List of Tables

17 IMMUNOLOGIC ASSESSMENT

17.1 INTRODUCTION

17.1.1 Background

Of the many chemical compounds known to cause immune system dysfunction in laboratory animals, the polyhalogenated aromatic hydrocarbons have been the most extensively studied and, among these, 2,3,7,8-tetrachlorodibenzo-p-dioxin (dioxin) has proven to be the most toxic. Since the early 1970s, when dioxin was shown to cause marked involution of the thymus gland in experimental animals (1–4), the extensive body of literature pertinent to dioxin-induced immunotoxicity has been summarized in several review articles (5–10).

In laboratory animals, dioxin has proven to have a wide range of toxic effects on all components of the immune system, including direct thymotoxic effects, particularly on the epithelial cells (8, 11–14), compromised cell mediated (1, 13, 15–18) and humoral (1, 17, 19–22) immune function, impaired myelo- (23, 24) and lymphoproliferative (13, 25–27) responses, and suppressed complement activity (28–31).

The crucial role of the immune system in resistance to infection has been well established, and numerous animal studies have demonstrated that exposure to dioxin increases host susceptibility to a broad range of bacterial (19, 23, 29, 32, 33), parasitic (34), and viral (35, 36) infectious agents.

The role of the aryl hydrocarbon (Ah) receptor as a mediator in dioxin toxicity has been long recognized (37, 38) and summarized in numerous reviews (6, 39, 40). Much of the basic research in laboratory animals has focused on the role of the Ah receptor in some but not all manifestations of dioxin-induced immunotoxicity, including suppressed humoral (20, 22, 41–46) and cellular (47, 48) responses and impaired complement activity (49). Other studies have demonstrated that dioxin exposure can cause immune system responses independent of the Ah receptor (42, 43, 45, 50–52). Although the Ah receptor has been identified in several human tissues (see references 43, 51–53, and 55 in Chapter 9, General Health Assessment), the relevance of these observations to dioxin toxicity in humans remains unknown. In an attempt to provide data more relevant to humans, two laboratories have conducted experiments of the effects of dioxin on peripheral lymphocyte subpopulations in marmoset (52–56) and rhesus (57) monkeys. These studies were carried out in vitro, employing lymphocyte cell cultures, and in vivo, with single-dose injections of dioxin in various concentrations. In these experiments, the ratios of selected lymphocyte subsets varied inconsistently in response to the dose (high versus low) and duration (acute versus chronic) of exposure. In none of the in vivo studies did the animals demonstrate any overt illness.

The demonstration that human tonsils contain the Ah receptor (58) and the development of a tonsillar lymphocyte culture model have established a scientifically valid basis for comparison of the effects of dioxin on experimental animals and humans at the cellular level. In published results from two series of experiments, dioxin had identical effects on both human and murine B lymphocytes with dose-dependent suppression of cellular proliferation and a significant reduction in the secretion of immunoglobulins IgM and IgG (59, 60). Although the mechanism is not known, these experiments provide strong evidence that the human lymphocyte is sensitive to dioxin. These results are consistent with those reported from another laboratory investigating the effect of dioxin on human lymphocytes isolated from peripheral blood (61). As noted below, these experimental models have been applied recently to human populations exposed to dioxin (62, 63).

Immune system indices have been included in epidemiological studies of populations exposed to dioxin consequent to industrial accidents (64–72), by occupation (62, 63, 73–75), by environmental contamination (76–81), and during military service in Vietnam (82–86). Industrial accidents have resulted in the most severe human exposure to dioxin on record. In three reports published shortly after the 1976 chemical explosion in Seveso, Italy, no immune system abnormalities were found in exposed children (64, 65) or cleanup workers (66). In contrast, other investigators documented abnormal immune indices in children with chloracne (67, 68) that resolved over time and were not associated with any clinical immune deficiency illness (69, 70). Similarly, the immunologic testing abnormalities noted in a cohort of chemical workers exposed to dioxin in an industrial accident in England in 1968 were not associated with any clinical illness (71, 72).

Most of the recently published epidemiological studies have reported on the results of clinical examinations of workers who experienced significant occupational exposure to dioxin during employment at chemical factories in Germany (62, 63, 73–75). These studies, which incorporated immune system parameters in the examination protocols, are strengthened by the inclusion of serum dioxin data in the analyses. None of these studies showed any evidence in those exposed for clinical illness associated with immune system disorders nor, in relation to the body burden of dioxin, any statistically significant abnormalities in the laboratory indices.

Resident populations in the Times Beach, Missouri, area have been the subject of several studies yielding conflicting results, some of which can be attributed to methodological limitations. In two early reports, abnormalities were documented in several indices of immune function, including impaired delayed sensitivity by skin testing and nonsignificant variations in several peripheral lymphocyte subsets and ratios (76–78). In subsequent follow-up examinations of the same subjects, there were no significant differences between the exposed and control cohorts (79, 80).

A subsequent report of the subject Missouri population included serum dioxin levels that ranged from less than 20 parts per trillion (ppt) to 750 ppt. In this study, a correlation was noted between serum dioxin and an increasing percentage of CD8+ (suppressor T cells) and T_{11}+ subsets of T lymphocytes, as well as statistically nonsignificant increases in serum IgA and complement components C3 and C4 (81). As in the other Missouri studies, there was no evidence for clinical illness in the exposed cohort relative to controls.

Finally, in the 1987 and 1992 examinations of the Air Force Health Study (AFHS), multiple immunologic indices have been examined in relation to serum dioxin levels (85, 86). In the 1987 examination and, to a lesser degree, in the 1992 examination, serum IgA immunoglobulin levels were significantly higher in the Ranch Hand cohort than controls in a pattern consistent with a dose-response effect. Although of uncertain significance, this finding is of interest as one that has been noted in two other epidemiological studies cited above (74, 81) and, separately, a report of a laboratory animal study (87) that documented a selective increase in the IgA globulin fraction after a single injection of dioxin. There have been no other significant immune system differences between the Ranch Hands and Comparisons across the baseline, 1985, 1987, and 1992 examinations.

17.1.2 Summary of Previous Analyses of the Air Force Health Study

17.1.2.1 1982 Baseline Study Summary Results

Immunologic function and phenotypic marker studies were performed on 592 participants (297 Ranch Hands, 295 Comparisons) randomly selected by the terminal digit of their case number. Because of laboratory problems (e.g., fluctuating quality control and lack of simultaneous differential counts on the peripheral mononuclear cells), data could be analyzed on a group basis only.

Analyses of the cell surface markers (CD2+ or T_{11} [T cells], CD3+ or T_3 [T cells], CD4+ or T_4 [helper T cells], CD8+ or T_8 [suppressor T cells], CD20+ [B cells], the CD4–CD8 or T_4-T_8 ratio) and the total lymphocyte count (TLC) showed no significant group differences. Smoking was significantly associated with increases in most cell counts, but not with the CD4-CD8 ratio and CD20+ cells, whereas increasing age was significantly associated with decreasing TLC and CD8+ cells.

Functional studies of T and B cells via reaction to antigenic (tetanus toxoid) or mitogen (phytohemagglutinin [PHA], concanavalin A, and pokeweed) stimulation showed no group differences. Similarly, unadjusted and adjusted mean values of the four assays were not significantly different between groups.

In summary, neither immunologic function nor cell marker studies showed significant impairment in the Ranch Hand group, nor did they show patterns supportive of an herbicide effect. Smoking was associated with a significant increase in the marker cells CD2+ (T cells), CD3+ (T cells), CD4+ (helper T cells), and CD8+ (suppressor T cells), and in the TLC, with a concomitant increase in lymphocytic response to pokeweed mitogen (PWM).

17.1.2.2 1985 Follow-up Summary Results

The 1985 AFHS physical examination placed more emphasis on the immunologic assessment than did the 1982 baseline examination profile. Immunologic competence was measured by cell surface marker (phenotypic) studies and cell stimulation studies on 47 percent of the study population, and by a series of four skin test antigens in 76 percent of the participants to assess the delayed hypersensitivity response.

Surface marker studies were conducted for CD2+ cells (T cells), CD4+ cells (T cells), CD8+ cells (suppressor T cells), CD20+ (B cells), CD14+ cells (monocytes), and HLA-DR cells. The ratio of CD4 to CD8 cells also was included in the analysis. Because of inherent significant day-to-day and batch-to-batch variation, all results (including functional stimulation studies) were adjusted for blood-draw day. Statistical testing of the seven phenotypic cell markers did not reveal any significant group differences, either unadjusted or adjusted, for the covariates of age, race, occupation, current smoking, lifetime smoking history, current alcohol use, or lifetime alcohol use. Similarly, none of the unadjusted or adjusted analyses of the functional stimulation studies (for PHA, PWM, or mixed lymphocyte culture [MLC]) showed any statistically significant group differences. Overall, no pattern was identified to suggest an adverse health effect in any subgroup of either the Ranch Hands or Comparisons.

The effects of age, race, smoking, and alcohol use affected most variables in the phenotypic and stimulation studies. Consistently decreasing values of all cell markers and stimulated cells were associated with increasing age, whereas increased levels of smoking usually were associated with increases in the values of those variables. Blacks had consistently higher stimulated cell counts than non-Blacks, but this effect was not observed for counts of T cells, B cells, or HLA-DR cells. Enlisted personnel generally had higher cell surface marker counts than officers.

The delayed hypersensitivity response was assessed by the skin test antigens of mumps, *Candida albicans*, Trichophyton, and staph-phage lysate. The 48-hour measurements of skin induration and erythema for the four tests showed marked inter-reader variation. Consequently, all skin test data were declared invalid and were not used in the assessment of group differences. The skin test reading problems led to the use of additional clinical quality control procedures for the 1987 follow-up examination.

