and Non-Vietnam Veterans With Selected Health Outcomes, by Military Occupational Specialty (MOS)**

Health Outcomes and MOS	Vietnam %	Vietnam No.	Non-Vietnam %	Non-Vietnam No.	Crude OR
Hearing Loss[a]					
Tactical	10.3	87	5.0	25	2.2
Nontactical	9.0	148	6.7	98	1.4
Hypertension[b]					
Tactical	34.0	288	32.1	160	1.1
Nontactical	33.3	547	31.2	459	1.1
Altered Peripheral Arterial Hemodynamics[c]					
Tactical	5.0	42	5.6	28	0.9
Nontactical	4.5	74	2.9	43	1.6
Pulmonary Function Test[d] Abnormalities					
Tactical	13.6	115	16.2	81	0.8
Nontactical	16.3	268	15.1	223	1.1
Peptic Ulcer Disease[e]					
Tactical	8.9	75	7.8	39	1.1
Nontactical	8.2	135	6.1	90	1.4

[a] Bilateral mid-to-high-frequency hearing loss.
[b] Systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, or current use of antihypertensive medications.
[c] Resting ankle-to-brachial blood pressure <1, an absent posterior tibial pulse waveform, or a femoral bruit.
[d] FEV1 ≤80% of predicted, FVC ≤80% of predicted, or FEV1/FVC % ratio <70.
[e] Physician-diagnosed condition reported during medical history interview.

Table 14.4 **Percent of Vietnam Veterans With Physical Health Findings and Symptoms, by Self-Reported Combat Exposure Index**

Findings and Symptoms[b]	Combat Exposure Index[a] 1 (N=576) %	2 (N=542) %	3 (N=711) %	4 (N=650) %
Peripheral Neuropathy				
Signs without symptoms	6.7	8.7	8.3	8.6
Symptoms regardless of signs	2.4	4.2	6.6	9.[illegible]
Pulmonary Dysfunction				
Abnormal PFT without symptoms	11.2	11.8	9.9	8.8
Any symptoms regardless of PFT results	16.1	20.7	25.5	30.3
Peripheral Vascular Disease				
APAH without symptoms	3.8	3.3	5.1	5.[illegible]
Claudication regardless of APAH findings	1.6	2.2	3.0	4.2
Cardiac Ischemia				
ECG signs without symptoms	0.9	1.9	0.8	1.5
Any symptoms regardless of ECG signs	14.2	18.3	22.5	24.9

[a] See text.
[b] See text for definitions of signs and symptoms. PFT = pulmonary function test; ECG = electrocardiogram; APAH = altered peripheral arterial hemodynamics.

In the medical history component of the examination, participants were questioned about the occurrence of a variety of symptoms during the year preceding the examination. These questions covered all organ systems and were designed to serve as the "review of systems" section of a standard medical history. Of the 57 symptoms about which study participants were questioned, Vietnam veterans reported 53 more frequently, non-Vietnam veterans reported 2 more frequently, and Vietnam and non-Vietnam veterans reported 2 with equal frequency. Group differences in the prevalence of each symptom were small. Most (48/57) of the symptoms were each reported by less than 10% of veterans in either cohort, and the absolute difference in prevalence between groups averaged about 1%. These results are in Appendix Table A.2.

Although Vietnam veterans were more likely than non-Vietnam veterans to report having had symptoms in the previous year, results of the medical examination showed few objective cohort differences. This discrepancy—between the reporting of symptoms and the lack of objective physical signs—may be related to the stress Vietnam veterans experienced and its subsequent psychological effects. Investigators recognize that stress can produce anxiety, depression, and a variety of somatic symptoms (Kellner, 1987). Persons who are anxious or depressed may have an increased awareness of symptoms and a heightened concern about physical health, and yet their test results may show no objective evidence of physical illness.

We evaluated the possibility that the Vietnam veterans' higher prevalence of psychological problems, including anxiety and depression, may have contributed to their increased reporting of somatic symptoms. For this analysis, "poor psychological status" was defined, as described in Volume IV, as meeting full DIS criteria for generalized anxiety, depression, or substance abuse in the month preceding examination *and* having elevated scores on at least two of eight MMPI clinical scales (scales 1-4, 6-9). Using these criteria, we identified about 10% of the veterans in the two cohorts combined who could be considered to have the poorest current psychological status. "Good psychological status" was defined as *not* meeting the DIS criteria for any of the three conditions in the past month and having elevated scores on no more than one MMPI scale. About 65% of the veterans in the two cohorts combined met these criteria.

