with the strongest Doppler sounds; (4) measured the ankle blood pressure at the selected artery, using the Doppler probe with an occlusive cuff around the ankle (with the lower edge of the cuff just above the malleolus); and (5) repeated steps 2 through 4 on the left leg. The participant's resting index for each leg was calculated by using the ankle blood pressure and the maximal (from either arm) brachial artery pressure.

The hyperemic and recovery indices are ratios of ankle-to-brachial blood pressure measured after the arterial flow to the lower extremity has been occluded. To occlude the flow, the technician inflated the sphygmomanometer cuffs, located bilaterally at the midcalf level, to 50 mm Hg above the systolic pressure and left the cuffs in place for 5 minutes. The hyperemic index for each leg was calculated by using ankle blood pressure measured immediately after the cuff was deflated. The recovery index was calculated by using measurements taken 1 minute after the cuff was deflated.

Because of data quality problems in the determination of the hyperemic and recovery indices, we did not use these postocclusive measures in assessing peripheral arterial flow. Since both legs were being tested simultaneously, the technician had difficulty in obtaining and recording the right and left ankle pressures at the precise times required—immediately after the cuff was deflated and 1 minute later. In our data quality analysis of repeat measures, we found that the coefficient of variation, as a measure of reliability, was higher for the hyperemic index (14.4%) than for the recovery index (7.0%) or the resting index (6.8%). Results of additional analyses indicated poor agreement between the resting index and the other two indices. Of the 173 veterans with a low (ratio <1.0) resting index, 6 (3.5%) also had a low (ratio ≤ 0.9) recovery index (kappa = 0.02). Similarly, 39 (22.5%) of the 173 veterans with a low resting index also had a low (ratio ≤ 0.8) hyperemic index (kappa = -0.02). Because of these problems with data quality, we did not use the recovery and hyperemic indices to further analyze cohort differences in peripheral arterial flow. We used the resting index for analyzing cohort differences because this Doppler measure has been in clinical use the longest.

We also used Doppler velocimetry to assess qualitatively the arterial wave morphology in the dorsalis pedis and posterior tibial arteries. In this technique the Doppler probe was used to obtain waveform tracings in both peripheral arteries bilaterally. With the participant lying down on his back, a trained technician used the Doppler probe to search for the artery being examined. After the technician located the artery, he or she tilted the probe until the Doppler sounds were strongest. The technician then recorded the waveform tracing.

Alterations in waveform morphology may indicate diminished arterial flow (Yao *et al.*, 1968). A multiphasic pattern is characteristic of a normal artery with unobstructed flow. Waveforms that exhibit either monophasic or absent pulsatility usually indicate the presence of proximal arterial stenosis (or, for monophasic patterns, decreased vascular resistance). Improper recording of the pulse, however, may produce artifacts in waveform morphology. Usually, the probe is held at an angle of about 45 degrees to the axis of blood flow. Small deviations (as little as 10 degrees) from the proper angle may alter the shape of the recorded waveform. Because of these technical problems, we found poor agreement (5.5%) between having a low resting index and having waveform abnormalities (monophasic or absent pulsatility). For this reason we did not use Doppler velocimetry measurements in our analysis of cohort differences.

We did, however, use the absence of a posterior tibial pulse as an indicator of altered peripheral arterial hemodynamics, since absence of this pulse is virtually always pathologic

(Barnhorst and Barner, 1968; Criqui *et al.*, 1985; Stephens, 1962). An absent dorsalis pedis pulse was not considered abnormal, since its absence may be congenital (Barnhorst and Barner, 1968; Stephens, 1962). During the examination the technician made several attempts to locate the posterior tibial pulse, using palpation and the Doppler probe, set at normal power. If the pulse could not be located with these techniques, the power of the probe was increased and the search continued before the pulse was declared absent.

9.2.3 Electrocardiograms

Electrocardiograms (ECGs) were obtained during the morning of the physical examination. Participants were requested not to drink caffeine-containing beverages or to smoke for 12 hours before the test. Trained technicians took standard 12-lead ECGs, using a Marquette MAC II automated ECG machine (Marquette Electronics). Initially, ECGs were analyzed by using a Marquette computer analysis program. Board-certified cardiologists reviewed all ECG tracings and their computer analyses. These physicians made corrections and additions, when necessary, to the computer-generated interpretations. Only physician-confirmed ECG readings were used in the analysis. In addition to each ECG being recorded on the data collection form as normal or abnormal, up to nine (of several hundred available) other specific ECG findings (*e.g.*, right bundle branch block) were recorded for analysis later.

9.2.4 Statistical Methods

We used the analytical methods described in detail in Chapter 2.

Systolic and diastolic blood pressures were analyzed as continuous measures. Because both measures were approximately log normally distributed, they were log transformed before being analyzed. In addition, we analyzed hypertension as a dichotomous variable. Hypertension was defined as either (1) diastolic pressure ⩾90 mm Hg, (2) systolic pressure ⩾140 mm Hg, or (3) current use of antihypertensive medications (NCHS, 1986).

Cohort differences in peripheral arterial disease were analyzed by treating the resting index (ratio of ankle-to-brachial blood pressure) as a continuous outcome measure. This index was log transformed before the analysis. In addition, we defined altered peripheral arterial hemodynamics (APAH) as a dichotomous measure. APAH was defined as having in either leg one or more of the following: (1) a resting index <1.0 (Carter, 1968, 1969; Yao *et al.*, 1969); (2) an absent posterior tibial pulse; (3) a femoral bruit.

In the Model 2 regression analyses, we used the following covariates (defined in Chapter 2): current alcohol consumption, current smoking status, body mass index, and self-reported occupational exposure to herbicides. We also included some covariates that were not commonly used in most other organ-specific analyses: family history of ischemic heart disease (a reported heart attack in an immediate family member before age 45) and a history of hypertension in an immediate family member. In addition, because results of quality control analyses indicated there was intertechnician variability in the measurement of systolic and diastolic brachial blood pressure and the resting index, we included "technician" as a covariate in Model 2 analyses of these measures. For completeness, "examiner" was also included as a covariate in the analysis of physical examination findings.

In the analysis, we considered several other important risk factors for cardiovascular diseases, including hypertension (as defined above in this section), diabetes (as defined in Chapter 11), total cholesterol (<220 mg/dL, ⩾220 mg/dL), and ratio of low-density lipoprotein to high-density lipoprotein (LDL/HDL; <3,⩾3) (NIH, 1985). The development of these risk factors may be related to military service in Vietnam, and, as such, they were considered *a priori* outcomes for analysis in this chapter and in Chapters 6 and 11. Thus, all of these factors may be considered intermediate components in the causal chain for subsequent cardiovascular outcomes. Since the primary purpose of the analysis was to estimate the association between service in Vietnam and specific health conditions and measures, we wanted to avoid adjusting for factors that may be in this causal chain. Thus, the Model 2 results presented here are not adjusted for hypertension, diabetes, cholesterol, or LDL/HDL ratio, except where indicated.

9.3 RESULTS

9.3.1 General Medical History

In general, Vietnam veterans were more likely than non-Vietnam veterans to report a history of physician-diagnosed cardiovascular conditions with onset after military service (Table 9.1). However, absolute differences between cohorts in the prevalences of these diagnoses were small. Hypertension, noted by about 10% of veterans in each group, was the most common of these conditions. Less than 1% of veterans in either group reported other conditions—angina, heart attack, or heart failure—that may be associated with either hypertension or ischemic heart disease.

Few (<3%) veterans in either group reported being hospitalized for cardiovascular diseases since being discharged (Table 9.2). Similar proportions of Vietnam and non-Vietnam veterans had been hospitalized for hypertension, ischemic heart disease, and other vascular disorders. Similarly, only a small number of veterans in each group had undergone cardiovascular surgery since being discharged from service. Only four Vietnam and five non-Vietnam veterans had had surgery on coronary vessels.

Although the two cohorts had similar histories of previous cardiovascular conditions, the Vietnam veterans were more likely than non-Vietnam veterans to report having had certain symptoms in the year before the examination (Table 9.3). Overall, 21.4% of Vietnam and 15.8% of non-Vietnam veterans reported having at least one cardiovascular symptom during this time. Symptoms included chest pain (after walking fast or uphill), unexplained rapid heart beating, fainting or other loss of consciousness, awakening from sleep because of breathing difficulties, and exertional leg pain that was relieved by rest. The most prevalent condition was rapid heart beating, reported by 12% of Vietnam and 9% of non-Vietnam veterans. The approximately 3% absolute difference between cohorts in the prevalence of this symptom was the largest difference for any of the reported symptoms.

More Vietnam than non-Vietnam veterans reported having past symptoms, but a similar proportion, about 8%, in each group reported current cardiovascular problems (Table 9.4).

Table 9.1 Percent and Number of Vietnam and Non-Vietnam Veterans Reporting Physician-Diagnosed Cardiovascular Conditions Since Discharge

	Vietnam		Non-Vietnam	
Condition	**%**	**No.**	**%**	**No.**
Hypertension	9.8	245	9.2	181
Heart murmur	2.7	66	2.4	48
Angina	0.8	20	0.5	10
Myocardial infarction	0.7	17	0.3	6
Congestive heart failure	0.1	3	0.1	1
Endocarditis	0.1	2	0.1	1
Pericarditis	0.4	11	0.3	6
Peripheral vascular disease	2.3	56	1.4	27

Table 9.2 Percent and Number of Vietnam and Non-Vietnam Veterans Reporting Cardiovascular Hospitalizations and Surgical Procedures Since Discharge

	Vietnam		Non-Vietnam	
	%	No.	%	No.
Reason for Hospitalization (ICD9-CM Codes)				
Rheumatic heart disease (390-398)	0.0	0	0.1	[illegible]
Hypertensive disease (401-405)	0.7	18	0.6	[illegible]
Ischemic heart disease (410-414)	0.4	11	0.6	12
Other cardiac diseases (415-429)	0.9	22	1.0	20
Cerebrovascular disease (430-438)	0.2	6	0.2	4
Vascular disease (440-454)	0.6	15	0.5	10
Any of above (390-454)	2.7	67	2.7	53
Site of Surgery				
Heart valves and septum (35)	<0.1	1	0.0	0
Cardiac vessels, including CABG[a] (36)	0.2	4	0.3	5
Other cardiac sites (37)	0.3	8	0.3	6
Vascular, excluding CABG (38-39)	0.6	15	0.4	8
Any of above (35-39)	1.0	25	0.9	18

[a] CABG = coronary artery bypass grafting.

Table 9.3 Percent and Number of Vietnam and Non-Vietnam Veterans With Self-Reported Cardiovascular Symptoms in Past Year

	Vietnam		Non-Vietnam	
Cardiovascular Symptom	%	No.	%	No.
Chest pain with exertion	7.3	181	5.2	102
Rapid heart beating	11.9	295	8.6	170
Fainting	2.1	52	1.9	38
Difficulty breathing at night	4.1	103	3.8	76
Leg pain with exercise	2.8	69	1.5	29
Any of above	21.4	532	15.8	311

Table 9.4 Percent and Number of Vietnam and Non-Vietnam Veterans Reporting Current Cardiovascular Problems[a]

	Vietnam		Non-Vietnam	
Condition (ICD9-CM Codes)	%	No.	%	No
Rheumatic heart disease (390-398)	0.1	2	0.1	1
Hypertensive disease (401-405)	6.2	155	7.0	138
Ischemic heart disease (410-414)	0.2	5	0.3	6
Other cardiac diseases (415-429)	1.1	27	0.8	16
Cerebrovascular disease (430-438)	<0.1	1	0.2	4
Vascular disease (440-454)	0.5	13	0.3	5
Any cardiovascular condition (390-454)	8.0	198	8.3	164

[a] From medical history: conditions that the veterans would like to discuss with a physician or that were currently being treated.

In each group hypertension was the most commonly cited problem. Only a handful of veterans in either group considered the two other cardiovascular conditions of particular interest in this study (ischemic heart disease and peripheral vascular disease) to be current problems. Veterans in the two cohorts reported these three conditions with similar frequency.

About 5% of the Vietnam and non-Vietnam veterans were currently using cardiovascular medications (Table 9.5). Use of any antihypertensive medication (as well as the distribution

Table 9.5 Percent and Number of Vietnam and Non-Vietnam Veterans Reporting Current Use of Cardiovascular Medications, by Type of Medication

Type of Medication	Vietnam		Non-Vietnam	
	%	No.	%	No.
Antihypertensive				
Diuretic	2.5	61	2.1	41
Beta blockers	1.4	34	0.9	18
Other antihypertensives[a]	2.3	56	2.3	45
Any antihypertensive[b]	4.9	121	4.7	92
Other				
Nitrates and other antianginals	0.4	11	0.4	8
Antiarrhythmics	0.4	9	0.1	2
Cardiac glycosides	0.2	6	0.2	3
Miscellaneous	0.2	5	0.2	3
Any of Above	5.4	135	5.0	99

[a] Includes combination diuretic/beta blocker medications and beta blockers whose sole indicated use is as an antihypertensive medication.
[b] Includes diuretics, beta blockers, and other antihypertensive medications.

of the use of specific types of medications) was similar in both cohorts. Similar proportions, less than 1%, of veterans in each group said that they were using nitrates or other medications for the treatment of angina.

9.3.2 Physical Examination

Abnormal heart sounds, the most common finding in the physical examination of the cardiovascular system, were noted for a similar percentage of veterans, about 12%, in each cohort (Table 9.6). The prevalence of specific types of heart sounds, such as systolic or diastolic murmurs, gallop sounds, or systolic clicks, was the same for both groups. Results of the physical examination of the vascular system showed few differences between cohorts in the prevalence of bruits—carotid, abdominal, or femoral. Each of these findings was noted for less than 1% of veterans in either group. Accounting for the six entry and other covariates did not affect the relative cohort differences for any of the physical examination findings.