In conclusion, no significant group differences were found for the comprehensive cell surface marker or functional stimulation studies. The effects of age, smoking, and alcohol use were observed in these immunologic tests.

17.1.2.3 1987 Follow-up Study Summary Results

For the assessment of the 1987 immunologic examination data, results from a composite skin reaction test were evaluated. Various laboratory examination measurements from cell surface marker studies, three groups of functional stimulation tests, and quantitative immunoglobulins also were analyzed. Ranch Hands had a higher frequency of individuals with possibly abnormal reactions on skin testing than Comparisons. The unadjusted analyses of the laboratory examination data indicated no significant group difference between Ranch Hands and Comparisons. For the adjusted analyses of the natural killer assay measurements with and without Interleukin 2 (IL-2), significant interactions between group and race were present. The clinical meaning of these findings was not apparent and did not point to any known clinical endpoints.

17.1.2.4 Serum Dioxin Analysis of 1987 Follow-up Study Summary Results

In general, the composite skin test diagnosis results were not associated with serum dioxin levels. The Ranch Hand analyses using initial dioxin and the analyses using current dioxin and time since duty in Southeast Asia (SEA) generally displayed nonsignificant decreased risks. For the analyses contrasting Ranch Hands with unknown, low, and high current dioxin to Comparisons with background current dioxin levels, the risks were increased but nonsignificant.

For the most part, the cell surface marker variables and TLC did not display significant associations with serum dioxin. The longitudinal analyses of the CD4-CD8 ratio did not consistently show significant differences in the 1987 ratio relative to the 1985 measurement of the ratio.

For the analyses of PHA net responses, significant or marginally significant positive associations with initial dioxin were found. For the analyses involving current dioxin and time since duty in SEA, the maximum PHA net response also displayed some significant or marginally significant positive associations. Depressed immune function would be expected to demonstrate lower PHA net response.

For unstimulated MLC and MLC net response, the three statistical analysis approaches generally displayed nonsignificant associations with serum dioxin. For the analysis involving Ranch Hands in the high current dioxin category and Comparisons in the background current dioxin category, Ranch Hands had a significantly higher unstimulated MLC mean. The analyses of the natural killer cell variables generally were nonsignificant.

Significant positive associations generally were found between IgA and initial dioxin. The analyses for IgA, IgG, and IgM using current dioxin and time since duty in SEA were, for the most part, nonsignificant. For the three immunoglobulins, the overall contrasts of Ranch Hands in the unknown, low, and high current dioxin categories versus Comparisons in the background current dioxin category generally were significant or marginally significant. For IgA and IgG, the contrasts of Ranch Hands in the unknown current dioxin category versus Comparisons in the background current dioxin category were significant with Ranch Hands having lower immunoglobulin averages. For IgM, the contrasts of Ranch Hands in the low current dioxin category versus Comparisons in the background current dioxin category were marginally significant with Ranch Hands again having lower averages. Ranch Hands in the high dioxin category were not significantly different from Comparisons.

The indices of immune responses analyzed in the 1987 examination provided a comprehensive reflection of in vivo and in vitro immune function in the study population. No clinically meaningful indicators reflecting a relation between the current body burden of dioxin or the extrapolated initial exposure and immune function were found. Increased IgA levels may have represented a chronic inflammatory response to dioxin exposure. Elevated erythrocyte sedimentation rates (as discussed in the general health assessment) and increased white blood cell and platelet counts (as discussed in the hematologic

assessment) were other examples of indicators that may have represented a chronic inflammatory response to dioxin exposure.

17.1.2.5 1992 Follow-up Study Summary Results

In general, the composite skin test diagnosis results did not differ significantly between Ranch Hands and Comparisons and were not positively associated with initial or current dioxin levels. For the most part, the cell surface marker variables and total lymphocyte count did not display significant associations with serum dioxin. The longitudinal analyses of the CD4-CD8 ratio did not consistently show significant differences between the 1992 ratio relative to the 1985 measurement of the ratio.

Marginally significant positive associations were found between IgA and initial dioxin. A negative association would be expected in immunologic deficiency, but the increased IgA levels could represent a chronic inflammatory response to dioxin exposure and thus suggested long-term evaluation.

The prevalence of some lupus panel antibodies, such as the MSK smooth muscle antibody and the rheumatoid factor, decreased as dioxin exposure increased. This finding was inconsistent with a harmful effect from dioxin. The presence of lupus panel antibodies generally was considered abnormal. A smaller prevalence of the lupus panel antibodies was found in this study than would be expected in the general population. The presence of a smaller prevalence of abnormalities than expected also may have been regarded as an abnormal finding, suggesting a possible early immune alteration.

17.1.3 Parameters for the 1997 Immunologic Assessment

17.1.3.1 Dependent Variables

Table 17-1 presents the immunologic parameters evaluated and describes their medical importance. The absolute lymphocyte and immunoglobulin studies and lupus panel tests were examined for all participants, whereas the cell surface marker studies were carried out on a random sample of approximately 40 percent of the participants because of the complexity of the assay and the expense of the tests.

Table 17-1. Medical Significance of the Immunologic Data

Immunologic Measure	Rationale of the Measurement	Disease/Syndrome/Condition Endpoint
Cell Surface Marker Studies		
CD3+	Pan-T cell marker (similar to CD2 in previous AFHS examinations). Measures all mature T cells (includes CD4, CD8, etc.). Generally 70% or more of peripheral blood lymphocytes are CD3 positive.	Decrease in absolute number of T cells indicates immunodeficiency. May occur because of direct effects of malignancy (e.g., lymphoma), acquired immune deficiency syndrome (AIDS), or chemotherapy. Increase may occur in lymphoproliferative disorders or in some infections.
CD4+	Measures T cells that exhibit helper/inducer phenotype. CD4 cells initiate an immune response to processed antigens.	Markedly decreased in people with AIDS because of human immunodeficiency virus (HIV) infection of CD4+ cells; increased in autoimmune diseases.
CD8+	Measures T cells that exhibit suppressor and cytotoxic functions. Responsible for appropriate down regulation of an immune response after antigen has been cleared.	Variable in autoimmune diseases; increased in some viral illnesses and immunodeficiencies.
CD20+ (B1)	Measures peripheral blood B cells; no reaction with T cells, granulocytes, or monocytes.	Decreased result in humoral immune deficiency with impaired production of antibodies; increased in lymphoproliferative disorders.
	Double Labeled Cells (cells that express both markers)	
CD3+CD4+	Helper T cells and excludes monocytes but more specific than CD4.	Same as CD4.
CD16+56+ (CD3-)	Normally these markers do not occur on the same cells. Measures natural killer (NK) cells that can lyse foreign cells independent of antibody or prior contact with the target. CD16 is an IgG receptor that appears on NK cells and neutrophils; CD56 is more restricted to NK cells; joint use of CD16 and CD56 enhances enumeration of NK cells.	NK cells are thought to attack neoplasms and naturally prevent growth of cancers.
Absolute Lymphocytes		
	Measures absolute number of total lymphocytes circulating in peripheral blood. Major immune mechanism against fungi and viruses.	Decreased in immunodeficiency; increased in lymphoproliferative disorders.

Table 17-1. Medical Significance of the Immunologic Data (Continued)

Immunologic Measure	Rationale of the Measurement	Disease/Syndrome/Condition Endpoint
Immunoglobulins		
IgG IgA IgM	Each measures ability of specific B cell subgroup to secrete specific antibody class of molecules. Antibodies normally rise in response to infections or immunizations with bacteria, fungi, and viruses. Major immune mechanism against bacteria.	Increased in hyperglobulinemia or myeloma (monoclonal). Decreased in selective or total B cell immunodeficiency. Polyclonal increases in chronic inflammation and liver disease (cirrhosis).
Lupus Panel		
	The test composition of this profile was chosen to include the most frequently encountered autoantibodies. Presence of autoantibodies may indicate specific autoimmune diseases, especially if multiple autoantibodies are present. The individually named autoantibodies (excluding ANA and B cell clones) are associated with specific diseases. Any of these tests may also turn positive as a participant's immune system ages or otherwise is dysregulated.	
Antinuclear Antibody (ANA) Test	Screening assay (performed with monolayers of HEP-2) for many clinically meaningful autoantibodies that occur in systemic rheumatologic diseases.	Positive result suggests possible rheumatologic disease; likelihood increases with number of different positive autoantibodies.
ANA Thyroid Microsomal Antibody	Measures autoantibodies against thyroid microsomal antigen.	Present in autoimmune thyroiditis.
MSK Smooth Muscle Antibody	MSK indicates the tissues used in the assay (mouse stomach kidney); measures autoantibodies against actin in smooth muscle.	Present in autoimmune liver diseases, especially chronic active hepatitis.
MSK Mitochondrial Antibody	Measures autoantibodies against mitochondrial antigens.	Present in autoimmune liver diseases, especially primary biliary cirrhosis.
MSK Parietal Antibody	Measures autoantibodies against parietal cells of the stomach that make intrinsic factor for the absorption of vitamin B_{12}.	Present in pernicious anemia (failure to absorb vitamin B_{12}).
Rheumatoid Factor	Autoantibodies reactive with a person's own antibodies.	Present in rheumatoid arthritis; also in some infections, chronic pulmonary diseases, and other inflammatory or autoimmune diseases.

17.1.3.1.1 Laboratory Examination Data

The results of cell surface marker studies, absolute lymphocytes, quantitative immunoglobulins, and a lupus panel were analyzed. Participants who were taking anti-inflammatory medication (except aspirin and nonsteroidal) or immunosuppressant medication at the time of the 1997 physical examination were excluded from analysis. Participants who had recently received x-ray treatment or chemotherapy for cancer and participants who tested positive for HIV also were excluded from analysis.