We examined those veterans who reported five or more symptoms during the medical history interview. About 21% of Vietnam and 14% of non-Vietnam veterans reported ≥5 symptoms, for an unadjusted OR of 1.7 (Table 14.5). After the results were adjusted for entry characteristics and current poor psychological status, the odds ratio remained about the same, suggesting that the differences in psychological status between cohorts do not explain why Vietnam veterans reported more symptoms.

For several conditions, we also examined the prevalence of reported symptoms among Vietnam and non-Vietnam veterans according to current psychological status. We selected the four medical conditions used in our analysis of herbicide and combat exposure (peripheral neuropathy, pulmonary dysfunction, peripheral vascular disease, and cardiac ischemia). Because we wanted to analyze the association between symptoms and psychological status, we restricted our analysis to those who reported symptoms and did not have any objective signs of disease.

In each cohort, for all four conditions, those with current poor psychological status were more likely to have symptoms than those with good psychological status (Table 14.6). Among Vietnam veterans, for example, those with poor psychological status were nearly three times as likely to have pulmonary symptoms as those with good psychological status (32.0% versus 12.5%). We saw a similar pattern when we compared non-Vietnam veterans with poor and good psychological status. Furthermore, with only one exception (pulmonary symptoms among those with poor psychological status), these results show that Vietnam veterans are more likely than non-Vietnam veterans to report symptoms related to each of these conditions, regardless of their current psychological status.

Table 14.5 Percent and Number of Vietnam and Non-Vietnam Veterans With Five or More Symptoms Reported During Medical Examination

	Vietnam		Non-Vietnam		Crude Results	Model 1[a]	Model 2[b]
	%	No.	%	No.	OR	OR	OR
Reported ≥5 symptoms during year preceding examination	21.2	529	13.9	275	1.7	1.6	1.5

[a] Model 1 contains the six entry characteristics.
[b] Model 2 contains the six entry characteristics and current psychological status (see text).

Thus, although reporting symptoms was associated with poor psychological status, and although psychological problems were more prevalent among Vietnam veterans, these two findings do not explain why Vietnam veterans reported more symptoms than non-Vietnam veterans. The Vietnam veterans' increased reporting of symptoms is not limited to those who are currently anxious or depressed or who currently exhibit other indicators of psychological distress. These results and others reported in this monograph indicate that the Vietnam experience has affected veterans' perceptions and feelings of health in a general way—characterized by a common pattern that is not limited to an easily identifiable subgroup of veterans with either physical or psychological problems.

14.7 CONCLUSIONS

Most Vietnam veterans who participated in this study believed that they were in good health. Compared with non-Vietnam veterans, however, the Vietnam veterans more frequently reported a wide range of current somatic symptoms and past diseases. Most of these conditions were not detected by the comprehensive physical and laboratory examinations conducted in this study. Results of the examinations did show, however, that Vietnam veterans, particularly those who served in tactical military occupational specialties, have more hearing loss than non-Vietnam veterans. Further, results of tests for the subsample of participants who had their semen evaluated showed differences between the two groups in semen characteristics. Compared with results for the non-Vietnam veterans, results for the Vietnam veterans showed decreased concentrations of sperm and a significant decrease in the average proportion of normal sperm cells. Despite these differences, however, Vietnam and non-Vietnam veterans have fathered similar numbers of children and similar proportions have fathered no children.

Table 14.6 Percent of Vietnam and Non-Vietnam Veterans With Self-Reported Symptoms by Type of Symptom and Current Psychological Status

	Current Psychological Status			
	Poor[a]		Good[a]	
Type of Symptom[b]	Vietnam (N=297) %	Non-Vietnam (N=144) %	Vietnam (N=1507) %	Non-Vietnam (N=1376) %
Peripheral neuropathy	8.4	3.5	1.5	1.1
Pulmonary dysfunction	32.0	34.7	12.5	11.4
Peripheral vascular disease	9.8	6.9	0.7	0.4
Cardiac ischemia	40.4	39.6	11.6	10.3

[a] See text for explanation.
[b] See text for definitions of symptoms.

More than 15 years after the end of the U.S. military involvement in Vietnam, the psychological and physical health of the veterans who served there remains a controversial issue. Many veterans are still concerned that, as a results of their service in Vietnam, they may be at increased risk for adverse health effects. Until now, we have had little objective evidence to use in comparing the health of Vietnam veterans with that of a similar group of veterans who served elsewhere at the same time. In the aftermath of the conflict, two popular views have arisen about Vietnam veterans. One view is that a large proportion of Vietnam veterans are psychologically disturbed and socially maladjusted. As we show in Volume IV, psychological problems are more prevalent among Vietnam veterans, but these affect a minority of veterans. Furthermore, as a group, Vietnam veterans have similar social and economic characteristics as non-Vietnam veterans. Another equally widespread view is that many Vietnam veterans are suffering from a myriad of physical ailments attributable to exposures encountered in Southeast Asia. The results of the Vietnam Experience Study indicate that relatively few Vietnam veterans have current physical health problems and that, for most conditions, their health is comparable to that of non-Vietnam veterans.