Table 9.6 Distribution of Cardiovascular Physical Examination Findings Among Vietnam and Non-Vietnam Veterans and Odds Ratios, by Type of Finding

							Multivariate Results			
	Vietnam		Non-Vietnam		Crude Results		Model 1[a]		Model 2[b]	
Finding	%	No.	%	No.	OR	95% CI	OR	95% CI	OR	95% CI
Abnormal Carotid Pulses	0.2	6	0.2	3	—	—	—	—	—	—
Carotid Bruits	0.2	4	0.3	5	—	—	—	—	—	—
Any Abnormal Heart Sounds	12.8	319	12.4	245	1.0	0.9-1.2	1.0	0.9-1.3	1.1	0.9-1.3
Any heart murmur	8.8	219	8.8	173	1.0	0.8-1.2	1.1	0.8-1.3	1.1	0.9-1.3
Systolic	8.5	211	8.6	169	1.0	0.8-1.2	1.0	0.8-1.3	1.1	0.8-1.3
Diastolic	0.5	12	0.3	6	1.6	0.6-4.2	—	—	—	—
Gallop	3.1	78	3.2	62	1.0	0.7-1.4	1.0	0.7-1.4	0.9	0.7-1.4
Systolic click	2.2	55	2.0	39	1.1	0.7-1.7	1.1	0.7-1.7	1.2	0.7-1.8
Abdominal Aortic Bruit	<0.1	1	0.1	1	—	—	—	—	—	—
Femoral Bruit	0.2	6	0.1	1	—	—	—	—	—	—

[a] Model 1 contains the six entry characteristics.
[b] Model 2 contains the six entry characteristics and alcohol consumption, smoking status, body mass index, occupational herbicide exposure, family history of myocardial infarction, and examiner.

9.3.3 Blood Pressure

For systolic blood pressure, the unadjusted geometric means were similar for the two cohorts (Table 9.7). Results were unchanged after being adjusted for entry characteristics or other covariates (alcohol consumption, current smoking status, body mass index, occupational exposure to herbicides, family history of hypertension, and technician). For diastolic blood pressure, the unadjusted geometric mean was significantly higher for Vietnam veterans, but the percent difference was only 0.8%. This difference decreased and was no longer statistically significant after the results were adjusted for entry characteristics. The group difference for this measure was even smaller after other covariates had been accounted for.

The percentages of Vietnam and non-Vietnam veterans who met the definition for hypertension (diastolic pressure ≥90 mm Hg, systolic pressure ≥140 mm Hg, or current use of antihypertensive medications) were, respectively, 33.5% and 31.4%, for an unadjusted OR of 1.1 (95% CI = 1.0-1.3). After the results were adjusted for entry characteristics, the OR was 1.1 (95% CI = 0.9-1.2). After they were further adjusted for other covariates (described in the preceding paragraph), the OR for hypertension was 1.0. Results were also unchanged when more restrictive cutoff values (diastolic pressure ≥95 mm Hg, systolic pressure ≥160 mm Hg, current medication use) were used to define hypertension (NCHS, 1986).

9.3.4 Doppler Measurement of Peripheral Pulses

The geometric mean resting index (ratio of ankle-to-brachial blood pressure) was the same, 1.1, for both cohorts, and results were unchanged after entry or other covariates had been taken into account. The prevalence of altered peripheral arterial hemodynamics (APAH) in each group was low, with less than 5% of veterans in each group meeting the criteria for this outcome. The absolute difference between cohorts for APAH was about 1% (Table 9.8). When APAH was redefined by using a resting index <0.9 as one of the three criteria (the other two being an absent posterior tibial pulse or a femoral bruit), the prevalence of this condition was less in both cohorts (1.3% for Vietnam versus 1.1% for non-Vietnam veterans), and the odds ratio was smaller.

9.3.5 Electrocardiograms

A similar proportion of veterans, about 14%, in each cohort had positive electrocardiogram (ECG) findings (Table 9.9). These findings included bradycardia, tachycardia, atrial arrhythmias, and extrasystoles. Less than 3% of Vietnam or non-Vietnam veterans had conduction abnormalities, primarily nonspecific intraventricular conduction delays. Few veterans had ECG patterns of ischemia or infarction. Few participants were found to have ECG evidence of chamber hypertrophy, but odds ratios for these types of abnormalities were all greater

Table 9.7 Means and Percent Difference Between Means for Systolic and Diastolic Blood Pressure of Vietnam and Non-Vietnam Veterans

					Multivariate Results			
	Crude Geometric Mean		Crude Results		Model 1[a]		Model 2[b]	
Blood Pressure	Vietnam	Non-Vietnam	% Diff	95% CI	% Diff	95% CI	% Diff	95% CI
Systolic, mm Hg	123.0	122.8	0.2	-0.4, 0.8	0.2	-0.4, 0.8	-0.1	-0.6, 0.5
Diastolic, mm Hg	83.9	83.3	0.8	0.1, 1.4	0.6	-0.1, 1.3	0.4	-0.3, 1.1

[a] Model 1 contains the six entry characteristics.

[b] Model 2 contains the six entry characteristics and alcohol consumption, smoking status, body mass index, occupational herbicide exposure, family history of hypertension, and technician.

Table 9.8 Distribution of Altered Peripheral Arterial Hemodynamics (APAH)[a] Among Vietnam and Non-Vietnam Veterans and Odds Ratios

	Vietnam		Non-Vietnam		Crude Results		Multivariate Results			
							Model 1[b]		Model 2[c]	
Condition	%	No.	%	No.	OR	95% CI	OR	95% CI	OR	95% CI
APAH	4.7	116	3.6	71	1.3	1.0-1.8	1.2	0.9-1.7	1.2	0.9-1.7

[a] Resting index (ankle-to-brachial blood pressure ratio) <1.0, an absent posterior tibial pulse waveform, or a femoral bruit.
[b] Model 1 contains the six entry characteristics.
[c] Model 2 contains the six entry characteristics and alcohol consumption, smoking status, body mass index, occupational herbicide exposure, family history of ischemic heart disease, and technician.

Table 9.9 Distribution of Electrocardiogram Findings Among Vietnam and Non-Vietnam Veterans and Odds Ratios, by Type of Finding

	Vietnam		Non-Vietnam		Crude Results		Multivariate Results			
							Model 1[a]		Model 2[b]	
Electrocardiogram Finding	**%**	**No.**	**%**	**No.**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Any Finding	14.3	357	13.9	274	1.0	0.9-1.2	1.1	0.9-1.3	1.1	0.9-1.3
Conduction Delays										
Right bundle branch block (BBB)[c]	0.5	12	0.7	13	0.7	0.3-1.6	0.8	0.3-1.8	—	—
Left BBB[d]	0.6	14	0.6	11	1.0	0.5-2.2	1.1	0.5-2.4	—	—
Bifascicular block	0.1	2	0.0	0	—	—	—	—	—	—
Any BBB	0.9	23	1.2	24	0.8	0.4-1.3	0.8	0.4-1.4	—	—
NSIVCD[e]	1.5	38	1.5	29	1.0	0.6-1.7	1.2	0.7-2.0	1.1	0.7-1.9
Any BBB or NSIVCD	2.4	61	2.6	52	0.9	0.6-1.3	1.0	0.7-1.5	1.0	0.7-1.5
Ischemia/Infarction										
Ischemia	0.8	21	0.7	13	1.3	0.6-2.6	1.3	0.6-2.8	—	—
Infarction	1.2	29	1.1	22	1.0	0.6-1.8	1.0	0.6-1.8	1.0	0.6-1.9
Ischemia or infarction	1.9	48	1.8	35	1.1	0.7-1.7	1.1	0.7-1.7	1.1	0.7-1.8
NSSTTW changes[f]	4.6	114	5.0	99	0.9	0.7-1.2	0.9	0.7-1.2	0.9	0.7-1.2
Chamber Hypertrophy										
Atrial	0.5	13	0.4	7	1.5	0.6-3.7	—	—	—	—
Right ventricular	0.2	4	0.1	2	1.6	0.3-8.7	—	—	—	—
Left ventricular	1.6	41	1.0	20	1.6	1.0-2.8	1.8	1.0-3.3	1.8	1.0-3.2
Biventricular	0.1	2	0.1	1	1.6	0.1-17.5	—	—	—	—
Any ventricular hypertrophy	1.9	47	1.2	23	1.6	1.0-2.7	1.8	1.1-3.1	1.8	1.1-3.1

[a] Model 1 contains the six entry characteristics.
[b] Model 2 contains the six entry characteristics and alcohol consumption, smoking status, body mass index, and family history of ischemic heart disease.
[c] Includes incomplete right BBB.
[d] Includes left anterior fascicular block.
[e] NSIVCD = nonspecific intraventricular conduction delay.
[f] NSSTTW = nonspecific ST and T wave.

than 1.0. The most prevalent type of chamber hypertrophy was left ventricular. After the results were adjusted for the six entry characteristics, the OR for left ventricular hypertrophy (LVH) was 1.8, and after they were adjusted for other covariates, including body mass index and hypertension, the OR was the same. Among the veterans with LVH, almost all in both groups had ECG tracings that met only the voltage criteria for LVH; two veterans, one Vietnam and one non-Vietnam, had LVH with repolarization changes (depressed ST segments with flattened or inverted T waves).

9.4 DISCUSSION

In the examination of the cardiovascular system, we focused on three health outcomes that we reasoned might be more prevalent among Vietnam veterans: peripheral vascular disease, hypertension, and ischemic heart disease. We selected these outcomes because results of previous studies have suggested that they may be associated with exposure to dioxin and dioxin-containing herbicides and because they may be a consequence of the psychological stress that Vietnam veterans have experienced as a result of their wartime service. As noted in Chapters 5 through 8 in this volume, Vietnam veterans reported more symptoms and past medical diagnoses than non-Vietnam veterans, yet results of objective medical examinations showed few current differences in the physical health of the two groups. We found a similar pattern in the results of our analysis of cardiovascular conditions.

There is little evidence to suggest that Vietnam veterans now have more peripheral vascular disease than non-Vietnam veterans. The Vietnam veterans reported more past physician-diagnoses of this disease, as well as more previous hospitalizations and surgical procedures for vascular disorders. They also noted having the symptom of claudication (exertional leg pain relieved by rest) more frequently. Yet, upon physical examination few veterans in either group had objective signs, such as bruits, of peripheral vascular disease. Further, retinal findings (described more fully in Chapter 12) noted during the ophthalmoscopic examination—such as arteriolar spasm and arteriovenous nicking—were uncommon in the two cohorts. Finally, when the veterans were examined with objective Doppler techniques, findings for the two groups were similar.

In this age group, the 30s to mid-40s, it is not surprising that, in each cohort, hypertension was the most frequently noted current cardiovascular problem. Again, the two groups were similar in the prevalence of this health outcome. Hypertension, defined by using standard criteria (NCHS, 1986), was found in about one-third of the veterans in each cohort. Both systolic and diastolic blood pressure measurements had similar distributions in the two cohorts. The overall frequency of antihypertensive medication use was also the same among Vietnam and non-Vietnam veterans.

Few participants in the medical examinations had any objective evidence of ischemic heart disease. Less than 1% in either group reported being told by a physician that they had angina or myocardial infarction. More Vietnam veterans reported having exertional chest pain, as well as other symptoms, during the year preceding the examination, but these symptoms are nonspecific and can be produced by a variety of noncardiac conditions. These symptoms could have been evaluated further only with more extensive testing (for example, the treadmill exercise test), which was beyond the scope of the study design. In any event, according to resting ECGs, the prevalence of ischemia or infarction patterns was similar, less than 2%, for both groups.

In this study, we analyzed numerous measures of cardiovascular health, but the results show relatively few differences between cohorts. One unexpected result was the higher prevalence of left ventricular hypertrophy (LVH), found on ECG examination, among Vietnam veterans. This finding is not explained by cohort differences in hypertension or body mass index, two factors that may be related to left ventricular enlargement. This condition is also a recognized consequence of both isometric and endurance exercise (Messerli, 1983). In the Vietnam Experience Study (VES) we did not gather information on physical activity; therefore, we cannot determine whether differences in cardiovascular fitness account for this finding. That the Vietnam cohort may have had somewhat better cardiovascular fitness is given some support by our finding lower mortality from cardiovascular diseases among Vietnam veterans than among non-Vietnam veterans (Centers for Disease Control Vietnam Experience Study, 1987).

The association between military service and LVH cannot be easily explained on the basis of available information. It would be speculative to suggest that, as a by-product of some kind of selection process that took place before the veterans were assigned to duty, the Vietnam veterans differed from non-Vietnam veterans in physical fitness and that these differences account for the LVH found in the ECG examinations. Furthermore, the large number of tests we performed complicates our interpretation of this difference. Including so many health outcome variables increased the pprobability of spurious or chance associations. In any event, this ECG abnormality was rare, found in <2% of the veterans in either group, and the absolute difference between cohorts was <1%. In addition, the prevalence of LVH among Vietnam veterans is about what would be expected among men of this age on the basis of results of other studies. In the Framingham study, the prevalence of LVH (without repolarization changes) among men of similar age was about 1.8% (Kannel *et al.*, 1969).

In this epidemiologic study, the possibility that biases in design or conduct may have affected the cardiovascular findings needs to be considered. Information or detection bias is one possible concern. Certainly, some of the increased prevalence of self-reported conditions among Vietnam veterans could have been due to either their enhanced recall of these conditions compared with non-Vietnam veterans or to differences in the health-care-seeking practices of the two groups. Such biases, however, should have had little effect on the examination findings. The examiners and technicians did not know the participants' cohort status, nor were they allowed to take any "history" from the participants as they conducted the examinations.

Selection bias is another concern, particularly since the participation rate for the medical examinations was lower for non-Vietnam veterans than for Vietnam veterans. However, in Chapter 3 we examined the reasons for nonparticipation (and the characteristics that influenced participation in the medical examinations) and found little evidence that selection bias influenced our study results.

For the three conditions of interest specified before the analysis—peripheral vascular disease, hypertension, and ischemic heart disease—the study findings are not likely to be explained on the basis of confounding by other factors. Risk factors for these conditions include age, sex, race, smoking, obesity, alcohol use, and family history. As detailed in Chapter 3, in relation to these health-influencing characteristics, the two cohorts were similar. Furthermore, results of additional analyses, adjusted for the effects of these characteristics, did not change the study findings.