17.1.3.1.1.1 Cell Surface Marker (Phenotypic) Studies

Quantification of the different cell populations was carried out with the use of reagent mouse monoclonal antibodies. Cell surface markers were analyzed in the statistical evaluation of the immunologic system. The unit of measurement was cells/mm^3. The CD3+CD4+ (helper T cells) double labeled cell surface marker was introduced to the AFHS for the 1997 follow-up examination.

17.1.3.1.1.2 Absolute Lymphocytes

Absolute lymphocytes indicate the density of lymphocytes in the blood. Lymphocytes recognize and destroy bacteria, fungi, viruses, and other foreign bodies. Statistical analyses were performed on absolute lymphocytes, measured in cells/mm^3.

Absolute lymphocytes also were analyzed in Chapter 15, Hematology Assessment (Table 15-19). The analysis of absolute lymphocytes in the Hematology Assessment chapter included nonreactive lymphocytes, whereas the analysis in this chapter included nonreactive and reactive lymphocytes. In addition, the analysis in this chapter included age, race, military occupation, current cigarette smoking, lifetime cigarette smoking history, current alcohol use, lifetime alcohol history, and a physical activity index as covariates. The analysis in the Hematology Assessment chapter did not include current alcohol use, lifetime alcohol history, or the physical activity index. The exclusions for analysis in the Hematology Assessment included participants with body temperatures greater than or equal to 100° Fahrenheit and participants testing positive for HIV. The exclusions in this chapter included participants who were taking anti-inflammatory (except aspirin and nonsteroidal) or immunosuppressant medication at the time of the 1997 physical examination. Participants who had recently received x-ray treatment or chemotherapy for cancer and participants who tested positive for HIV also were excluded from analysis in this chapter.

17.1.3.1.1.3 Immunoglobulins

Immunoglobulins measure the ability of a specific B cell subgroup to secrete a specific antibody class of molecules. The antibodies usually rise in response to infections or immunizations with bacteria, fungi, and viruses. Statistical analyses were performed on the immunoglobulins IgA, IgG, and IgM, measured in mg/dl.

17.1.3.1.1.4 Lupus Panel

This group of laboratory tests was configured to detect the most frequent autoantibodies found in both patients and asymptomatic individuals. Autoantibodies are markers for autoimmune diseases, and the lupus panel is considered a screening assay for a wide spectrum of autoimmune disorders (e.g., rheumatoid arthritis, systemic lupus erythematosus). Occasionally, autoantibodies are detected in asymptomatic persons; this is alternatively explained as evidence for incipient autoimmune disease or a finding of unknown meaning. In any instance, the finding of an autoantibody is not normal and should be

interpreted as an aberration of the immune system. The lupus panel was composed of the following individual tests on serum:

- Antinuclear antibody (ANA) performed on HEP-2 cells
- Mouse stomach kidney (MSK) section stain for the following specific autoantibodies:
  - Smooth muscle
  - Mitochondrial
  - Parietal cell
- Thyroid microsomal antibody
- Rheumatoid factor.

All of the autoantibodies derive from abnormalities of the B cell portion, the part of the immune system that produces immunoglobulins.

Statistical analyses were performed on the ANA, ANA thyroid microsomal antibody, MSK smooth muscle antibody, MSK mitochondrial antibody, MSK parietal cell antibody, and rheumatoid factor, with the response to these tests scored as present or absent.

17.1.3.2 Covariates

Covariates to be used in the immunologic evaluation for adjusted statistical analyses included age, race, military occupation, current alcohol use (drinks/day), lifetime alcohol history (drink-years), current cigarette smoking (cigarettes/day), lifetime cigarette smoking history (pack-years), and exercise history (an index combining both duration and intensity).

Age, race, and military occupation were determined from military records. Lifetime alcohol history was based on information from the 1997 questionnaire and combined with similar information gathered at the 1987 and 1992 follow-up examinations. Each participant was asked about his drinking patterns throughout his lifetime. When a participant's drinking patterns changed, he was asked to describe how his alcohol consumption differed and the duration of time that the drinking pattern lasted. The participant's average daily alcohol consumption was determined for each of the reported drinking pattern periods throughout his lifetime, and an estimate of the corresponding total number of drink-years was derived. One drink-year was the equivalent of drinking 1.5 ounces of an 80-proof alcoholic beverage, one 12-ounce beer, or one 5-ounce glass of wine per day for 1 year. Current alcohol use was defined as the average number of drinks per day during the month prior to completing the questionnaire.

Current cigarette smoking and lifetime cigarette smoking history were based on questionnaire data. For lifetime cigarette smoking history, the respondent's average smoking was estimated over his lifetime based on his responses to the 1997 questionnaire, with 1 pack-year defined as 365 packs of cigarettes smoked during a single year.

A series of questions concerning exercise patterns in the 2 weeks prior to the physical examination were included as part of the 1997 questionnaire. The participants were asked questions on frequency, average duration per frequency, and increase of heart rate or breathing for more than 20 different activities. The answers to these questions were used and combined to determine an index of physical activity incorporating duration and intensity (88, 89), and this covariate was used in adjusted statistical analyses. A participant was classified as active, moderately active, or sedentary based on his responses to the series of questions regarding exercise patterns.

17.1.4 Statistical Methods

Chapter 7, Statistical Methods, describes the basic statistical methods to be used in the immunologic assessment. For the 1985, 1897, and 1992 follow-up studies, large variation was observed from examination group variability. Because of the variation, this covariate generally was incorporated into the unadjusted and the adjusted models of the respective immunologic assessments for the 1985, 1987, and 1992 studies. Plans had been made to use examination group as a covariate in the analysis of the 1997 immunologic data; however, examination group was not significantly associated with immunologic data in the 1997 follow-up study and, consequently, examination group was not used as a covariate in the analyses described in this chapter.

Table 17-2 summarizes the statistical analyses to be performed for the analysis of the immunologic assessment. The first part of this table lists the dependent variables to be analyzed. The second part of the table further describes the covariates to be examined. A covariate was used in its continuous form whenever possible for all adjusted analyses. If the covariate was inherently discrete (e.g., military occupation), or if a categorized form was needed to develop measures of association with the dependent variables, the covariate was categorized as shown in Table 17-2.

Table 17-2. Statistical Analysis for the Immunologic Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Normal Range/ Cutpoints[a]	Covariates[b]	Exclusions[c]	Statistical Analysis and Methods
CD3+ Cells (T Cells) (cells/mm^3)	LAB	C	700–2,400	(1)	(a)	U:GLM A:GLM
CD4+ Cells (Helper T Cells) (cells/mm^3)	LAB	C	400–1,400	(1)	(a)	U:GLM A:GLM
CD8+ Cells (Suppressor Cells) (cells/mm^3)	LAB	C	300–900	(1)	(a)	U:GLM A:GLM
CD16+56+ Cells (Natural Killer Cells) (cells/mm^3)	LAB	C	48–450	(1)	(a)	U:GLM A:GLM
CD20+ Cells (B Cells) (cells/mm^3)	LAB	C	--	(1)	(a)	U:GLM A:GLM
CD3+CD4+ Cells (Helper T Cells) (cells/mm^3)	LAB	C	400–1,400	(1)	(a)	U:GLM A:GLM
Absolute Lymphocytes (cells/mm^3)	LAB	C	1,000–4,800	(1)	(a)	U:GLM A:GLM
IgA (mg/dl)	LAB	C	69–382	(1)	(a)	U:GLM A:GLM
IgG (mg/dl)	LAB	C	723–1,685	(1)	(a)	U:GLM A:GLM
IgM (mg/dl)	LAB	C	63–277	(1)	(a)	U:GLM A:GLM
Lupus Panel: ANA Test	LAB	D	Present Absent	(1)	(a)	U:LR A:LR
Lupus Panel: ANA Thyroid Microsomal Antibody	LAB	D	Present Absent	(1)	(a)	U:LR A:LR

Table 17-2. Statistical Analysis for the Immunologic Assessment (Continued)

Variable (Units)	Data Source	Data Form	Normal Range/ Cutpoints[a]	Covariates[b]	Exclusions[c]	Statistical Analysis and Methods
Lupus Panel: MSK Smooth Muscle Antibody	LAB	D	Present Absent	(1)	(a)	U:LR A:LR
Lupus Panel: MSK Mitochondrial Antibody	LAB	D	Present Absent	(1)	(a)	U:LR,CS A:LR
Lupus Panel: MSK Parietal Antibody	LAB	D	Present Absent	(1)	(a)	U:LR A:LR
Lupus Panel: Rheumatoid Factor	LAB	D	Present Absent	(1)	(a)	U:LR A:LR

[a] Normal ranges are presented for cell surface markers, absolute lymphocytes, and immunoglobulins for reference purposes. Statistical analyses were done only on the continuous form of these dependent variables.

[b] Covariates:
(1): age, race, military occupation, current cigarette smoking, lifetime cigarette smoking history, current alcohol use, lifetime alcohol history, physical activity index.

[c] Exclusions:
(a): participants taking anti-inflammatory (except aspirin and nonsteroidal) or immunosuppression medications, participants testing positive for HIV, participants who recently received x-ray treatment or chemotherapy for cancer.