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APPENDIX A

Medical History Results

Table A.1 Percent and Number of Vietnam and Non-Vietnam Veterans Reporting Physician-Diagnosed Health Conditions, and Odds Ratios, by Selected Medical History Items

Condition	Vietnam (N=2490)		Non-Vietnam (N=1972)		Crude Results[a]	
	%	No.	%	No.	OR	95% CI
Arthritis	8.6	211	9.0	174	1.0	0.8-1.2
Gout	2.1	51	1.5	29	1.4	0.9-2.2
Diabetes	1.2	31	0.8	15	1.6	0.9-3.0
Overactive thyroid	0.6	14	0.2	3	3.7	1.1-13.0
Underactive thyroid	0.5	12	0.7	13	0.7	0.3-1.6
Eczema	2.1	51	1.7	34	1.2	0.8-1.8
Psoriasis	1.9	46	1.2	24	1.5	0.9-2.5
Chloracne	0.7	17	0.1	1	13.6	1.8-102.5
Asthma	1.1	27	1.5	28	0.8	0.4-1.3
Chronic bronchitis	0.9	23	0.4	8	2.3	1.0-5.1
Emphysema	0.6	16	0.5	9	1.4	0.6-3.2
Tuberculosis	0.1	2	0.2	4	–	–
Pneumonia	7.4	166	6.7	119	1.1	0.9-1.4
Hypertension	10.0	245	9.2	181	1.1	0.9-1.3
Heart murmur	2.8	66	2.6	48	1.1	0.8-1.6
Angina	0.8	20	0.5	10	1.6	0.7-3.4
Heart attack	0.7	17	0.3	6	2.2	0.9-5.7
Heart failure	0.1	3	0.1	1	–	–
Endocarditis	0.1	2	0.1	1	–	–
Pericarditis	0.4	11	0.3	6	1.5	0.5-3.9
Peripheral vascular disease	2.3	56	1.4	27	1.7	1.0-2.6
Phlebitis	0.5	13	0.7	13	0.8	0.4-1.7
Stomach/duodenal ulcer	8.6	210	6.7	129	1.3	1.0-1.7
Gastritis	6.2	152	5.2	102	1.2	0.9-1.5
Irritable bowel syndrome	1.2	29	1.1	22	1.0	0.6-1.8
Hemorrhoids	18.4	441	16.7	313	1.1	.0-1.3
Diverticulitis	0.2	6	0.3	5	1.0	0.3-3.1
Crohn's disease	–	0	0.1	2	–	–
Ulcerative colitis	0.1	3	0.1	1	–	–
Pancreatitis	0.5	12	0.4	8	1.2	0.5-2.9

Table A.1 Percent and Number of Vietnam and Non-Vietnam Veterans Reporting Physician-Diagnosed Health Conditions, and Odds Ratios, by Selected Medical History Items – Continued

Condition	Vietnam (N=2490)		Non-Vietnam (N=1972)		Crude Results[a]	
	%	No.	%	No.	OR	95% CI
Alcohol-induced liver damage	1.5	38	0.9	17	1.8	1.0-3.2
Hepatitis	3.1	74	2.6	50	1.2	0.8-1.7
Cirrhosis	0.2	5	0.3	5	0.8	0.2-2.7
Porphyria	–	0	–	0	–	–
Gallstones	0.8	21	0.9	17	1.0	0.5-1.9
Anemia	0.9	23	0.9	18	1.0	0.5-1.9
Blood clotting abnormality	0.1	3	0.1	1	–	–
Glaucoma	0.3	7	0.1	1	–	–
Migraine headaches	3.9	95	3.2	61	1.2	0.9-1.7
Meningitis	0.2	6	0.2	3	–	–
Peripheral neuropathy	4.1	100	4.7	92	0.9	0.6-1.2
Post-traumatic stress disorder	2.0	50	0.2	4	10.1	3.6-28.1
Kidney/bladder stones	4.9	121	4.4	86	1.1	0.8-1.5
Urinary tract infection	9.5	228	9.1	173	1.1	0.9-1.3
Chronic kidney disease	0.2	6	0.1	2	–	–
Prostatitis	5.3	130	5.6	110	0.9	0.7-1.2
Epididymitis	0.8	19	0.9	18	0.8	0.4-1.6
Varicocele	0.8	20	0.8	16	1.0	0.5-1.9
Gonorrhea	6.1	133	5.0	90	1.2	0.9-1.6
Syphilis	0.4	11	0.6	11	0.8	0.3-1.8
Genital herpes	1.3	33	1.9	37	0.7	0.4-1.[illegible]
Infectious mononucleosis	1.2	30	1.4	26	0.9	0.5-1.5
Malaria	0.7	17	0.1	1	14.3	1.9-107.7
Melioidosis	0.1	2	0.1	1	–	–
Benign tumor	3.5	87	3.8	74	0.9	0.7-1.3
Any cancer	1.7	42	1.2	24	1.4	0.8-2.3

