

CHAPTER 13

GASTROINTESTINAL ASSESSMENT

INTRODUCTION

Background

This system assessment centers on reported peptic ulcer and liver disease, and current hepatic function and porphyria as determined by comprehensive laboratory testing and the physical examination. The liver is a major target organ for single high-dose and continued low-dose exposure to chlorophenols and 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). Peptic and stomach ulcer disease and porphyria cutanea tarda (PCT) are suspected clinical endpoints following moderate- to high-level exposures.

A variety of experimental animal studies¹⁻⁶ have demonstrated hepatic dysfunction and porphyria following a wide range of exposures to TCDD. The effects of exposure, as measured by enzymatic change, however, generally appear to be more related to species than to dose and route of administration.

Gross organ pathology in the digestive system and associated clinical symptoms have been observed following TCDD oral administration to animals (or by accidental ingestion). Pathological lesions have included gastric ulcers, metaplasia of the gastric mucosa, ileitis, hepatic hypertrophy and degeneration, hepatic parenchymal cell necrosis, and hepatic lipid accumulation.

Scientific interest has centered on changes in hepatic enzymes following TCDD administration. Studies involving the metabolism of TCDD have indicated that 74 to 81 percent of the intestinal uptake in rats is absorbed into the liver and adipose tissue, making the liver a key organ for TCDD effects. Clearly, TCDD has proved to be an exceptional inducer of hepatic enzymes and mixed function oxidases, and a powerful inhibitor of other enzymes. Specifically, the induction of cytochrome P-450, a ferrocyclochrome enzyme, has been demonstrated in many species and most of their tissues. Further, marked increases in cytochrome P-450 have been implicated as a mechanism of hepatotoxicity, although other factors, such as genetic susceptibility, are also contributory.⁸⁻¹⁰

Extensive work has been done investigating the TCDD-binding capacity of hepatic Ah receptors and the enhancement of lipid peroxidase and glutathione peroxidase activity in the presence of TCDD in a variety of experimental animals.¹¹⁻²³ Other hepatic effects include the inhibition of cholesterol synthesis and fatty acid synthesis, a decrease in estrogen receptors, a change in the proteins found in plasma membranes, and an increase in liver weight as a result of hepatocellular hypertrophy.^{7,24-27} TCDD has also been shown to cause the disruption of subcellular distributions of iron, copper, zinc, and magnesium.²⁸ Peroxisome proliferation has been shown with 2,4-D and 2,4,5-T and appears to depend on the location of the chlorine atoms on the phenoxy molecule.²⁹

TCDD has also been shown to produce hepatic porphyria in animals by a reduction in uroporphyrinogen decarboxylase, possibly due to the activation of the P-450 enzyme.^{30,31} The porphyrinogenic effect of TCDD has also been influenced by genetic susceptibility, iron levels, sex, and ambient temperature.^{32,33} In correlation with some human studies, hexachlorobenzene was found to be more porphyrinogenic than TCDD.³² Work in humans has located cytochrome P-450 receptors that bind TCDD in the liver.^{34,35}

Numerous morbidity studies, predominantly from the industrial sector, have noted significant abnormal liver function in exposed workers, with and without the presence of clinical hepatic disease. Abnormal liver function test results have been found for direct bilirubin, alkaline phosphatase, triglycerides, cholesterol, aspartate aminotransferase (AST; previously called serum glutamic-oxaloacetic transaminase or SGOT), gamma-glutamyl transpeptidase (GGT; previously GGTP), urine d-glucaric acid, etc.³⁶⁻⁴⁹ The consistent finding of elevated cholesterol levels may have predictive significance with respect to future heart disease (see Chapter 15).

Contemporary studies have focused on two indirect measures of hepatic microsomal activity, GGT and urine d-glucaric acid. In the study of an English industrial incident, several Seveso investigations, and two studies of the Monsanto plant in Nitro, West Virginia, there was modest agreement in observing elevated GGT and urine d-glucaric acid levels in exposed individuals.^{41,42,44,45} Common to all studies was the observation that individuals with chloracne manifested significantly more abnormal liver function tests than exposed individuals without chloracne or unexposed individuals, suggesting a link to TCDD exposure.

Several industrial studies have shown altered porphyrin excretion patterns (predominantly an increase in uroporphyrin) or clinical evidence of PCT, particularly in chronically exposed workers.⁵⁰⁻⁵² Individuals with low chronic exposure or high acute exposure (Seveso) have not shown these signs. Reviews of the suspected association have identified the following difficulties in interpreting these studies: (1) multiple etiologies of PCT or abnormal porphyrin excretion patterns (chemical exposure, genetic makeup, alcohol consumption), (2) potential misdiagnosis of PCT, and (3) confounding by other chemical exposures in the industrial cohorts. Some investigators believe that the PCT cases found in the early U.S. and European studies were more likely caused by exposure to chlorobenzenes than to TCDD.⁵³ Overall, the evidence at present is inconclusive to establish a causal association between PCT and TCDD exposure.

A recent industrial study based on questionnaire data has suggested an association of stomach and peptic ulcers with exposure to TCDD.⁴⁵ This finding at the Monsanto plant differs from similar research using a slightly different cohort at the same plant that produced a negative conclusion on peptic ulcer disease.⁴⁴ The gastric ulcer-TCDD association has not been reported in other cohort dioxin morbidity studies, but ulcer disease has generally not been a major research focus. The preliminary gastric ulcer-TCDD association is fortified somewhat by studies that have shown significant gastric mucosal damage in monkeys following oral administration of TCDD.²

Baseline Summary Results

The 1982 Air Force Health Study (AFHS) examination included an extensive evaluation of hepatic status by questionnaire, physical examination, and laboratory testing. The questionnaire elicited data on liver conditions, liver disease, and symptoms compatible with PCT, as well as detailed information on PCT risk factors (e.g., alcohol consumption, chemical exposures). The physical examination measured hepatomegaly when present and determined liver function and porphyrin patterns by a comprehensive battery of 12 laboratory tests.

The questionnaire showed that Ranch Hands reported more miscellaneous liver conditions (verified by medical record reviews) and more skin changes compatible with PCT than their Comparisons. Although the reported skin changes were statistically significant, no cases of PCT were diagnosed at examination in either cohort.

The physical examination detected a twofold increase in hepatomegaly in the Ranch Hands, but the numbers were small and not statistically significant. Many analyses of the laboratory test variables involved group-by-covariate interactions. Ranch Hands had slightly higher GGT and lactic dehydrogenase (LDH) results and lower cholesterol levels; no differences were found for bilirubin or alkaline phosphatase levels.

AST, alanine aminotransferase (ALT; previously called serum glutamic-pyruvic transaminase or SGPT), and LDH results in the Ranch Hands interacted with the alcohol, degreasing chemicals, and industrial chemicals covariates differently than they did in the Comparisons. All of these two-factor interactions were statistically significant ($p < 0.05$). There were no significant group differences in uroporphyrin, coproporphyrin, or d-aminolevulinic acid levels, nor did any test set support a diagnosis of PCT. Exposure analyses were essentially negative.

The comprehensive hepatic evaluation did not reveal any consistent pattern of significant liver damage in the Ranch Hand group.

1985 Followup Study Summary Results

The 1985 AFHS examination continued the emphasis on hepatic function and expanded the porphyrin test battery to six assays. In addition, new components were added to the questionnaire to assess past and current diagnosed peptic ulcer disease, along with a series of screening questions to assess possible undiagnosed disease. Covariate data on aspirin usage, blood group, and family history of peptic ulcer and additional probes on intestinal parasites, gallbladder disease, and other liver conditions were also added. Because of the known effects of alcohol ingestion on hepatic function, a detailed alcohol consumption history was obtained by questionnaire.

The interval questionnaire revealed sparse reporting of liver disorders from 1982 to 1985 that was not significantly different between groups. Reported liver diseases were verified by medical records, and these data were added to the verified Baseline history to assess possible lifetime differences. No significant differences were found. The medical record verifica-

tion process showed that the historical data were generally correctly reported and classified between groups, except for the category of enlarged liver, which showed a higher verification rate in the Comparison group.

No differences were found for past or current peptic ulcer disease in the Ranch Hand and Comparison groups, after adjustment for blood type.

The physical examination disclosed a borderline significant increase of hepatomegaly in the Ranch Hand group. Emphasis was placed on nine laboratory test variables measuring liver function, i.e., AST, ALT, GGT, alkaline phosphatase, total and direct bilirubin, LDH, cholesterol, and triglycerides. In addition, uroporphyrin and coproporphyrin measurements were obtained to assess liver function and the likelihood of PCT. The nine hepatic variables were subjected to continuous and discrete statistical tests, and were adjusted for the covariates of age, race, occupation, current alcohol use, and unprotected exposure to both industrial chemicals and degreasing chemicals. Final statistical models used only the significant covariates and two-way interactions for adjustment. The two porphyrin measurements were analyzed only in the continuous form.

The results showed a significantly lower mean ALT level, a greater mean alkaline phosphatase level, a lower mean uroporphyrin level, and a marginally significant greater mean coproporphyrin level in the Ranch Hands. Only in the instance of alkaline phosphatase was the discrete analysis statistically significant. No group differences were noted for AST, GGT, total and direct bilirubin, LDH, cholesterol, or triglycerides. A review of the covariate effects in the adjusted statistical models revealed that all covariates behaved as expected with the exception of alcohol consumption for the alkaline phosphatase analysis, which showed an inverse relationship with wine consumption.

Exploration of group-by-covariate interactions for alkaline phosphatase, direct bilirubin, triglycerides, AST, and uroporphyrins revealed significant group differences within specific covariate strata. In particular, Ranch Hands exposed to industrial chemicals had a significantly higher adjusted mean level of alkaline phosphatase and a significantly higher prevalence rate of abnormal direct bilirubin levels than similarly exposed Comparisons. For triglycerides, Ranch Hands born in or before 1922 had a significantly higher adjusted mean level than similar aged Comparisons, while Ranch Hand officers exhibited a significantly higher prevalence rate of abnormal levels than Comparison officers. For AST, Ranch Hand moderate current drinkers (more than one to four drinks per day) had a significantly higher mean level than corresponding Comparisons. In the opposite direction, Comparisons with a mean blood urea nitrogen level less than or equal to 14 mg/dl (median for all participants) were found to have a significantly higher adjusted mean uroporphyrin level than similar Ranch Hands. These results did not disclose any common pattern suggesting a detriment in the Ranch Hand group.

These findings were generally consistent with the 1982 Baseline data. Slight differences in analytic results are probably due to the use of more fully adjusted models used for the 1985 followup examination data.

Overall, the followup examination laboratory data showed no adverse clinical or exposure patterns in either group. Further, the detection of

significant mean shifts (still within normal range) by the continuous statistical tests, not mirrored by the discrete tests, highlights the difference between statistical significance and biological relevance.

The results of the exposure index analyses were generally not significant. Significant or marginally significant results that supported a herbicide effect were found for ALT and total bilirubin in the enlisted flyer cohort, and for AST in the enlisted groundcrew cohort.

Longitudinal analyses for AST, ALT, and GGT disclosed no statistically significant group differences in the mean shifts from the Baseline to the 1985 followup examination.

Interval reporting of PCT-like symptoms of skin patches, bruises, and sensitivity was significantly increased in the Ranch Hands. However, when these historic data were contrasted to both uroporphyrin and coproporphyrin abnormalities, no correlation was apparent, nor were there any significant group differences. Since an elevation in the uroporphyrin level is required for a diagnosis of PCT, the historic data were retabulated with only uroporphyrin abnormalities; again, no group differences were apparent, and uroporphyrin abnormalities in both groups were higher in those participants without a history of skin disorders than in those participants with such a history. The likelihood of bona fide PCT among study participants, and particularly among the Ranch Hands, appears to be remote.

The 1985 followup examination disclosed more statistically significant findings for tests of liver function than the Baseline examination, but they were equally divided between the two groups and did not demonstrate clinical, statistical, or exposure patterns consistent with a herbicide-related effect on health. No evidence was found to suggest an increased likelihood of PCT in the Ranch Hand group.

Parameters of the 1987 Gastrointestinal Assessment

Dependent Variables

Questionnaire, physical examination, and laboratory data were used in the 1987 gastrointestinal assessment.

Questionnaire Data

During the health interview, each study participant was asked about the occurrence of hepatitis, jaundice, cirrhosis, enlarged liver, and other liver conditions. This self-reported information was verified by medical record review. The verified results were then grouped into eight categories of disorders for analysis: viral hepatitis, acute and subacute necrosis of the liver, chronic liver disease and cirrhosis (alcoholic-related and non-alcoholic-related were analyzed separately), liver abscess and sequelae of chronic liver disease, other disorders of the liver, jaundice (unspecified, not of the newborn), and hepatomegaly.

Information on the occurrence of peptic or stomach ulcers and on skin bruises, patches, and sensitivity was also captured in the questionnaire. This self-reported information was analyzed as part of the 1987 assessment. A verified ulcer variable based on gastric, duodenal, peptic, and gastrojejunal ulcers was also analyzed.

For each condition (other than reported ulcer and skin patches, bruises, and sensitivity), participants with a pre-Southeast Asia (SEA) diagnosis were excluded from the analysis.

The frequency of digestive system mortality was tabulated.

Physical Examination Data

One variable from the physical examination, diagnosed hepatomegaly, was analyzed in the gastrointestinal assessment. This variable was coded as yes/no.

Participants whose blood contained hepatitis B surface antigen (HB_sAg) were excluded from the analysis of hepatomegaly.

Laboratory Examination Data

The 1987 followup examination emphasized evaluation of laboratory data, particularly for the hepatic function. Thirteen laboratory variables were analyzed: AST (U/L), ALT (U/L), GGT (U/L), alkaline phosphatase (U/L), total bilirubin (mg/dl), direct bilirubin (mg/dl), LDH (U/L), cholesterol (mg/dl), high-density lipoproteins (HDL in mg/dl), cholesterol-HDL ratio, triglycerides (mg/dl), creatine kinase (U/L), and fasting glucose (mg/dl). Each of these was analyzed as a continuous variable and as a discrete variable. All were dichotomized as normal versus high for the discrete analyses except HDL, which was dichotomized as normal versus low. For all variables other than HDL, only values greater than the normal range were considered as important in the assessment of dysfunction and coded as abnormal. A natural logarithm transformation was applied to all the variables except HDL and cholesterol-HDL ratio. These two exceptions were analyzed in original units. For total bilirubin and direct bilirubin, the transformation was done after adding 0.1 to each value because several participants had levels of 0 mg/dl.

Participants whose blood contained HB_sAg and participants with body temperature greater than or equal to 100 degrees Fahrenheit were excluded from the analysis of the laboratory variables.

Covariates

The effects of covariates were examined in the gastrointestinal assessment, both in pairwise associations with the dependent variables and in adjusted statistical analyses. Blood type was a candidate covariate for the adjusted analysis of reported and verified ulcer. The matching variables age, race, and occupation were used for analyses with all laboratory variables. In addition, current alcohol use, lifetime alcohol history, lifetime industrial

chemical exposure, and lifetime degreasing chemical exposure were candidate covariates for the adjusted analyses of all of the laboratory variables except alkaline phosphatase. For alkaline phosphatase, current wine consumption was used instead of current alcohol use, and lifetime wine history was used instead of lifetime alcohol history since wine consumption showed a strong negative association with alkaline phosphatase in the 1985 followup.

The lifetime alcohol history and current alcohol use covariates were based on self-reported information from the questionnaire. For lifetime alcohol history, the respondent's average daily alcohol consumption was determined for various drinking stages throughout his lifetime, and an estimate of the corresponding total number of drink-years (1 drink-year is the equivalent of drinking 1.5 ounces of 80-proof alcoholic beverage per day for 1 year) was derived. The current alcohol use covariate was based on the average drinks per day for the month prior to completing the questionnaire.

Age, current alcohol use, and lifetime alcohol history were treated as continuous variables for all adjusted analyses. However, for the discrete covariate tests of association, and to explore interactions, they were categorized for presentation. Current wine use and lifetime wine history were treated as continuous variables for the adjusted alkaline phosphatase analyses, and were similarly categorized for presentation. Degreasing chemical exposure and industrial chemical exposure were categorized for all analyses. The cutpoints used for categorization are specified in Table 13-1. In discussing the alcohol-related covariates, the terms light, moderate, and heavy are frequently used to describe the current drinking habits of the participants; for lifetime alcohol use, never replaces light. These distinctions correspond to the three drinking categories in Table 13-1 for current alcohol use and lifetime drinking history.

Relation to Baseline and 1985 Followup Studies

The verified questionnaire data analyzed in the 1987 assessment were organized by International Classification of Disease (ICD) medical coding categories. The analysis of ulcers was added in the 1985 assessment.

For the laboratory variables, the 1987 assessment was expanded to include HDL, cholesterol-HDL ratio, creatine kinase, and fasting glucose; all other laboratory variables analyzed in the 1987 followup were analyzed in the Baseline and 1985 followup studies.

The longitudinal assessment was based on the analysis of AST, ALT, and GGT.

Statistical Methods

The basic statistical analysis methods used in the gastrointestinal assessment are described in Chapter 7.

Table 13-1 summarizes the statistical analyses performed for the 1987 gastrointestinal assessment. The first part of this table identifies the dependent variables, source of the data, form(s) of the data, cutpoints,

TABLE 13-1.