Several cardiovascular risk factors—hypertension, increased cholesterol, elevated LDL/HDL ratio, and diabetes—were also considered health outcomes that may be related to service in Vietnam. As stated earlier in this chapter, the prevalence of hypertension was the same for the two cohorts, and, as shown in Chapter 6, Vietnam and non-Vietnam veterans had similar levels of total cholesterol, high-density lipoprotein (HDL) cholesterol, and total triglycerides. As noted in Chapter 11, the two cohorts were also similar in measures of glucose and in the prevalence of diabetes. As expected, given the similarity between the Vietnam and non-Vietnam groups in these risk factors, additional analyses in which these factors were accounted for did not change the results.

Some investigators have suggested that psychological stress plays a role in the development of both hypertension and ischemic heart disease (Kasl, 1984; Shapiro, 1978; Syme and Torfs, 1978). Vietnam veterans who were engaged in combat might be at greater risk for these diseases because they experienced higher levels of stress than those who were not engaged in combat. Yet, in our study, the results gave little indication that combat exposure was a risk factor for cardiovascular disease. The relative risk for hypertension was the same regardless of military occupational specialty (MOS). Those with a tactical MOS included infantrymen, armored vehicle crewmen, artillery crewmen, and combat engineers. These results are presented in Chapter 14, where the issue of combat experience and physical health is discussed in detail.

In summary, Vietnam and non-Vietnam veterans differed little in the prevalence of peripheral vascular disease, hypertension, or ischemic heart disease. For unknown reasons, left ventricular hypertrophy, as evidenced on electrocardiograms, was more common among Vietnam veterans, but this finding was rare, affecting less than 2% of the veterans, and the absolute difference between cohorts was less than 1%. With this one exception, at the time of the medical examinations, the cardiovascular status of the two groups was similar.

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CHAPTER 10

Respiratory System

10. RESPIRATORY SYSTEM

10.1 INTRODUCTION

In this chapter we present our evaluation of the respiratory system. In general, little is known about the long term effects of wartime service or exposure to dioxin-containing herbicides on respiratory function. Nonetheless, as in other parts of this study, before we began our analysis, we identified conditions that might be expected to be more prevalent among Vietnam veterans. On the basis of our review of the scientific literature, we hypothesized that Vietnam veterans would be more likely than non-Vietnam veterans to have (1) evidence of *Mycobacterium tuberculosis* infection and (2) diminished pulmonary function. The rationale for selecting these two conditions for more detailed analysis follows.

During the Vietnam conflict, acute respiratory infection was one of the main medical conditions for which U.S. Army personnel were hospitalized. Between 1965 and 1970, annual hospitalization rates ranged from 31 to 47 admissions per 1,000 servicemen (Neel, 1973). However, since most of these respiratory infections had short incubation periods and were self-limited, residual effects from these previous infections would be unusual.

Tuberculosis, on the other hand, may be characterized as a chronic infection with a long latency period from exposure to clinical disease. Since tuberculosis infection is endemic in Southeast Asia, health personnel were concerned about tuberculosis among the troops in Vietnam. Prevalence surveys indicated that for nearly all Vietnamese adults, tuberculin skin tests were positive (Houk, 1967). In 1968, results of a chest roentgenogram survey of Vietnamese civilians showed that nearly a third of those over 15 years of age had evidence of active pulmonary tuberculosis (Cowley, 1970). Further, skin test conversion (from negative to positive) rates for U.S. troops stationed in Vietnam seemed to be higher than rates for servicemen stationed elsewhere. Among servicemen evacuated from Vietnam for other medical conditions and skin tested, the conversion rate was 4.7% per year compared with annual rates of 1.0% and 2.5% among Army personnel stationed, respectively, in the United States and Europe (Guiton and Barrett, 1982).

Researchers have suggested that dioxin and phenoxyherbicides cause a wide variety of health effects (Sterling and Arundel, 1986), but they have only rarely associated exposure to these substances with respiratory effects (Webb *et al.*, 1986). However, in one study of chemical workers involved in the industrial production of 2,4,5-trichlorophenoxyacetic acid (2,4,5-T), investigators found that current smokers who had been exposed to the compound had diminished pulmonary function—both forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV1)—compared with current smokers who had not been exposed (Suskind and Hertzberg, 1984). In contrast, in the U.S. Air Force Study of personnel involved in the aerial spraying of Agent Orange in Vietnam, investigators found no differences in pulmonary function between the exposed and comparison groups in either the baseline or the first follow-up examinations (Lathrop *et al.*, 1984, 1987).

10.2 METHODS

In this chapter, we present five types of data: (1) information from the medical history interview; (2) findings from the physical examination; (3) results of chest roentgenograms; (4) results of tuberculin skin testing done with the Multitest cell-mediated immunity (CMI) delayed hypersensitivity test; and (5) values from spirometric tests of pulmonary function. During the study all examiners and technicians were unaware of which cohort the veterans were in.

10.2.1 Medical History and Physical Examination

All participants completed standardized medical history interviews, as described in Chapter 2. Board-certified internists conducted standardized physical examinations, using techniques that are also described in Chapter 2.

10.2.2 Chest Roentgenograms

Standard 14- by 17-inch posteroanterior chest roentgenograms were obtained for all study participants. Board-certified radiologists read the x-ray films and classified them as normal or abnormal. For each abnormal film, the radiologist recorded the specific findings, up to a maximum of five, on the data collection form. For data entry and subsequent analysis, the findings were abstracted according to location and disease codes from the *Index for Roentgen Diagnoses* (American College of Radiology, 1975).

For quality control, during each examination day one x-ray film was randomly selected for an independent rereading by another board-certified radiologist who was unaware of the first radiologist's interpretation. The percent agreement between radiologists (for classifying the x-ray films as normal or abnormal) was 81.2% and 78.6% for Vietnam and non-Vietnam veterans' films, respectively. We present other assessments of data quality in Supplement B (Medical and Psychological Data Quality).

10.2.3 Tuberculin Skin Testing

As noted in Chapter 8, one of the seven antigens in the cell-mediated immunity (CMI) test was the same old tuberculin antigen used in the Monovacc-tuberculin applicator (Merieux Institute) (Kniker *et al.*, 1984). We included the CMI test in the medical examination so that we could evaluate cell-mediated immunity (specifically the prevalence of anergy) in the two cohorts; we did not intend for the test to be a substitute for a standard intradermal 5 TU PPD test. The CMI test was not designed to be a screening test for past *M. tuberculosis* infection, so we limited our analysis to comparing the distribution, in the two cohorts, of values for skin induration to the tuberculin antigen.

The CMI was applied to the volar aspect of the participant's forearm, and, 48 hours later, trained technicians measured the amount of induration to each antigen. A second technician, unaware of the first technician's measurements, remeasured the indurations of a random sample of about 5% of the veterans. For the tuberculin antigen, the interclass correlation coefficients, as a measure of variability among the six technicians "reading" this test, were 0.66 and 0.61 for the Vietnam and non-Vietnam veterans, respectively.

10.2.4 Pulmonary Function Tests

In developing procedures for testing pulmonary function, we followed the recommendations of the American Thoracic Society (Gardner, 1979). Each participant underwent spirometric testing to measure his forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV1). Flow-volume loops were recorded with a MedScience 570 Wedge Spirometer. The spirometer was calibrated weekly by using a 3 liter calibrated syringe. To calculate the FVC and FEV1, we used a Digital DEC Writer III to transmit analog data from the spirometer to the pulmonary function computer. At the beginning of each day the atmospheric pressure and temperature were determined and entered into the computer.

All participants were tested under the direction of trained and experienced technicians. First, the participant performed one slow vital capacity test. After his breathing pattern had returned to normal, he then performed a minimum of three forced expiratory maneuvers. The technician assessed adequacy of effort by using LED ladder lights on the spirometer. If the technician judged the participant's effort to be less than optimal, the participant performed additional trials. If, after eight maneuvers, the participant had not shown adequate effort, his testing was terminated, and he was retested later.

The pulmonary function computer selected the single curve with the largest sum of FVC and FEV1 as the best effort. The flow volume curve for the best effort was printed, and the technician reviewed the curve on the printout. If the effort was judged unsatisfactory, the test was repeated and another printout was generated. Test values obtained during the best effort, corrected for atmospheric pressure and temperature, were recorded for data entry and subsequent analysis.

For quality control, on each examination day one randomly selected participant repeated the pulmonary function tests under the direction of a different technician. Analysis of these paired observations showed that reproducibility was good. Overall, the coefficients of variation for FVC and FEV1 were 4.0% and 4.4%, respectively, and they did not vary by cohort status.

We used multiple linear regression to develop prediction equations for expected values of FVC and FEV1, based upon age, race, and height. We defined the normal referent group as those veterans in both cohorts combined who had never smoked and who had never been told by a physician that they had asthma, chronic bronchitis, or emphysema. The mean age, height, and ethnic composition of the referent group was similar to that of the entire examination sample. The values for coefficients derived in our regression analyses were similar to those previously reported (Morris *et al.*, 1971).

For the categorical analysis of cohort differences, we classified individual test results by two methods: the percent-predicted method and the residual method (Hankinson, 1986; Miller, 1986; Morris *et al.*, 1971). Since the methods produced similar results, we present findings for the percent-predicted method only. The following results were considered abnormal: an observed value for FVC or FEV1 that was ≤80% of its respective predicted value or a FEV1/FVC percentage ratio <70%.

10.2.5 Statistical Methods

We used the analytical methods described in Chapter 2. Pulmonary function test results were treated as both continuous and categorical (normal/abnormal) outcome variables, and thus were analyzed by multiple linear and logistic regression, respectively.

In the Model 2 regression analyses we used three covariates (defined in Chapter 2): current alcohol consumption, body mass index, and self-reported occupational exposure to herbicides. In addition, results were either stratified by current smoking status or adjusted for this covariate during multivariate analyses.

10.3 RESULTS

10.3.1 General Medical History

Pneumonia, reported by similar proportions of Vietnam (8.0%) and non-Vietnam (7.1%) veterans, was the most frequently reported respiratory condition that had been diagnosed by a physician since the veterans were discharged (Table 10.1). Only two Vietnam and four

Table 10.1 Percent and Number of Vietnam and Non-Vietnam Veterans Reporting Physician-Diagnosed Respiratory Conditions Since Discharge

Condition	Vietnam %	Vietnam No.	Non-Vietnam %	Non-Vietnam No.
Tuberculosis	0.1	2	0.2	4
Pneumonia	8.0	198	7.1	140
Asthma	1.1	27	1.4	28
Chronic bronchitis	0.9	23	0.4	8
Emphysema	0.6	16	0.5	9

non-Vietnam veterans reported past diagnoses of tuberculosis. Few veterans in either cohort reported having asthma or emphysema diagnosed since discharge. The largest relative difference in physician-diagnosed conditions was for chronic bronchitis, but this diagnosis was also rare, being reported by <1% of veterans in either group.

Overall, few Vietnam (4.6%) or non-Vietnam (3.1%) veterans had been hospitalized for respiratory conditions since their discharge (Table 10.2). The most common reasons for hospitalization were for treatment of upper respiratory diseases, pneumonia, and influenza. One Vietnam veteran was hospitalized for tuberculosis. No hospitalizations for intrathoracic malignancies were reported. A similar proportion, about 1%, of Vietnam and non-Vietnam veterans reported surgery involving the respiratory system, and the anatomic sites of these procedures were comparable for the two groups.

Although the two groups were similar regarding past respiratory conditions, the Vietnam veterans were more likely to report having respiratory symptoms during the year preceding the examination (Table 10.3). Overall, about 22% of Vietnam veterans and 18% of non-Vietnam veterans reported having at least one respiratory symptom during the year. Vietnam veterans reported most of the specific symptoms—including shortness of breath, persistent coughing, and wheezing—more frequently than non-Vietnam veterans. The largest relative difference was for shortness of breath, which 5.7% of Vietnam and 3.6% of non-Vietnam veterans reported.

Table 10.2 Percent and Number of Vietnam and Non-Vietnam Veterans Reporting Respiratory Hospitalizations and Surgical Procedures Since Discharge

	Vietnam %	Vietnam No.	Non-Vietnam %	Non-Vietnam No
Reason for Hospitalization (ICD9-CM Codes)				
Pulmonary tuberculosis (010-012)	<0.1	1	0.0	0
Intrathoracic malignancy (162-165)	0.0	0	0.0	0
Upper respiratory disease (460-466)	1.3	33	0.8	15
Pneumonia and influenza (480-487)	2.0	49	1.4	28
Asthma and COPD[a] (490-496)	0.4	11	0.3	6
Pneumoconioses (500-508)	<0.1	1	0.0	0
Empyema, abcess or pleural disease (510-514)	0.7	18	0.6	11
Other pulmonary diseases (515-519)	0.3	8	0.2	5
Any of above (010-012, 460-519)	4.6	115	3.1	61
Site of Surgery				
Larynx and trachea (30-31)	0.2	4	0.3	5
Lung and bronchus (32-33)	0.2	6	0.4	8
Chest wall and pleura (34)	0.6	15	0.5	10
Any of above (30-34)	1.0	24	1.1	22

[a] COPD = chronic obstructive pulmonary disease.

Table 10.3 Percent and Number of Vietnam and Non-Vietnam Veterans With Self-Reported Respiratory Symptoms in Past Year

	Vietnam		Non-Vietnam	
Respiratory Symptom	%	No.	%	No.
Shortness of breath	5.7	142	3.6	72
Persistent cough	11.0	274	9.2	182
Coughing spells	11.1	277	9.6	189
Cough with phlegm	8.7	216	7.0	137
Wheezing	2.5	63	2.1	41
Cough blood	1.1	27	1.5	29
Any of above	22.1	551	18.0	355

Only about 2% of the participants in either group stated that they had current respiratory problems (Table 10.4). The types of problems were similar among Vietnam and non-Vietnam veterans. None of the veterans in either cohort reported tuberculosis or intrathoracic malignancies as current health concerns.

10.3.2 Physical Examination

During the physical examination of the respiratory system, physicians noted few abnormalities for either Vietnam or non-Vietnam veterans. At auscultation, only 2.5% of the Vietnam and 2.6% of non-Vietnam veterans had diminished breath sounds (OR=1.0). Similarly, only 2.6% Vietnam and 2.0% non-Vietnam veterans had adventitial lung sounds (crackles or wheezes) (OR=1.3, 95% CI=0.9-1.9). Results of these and other physical examination items are listed in Appendix Table C.1.

