

CHAPTER 14

DERMATOLOGIC ASSESSMENT

INTRODUCTION

Background

Chloracne, a chronic acneiform eruption with a highly specific cutaneous distribution, was first described by Von Bettman in 1897 as an occupational disease in German industrial workers. It was not until 1957 that it became recognized as a very specific consequence of exposure to chlorophenols (1,2). A recent review article summarizes the unique clinical manifestations of this skin condition (3).

Early animal researchers employed the rabbit's ear as a model for assaying the effects of chloracnegenic compounds (4,5). Other experiments on hairless mice produced histopathologic changes similar to those that occur in humans exposed to tetrachlorodibenzo-p-dioxin (TCDD, or dioxin) including hyperkeratotic changes in the sebaceous follicle with plugging of the orifice, hyperkeratinization of the stratum corneum, and keratin cyst formation (6,7).

The earliest descriptions of chloracne-like disease date back to the turn of the century (8). It is a relatively rare dermatitis with fewer than 4,000 cases documented world-wide (9); most cases have occurred in chemical plant workers or in victims of industrial accidents (10-13). Chronic conditions associated with severe chloracne include actinic elastosis, acne scars, and hypertrichosis (14,15). Epidermoid inclusion cysts seen in biopsy specimens are considered pathognomonic (16). The occurrence and severity of chloracne appear to be dose-related but may depend on other factors including the route of administration, age, genetic predisposition, and the presence of acne vulgaris and other dermatoses (14,17,18). More recent studies in rats have documented that the extent of dermal absorption is inversely related to age (19). This observation may be relevant to the finding in the industrial explosion at Seveso, Italy, that most cases (170 of 193 exposed) of chloracne occurred in children (10,11,13).

Monkeys given lethal doses of TCDD develop acneiform lesions of the lips, retention cysts of the Meibomian glands of the eyelids, facial alopecia, and loss of eyelashes (20). Other studies have demonstrated that TCDD induced squamous cell carcinomas in hamsters (21) and also induced chloracne, hirsutism, and hyperpigmentation in association with suppression of selected androgens in rats (22). Domestic animals accidentally exposed to TCDD in contaminated soil have developed alopecia, mucous membrane inflammation, hyperkeratosis, and ulcerative dermatitis (23,24).

A genetic basis for the dermal responses to TCDD has been defined in selected laboratory animals. In one series of experiments, investigators found strain-specific differences in the cutaneous reactions of haired and hairless mice to the topical application of TCDD (25). The involvement of sebaceous glands and increased transglutaminase activity

were noted in both strains, while epidermal proliferation and hyperkeratinization occurred in the responsive (haired) strain only. Furthermore, in a subsequent study from the same laboratory, these TCDD-induced dermal changes were associated with an increased density of Langerhans cells in mouse skin unique to the responsive strain (26). Based on these and other studies (27-29), it is clear that these strain-specific responses are determined genetically, and there is evidence that they may be mediated by the aryl hydrocarbon (Ah) receptor (30,31). Of the industrial compounds known to cause chloracne, TCDD is by far the most potent. Studies of the application of dioxin to the skin of human volunteers have defined the changes described earlier in animals (32). Chloracne is characterized by a maculopapular rash of active comedones conforming to an eyeglass or facial butterfly distribution, often accompanied by chest, back, or periorbital lesions (3,14,17,33). Clinically, the presence of chloracne, which can persist for more than 30 years after exposure (15), can be strongly suspected based on the history of cutaneous contact. Definitive diagnosis, however, requires biopsy and histologic confirmation particularly in light of reports that chloracne can occur after oral ingestion of chlorophenols (34).

The use of chloracne as a marker for the severity of TCDD exposure has been the subject of controversy. At issue is whether long-term consequences can occur at levels of exposure less than that required to produce chloracne. Earlier reports in subjects with chloracne found extreme variations in adipose tissue levels of TCDD (35-37), observations confirmed as well in serum levels from populations exposed in industrial accidents (11,38) and by occupation (39).