Statistical Analysis for the Gastrointestinal Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Viral Hepatitis	Q-V	D	Yes No	--	UC:FT
Acute and Sub- acute Necrosis of the Liver	Q-V	D	Yes No	--	UC:FT
Chronic Liver Disease and Cirrhosis (Alco- hol Related)	Q-V	D	Yes No	--	UC:FT
Chronic Liver Disease and Cirrhosis (Non- alcohol Related)	Q-V	D	Yes No	--	UC:FT
Liver Abscess and Sequelae of Chronic Liver Disease	Q-V	D	Yes No	--	UC:FT
Other Disorders of the Liver	Q-V	D	Yes No	--	UC:FT
Jaundice (Unspecified)	Q-V	D	Yes No	--	UC:FT
Hepatomegaly	Q-V	D	Yes No	--	UC:FT
Reported Ulcer	Q-SR	D	Yes-Current Yes-Past No	BLOOD	UC:CS AC:LL
Skin Bruises, Patches, or Sensitivity	Q-SR	D	Yes No	--	UC:FT
Verified Ulcer	Q-V	D	Yes No	BLOOD	UC:FT AC:LR

TABLE 13-1. (continued)

Statistical Analysis for the Gastrointestinal Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Diagnosed Hepatomegaly	PE	D	Yes No	AGE RACE OCC ALC DRKYR IC DC	UC:FT AC:LR CA:CS,FT
AST (U/L)	LAB	D/C	Normal: <47 High: ≥ 48	AGE RACE OCC ALC DRKYR IC DC	UC:FT,TT AC:LR,GLM CA:CC,TT,GLM,CS,FT UE:CS,FT,GLM,TT AE:LR,GLM L:RM
ALT (U/L)	LAB	D/C	Normal: <36 High: ≥ 37	AGE RACE OCC ALC DRKYR IC DC	UC:FT,TT AC:LR,GLM CA:CC,TT,GLM,CS,FT UE:CS,FT,GLM,TT AE:LR,GLM L:RM
GGT (U/L)	LAB	D/C	Normal: <85 High: ≥ 86	AGE RACE OCC ALC DRKYR IC DC	UC:FT,TT AC:LR,GLM CA:CC,TT,GLM,CS,FT UE:CS,FT,GLM,TT AE:LR,GLM L:RM
Alkaline Phosphatase (U/L)	LAB	D/C	Normal: <136 High: ≥ 137	AGE RACE OCC WINE LWINE IC DC	UC:FT,TT AC:LR,GLM CA:CC,TT,GLM,CS,FT UE:CS,FT,GLM,TT AE:LR,GLM

TABLE 13-1. (continued)

Statistical Analysis for the Gastrointestinal Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Total Bilirubin (mg/dl)	LAB	D/C	Normal: <1.5 High: ≥ 1.5	AGE RACE OCC ALC DRKYR IC DC	UC: FT, TT AC: LR, GLM CA: CC, TT, GLM, CS, FT UE: CS, FT, GLM, TT AE: LR, GLM
Direct Bilirubin (mg/dl)	LAB	D/C	Normal: <0.40 High: ≥ 0.41	AGE RACE OCC ALC DRKYR IC DC	UC: FT, TT AC: LR, GLM CA: CC, TT, GLM, CS, FT UE: CS, FT, GLM, TT AE: LR, GLM
LDH (U/L)	LAB	D/C	Normal: <190 High: ≥ 191	AGE RACE OCC ALC DRKYR IC DC	UC: FT, TT AC: LR, GLM CA: CC, TT, GLM, CS, FT UE: CS, FT, GLM, TT AE: LR, GLM
Cholesterol (mg/dl)	LAB	D/C	Normal: <260 High: ≥ 261	AGE RACE OCC ALC DRKYR IC DC	UC: FT, TT AC: LR, GLM CA: CC, TT, GLM, CS, FT UE: CS, FT, GLM, TT AE: LR, GLM
HDL (mg/dl)	LAB	D/C	Normal: ≥ 25 Low: <25	AGE RACE OCC ALC DRKYR IC DC	UC: FT, TT AC: LR, GLM CA: CC, TT, GLM, CS, FT UE: CS, FT, GLM, TT AE: LR, GLM

TABLE 13-1. (continued)

Statistical Analysis for the Gastrointestinal Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Cholesterol-HDL Ratio	LAB	D/C	Normal: <5 High: >5	AGE RACE OCC ALC DRKYR IC DC	UC: FT, TT AC: LR, GLM CA: CC, TT
Triglycerides (mg/dl)	LAB	D/C	Normal: <320 High: >321	AGE RACE OCC ALC DRKYR IC DC	UC: FT, TT AC: LR, GLM CA: CC, TT, GLM, CS, FT UE: CS, FT, GLM, TT AE: LR, GLM
Creatine Kinase (U/L)	LAB	D/C	Normal: <232 High: >233	AGE RACE OCC ALC DRKYR IC DC	UC: FT, TT AC: LR, GLM CA: CC, TT, GLM, CS, FT UE: CS, FT, GLM, TT AE: LR, GLM
Fasting Glucose (mg/dl)	LAB	D/C	Normal: <110 High: >111	AGE RACE OCC ALC DRKYR IC DC	UC: FT, TT AC: LR, GLM CA: CC, TT, GLM, CS, FT UE: CS, FT, GLM, TT AE: LR, GLM

TABLE 13-1. (continued)

Statistical Analysis for the Gastrointestinal Assessment

Covariates

Variable (Abbreviation)	Data Source	Data Form	Cutpoints
Age (AGE)	MIL	D/C	Born >1942 Born 1923-1941 Born ≤1922
Race (RACE)	MIL	D	Nonblack Black
Occupation (OCC)	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Current Alcohol Use (ALC) (drinks/day)	Q-SR	D/C	0-1 >1-4 >4
Current Wine Use (WINE) (drinks/day)	Q-SR	D/C	0 >0
Lifetime Alcohol History (DRKYR) (drink-years)	Q-SR	D/C	0 >0-40 >40
Lifetime Wine History (LWINE) (drink-years of wine)	Q-SR	D/C	0 >0-10 >10
Industrial Chemical Exposure (IC)	Q-SR	D	Yes No
Degreasing Chemical Exposure (DC)	Q-SR	D	Yes No
Blood Type (BLOOD)	MIL	D	A B AB O

Abbreviations:

Data Source: LAB--1987 SCRF laboratory results
MIL--Air Force military records
PE--1987 SCRF physical examination
Q-SR--1987 NORC questionnaire (self-reported)
Q-V--1987 NORC questionnaire (verified)

TABLE 13-1. (continued)

Statistical Analysis for the Gastrointestinal Assessment

Abbreviations (continued):

Data Form: D--Discrete analysis only
D/C--Discrete and continuous analyses for dependent variables; appropriate form for analysis (either discrete or continuous) for covariates

Statistical Analyses: UC--Unadjusted core analyses
AC--Adjusted core analyses
CA--Dependent variable-covariate associations
UE--Unadjusted exposure index analyses
AE--Adjusted exposure index analyses
L--Longitudinal analyses

Statistical Methods: CC--Pearson's product moment correlation coefficient
CS--Chi-square contingency table test
FT--Fisher's exact test
GLM--General linear models analysis
LL--Log-linear models analysis
LR--Logistic regression analysis
RM--Repeated measures analysis
TT--Two-sample t-test

candidate covariates, and statistical methods. The second part of the table provides additional information on the candidate covariates. Abbreviations are used extensively in the body of the table and are defined in footnotes.

Dependent variable and covariate data were missing for some participants. Table 13-2 summarizes the number of participants with missing data, and the number who were excluded from analyses for medical reasons, by group and variable.

RESULTS

Ranch Hand and Comparison Group Contrast

Table 13-3 presents unadjusted results for verified questionnaire variables. Unadjusted results for ulcers, presence of skin bruises, patches, or sensitivity, and diagnosed hepatomegaly are given in Table 13-4; adjusted results for hepatomegaly and peptic ulcer are shown in Table 13-5. Unadjusted and adjusted results for the laboratory examination variables are provided in Tables 13-6 and 13-7, respectively. Table J-1 of Appendix J summarizes the results of the covariate tests of association for hepatomegaly and the laboratory examination variables. Table J-2 details the relationship between ulcer and blood type. Stratified results to explore group-by-covariate interactions are presented in Table J-3.

Questionnaire Variables

Verified questionnaire data on viral hepatitis, acute and subacute necrosis of the liver, chronic liver disease and cirrhosis (alcohol-related and nonalcohol-related analyzed separately), liver abscess and sequelae of chronic liver disease, other disorders of the liver, jaundice (unspecified, not of newborn), and hepatomegaly were analyzed. Additional self-reported information from the questionnaire was analyzed on occurrences of ulcers, and on skin patches, bruises, and sensitivity. As seen in Tables 13-3 and 13-4, no significant group differences were noted for any of these conditions.

An additional analysis was done for reported ulcer, adjusting for blood type and the group-by-blood type interaction. However, since neither of these effects were statistically significant, they were deleted from the adjusted model. Thus, results for this adjusted analysis paralleled the unadjusted analysis.

Verified Ulcer

The unadjusted prevalence of verified ulcer was not significantly different between groups ($p=0.950$). An adjusted analysis was done examining the effects of blood type and the group-by-blood type interaction. This analysis found no significant result.

TABLE 13-2.

Number of Participants Excluded and With Missing Data for the
Gastrointestinal Assessment by Group

Variable	Analysis Use	Group		Total
		Ranch Hand	Comparison	
All 13 Laboratory Examination Variables	DEP	1	2	3
Reported Ulcer	DEP	1	0	1
Current Alcohol Use	COV	5	1	6
Current Wine Use	COV	6	2	8
Lifetime Alcohol History	COV	10	3	13
Lifetime Wine History	COV	6	3	9
Blood Type	COV	6	7	13
Pre-SEA Viral Hepatitis	EXC	27	42	69
Pre-SEA Acute and Subacute Necrosis of the Liver	EXC	0	1	1
Pre-SEA Chronic Liver Disease and Cirrhosis (Alcohol-Related)	EXC	1	5	6

TABLE 13-2. (continued)

Number of Participants Excluded and With Missing Data for the
Gastrointestinal Assessment by Group

Variable	Analysis Use	Group		Total
		Ranch Hand	Comparison	
Pre-SEA Chronic Liver Disease and Cirrhosis (Nonalcohol-Related)	EXC	0	1	1
Pre-SEA Other Disorders of the Liver	EXC	6	12	18
Pre-SEA Jaundice	EXC	27	39	66
Pre-SEA Hepatomegaly	EXC	2	2	4
Pre-SEA Verified Ulcer	EXC	23	32	55
Positive HB _s Ag	EXC	7	8	15
Temperature >100° at Laboratory Examination	EXC	1	3	4

Abbreviations: DEP--Dependent variable (missing data)
COV--Covariate (missing data)
EXC--Exclusion

TABLE 13-3.

Unadjusted Analysis for Verified Gastrointestinal Questionnaire Variables by Group

Variable	Statistic	Group		Est. Relative Risk (95% C.I.)	p-Value
		Ranch Hand	Comparison		
Viral Hepatitis	n	968		0.93 (0.78,1.10)	0.406
	Number/%	1,257			
	Yes	375 38.7%	510 40.6%		
	No	593 61.3%	747 59.4%		
Acute and Sub-acute Necrosis of the Liver	n	995		-- ^a	0.640
	Number/%	1,298			
	Yes	0 0.0%	2 0.2%		
	No	995 100.0%	1,296 99.8%		
Chronic Liver Disease and Cirrhosis (Alcohol Related)	n	994		1.18 (0.79,1.78)	0.480
	Number/%	1,294			
	Yes	46 4.6%	51 3.9%		
	No	948 95.4%	1,243 96.1%		
Chronic Liver Disease and Cirrhosis (Non-alcohol Related)	n	995		1.60 (0.66,3.88)	0.408
	Number/%	1,298			
	Yes	11 1.1%	9 0.7%		
	No	984 98.9%	1,289 99.3%		
Liver Abscess and Sequelae of Chronic Liver Disease	n	995		-- ^a	0.999
	Number/%	1,299			
	Yes	0 0.0%	1 0.1%		
	No	995 100.0%	1,298 99.9%		

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TABLE 13-3. (continued)

Unadjusted Analysis for Verified Gastrointestinal Questionnaire Variables by Group

Variable	Statistic	Group		Est. Relative Risk (95% C.I.)	p-Value
		Ranch Hand	Comparison		
Other Disorders of the Liver	n	989		1,287	
	Number/%				
	Yes	90	9.1%	95	7.4%
	No	899	90.9%	1,192	92.6%
				1.26 (0.93,1.70)	0.159
Jaundice (Unspecified)	n	968		1,260	
	Number/%				
	Yes	17	1.8%	32	2.5%
	No	951	98.2%	1,228	97.5%
				0.69 (0.38,1.24)	0.268
Hepatomegaly	n	993		1,297	
	Number/%				
	Yes	16	1.6%	25	1.9%
	No	977	98.4%	1,272	98.1%
				0.83 (0.44,1.57)	0.690

*Estimated relative risk/confidence interval not given due to a cell with zero frequency.

TABLE 13-4.

Unadjusted Analysis for Other Gastrointestinal Questionnaire and Physical Examination Variables by Group

Variable	Statistic	Group		Contrast	Est. Relative Risk (95% C.I.)	p-Value
		Ranch Hand	Comparison			
Reported Ulcer	n	994		1,299		
	Number/%					
	Yes-Current	11	1.1%	10	0.8%	Overall Yes-Current vs. No Yes-Past vs. No
	Yes-Past	10	1.0%	12	0.9%	
No	973	97.9%	1,277	98.3%	1.44 (0.61,3.41)	0.688
					1.09 (0.47,2.54)	0.532
						0.998
Verified Ulcer (Questionnaire and Physical Exam)	n	972		1,267		
	Number/%					
	Yes	69	7.1%	92	7.3%	0.98 (0.71,1.35)
No	903	92.9%	1,175	92.7%		
Skin Bruises, Patches, or Sensitivity	n	995		1,299		
	Number/%					
	Yes	184	18.5%	207	15.9%	1.20 (0.96,1.49)
No	811	81.5%	1,092	84.1%		
Diagnosed Hepatomegaly (Physical Exam)	n	988		1,291		
	Number/%					
	Yes	11	1.1%	15	1.2%	0.96 (0.44,2.10)
No	977	98.9%	1,276	98.8%		

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TABLE 13-5.

Adjusted Analysis for Reported Gastrointestinal Questionnaire and Physical Examination Variables by Group

Variable	Statistic	Group		Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
		Ranch Hand	Comparison				
Reported Ulcer	n	994	1,299	Overall		0.688	—
				Yes-Current vs. No	1.44 (0.61,3.41)	0.532	
				Yes-Past vs. No	1.09 (0.47,2.54)	0.998	
Verified Ulcer (Questionnaire and Physical Exam)	n	972	1,267		0.98 (0.71,1.35)	0.950	—
Diagnosed Hepatomegaly (Physical Exam)	n	978	1,288		0.95 (0.43,2.07)**	0.888**	GRP*DC (p=0.016) OCC (p=0.049) RACE*DRKYR (p=0.031)

—No covariates significant in final model ($p > 0.05$).

GRP: Group (Ranch Hand, Comparison).

**Group-by-covariate interaction ($0.01 < p < 0.05$)—adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

TABLE 13-6.

Unadjusted Analysis for Hepatic Laboratory Examination Variables by Group

Variable	Statistic	Group		Est. Relative Risk (95% C.I.)	p-Value
		Ranch Hand	Comparison		
AST	n	986	1,286	--	0.695
	Mean ^a	25.8	25.6		
	95% C.I. ^a	(25.3,26.3)	(25.2,26.1)	1.17 (0.78,1.74)	0.508
	Number/%				
High	48 4.9%	54 4.2%			
Normal	938 95.1%	1,232 95.8%			
ALT	n	986	1,286	--	0.817
	Mean ^a	20.6	20.7		
	95% C.I. ^a	(19.9,21.2)	(20.1,21.2)	1.10 (0.85,1.42)	0.514
	Number/%				
High	120 12.2%	144 11.2%			
Normal	866 87.8%	1,142 88.8%			
GGT	n	986	1,286	--	0.552
	Mean ^a	33.2	32.6		
	95% C.I. ^a	(31.8,34.6)	(31.5,33.8)	1.05 (0.77,1.41)	0.834
	Number/%				
High	83 8.4%	104 8.1%			
Normal	903 91.6%	1,182 91.9%			
Alkaline Phosphatase	n	986	1,286	--	<0.001
	Mean ^a	93.7	90.3		
	95% C.I. ^a	(92.3,95.1)	(89.1,91.5)	1.01 (0.69,1.49)	0.999
	Number/%				
High	48 4.9%	62 4.8%			
Normal	938 95.1%	1,224 95.2%			

TABLE 13-6. (continued)

Unadjusted Analysis for Hepatic Laboratory Examination Variables by Group

Variable	Statistic	Group		Est. Relative Risk (95% C.I.)	p-Value
		Ranch Hand	Comparison		
Total Bilirubin	n	986	1,286		
	Mean ^b	0.780	0.785	--	0.611
	95% C.I. ^b	(0.765,0.795)	(0.771,0.800)		
	Number/%				
	High	28 2.8%	48 3.7%	0.75 (0.47,1.21)	0.292
	Normal	958 97.2%	1,238 96.3%		
Direct Bilirubin	n	986	1,286		
	Mean ^b	0.158	0.158	--	0.969
	95% C.I. ^b	(0.151,0.165)	(0.151,0.165)		
	Number/%				
	High	35 3.5%	57 4.4%	0.79 (0.52,1.22)	0.342
	Normal	951 96.5%	1,229 95.6%		
LDH	n	986	1,286		
	Mean ^a	128.1	127.8	--	0.692
	95% C.I. ^a	(126.8,129.5)	(126.6,129.0)		
	Number/%				
	High	12 1.2%	16 1.2%	0.98 (0.46,2.08)	0.999
	Normal	974 98.8%	1,270 98.8%		
Cholesterol	n	986	1,286		
	Mean ^a	214.8	213.4	--	0.379
	95% C.I. ^a	(212.3,217.3)	(211.3,215.5)		
	Number/%				
	High	141 14.3%	158 12.3%	1.19 (0.93,1.52)	0.179
	Normal	845 85.7%	1,128 87.7%		

TABLE 13-6. (continued)

Unadjusted Analysis for Hepatic Laboratory Examination Variables by Group

Variable	Statistic	Group		Est. Relative Risk (95% C.I.)	p-Value
		Ranch Hand	Comparison		
HDL	n	986		--	0.847
	Mean	49.08			
	95% C.I.	(47.83,50.38)			
	Number/%				
Low		9	0.9%	13	1.0%
	Normal	977	99.1%		
				0.90 (0.38,2.12)	0.992
Cholesterol-HDL Ratio	n	986		--	0.357
	Mean	4.75			
	95% C.I.	(4.60,4.90)			
	Number/%				
High		432	43.8%	537	41.8%
	Normal	554	56.2%		
				1.09 (0.92,1.29)	0.348
Triglycerides	n	986		--	0.355
	Mean ^a	119.5			
	95% C.I. ^a	(114.8,124.4)			
	Number/%				
High		66	6.7%	70	5.4%
	Normal	920	93.3%		
				1.25 (0.88,1.76)	0.248
Creatine Kinase	n	986		--	0.611
	Mean ^a	110.0			
	95% C.I. ^a	(106.8,113.4)			
	Number/%				
High		57	5.8%	97	7.5%
	Normal	929	94.2%		
				0.75 (0.54,1.06)	0.114

TABLE 13-6. (continued)
Unadjusted Analysis for Hepatic Laboratory Examination Variables by Group

Variable	Statistic	Group		Est. Relative Risk (95% C.I.)	p-Value
		Ranch Hand	Comparison		
Fasting Glucose	n	986	1,286	--	0.504
	Mean ^a	100.6	100.1		
	95% C.I. ^a	(99.5,101.7)	(99.3,100.9)	0.93 (0.72,1.19)	0.606
	Number/%				
High	120 12.2%	167 13.0%			
Normal	866 87.8%	1,119 87.0%			

--Estimated relative risk not applicable for continuous analysis of a variable.