10.3.3 Chest Roentgenograms

The proportions of Vietnam (22.4%) and non-Vietnam (20.5%) veterans with positive findings on the chest roentgenogram examination were comparable, as were the types of findings noted (Table 10.5). Almost all of the spinal findings were thoracic scoliosis. Most of the other skeletal findings were either congenital anomalies or healed fractures of the clavicles or ribs. About 1% of the veterans in each group had cardiac abnormalities. These included 12 Vietnam veterans and 6 non-Vietnam veterans with left ventricular enlargement (or nonspecific cardiomegaly).

The most prevalent types of findings were those of the lung, mediastinum, and pleura, which were noted for 16.0% of Vietnam and 14.1% of non-Vietnam veterans Specific pulmonary findings are characterized in Table 10.6. Of these, pulmonary nodules were the

Table 10.4 Percent and Number of Vietnam and Non-Vietnam Veterans Reporting Current Respiratory Problems[a]

	Vietnam		Non-Vietnam	
Condition (ICD9-CM Codes)	%	No.	%	No.
Pulmonary tuberculosis (010-012)	<0.1	1	0.0	0
Intrathoracic malignancy (162-165)	0.0	0	0.0	0
Upper respiratory disease (460-466)	1.0	24	1.0	19
Pneumonia and influenza (480-487)	0.1	2	0.1	1
Asthma and COPD[b] (490-496)	0.6	15	1.1	22
Pneumoconioses (500-508)	<0.1	1	0.0	0
Empyema, abcess or pleural disease (510-514)	0.1	2	0.1	1
Other pulmonary diseases (515-519)	0.4	9	0.2	4
Any respiratory condition (010-012, 460-519)	2.2	54	2.3	46

[a] From medical history: conditions that the veteran would like to discuss with a physician or that were currently being treated.

[b] COPD = chronic obstructive pulmonary disease.

Table 10.5 Distribution of Chest Roentgenogram Abnormalities Among Vietnam and Non-Vietnam Veterans and Odds Ratios, by Location of Abnormality

		Vietnam		Non-Vietnam		Crude Results		Multivariate Results: Model 1[a]		Multivariate Results: Model 2[b]	
Location of Abnormality	Location Codes[c]	%	No.	%	No.	OR	95% CI	OR	95% CI	OR	95% CI
Spinal	30-39	3.2	79	3.5	68	0.9	0.7-1.3	1.0	0.7-1.3	1.0	0.7-1.4
Other skeletal	40-49	4.1	103	3.6	70	1.2	0.9-1.6	1.1	0.8-1.5	1.0	0.8-1.4
Cardiac	50-59	1.0	26	0.9	18	1.1	0.6-2.1	1.3	0.7-2.5	–	–
Lung, mediastinal, and pleural	60-69	16.0	399	14.1	277	1.2	1.0-1.4	1.1	1.0-1.4	1.1	1.0-1.4
Gastrointestinal	70-79	0.4	11	0.1	2	4.4	1.0-19.7	–	–	–	–
Any abnormality	30-79	22.4	557	20.5	404	1.1	1.0-1.3	1.1	1.0-1.3	1.1	0.9-1.3

[a] Model 1 contains the six entry characteristics.
[b] Model 2 contains the six entry characteristics and smoking status, alcohol consumption, body mass index, occupational exposure to herbicides, and radiologist.
[c] Location codes from *Index for Roentgen Diagnoses.*

Table 10.6 Distribution of Lung, Mediastinal, and Pleural Abnormalities on Chest Roentgenograms Among Vietnam and Non-Vietnam Veterans and Odds Ratios, by Type of Abnormality

		Vietnam		Non-Vietnam		Crude Results		Multivariate Results: Model 1[a]		Multivariate Results: Model 2[b]	
Type of Abnormality	Disease Codes[c]	%	No.	%	No.	OR	95% CI	OR	95% CI	OR	95% CI
Normal Variants	10-19	0.6	15	0.8	15	0.8	0.4-1.6	0.9	0.4-1.8	–	–
Infection	20-29	7.7	191	6.4	127	1.2	1.0-1.5	1.2	0.9-1.5	1.2	0.9-1.5
Tuberculosis	23	0.4	9	0.3	6	1.2	0.4-3.3	–	–	–	–
Pulmonary nodules	28	7.2	180	6.2	122	1.2	0.9-1.5	1.2	0.9-1.5	1.2	0.9-1.5
Neoplasm or Neoplastic-Like Conditions	30-39	0.9	23	0.4	8	2.3	1.0-5.1	2.1	0.9-4.7	–	–
Traumatic Conditions	40-49	1.2	29	1.0	19	1.2	0.7-2.2	1.1	0.6-2.1	–	–
Metabolic, Endocrine or Toxic Conditions	50-59	0.0	0	0.0	0	–	–	–	–	–	–
Systemic Disorders	60-69	0.0	0	0.0	0	–	–	–	–	–	–
Miscellaneous	70-79	4.5	113	3.8	75	1.2	0.9-1.6	1.2	0.9-1.6	1.2	0.9-1.6
Calcifications	80-89	3.5	87	3.2	63	1.1	0.8-1.5	1.1	0.8-1.5	1.0	0.7-1.5
Other	90-99	0.8	19	0.4	8	1.9	0.8-4.3	2.0	0.8-4.7	–	–

[a] Model 1 contains the six entry characteristics.
[b] Model 2 contains the six entry characteristics and smoking status, alcohol consumption, body mass index, occupational exposure to herbicides, and radiologist.
[c] Disease codes from *Index for Roentgen Diagnoses.*

most common abnormality noted in each cohort. Few Vietnam or non-Vietnam veterans had radiographic evidence of tuberculosis. More Vietnam than non-Vietnam veterans had pulmonary findings categorized as neoplasms or neoplastic-like conditions. Most of this increase consisted of a larger number of Vietnam veterans (15 versus 3 non-Vietnam veterans) with blebs or bullae (air-filled blisters on the surface of the lung). Only one participant, a Vietnam veteran, had a finding categorized as a primary malignant tumor, and seven Vietnam and four non-Vietnam veterans had "masses of unknown etiology' (Disease Code 39).

10.3.4 Tuberculin Skin Testing

Figure 10.1 shows the distribution of the size of skin reactions to the old tuberculin antigen in the Multitest CMI test. Overall, the distributions for the Vietnam and non-Vietnam veterans are similar. Nearly two-thirds of the veterans in each group had no reaction to the antigen, and most of the positive reactions were 2 to 5 millimeters in diameter.

10.3.5 Pulmonary Function Tests

Vietnam and non-Vietnam veterans had similar mean values for each of the three pulmonary function tests—forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC), and ratio of FEV1 to FVC (FEV1/FVC)—regardless of current smoking status (Table 10.7). Results were unchanged after being adjusted for entry characteristics and other secondary covariates. The proportions of Vietnam and non-Vietnam veterans with abnormal

Figure 10.1 Distribution of Skin Reactions to Old Tuberculin Antigen Among Vietnam and Non-Vietnam Veterans

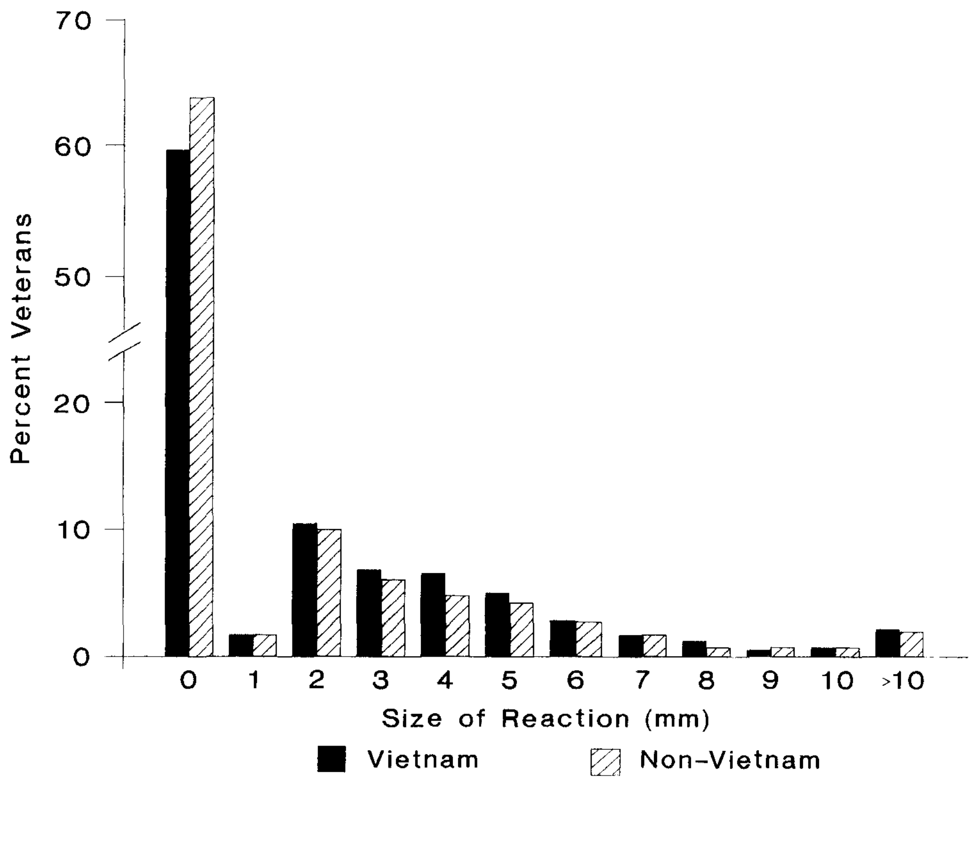

Table 10.7 Arithmetic Means and Mean Differences for Pulmonary Function Test Results Among Vietnam and Non-Vietnam Veterans, by Current Smoking Status

	Crude Arithmetic Mean		Crude Results		Multivariate Results			
					Model 1[a]		Model 2[b]	
Test[c]	Vietnam	Non-Vietnam	Diff	95% CI	Diff	95% CI	Diff	95% CI
FEV1, liters								
Nonsmokers	4.12	4.17	-0.05	-0.12, 0.03	-0.03	-0.10, 0.05	-0.03	-0.10, 0.05
Former smokers	4.17	4.13	0.04	-0.03, 0.11	0.05	-0.02, 0.12	0.05	-0.02, 0.13
Current smokers	3.91	3.89	0.02	-0.04, 0.08	0.03	-0.02, 0.09	0.03	-0.02, 0.09
FVC, liters								
Nonsmokers	5.00	5.07	-0.08	-0.17, 0.01	-0.04	-0.13, 0.05	-0.04	-0.13, 0.05
Former smokers	5.12	5.11	0.01	-0.08, 0.10	0.03	-0.05, 0.12	0.03	-0.05, 0.12
Current smokers	4.87	4.86	0.01	-0.06, 0.07	0.01	-0.06, 0.08	0.01	-0.06, 0.08
FEV1/FVC								
Nonsmokers	0.82	0.82	0.00	0.00, 0.01	0.00	0.00, 0.01	0.00	0.00, 0.01
Former smokers	0.81	0.81	0.01	0.00, 0.01	0.01	0.00, 0.01	0.01	0.00, 0.01
Current smokers	0.80	0.80	0.00	0.00, 0.01	0.01	0.00, 0.01	0.01	0.00, 0.01

[a] Model 1 contains the six entry characteristics.
[b] Model 2 contains the six entry characteristics and alcohol consumption, body mass index, and occupational exposure to herbicides.
[c] FEV1 = forced expiratory volume in 1 second; FVC = forced vital capacity; FEV1/FVC = ratio of FEV1 to FVC.

results for each pulmonary test were also similar (Table 10.8). Adjustment for entry and other characteristics did not alter these findings. Within each cohort, for current smokers compared with other veterans, mean values for FEV1, FVC, and FEV1/FVC ratio were lower and the proportions of men with abnormal results on each of the three tests were higher.

10.4 DISCUSSION

In the analysis of data on the respiratory system, we focused on two health outcomes that we reasoned might be more prevalent among Vietnam veterans. We selected these two conditions—tuberculosis and diminished pulmonary function—because researchers have suggested that they might be associated with service in Vietnam or with exposure to

Table 10.8 Percent and Number of Vietnam and Non-Vietnam Veterans With Abnormal Pulmonary Function Test Results and Odds Ratios, by Current Smoking Status

	Vietnam		Non-Vietnam		Crude Results		Multivariate Results			
							Model 1[a]		Model 2[b]	
Test[c]	%	No.	%	No.	OR	95% CI	OR	95% CI	OR	95% CI
FEV1 ≤80% Predicted										
Nonsmokers	6.0	37	5.9	32	1.0	0.6-1.7	0.9	0.5-1.5	0.9	0.5-1.5
Former smokers	6.4	46	7.6	44	0.8	0.5-1.3	0.8	0.5-1.2	0.8	0.5-1.2
Current smokers	14.8	171	16.2	138	0.9	0.7-1.1	0.9	0.7-1.1	0.9	0.7-1.3
FVC ≤80% Predicted										
Nonsmokers	6.0	37	5.0	27	1.2	0.7-2.0	1.2	0.7-2.0	1.2	0.7-2.0
Former smokers	4.8	34	5.7	33	0.8	0.5-1.3	0.8	0.5-1.3	0.8	0.5-1.3
Current smokers	9.3	107	8.8	75	1.1	0.8-1.4	1.0	0.7-1.4	1.0	0.7-1.4
FEV1/FVC % <70%										
Nonsmokers	3.1	19	3.3	18	0.9	0.5-1.8	1.0	0.5-2.0	—	—
Former smokers	5.2	37	5.5	32	0.9	0.6-1.5	0.9	0.5-1.5	0.9	0.6-1.5
Current smokers	8.4	97	8.3	71	1.0	0.7-1.4	1.0	0.7-1.4	1.0	0.7-1.4

[a] Model 1 contains the six entry characteristics.
[b] Model 2 contains the six entry characteristics and alcohol consumption, body mass index, and occupational exposure to herbicides.
[c] FEV1 = forced expiratory volume in 1 second; FVC = forced vital capacity.

phenoxyherbicides. At the time of the examination, the Vietnam and non-Vietnam veterans were similar regarding these two health outcomes and other measures of respiratory status.