Although the high occurrence of dermatologic disease in Vietnam veterans has been well documented (40), there is no objective evidence to support an association with herbicide exposure. In a study of American Legion veterans (41), a higher prevalence of self-reported cutaneous disease was found in veterans who served in Vietnam when compared with controls, but no attempt was made to confirm the history by physical examination and the exposure indices have not been validated. In the Vietnam Experience Study (VES) conducted by the U.S. Centers for Disease Control (CDC), the occurrence of dermatologic disorders found upon physical examination was similar in Vietnam and non-Vietnam veterans (42).

Though initial examination cycles of the Air Force Health Study (AFHS) appeared to reveal an increased prevalence of basal cell and other sun-related skin cancers, the most recent analysis, using serum dioxin levels as the measure of exposure (43) did not find an association between these malignancies and TCDD.

Summary of Previous Analyses of the Air Force Health Study

1982 Baseline Study Summary Results

The 1982 Baseline clinical examination revealed an unexpected significant excess ($p=0.03$) of basal cell carcinoma in the Ranch Hand group. Risk factor data for skin cancer, including sun exposure, host factors of tannability, and complexion, were not collected in 1982. The 1982 examination focused on the diagnosis of chloracne both in historical terms by a detailed questionnaire and in contemporary terms via a comprehensive clinical assessment. The questionnaire data did not demonstrate anatomic, incidence, or onset-time

patterns of acne in the Ranch Hand group that might support an inference of past chloracne, nor did the physical examination detect a single case. Fourteen biopsies from 11 participants also did not document a chloracne diagnosis. A dermatology index (the number of clinically detected skin abnormalities per individual) was virtually identical between the Ranch Hand and Comparison groups. No exposure level associations were noted in any occupational category of the Ranch Hand group. The comprehensive dermatologic assessment did not reveal evidence of past or current chloracne in the Ranch Hand group.

1985 Followup Study Summary Results

Questionnaire data recaptured many of the acne parameters of the 1982 Baseline Questionnaire, and the physical examination parameters were similar to the 1982 Baseline examination. Particular emphasis was given to the diagnosis of basal cell carcinoma and to the collection of risk factor data, including skin color, hair color, reaction to sun exposure, and ethnicity (44).

Interval questionnaire data on the occurrence, time, and location of acne were analyzed to assess the possible historical diagnosis of chloracne. No significant difference was observed between groups for reported occurrence of acne. A marginally significant difference in the occurrence of post-1961 acne was found, with more Ranch Hands than Comparisons reporting acne. The duration of post-1961 acne was not significantly different between the two groups.

For participants with post-Southeast Asia (SEA) acne, the spatial eyeglass distribution of acne (suggesting chloracne) was observed to be similar for the Ranch Hand and Comparison groups, both for individual sites and the combination of acne on the eyelids, ears, and temples. This analysis suggested that the occurrence of skin disease compatible with chloracne was not different in the two groups.

Analyses of the 1985 followup physical examination data, as with the Baseline examination, placed primary emphasis on six dermatologic disorders: comedones, acneiform lesions, acneiform scars, inclusion cysts, depigmentation, and hyperpigmentation. Secondary emphasis was given to a composite variable consisting of 16 other minor conditions (generally not associated with chloracne). No significant difference was found for any of these variables in the unadjusted analyses. The adjusted analyses closely mirrored the unadjusted analyses, with no significant difference noted between groups for any variable. Exposure index analyses did support dose-response relationships for some of the variables in certain occupational strata, but did not reveal a strong pattern of results suggesting a relationship between skin disease and herbicide exposure.

Overall, the 1985 followup examination results paralleled the Baseline findings. Although the followup examination detected more dermatologic abnormalities than those present at Baseline, slightly more abnormalities were found in the Comparisons, and most relative risks approached unity.

1987 Followup Study Summary Results

With the exception of more Ranch Hands than Comparisons reporting at least one occurrence of acne during their lifetime, no significant group differences were detected in the Dermatologic Assessment. Subsequent analysis of the occurrence of acne indicated that, for participants with no history of acne before the start of the first SEA duty, a higher percentage of Ranch Hands than Comparisons reported the occurrence of acne after the start of the first SEA duty. However, the anatomic distribution of these lesions did not suggest chloracne as a cause. No cases of chloracne were diagnosed in the physical examination. Analyses were conducted on historical occurrence and duration of acne, six dermatologic disorders, a composite variable of other disorders, and a dermatology index of four disorders. All of these analyses found no significant group differences. The longitudinal analysis, based on the dermatology index, showed no significant differences between groups over time.