^aTransformed from natural logarithm scale.

^bTransformed from natural logarithm (X + 0.1) scale.

TABLE 13-7.

Adjusted Analysis for Hepatic Laboratory Examination Variables by Group

Variable	Statistic	Group		Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
		Ranch Hand	Comparison			
AST	n	981	1,285			
	Adj. Mean ^a 95% C.I. ^a	26.7 (25.9,27.6)	26.5 (25.7,27.3)	--	0.453	ALC*RACE (p=0.016) ALC*IC (p=0.028)
	n	981	1,285	1.23 (0.82,1.84)	0.326	ALC (p<0.001)
ALT	n	976	1,283			
	Adj. Mean ^{**a} 95% C.I. ^{**a}	20.8 (19.7,21.8)	20.7 (19.8,21.7)	--	0.915**	GRP*DRKYR (p=0.020) AGE (p<0.001) ALC*RACE (p<0.001) ALC*IC (p=0.011) DC*IC (p=0.038)
	n	981	1,285	1.14 (0.88,1.49)	0.313	AGE*OCC (p=0.003) AGE*IC (p=0.009) ALC*IC (p=0.031)
GGT	n	976	1,283			
	Adj. Mean ^a 95% C.I. ^a	37.6 (35.2,40.1)	36.7 (34.5,39.0)	--	0.365	RACE (p<0.001) DC (p=0.022) ALC*DRKYR (p<0.001)
	n	976	1,283	1.07 (0.78,1.46)	0.695	OCC*DC (p=0.043) RACE*DC (p=0.038) ALC*DRKYR (p=0.028)

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TABLE 13-7. (continued)

Adjusted Analysis for Hepatic Laboratory Examination Variables by Group

Variable	Statistic	Group		Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
		Ranch Hand	Comparison			
Alkaline Phosphatase	n	979	1,283			
	Adj. Mean ^a 95% C.I. ^a	93.4 (91.1,95.7)	89.9 (87.8,92.1)	--	<0.001	AGE (p<0.001) LWINE (p=0.028) OCC*WINE (p=0.007) RACE*IC (p=0.006)
	n	979	1,283	1.03 (0.70,1.52)	0.892	AGE (p<0.001) IC (p=0.003) LWINE (p=0.013)
Total Bilirubin	n	976	1,283			
	Adj. Mean ^b 95% C.I. ^b	0.778 (0.763,0.794)	0.784 (0.770,0.798)	--	0.622	ALC*DRKYR (p=0.023) AGE*IC (p=0.032)
	n	976	1,283	0.75 (0.47,1.21)**	0.237**	GRP*ALC (p=0.036) GRP*DRKYR (p=0.040)
Direct Bilirubin	n	986	1,286			
	Adj. Mean ^{ab} 95% C.I. ^{ab}	0.156 (0.148,0.164)	0.156 (0.149,0.163)	--	0.985**	GRP*RACE (p=0.022) OCC (p=0.029)
	n	986	1,286	****	****	GRP*DC (p=0.009) OCC (p=0.044)
LDH	n	976	1,283			
	Adj. Mean ^a 95% C.I. ^a	127.3 (125.9,128.8)	127.1 (125.8,128.4)	--	0.804	ALC*DRKYR (p=0.025) AGE*OCC (p=0.025)
	n	986	1,286	0.98 (0.46,2.08)	0.954	--

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TABLE 13-7. (continued)

Adjusted Analysis for Hepatic Laboratory Examination Variables by Group

Variable	Statistic	Group		Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
		Ranch Hand	Comparison			
Cholesterol	n	981	1,285	--	0.437	AGE (p<0.001) ALC (p=0.021) IC (p=0.023) OCC*RACE (p=0.003)
	Adj. Mean ^a 95% C.I. ^a	216.2 (211.4,221.2)	215.0 (210.3,219.7)			
	n	986	1,286	1.18 (0.93,1.51)	0.177	AGE (p=0.048) OCC (p=0.034)
HDL	n	976	1,283	--	0.648**	GRP*DRKYR (p=0.036) OCC (p=0.042) ALC (p=0.001) RACE*DC (p=0.004) ALC*DRKYR (p<0.001) RACE*IC (p=0.042)
	Adj. Mean** 95% C.I.**	48.31 (46.03,50.63)	47.71 (45.72,49.70)			
	n	976	1,283	1.01 (0.42,2.45)	0.999	DC (p=0.040)
Cholesterol- HDL Ratio	n	976	1,283	--	0.509	ALC (p=0.002) RACE*DC (p=0.017) AGE*DRKYR (p=0.040) ALC*DRKYR (p=0.004)
	Adj. Mean 95% C.I.	4.77 (4.48,5.05)	4.89 (4.64,5.13)			
	n	976	1,283	1.07 (0.90,1.27)	0.434	AGE (p=0.038) RACE (p=0.036) OCC (p<0.001) ALC (p<0.001)

13-27

TABLE 13-7. (continued)

Adjusted Analysis for Hepatic Laboratory Examination Variables by Group

Variable	Statistic	Group		Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
		Ranch Hand	Comparison			
Triglycerides	n	976	1,283	--	0.459	AGE (p<0.001) OCC (p=0.001) DC (p=0.009) DRKYR*RACE (p=0.038)
	Adj. Mean ^a	107.8	105.6			
	95% C.I. ^a	(101.0,115.0)	(99.4,112.3)			
	n	976	1,283	1.28 (0.90,1.82)	0.172	RACE (p=0.039) ALC*DRKYR (p=0.043)
Creatine Kinase	n	981	1,285	--	0.500	AGE (p=0.002) RACE (p<0.001) ALC*OCC (p=0.045)
	Adj. Mean ^a	145.4	143.4			
	95% C.I. ^a	(138.2,153.0)	(136.7,150.5)			
	n	986	1,286	0.76 (0.53,1.08)	0.122	RACE (p<0.001) AGE*DC (p=0.019)

TABLE 13-7. (continued)

Adjusted Analysis for Hepatic Laboratory Examination Variables by Group

Variable	Statistic	Group		Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
		Ranch Hand	Comparison			
Fasting Glucose	n	976	1,283			
	Adj. Mean ^a	102.5	102.0	--	0.534	DRKYR*OCC (p<0.001) AGE*RACE (p=0.002) DRKYR*RACE (p=0.050)
	95% C.I. ^a	(100.8,104.2)	(100.4,103.7)			
	n	976	1,283	0.93 (0.72,1.20)	0.565	AGE (p<0.001) RACE (p=0.008) DC (p=0.024) DRKYR (p=0.021)

^aTransformed from natural logarithm scale.

--Adjusted relative risk not applicable for continuous analysis of a variable; no covariates significant in final model (p>0.05).

^bTransformed from natural logarithm (X + 0.1) scale.

**Group-by-covariate interaction (0.01<p<0.05)--adjusted means or relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

***Group-by-covariate interaction (p<0.01)--adjusted relative risk, confidence interval, and p-value not presented.

Physical Examination Variables

Diagnosed Hepatomegaly

The percentage of participants diagnosed with hepatomegaly at the physical examination did not differ significantly between groups ($p=0.999$).

Using pooled group data, the covariate tests of association showed that hepatomegaly was associated with current alcohol use ($p=0.019$) and lifetime alcohol history ($p=0.016$). The percentages of participants with hepatomegaly increased with current alcohol use (0.9%, 1.8%, and 4.1% for the ≤ 1 drink/day, $>1-4$ drinks/day, and >4 drinks/day categories, respectively). Relatively fewer cases of hepatomegaly were seen for moderate lifetime drinkers (0.7% for individuals who drank and had at most 40 drink-years) than for men who had never drunk (2.0%) or for heavy lifetime drinkers (2.1% for men who had more than 40 drink-years).

A significant group-by-degreasing chemical exposure interaction was detected for the adjusted analysis ($p=0.016$). Occupation ($p=0.049$) and a race-by-lifetime alcohol history interaction ($p=0.031$) were also included for adjustment. Results were derived for each level of degreasing chemical exposure to explore the interaction. They showed that the adjusted group relative risk for participants who had never been exposed to degreasing chemicals was marginally less than one (Adj. RR: 0.27, 95% C.I.: [0.06,1.26], $p=0.095$). Conversely, the relative risk for individuals who had been exposed to degreasing chemicals was greater than one, but not significant (Adj. RR: 2.04, 95% C.I.: [0.72,5.81], $p=0.181$). Further analysis was done excluding the group-by degreasing chemical interaction. No significant group difference was found ($p=0.888$) after adjusting for the race-by-lifetime alcohol history interaction ($p=0.037$).

Laboratory Examination Variables

AST

Group differences for AST were not significant for both the unadjusted continuous ($p=0.695$) and discrete ($p=0.508$) analyses.

Examining the relationship between AST and the covariates revealed significant associations with race ($p=0.004$), current alcohol use ($p<0.001$), and lifetime alcohol history ($p<0.001$). A marginally significant association with degreasing chemical exposure was also found ($p=0.091$). Blacks had a higher mean level than nonblacks (27.7 U/L vs. 25.6 U/L). Both alcohol-related variables were positively correlated with AST ($r=0.220$ for current alcohol use; $r=0.096$ for lifetime alcohol history). Correspondingly, the percentage of abnormal AST values increased with current alcohol use (2.8%, 9.6%, and 19.2% for ≤ 1 drink/day, $>1-4$ drinks/day, and >4 drinks/day, respectively), but this pattern was not observed for lifetime alcohol history. The highest percentage of abnormal values was found for the heaviest drinkers (8.4% for participants with >40 drink-years), but men who had never drunk showed a slightly higher percentage of abnormalities than moderate drinkers

(3.9% vs. 3.2% for men with 0 drink-years and >0-40 drink-years, respectively). Relatively more AST abnormal levels were found for participants exposed to degreasing chemicals (5.1%) than for those who had not been exposed (3.5%).

Group differences remained nonsignificant after covariate adjustment ($p=0.453$, $p=0.326$ for the continuous and discrete analysis, respectively). The continuous model was adjusted for interactions between current alcohol use and race ($p=0.016$), and between current alcohol use and industrial chemical exposure ($p=0.028$). The discrete analysis was adjusted only for current alcohol use ($p<0.001$).

ALT

No significant group difference for ALT was found for either the unadjusted continuous ($p=0.817$) or discrete ($p=0.514$) analysis.

The relationship between ALT and the covariates was examined using pooled group data. As seen in Table J-1, significant associations were found with age, both alcohol-related variables, and degreasing chemical exposure. Age was negatively correlated with ALT ($r=-0.109$, $p<0.001$). This finding was also seen after categorizing ALT; the percentage of abnormalities decreased with age (14.3% abnormal values for participants born in or after 1942, 10.0% abnormal values for participants born between 1923 and 1941, and 4.8% abnormal values for participants born in or before 1922, $p=0.001$). The correlation with current alcohol use was 0.125 ($p<0.001$). Correspondingly, the percentage of abnormal levels increased with current alcohol use (10.2%, 17.0%, and 19.2% for individuals currently drinking ≤ 1 drink/day, $>1-4$ drinks/day, and >4 drinks/day, respectively; $p<0.001$). The percentages of abnormal values were 14.2 percent, 10.1 percent, and 15.5 percent for participants who had never drunk, drinkers who had up to 40 drink-years, and those with more than 40 drink-years, respectively ($p=0.007$). Participants exposed to degreasing chemicals had a higher mean ALT than those not exposed (21.0 U/L vs. 20.1 U/L, $p=0.032$).

For the adjusted continuous analysis, a significant group-by-lifetime alcohol history interaction was found ($p=0.020$). Other significant covariates in the model were age ($p<0.001$), current alcohol use-by-race ($p<0.001$), current alcohol use-by-industrial chemical exposure ($p=0.011$), and industrial chemical exposure-by-degreasing chemical exposure ($p=0.038$). Lifetime alcohol history was categorized to explore the interaction with group. Table J-3 presents adjusted mean ALT levels by group for the three levels of lifetime alcohol history. The interaction can partly be explained by a marginally significant group difference for participants with greater than 40 lifetime drink-years ($p=0.095$). Of the three lifetime alcohol history categories, the Ranch Hand adjusted mean was highest for this category (21.8 U/L) in contrast to the Comparison adjusted mean, which was lowest (20.3 U/L). Also, the Comparison adjusted means decreased as lifetime drinking increased. This pattern contrasted with the Ranch Hand group, which showed the lowest adjusted mean for moderate drinkers and higher adjusted means for the other categories. Because the statistical significance of the group-by-lifetime alcohol history interaction was greater than 0.01, an additional adjusted analysis was done to assess the overall group difference. This analysis excluded the group-by-

lifetime alcohol history interaction. The group difference was not significant ($p=0.915$) after adjusting for the covariates discussed above.

The adjusted relative risk was not significant for the discrete analysis ($p=0.313$). Three pairwise covariate interactions were used for adjustment (age-by-occupation, $p=0.003$; age-by-industrial chemical exposure, $p=0.009$; and current alcohol use-by-industrial chemical exposure, $p=0.031$).

GGT

Neither the GGT mean level nor the percentage of abnormal GGT values was significantly different between groups ($p=0.552$ and $p=0.834$, respectively) in unadjusted analyses.

Using pooled group data, significant associations with race, current alcohol use, and lifetime alcohol history were found, along with marginal associations with occupation and degreasing chemical exposure. The GGT mean was much larger for Blacks than nonblacks (44.1 U/L vs. 32.3 U/L, respectively; $p<0.001$), as was the percentage of abnormal values (14.9% abnormal vs. 7.8% abnormal, respectively; $p=0.011$). GGT was highly correlated with current alcohol use ($r=0.271$, $p<0.001$), and the percentage of abnormal values steadily increased with drinking (5.6%, 16.5%, and 28.8% for participants currently drinking ≤ 1 drinks/day, $>1-4$ drinks/day, and >4 drinks/day, respectively; $p<0.001$). The correlation with lifetime alcohol history was 0.110 ($p<0.001$). As with AST and ALT, the percentage of abnormal values was highest for heavy drinkers (14.9% for participants with more than 40 drink-years), less for individuals who had never drunk (7.8%), and lowest for the middle lifetime alcohol history category (6.0% for $>0-40$ drink-years, $p<0.001$). Relatively more abnormal levels were seen for the enlisted flyers than for the other occupational cohorts (7.8% abnormal for officers, 11.1% abnormal for enlisted flyers, and 7.6% abnormal for enlisted groundcrew; $p=0.089$). The mean for participants exposed to degreasing chemicals, 33.6 U/L, was larger than the mean for those not exposed, 31.9 U/L ($p=0.068$).

No significant group differences were found in the adjusted continuous ($p=0.365$) and discrete ($p=0.695$) analyses. The continuous model was adjusted for race ($p<0.001$), degreasing chemical exposure ($p=0.022$), and a current alcohol use-by-lifetime alcohol history interaction ($p<0.001$). Covariates used for adjustment in the discrete analysis were an occupation-by-degreasing chemical exposure interaction ($p=0.043$), a race-by-degreasing chemical exposure interaction ($p=0.038$), and a current alcohol use-by-lifetime alcohol history interaction ($p=0.028$).

Alkaline Phosphatase

For the unadjusted continuous analysis, the Ranch Hand group alkaline phosphatase mean, 93.7 U/L, was significantly higher than the Comparison group mean, 90.3 U/L ($p<0.001$). In contrast, the discrete analysis was not significant ($p=0.999$).

Significant covariate associations were found with occupation, current wine use, lifetime wine history, industrial chemical exposure, and degreasing

chemical exposure. A marginally significant association was found with age. The occupational effect ($p < 0.001$) showed a much higher mean level for enlisted flyers, 95.6 U/L, than for officers, 87.6 U/L. The enlisted groundcrew mean, 93.9 U/L, fell in between. After categorizing alkaline phosphatase, the percentage of abnormalities was lowest for officers, 3.5 percent; higher for enlisted flyers, 5.5 percent; and highest for enlisted groundcrew, 5.7 percent. This relationship was marginally significant ($p = 0.059$). A strong negative association with current wine use was noted at the 1985 followup analysis and was explored further in this study. Both wine-related variables were negatively correlated with alkaline phosphatase ($r = -0.048$, $p = 0.023$, for current wine use; $r = -0.071$, $p < 0.001$, for lifetime wine history). These findings were opposite of expectation. The percentage of abnormal values was higher for participants who do not currently drink wine than for current wine drinkers (5.9% vs. 3.4%, $p = 0.006$). Men who had never drunk wine had relatively more abnormal levels than moderate and heavy wine drinkers (6.3%, 3.5%, and 2.1% for 0 drink-years of wine, >0-10 drink-years of wine, and >10 drink-years of wine, respectively; $p = 0.005$). The alkaline phosphatase mean for individuals exposed to industrial chemicals was larger than for those not exposed (93.1 U/L vs. 90.1 U/L, $p = 0.001$). Similarly, the percentage of abnormal values was significantly higher (5.9% vs. 3.5%, respectively; $p = 0.010$). Participants exposed to degreasing chemicals had a higher mean, 92.5 U/L, than those not exposed, 90.6 U/L ($p = 0.050$); the percentage of abnormalities was marginally significantly higher (5.5% vs. 3.9%, respectively; $p = 0.096$). A positive correlation with age ($r = 0.040$, $p = 0.054$) was found.