The hypothesis that Vietnam veterans, who served in a country where tuberculosis is endemic among the native population, are at increased risk for this infectious disease is attractive, but there is no evidence to support it. Only a handful of Vietnam veterans, and a similar proportion of veterans who served elsewhere, have been diagnosed as having tuberculosis since they were discharged from the Army. Additionally, we found radiographic evidence of tuberculosis for only a few veterans in either cohort.

The men who participated in this study had completed their Army service 10 to 20 years earlier. Since active tuberculosis may develop from a breakdown of latent infection after an even longer time, differences between Vietnam and non-Vietnam veterans may become more apparent later. This is, however, unlikely, because the proportions of veterans who had skin reactions to the old tuberculin antigen (presumably those who are at increased risk for subsequent disease) were similar in the two groups. These skin test results should be interpreted cautiously, however, since the Multitest CMI was not designed to be a screening test for past exposure to tuberculosis. Nonetheless, these test results, combined with other findings from the medical examinations, suggest that, despite earlier concerns (Cowley, 1970), tuberculosis will not be a greater problem among Vietnam veterans than among men who served elsewhere.

Service in Vietnam was not associated with having diminished pulmonary function. We had little reason to expect that our test results would show differences between Vietnam and non-Vietnam veterans because only one report of diminished pulmonary function following exposure to phenoxyherbicides has been published (Suskind and Hertzberg, 1984). Furthermore, in studies of Vietnam veterans involved in the aerial spraying of Agent Orange, investigators found no association between pulmonary function and herbicide exposure (Lathrop *et al.*, 1984, 1987). Even if there is some relationship, the two cohorts in our study may not differ in pulmonary function because few of the study participants were heavily exposed to herbicides that contained dioxin. In a recently completed CDC comparison study of enlisted Vietnam veterans, we found that few Army ground troops had been heavily exposed to dioxin-containing herbicides (Centers for Disease Control Veterans Health Studies, in press).

The prevalence of spirometric abnormalities among veterans in this study is comparable to that found in the general population. In two separate surveys, the proportion of nonsmoking males aged 18 to 79 years with a low FVC ($\leq$80% of predicted value) ranged from 4.1% to 7.0%, and the proportion of current smokers with a low FVC ranged from 10% to 13% (Babbott *et al.*, 1980; Miller *et al.*, 1982). In our study, about 6.0% of the nonsmokers and 15% of the current smokers had low FVCs.

In summary, the current respiratory status of the Vietnam veterans was comparable to that of the non-Vietnam veterans. The Vietnam veterans reported having respiratory symptoms in the year preceding examination more frequently than did non-Vietnam veterans. Yet, when we compared the two groups on the basis of results of pulmonary function tests and chest roentgenogram findings, we found few differences between the cohorts.

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CHAPTER 11

Endocrine System

11. ENDOCRINE SYSTEM

11.1 INTRODUCTION

In this chapter we summarize the results of several laboratory tests of endocrine function and examine the prevalence of certain endocrine disorders among veterans who participated in the medical examination. Before the study we did not have any strong reasons for expecting to find major endocrinologic differences between Vietnam and non-Vietnam veterans, but we did recognize that, theoretically, two potential components of the Vietnam experience—psychological stress (both chronic and acute) and exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)—can alter endocrinologic status.

Both chronic and acute stress may cause serum cortisol levels to rise (Leedy and Wilson, 1985; Schaeffer and Baum, 1984). Stress may also decrease serum testosterone levels (Leedy and Wilson, 1985) and serum thyroxine levels (Kirkeby *et al.*, 1984). In the psychological evaluations (see Volume IV), we found that a greater proportion of Vietnam veterans were currently anxious and depressed, two recognized sequelae of chronic stress (Kellner, 1987). In addition, Vietnam veterans might have found participation in the Vietnam Experience Study (VES) at Lovelace Medical Center more acutely stressful than the comparison veterans.

Investigators have found that TCDD may affect several endocrine functions. Experimental animals fed TCDD have exhibited lowered blood glucose, decreased serum thyroxine, and increased thyroid-stimulating hormone (TSH) levels (Potter *et al.*, 1983), as well as decreased serum testosterone concentrations (Moore *et al.*, 1985). These studies, however, involved high dose exposures, so their relevance to lower levels of exposure in humans is questionable.

In the Air Force Health Study, investigators compared the health of servicemen (Ranch Hands) who had handled or sprayed Agent Orange in Vietnam with the health of Vietnam-era Air Force veterans who had not participated in defoliation activities. The participants were examined in 1982 (Lathrop *et al.*, 1984) and again in 1985 (Lathrop *et al.*, 1987). The mean for serum testosterone was higher for Ranch Hands than for the comparison group in both 1982 and 1985; otherwise, the groups were endocrinologically comparable. Measures of diabetes and serum cortisol were similar between the Ranch Hands and the comparison group. The mean for TSH was significantly higher among Ranch Hands, but similar proportions in both groups had high TSH levels (>7.5 mIU/L), and more comparison veterans were excluded from the TSH analysis because of a previous diagnosis of thyroid disease. Some Ranch Hands have substantially elevated current serum TCDD levels (Pirkle *et al.*, 1987), but these levels have not been correlated with laboratory measures of endocrine function.

On the basis of the findings discussed above, we would expect Vietnam veterans in general to be similar in endocrine function to the comparison group of veterans. Furthermore, we would expect differences—if there were any—to be stress-related, such as differences in serum cortisol, testosterone, or thyroxine levels.

11.2 METHODS

The three sources of information for this chapter are (1) self-reported medical histories, (2) general physical examinations, and (3) laboratory assays. During the examinations, all interviewers, physicians, and technicians were unaware of the veterans' cohort status.

11.2.1 Medical History and Physical Examination

Physician's assistants administered a standardized medical history questionnaire, as described in Chapter 2. The veterans were asked if they had ever had diabetes mellitus or an overactive or underactive thyroid gland. Veterans who reported having diabetes, hyperthyroidism, or hypothyroidism before discharge from the service were excluded from the analysis of the self-reported postdischarge prevalence of that condition, but not from other analyses. Veterans were also asked about current medication use, hospitalizations and surgery for endocrine conditions, and adherence to a diabetic diet.

Board-certified internists conducted physical examinations. The thyroid and testes were examined. If the thyroid was palpably abnormal, the examiner specified if it was enlarged, tender, or nodular. Results of the testes examination are in Chapter 12.

11.2.2 Laboratory Tests

The participants were placed on an overnight fast, with only drinking water permitted. The fast began at 7 p.m. on the evening before the medical examination and ended after blood specimens had been taken the next morning.

The laboratory tests and their units of measurement are shown in Table 11.1 Fasting serum glucose (FSG) was determined from serum samples by using a standard adaptation of the glucose oxidase-peroxidase-chromogen-coupled system for glucose determination in biologic fluids. Other endocrine assays were performed by using a standard double antibody radioimmunoassay system (test protocol, Leeco Diagnostics, Inc.). All laboratory determinations were monitored by using bench and "blind" repeat quality control procedures. Controls were run in duplicate for approximately each set of 20 participant samples. A blind repeat test was run for one randomly chosen specimen in each set. In general, correlation between first and repeat measures was high for each of these assays; bench controls were maintained well within the acceptable performance criteria (coefficients of variation $< 10\%$) throughout the study. Analytic procedures and quality control methods are described in Supplement A (Laboratory Methods and Quality Control), which also contains the data on bench controls. Data on blind repeats and intertechnician variability are in Supplement B (Medical and Psychological Data Quality).

For most assays, low and high reference values were defined as the 5th and 95th percentiles, respectively, for the combined cohort of Vietnam and non-Vietnam veterans (Table 11.1). Clinically relevant upper limits were used for FSG (≥ 140 mg/dL) (National

Table 11.1 Reference Values[a] for Laboratory Tests Associated With Endocrine Function

Test	Low Value	High Value
Fasting serum glucose, mg/dL	81.0	140.0
Free thyroxine index	1.7	2.8
Thyroid-stimulating hormone, mIU/L	–	10.0
Cortisol, µg/dL	10.4	28.2
Dehydroepiandrosterone, µg/dL	109.0	421.0
Testosterone, ng/dL	348.2	1102.9
Follicle-stimulating hormone, IU/L	3.0	16.9
Luteinizing hormone, IU/L	7.0	24.0

[a] See Section 11.2.2 for definition of low and high reference values.

Diabetes Data Group, 1979) and thyroid-stimulating hormone (TSH >10 mIU/L). Thyroxine and triiodothyronine uptake values were used to calculate the free thyroxine index (FTI), but are not shown in the results.

11.2.3 Case Definitions for Diabetes Mellitus and Hypothyroidism

To calculate prevalences that reflect both treated and untreated veterans, we used definitions of diabetes and hypothyroidism that combined laboratory results with treatment information. A veteran was considered diabetic if he reported he was currently using diabetic medication or following a diabetic diet, or if he had an elevated FSG (≥140 mg/dL). A veteran who used thyroid replacement medication or whose TSH was >10 mIU/L was considered hypothyroid.

11.2.4 Statistical Methods

The statistical methods and strategies for conducting multiple linear and multiple logistic regression analyses are described in Chapter 2. Logistic and linear regression analyses were conducted for the laboratory tests listed in Table 11.1. The distributions of the laboratory assay results were investigated before other statistical analyses were performed. Most of the distributions were approximately log-normal; the logarithmic transformations were therefore used for statistical analysis. The distributions of FSG and of TSH, however, were not well approximated by a normal distribution, even after they had been logarithmically transformed. For FSG and TSH, confidence limits from the linear regression results must be considered approximate.

Primary covariates for Model 1 regression analyses consisted of the six entry characteristics. Covariates for cigarette smoking status and alcohol consumption (defined in Chapter 2) were included in all Model 2 analyses. Other covariates included in Model 2 analyses differed somewhat by laboratory test as follows: FSG—body mass index and current use of a medication known to affect glucose metabolism; TSH and FTI—current use of a medication known to affect thyroid measurements or function; and testosterone, follicle-stimulating hormone (FSH) and luteinizing hormone (LH)—illicit drug use (defined in Chapter 2). For testosterone, FSH, and LH, we evaluated other categorical variables individually for potential influence on point estimates; their effects were minimal, and we therefore did not include them in the final regression models.

Values from 83 veterans were excluded from the analysis of FSG: 32 Vietnam (1.3%) and 17 non-Vietnam (0.9%) veterans had not maintained the required overnight fast, and 23 Vietnam (0.9%) and 11 non-Vietnam (0.6%) veterans reported using a medication for diabetes. Values from 12 (4 Vietnam and 8 non-Vietnam) veterans who reported using thyroid-replacement medication were excluded from the analyses of thyroid tests.

11.3 RESULTS

11.3.1 Medical History and Physical Examination

The veterans were asked whether, since their discharge from the service, they had been told by a physician that they had certain diseases. Vietnam veterans more frequently reported diabetes mellitus and hyperthyroidism and less frequently reported hypothyroidism than did other veterans (Table 11.2). The excess of reported hyperthyroidism was statistically significant, although the prevalence of either thyroid disorder was less than 1% in each cohort. Of the 17 veterans who reported having hyperthyroidism, 6 Vietnam and 2

Table 11.2 Percent and Number of Vietnam and Non-Vietnam Veterans Reporting Physician-Diagnosed Endocrine Conditions Since Discharge

	Vietnam		Non-Vietnam	
Condition	%	No.	%	No.
Diabetes mellitus	1.2	31	0.8	15
Hyperthyroidism	0.6	14	0.2	3
Hypothyroidism	0.5	12	0.7	13

non-Vietnam veterans had other evidence (a past hospitalization for thyrotoxicosis, a thyroid examination abnormality, or an FTI >2.8) consistent with this diagnosis. However, since treatment for hyperthyroidism does not necessarily require hospitalization or the continued use of medication, we could not accurately assess the validity of the other 9 veterans' reports.

Vietnam veterans more often reported use of a diabetic medication or adherence to a diabetic diet, but more non-Vietnam veterans reported using thyroid replacement medication (Table 11.3). Reports of hospitalization or surgery for endocrinologic diseases were rare in both groups. Vietnam veterans reported a postdischarge hospitalization for diabetes mellitus slightly more often than other veterans (0.5% versus 0.4%). Four Vietnam veterans and one non-Vietnam veteran reported a postdischarge hospitalization for hypothyroidism or goiter. Two veterans from each group had been hospitalized for thyrotoxicosis. Two members of each group reported that they had undergone thyroid surgery after their discharge.

Vietnam veterans were more likely than other veterans to have an abnormality detected on thyroid examination; thyromegaly was the most common finding (Table 11.4). Abnormalities were detected in <1% of participants in both groups, however, and the estimates of the odds ratios were unstable.

11.3.2 Laboratory Tests

The percent differences in the means for all endocrinologic measures except TSH were less than 2% (Table 11.5). The unadjusted difference in TSH was 3.4%; when adjusted by multivariate analysis, the difference increased to 4.5%. Although the unadjusted geometric mean FSG for Vietnam veterans was only 1.0% higher than that for non-Vietnam veterans, the confidence interval did not include 0.0% (*i.e.* the result was statistically significant).

The proportions of Vietnam and other veterans with serum assay values above the reference range were similar, except that Vietnam veterans were about twice as likely to have a high TSH value (Table 11.6). The proportions of Vietnam and other veterans with values below the reference range were similar for all assays (Table 11.7).

11.3.3 Diabetes Mellitus and Hypothyroidism

On the basis of the case definitions of these conditions, rates for diabetes and hypothyroidism were somewhat higher among Vietnam veterans (Table 11.8), but the

Table 11.3 Percent and Number of Vietnam and Non-Vietnam Veterans Reporting Current Treatment for Diabetes or Hypothyroidism

	Vietnam		Non-Vietnam	
Treatment	%	No.	%	No.
Diabetic medication	0.9	23	0.6	11
Diabetic diet[a]	0.8	21	0.5	9
Thyroid replacement	0.2	4	0.4	8

[a] Includes veterans who also report diabetic medication.