[a] A dash (–) indicates the value was not computed. This occurs when there are fewer than 10 cases in both cohorts combined.

Table A.2 Percent and Number of Vietnam and Non-Vietnam Veterans Reporting Medical Symptoms in the Past Year, and Odds Ratios, by Selected Medical History Items

	Vietnam (N=2490)		Non-Vietnam (N=1972)		Crude Results[a]	
Symptom	%	No.	%	No.	OR	95% CI
Common Cold at Time of Exam	12.1	298	12.2	238	1.0	0.8-1.2
Frequent Skin Boils	4.9	121	2.8	56	1.7	1.3-2.4
Jaundice, Skin/Eyes	0.9	23	0.4	8	2.3	1.0-5.1
Unexplained Skin Darkening	3.8	95	2.4	48	1.6	1.1-2.3
Abnormal Temple Hair Growth	0.1	3	0.1	1	—	—
Sudden Vision Loss	1.6	40	1.0	20	1.6	0.9-2.7
Double Vision	7.8	193	4.8	94	1.7	1.3-2.2
Bright Light Pain	5.0	125	3.1	62	1.6	1.2-2.2
Ringing in Ear	9.6	238	6.2	122	1.6	1.3-2.0
Severe Spinning Sensation	3.3	82	2.1	41	1.6	1.1-2.3
Persistent Nose Bleed	0.5	13	0.2	3	3.4	1.0-12.1
Shortness of Breath at Rest	5.7	142	3.7	72	1.6	1.2-2.1
Persistent Cough	11.0	274	9.2	182	1.2	1.0-1.5
Cough Phlegm	8.7	216	7.0	137	1.3	1.0-1.6
Coughing Spells	11.1	277	9.6	189	1.2	1.0-1.4
Sudden Attacks of Wheezing	2.5	63	2.1	41	1.2	0.8-1.8
Coughing Up Blood	1.1	27	1.5	29	0.7	0.4-1.2
Chest Pain/Pressure	7.3	181	5.2	102	1.4	1.1-1.9
Rapid Heart Beating	11.9	295	8.6	170	1.4	1.2-1.7
Fainting	2.1	52	1.9	38	1.1	0.7-1.7
Night Breathing Difficulty	4.1	103	3.9	76	1.1	0.8-1.5
Calf Pain/Cramps at Walking	2.8	69	1.5	29	1.9	1.2-3.0
Appetite Loss, >2 Weeks	3.6	90	2.1	41	1.8	1.2-2.6
Rapid Weight Loss, >10 Pounds	2.3	58	1.2	24	1.9	1.2-3.1
Difficulty Swallowing Food	2.7	68	1.6	31	1.8	1.1-2.7
Recurrent Abdominal Pain	10.2	254	8.1	160	1.3	1.0-1.6
Vomiting Up Blood	1.1	27	0.7	14	1.5	0.8-2.9
Black Stools	7.6	188	6.4	126	1.2	0.9-1.5
Frequent Loose Stools	9.7	240	8.3	164	1.2	1.0-1.4
Bleed/Bruise Easily	3.3	82	1.5	30	2.2	1.4-3.4
Enlarged Lymph Nodes	2.3	56	1.5	30	1.5	1.0-2.3
Frequent Urination	3.6	88	1.8	35	2.0	1.4-3.0
Bladder Control Loss	1.1	28	0.7	13	1.7	0.9-3.3
Frequent Night Urination	9.2	229	6.6	130	1.4	1.1-1.8
Difficulty Urinating	5.6	140	4.3	85	1.3	1.0-1.7
Weak, Dribbly Urine Stream	6.8	170	5.0	99	1.4	1.1-1.8