The results of the adjusted analyses supported the unadjusted analyses. A highly significant group difference was found in the continuous analysis ($p < 0.001$), but the adjusted relative risk was not significant for the discrete analysis ($p = 0.892$). Age ($p < 0.001$), lifetime wine history ($p = 0.028$), occupation-by-current wine use ($p = 0.007$), and race-by-industrial chemical exposure ($p = 0.006$) were used for adjustment in the continuous analysis. The discrete model was adjusted for age ($p < 0.001$), industrial chemical exposure ($p = 0.003$), and lifetime wine history ($p = 0.013$).

Total Bilirubin

No significant group difference was found for total bilirubin in either the unadjusted continuous ($p = 0.611$) or discrete ($p = 0.292$) analyses.

Treating total bilirubin as a continuous variable, significant associations with age ($p = 0.042$) and occupation ($p = 0.035$) were found, along with a marginally significant association with current alcohol use ($p = 0.092$). No covariates were significantly associated after categorizing total bilirubin; industrial chemical exposure showed a marginal effect ($p = 0.069$). A positive correlation with age was seen ($r = 0.043$), and officers had a larger mean, 0.80 mg/dl, than either enlisted groundcrew (0.77 mg/dl) or enlisted flyers (0.77 mg/dl). The correlation with current alcohol use was 0.035. Participants exposed to industrial chemicals had a higher percentage of abnormal total bilirubin levels than participants not exposed (4.0% vs. 2.5%, respectively).

The group difference was not significant for the adjusted continuous analysis ($p = 0.622$). An age-by-industrial chemical exposure interaction

($p=0.032$) and a current alcohol use-by-lifetime alcohol history interaction ($p=0.023$) were used for adjustment. Group interactions with both alcohol-related variables were found for the adjusted discrete analysis (group-by-current alcohol use, $p=0.036$; group-by-lifetime alcohol history, $p=0.040$). To investigate these interactions, unadjusted relative risks were derived for each of six current alcohol use-by-lifetime alcohol history covariate stratum. As seen in Table J-3, none of these relative risks were significantly different from one. After excluding the interactions, no significant group difference was found ($p=0.237$). No covariates were used for adjustment in this analysis.

Direct Bilirubin

The results of the unadjusted continuous and discrete analyses showed no significant group differences for direct bilirubin ($p=0.969$ and $p=0.342$, respectively).

Of the candidate covariates, only occupation was significantly associated with direct bilirubin; current alcohol use was marginally associated. Although both the continuous and discrete tests of association showed an effect due to occupation, the pattern of the relationship was inconsistent. Officers had the largest mean, 0.17 mg/dl, followed by enlisted groundcrew, 0.16 mg/dl, and enlisted flyers, 0.15 mg/dl ($p=0.022$). In contrast, the highest percentage of abnormal values was found for enlisted flyers, 6.1 percent, followed by officers, 4.2 percent, and enlisted groundcrew, 3.2 percent ($p=0.054$). The correlation between direct bilirubin and current alcohol use was 0.040 ($p=0.059$). The percentages of abnormal values were 3.7%, 6.1%, and 2.7% for men who currently had no more than one drink per day, those who had more than one but at most four drinks per day, and those who daily consumed more than four drinks, respectively ($p=0.074$).

A significant group-by-race interaction was found for the adjusted continuous analysis ($p=0.022$). The only significant covariate included for adjustment was occupation ($p=0.029$). Exploration of the interaction showed no significant group difference for nonblacks ($p=0.565$), but revealed a significantly higher adjusted mean for Black Ranch Hands than for Black Comparisons (0.181 mg/dl vs. 0.134 mg/dl, respectively; $p=0.026$). A further adjusted analysis was done ignoring the group-by-race interaction. Adjusting for occupation ($p=0.023$), the result for this analysis found no significant difference between groups ($p=0.985$).

The adjusted discrete analysis detected a highly significant group-by-degreasing chemical exposure interaction ($p=0.009$). Occupation ($p=0.044$) was included for adjustment. Ranch Hands who had been exposed to degreasing chemicals had significantly fewer abnormal direct bilirubin levels than Comparisons who had been exposed (Adj. RR: 0.48, 95% C.I.: [0.27,0.87], $p=0.016$). Conversely, the relative risk for Ranch Hands who never had been exposed to degreasing chemicals was greater than one, but not significant (Adj. RR: 1.59, 95% C.I.: [0.81,3.14], $p=0.180$).

LDH

The Ranch Hand group LDH mean and percentage of abnormal values were not significantly different from the Comparison group mean and percentage of abnormalities for the unadjusted analyses ($p=0.692$ and $p=0.999$, respectively).

Using pooled group data, a significant positive correlation between LDH and age was found ($r=0.102$, $p<0.001$). Current alcohol use ($p=0.058$) and lifetime alcohol history ($p=0.031$) were also associated with LDH, after categorization. For both alcohol-related variables, the percentage of abnormalities increased with drinking (1.1%, 1.5%, and 4.1% for the ≤ 1 drink/day, $>1-4$ drinks/day, and the >4 drinks/day categories, respectively; and 0.5%, 1.0%, and 2.4% for the 0 drink-years, $>0-40$ drink-years, and the >40 drink-years categories, respectively).

Both the adjusted continuous and discrete analyses showed no significant group difference ($p=0.804$ and $p=0.954$, respectively). The continuous analysis was adjusted for age-by-occupation ($p=0.025$) and current alcohol use-by-lifetime alcohol history ($p=0.025$). No covariates were included for adjustment in the discrete analysis.

Cholesterol

No significant group differences were found for cholesterol for either the continuous or the discrete analysis ($p=0.379$ and $p=0.179$, respectively) without adjustment for covariates.

The covariate tests of association showed significant relationships between cholesterol and age, occupation, current alcohol use, and industrial chemical exposure. The correlation with age was 0.079 ($p<0.001$). Participants born between 1923 and 1941 had a higher percentage of abnormal values, 15.0 percent, than those born in or before 1922, 10.7 percent, and those born in or after 1942, 11.0 percent ($p=0.018$). For occupation ($p=0.012$), enlisted flyers had a larger mean (219.5 mg/dl) than officers (212.8 mg/dl) and enlisted groundcrew (213.0 mg/dl). This pattern was also evident in the discrete analysis, where 17.4 percent of enlisted flyers had abnormal values, in contrast to 12.1 percent and 12.5 percent of officers and enlisted groundcrew, respectively ($p=0.028$). Current alcohol use was positively correlated with cholesterol ($r=0.048$, $p=0.023$); the percentage of abnormal values increased with drinking (12.7%, 13.7%, and 21.9% for the ≤ 1 drinks/day, $>1-4$ drinks/day, and >4 drinks/day categories, respectively; $p=0.068$). The mean for individuals exposed to industrial chemicals was higher than for those not exposed (215.6 mg/dl vs. 212.0 mg/dl, respectively; $p=0.030$).

Group differences in cholesterol remained nonsignificant after covariate adjustment for both the continuous analysis ($p=0.437$) and the discrete analysis ($p=0.177$). Age ($p<0.001$), current alcohol use ($p=0.021$), industrial chemical exposure ($p=0.023$), and an occupation-by-race interaction ($p=0.003$) were used for adjustment in the continuous analysis. The discrete analysis was adjusted for age ($p=0.048$) and occupation ($p=0.034$).

HDL

No significant group differences were found for HDL for either the unadjusted continuous or discrete analyses ($p=0.847$ and $p=0.992$, respectively).

The covariate tests of association showed significant relationships between HDL and race, occupation, current alcohol use, lifetime alcohol history, industrial chemical exposure, and degreasing chemical exposure. Dichotomized HDL was significantly associated with degreasing chemical exposure. The HDL mean changed significantly with race ($p<0.001$); the HDL mean among Blacks was 51.13 mg/dl and the mean among nonblacks was 46.69 mg/dl. For occupation ($p<0.001$), officers had a higher HDL mean (48.23 mg/dl) than enlisted flyers (46.13 mg/dl) or enlisted groundcrew (46.18 mg/dl). Current alcohol use was positively associated with HDL ($p<0.001$), with the HDL means for light, moderate, and heavy drinkers being 45.50 mg/dl, 51.35 mg/dl, and 58.71 mg/dl, respectively. For lifetime alcohol history ($p<0.001$), the HDL means for never, moderate, and heavy drinkers were 43.85 mg/dl, 46.62 mg/dl, and 49.14 mg/dl, respectively. The mean HDL for participants reporting exposure to industrial chemicals (46.45 mg/dl) was significantly less ($p=0.029$) than the mean HDL for participants not exposed to industrial chemicals (47.56 mg/dl). The dichotomized HDL was significantly associated with degreasing chemical exposure ($p=0.037$); 1.3 percent of participants who reported exposure and 0.4 percent of participants who reported no exposure had HDL below 25 mg/dl.

A significant group-by-lifetime alcohol history interaction was found for the adjusted continuous analysis of HDL ($p=0.036$). Occupation ($p=0.042$), current alcohol use ($p=0.001$), a race-by-degreasing chemical interaction ($p=0.004$), a current alcohol use-by-lifetime alcohol history interaction ($p<0.001$), and a race-by-industrial chemical exposure interaction ($p=0.042$) were used for adjustment. Results were derived for each level of lifetime alcohol history to explore the interaction. The Ranch Hand HDL means among never, moderate, and heavy drinkers with reference to lifetime alcohol history, were 47.23 mg/dl, 49.60 mg/dl, and 47.41 mg/dl, respectively; the corresponding Comparison HDL means were 47.58 mg/dl, 48.84 mg/dl, and 49.33 mg/dl. The difference between Ranch Hands and Comparisons for heavy drinkers was marginally significant ($p=0.067$). The adjusted group means were not significantly different ($p=0.648$) after excluding the group-by-lifetime alcohol history interaction.

No significant group difference was found for the adjusted discrete analysis of HDL ($p=0.999$). Degreasing chemical exposure was the only covariate used for adjustment ($p=0.040$).

Cholesterol-HDL Ratio

No significant group differences were found for cholesterol-HDL ratio for either the unadjusted continuous or discrete analyses ($p=0.357$ and $p=0.348$, respectively).

The covariate tests of association showed significant relationships between the continuously distributed cholesterol-HDL ratio and age, race,

occupation, current alcohol use, lifetime alcohol history, industrial chemical exposure, and degreasing chemical exposure. The discretized cholesterol-HDL ratio was significantly associated with race, occupation, current alcohol use, and degreasing chemical exposure. The cholesterol-HDL ratio mean changed significantly with age ($p=0.009$); the cholesterol-HDL ratio means among participants born in or after 1942, between 1923 and 1941, and in or before 1922 were 4.80, 4.99, and 4.84, respectively. The cholesterol-HDL ratio mean for Blacks (4.51) was significantly different from the cholesterol-HDL ratio mean for nonblacks (4.93) ($p=0.001$).

For occupation, the officer, enlisted flyer, and enlisted groundcrew cholesterol-HDL ratio means (4.73, 5.13, and 4.96, respectively) were significantly different ($p<0.001$). The cholesterol-HDL ratio mean changed significantly with current alcohol use ($p<0.001$); the cholesterol-HDL ratio means for light, moderate, and heavy drinkers were 5.00, 4.60, and 4.16, respectively. The cholesterol-HDL ratio mean also changed significantly with lifetime alcohol history ($p=0.003$); the cholesterol-HDL ratio means for never, moderate, and heavy drinkers were 5.13, 4.93, and 4.75, respectively. The cholesterol-HDL ratio means changed significantly with industrial chemical exposure ($p=0.002$); the cholesterol-HDL ratio mean among participants who reported industrial chemical exposure was 4.99 and the mean among those who reported no exposure was 4.80. The cholesterol-HDL ratio means also changed significantly with degreasing chemical exposure ($p<0.001$); the cholesterol-HDL ratio mean among participants who reported degreasing chemical exposure was 5.00 and the mean among those who reported no exposure was 4.76.

The dichotomized cholesterol-HDL ratio was significantly associated with race ($p=0.045$); a greater percentage of nonblacks had abnormalities (43.2%) than Blacks (34.3%). There was a significant association between cholesterol-HDL ratio and occupation ($p=0.002$); the percentages of participants with cholesterol-HDL ratio abnormalities among officers, enlisted flyers, and enlisted groundcrew were 38.5 percent, 48.4 percent, and 44.0 percent, respectively. There was also a significant association between the dichotomized cholesterol-HDL ratio and current alcohol use ($p<0.001$); the percentages of participants with cholesterol-HDL ratio abnormalities for light, moderate, and heavy drinkers were 45.4 percent, 35.0 percent, and 16.4 percent, respectively. There was a significant association between the dichotomized cholesterol-HDL ratio and degreasing chemical exposure ($p=0.008$); 44.9 percent of participants who reported exposure, and 39.3 percent of participants who reported no exposure to degreasing chemicals had cholesterol-HDL ratio abnormalities.

Group differences in the cholesterol-HDL ratio remained nonsignificant after adjustment for covariates in both the continuous analysis ($p=0.509$) and the discrete analysis ($p=0.434$). Current alcohol use ($p=0.002$), a race-by-degreasing chemical exposure interaction ($p=0.017$), an age-by-lifetime alcohol history interaction ($p=0.040$), and a current alcohol use-by-lifetime alcohol history interaction ($p=0.004$) contributed to the continuous model. The discrete analysis was adjusted for age ($p=0.038$), race ($p=0.036$), occupation ($p<0.001$), and current alcohol use ($p<0.001$).

Triglycerides

Group differences for triglycerides were not significant for both the unadjusted continuous ($p=0.355$) and discrete ($p=0.248$) analyses.

Treating triglycerides as a continuous variable, significant covariate associations were found with age ($p=0.009$), race ($p<0.001$), occupation ($p=0.003$), industrial chemical exposure ($p=0.027$), and degreasing chemical exposure ($p<0.001$). After categorizing triglycerides, no significant covariate associations were found. The correlation with age was 0.055. Non-blacks had a much higher mean, 119.3 mg/dl, than did Blacks, 96.1 mg/dl. For occupation, enlisted flyers had the highest mean, 126.5 mg/dl, followed by enlisted groundcrew, 119.9 mg/dl, and officers, 111.7 mg/dl. The mean for participants exposed to industrial chemicals (121.0 mg/dl) was larger than for those not exposed (114.0 mg/dl), and the mean for individuals exposed to degreasing chemicals was larger than the mean for those not exposed (122.7 mg/dl vs. 110.7 mg/dl, respectively).

The results of the adjusted analyses and triglycerides did not show a significant group difference ($p=0.459$ and $p=0.172$ for the continuous and discrete analysis, respectively). Significant covariates used to adjust the continuous model were age ($p<0.001$), occupation ($p=0.001$), degreasing chemical exposure ($p=0.009$), and a race-by-lifetime alcohol history interaction ($p=0.038$). Race ($p=0.039$) and current alcohol use-by-lifetime alcohol history ($p=0.043$) were used for the adjusted discrete analysis.

Creatine Kinase

No significant group differences were found for creatine kinase for either the unadjusted continuous ($p=0.611$) or the discrete ($p=0.114$) analyses.

Examining the relationship with the covariates revealed an extremely large creatine kinase difference between races that was highly significant ($p<0.001$, continuous and discrete), and a strong association with age ($p<0.001$). A marginally significant negative association with lifetime alcohol history was also noted ($p=0.055$). The mean for Blacks, 197.5 U/L, was nearly twice as large as the mean for nonblacks, 105.4 U/L. This finding was supported by the discrete test of association, in which 34.3 percent of Blacks had abnormal values, versus only 5.1 percent of nonblacks. Age was negatively correlated with creatine kinase ($r=-0.074$). The correlation with lifetime alcohol history was -0.040 .

Group differences in creatine kinase were not significant for the adjusted continuous analysis ($p=0.500$) and the discrete analysis ($p=0.122$), supporting the unadjusted results. The continuous model was adjusted for age ($p=0.002$), race ($p<0.001$), and current alcohol use-by occupation ($p=0.045$). Race ($p<0.001$) and an age-by-degreasing chemical exposure interaction ($p=0.019$) were included in the final adjusted discrete model.

Fasting Glucose

No significant differences were found between groups in the unadjusted continuous or discrete analyses for fasting glucose ($p=0.504$ and $p=0.606$, respectively).

Age was highly correlated with fasting glucose ($r=0.195$, $p<0.001$). The percentage of abnormal values increased with age (5.3% for participants born in or after 1942, 17.4% for those born between 1923 and 1941, and 25.0% for those born in or before 1922). The correlation with lifetime alcohol history was 0.067 ($p=0.002$). The percentages of abnormal values were 13.2 percent, 9.9 percent, and 20.7 percent for never, moderate, and heavy drinkers, respectively ($p<0.001$).

Group differences in fasting glucose were not significant for the adjusted continuous ($p=0.534$) and the discrete analysis ($p=0.565$). Significant covariates included in the continuous analysis were age-by-race ($p=0.002$), race-by-lifetime alcohol history ($p=0.050$), and occupation-by-lifetime alcohol history ($p<0.001$). The discrete analysis included age ($p<0.001$), race ($p=0.008$), lifetime alcohol history ($p=0.021$), and degreasing chemical exposure ($p=0.024$) for adjustment.

Exposure Index Analysis

Laboratory Examination Variables

Exposure index analyses were done for all 13 laboratory examination variables. Each variable was analyzed in both continuous and discrete forms. Unadjusted and adjusted results are presented in Tables 13-8 and 13-9, respectively. Many exposure index-by-covariate interactions were detected in the adjusted analyses, particularly for the discrete analyses. These interactions are listed in Table 13-10, and stratified results are presented in Table J-4. In several instances, meaningful interpretation of the interaction was obscured because the cell sizes were very small after stratification.

Both the statistical significance of the results and whether trends in the data supported a herbicide effect were investigated. Examination of Table 13-8 shows that many variables exhibited increasing dose-response relationships, without a significant result. Of the 39 unadjusted continuous analyses for the three occupational cohorts, the means for 14 analyses exhibited increasing dose-response patterns. However, the overall result was not significant for any of these analyses. The means for five analyses decreased with the exposure index categories, also without a statistically significant finding. Breaking this down by occupation showed that the means for officers increased with exposure level for five variables (AST, ALT, GGT, alkaline phosphatase, and triglycerides) and decreased for HDL; the enlisted flyer means for GGT and direct bilirubin increased and the mean for alkaline phosphatase and HDL decreased; and the enlisted groundcrew means increased with exposure level for seven variables (AST, alkaline phosphatase, total bilirubin, direct bilirubin, LDH, cholesterol, and HDL) and decreased for two variables (GGT and fasting glucose). Trends such as these are discussed in Chapter 21.