Table 11.4 **Percent and Number of Vietnam and Non-Vietnam Veterans With Thyroid Examination Abnormalities and Odds Ratios, by Abnormality**

	Vietnam		Non-Vietnam		Crude Results		Multivariate Results Model 1[a]	
Abnormality	**%**	**No.**	**%**	**No.**	**OR**	**95% CI**	**OR**	**95% CI**
Thyromegaly	0.8	20	0.5	9	1.8	0.8-3.9	2.1	0.9-4.7
Thyroid tenderness	<0.1	1	0.0	0	—	—	—	—
Thyroid nodule	<0.1	1	0.1	2	—	—	—	—
Any of above	0.9	22	0.6	11	1.6	0.8-3.3	1.8	0.9-3.9

[a] Model 1 contains the six entry characteristics.

confidence intervals for both conditions included 1.0. Various exclusions did not alter these point estimates. When the veterans with a history of pancreatitis were excluded from the analysis, the results for diabetes were basically unchanged (Vietnam: 1.6%, non-Vietnam: 1.1%; crude OR=1.4, 95% CI= 0.9-2.4). Similarly, when adherence to a diabetic diet was not included in the "definition" of diabetes, 1.5% of Vietnam and 1.1% of non-Vietnam veterans met the case definition for diabetes (crude OR=1.4, 95% CI=0.8-2.3). After veterans with a history of thyroid surgery were excluded from the hypothyroidism analysis, 1.2% of Vietnam and 1.1% of non-Vietnam veterans met the case definition for this thyroid disorder (crude OR=1.4, 95% CI=0.8-2.5).

11.4 DISCUSSION

Vietnam veterans more frequently reported that they had had diabetes and that they were currently under treatment for diabetes. The mean FSG was also 1% higher for Vietnam veterans than for non-Vietnam veterans. When either treatment for diabetes or an elevated FSG (≥140 mg/dL) was considered an indication of diabetes, the prevalence of this condition was about 1.7% among Vietnam veterans and 1.2% among non-Vietnam veterans.

The small differences in diabetes-related findings could well be due to chance, because the only statistically significant finding was the difference in mean FSG. A number of possible biases should also be considered. As with any of the self-reports, the information on diabetes could be biased if Vietnam veterans were more likely than non-Vietnam veterans to recall items related to diabetes. Increased concern about health or increased access to health care might cause Vietnam veterans to have more opportunities to be treated for diabetes. Selection bias might be present if diabetic Vietnam veterans were more likely than diabetic non-Vietnam veterans to participate in the medical examination. As we show in Chapter 3, however, having a history of diabetes does not appear to have differentially affected participation in the examination (see Table 3.8). Further, these findings are not the result of confounding by known risk factors for diabetes, such as age, race, or body mass index, because adjusting for these factors did not alter the results.

When both treated and untreated hypothyroidism were considered together, the prevalence of hypothyroidism was similar in the two groups of veterans. However, as indicated by their almost twofold excess of high TSH values (>10 mIU/L), rates of untreated hypothyroidism were higher for Vietnam veterans. The reason for this excess is unclear, and it could be due to chance.

The excess of self-reported hyperthyroidism among Vietnam veterans, though based on very few cases, is striking and not easily explained. Some veterans may have confused hyperthyroidism with hypothyroidism, but Vietnam veterans should not be any more likely

Table 11.5 Means and Percent Differences Between Means for Endocrine Laboratory Tests for Vietnam and Non-Vietnam Veterans

					Multivariate Results			
	Crude Geometric Mean		Crude Results		Model 1[a]		Model 2	
Test	Vietnam	Non-Vietnam	% Diff	95% CI	% Diff	95% CI	% Diff	95% CI
Fasting serum glucose, mg/dL	93.4	92.4	1.0	0.3,1.7	0.9	0.2,1.6	0.7[b]	0.1,1.4
Free thyroxine index	2.18	2.20	-0.7	-1.6,0.3	-0.8	-1.8, 0.3	-0.8[c]	-1.8, 0.2
Thryoid-stimulating hormone, mIU/L	1.61	1.55	3.4	-0.2,7.2	4.3	0.5,8.2	4.5[c]	0.7,8.4
Cortisol, μg/dL	17.5	17.3	1.2	-0.7,3.0	1.1	-0.8,3.0	0.9[d]	-1.0,2.8
Dehydroepiandrosterone, μg/dL	219.0	221.6	-1.2	-3.7,1.3	-0.9	-3.4,1.8	-1.0[d]	-3.6,1.6
Testosterone, ng/dL	636.6	643.7	-1.1	-3.2,1.0	-1.3	-3.5,0.8	-1.5[e]	-3.6,0.6
Follicle-stimulating hormone, IU/L	6.6	6.5	1.7	-1.8,5.4	0.9	-2.7,4.7	0.8[e]	-2.9,4.6
Luteinizing hormone, IU/L	13.3	13.1	1.5	-0.7,3.7	1.1	-1.2,3.4	1.0[e]	-1.2,3.3

[a] Model 1 contains the six entry characteristics.
[b] Model 2 contains the six entry characteristics and alcohol consumption, smoking status, body mass index, and medications known to affect blood glucose.
[c] Model 2 contains the six entry characteristics and alcohol consumption, smoking status, and medications that can decrease thyroid hormone levels.
[d] Model 2 contains the six entry characteristics and alcohol consumption and smoking status.
[e] Model 2 contains the six entry characteristics and alcohol consumption, smoking status, and illicit drug use.

Table 11.6 Percent and Number of Vietnam and Non-Vietnam Veterans With Endocrine Test Results Above Reference Range, and Odds Ratios

							Multivariate Results			
	Vietnam		Non-Vietnam		Crude Results		Model 1[a]		Model 2	
Test	%	No.	%	No.	OR	95% CI	OR	95% CI	OR	95% CI
Fasting serum glucose	0.6	15	0.6	11	1.1	0.5-2.4	1.0	0.4-2.2	—	—
Free thyroxine index	4.6	114	5.1	101	0.9	0.7-1.2	0.8	0.6-1.1	0.8[b]	0.6-1.1
Thryoid-stimulating hormone	1.1	26	0.6	11	1.9	0.9-3.8	2.0	0.9-4.3	—	—
Cortisol	5.0	124	4.8	94	1.0	0.8-1.4	1.1	0.8-1.4	1.0[c]	0.8-1.4
Dehydroepiandrosterone	4.5	113	5.4	106	0.8	0.6-1.1	0.8	0.6-1.1	0.8[c]	0.6-1.1
Testosterone	5.1	128	4.8	95	1.1	0.8-1.4	1.0	0.8-1.4	1.[illegible] [d]	0.8-1.4
Follicle-stimulating hormone	5.0	124	5.0	99	1.0	0.8-1.3	1.0	0.7-1.3	0.9[d,e]	0.7-1.2
Luteinizing hormone	4.3	107	4.3	85	1.0	0.7-1.3	1.0	0.7-1.4	1.0[d]	0.7-1.4

[a] Model 1 contains the six entry characteristics.
[b] Model 2 contains the six entry characteristics and alcohol consumption, smoking status, and medications that can decrease thyroid hormone levels.
[c] Model 2 contains the six entry characteristics and alcohol consumption and smoking status.
[d] Model 2 contains the six entry characteristics and alcohol consumption, smoking status, and illicit drug use.
[e] Standardized for alcohol consumption.

than other veterans to make that mistake, and any resulting bias would lessen any difference between the groups. Since patients with hyperthyroidism can be treated, the current similarity in the free thyroxine index between the groups does not exclude the possibility that Vietnam veterans were more likely to have hyperthyroidism after their discharge. The current prevalence of hyperthyroidism among Vietnam veterans is, however, similar to that among non-Vietnam veterans.

Results for the other endocrine measures were similar for both groups of veterans. In particular, for the Vietnam veterans, we found no evidence of a deficiency in either cortisol or testosterone.

In summary, Vietnam veterans exhibited a small excess of diabetes and a twofold excess of untreated hypothyroidism. They also reported having had hyperthyroidism more often

Table 11.7 Percent and Number of Vietnam and Non-Vietnam Veterans With Endocrine Assays Below Reference Range, and Odds Ratios

							Multivariate Results			
	Vietnam		Non-Vietnam		Crude Results		Model 1[a]		Model 2	
Assay	%	No.	%	No.	OR	95% CI	OR	95% CI	OR	95% CI
Free thyroxine index	5.4	134	4.6	91	1.2	0.9-1.5	1.2	0.9-1.5	1.2[b]	0.9-1.5
Cortisol	4.6	114	5.4	106	0.8	0.6-1.1	0.9	0.6-1.1	0.9[c]	0.6-1.1
Dehydroepiandrosterone	5.3	132	4.6	90	1.2	0.9-1.5	1.1	0.9-1.5	1.[illegible] [c]	0.8-1.5
Testosterone	5.0	125	5.0	98	1.0	0.8-1.3	1.0	0.8-1.3	1.0[d]	0.8-1.3
Follicle-stimulating hormone	4.7	117	5.2	103	0.9	0.7-1.2	0.9	0.7-1.2	0.9[d]	0.6-1.1
Luteinizing hormone	5.2	129	5.2	103	1.0	0.8-1.3	1.0	0.8-1.3	1.0[d]	0.8-1.3

[a] Model 1 contains the six entry characteristics.
[b] Model 2 contains the six entry characteristics and alcohol consumption, smoking status, and thyroid medications.
[c] Model 2 contains the six entry characteristics and alcohol consumption and smoking status.
[d] Model 2 contains the six entry characteristics and alcohol consumption, smoking status, and illicit drug use.

than did other veterans. Each of these three conditions, however, occurred in <2% of veterans in each cohort, and the differences may well be due to chance or bias. We observed no endocrinologic differences that could be attributed to chronic or acute stress.

Table 11.8 Percent and Number of Vietnam and Non-Vietnam Veterans Who Met Case Definitions for Diabetes or Hypothyroidism, and Odds Ratios

							Multivariate Results			
	Vietnam		Non-Vietnam		Crude Results		Model 1[a]		Model 2	
Condition	%	No.	%	No.	OR	95% CI	OR	95% CI	OR	95% CI
Diabetes[b]	1.7	42	1.2	23	1.5	0.9-2.4	1.4	0.8-2.4	1.4[c]	0.8-2.3
Hypothyroidism[d]	1.2	30	1.0	19	1.3	0.7-2.2	1.3	0.7-2.4	–	–

[a] Model 1 contains the six entry characteristics.
[b] Fasting serum glucose ≥140 mg/dL, adherence to a diabetic diet, or current use of a glucose-regulating medication.
[c] Model 2 contains the six entry characteristics and alcohol consumption, smoking status, body mass index, and medications that can increase serum glucose.
[d] TSH >10 mIU/L or current use of thyroid-replacement medication

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CHAPTER 12

Other Medical Conditions and Organ Systems

12. OTHER MEDICAL CONDITIONS AND ORGAN SYSTEMS

Thus far in this volume we have described the medical examination results of the Vietnam Experience Study (VES) for most of the major organ systems. In Chapters 5-11 we presented information on the dermatologic, gastrointestinal, neurologic, immunologic, cardiovascular, respiratory, and endocrine systems. In this chapter, we first summarize the information from the examinations concerning tumors, growths, and masses. Then, according to the format used elsewhere in the volume, we describe the results for four organ systems: (1) head, eyes, ears, nose, and throat (HEENT); (2) musculoskeletal; (3) genitourinary; and (4) hematologic.

In this chapter, we present information obtained from three sources: (1) self-reported medical histories, (2) general physical examinations, and (3) laboratory tests. The methods used to obtain this information are described in Chapter 2. Additional details on specific laboratory test procedures are in Supplement A (Laboratory Methods and Quality Control). The statistical methods, and the covariates used in the secondary analyses, are also described in Chapter 2.

12.1 TUMORS, GROWTHS, AND MASSES

12.1.1 Background

Some Vietnam veterans have expressed concern that their military service, as a result of exposure to the herbicide Agent Orange, may have put them at increased risk for developing cancer. Several investigators have suggested that certain cancers may be related to exposure to phenoxyherbicides or 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). These cancers include the following six: non-Hodgkin's lymphoma (Hoar *et al.*, 1986), Hodgkin's disease (Hardell *et al.*, 1981), soft tissue sarcoma (Eriksson *et al.*, 1981), nasal cancer and nasopharyngeal cancer (Hardell *et al.*, 1982), and primary liver cancer (Hardell *et al.*, 1984). Most of these cancers are rare. Considering the size of the VES, a retrospective cohort study, we expected to find few, if any, veterans in either cohort with these malignancies. Accordingly, the Vietnam veterans' risks for developing these six types of cancer will be more adequately assessed in the Selected Cancers Study, a case-control investigation, as noted in Chapter 1. Nonetheless, for completeness, we herein describe findings from the VES medical history interviews and physical examinations that are related to tumors, growths, and masses. The prevalences of skin cancer and chest x-ray masses among VES participants are discussed in detail in Chapters 6 and 10, respectively. Results of tests of immune function are presented in Chapter 8.

12.1.2 Results

A slightly higher proportion of Vietnam (1.7%) than non-Vietnam (1.2%) veterans reported having a physician-diagnosed cancer since being discharged from the service. More Vietnam veterans reported being hospitalized since discharge for malignant cancers than non-Vietnam veterans, but the proportion in each cohort who were hospitalized was <1% (Table 12.1). Regarding cancers believed to be associated with exposure to phenoxyherbicides or TCDD, two Vietnam veterans reported soft tissue sarcomas, and one participant from each cohort was hospitalized for Hodgkin's disease. No veteran reported having any of the other cancers that have been associated with exposure to herbicides. Except for skin cancer, the most frequently reported type of cancer involved the genitourinary system. Five Vietnam and one non-Vietnam veteran reported hospitalizations for testicular cancer.