Covariates

Variable (Units)	Data Source	Data Form	Cutpoints
Age (years)	MIL	D/C	Born≥1942 Born<1942
Race	MIL	D	Black Non-Black
Occupation	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Current Cigarette Smoking (cigarettes/day)	Q-SR	D/C	0-Never 0-Former >0–20 >20
Lifetime Cigarette Smoking History (pack-years)	Q-SR	D/C	0 >0–10 >10
Current Alcohol Use (drinks/day)	Q-SR	D/C	0–1 >1–4 >4

Table 17-2. Statistical Analysis for the Immunologic Assessment (Continued)

Variable (Units)	Data Source	Data Form	Cutpoints
Lifetime Alcohol History (drink-years)	Q-SR	D/C	0 >0–40 >40
Physical Activity Index (kcal/kg/day)	Q-SR	D	Sedentary: <1.45 Moderate: 1.45–<2.95 Very Active: ≥2.95

Abbreviations

Data Source: LAB: 1997 laboratory results
MIL: Air Force military records
Q-SR: Health questionnaires (self-reported)

Data Form: D: Discrete analysis only
C: Continuous analysis only
D/C: Appropriate form for analysis (either discrete or continuous) for covariates

Statistical Analysis: U: Unadjusted analysis
A: Adjusted analysis

Statistical Methods: CS: Chi-square contingency table analysis (continuity-adjusted)
GLM: General linear models analysis
LR: Logistic regression analysis

Table 17-3 provides a summary of participants with missing dependent variable and covariate data. In addition, the number of participants excluded is given. Because approximately 40 percent of the participants were assayed for cell surface markers, Table 17-3 is divided into two parts: (1) a summary for cell surface markers and (2) a summary for absolute lymphocytes, immunoglobulins, and the lupus panel.

Table 17-3. Number of Participants Excluded or with Missing Data for the Immunologic Assessment

		Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
Variable	Variable Use	Ranch Hand	Comparison	Initial	1987	Ranch Hand	Comparison
Cell Surface Markers							
CD20+ Cells (B Cells)	DEP	1	0	1	1	1	0
Current Cigarette Smoking	COV	1	0	0	1	1	0
Lifetime Cigarette Smoking History	COV	2	1	1	2	2	1
Current Alcohol Use	COV	1	0	0	1	1	0
Lifetime Alcohol History	COV	2	0	1	2	2	0
Physical Activity Index	COV	3	3	1	3	3	3

Table 17-3. Number of Participants with Missing Data for the Immunologic Assessment (Continued)

Variable	Variable Use	Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
		Ranch Hand	Comparison	Initial	1987	Ranch Hand	Comparison
Taking Anti-Inflammatory or Immunosuppressant Medications	EXC	12	12	8	12	12	11
Recent X-ray Treatment or Chemotherapy for Cancer	EXC	10	8	9	10	10	7
HIV Positive	EXC	0	2	0	0	0	2
Absolute Lymphocytes, Immunoglobulins, and Lupus Panel							
Current Cigarette Smoking	COV	1	0	0	1	1	0
Lifetime Cigarette Smoking History	COV	2	1	1	2	2	1
Current Alcohol Use	COV	1	0	0	1	1	0
Lifetime Alcohol History	COV	6	2	3	6	6	1
Physical Activity Index	COV	6	8	2	6	6	8
Taking Anti-Inflammatory or Immunosuppressant Medications	EXC	23	34	14	23	23	32
Recent X-ray Treatment or Chemotherapy for Cancer	EXC	14	17	12	13	13	16
HIV Positive	EXC	3	2	3	3	3	2

Note: DEP = Dependent variable.
COV = Covariate.
EXC = Exclusion.

Cell Surface Markers:
341 Ranch Hands and 477 Comparisons.
192 Ranch Hands for initial dioxin; 339 Ranch Hands for 1987 dioxin.
339 Ranch Hands and 460 Comparisons for categorized dioxin.

Absolute Lymphocytes, Immunoglobulins, and Lupus Panel:
870 Ranch Hands and 1,251 Comparisons.
482 Ranch Hands for initial dioxin; 863 Ranch Hands for 1987 dioxin.
863 Ranch Hands and 1,213 Comparisons for categorized dioxin.

17.2 RESULTS

17.2.1 Dependent Variable-Covariate Associations

Tests of association between the immunologic dependent variables and each of the covariates given in Table 17-2 were conducted. The results are presented in Appendix Table F-9. These associations are pairwise between the dependent variable and the covariate and are not adjusted for any other covariates. Participants taking anti-inflammatory medications, taking immunosuppression medication, testing

positive for HIV, or who have recently received x-ray treatment or chemotherapy for cancer were excluded from all analyses.

The analysis of CD3+ cells (T cells) revealed a significant association with age ($p=0.006$), indicating a decrease in the CD3+ cell count as age increased. A marginally significant association was found between race and CD3+ cell count ($p=0.095$). Blacks displayed a higher mean CD3+ cell count (mean=1,363.1 cells/mm^3) than non-Blacks (mean=1,239.6 cells/mm^3). Analyses also revealed significant associations between CD3+ cell count and current cigarette smoking ($p<0.001$) and between CD3+ cell count and the physical activity index ($p<0.001$). CD3+ cell count increased as the number of cigarettes per day increased and as the activity level decreased.

Tests of association for CD4+ cell (helper T cell) count were significant for age ($p<0.001$), race ($p=0.023$), current cigarette smoking ($p<0.001$), and the physical activity index ($p=0.001$). A marginally significant association was found with lifetime cigarette smoking history ($p=0.053$). The CD4+ cell count decreased with age, and the CD4+ cell count mean was higher for Blacks (mean=958.7 cells/mm^3) than for non-Blacks (mean=844.4 cells/mm^3). As the number of cigarettes per day increased, the CD4+ cell count increased. Participants with the lowest activity level displayed the highest average CD4+ cell counts (mean=889.2 cells/mm^3); the cell count increased as the number of cigarette pack-years increased.

Significant associations with the CD8+ cell (suppressor T cell) count were found for the current cigarette smoking ($p<0.001$) and the physical activity index covariates ($p=0.005$). The CD8+ cell count increased as the number of cigarettes smoked per day increased. The mean CD8+ cell count was highest among those participants classified as sedentary (mean=608.3 cells/mm^3). Participants classified as active displayed the next highest CD8+ cell count mean (mean=548.3 cells/mm^3), followed by those with a moderately active index (mean=539.1 cells/mm^3).

Covariate association tests conducted for the CD16+56+ cell (natural killer cell) count analysis resulted in significant findings for age ($p=0.005$) and current cigarette smoking ($p<0.001$). The CD16+56+ cell count increased as age increased and as the number of cigarettes smoked per day decreased.

Significant covariate associations with the CD20+ cell (B cell) count were found for age ($p<0.001$), race ($p=0.007$), occupation ($p=0.002$), current cigarette smoking ($p<0.001$), current alcohol use ($p=0.007$), and the physical activity index ($p=0.017$). The CD20+ cell count decreased with age, and the CD20+ cell count mean was higher for Blacks (mean=232.9 cells/mm^3) than for non-Blacks (mean=182.2 cells/mm^3). Enlisted groundcrew showed the highest average CD20+ cell count (mean=200.9 cells/mm^3), followed by enlisted flyers (mean=178.8 cells/mm^3) and officers (mean=170.8 cells/mm^3). The CD20+ cell count increased as the number of cigarettes smoked per day increased and as the number of drinks per day decreased. The CD20+ cell count increased as the physical activity level decreased.

Tests of covariate associations with the CD3+CD4+ cell (helper T cell) count were significant for age ($p<0.001$), current cigarette smoking ($p<0.001$), lifetime cigarette smoking history ($p=0.032$), and the physical activity index ($p=0.001$), and marginally significant for race ($p=0.061$). The CD3+CD4+ cell count decreased with age. The mean CD3+CD4+ cell count was higher for Blacks (mean=860.6 cells/mm^3) than for non-Blacks (mean=770.2 cells/mm^3). The CD3+CD4+ cell count increased as current and lifetime cigarette smoking increased. Participants in the sedentary category of the physical activity index showed the highest CD3+CD4+ cell count (mean=814.3 cells/mm^3).

Association tests for absolute lymphocytes revealed significant findings for age ($p<0.001$), occupation ($p<0.001$), current cigarette smoking ($p<0.001$), lifetime cigarette smoking history ($p<0.001$), and the physical activity index ($p<0.001$). The association between absolute lymphocytes and race was

marginally significant (p=0.070). Absolute lymphocytes decreased with age and increased as cigarette smoking increased. Enlisted groundcrew had the highest average absolute lymphocyte count (mean=1,845.8 cells/mm^3), followed by enlisted flyers (mean=1,788.5 cells/mm^3), then officers (mean=1,703.3 cells/mm^3). Blacks displayed a higher mean absolute lymphocyte count (mean=1,879.4 cells/mm^3) than did non-Blacks (mean=1,772.9 cells/mm^3). The least active participants displayed the highest average absolute lymphocyte count (mean=1,831.0 cells/mm^3), compared to those who were moderately active (mean=1,722.7 cells/mm^3) and active (mean=1,719.7 cells/mm^3).

The covariate association analysis for IgA displayed significant findings for age (p=0.012), occupation (p=0.030), and current alcohol use (p=0.032). Marginally significant findings resulted for lifetime alcohol use (p=0.086) and the physical activity index (p=0.088). IgA levels increased with age, current alcohol use, and lifetime alcohol use. Average IgA levels were highest among enlisted groundcrew (mean=238.7 mg/dl), followed by enlisted flyers (mean=237.3 mg/dl), then officers (mean=225.0 mg/dl). Participants with the lowest activity levels displayed the highest mean IgA levels.

Analysis of IgG revealed significant associations with race (p<0.001), occupation (p=0.019), current cigarette smoking (p<0.001), lifetime cigarette smoking (p<0.001), current alcohol use (p<0.001), and lifetime alcohol history (p=0.007). Blacks exhibited a higher average IgG level (mean=1,266.8 mg/dl) than non-Blacks (mean=1,029.2 mg/dl). Enlisted groundcrew exhibited the highest average IgG level (mean=1,058.6 mg/dl) among the occupational strata, followed by enlisted flyers (mean=1,036.8 mg/dl), then officers (mean=1,026.7 mg/dl). IgA levels decreased as current and lifetime cigarette smoking increased and as current and lifetime alcohol use increased.