TABLE 13-8.

Unadjusted Exposure Index for Hepatic Variables by Occupation

Variable	Occupation	Statistic	Exposure Index				Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value		
			Low		Medium					High	
AST	Officer	n	128		124		122		Overall		0.429
		Mean ^a	25.4		26.1		26.7		M vs. L	--	0.450
		95% C.I. ^a	(24.3,26.5)		(24.6,27.6)		(25.0,28.6)		H vs. L	--	0.196
		Number/%							Overall		0.086
		High	4	3.1%	5	4.0%	11	9.0%	M vs. L	1.30 (0.34,4.97)	0.960
		Normal	124	96.9%	119	96.0%	111	91.0%	H vs. L	3.07 (0.95,9.93)	0.088
	Enlisted Flyer	n	55		63		53		Overall		0.898
		Mean ^a	24.8		24.4		25.0		M vs. L	--	0.778
		95% C.I. ^a	(22.9,26.8)		(22.5,26.4)		(23.4,26.7)		H vs. L	--	0.873
		Number/%							Overall		0.552
		High	1	1.8%	3	4.8%	1	1.9%	M vs. L	2.70 (0.27,26.74)	0.724
		Normal	54	98.2%	60	95.2%	52	98.1%	H vs. L	1.04 (0.06,17.04)	0.999
Enlisted Groundcrew	n	146		155		140		Overall		0.524	
	Mean ^a	25.5		25.8		26.6		M vs. L	--	0.790	
	95% C.I. ^a	(24.4,26.7)		(24.4,27.2)		(25.2,28.1)		H vs. L	--	0.255	
	Number/%							Overall		0.226	
	High	5	3.4%	7	4.5%	11	7.9%	M vs. L	1.33 (0.41,4.30)	0.854	
	Normal	141	96.6%	148	95.5%	129	92.1%	H vs. L	2.41 (0.81,7.11)	0.168	

TABLE 13-8. (continued)

Unadjusted Exposure Index for Hepatic Variables by Occupation

Variable	Occupation	Statistic	Exposure Index				Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High				
ALT	Officer	n	128	124	122		Overall		0.592
		Mean ^a	20.1	20.4	21.4		H vs. L	--	0.812
		95% C.I. ^a	(18.6,21.7)	(18.6,22.3)	(25.0,28.6)		H vs. L	--	0.325
		Number/%					Overall		0.783
		High	14 10.9%	17 13.7%	16 13.1%		H vs. L	1.29 (0.61,2.75)	0.632
		Normal	114 89.1%	107 86.3%	106 86.9%		H vs. L	1.23 (0.57,2.64)	0.738
	Enlisted Flyer	n	55	63	53		Overall		0.394
		Mean ^a	18.6	20.7	20.5		H vs. L	--	0.211
		95% C.I. ^a	(16.6,20.8)	(18.3,23.4)	(18.2,23.1)		H vs. L	--	0.259
		Number/%					Overall		0.775
		High	4 7.3%	7 11.1%	5 9.4%		H vs. L	1.59 (0.44,5.77)	0.696
		Normal	51 92.7%	56 88.9%	48 90.6%		H vs. L	1.33 (0.34,5.24)	0.952
	Enlisted Groundcrew	n	146	155	140		Overall		0.368
		Mean ^a	20.2	21.7	20.3		H vs. L	--	0.207
		95% C.I. ^a	(18.8,21.8)	(20.0,23.6)	(18.6,22.1)		H vs. L	--	0.967
Number/%						Overall		0.301	
High		15 10.3%	25 16.1%	17 12.1%		H vs. L	1.68 (0.85,3.33)	0.184	
Normal		131 89.7%	130 83.9%	123 87.9%		H vs. L	1.21 (0.58,2.52)	0.754	

TABLE 13-8. (continued)

Unadjusted Exposure Index for Hepatic Variables by Occupation

Variable	Occupation	Statistic	Exposure Index				Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High				
GGT	Officer	n	128	124	122		Overall		0.140
		Mean ^a	30.9	31.4	36.2		M vs. L	--	0.839
		95% C.I. ^a	(27.7,34.4)	(27.9,35.3)	(31.6,41.4)		H vs. L	--	0.076
		Number/%					Overall		0.018
		High	7 5.5%	8 6.5%	18 14.8%		M vs. L	1.19 (0.42,3.39)	0.948
		Normal	121 94.5%	116 93.5%	104 85.2%		H vs. L	2.99 (1.20,7.44)	0.024
	Enlisted Flyer	n	55	63	53		Overall		0.875
		Mean ^a	32.5	34.1	34.7		M vs. L	--	0.720
		95% C.I. ^a	(26.1,40.5)	(29.2,39.9)	(29.5,40.8)		H vs. L	--	0.637
		Number/%					Overall		0.681
		High	7 12.7%	5 7.9%	6 11.3%		M vs. L	0.59 (0.18,1.98)	0.578
		Normal	48 87.3%	58 92.1%	47 88.7%		H vs. L	0.88 (0.27,2.80)	0.999
Enlisted Groundcrew	n	146	155	140		Overall		0.760	
	Mean ^a	34.0	33.8	32.3		M vs. L	--	0.932	
	95% C.I. ^a	(30.5,37.9)	(30.7,37.3)	(28.8,36.1)		H vs. L	--	0.510	
	Number/%					Overall		0.461	
	High	8 5.5%	11 7.1%	13 9.3%		M vs. L	1.32 (0.52,3.37)	0.736	
	Normal	138 94.5%	144 92.9%	127 90.7%		H vs. L	1.77 (0.71,4.40)	0.314	

TABLE 13-8. (continued)

Unadjusted Exposure Index for Hepatic Variables by Occupation

Variable	Occupation	Statistic	Exposure Index				Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value		
			Low		Medium					High	
Alkaline Phosphatase	Officer	n	128		124		122		Overall		0.302
		Mean ^a	87.9		88.9		92.0		M vs. L	--	0.699
		95% C.I. ^a	(84.5,91.4)		(84.8,93.2)		(88.3,95.9)		H vs. L	--	0.115
		Number/%							Overall		0.117
		High	2	1.6%	8	6.5%	4	3.3%	M vs. L	4.35 (0.90,20.88)	0.092
		Normal	126	98.4%	116	93.5%	118	96.7%	H vs. L	2.14 (0.38,11.88)	0.638
	Enlisted Flyer	n	55		63		53		Overall		0.334
		Mean ^a	99.4		96.0		92.2		M vs. L	--	0.505
		95% C.I. ^a	(91.3,108.3)		(90.8,101.5)		(86.3,98.4)		H vs. L	--	0.170
		Number/%							Overall		0.702
		High	2	3.6%	3	4.8%	1	1.9%	M vs. L	1.33 (0.21,8.24)	0.999
		Normal	53	96.4%	60	95.2%	52	98.1%	H vs. L	0.51 (0.05,5.79)	0.999
Enlisted Groundcrew	n	146		155		140		Overall		0.241	
	Mean ^a	94.1		97.2		98.3		M vs. L	--	0.201	
	95% C.I. ^a	(90.7,97.6)		(94.0,100.6)		(94.4,102.3)		H vs. L	--	0.117	
	Number/%							Overall		0.994	
	High	9	6.2%	10	6.5%	9	6.4%	M vs. L	1.05 (0.41,2.66)	0.999	
	Normal	137	93.8%	145	93.5%	131	93.6%	H vs. L	1.05 (0.40,2.72)	0.999	

TABLE 13-8. (continued)

Unadjusted Exposure Index for Hepatic Variables by Occupation

Variable	Occupation	Statistic	Exposure Index				Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value	
			Low		Medium					High
Total Bilirubin	Officer	n	128		124		122		Overall	0.415
		Mean ^b	0.805		0.776		0.815		M vs. L	0.315
		95% C.I. ^b	(0.766, 0.844)		(0.739, 0.815)		(0.769, 0.863)		H vs. L	0.740
		Number/%							Overall	0.694
		High	3	2.3%	2	1.6%	4	3.3%	M vs. L	0.68 (0.11,4.16)
		Normal	125	97.7%	122	98.4%	118	96.7%	H vs. L	1.41 (0.31,6.45)
	Enlisted Flyer	n	55		63		53		Overall	0.195
		Mean ^b	0.744		0.735		0.809		M vs. L	0.813
		95% C.I. ^b	(0.692, 0.800)		(0.678, 0.796)		(0.745, 0.876)		H vs. L	0.139
		Number/%							Overall	0.552
		High	1	1.8%	3	4.8%	1	1.9%	M vs. L	2.70 (0.27,26.74)
		Normal	54	98.2%	60	95.2%	52	98.1%	H vs. L	1.04 (0.06,17.04)
Enlisted Groundcrew	n	146		155		140		Overall	0.382	
	Mean ^b	0.753		0.773		0.791		M vs. L	0.434	
	95% C.I. ^b	(0.718, 0.789)		(0.737, 0.811)		(0.751, 0.833)		H vs. L	0.164	
	Number/%							Overall	0.664	
	High	2	1.4%	3	1.9%	1	0.7%	M vs. L	1.42 (0.23,8.63)	
	Normal	144	98.6%	152	98.1%	139	99.3%	H vs. L	0.52 (0.05,5.78)	

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TABLE 13-8. (continued)

Unadjusted Exposure Index for Hepatic Variables by Occupation

Variable	Occupation	Statistic	Exposure Index				Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value		
			Low		Medium					High	
Direct Bilirubin	Officer	n	128		124		122		Overall		0.191
		Mean ^b	0.176		0.150		0.169		M vs. L	--	0.055
		95% C.I. ^b	(0.157, 0.196)		(0.132, 0.169)		(0.145, 0.195)		H vs. L	--	0.641
		Number/%							Overall		0.010
		High	4	3.1%	1	0.8%	10	8.2%	M vs. L	0.25 (0.03, 2.29)	0.390
		Normal	124	96.9%	123	99.2%	112	91.8%	H vs. L	2.77 (0.84, 9.07)	0.140
	Enlisted Flyer	n	55		63		53		Overall		0.598
		Mean ^b	0.134		0.145		0.156		M vs. L	--	0.565
		95% C.I. ^b	(0.109, 0.116)		(0.118, 0.175)		(0.122, 0.195)		H vs. L	--	0.315
		Number/%							Overall		0.609
		High	2	3.6%	5	7.9%	3	5.7%	M vs. L	2.28 (0.43, 12.28)	0.548
		Normal	53	96.4%	58	92.1%	50	94.3%	H vs. L	1.59 (0.26, 9.92)	0.964
Enlisted Groundcrew	n	146		155		140		Overall		0.085	
	Mean ^b	0.141		0.163		0.168		M vs. L	--	0.089	
	95% C.I. ^b	(0.124, 0.160)		(0.146, 0.181)		(0.151, 0.187)		H vs. L	--	0.041	
	Number/%							Overall		0.719	
	High	4	2.7%	4	2.6%	2	1.4%	M vs. L	0.94 (0.23, 3.83)	0.999	
	Normal	142	97.3%	151	97.4%	138	98.6%	H vs. L	0.51 (0.09, 2.86)	0.724	

TABLE 13-8. (continued)

Unadjusted Exposure Index for Hepatic Variables by Occupation

Variable	Occupation	Statistic	Exposure Index				Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value		
			Low		Medium					High	
LDH	Officer	n	128		124		122		Overall		0.780
		Mean ^a	127.3		128.9		127.1		M vs. L	--	0.563
		95% C.I. ^a	(124.1, 130.6)		(124.8, 133.1)		(123.4, 131.0)		H vs. L	--	0.950
		Number/%							Overall		0.859
		High	2	1.6%	3	2.4%	2	1.6%	M vs. L	1.56 (0.26, 9.51)	0.970
		Normal	126	98.4%	121	97.6%	120	98.4%	H vs. L	1.05 (0.15, 7.57)	0.999
	Enlisted Flyer	n	55		63		53		Overall		0.082
		Mean ^a	128.7		120.8		128.8		M vs. L	--	0.042
		95% C.I. ^a	(123.2, 134.5)		(115.9, 125.9)		(122.0, 136.0)		H vs. L	--	0.987
		Number/%							Overall		0.346
		High	1	1.8%	0	0.0%	0	0.0%	M vs. L	-- ^c	0.932
		Normal	54	98.2%	63	100.0%	53	100.0%	H vs. L	-- ^c	0.999
Enlisted Groundcrew	n	146		155		140		Overall		0.245	
	Mean ^a	127.8		128.6		131.7		M vs. L	--	0.726	
	95% C.I. ^a	(124.8, 130.9)		(125.2, 132.1)		(128.2, 135.3)		H vs. L	--	0.099	
	Number/%							Overall		0.769	
	High	2	1.4%	1	0.7%	1	0.7%	M vs. L	0.47 (0.04, 5.21)	0.956	
	Normal	144	98.6%	154	99.3%	139	99.3%	H vs. L	0.52 (0.05, 5.78)	0.999	

13-46

TABLE 13-8. (continued)

Unadjusted Exposure Index for Hepatic Variables by Occupation

Variable	Occupation	Statistic	Exposure Index				Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value	
			Low		Medium					High
Cholesterol	Officer	n	128		124		122		Overall	0.063
		Mean ^a	220.5		209.9		210.1		M vs. L	0.043
		95% C.I. ^a	(213.0, 228.4)		(203.2, 216.8)		(203.3, 217.1)		H vs. L	0.049
		Number/%							Overall	0.215
		High	22	17.2%	12	9.7%	18	14.8%	M vs. L	0.118
		Normal	106	82.8%	112	90.3%	104	85.2%	H vs. L	0.726
	Enlisted Flyer	n	55		63		53		Overall	0.509
		Mean ^a	219.7		212.8		221.4		M vs. L	0.388
		95% C.I. ^a	(207.8, 232.4)		(203.0, 223.1)		(210.4, 233.1)		H vs. L	0.843
		Number/%							Overall	0.762
		High	11	20.0%	10	15.9%	8	15.1%	M vs. L	0.730
		Normal	44	80.0%	53	84.1%	45	84.9%	H vs. L	0.678
Enlisted Groundcrew	n	146		155		140		Overall	0.491	
	Mean ^a	213.3		213.4		217.9		M vs. L	0.996	
	95% C.I. ^a	(207.9, 219.0)		(207.7, 219.2)		(211.2, 225.0)		H vs. L	0.308	
	Number/%							Overall	0.474	
	High	17	11.6%	20	12.9%	23	16.4%	M vs. L	0.876	
	Normal	129	88.4%	135	87.1%	117	83.6%	H vs. L	0.320	

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TABLE 13-8. (continued)

Unadjusted Exposure Index for Hepatic Variables by Occupation

Variable	Occupation	Statistic	Exposure Index				Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High				
HDL	Officer	n	128	124	122		Overall		0.151
		Mean	49.28	48.58	46.38		M vs. L	--	0.650
		95% C.I.	(47.15, 51.41)	(46.21, 50.95)	(44.31, 48.45)		H vs. L	--	0.062
		Number/%					Overall		0.593
		Low	0 0.0%	1 0.8%	1 0.8%		M vs. L	--- ^c	0.309
		Normal	128 100.0%	123 99.2%	121 99.2%		H vs. L	--- ^c	0.305
	Enlisted Flyer	n	55	63	53		Overall		0.700
		Mean	46.91	45.68	45.04		M vs. L	--	0.571
		95% C.I.	(43.16, 50.66)	(43.12, 48.24)	(42.02, 48.05)		H vs. L	--	0.408
		Number/%					Overall		0.127
		Low	1 1.8%	0 0.0%	3 5.7%		M vs. L	--- ^c	0.282
		Normal	54 98.2%	63 100.0%	50 94.3%		H vs. L	--- ^c	0.291
	Enlisted Groundcrew	n	146	155	140		Overall		0.882
		Mean	45.86	46.21	46.61		M vs. L	--	0.810
		95% C.I.	(43.79, 47.92)	(44.13, 48.28)	(44.49, 48.73)		H vs. L	--	0.616
		Number/%					Overall		0.395
		Low	0 0.0%	2 1.3%	1 0.7%		M vs. L	--- ^c	0.168
		Normal	146 100.0%	153 98.7%	139 99.3%		H vs. L	--- ^c	0.306

TABLE 13-8. (continued)

Unadjusted Exposure Index for Hepatic Variables by Occupation

Variable	Occupation	Statistic	Exposure Index				Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value		
			Low		Medium					High	
Cholesterol- HDL Ratio	Officer	n	128		124		122		Overall		0.536
		Mean	4.82		4.68		4.88		M vs. L	--	0.441
		95% C.I.	(4.56,5.08)		(4.42,4.93)		(4.61,5.14)		H vs. L	--	0.744
		Number/%							Overall		0.311
		High	50	39.1%	47	37.9%	57	46.7%	M vs. L	0.95 (0.57,1.58)	0.850
		Normal	78	60.9%	77	62.1%	65	53.3%	H vs. L	1.37 (0.83,2.26)	0.221
	Enlisted Flyer	n	55		63		53		Overall		0.349
		Mean	5.08		4.93		5.37		M vs. L	--	0.625
		95% C.I.	(4.69,5.47)		(4.60,5.26)		(4.78,5.97)		H vs. L	--	0.356
		Number/%							Overall		0.510
		High	26	47.3%	24	38.1%	25	47.2%	M vs. L	0.69 (0.33,1.43)	0.314
		Normal	29	52.7%	39	61.9%	28	52.8%	H vs. L	1.00 (0.47,2.12)	0.991
Enlisted Groundcrew	n	146		155		140		Overall		0.965	
	Mean	5.02		4.98		5.01		M vs. L	--	0.815	
	95% C.I.	(4.77,5.27)		(4.74,5.22)		(4.79,5.24)		H vs. L	--	0.994	
	Number/%							Overall		0.681	
	High	69	47.3%	67	43.2%	67	47.9%	M vs. L	0.85 (0.54,1.34)	0.482	
	Normal	77	52.7%	88	56.8%	73	52.1%	H vs. L	1.02 (0.64,1.63)	0.920	

TABLE 13-8. (continued)