Table 12.1 Percent and Number of Vietnam and Non-Vietnam Veterans Reporting Hospitalizations for Malignant Neoplasms Since Discharge, by Site of Neoplasm

	Vietnam		Non-Vietnam	
Site of Neoplasm (ICD9-CM Codes)	%	No.	%	No.
Lip, Oral Cavity, and Pharynx (140-149)	0.0	0	0.0	0
Digestive Organs and Peritoneum (150-159)	0.1	3	0.0	0
Respiratory and Intrathoracic (160-165)	0.0	0	0.0	0
Bone, Connective Tissue, Skin, and Breast (170-175)	0.2	6	0.1	1
Melanoma (172)	<0.1	1	0.0	0
Other skin (173)	0.2	4	0.1	1
Genitourinary Organs (179-189)	0.2	5	0.1	2
Other and Unspecified (190-199)	<0.1	1	0.1	2
Hematopoietic and Lymphatic Tissue (200-208)	0.1	2	0.1	1
Any Malignant Neoplasm (140-208)	0.7	17	0.3	6

Both groups of veterans more frequently reported having benign tumors than malignant cancers, but the proportion of Vietnam (3.5%) and non-Vietnam (3.8%) veterans with physician-diagnosed benign tumors since discharge was about the same. A small, identical proportion (0.8%) of veterans from each cohort reported being hospitalized for benign tumors. Slightly more Vietnam veterans were hospitalized for lipomas (0.3% versus 0.1%); the frequency of the other types of benign tumors was similar for the two groups.

Less than 1% of veterans in either group reported that malignant tumors were a current health problem or concern. Five participants, all Vietnam veterans, reported current use of medications for treatment of cancer. A similar proportion (0.8%) of veterans in each group stated that benign tumors were a current health problem or concern.

The prevalences of several physical examination findings that might be associated with tumors, growths, or masses differed between cohorts (Table 12.2). A larger proportion of Vietnam than non-Vietnam veterans had neck masses, which were primarily benign conditions that included lipomas, epidermal inclusion cysts, and sebaceous cysts. No single condition accounted for the observed difference between cohorts in the prevalence of neck masses. Although more Vietnam (2.4%) than non-Vietnam (1.8%) veterans reported having swollen testicles during the year preceding examination, at the physical examination similar

Table 12.2 Percent and Number of Vietnam and Non-Vietnam Veterans With Physical Examination Findings Associated With Tumors, Growths, and Masses and Odds Ratios, by Type of Finding

							Multivariate Results			
	Vietnam		Non-Vietnam		Crude Results		Model 1[a]		Model 2[b]	
Finding	%	No.	%	No.	OR	95% CI	OR	95% CI	OR	95% CI
Mouth mass	0.2	6	0.0	0	—	—	—	—	—	—
Salivary gland mass	0.0	0	0.0	0	—	—	—	—	—	—
Neck mass	0.9	22	0.3	6	2.9	1.2-7.2	2.8	1.1-7.0	—	—
Abdominal mass	0.4	9	0.2	4	1.8	0.5-5.8	—	—	—	—
Scrotal mass	2.8	69	2.9	58	0.9	0.7-1.3	0.9	0.6-1.3	0.9	0.6-1.3
Prostatic nodule	0.4	11	0.3	5	1.7	0.6-5.0	—	—	—	—
Rectal mass	0.2	4	0.4	8	0.4	0.1-1.3	—	—	—	—
Soft tissue mass of extremity	1.7	41	1.0	20	1.6	1.0-2.8	1.4	0.8-2.4	1.4	0.8-2.4
Abnormal lymph nodes	2.4	60	2.7	53	0.9	0.6-1.3	0.9	0.6-1.3	0.9	0.6-1.3

[a] Model 1 contains the six entry characteristics.
[b] Model 2 contains the six entry characteristics and smoking status, alcohol consumption, and occupational exposure to herbicides.

proportions (2.8% versus 2.9%) were found to have scrotal masses. Soft tissue masses of the extremities were noted more frequently among the Vietnam veterans, but, as with the neck masses, these soft tissue masses varied. They included lipomas, ganglia, and prepatellar cysts, for example, and no single finding accounted for the observed difference between cohorts in the prevalence of soft tissue masses of the extremities.

12.2 HEAD, EYES, EARS, NOSE, AND THROAT

12.2.1 Background

Modern military weapons can produce levels of sound that permanently damage hearing. The results of audiometric testing, which show that Vietnam veterans are more likely than non-Vietnam veterans to have mid-to-high-frequency hearing loss, were presented in Chapter 7. There is little reason to suspect that other aspects of military service in Vietnam—such as exposure to infectious diseases, trauma, or psychological stress—would adversely affect the head, eyes, ears, nose, or throat (HEENT) of the veterans.

In general, investigators do not believe that exposure to TCDD causes many HEENT problems, although a few investigators have reported eye problems among persons exposed to this compound. Investigators have noted chronic conjunctivitis and blepharitis, in association with chloracne, among several groups of workers exposed to TCDD and 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) (Goldman, 1972; Kimmig and Schulz, 1957; May, 1973). In addition, researchers have reported that, among the large number of persons exposed to TCDD during an industrial explosion in Seveso, Italy, 118 persons were treated for ocular irritation and 4 were treated for other unspecified ocular disorders (Greim and Loprieno, 1978). However, no data have been published on the long-term follow-up of persons with ocular problems who were exposed at Seveso. Finally, swollen eyelids and reading difficulties have been reported among Vietnamese refugees who lived in areas sprayed with herbicides during the Vietnam conflict (Tung *et al.*, 1971).

12.2.2 Results

Vietnam veterans reported having had, in the year preceding the examination, six symptoms referable to the eye, ear, or nose more frequently than non-Vietnam veterans. The prevalences of these six symptoms—sudden vision loss, periods of double vision, pain upon looking at a bright light, ringing in the ears, a severe spinning sensation, and persistent nosebleeds—are presented in Appendix Table A.2. The largest relative difference between cohorts was for persistent nosebleeds, but only 0.5% of Vietnam and 0.2% of non-Vietnam veterans reported having had this symptom.

At examination, only one participant, a Vietnam veteran, had a conjunctival discharge (Table 12.3). Other abnormal findings noted during eye examination were uncommon, but several were more prevalent among Vietnam veterans. More Vietnam (0.5%) than non-Vietnam (0.1%) veterans had corneal scarring. Arteriovenous nicking and arteriolar spasm, manifestations of arteriolar sclerosis and hypertension, respectively, were more frequent among Vietnam veterans.

Other physical examination findings of the head, ear, nose, and throat are listed in Appendix Table C.1. Of the 19 participants with skull abnormalities, 16 were Vietnam veterans. Skull abnormalities included healed scars, boney protuberances, and cystic lesions. For Vietnam and non-Vietnam veterans, the frequency of specific middle ear

Table 12.3 Percent and Number of Vietnam and Non-Vietnam Veterans With Abnormal Findings on Eye Examination and Odds Ratios, by Type of Finding

							Multivariate Results			
	Vietnam		Non-Vietnam		Crude Results		Model 1[a]		Model 2[b]	
Finding	%	No.	%	No.	OR	95% CI	OR	95% CI	OR	95% CI
Globe Missing	0.2	4	0.1	1	–	–	–	–	–	–
Conjunctival Discharge	<0.1	1	0.0	0	–	–	–	–	–	–
Corneal Scarring	0.5	13	0.1	2	5.2	1.2-22.9	–	–	–	–
Cataract	0.3	8	0.3	5	1.3	0.4-3.9	–	–	–	–
Scleral Icterus	0.1	3	0.1	2	–	–	–	–	–	–
Fundoscopic Abnormality	2.9	73	2.1	42	1.4	0.9-2.0	1.3	0.9-1.9	1.3	0.8-1.9
Arteriovenous nicking	1.8	44	1.3	26	1.3	0.8-2.2	1.3	0.8-2.1	1.2	0.7-2.0
Arteriolar spasm	0.7	18	0.4	8	1.8	0.8-4.1	1.7	0.7-4.0		
Exudates	0.1	2	0.2	3	–	–	–	–	–	–
Hemorrhages	<0.1	1	0.1	2	–	–	–	–	–	–
Papilledema	<0.1	1	0.0	0	–	–	–	–	–	–
Disc cupping	0.3	7	0.3	5	1.1	0.4-3.5	–	–	–	–
Disc pallor	0.2	4	0.1	2						

[a] Model 1 contains the six entry characteristics.
[b] Model 2 contains the six entry characteristics and smoking status, alcohol consumption, hypertension, and diabetes.

abnormalities (such as retracted or scarred tympanic membranes) was similar. Comparable proportions (<1%) of each group had nasal abnormalities—polyps, ulcers, perforated septa, or bleeding—and for about one-third of each group dental status was judged to be fair or poor.

12.3 MUSCULOSKELETAL SYSTEM

12.3.1 Background

We reasoned that musculoskeletal disorders would be more prevalent among Vietnam veterans for two reasons. First, many of the Vietnam veterans had used combat weapons and had been exposed to hostile fire. Second, after discharge from service, Vietnam veterans might well have had more injuries than non-Vietnam veterans. In the mortality follow-up of the Vietnam Experience Study, we found that, in the first 5 years after discharge from active duty, the mortality for Vietnam veterans was about 45% higher than for non-Vietnam veterans (Centers for Disease Control Vietnam Experience Study, 1987). This excess mortality resulted from motor vehicle collisions, suicides, homicides, and unintentional poisonings. During the entire follow-up period, mortality from motor vehicle collisions was 48% higher for Vietnam veterans than for non-Vietnam veterans. Thus, we expected trauma-related musculoskeletal disorders, such as missing extremities, to be more common among the Vietnam veterans.

12.3.2 Results

An equal proportion of Vietnam (6.5%) and non-Vietnam (6.4%) veterans reported being hospitalized for musculoskeletal disorders since discharge. In each cohort about half of these hospitalizations were for treatment of dorsopathies (disorders of the back and spine); the remainder were for arthropathies (disorders of joints) and rheumatism (disorders of muscles and tendons). Fractures or dislocations since discharge were reported by 33.8% of the Vietnam and 30.6% of the non-Vietnam veterans. Arthritis, diagnosed by a physician, was reported by 8.6% of the Vietnam and by 9.0% of the non-Vietnam veterans.

About 14% of the veterans in each group stated that musculoskeletal conditions were current health problems. The distributions of the types of disorders were similar for the two groups. Vietnam veterans, however, were more likely to report having had musculoskeletal symptoms in the year preceding the examination. The percentage of veterans with these symptoms—neck pain, back pain, and other pains or stiffness—are listed in Appendix Table A.2.

At physical examination, findings were similar for the two groups (Table 12.4). Absent extremities, primarily missing fingers, were noted in <2% of the men in either cohort. Spinal abnormalities were rare, and similarly distributed, in each cohort.

12.4 GENITOURINARY SYSTEM

12.4.1 Background

On the basis of our review of the scientific literature, we had several reasons to suspect that disorders of the genitourinary system might be associated with military service in Vietnam, but we expected the overall prevalence of these disorders to be low. Military physicians estimated that post-traumatic acute renal insufficiency (ARI) occurred in 1 of 600 men severely wounded in battle in Vietnam and that about one-third of those with ARI survived (Stone and Knepshield, 1982). Survivors could have chronic renal insufficiency as a sequela of ARI. In Vietnam, other medical conditions, such as infection with *Plasmodium falciparum* or hemolytic anemia, caused ARI, but ARI caused by these conditions was rare (Stone *et al.*, 1982).

Chronic renal insufficiency may also result from an obstructive uropathy that is secondary to a sexually transmitted disease (STD). Among Army personnel in Vietnam from 1963 to 1970, the average annual incidence rate for STDs was 261.9 cases per 1,000 men, whereas

Table 12.4 Percent and Number of Vietnam and Non-Vietnam Veterans With Abnormalities of the Musculoskeletal System Noted During Physical Examination and Odds Ratios, by Type of Finding

							Multivariate Results			
	Vietnam		Non-Vietnam		Crude Results		Model 1[a]		Model 2[b]	
Finding	%	No.	%	No.	OR	95% CI	OR	95% CI	OR	95% CI
Extremity										
Absent	1.1	28	1.3	26	0.9	0.5-1.5	0.8	0.5-1.4	0.8	0.5-1.4
Decreased range of motion	4.2	105	5.0	98	0.8	0.6-1.1	0.8	0.6-1.1	0.8	0.6-1.1
Painful straight leg raising	4.3	108	3.9	76	1.1	0.8-1.5	1.1	0.8-1.5	1.1	0.8-1.5
Joint swelling	1.3	33	1.2	23	1.1	0.7-1.9	1.1	0.7-2.0	1.1	0.6-1.9
Spine	6.3	158	6.6	130	1.0	0.8-1.2	0.9	0.7-1.2	0.9	0.7-1.2
Scoliosis	1.0	24	0.7	14	1.4	0.7-2.6	1.5	0.7-2.9	–	–
Kyphosis	0.4	11	0.6	11	0.8	0.3-1.8	–	–	–	–
Decreased range of motion	4.2	105	5.0	98	0.8	0.6-1.1	.0.8	0.6-1.1	0.8	0.6-1.1
Tenderness	1.5	37	1.1	22	1.3	0.8-2.3	1.3	0.7-2.2	1.2	0.7-2.1
Abnormal pelvic tilt	0.4	11	0.6	11	0.8	0.3-1.8	–	–	–	–

[a] Model 1 contains the six entry characteristics.
[b] Model 2 contains the six entry characteristics and alcohol consumption, illicit drug use, education and body mass index.

the corresponding rate for Army personnel stationed elsewhere was 74.3 cases per 1,000 men (Deller *et al.*, 1982). Over 90% of the men who were treated for STDs in Vietnam had gonorrhea. Since gonorrhea is readily diagnosed and easily treated, local complications such as periurethral abscesses and fistulas (that might cause stricture) are uncommon; thus, it would be unusual to find chronic renal insufficiency among Vietnam veterans as a sequela of this infection.