The covariate analysis of IgM levels revealed significant associations with age (p=0.005), race (p=0.004), and current alcohol use (p=0.010). IgM levels decreased as age increased. Non-Blacks displayed higher average levels of IgM (mean=98.4 mg/dl) as compared to Blacks (mean=85.4 mg/dl). IgM levels increased as the current alcohol use increased.

Tests of association between covariates and ANA revealed a marginally significant relation with age (p=0.098) and significant relations with current cigarette smoking (p=0.001) and lifetime cigarette smoking history (p=0.033). The presence of the ANA was higher among older participants (53.7%) than among younger participants (49.9%). Cigarette smokers who smoke at most 20 cigarettes per day and those with more than 10 pack-years exhibited the greatest percentages of the ANA present (63.2% and 55.1%, respectively).

A marginally significant association between thyroid microsomal antibody and the physical activity index was observed (p=0.061). The highest percentage of participants with the thyroid microsomal antibody present was found in the moderately active category (4.3%), followed by those classified as sedentary (2.9%), then those classified as active (1.7%).

Significant covariate associations for the MSK smooth muscle antibody test included race (p=0.018) and current cigarette smoking (p=0.037). A marginally significant association with the physical activity index was observed (p=0.085). Blacks exhibited a higher presence of the MSK smooth muscle antibody than non-Blacks (19.2% vs. 11.7%, respectively). Cigarette smokers who smoked at most 20 cigarettes per day displayed the highest presence of the smooth muscle antibody (17.2%). Participants categorized as moderately active exhibited the highest presence of the smooth muscle antibody (13.5%), followed by those who were classified as sedentary (12.9%), then those who were active (9.5%).

Tests of covariate association for the MSK mitochondrial antibody revealed a marginally significant association with occupation (p=0.060). Officers had the highest prevalence of the antibody (0.6%), followed by enlisted flyers (0.3%), then enlisted groundcrew (0.0%).

The MSK parietal antibody test displayed a significant covariate association with race (p=0.001). For Blacks, 10.4 percent exhibited the presence of the antibody, as compared to 3.9 percent of non-Blacks.

Association tests for the rheumatoid factor showed age to be marginally significant (p=0.064) and occupation and lifetime cigarette smoking history to be significant (p=0.038 and p=0.006, respectively). The presence of the rheumatoid factor was higher among the older participants (12.2%), compared to a prevalence of 9.5 percent for the younger participants. Enlisted flyers displayed the highest prevalence of a positive rheumatoid factor (13.1%), followed by officers (12.3%), then enlisted groundcrew (9.0%). The heaviest lifetime smokers (in terms of pack-years) showed the highest presence of the rheumatoid factor (12.8%), followed by nonsmokers (11.6%), then moderate lifetime smokers (7.4%).

17.2.2 Exposure Analysis

The following section presents results of the statistical analyses of the dependent variables shown in Table 17-2. Dependent variables were derived from the results of the laboratory portion of the 1997 follow-up examination.

Four models were examined for each dependent variable given in Table 17-2. The analyses of these models are presented below. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7, respectively. These analyses were performed both unadjusted and adjusted for relevant covariates. Model 1 examined the relation between the dependent variable and group (i.e., Ranch Hand or Comparison). In this model, exposure was defined as "yes" for Ranch Hands and "no" for Comparisons without regard to the magnitude of the exposure. As an attempt to quantify exposure, three contrasts of Ranch Hands and Comparisons were performed along with the overall Ranch Hand versus Comparison contrast. These three contrasts compared Ranch Hands and Comparisons within each occupational category (i.e., officers, enlisted flyers, and enlisted groundcrew). As described in previous reports and Table 2-8, the average levels of exposure to dioxin were highest for enlisted groundcrew, followed by enlisted flyers, then officers.

Model 2 explored the relation between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt. If a participant did not have a 1987 dioxin level, the 1992 level was used to estimate the initial dioxin level. If a participant did not have a 1987 or a 1992 dioxin level, the 1997 level was used to estimate the initial dioxin level. A statistical adjustment for the percentage of body fat at the time of the participant's blood measurement of dioxin was included in this model to account for body-fat-related differences in elimination rate (90).

Model 3 divided the Ranch Hands examined in Model 2 into two categories based on their initial dioxin measures. These two categories are referred to as "low Ranch Hand" and "high Ranch Hand." Two additional categories, Ranch Hands with 1987 serum dioxin levels at or below 10 ppt and Comparisons with 1987 serum dioxin levels at or below 10 ppt, were formed and included in the model. Ranch Hands with 1987 serum dioxin levels at or below 10 ppt are referred to as the "background Ranch Hand" category. Dioxin levels in 1992 were used if the 1987 level was not available and dioxin levels in 1997 were used if the 1987 and 1992 levels were not available. These four categories—Comparison, background Ranch Hands, low Ranch Hands, and high Ranch Hands—were used in Model 3 analyses. The relation between the dependent variable in each of the three Ranch Hand categories and the dependent variable in the Comparison category was examined. A fourth contrast, exploring the relation

of the dependent variable in the combined low and high Ranch Hand categories relative to Comparisons, also was conducted. This combination is referred to in the tables as the "low plus high Ranch Hand" category. As in Model 2, a statistical adjustment for the percentage of body fat at the time of the participant's blood measurement of dioxin was included in this model.

Model 4 examined the relation between the dependent variable and 1987 lipid-adjusted dioxin levels in all Ranch Hands with a dioxin measurement. If a participant did not have a 1987 dioxin measurement, the 1992 measurement was used to determine the dioxin level. If a participant did not have a 1987 or a 1992 dioxin measurement, the 1997 measurement was used to determine the dioxin level.

17.2.2.1 Laboratory Variables

17.2.2.1.1 CD3+ Cells (T Cells)

The Model 1 adjusted analysis of CD3+ cells revealed a marginally significant difference in means between Ranch Hands and Comparisons within the enlisted groundcrew stratum (Table 17-4(b): p=0.073, difference of adjusted means=–91.7 cells/mm^3). The mean CD3+ cell count was higher for Comparisons than for Ranch Hands. All other Model 1 contrasts, as well as the Model 2 and Model 3 analyses, were nonsignificant (Table 17-4(a–f): p>0.11 for all analyses).

Results from the Model 4 unadjusted analysis of CD3+ cells were nonsignificant (Table 17-4(g): p=0.316). After adjustment for covariates, a significant and positive association between the 1987 dioxin levels and CD3+ cell count was observed (Table 17-4(h): p=0.046, adjusted slope=0.035). CD3+ cell counts increased as 1987 dioxin levels increased.

Table 17-4. Analysis of CD3+ Cells (T Cells) (cells/mm^3)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***319***	***1,231.0***	***–26.7 --***	***0.431***
	Comparison	***455***	***1,257.7***		
Officer	Ranch Hand	135	1,230.0	39.8 --	0.449
	Comparison	164	1,190.2		
Enlisted Flyer	Ranch Hand	56	1,197.2	–89.6 --	0.270
	Comparison	78	1,286.8		
Enlisted Groundcrew	Ranch Hand	128	1,247.1	–54.2 --	0.308
	Comparison	213	1,301.3		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 17-4. Analysis of CD3+ Cells (T Cells) (cells/mm^3) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	*Ranch Hand*	*316*	*1,245.2*	*–38.5 --*	*0.255*
	Comparison	*451*	*1,283.7*		
Officer	Ranch Hand	134	1,313.3	46.8 --	0.392
	Comparison	162	1,266.5		
Enlisted Flyer	Ranch Hand	56	1,201.6	–96.8 --	0.224
	Comparison	77	1,298.4		
Enlisted Groundcrew	Ranch Hand	126	1,205.6	–91.7 --	0.073
	Comparison	212	1,297.3		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[a,b]	R^2	Slope (Std. Error)[c]	p-Value
Low	52	1,163.0	1,166.8	0.013	0.023 (0.023)	0.317
Medium	61	1,288.6	1,285.9			
High	62	1,263.7	1,262.9			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of CD3+ cells versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	52	1,237.6	0.132	0.042 (0.027)	0.113
Medium	60	1,358.6			
High	62	1,388.6			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD3+ cells versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 17-4. Analysis of CD3+ Cells (T Cells) (cells/mm^3) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	440	1,252.8	1,252.1		
Background RH	142	1,210.4	1,220.8	–31.3 --	0.490
Low RH	84	1,230.2	1,225.9	–26.2 --	0.636
High RH	91	1,251.6	1,242.7	–9.4 --	0.862
Low plus High RH	175	1,241.3	1,234.6	–17.5 --	0.676

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	436	1,284.8		
Background RH	140	1,237.1	–47.7 --	0.308
Low RH	83	1,272.3	–12.5 --	0.823
High RH	91	1,239.3	–45.5 --	0.403
Low plus High RH	174	1,254.9	–29.9 --	0.474

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 17-4. Analysis of CD3+ Cells (T Cells) (cells/mm³) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	110	1,196.2	0.003	0.015 (0.015)	0.316
Medium	100	1,216.1			
High	107	1,271.3			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD3+ cells versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	108	1,149.8	0.088	0.035 (0.018)	0.046
Medium	100	1,220.5			
High	106	1,286.6			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD3+ cells versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

17.2.2.1.2 CD4+ Cells (Helper T Cells)

The unadjusted and adjusted analyses of CD4+ cells in Models 1, 2, and 3, as well as the unadjusted analysis in Model 4, were nonsignificant (Table 17-5(a–g): $p>0.11$ for all analyses). The adjusted analysis of Model 4 revealed a significant and positive association between the 1987 dioxin levels and the CD4+ cell count (Table 17-5(h): $p=0.033$, adjusted slope=0.038). CD4+ cell counts increased as 1987 dioxin increased.