Unadjusted Exposure Index for Hepatic Variables by Occupation

Variable	Occupation	Statistic	Exposure Index				Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value		
			Low		Medium					High	
Triglycerides	Officer	n	128		124		122		Overall		0.689
		Mean ^a	112.7		113.2		120.4		M vs. L	--	0.953
		95% C.I. ^a	(100.8, 125.9)		(99.7, 128.6)		(107.4, 134.9)		H vs. L	--	0.417
		Number/%							Overall		0.876
		High	9	7.0%	9	7.3%	7	5.7%	M vs. L	1.04 (0.40, 2.70)	0.999
		Normal	119	93.0%	115	92.7%	115	94.3%	H vs. L	0.81 (0.29, 2.23)	0.876
	Enlisted Flyer	n	55		63		53		Overall		0.412
		Mean ^a	131.1		112.4		126.8		M vs. L	--	0.180
		95% C.I. ^a	(111.3, 154.5)		(96.5, 130.9)		(103.5, 155.4)		H vs. L	--	0.803
		Number/%							Overall		0.238
		High	6	10.9%	2	3.2%	5	9.4%	M vs. L	0.27 (0.05, 1.39)	0.193
		Normal	49	89.1%	61	96.8%	48	90.6%	H vs. L	0.85 (0.24, 2.98)	0.999
Enlisted Groundcrew	n	146		155		140		Overall		0.684	
	Mean ^a	125.6		118.1		122.3		M vs. L	--	0.392	
	95% C.I. ^a	(112.5, 140.2)		(108.1, 129.0)		(110.6, 135.3)		H vs. L	--	0.733	
	Number/%							Overall		0.181	
	High	13	8.9%	10	6.5%	5	3.6%	M vs. L	0.71 (0.30, 1.66)	0.560	
	Normal	133	91.1%	145	93.5%	135	96.4%	H vs. L	0.38 (0.13, 1.09)	0.104	

TABLE 13-8. (continued)

Unadjusted Exposure Index for Hepatic Variables by Occupation

Variable	Occupation	Statistic	Exposure Index				Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High				
Creatine Kinase	Officer	n	128	124	122		Overall		0.971
		Mean ^a	110.4	109.4	111.1		M vs. L	--	0.880
		95% C.I. ^a	(101.2, 120.6)	(100.2, 119.4)	(102.0, 120.9)		H vs. L	--	0.928
		Number/% High	10 7.8%	6 4.8%	8 6.6%		Overall		0.627
		Normal	118 92.2%	118 95.2%	114 93.4%		M vs. L	0.60 (0.21,1.70)	0.480
							H vs. L	0.83 (0.32,2.17)	0.892
	Enlisted Flyer	n	55	63	53		Overall		0.735
		Mean ^a	102.9	102.7	109.9		M vs. L	--	0.978
		95% C.I. ^a	(88.8, 119.2)	(92.2, 114.2)	(94.3, 128.1)		H vs. L	--	0.543
		Number/% High	4 7.3%	3 4.8%	5 9.4%		Overall		0.615
		Normal	51 92.7%	60 95.2%	48 90.6%		M vs. L	0.64 (0.14,2.98)	0.848
							H vs. L	1.33 (0.34,5.24)	0.952
Enlisted Groundcrew	n	146	155	140		Overall		0.986	
	Mean ^a	112.4	111.5	111.6		M vs. L	--	0.876	
	95% C.I. ^a	(103.7, 121.9)	(104.2, 119.2)	(103.5, 120.4)		H vs. L	--	0.902	
	Number/% High	9 6.2%	6 3.9%	6 4.3%		Overall		0.614	
	Normal	137 93.8%	149 96.1%	134 95.7%		M vs. L	0.61 (0.21,1.77)	0.516	
						H vs. L	0.68 (0.24,1.97)	0.658	

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TABLE 13-8. (continued)

Unadjusted Exposure Index for Hepatic Variables by Occupation

Variable	Occupation	Statistic	Exposure Index				Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value		
			Low		Medium					High	
Fasting Glucose	Officer	n	128		124		122		Overall	0.186	
		Mean ^a	101.2		99.9		104.0		M vs. L	--	0.491
		95% C.I. ^a	(98.3, 104.1)		(97.6, 102.2)		(100.0, 108.0)		H vs. L	--	0.269
		Number/%							Overall		0.698
		High	18	14.1%	14	11.3%	18	14.8%	M vs. L	0.78 (0.37,1.64)	0.638
		Normal	110	85.9%	110	88.7%	104	85.2%	H vs. L	1.06 (0.52,2.14)	0.999
	Enlisted Flyer	n	55		63		53		Overall	0.127	
		Mean ^a	98.5		103.3		98.0		M vs. L	--	0.143
		95% C.I. ^a	(94.2, 103.1)		(99.0, 107.7)		(95.3, 100.7)		H vs. L	--	0.831
		Number/%							Overall		0.288
		High	5	9.1%	11	17.5%	5	9.4%	M vs. L	2.12 (0.69,6.52)	0.292
		Normal	50	90.9%	52	82.5%	48	90.6%	H vs. L	1.04 (0.28,3.83)	0.999
Enlisted Groundcrew	n	146		155		140		Overall	0.853		
	Mean ^a	100.3		100.0		99.1		M vs. L	--	0.863	
	95% C.I. ^a	(97.6, 103.1)		(96.7, 103.4)		(96.6, 101.7)		H vs. L	--	0.536	
	Number/%							Overall		0.757	
	High	18	12.3%	15	9.7%	16	11.4%	M vs. L	0.76 (0.37,1.58)	0.582	
	Normal	128	87.7%	140	90.3%	124	88.6%	H vs. L	0.92 (0.45,1.88)	0.960	

^aTransformed from natural logarithm scale.

--Estimated relative risk not applicable for continuous analysis of a variable.

^bTransformed from natural logarithm (X + 0.1) scale.

^cRelative risk/confidence interval not given due to a cell with zero frequency.

TABLE 13-9.

Adjusted Exposure Index for Hepatic Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value	
			Low	Medium	High				
AST	Officer	n	127	122	122	Overall		****	
		Adj. Mean	****	****	****	M vs. L	--	****	
		95% C.I.	****	****	****	H vs. L	--	****	
			n	127	122	122	Overall		0.152
						M vs. L	1.62 (0.39,6.73)	0.504	
						H vs. L	3.15 (0.89,11.14)	0.075	
		Enlisted Flyer	n	54	62	53	Overall		0.618
			Adj. Mean ^a	22.6	22.2	23.3	M vs. L	--	0.697
			95% C.I. ^a	(20.1,25.5)	(19.9,24.8)	(20.8,26.1)	H vs. L	--	0.568
			n	54	62	53	Overall		****
						M vs. L	****	****	
						H vs. L	****	****	
	Enlisted Groundcrew	n	144	155	138	Overall		0.412	
		Adj. Mean ^a	27.0	27.5	28.4	M vs. L	--	0.665	
		95% C.I. ^a	(25.3,28.9)	(25.6,29.4)	(26.5,30.5)	H vs. L	--	0.190	
		n	144	155	138	Overall		0.191	
					M vs. L	1.52 (0.45,5.12)	0.499		
					H vs. L	2.71 (0.87,8.46)	0.086		

TABLE 13-9. (continued)

Adjusted Exposure Index for Hepatic Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value	
			Low	Medium	High				
ALT	Officer	n	127	122	122	Overall		****	
		Adj. Mean	****	****	****	M vs. L	--	****	
		95% C.I.	****	****	****	H vs. L	--	****	
			n	127	122	122	Overall		****
						M vs. L	****	****	
						H vs. L	****	****	
		Enlisted Flyer	n	54	62	53	Overall		0.378
	Adj. Mean ^a		17.1	18.8	19.2	M vs. L	--	0.274	
	95% C.I. ^a		(14.0,20.9)	(15.6,22.5)	(15.8,23.2)	H vs. L	--	0.192	
			n	54	62	53	Overall		****
						M vs. L	****	****	
						H vs. L	****	****	
	Enlisted Groundcrew	n	143	155	138	Overall		0.662	
Adj. Mean ^a		20.6	21.7	21.0	M vs. L	--	0.372		
95% C.I. ^a		(18.5,23.0)	(19.5,24.3)	(18.7,23.5)	H vs. L	--	0.770		
		n	143	155	138	Overall		0.442	
					M vs. L	1.57 (0.78,3.14)	0.207		
					H vs. L	1.31 (0.62,2.77)	0.478		

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TABLE 13-9. (continued)

Adjusted Exposure Index for Hepatic Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value	
			Low	Medium	High				
GGT	Officer	n	127	122	122	Overall		0.209**	
		Adj. Mean** ^a	29.4	30.0	33.8	M vs. L	--	0.817**	
		95% C.I.** ^a	(22.3,38.7)	(22.9,39.3)	(25.8,44.3)	H vs. L	--	0.103**	
			n	127	122	122	Overall		0.038
						M vs. L	1.34 (0.44,4.04)	0.607	
						H vs. L	3.09 (1.16,8.24)	0.024	
		Enlisted Flyer	n	54	62	53	Overall		0.776
			Adj. Mean ^a	31.0	32.7	33.9	M vs. L	--	0.665
			95% C.I. ^a	(23.2,41.5)	(25.0,42.7)	(25.6,44.8)	H vs. L	--	0.480
			n	54	62	53	Overall		0.267**
						M vs. L	0.37 (0.07,1.88)**	0.233**	
						H vs. L	1.26 (0.33,4.89)**	0.736**	
	Enlisted Groundcrew	n	143	155	138	Overall		0.937	
		Adj. Mean ^a	38.5	39.0	37.9	M vs. L	--	0.880	
		95% C.I. ^a	(33.6,44.2)	(33.9,44.7)	(32.9,43.8)	H vs. L	--	0.832	
		n	143	155	138	Overall		0.324	
					M vs. L	1.33 (0.51,3.47)	0.562		
					H vs. L	2.01 (0.79,5.12)	0.145		

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TABLE 13-9. (continued)

Adjusted Exposure Index for Hepatic Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value	
			Low	Medium	High				
Alkaline Phosphatase	Officer	n	127	122	122	Overall		0.314**	
		Adj. Mean** ^a	77.9	79.3	81.6	M vs. L	--	0.561**	
		95% C.I.** ^a	(70.4,86.1)	(71.9,87.5)	(73.9,90.1)	H vs. L	--	0.132**	
			n	127	122	122	Overall		0.119
							M vs. L	4.32 (0.87,21.41)	0.073
							H vs. L	1.84 (0.32,10.51)	0.491
	Enlisted Flyer	n	n	54	62	53	Overall		0.414
			Adj. Mean ^a	95.5	93.1	89.3	M vs. L	--	0.606
			95% C.I. ^a	(84.9,107.4)	(83.5,103.8)	(79.8,99.0)	H vs. L	--	0.189
			n	54	62	53	Overall		0.379
							M vs. L	1.96 (0.27,14.14)	0.504
							H vs. L	0.39 (0.03,4.85)	0.463
Enlisted Groundcrew	n	n	144	155	138	Overall		0.294**	
		Adj. Mean** ^a	94.8	98.6	98.1	M vs. L	--	0.150**	
		95% C.I.** ^a	(90.3,99.6)	(93.8,103.6)	(93.2,103.3)	H vs. L	--	0.213**	
		n	144	155	138	Overall		0.941**	
						M vs. L	1.14 (0.44,2.93)**	0.791**	
						H vs. L	0.97 (0.36,2.58)**	0.948**	

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TABLE 13-9. (continued)

Adjusted Exposure Index for Hepatic Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value	
			Low	Medium	High				
Total Bilirubin	Officer	n	127	122	122	Overall		0.431	
		Adj. Mean ^b	0.780	0.760	0.799	M vs. L	--	0.510	
		95% C.I. ^b	(0.688, 0.883)	(0.672, 0.858)	(0.706, 0.902)	H vs. L	--	0.530	
		n		127	122	122	Overall		0.763**
							M vs. L	0.78 (0.17, 3.54)**	0.748**
							H vs. L	1.36 (0.35, 5.26)**	0.656**
	Enlisted Flyer	n	n	54	62	53	Overall		0.277
			Adj. Mean ^b	0.719	0.710	0.774	M vs. L	--	0.833
			95% C.I. ^b	(0.626, 0.823)	(0.625, 0.805)	(0.679, 0.881)	H vs. L	--	0.210
		n		54	62	53	Overall		****
							M vs. L	****	****
							H vs. L	****	****
Enlisted Groundcrew	n	n	143	155	138	Overall		0.353**	
		Adj. Mean ^{**b}	0.775	0.794	0.816	M vs. L	--	0.495**	
		95% C.I. ^{**b}	(0.726, 0.827)	(0.743, 0.847)	(0.763, 0.873)	H vs. L	--	0.149**	
	n		143	155	138	Overall		0.670	
						M vs. L	1.82 (0.38, 8.67)	0.455	
						H vs. L	0.70 (0.11, 4.70)	0.718	

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TABLE 13-9. (continued)

Adjusted Exposure Index for Hepatic Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value	
			Low	Medium	High				
Direct Bilirubin	Officer	n	127	122	122	Overall		0.160	
		Adj. Mean ^b	0.158	0.131	0.151	M vs. L	--	0.066	
		95% C.I. ^b	(0.113, 0.212)	(0.092, 0.179)	(0.108, 0.203)	H vs. L	--	0.631	
			n	127	122	122	Overall		0.006
						M vs. L	0.29 (0.03, 2.73)	0.278	
						H vs. L	3.42 (0.98, 11.99)	0.054	
		Enlisted Flyer	n	54	62	53	Overall		0.676
			Adj. Mean ^b	0.135	0.138	0.153	M vs. L	--	0.866
			95% C.I. ^b	(0.090, 0.190)	(0.096, 0.189)	(0.107, 0.210)	H vs. L	--	0.407
			n	54	62	53	Overall		0.575
						M vs. L	2.47 (0.41, 14.79)	0.321	
						H vs. L	1.97 (0.29, 13.52)	0.488	
	Enlisted Groundcrew	n	143	155	138	Overall		0.064**	
		Adj. Mean** ^b	0.166	0.189	0.199	M vs. L	--	0.096**	
		95% C.I.** ^b	(0.143, 0.192)	(0.163, 0.217)	(0.171, 0.229)	H vs. L	--	0.024**	
		n	143	155	138	Overall		0.905	
					M vs. L	1.08 (0.24, 4.90)	0.919		
					H vs. L	0.73 (0.12, 4.43)	0.736		

TABLE 13-9. (continued)

Adjusted Exposure Index for Hepatic Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value	
			Low	Medium	High				
LDH	Officer	n	127	122	122	Overall		0.831**	
		Adj. Mean** ^a	133.9	133.5	132.3	M vs. L	--	0.892**	
		95% C.I.** ^a	(124.9, 143.5)	(124.8, 142.9)	(123.5, 141.6)	H vs. L	--	0.563**	
			n	127	122	122	Overall		0.836
						M vs. L	1.54 (0.24, 9.92)	0.650	
						H vs. L	0.92 (0.12, 7.04)	0.938	
		Enlisted Flyer	n	54	62	53	Overall		****
			Adj. Mean	****	****	****	M vs. L	--	****
			95% C.I.	****	****	****	H vs. L	--	****
			n	54	62	53	Overall		--
						M vs. L	--	--	
						H vs. L	--	--	
	Enlisted Groundcrew	n	143	155	138	Overall		0.381	
		Adj. Mean ^a	131.5	132.9	135.0	M vs. L	--	0.558	
		95% C.I. ^a	(127.0, 136.1)	(128.4, 137.6)	(130.2, 140.0)	H vs. L	--	0.166	
		n	143	155	138	Overall		****	
					M vs. L	****	****		
					H vs. L	****	****		

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TABLE 13-9. (continued)

Adjusted Exposure Index for Hepatic Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value	
			Low	Medium	High				
Cholesterol	Officer	n	127	122	122	Overall		0.057	
		Adj. Mean ^a	231.4	219.2	220.4	M vs. L	--	0.030	
		95% C.I. ^a	(213.7, 250.5)	(202.9, 236.9)	(203.9, 238.3)	H vs. L	--	0.050	
			n	127	122	122	Overall		0.199
							M vs. L	0.52 (0.23,1.13)	0.098
							H vs. L	0.91 (0.45,1.85)	0.794
	Enlisted Flyer	n	n	54	62	53	Overall		0.524
			Adj. Mean ^a	201.8	194.9	202.1	M vs. L	--	0.344
			95% C.I. ^a	(185.0, 220.1)	(179.9, 211.1)	(186.0, 219.7)	H vs. L	--	0.961
			n	54	62	53	Overall		****
							M vs. L	****	****
							H vs. L	****	****
Enlisted Groundcrew	n	n	143	155	138	Overall		0.494	
		Adj. Mean ^a	214.6	215.7	219.8	M vs. L	--	0.796	
		95% C.I. ^a	(206.6, 222.8)	(207.6, 224.1)	(211.2, 228.6)	H vs. L	--	0.256	
		n	143	155	138	Overall		0.630	
						M vs. L	1.18 (0.58,2.38)	0.646	
						H vs. L	1.40 (0.70,2.78)	0.338	

TABLE 13-9. (continued)

Adjusted Exposure Index for Hepatic Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value	
			Low	Medium	High				
HDL	Officer	n	127	122	122	Overall		0.302	
		Adj. Mean	52.26	52.44	50.30	M vs. L	--	0.804	
		95% C.I.	(47.20, 57.31)	(47.50, 57.38)	(45.33, 55.27)	H vs. L	--	0.205	
			n	127	122	122	Overall		0.433
						M vs. L	--	--	
						H vs. L	--	--	
		Enlisted Flyer	n	54	62	53	Overall		0.780
	Adj. Mean		43.82	42.90	42.21	M vs. L	--	0.679	
	95% C.I.		(38.43, 49.20)	(37.93, 47.86)	(37.04, 47.37)	H vs. L	--	0.483	
			n	54	62	53	Overall		0.089
						M vs. L	--	--	
						H vs. L	--	--	
	Enlisted Groundcrew	n	143	155	138	Overall		0.575	
Adj. Mean		49.1	49.58	50.62	M vs. L	--	0.740		
95% C.I.		(46.43, 51.80)	(46.87, 52.30)	(47.81, 53.43)	H vs. L	--	0.302		
		n	143	155	138	Overall		0.270	
					M vs. L	--	--		
					H vs. L	--	--		

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TABLE 13-9. (continued)