The results of only a few, isolated studies have suggested that exposure to TCDD may have toxic effects on the kidney. Investigators reported a single case of hemorrhagic cystitis in a young girl exposed to TCDD-contaminated soil in a horse arena (Carter *et al.*, 1975). In the Ranch Hand Study of men exposed to TCDD during defoliant spraying in Vietnam, Lathrop *et al.* (1984) found no difference in results of urinalyses for the exposed and comparison groups. These investigators noted that the exposed group had an increased prevalence of self-reported kidney disease, but these reports were not verified, and the investigators did not give details on the types of kidney diseases that were increased. In a pilot study of 104 Missouri residents who lived where TCDD-contaminated oil had been used to control dust on roadways, Webb (1984) reported that exposed persons had urinary tract problems and several urine abnormalities, including microscopic hematuria. In the full-scale study of these residents, however, investigators found no differences in genitourinary conditions or urinalysis results between the exposed and comparison group (Hoffman *et al.*, 1986). Thus, we have little reason for expecting renal disorders to be long-term consequences of exposure to TCDD.

12.4.2 Methods

Blood urea nitrogen and serum creatinine were determined by using a Kodak Ektachem 700 autoanalyzer. Results of tests of sex hormones (serum testosterone, follicle-stimulating hormone, and luteinizing hormone) are presented in Chapter 11, and results of semen analysis are presented in Chapter 13.

Each participant provided a first-morning urine specimen for analysis. Trained technicians, using Ames Multistix, performed standard urinalyses; dipstick results were quantified with a Clintek 200 reflectance spectrophotometer. Technicians also examined miscroscopically a centrifuged urine sediment.

12.4.3 Results

The same proportion of Vietnam (5.7%) and non-Vietnam (5.5%) veterans reported being hospitalized for genitourinary conditions since discharge. In both cohorts half of these hospitalizations were for renal or bladder calculi; urethral disorders, the next most frequent reason cited, accounted for about one-tenth of the hospitalizations. The prevalences of medical conditions, such as prostatitis and epididymitis, diagnosed by a physician since discharge were comparable in the two cohorts (Table 12.5). The Vietnam veterans more frequently reported having urinary symptoms—frequent urination, difficulty in urinating, blood in urine, and the like—during the year preceding the examination. The percentages of veterans with these and other urinary symptoms are listed in Appendix Table A.2. Few Vietnam (2.7%) or non-Vietnam (2.2%) veterans, however, reported having current genitourinary problems. The most common current problems in both groups were kidney and bladder calculi and prostatic disorders.

At physical examination, few veterans had genital or prostatic abnormalities. The most common of these, varicocele, was noted in 5.5% of the veterans in each cohort. The

Table 12.5 **Percent and Number of Vietnam and Non-Vietnam Veterans Reporting Physician-Diagnosed Genitourinary Conditions Since Discharge**

	Vietnam		Non-Vietnam	
Condition	**%**	**No.**	**%**	**No.**
Kidney or bladder stones	4.9	121	4.4	86
Urinary tract infection	9.5	228	9.1	173
Chronic kidney disease	0.2	6	0.1	2
Prostatitis	5.3	130	5.6	110
Epididymitis	0.8	19	0.9	18
Varicocele	0.8	20	0.8	16

proportion of veterans with other abnormalities are listed in Appendix Table C.1. Twelve Vietnam veterans had no right testis, 6 had no left testis, and 6 had no testes. The corresponding number of non-Vietnam veterans were 2, 4, and 1, respectively. The Vietnam and non-Vietnam veterans had testes of similar size. The size was measured either with calipers (during the first 7 months of the study) or orchidometers (during the rest of the study). For each cohort, the distributions of these measurements are presented in Appendix Tables C.9-12.

The means for blood urea nitrogen and serum creatinine were similar for Vietnam and non-Vietnam veterans (Table 12.6). Results did not change after they were adjusted for the six entry or other covariates. The distributions of values for these two tests are presented by cohort status in Appendix Tables E.26-27. For both tests, the proportions in each cohort with values above the reference range were similar. Results of urinalyses are summarized in Table 12.7. More Vietnam veterans had urobilinogen in their urine, but this abnormality was found in <1% of either cohort. Ketones were also detected slightly more frequently among Vietnam veterans (2.9% versus 1.9%), but other substances and elements were found with similar frequency in the two cohorts.

12.5 HEMATOLOGY

12.5.1 Background

We did not expect prior military service in Vietnam to directly cause hematologic disorders among veterans, but we reasoned that such service could indirectly contribute to the development of anemia in several ways. One way is via contracting infections that are endemic in Southeast Asia. Anemia can be a manifestation of many infectious diseases, including malaria, hepatitis B, melioidosis, and tuberculosis. We have shown, however, that these infections are not now more of a problem to the Vietnam veterans than to others.

Table 12.6 **Means and Percent Differences Between Means for Laboratory Tests of Renal Function for Vietnam and Non-Vietnam Veterans**

					Multivariate Results			
	Crude Geometric Mean		Crude Results		Model 1[a]		Model 2[b]	
Test	**Vietnam**	**Non-Vietnam**	**% Diff**	**95% CI**	**% Diff**	**95% CI**	**% Diff**	**95% CI**
Blood urea nitrogen, mg/dL	13.6	13.7	-0.4	-1.7,1.0	-0.4	-1.8,1.0	-0.1	-1.5,1.3
Serum creatinine, mg/dL	1.1	1.1	-0.2	-1.2,0.7	-0.1	-1.1,0.9	0.0	-1.0,1.0

[a] Model 1 contains the six entry characteristics.
[b] Model 2 contains the six entry characteristics and smoking status, alcohol consumption, and illicit drug use.

Table 12.7 Percent and Number of Vietnam and Non-Vietnam Veterans With Abnormalities on Urinalysis and Odds Ratios, by Type of Abnormality

	Vietnam		Non-Vietnam		Crude Results	
Urine Abnormality	**%**	**No.**	**%**	**No.**	**OR**	**95% CI**
Glucose	0.7	18	0.6	12	1.2	0.6-2.5
Ketones[a]	2.9	71	1.9	37	1.5	1.0-2.3
Protein[a]	7.4	184	5.9	117	1.3	1.0-1.6
Bilirubin[a]	8.2	204	7.9	155	1.0	0.8-1.3
Urobilinogen	0.8	20	0.5	9	1.8	0.8-3.9
Hemoglobin[a]	1.6	40	1.6	31	1.0	0.6-1.6
RBCs[b]	1.7	41	1.7	33	1.0	0.6-1.6
WBCs[c]	5.3	131	4.8	95	1.1	0.8-1.4
Renal tubular cells	0.7	18	1.0	19	0.7	0.4-1.4
Hyaline casts	5.1	127	4.2	82	1.2	0.9-1.6
Granular casts	0.4	10	0.7	14	0.6	0.3-1.3
Red cell casts	<0.1	1	0.1	1	—	—
White cell casts	0.1	3	0.1	2	—	—
Other casts	<0.1	1	0.0	0	—	—

[a] >trace amount.
[b] >5 red blood cells per high powered field.
[c] >5 white blood cells per high powered field.

Another way is through the influence of certain behavioral habits that may have been acquired as a result of service in Vietnam. Dietary habits (resulting in nutritional deficiencies), excessive alcohol ingestion, cigarette smoking, and illicit drug use are factors that may contribute to the development of anemia. We did not find much difference between the two cohorts in the prevalence of any of these factors.

A third way is through some disease that can cause anemia, if that disease is more prevalent among the Vietnam veterans. As noted in Chapter 6, Vietnam veterans were more likely than non-Vietnam veterans to have occult blood in their stools. In adult males of this age, chronic occult blood loss, usually from some gastrointestinal site, is the most frequent cause of anemia.

The evidence suggesting that prior exposure to TCDD causes chronic hematologic abnormalities is slight. In only a few studies of humans potentially exposed to dioxin have investigators reported hematologic results in any detail, and in these, the differences have generally been minor, if present at all. Suskind and Hertzberg (1984), for example, reported no differences in complete blood cell counts or differential cell counts among industrial workers exposed to TCDD compared with their controls. In the baseline examination of the Ranch Hand Study, Lathrop *et al.* (1984) noted that the mean corpuscular hemoglobin was higher for the exposed group, but at the first follow-up examination, they did not find this difference (Lathrop *et al.*, 1987). In a study of residents of a Missouri trailer park who had been exposed to dioxin-contaminated oils used to control dust on roadways, Hoffman *et al.* (1986) found that leukocyte counts were higher among exposed persons than among controls. The investigators, however, did not adjust for other conditions that might affect this measure, nor did they report hemoglobin or hematocrit values for the two study groups.

12.5.2 Methods

Personnel at Lovelace Clinical Laboratory, using a Contraves Autolyzer 800, performed standard hematologic measures on whole blood samples. In addition, with a Geometric Data Hematrak automated counter, they determined differential counts of whole blood smears, and then reviewed each slide for cell morphology. Technicians determined plasma prothrombin times by using an MLA 700 Automatic Coagulation Timer.

12.5.3 Results

Less than 1% of veterans in either group reported that, since their discharge from service, a physician had told them that they had anemia or a blood clotting abnormality. The proportions of veterans in each cohort with these diagnoses are listed in Appendix Table A.1. More Vietnam (3.3%) than non-Vietnam (1.5%) veterans reported bleeding or bruising easily during the year preceding the examination, but results of tests of prothrombin time and platelet count showed no differences between the groups (Table 12.8).

Mean hemoglobin values were nearly identical for Vietnam and non-Vietnam veterans, as were the mean values for other hemotologic tests (Table 12.8). The proportions in each cohort with values above or below the reference ranges for all test measurements were similar (see Appendix D). The prevalence of anemia (hemoglobin <14 g/dL) was 2.4% and 2.3% for Vietnam and non-Vietnam veterans, respectively.

12.6 DISCUSSION

In this chapter we have summarized the information from the Vietnam Experience Study (VES) that relates to tumors, growths, and masses and have presented the results of our analysis of four organ systems—head, eyes, ears, nose, and throat (HEENT); musculoskeletal; genitourinary; and hematologic—evaluated in the medical examination. Although we considered many health outcomes, we found relatively few objective differences between the Vietnam and non-Vietnam cohorts.

Overall, slightly more Vietnam than non-Vietnam veterans reported having physician-diagnosed malignant tumors and having been hospitalized for these tumors since being discharged from service. The significance of these differences is difficult to evaluate for two reasons: first, because the number of veterans in each group with cancers is small (less than 2% in either cohort reported prior physician diagnoses); and second, because having a history of cancer was associated with an increased participation rate in the Vietnam group but not in the non-Vietnam group (see Chapter 3).

That we found only a few veterans with malignant neoplasms is not surprising, particularly when one considers the size of the cohorts in our study, and the rarity of most cancers. For Hodgkin's disease, the average age-adjusted incidence among males age 20-40 years old ranges from 4.0 to 5.4 cases per 100,000 persons per year; for non-Hodgkin's disease, the corresponding rate ranges from 1.9 to 4.1 cases per 100,000 persons per year (National Cancer Institute, 1981). Incidence rates for the other types of cancers believed to be associated with exposure to phenoxyherbicides or TCDD are even lower. Thus, in a study the size of ours, with 4,462 veterans who served in the Army 10 to 20 years earlier, we would expect to find few, if any, participants with these types of tumors. Methodologically, in the VES, our ability to study the relative prevalence of specific cancers was limited. The risk for certain specific cancers among Vietnam veterans is, however, being evaluated in the Selected Cancers Study (SCS). The results of the SCS, now being conducted by the Centers for Disease Control, should help clarify the issue of the risk of certain cancers among Vietnam veterans.

More Vietnam than non-Vietnam veterans reported having testicular cancers, but the overall number of study participants with this tumor was small, and group differences were

Table 12.8 **Means and Mean Differences for Hematologic Tests for Vietnam and Non-Vietnam Veterans**

					Multivariate Results			
	Crude Arithmetic Mean		Crude Results		Model 1[a]		Model 2[b]	
Laboratory Test	**Vietnam**	**Non-Vietnam**	**Diff**	**95% CI**	**Diff**	**95% CI**	**Diff**	**95% CI**
Red cell count, 10^6 cells/mm^3	5.2	5.2	0.0	-0.02,0.03	0.0	-0.02,0.02	0.0	-0.02,0.02
Hemoglobin, g/dL	16.2	16.1	0.1	-0.02,0.12	0.0	-0.05,0.09	0.0	-0.06,0.08
Hematocrit, vol %	48.5	48.4	0.1	-0.04,0.33	0.1	-0.12,0.26	0.0	-0.14,0.23
Mean corpuscular volume, fL	93.1	92.9	0.2	-0.04,0.50	0.2	-0.13,0.43	0.1	-0.17,0.35
Mean corpuscular hemoglobin, pg	31.1	31.0	0.1	-0.03,0.19	0.1	-0.06,0.16	0.0	-0.08,0.13
Mean corpuscular hemoglobin concentration, %	33.4	33.4	0.0	-0.05,0.06	0.0	-0.06,0.06	0.0	-0.06,0.05
White cell count, 10^3 cells/mm^3	6.7	6.6	0.2	0.04,0.27	0.1	-0.04,0.20	0.1	-0.05,0.16
Segmented neutrophil, 10^3 cells/mm^3	3.8	3.6	0.1	0.03,0.20	0.1	-0.03,0.15	0.1	-0.04,0.13
Band neutrophil, 10^3 cells/mm^3	0.2	0.2	0.0	-0.01,0.01	0.0	-0.02,0.01	0.0	-0.02,0.01
Lymphocyte, 10^3 cells/mm^3	2.0	1.9	0.0	0.00,0.07	0.0	-0.01,0.06	0.0	-0.02,0.05
Monocyte, 10^3 cells/mm^3	0.4	0.4	0.0	-0.01,0.01	0.0	-0.01,0.01	0.0	-0.02,0.00
Eosinophil, 10^3 cells/mm^3	0.1	0.1	0.0	0.00,0.01	0.0	-0.01,0.01	0.0	-0.01,0.01
Basophil, 10^3 cells/mm^3	0.0	0.0	0.0	0.00,0.00	0.0	0.00,0.00	0.0	0.00,0.00
Platelet count, 10^3 cells/mm^3	280.4	278.5	1.9	-1.69,5.52	1.2	-2.58,4.92	1.4	2.33,5.18
Prothrombin time, sec	12.4	12.4	0.0	-0.10,0.00	0.0	-0.05,0.01	0.0	-0.04,0.01

[a] Model 1 contains the six entry characteristics.

[b] Model 2 contains the six entry characteristics and smoking status, alcohol consumption, illicit drug use, and occupational exposure to herbicides.