Table 17-5. Analysis of CD4+ Cells (Helper T Cells) (cells/mm^3)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***319***	***842.0***	***–15.0 --***	***0.511***
	Comparison	***455***	***857.0***		
Officer	Ranch Hand	135	838.0	13.3 --	0.708
	Comparison	164	824.7		
Enlisted Flyer	Ranch Hand	56	808.4	–61.8 --	0.254
	Comparison	78	870.2		
Enlisted Groundcrew	Ranch Hand	128	861.4	–16.5 --	0.646
	Comparison	213	877.9		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***316***	***871.6***	***–22.4 --***	***0.333***
	Comparison	***451***	***894.0***		
Officer	Ranch Hand	134	926.9	20.0 --	0.601
	Comparison	162	906.9		
Enlisted Flyer	Ranch Hand	56	835.6	–61.0 --	0.261
	Comparison	77	896.5		
Enlisted Groundcrew	Ranch Hand	126	842.4	–44.0 --	0.205
	Comparison	212	886.4		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	52	804.2	807.5	0.018	0.027 (0.023)	0.254
Medium	61	883.0	880.6			
High	62	869.6	868.8			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of CD4+ cells versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 17-5. Analysis of CD4+ Cells (Helper T Cells) (cells/mm^3) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	52	885.8	0.152	0.041 (0.026)	0.119
Medium	60	961.1			
High	62	967.0			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD4+ cells versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	440	855.4	854.9		
Background RH	142	823.0	830.4	–24.5 --	0.421
Low RH	84	838.7	835.6	–19.3 --	0.605
High RH	91	868.7	862.2	7.3 --	0.842
Low plus High RH	175	854.2	849.3	–5.6 --	0.844

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	436	897.9		
Background RH	140	854.8	–43.1 --	0.176
Low RH	83	893.6	–4.3 --	0.911
High RH	91	886.1	–11.8 --	0.752
Low plus High RH	174	889.7	–8.2 --	0.774

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 17-5. Analysis of CD4+ Cells (Helper T Cells) (cells/mm^3) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	110	813.6	0.004	0.017 (0.015)	0.255
Medium	100	825.4			
High	107	882.5			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD4+ cells versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	108	821.6	0.091	0.038 (0.018)	0.033
Medium	100	865.5			
High	106	944.0			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD4+ cells versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

17.2.2.1.3 CD8+ Cells (Suppressor T Cells)

All results from the analyses of CD8+ cells in Models 1 through 4 were nonsignificant (Table 17-6(a–h): p>0.11 for all analyses).

Table 17-6. Analysis of CD8+ Cells (Suppressor T Cells) (cells/mm^3)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.L)[b]	p-Value[c]
All	***Ranch Hand***	***319***	***564.5***	***–22.6 --***	***0.254***
	Comparison	***455***	***587.1***		
Officer	Ranch Hand	135	558.7	7.0 --	0.818
	Comparison	164	551.7		
Enlisted Flyer	Ranch Hand	56	563.9	–61.7 --	0.207
	Comparison	78	625.6		
Enlisted Groundcrew	Ranch Hand	128	571.0	–30.7 --	0.319
	Comparison	213	601.7		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 17-6. Analysis of CD8+ Cells (Suppressor T Cells) (cells/mm^3) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***316***	***565.6***	***–27.4 --***	***0.169***
	Comparison	***451***	***593.0***		
Officer	Ranch Hand	134	565.9	7.3 --	0.812
	Comparison	162	558.6		
Enlisted Flyer	Ranch Hand	56	551.8	–72.5 --	0.132
	Comparison	77	624.3		
Enlisted Groundcrew	Ranch Hand	126	564.7	–42.2 --	0.170
	Comparison	212	606.9		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	52	531.7	531.9	0.001	0.012 (0.029)	0.688
Medium	61	584.9	584.7			
High	62	568.7	568.7			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of CD8+ cells versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	52	546.2	0.039	0.023 (0.034)	0.505
Medium	60	608.0			
High	62	609.7			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD8+ cells versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 17-6. Analysis of CD8+ Cells (Suppressor T Cells) (cells/mm^3) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	440	584.2	584.1		
Background RH	142	563.2	565.3	–18.8 --	0.479
Low RH	84	572.7	571.8	–12.3 --	0.706
High RH	91	554.1	552.4	–31.7 --	0.307
Low plus High RH	175	562.9	561.6	–22.5 --	0.355

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	436	592.0		
Background RH	140	576.2	–15.8 --	0.574
Low RH	83	576.2	–15.8 --	0.634
High RH	91	541.9	–50.1 --	0.112
Low plus High RH	174	558.0	–34.0 --	0.164

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 17-6. Analysis of CD8+ Cells (Suppressor T Cells) (cells/mm^3) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	110	550.0	0.001	0.009 (0.019)	0.640
Medium	100	571.5			
High	107	569.0			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD8+ cells versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	108	519.5	0.049	0.014 (0.022)	0.540
Medium	100	553.2			
High	106	539.0			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD8+ cells versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

17.2.2.1.4 CD16+56+ Cells (Natural Killer Cells)

The Model 1 unadjusted analysis of CD16+56+ cell count revealed a marginally significant difference between Ranch Hands and Comparisons when examined across all occupational strata (Table 17-7(a): p=0.082, difference of means=–16.6 cells/mm^3). In addition, a significant difference among Ranch Hands and Comparisons was found within the enlisted flyer stratum for both the unadjusted and adjusted analyses (Table 17-7(a,b): p=0.018, difference of means=–53.5 cells/mm^3; p=0.011, difference of adjusted means=–58.7 cells/mm^3). Each analysis displayed a higher CD16+56+ cell count mean for Comparisons. All other Model 1 contrasts and both the unadjusted and adjusted analyses from Model 2 were nonsignificant (Table 17-7(a–d): p>0.10 for all analyses).

Table 17-7. Analysis of CD16+56+ Cells (Natural Killer Cells) (cells/mm^3)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***319***	***259.3***	***–16.6 --***	***0.082***
	Comparison	***455***	***275.9***		
Officer	Ranch Hand	135	266.2	–9.9 --	0.521
	Comparison	164	276.1		
Enlisted Flyer	Ranch Hand	56	236.7	–53.5 --	0.018
	Comparison	78	290.2		
Enlisted Groundcrew	Ranch Hand	128	262.4	–8.2 --	0.572
	Comparison	213	270.6		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***316***	***265.8***	***–15.8 --***	***0.106***
	Comparison	***451***	***281.6***		
Officer	Ranch Hand	134	261.0	–10.7 --	0.478
	Comparison	162	271.7		
Enlisted Flyer	Ranch Hand	56	241.8	–58.7 --	0.011
	Comparison	77	300.4		
Enlisted Groundcrew	Ranch Hand	126	280.8	–2.5 --	0.869
	Comparison	212	283.3		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[a,b]	R^2	Slope (Std. Error)[c]	p-Value
Low	52	273.6	276.7	0.038	–0.029 (0.032)	0.370
Medium	61	265.1	263.2			
High	62	254.8	254.2			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of CD16+56+ cells versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 17-7. Analysis of CD16+56+ Cells (Natural Killer Cells) (cells/mm^3) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	52	265.4	0.112	–0.030 (0.038)	0.429
Medium	60	268.8			
High	62	246.9			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD16+56+ cells versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	440	275.8	275.4		
Background RH	142	254.1	258.9	–16.5 --	0.192
Low RH	84	283.3	281.1	5.7 --	0.726
High RH	91	247.1	243.3	–32.1 --	0.028
Low plus High RH	175	263.9	260.7	–14.7 --	0.209

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	436	282.6		
Background RH	140	268.0	–14.6 --	0.285
Low RH	83	286.7	4.1 --	0.805
High RH	91	252.0	–30.6 --	0.046
Low plus High RH	174	268.0	–14.6 --	0.227

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 17-7. Analysis of CD16+56+ Cells (Natural Killer Cells) (cells/mm^3) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	110	258.5	<0.001	0.006 (0.021)	0.772
Medium	100	263.0			
High	107	257.1			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD16+56+ cells versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	108	265.6	0.059	–0.001 (0.025)	0.960
Medium	100	263.8			
High	106	258.6			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD16+56+ cells versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

The results from the Model 3 analysis of CD16+56+ cell count revealed similar results in the unadjusted and adjusted analyses. Comparisons were found to have a significantly higher mean CD16+56+ cell count than Ranch Hands in the high dioxin category in both the unadjusted and adjusted analyses (Table 17-7(e,f): p=0.028, difference of adjusted means=–32.1 cells/mm^3; p=0.046, difference of adjusted means=–30.6 cells/mm^3, respectively). All other Model 3 contrasts, as well as each analysis for Model 4, were nonsignificant (Table 17-7(e–h): p>0.19 for all analyses).

17.2.2.1.5 CD20+ Cells (B Cells)

All results from the analysis of CD20+ cell count were nonsignificant for Models 1, 3, and 4 (Table 17-8(a,b,e–h): p>0.14 for each analysis). The Model 2 unadjusted analysis revealed a significant and positive association between initial dioxin and CD20+ cell count (Table 17-8(c): p=0.024, slope=0.081). The Model 2 results became marginally significant after adjustment for covariates (Table 17-8(d): p=0.052, adjusted slope=0.075).