Adjusted Exposure Index for Hepatic Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
Cholesterol- HDL Ratio	Officer	n	127	122	122	Overall		0.340
		Adj. Mean	4.78	4.52	4.73	M vs. L	--	0.169
		95% C.I.	(4.17,5.38)	(3.93,5.11)	(4.14,5.32)	H vs. L	--	0.801
	Enlisted Flyer	n	127	122	122	Overall		0.285**
		Adj. Mean	4.92	4.73	5.18	M vs. L	1.10 (0.64,1.86)**	0.732**
		95% C.I.	(4.16,5.69)	(4.03,5.44)	(4.44,5.91)	H vs. L	0.73 (0.43,1.23)**	0.225**
	Enlisted Groundcrew	n	54	62	53	Overall		0.374
		Adj. Mean	4.92	4.73	5.18	M vs. L	--	0.550
		95% C.I.	(4.16,5.69)	(4.03,5.44)	(4.44,5.91)	H vs. L	--	0.436
	Enlisted Groundcrew	n	54	62	53	Overall		0.524
		Adj. Mean	4.92	4.73	5.18	M vs. L	0.65 (0.30,1.42)	0.270
		95% C.I.	(4.16,5.69)	(4.03,5.44)	(4.44,5.91)	H vs. L	0.96 (0.44,2.09)	0.919
Enlisted Groundcrew	n	143	155	138	Overall		0.938	
	Adj. Mean	4.84	4.81	4.78	M vs. L	--	0.873	
	95% C.I.	(4.52,5.16)	(4.49,5.13)	(4.44,5.11)	H vs. L	--	0.720	
Enlisted Groundcrew	n	143	155	138	Overall		0.135	
	Adj. Mean	4.84	4.81	4.78	M vs. L	0.82 (0.51,1.31)	0.394	
	95% C.I.	(4.52,5.16)	(4.49,5.13)	(4.44,5.11)	H vs. L	1.04 (0.65,1.68)	0.867	

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TABLE 13-9. (continued)

Adjusted Exposure Index for Hepatic Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value	
			Low	Medium	High				
Triglycerides	Officer	n	127	122	122	Overall		****	
		Adj. Mean	****	****	****	M vs. L	--	****	
		95% C.I.	****	****	****	H vs. L	--	****	
			n	127	122	122	Overall		****
							M vs. L	****	****
							H vs. L	****	****
	Enlisted Flyer	n		54	62	53	Overall		0.316**
			Adj. Mean** ^a	118.6	99.1	114.6	M vs. L	--	0.157**
			95% C.I.** ^a	(87.8, 160.1)	(75.2, 130.8)	(86.0, 152.9)	H vs. L	--	0.796**
		n		54	62	53	Overall		0.291**
							M vs. L	0.30 (0.05,1.70)**	0.174**
							H vs. L	0.95 (0.25,3.59)**	0.945**
Enlisted Groundcrew	n		143	155	138	Overall		0.706	
		Adj. Mean ^a	114.0	107.6	108.9	M vs. L	--	0.426	
		95% C.I. ^a	(99.7, 130.2)	(94.0, 123.1)	(94.7, 125.3)	H vs. L	--	0.543	
	n		143	155	138	Overall		0.132**	
						M vs. L	0.70 (0.29,1.66)**	0.417**	
					H vs. L	0.35 (0.12,1.03)**	0.057**		

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TABLE 13-9. (continued)

Adjusted Exposure Index for Hepatic Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value	
			Low	Medium	High				
Creatine Kinase	Officer	n	127	122	122	Overall		0.964**	
		Adj. Mean** ^a	135.2	134.3	136.6	M vs. L	--	0.921**	
		95% C.I.** ^a	(109.9, 166.3)	(109.7, 164.4)	(111.5, 167.5)	H vs. L	--	0.867**	
		n	127	122	122	Overall		0.550**	
						M vs. L	0.56 (0.19,1.66)**	0.296**	
						H vs. L	0.68 (0.25,1.87)**	0.457**	
		Enlisted Flyer	n	54	62	53	Overall		****
	Adj. Mean		****	****	****	M vs. L	--	****	
	95% C.I.		****	****	****	H vs. L	--	****	
		n	54	62	53	Overall		****	
						M vs. L	****	****	
						H vs. L	****	****	
	Enlisted Groundcrew	n	143	155	138	Overall		0.928	
Adj. Mean ^a		145.8	147.4	148.7	M vs. L	--	0.819		
95% C.I. ^a		(133.0, 159.8)	(134.4, 161.7)	(135.1, 163.6)	H vs. L	--	0.701		
	n	143	155	138	Overall		0.970		
					M vs. L	0.87 (0.26,2.83)	0.810		
					H vs. L	0.97 (0.29,3.18)	0.954		

TABLE 13-9. (continued)

Adjusted Exposure Index for Hepatic Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
Fasting Glucose	Officer	n	127	122	122	Overall		****
		Adj. Mean	****	****	****	M vs. L	--	****
		95% C.I.	****	****	****	H vs. L	--	****
		n	127	122	122	Overall		0.311**
						M vs. L	0.54 (0.24,1.21)**	0.133**
						H vs. L	0.78 (0.37,1.66)**	0.526**
	Enlisted Flyer	n	54	62	53	Overall		0.083**
		Adj. Mean** ^a	102.7	107.9	101.5	M vs. L	--	0.090**
		95% C.I.** ^a	(95.8, 110.0)	(101.2, 115.0)	(95.0, 108.5)	H vs. L	--	0.706**
		n	54	62	53	Overall		****
						M vs. L	****	****
						H vs. L	****	****
Enlisted Groundcrew	n	143	155	138	Overall		****	
	Adj. Mean	****	****	****	M vs. L	--	****	
	95% C.I.	****	****	****	H vs. L	--	****	
	n	143	155	138	Overall		0.649**	
					M vs. L	0.92 (0.43,1.97)**	0.823**	
					H vs. L	0.70 (0.32,1.52)**	0.370**	

^aTransformed from natural logarithm scale.

****Exposure index-by-covariate interaction ($p < 0.01$)--adjusted mean, confidence interval, and p-value not presented.

--Adjusted relative risk not applicable for continuous analysis of a variable; analysis not done due to sparse number of abnormalities.

**Exposure index-by-covariate interaction ($0.01 < p < 0.05$)--adjusted mean/relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

^bTransformed from natural logarithm ($X + 0.1$) scale.

TABLE 13-10.

**Summary of Exposure Index-by-Covariate
Interactions From Adjusted Analyses for Hepatic Variables***

Variable	Occupation	Covariate	p-Value
AST (C)	Officer	Current Alcohol Use	<0.001
AST (D)	Enlisted Flyer	Age	0.004
ALT (C)	Officer	Current Alcohol Use	0.003
ALT (D)	Officer	Lifetime Alcohol History	0.006
ALT (D)	Enlisted Flyer	Age	0.001
		Current Alcohol Use	0.042
		Lifetime Alcohol History	0.030
		Degreasing Chemical Exposure	0.009
GGT (C)	Officer	Degreasing Chemical Exposure	0.042
GGT (D)	Enlisted Flyer	Lifetime Alcohol History	0.032
		Current Alcohol Use	0.017
Alkaline Phosphatase (C)	Officer	Lifetime Wine History	0.050
Alkaline Phosphatase (C)	Enlisted Groundcrew	Degreasing Chemical Exposure	0.037
Alkaline Phosphatase (D)	Enlisted Groundcrew	Lifetime Wine History	0.041
Total Bilirubin (D)	Officer	Age	0.017
		Industrial Chemical Exposure	0.023
Total Bilirubin (D)	Enlisted Flyer	Age	0.003
		Industrial Chemical Exposure	0.008
		Degreasing Chemical Exposure	0.004
Total Bilirubin (C)	Enlisted Groundcrew	Age	0.040
		Current Alcohol Use	0.046
Direct Bilirubin (C)	Enlisted Groundcrew	Current Alcohol Use	0.026
LDH (C)	Officer	Lifetime Alcohol History	0.026
LDH (C)	Enlisted Flyer	Age	0.009
		Race	0.035
LDH (D)	Enlisted Groundcrew	Race	0.009
		Current Alcohol Use	0.003

TABLE 13-10. (continued)

Summary of Exposure Index-by-Covariate
Interactions From Adjusted Analyses for Hepatic Variables*

Variable	Occupation	Covariate	p-Value
Cholesterol (D)	Enlisted Flyer	Degreasing Chemical Exposure	<0.001
Cholesterol-HDL Ratio (D)	Officer	Lifetime Alcohol History	0.014
		Degreasing Chemical Exposure	0.017
Triglycerides (C)	Officer	Current Alcohol Use	0.009
Triglycerides (D)	Officer	Lifetime Alcohol History	0.018
		Industrial Chemical Exposure	0.005
Triglycerides (C)	Enlisted Flyer	Age	0.043
Triglycerides (D)	Enlisted Flyer	Age	0.022
Triglycerides (D)	Enlisted Groundcrew	Current Alcohol Use	0.023
Creatine Kinase (C)	Officer	Industrial Chemical Exposure	0.017
Creatine Kinase (D)	Officer	Current Alcohol Use	0.027
Creatine Kinase (C)	Enlisted Flyer	Age	0.009
Creatine Kinase (D)	Enlisted Flyer	Age	<0.001
Fasting Glucose (C)	Officer	Lifetime Alcohol History	<0.001
Fasting Glucose (D)	Officer	Degreasing Chemical Exposure	0.026
Fasting Glucose (C)	Enlisted Flyer	Race	0.011
Fasting Glucose (D)	Enlisted Flyer	Industrial Chemical Exposure	0.005
Fasting Glucose (C)	Enlisted Groundcrew	Race	<0.001
		Current Alcohol Use	0.019
Fasting Glucose (D)	Enlisted Groundcrew	Race	0.013

*Refer to Table J-4 for a further investigation of these interactions.

C: Continuous Analysis.

D: Discrete Analysis.

The final interpretation of these exposure index data must await the reanalysis of the clinical data using the results of the serum dioxin assay. The report is expected in 1991.

AST

The unadjusted exposure index means and the percentages of abnormal AST values both exhibited increasing dose-response patterns for the officer cohort (25.4 U/L, 26.1 U/L, and 26.7 U/L; and 3.1%, 4.0%, and 9.0% for the low, medium, and high exposure categories, respectively). The means were not significantly different ($p=0.429$), and the overall discrete association was marginally significant ($p=0.086$). After covariate adjustment, the overall discrete result became nonsignificant ($p=0.152$), yet a marginally significant result remained for the high versus low contrast (Adj. RR: 3.15, 95% C.I.: [0.89,11.14], $p=0.075$). A highly significant exposure index-by-current alcohol use interaction was found for the adjusted continuous analysis ($p<0.001$). Results stratified by current alcohol use are presented in Table J-4. Increasing dose-response patterns were seen for moderate and heavy drinkers, in contrast to a decreasing dose-response effect for light drinkers. The adjusted mean for moderate drinkers in the high exposure category, 33.0 U/L, was significantly higher than the adjusted mean for moderate drinkers in the lowest exposure category, 25.9 U/L ($p=0.006$). No significant unadjusted results were found for the enlisted flyer cohort; a significant exposure index-by-age interaction was found for the adjusted discrete analysis ($p=0.004$). For the enlisted groundcrew, AST means and the percentages of abnormal values exhibited increasing dose-response trends. However, results for the unadjusted continuous and discrete analyses were not significant. The trends remained after covariate adjustment. The adjusted relative risk for the high versus low contrast was marginally significant (Adj. RR: 2.71, 95% C.I.: [0.87,8.46], $p=0.086$).

ALT

No significant results for ALT were found for the unadjusted exposure index analyses for each occupational cohort, although the means for officers increased with exposure level (20.1 U/L, 20.4 U/L, and 21.4 U/L for the low, medium, and high exposure categories, respectively). For the adjusted analyses, significant exposure index-by-covariate interactions were found for the officer and enlisted flyer cohorts. Adjusted results for the enlisted groundcrew were not significant. The adjusted continuous analysis for officers detected a significant exposure index-by-current alcohol use interaction ($p=0.003$). Results stratified by current drinking exhibited the same patterns as the results for AST. Increasing dose-response effects were seen for moderate and heavy drinkers, in contrast to a decreasing dose-response pattern for Ranch Hands who currently had no more than one drink per day. With ALT, the adjusted mean for high exposure moderate drinkers was significantly higher than the mean for low exposure moderate drinkers, (26.9 U/L vs. 17.0 U/L, respectively; $p=0.001$). The adjusted discrete analysis found a significant interaction with lifetime alcohol history ($p=0.006$) for officers. Four significant exposure index-by-covariate interactions were found for the enlisted flyer cohort in the adjusted discrete analysis (exposure index-by-age, $p=0.001$; exposure index-by-current alcohol use, $p=0.042$; exposure index-

by-degreasing chemical exposure, $p=0.009$; and exposure index-by-lifetime alcohol history, $p=0.030$).

GGT

A significant overall result, supportive of a herbicide effect, was found for officers in both the unadjusted and adjusted discrete exposure index analyses for GGT ($p=0.018$ and $p=0.038$, respectively). The percentage of abnormal GGT values increased with exposure (5.5%, 6.5%, and 14.8% for the low, medium, and high exposure categories, respectively). The adjusted discrete analysis also exhibited a dose-response effect; medium versus low (Adj. RR: 1.34, 95% C.I.: [0.44, 4.04], $p=0.607$), and high versus low (Adj. RR: 3.09, 95% C.I.: [1.16, 8.24], $p=0.024$). The unadjusted and adjusted officer GGT means also increased with exposure, but the overall results were not significant ($p=0.140$ and $p=0.209$, respectively). A significant exposure index-by-degreasing chemical exposure interaction was found for the adjusted continuous analysis ($p=0.042$). There was an increasing dose-response relationship for officers who had not been exposed to degreasing chemicals, and the high versus low contrast was significant ($p=0.007$). For the enlisted flyer cohort, the only significant findings were two covariate interactions with exposure index in the adjusted discrete analysis (exposure index-by-current alcohol use, $p=0.017$; and exposure index-by-lifetime alcohol history, $p=0.032$). The discrete data exhibited a dose-response effect within the enlisted groundcrew cohort, but the results were not statistically significant.

Alkaline Phosphatase

The alkaline phosphatase means for officers increased with exposure level (87.9 U/L, 88.9 U/L, and 92.0 U/L for the low, medium, and high exposure categories, respectively), but the overall difference was not significant ($p=0.302$). The adjusted continuous analysis revealed a significant exposure index-by-lifetime wine history interaction ($p=0.050$). Stratifying by wine consumption revealed an increasing dose-response effect for heavy wine drinkers. The high versus low contrast for this stratum was significant ($p=0.017$). The adjusted mean for the 11 officers in the high exposure category who had more than 10 drink-years of wine, 79.9 U/L, was significantly higher than the adjusted mean for the 9 officers in the low exposure category who had more than 10 drink-years of wine, 61.3 U/L.

Excluding this interaction, the adjusted continuous results remained nonsignificant ($p=0.314$), with the adjusted means exhibiting a positive dose-response trend. The percentage of abnormal values was highest for the medium exposure category (6.5%) and lower for the high (3.3%) and low (1.6%) categories for officers. Both the unadjusted and adjusted relative risk for the medium versus low contrast were marginally significant (Est. RR: 4.35, 95% C.I.: [0.90, 20.88], $p=0.092$; Adj. RR: 4.32, 95% C.I.: [0.87, 21.41], $p=0.073$). No significant results, either unadjusted or adjusted, were found for the enlisted flyers.

A significant exposure index-by-degreasing chemical exposure interaction was found in the adjusted continuous analysis for the enlisted groundcrew

cohort ($p=0.037$). The adjusted mean for the medium exposure category was significantly higher than the adjusted mean for the low exposure category for enlisted groundcrew exposed to degreasing chemicals (100.1 U/L vs. 93.5 U/L, respectively; $p=0.028$). The adjusted discrete analysis for the enlisted groundcrew revealed a significant exposure index-by-lifetime wine history interaction ($p=0.041$). A marginally significant result ($p=0.052$), not supportive of a dose-response relationship, was found for enlisted groundcrew who had more than 0 and no more than 10 drink-years of wine.

Total Bilirubin

Unadjusted continuous and discrete exposure index results for total bilirubin were not significant for each occupational cohort. The means for the enlisted groundcrew increased with exposure level. Significant exposure index-by-covariate interactions were found for all occupations in the adjusted analyses. They are listed in Table 13-10 and stratified results are presented in Table J-4.

Direct Bilirubin

The unadjusted and adjusted discrete exposure index analyses for direct bilirubin showed significant differences among exposure categories for officers, but not in a dose-response pattern ($p=0.010$ and $p=0.006$, respectively). The percentage of abnormal values was highest for the high exposure category (8.2%), but lowest for the medium exposure category (0.8%). There were 3.1 percent abnormal in the low exposure category. The relative risk for the high versus low contrast was marginally significant after covariate adjustment ($p=0.054$). The means increased with exposure level, but results were not significant for the enlisted flyer cohort. For the enlisted groundcrew, a marginally significant result supportive of a dose-response effect was found for the unadjusted continuous analysis ($p=0.085$). The means were 0.141 mg/dl, 0.163 mg/dl, and 0.168 mg/dl for the low, medium, and high exposure categories, respectively. The high versus low contrast was significant ($p=0.041$). The adjusted analysis revealed a significant exposure index-by-current alcohol use interaction ($p=0.026$). Increasing dose-response patterns were seen for light and moderate drinkers; for Ranch Hands who currently consume more than four drinks per day, the adjusted mean for the medium exposure category was significantly higher than the adjusted mean for the low exposure category ($p=0.031$). After excluding this interaction, the adjusted results agreed with the unadjusted findings; the overall difference was marginally significant ($p=0.064$), and the high versus low contrast was significant ($p=0.024$).

LDH

Unadjusted exposure index results for LDH were not significant for officers. A significant exposure index-by-lifetime alcohol history interaction ($p=0.026$) was found in the adjusted continuous analysis. An increasing dose-response pattern was observed for officers who had more than 40 drink-years. The medium versus low contrast was marginally significant ($p=0.070$) and the high versus low contrast was significant ($p=0.017$) for this stratum.