Table 17-8. Analysis of CD20+ Cells (B Cells) (cells/mm^3)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***318***	***184.0***	***–1.5 --***	***0.858***
	Comparison	***455***	***185.5***		
Officer	Ranch Hand	134	175.3	8.1 --	0.496
	Comparison	164	167.1		
Enlisted Flyer	Ranch Hand	56	170.2	–15.0 --	0.420
	Comparison	78	185.2		
Enlisted Groundcrew	Ranch Hand	128	200.4	–0.7 --	0.961
	Comparison	213	201.1		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***315***	***196.2***	***–2.0 --***	***0.808***
	Comparison	***451***	***198.2***		
Officer	Ranch Hand	133	211.3	13.1 --	0.343
	Comparison	162	198.2		
Enlisted Flyer	Ranch Hand	56	185.0	–14.7 --	0.450
	Comparison	77	199.7		
Enlisted Groundcrew	Ranch Hand	126	189.2	–10.1 --	0.422
	Comparison	212	199.3		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	51	153.6	154.9	0.052	0.081 (0.035)	0.024
Medium	61	198.4	197.3			
High	62	191.7	191.4			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of CD20+ cells versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 17-8. Analysis of CD20+ Cells (B Cells) (cells/mm^3) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	51	203.2	0.236	0.075 (0.038)	0.052
Medium	60	247.8			
High	62	238.9			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD20+ cells versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	440	185.0	185.0		
Background RH	142	182.9	183.9	–1.1 --	0.918
Low RH	83	167.1	166.7	–18.3 --	0.141
High RH	91	196.4	195.5	10.5 --	0.419
Low plus High RH	174	181.8	181.1	–3.9 --	0.694

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	436	198.1		
Background RH	140	200.6	2.5 --	0.827
Low RH	82	185.2	–12.9 --	0.325
High RH	91	194.6	–3.5 --	0.788
Low plus High RH	173	190.1	–8.0 --	0.419

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 17-8. Analysis of CD20+ Cells (B Cells) (cells/mm^3) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	110	179.1	0.004	0.026 (0.023)	0.260
Medium	99	170.0			
High	107	197.9			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD20+ cells versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	108	199.9	0.105	0.030 (0.026)	0.253
Medium	99	194.4			
High	106	214.6			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD20+ cells versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

17.2.2.1.6 CD3+CD4+ Cells (Helper T Cells)

All contrasts examined within the CD3+CD4+ cell count analysis of Models 1 and 3 were nonsignificant (Table 17-9(a,b and e,f): p>0.15 for all contrasts). The Model 2 unadjusted analysis of CD3+CD4+ cell count was also nonsignificant (Table 17-9(c): p=0.226), although the adjusted analysis revealed a marginally significant and positive association between initial dioxin and the CD3+CD4+ cell count (Table 17-9(d): p=0.098, adjusted slope=0.046). The Model 4 analysis of CD3+CD4+ cell count was also nonsignificant in the unadjusted analysis (Table 17-9(g): p=0.228) and significant in the adjusted analysis, with a positive association between the 1987 dioxin levels and the CD3+CD4+ cell count (Table 17-9(h): p=0.025, adjusted slope=0.042).

Table 17-9. Analysis of CD3+CD4+ Cells (Helper T Cells) (cells/mm^3)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***319***	***767.4***	***–13.4 --***	***0.541***
	Comparison	***455***	***780.9***		
Officer	Ranch Hand	135	763.1	13.5 --	0.693
	Comparison	164	749.6		
Enlisted Flyer	Ranch Hand	56	737.4	–54.5 --	0.296
	Comparison	78	791.9		
Enlisted Groundcrew	Ranch Hand	128	785.6	–16.1 --	0.641
	Comparison	213	801.8		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***316***	***786.5***	***–20.7 --***	***0.347***
	Comparison	***451***	***807.2***		
Officer	Ranch Hand	134	839.6	19.6 --	0.589
	Comparison	162	820.0		
Enlisted Flyer	Ranch Hand	56	753.7	–53.8 --	0.296
	Comparison	77	807.5		
Enlisted Groundcrew	Ranch Hand	126	758.1	–42.5 --	0.196
	Comparison	212	800.7		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	52	730.7	733.6	0.018	0.030 (0.024)	0.226
Medium	61	807.5	805.4			
High	62	798.1	797.5			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of CD3+CD4+ cells versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 17-9. Analysis of CD3+CD4+ Cells (Helper T Cells) (cells/mm^3) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	52	790.9	0.159	0.046 (0.028)	0.098
Medium	60	861.0			
High	62	874.2			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD3+CD4+ cells versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	440	779.1	778.6		
Background RH	142	747.7	753.7	–24.9 --	0.395
Low RH	84	764.0	761.5	–17.1 --	0.632
High RH	91	796.2	790.8	12.2 --	0.731
Low plus High RH	175	780.6	776.6	–2.0 --	0.940

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	436	809.9		
Background RH	140	766.6	–43.3 --	0.151
Low RH	83	806.9	–3.0 --	0.935
High RH	91	803.8	–6.1 --	0.865
Low plus High RH	174	805.3	–4.6 --	0.866

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 17-9. Analysis of CD3+CD4+ Cells (Helper T Cells) (cells/mm^3) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	110	738.7	0.005	0.019 (0.016)	0.228
Medium	100	750.2			
High	107	809.7			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD3+CD4+ cells versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	108	731.1	0.097	0.042 (0.019)	0.025
Medium	100	775.5			
High	106	854.8			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of CD3+CD4+ cells versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

17.2.2.1.7 Absolute Lymphocytes

All analysis results from Models 1 through 4 for absolute lymphocytes were nonsignificant (Table 17-10(a–h): p>0.10).

Table 17-10. Analysis of Absolute Lymphocytes (cells/mm^3)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***830***	***1,781.2***	***3.2 --***	***0.909***
	Comparison	***1,199***	***1,777.9***		
Officer	Ranch Hand	327	1,730.0	44.8 --	0.292
	Comparison	475	1,685.2		
Enlisted Flyer	Ranch Hand	142	1,753.3	–63.8 --	0.360
	Comparison	178	1,817.2		
Enlisted Groundcrew	Ranch Hand	361	1,840.2	–9.5 --	0.828
	Comparison	546	1,849.6		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 17-10. Analysis of Absolute Lymphocytes (cells/mm^3) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	*Ranch Hand*	*820*	*1,787.3*	*–6.1 --*	*0.827*
	Comparison	*1,188*	*1,793.3*		
Officer	Ranch Hand	324	1,805.1	52.9 --	0.227
	Comparison	470	1,752.2		
Enlisted Flyer	Ranch Hand	140	1,740.1	–74.3 --	0.279
	Comparison	176	1,814.4		
Enlisted Groundcrew	Ranch Hand	356	1,795.4	–34.6 --	0.412
	Comparison	542	1,830.0		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	148	1,731.1	1,737.8	0.019	0.019 (0.012)	0.121
Medium	152	1,777.4	1,777.7			
High	153	1,838.8	1,831.7			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of absolute lymphocytes versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	148	1,742.9	0.066	0.023 (0.014)	0.109
Medium	150	1,781.8			
High	151	1,837.5			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute lymphocytes versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 17-10. Analysis of Absolute Lymphocytes (cells/mm^3) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.L)[c]	p-Value[d]
Comparison	1,164	1,776.6	1,775.7		
Background RH	371	1,772.5	1,786.3	10.6 --	0.777
Low RH	222	1,757.0	1,752.0	–23.7 --	0.598
High RH	231	1,807.3	1,794.5	18.8 --	0.676
Low plus High RH	453	1,782.5	1,773.5	–2.2 --	0.959

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,154	1,794.7		
Background RH	365	1,821.6	26.9 --	0.477
Low RH	220	1,768.7	–26.0 --	0.562
High RH	229	1,755.8	–38.9 --	0.389
Low plus High RH	449	1,762.1	–32.6 --	0.340

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	281	1,730.6	0.002	0.010 (0.008)	0.222
Medium	271	1,788.5			
High	272	1,817.6			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute lymphocytes versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 17-10. Analysis of Absolute Lymphocytes (cells/mm³) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	277	1,723.8	0.046	0.008 (0.009)	0.393
Medium	269	1,783.7			
High	268	1,776.6			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of absolute lymphocytes versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

17.2.2.1.8 IgA

Examination of contrasts for Models 1 and 3 in both the unadjusted and adjusted analyses revealed no significant differences in IgA levels between Ranch Hands and Comparisons (Table 17-11(a,b and e,f): p>0.29 for all contrasts). The Model 2 unadjusted analysis of IgA was also nonsignificant (Table 17-11(c): p=0.224), although after adjustment for covariates, the association between initial dioxin and IgA levels was significant and positive (Table 17-11(d): p=0.046, adjusted slope=0.040). The Model 4 unadjusted analysis of IgA revealed a marginally significant and positive association between the 1987 dioxin levels and IgA levels (Table 17-11(g): p=0.051, adjusted slope=0.022), whereas the adjusted Model 4 analysis was nonsignificant (Table 17-11(h): p=0.115).