In contrast, a significant result, not supportive of a dose-response effect, was seen for officers who had never drunk alcohol. The adjusted mean for the high exposure category was significantly lower than the adjusted mean for the low exposure category for this stratum ($p=0.041$). A marginally significant result that did not suggest a dose-response relationship was found in the unadjusted continuous analysis for the enlisted flyers ($p=0.082$); the medium exposure category LDH mean was significantly lower than the low exposure category mean ($p=0.042$). Significant exposure index-by-covariate interactions were found in the adjusted continuous analysis for enlisted flyers. The enlisted groundcrew means increased with exposure level (127.8 U/L, 128.6 U/L, and 131.7 U/L for the low, medium, and high exposure categories, respectively), but the overall unadjusted result was not significant ($p=0.245$). The mean for the high exposure category was marginally significantly different from the low exposure mean ($p=0.099$), but after covariate adjustment, this finding was not significant ($p=0.166$). Two significant exposure index-by-covariate interactions were found for the adjusted discrete analysis for the enlisted groundcrew; the unadjusted results were not significant.

Cholesterol

Unadjusted and adjusted cholesterol means for officers were marginally significantly different among exposure categories ($p=0.063$ and $p=0.057$, respectively). The adjusted mean for the low exposure category, 231.4 mg/dl, was significantly higher than the means for both the medium, 219.2 mg/dl, and high exposure categories, 220.4 mg/dl ($p=0.030$ and $p=0.050$, respectively). Results of the discrete analyses were not significant for officers. A significant exposure index-by-degreasing chemicals exposure interaction ($p<0.001$) was found for enlisted flyers in the adjusted discrete analysis. All other enlisted flyer results were not significant. The percentage of abnormal cholesterol levels exhibited an increasing dose-response effect for enlisted flyers who had never been exposed to degreasing chemicals (0.0%, 7.1%, and 41.7% for the low, medium, and high exposure categories, respectively; overall, $p=0.013$). Conversely, a decreasing pattern was seen for enlisted flyers exposed to degreasing chemicals (25.6%, 16.7%, and 7.3% for the low, medium, and high exposure categories, respectively; overall, $p=0.080$). For each stratum, the high versus low contrast was significant ($p=0.048$ and $p=0.047$, for exposed to degreasing chemicals and not exposed to degreasing chemicals, respectively). Cholesterol means and the percentages of abnormal values increased with exposure category for the enlisted groundcrew, but unadjusted and adjusted results were not significant.

HDL

Results for the unadjusted exposure index analyses of HDL were not significant for each occupational cohort. HDL means exhibited a negative dose-response effect for officers (49.28 mg/dl, 48.58 mg/dl, and 46.38 mg/dl for the low, medium, and high exposure categories, respectively). Results for the adjusted exposure index analyses were not significant for each occupational cohort.

Cholesterol-HDL Ratio

Results for the unadjusted exposure index analyses of the cholesterol-HDL ratio were not significant for each occupational cohort. There were no apparent dose-response patterns with regard to cholesterol-HDL ratio means or percent abnormal. Results for the adjusted exposure index analyses were not significant for enlisted flyers and enlisted groundcrew. Significant exposure index-by-covariate interactions were found in the adjusted analyses for officers. Stratified analyses revealed no significant results supportive of a herbicide effect.

Triglycerides

Results for the unadjusted exposure index analyses of triglycerides were not significant for each occupational cohort. Triglycerides means exhibited a positive dose-response effect for officers (112.7 mg/dl, 113.2 mg/dl, and 120.4 mg/dl for the low, medium, and high exposure categories, respectively). The percentage of abnormal values decreased with exposure for the enlisted groundcrew (8.9%, 6.5%, and 3.6% for the low, medium, and high exposure categories, respectively). Significant exposure index-by-covariate interactions were found in the adjusted analyses for all occupations. Stratified analyses revealed no significant results supportive of a herbicide effect.

Creatine Kinase

For creatine kinase, no significant unadjusted exposure index results were found for any occupational cohort. Adjusted analyses showed significant exposure index-by-covariate interactions for officers and enlisted flyers. These interactions are listed in Table 13-10. Creatine kinase means, for officers who were exposed to industrial chemicals, decreased with exposure level (144.5 U/L, 140.9 U/L, and 117.3 U/L for the low, medium, and high exposure categories, respectively). Conversely, an increasing trend was seen for officers who had not been exposed to industrial chemicals (132.4 U/L, 132.7 U/L, and 150.7 U/L for the low, medium, and high exposure categories, respectively). The high versus low contrast was marginally significant for each stratum ($p=0.052$ for exposed to industrial chemicals, $p=0.098$ for not exposed to industrial chemical exposure). Stratified analyses for the other interactions showed no significant results supportive of a dose-response effect. Adjusted results for the enlisted groundcrew were not significant.

Fasting Glucose

Unadjusted exposure index results for fasting glucose were not significant for each occupation. Significant exposure index-by-covariate interactions were found in all adjusted analyses for all occupations. Stratified analyses were done to explore these interactions. As seen in Table J-4, several significant results were found, but none suggested a herbicide effect. A marginally significant result, supportive of a dose-response relationship, was found for the discrete analysis of enlisted flyers who had not been exposed to industrial chemicals ($p=0.099$).

Longitudinal Analysis

AST, ALT, and GGT were investigated to assess longitudinal group differences between the 1982 Baseline examination and the 1987 followup. Each variable was analyzed in its continuous form. Longitudinal results are summarized in Table 13-11. No significant findings were noted. Both groups showed a large decrease in AST between 1982 and 1987.

Mortality Count Data

Cumulative digestive system mortality through the end of 1987 by group and ICD code is shown in Table 13-12. The overall numbers at risk are 1,261 Ranch Hands and 19,101 Comparisons (approximately a 15:1 ratio). An unadjusted analysis of digestive system mortality revealed a statistically significant group difference ($p=0.01$). This difference was attributed to increased alcohol-related liver disease in the Ranch Hands.

TABLE 13-11.

Longitudinal Analysis of Selected Hepatic Variables:
A Contrast of 1982 Baseline and 1987 Followup Examination Means

Variable	Examination	Group Means		p-Value (Equality of Differences)
		Ranch Hand	Comparison	
AST*	1982 Baseline	32.71	32.91	0.219
	1985 Followup	33.81	33.54	
	1987 Followup	25.82	25.56	
ALT*	1982 Baseline	19.87	20.35	0.198
	1985 Followup	21.78	22.45	
	1987 Followup	20.61	20.55	
GGT*	1982 Baseline	39.28	38.60	0.478
	1985 Followup	32.80	32.22	
	1987 Followup	33.48	32.43	

Note: Summary statistics for the 1982 Baseline and the 1987 followup are based on 931 Ranch Hands and 1,096 Comparisons who participated in the 1982 Baseline and the 1987 followup examinations. P-value given is in reference to the hypothesis test involving 1982 Baseline and 1987 followup results. Summary statistics on 911 of these Ranch Hands and 1,077 of these Comparisons who also participated in the 1985 followup are also included for reference purposes only.

*Means transformed from the natural logarithm scale; hypothesis test performed on the natural logarithm scale.

TABLE 13-12.

Group Cumulative Site-Specific Digestive System Mortality

ICD Code	Category	Number of Deaths	
		Ranch Hand	All Comparison
530-537	Esophagus, Stomach, and Duodenum		
531.9	Gastric Ulcer	0	1
532.4	Duodenal Ulcer with Hemorrhage	0	1
532.5	Duodenal Ulcer with Perforation	0	1
533.4	Peptic Ulcer with Hemorrhage	0	1
540-543	Appendicitis		
540.0	Acute Appendicitis, Peritonitis	0	1
560-569	Intestine and Peritonium, Other		
564.1	Irritable Colon	0	1
570-579	Digestive System, Other		
571.0	Alcoholic Fatty Liver	1	1
571.1	Acute Alcoholic Hepatitis	0	3
571.2	Alcoholic Cirrhosis of Liver	4	15
571.3	Alcoholic Liver Damage, Unspecified	0	4
571.5	Cirrhosis of Liver, Nonalcoholic	0	5
571.9	Unspecified Chronic Liver Disease		
	Without Mention of Alcohol	0	1
572.9	Other Sequelae of Chronic Liver Disease	1	0
577.0	Acute Pancreatitis	0	2
	Totals	6	37

DISCUSSION

Signs and symptoms referable to the gastrointestinal system are among those most frequently encountered in ambulatory medicine. As screening tools in the outpatient investigation of digestive disorders, the historical, physical examination, and laboratory parameters included in the gastrointestinal assessment are well established in clinical practice. More definitive diagnostic studies, such as barium and endoscopic surveys of the bowel, were not included in the current study and, except in emergent circumstances, are rarely indicated in the initial evaluation of gastrointestinal disease.

In the diagnosis of digestive disorders it is important to recognize certain limitations in the extent to which data from the history and physical examination can be relied upon. Rather than pointing to a particular diagnosis, digestive symptoms are frequently nonspecific and intermittent. In this setting, even the best designed medical history questionnaire can be subject to error. "Ulcer" and "colitis" are diagnoses that are commonly reported but often not accurately established. In contrast, most cases of

hepatitis are anicteric and escape detection. As a common target organ for situational stress, the bowel frequently gives rise to symptoms that can be severe but that are functional in nature and resolve over time. These caveats highlight the importance of the type of medical record verification conducted in the current study and, in the case of hepatitis, the need for serologic confirmation.

In contrast to some organ systems, the physical examination in gastrointestinal disease is often of limited value and can be misleading in the differential diagnosis. The ability of the examiner to detect hepatomegaly will be unreliable in the obese patient. In obstructive airway disease, with hyperinflation of the lungs and flattening of the diaphragms, the liver edge may descend abnormally below the right costal margin in the absence of hepatomegaly. In the best of circumstances, the span of the liver by palpation or percussion is often an unreliable index of liver size. Recognizing that in the most advanced stages of cirrhosis hepatomegaly is often not present, other stigmata of chronic liver disease were sought during the physical examination. Palmar erythema, ascites, telangiectasias, and gynecomastia were examined as part of this physical examination.

In contrast to the limitations of the history and physical examination outlined above, data collected in the laboratory can provide early insight into the presence of occult liver disease. The four hepatic enzymes analyzed as dependent variables (AST, ALT, GGT, and LDH) are common to most chemistry panels ordered in the outpatient setting. Present in high intracellular concentration, these enzymes are released in virtually all toxic, inflammatory, and neoplastic diseases with hepatic involvement. As reliable laboratory markers of liver disease, the GGT is considered the most sensitive, while the LDH, with iso-enzymes derived from multiple organ systems, is the least specific.

As the hepatic enzymes are used in the detection and followup of parenchymal disease, so are the serum alkaline phosphatase and bilirubin reflective of hepatobiliary function in "cholestatic" or "obstructive" disease. Though present in virtually all organ systems, the serum alkaline phosphatase in the adult population under study is of dual origin and close to a 50-50 mixture of liver- and bone-derived fractions. An elevated alkaline phosphatase is by no means diagnostic of liver disease and can occur in a broad range of unrelated clinical conditions including drug-induced cholestasis, Paget's disease (3% of males over age 40), neoplasia with metastases to bone, and congestive heart failure.

Similarly, and pertinent to the current study, the bilirubin indices are subject to numerous hereditary and acquired disorders unrelated to intrinsic hepatic disease. The benign hyperbilirubinemia of Gilbert's syndrome will occur in 5 percent of the population under study. A long list of medications, including many over-the-counter preparations, have been implicated in the overproduction of bilirubin in the hemolytic reactions associated with glucose-6-phosphate dehydrogenase deficiency, which may occur in up to 15 percent of Black American males.

Most of the dependent variable-covariate associations analyzed in the present section are consistent with established clinical observations. Alcohol consumption was associated with hepatomegaly and elevated liver

enzymes with the most sensitive GGT showing the greatest deviation from the normal. The difficulty in estimating alcohol consumption by history may account for the unexpectedly higher percentage of two enzyme abnormalities (ALT and GGT) in non- versus moderate alcohol consumption. Alcohol use per se should not affect the bilirubin indices, and the slight differences related to current consumption were not significant.

Documented in the adjusted analyses were a number of covariate associations that would be expected with age including gradual elevations in serum cholesterol, triglycerides, and fasting blood sugar. The decrease in ALT over time is not readily explained and probably not significant as an isolated finding. The decline in serum creatine kinase would be consistent with decreasing muscle mass over time.

Significant ($p < 0.001$) race-related differences in two serum enzymes (GGT and creatine kinase) were documented and, in the case of the creatine kinase, the mean for Blacks was almost twice that for nonblacks. These data are consistent with observations first reported by H.Y. Meltzer⁵⁴ and subsequently confirmed in a small number of studies over the past decade. The elevation, not yet explained, appears to be race- and gender-specific and is limited to Black males.

With reference to prior herbicide exposure, most group differences were not statistically significant, though, as in the 1985 followup examination, Ranch Hands had a significantly higher mean alkaline phosphatase (93.7 U/L) than did the Comparisons (90.3 U/L). As an index subject to multiple organ variables, however, this difference should not be considered clinically significant. Longitudinal analysis of three enzyme variables confirmed no significant group differences over time. The decline in serum AST in both groups cannot be explained on the basis of any difference in methodology as the laboratory assay techniques in the 1985 and 1987 examination cycles were identical.

In summary, the gastrointestinal assessment data confirmed observations that are well established in clinical practice and reflect no apparent increase in organ-specific mortality or morbidity in the Ranch Hand group versus the Comparison group over time.

SUMMARY

Table 13-13 summarizes the statistical results of the Ranch Hand and Comparison group contrasts that were analyzed for the 1987 gastrointestinal assessment.

Information collected at the health interview was verified and grouped into eight categories of liver disorders. There were no significant group differences for any of these conditions. Self-reported data on history of ulcers and on occurrences of skin patches, bruises, and sensitivity also did not differ significantly between groups. In contrast, Ranch Hands reported significantly more skin patches, bruises, and sensitivity than Comparisons at both the Baseline and 1985 followup examinations.

TABLE 13-13.

**Overall Summary Results of Unadjusted and Adjusted
Group Contrast Analyses of Gastrointestinal Variables**

Variable	Unadjusted		Adjusted		Direction of Results
	Discrete	Continuous	Discrete	Continuous	
<u>Questionnaire</u>					
Viral Hepatitis	NS	--	--	--	
Acute and Subacute Necrosis of the Liver	NS	--	--	--	
Chronic Liver Disease and Cirrhosis (Alcohol Related)	NS	--	--	--	
Chronic Liver Disease and Cirrhosis (Nonalcohol Related)	NS	--	--	--	
Liver Abscess and Sequelae of Chronic Liver Disease	NS	--	--	--	
Other Disorders of the Liver	NS	--	--	--	
Jaundice (Unspecified)	NS	--	--	--	
Hepatomegaly	NS	--	--	--	
Reported Ulcer	NS	--	NS	--	
Skin Patches, Bruises, or Sensitivity	NS	--	--	--	
Verified Ulcer	NS	--	NS	--	
<u>Physical Examination</u>					
Diagnosed Hepatomegaly	NS	--	** (NS)	--	
<u>Laboratory</u>					
AST	NS	NS	NS	NS	
ALT	NS	NS	NS	** (NS)	
GGT	NS	NS	NS	NS	
Alkaline Phosphatase	NS	<0.001	NS	<0.001	RH>C
Total Bilirubin	NS	NS	** (NS)	NS	
Direct Bilirubin	NS	NS	****	** (NS)	
LDH	NS	NS	NS	NS	
Cholesterol	NS	NS	NS	NS	
HDL	NS	NS	NS	** (NS)	
Cholesterol-HDL Ratio	NS	NS	NS	NS	

TABLE 13-13. (continued)

Overall Summary Results of Unadjusted and Adjusted
Group Contrast Analyses of Gastrointestinal Variables

Variable	Unadjusted		Adjusted		Direction of Results
	Discrete	Continuous	Discrete	Continuous	
Triglycerides	NS	NS	NS	NS	
Creatine Kinase	NS	NS	NS	NS	
Fasting Glucose	NS	NS	NS	NS	

--Analysis not performed or not applicable.

NS: Not significant ($p > 0.10$).

****: Group-by-covariate interaction ($p < 0.01$).

** (NS): Group-by-covariate interaction ($0.01 < p < 0.05$); not significant when interaction is deleted.

RH>C: Higher mean value in Ranch Hands than in Comparisons.

Hepatomegaly was diagnosed at the physical exam. No significant group difference was found for the unadjusted analysis. The adjusted analysis detected a significant group-by-degreasing chemical exposure interaction; the group relative risk for participants never exposed to degreasing chemicals was marginally significant and less than 1. After excluding the interaction, the adjusted group difference was not significant.

Ranch Hand and Comparison group contrasts were assessed for 13 laboratory variables. Each variable was examined in both continuous and discrete forms. Statistical analysis of these variables revealed only one significant group difference. The Ranch Hand alkaline phosphatase mean was significantly higher than the Comparison mean, a finding also noted at the 1985 followup study. In contrast, the percentage of abnormal alkaline phosphatase values was very similar between groups. Aside from significant group-by-covariate interactions, results of the adjusted analyses always supported the unadjusted analyses results. Results based on stratified analyses to explore group-by-covariate interactions were generally not significant. The following stratum specific significant results were noted: for participants with more than 40 drink-years, the Ranch Hand ALT mean was marginally higher than the Comparison mean; the direct bilirubin mean for Black Ranch Hands was significantly higher than the mean for Black Comparisons; and Ranch Hands exposed to degreasing chemicals had significantly fewer direct bilirubin abnormal levels than Comparisons who had been exposed to degreasing chemicals.

The adjusted exposure index analyses detected one statistically significant result supportive of a herbicide effect (GGT discretized for the officer cohort), and one marginally significant result that suggested a herbicide effect (direct bilirubin treated as a continuous variable for the enlisted groundcrew cohort). Other significant or marginally significant results did not indicate an effect due to dioxin exposure. Although few exposure index results were statistically significant, trends in the data showed positive dose-response relationships for many variables, particularly for the officer and enlisted groundcrew cohorts.

Longitudinal analyses for AST, ALT, and GGT disclosed no statistically significant differences over time between groups.

In conclusion, results of the 1987 gastrointestinal assessment did not indicate an overall detriment to the health of the Ranch Hand group. The Ranch Hand alkaline phosphatase mean was significantly higher than the Comparison mean, but for all other variables, differences between groups were not statistically significant. In many instances, patterns in the data for the exposure index analyses supported a herbicide effect, but the results were generally not significant.

CHAPTER 13

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