Table 17-11. Analysis of IgA (mg/dl)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***830***	***232.4***	***–0.9 --***	***0.860***
	Comparison	***1,199***	***233.3***		
Officer	Ranch Hand	327	224.8	–0.4 --	0.958
	Comparison	475	225.2		
Enlisted Flyer	Ranch Hand	142	238.1	1.4 --	0.912
	Comparison	178	236.6		
Enlisted Groundcrew	Ranch Hand	361	237.3	–2.2 --	0.779
	Comparison	546	239.5		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 17-11. Analysis of IgA (mg/dl) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	*Ranch Hand*	*820*	*234.9*	*–1.4 --*	*0.790*
	Comparison	*1,188*	*236.2*		
Officer	Ranch Hand	324	221.5	–2.5 --	0.740
	Comparison	470	224.0		
Enlisted Flyer	Ranch Hand	140	238.2	0.1 --	0.995
	Comparison	176	238.1		
Enlisted Groundcrew	Ranch Hand	356	246.1	–0.7 --	0.927
	Comparison	542	246.8		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	148	230.8	231.4	0.007	0.021 (0.017)	0.224
Medium	152	241.6	241.6			
High	153	241.1	240.4			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of IgA versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	148	257.2	0.049	0.040 (0.020)	0.046
Medium	150	270.3			
High	151	275.8			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of IgA versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 17-11. Analysis of IgA (mg/dl) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,164	233.8	233.6		
Background RH	371	225.0	226.8	–6.8 --	0.297
Low RH	222	233.0	232.3	–1.3 --	0.868
High RH	231	242.6	240.9	7.3 --	0.373
Low plus High RH	453	237.8	236.6	3.0 --	0.629

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,154	236.3		
Background RH	365	231.0	–5.3 --	0.435
Low RH	220	233.2	–3.1 --	0.707
High RH	229	241.0	4.7 --	0.575
Low plus High RH	449	237.1	0.8 --	0.890

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	281	221.1	0.005	0.022 (0.011)	0.051
Medium	271	231.1			
High	272	244.7			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of IgA versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 17-11. Analysis of IgA (mg/dl) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	277	240.7	0.031	0.021 (0.013)	0.115
Medium	269	247.3			
High	268	265.1			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of IgA versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

17.2.2.1.9 IgG

All analyses of IgG from Models 1 through 4 were nonsignificant (Table 17-12 (a–h): p>0.21).

Table 17-12. Analysis of IgG (mg/dl)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.L.)[b]	p-Value[c]
All	***Ranch Hand***	***830***	***1,035.5***	***–11.8 --***	***0.273***
	Comparison	***1,199***	***1,047.3***		
Officer	Ranch Hand	327	1,022.2	–7.7 --	0.649
	Comparison	475	1,029.8		
Enlisted Flyer	Ranch Hand	142	1,021.8	–27.2 --	0.307
	Comparison	178	1,048.9		
Enlisted Groundcrew	Ranch Hand	361	1,053.3	–8.9 --	0.587
	Comparison	546	1,062.2		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 17-12. Analysis of IgG (mg/dl) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***820***	***1,121.4***	***–13.9 --***	***0.217***
	Comparison	***1,188***	***1,135.4***		
Officer	Ranch Hand	324	1,101.3	–14.3 --	0.417
	Comparison	470	1,115.6		
Enlisted Flyer	Ranch Hand	140	1,111.7	–32.3 --	0.251
	Comparison	176	1,144.1		
Enlisted Groundcrew	Ranch Hand	356	1,145.3	–6.8 --	0.694
	Comparison	542	1,152.2		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	148	1,040.7	1,039.6	0.002	–0.001 (0.009)	0.922
Medium	152	1,061.9	1,061.8			
High	153	1,025.2	1,026.3			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of IgG versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	148	1,132.3	0.119	–0.003 (0.010)	0.761
Medium	150	1,162.9			
High	151	1,107.0			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of IgG versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 17-12. Analysis of IgG (mg/dl) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,164	1,048.3	1,048.1		
Background RH	371	1,029.2	1,031.9	–16.2 --	0.254
Low RH	222	1,042.7	1,041.7	–6.4 --	0.713
High RH	231	1,042.2	1,039.6	–8.5 --	0.621
Low plus High RH	453	1,042.5	1,040.7	–7.4 --	0.572

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,154	1,136.6		
Background RH	365	1,122.1	–14.5 --	0.340
Low RH	220	1,121.4	–15.2 --	0.404
High RH	229	1,125.1	–11.5 --	0.535
Low plus High RH	449	1,123.3	–13.3 --	0.340

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	281	1,019.6	<0.001	0.002 (0.005)	0.652
Medium	271	1,040.5			
High	272	1,050.1			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of IgG versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 17-12. Analysis of IgG (mg/dl) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED					
1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	277	1,115.5	0.073	–0.001 (0.006)	0.920
Medium	269	1,132.4			
High	268	1,142.7			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of IgG versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

17.2.2.1.10 IgM

Each result from the analyses of IgM was nonsignificant for Models 1 through 4 (Table 17-13 (a–h): p>0.10 for all analyses).

Table 17-13. Analysis of IgM (mg/dl)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***830***	***96.3***	***–2.1 --***	***0.373***
	Comparison	***1,199***	***98.4***		
Officer	Ranch Hand	327	95.2	–0.6 --	0.862
	Comparison	475	95.9		
Enlisted Flyer	Ranch Hand	142	94.6	–9.7 --	0.102
	Comparison	178	104.4		
Enlisted Groundcrew	Ranch Hand	361	98.0	–0.8 --	0.831
	Comparison	546	98.7		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Table 17-13. Analysis of IgM (mg/dl) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***820***	***90.5***	***–2.0 --***	***0.365***
	Comparison	***1,188***	***92.4***		
Officer	Ranch Hand	324	89.2	–0.7 --	0.831
	Comparison	470	89.9		
Enlisted Flyer	Ranch Hand	140	89.3	–8.7 --	0.120
	Comparison	176	98.1		
Enlisted Groundcrew	Ranch Hand	356	90.7	–0.7 --	0.824
	Comparison	542	91.4		

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	148	93.9	93.5	0.005	0.007 (0.019)	0.711
Medium	152	96.5	96.5			
High	153	96.0	96.3			

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Slope and standard error based on natural logarithm of IgM versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adj. Mean[a]	R^2	Adj. Slope (Std. Error)[b]	p-Value
Low	148	86.3	0.046	–0.003 (0.022)	0.896
Medium	150	89.7			
High	151	87.9			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of IgM versus log_2 (initial dioxin).

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 17-13. Analysis of IgM (mg/dl) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,164	98.2	98.2		
Background RH	371	97.1	96.1	–2.1 --	0.487
Low RH	222	95.5	95.8	–2.4 --	0.525
High RH	231	95.5	96.4	–1.8 --	0.619
Low plus High RH	453	95.5	96.1	–2.1 --	0.459

[a] Transformed from natural logarithm scale.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[c] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[b]	p-Value[c]
Comparison	1,154	92.5		
Background RH	365	91.2	–1.3 --	0.659
Low RH	220	90.7	–1.8 --	0.599
High RH	229	89.4	–3.1 --	0.390
Low plus High RH	449	90.0	–2.5 --	0.358

[a] Transformed from natural logarithm scale.
[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c] P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin +1)		
1987 Dioxin	n	Mean[a]	R^2	Slope (Std. Error)[b]	p-Value
Low	281	96.4	<0.001	–0.001 (0.012)	0.937
Medium	271	96.4			
High	272	95.7			

[a] Transformed from natural logarithm scale.
[b] Slope and standard error based on natural logarithm of IgM versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 17-13. Analysis of IgM (mg/dl) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin + 1)		
1987 Dioxin	n	Adj. Mean[a]	R^2	Adjusted Slope (Std. Error)[b]	p-Value
Low	277	88.6	0.025	–0.008 (0.014)	0.586
Medium	269	89.3			
High	268	86.4			

[a] Transformed from natural logarithm scale
[b] Slope and standard error based on natural logarithm of IgM versus log_2 (1987 dioxin + 1).

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

17.2.2.1.11 Lupus Panel: ANA Test

All analysis results from Models 1 through 4 for the antinuclear antibody were nonsignificant (Table 17-14(a–h): p>0.20).

Table 17-14. Analysis of Lupus Panel: ANA Test

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Present	Est. Relative Risk (95% C.L)	p-Value
All	***Ranch Hand***	***830***	***432 (52.1)***	***1.00 (0.84,1.19)***	***0.998***
	Comparison	***1,199***	***624 (52.0)***		
Officer	Ranch Hand	327	168 (51.4)	0.94 (0.71,1.25)	0.683
	Comparison	475	251 (52.8)		
Enlisted Flyer	Ranch Hand	142	73 (51.4)	1.11 (0.71,1.72)	0.653
	Comparison	178	87 (48.9)		
Enlisted Groundcrew	Ranch Hand	361	191 (52.9)	1.02 (0.78,1.33)	0.876
	Comparison	546	286 (52.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Adjusted Relative Risk (95% C.L)	p-Value
All	***1.01 (0.84,1.20)***	***0.946***
Officer	0.95 (0.72,1.27)	0.736
Enlisted Flyer	1.07 (0.68,1.67)	0.778
Enlisted Groundcrew	1.04 (0.79,1.36)	0.801

Table 17-14. Analysis of Lupus Panel: ANA Test (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Number (%) Present	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	148	76 (51.4)	1.08 (0.94,1.24)	0.301
Medium	152	71 (46.7)		
High	153	85 (55.6)		

[a] Adjusted for percent body fat at the time of the blood measurement of dioxin.
[b] Relative risk for a twofold increase in initial dioxin.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
449	1.04 (0.88,1.24)	0.622

[a] Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Present	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,164	606 (52.1)		
Background RH	371	199 (53.6)	1.05 (0.83,1.33)	0.674
Low RH	222	105 (47.3)	0.83 (0.62,1.11)	0.202
High RH	231	127 (55.0)	1.14 (0.85,1.51)	0.380
Low plus High RH	453	232 (51.2)	0.97 (0.78,1.21)	0.810

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,154		
Background RH	365	1.04 (0.82,1.33)	0.738
Low RH	220	0.85 (0.63,1.14)	0.276
High RH	229	1.15 (0.85,1.55)	0.364
Low plus High RH	449	0.99 (0.79,1.24)	0.936

[a] Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Comparison: 1987 Dioxin ≤ 10 ppt.
Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.
High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.