Serum Dioxin Analysis of 1987 Followup Study Summary Results

In general, the occurrence and location of acne were not associated with initial dioxin. However, in the stratified analysis of acne relative to duty in SEA, the association with initial dioxin showed a decreasing occurrence of post-SEA acne for increasing levels of initial dioxin in the stratum consisting of Ranch Hands without pre-SEA acne and an increasing occurrence of post-SEA acne for increasing levels of initial dioxin in the pre-SEA acne stratum. Of the physical examination variables, only hyperpigmentation had a significant positive association with initial dioxin under the maximal assumption.

The association between current dioxin and the occurrence of acne (lifetime), under the maximal assumption, differed between the time since SEA duty strata, with a positive association for Ranch Hands with a later duty in SEA and a negative association for those with an earlier duty in SEA. The same pattern was exhibited in the analysis of acne relative to time of duty in SEA. In the stratified analysis of acne relative to time of duty in SEA, the association with current dioxin, within the earlier duty stratum (greater than 18.6 years since duty in SEA), was similar to the association with initial dioxin—negative for Ranch Hands without pre-SEA acne and positive for those with pre-SEA acne.

Several of the physical examination variables also had significant or marginally significant positive associations with current dioxin in the later duty stratum (18.6 years or fewer since duty in SEA) but had nonsignificant associations in the earlier duty stratum. In contrast, the association between current dioxin and location of acne was negative in the later duty stratum and positive in the earlier duty stratum. No significant differences were found between the low and background current dioxin categories nor between the high and background categories for any of the variables. No cases of chloracne were defined, nor were there any dermatologic endpoints consistently related to the current body burden of dioxin. Also, the longitudinal analysis of the dermatology index showed no significant associations with dioxin. In summary, there was no consistent evidence in these data to suggest a dioxin effect on the dermatologic system.

Parameters for the Dermatologic Assessment

Dependent Variables

The dermatologic assessment was based on physical examination data and information regarding acne, as obtained in a face-to-face interview with the participant and subsequently verified by a medical records review.

Medical Records Data

During the health interview conducted as part of the questionnaire, each study participant was asked about occurrences of acne since the date of the last health interview. In addition, data regarding occurrence of acne were collected at the physical examination. This information was used to update data gathered through the 1987 examination, and was subsequently verified through a review of the participant's medical records. The definition of acne was expanded for the 1992 followup to include all reasonable conditions that could be confused with acne. This definition included the following conditions: erythematous-squamous dermatoses, toxic erythema-rosacea, unspecified erythematous, other dermatoses, diseases of hair and hair follicles, acne varioliformia, other acne, sebaceous cysts, specified and unspecified diseases of sebaceous glands, and other specified disorders of the skin. Information regarding the date and location of each acne occurrence also was collected and verified. The variables defined below were constructed from the acne data and analyzed in the dermatologic assessment.

- Occurrence of Acne (lifetime):
 - Yes: at least one occurrence of acne
 - No: no occurrences of acne.

- Acne Relative to Time of Duty in SEA:
 - Post-SEA: all occurrences were after the start of the first duty in SEA
 - Pre and post-SEA: multiple occurrences, both before and after the start of the first duty in SEA, or a case of acne that began before the start of the first duty in SEA and ended after starting duty in SEA
 - Pre-SEA: last occurrence was before the start of duty in SEA
 - None: no occurrences of acne.

- Location of Acne (post-SEA; post-SEA combined with pre- and post-SEA):
 - Temples
 - Eyes or eyelids
 - Ears
 - Temples and eyes
 - Eyes and ears
 - Temples and ears
 - Temples, eyes, and ears
 - Other sites (cheeks, nose, forehead, jaw or chin, chest, and back).

If an individual had multiple site involvement for one or more of the seven specified sites and for the category "other sites," then the specified site(s) category was assigned.

The analysis of the occurrence of acne was based on responses from all of the participants of the 1992 examination. Acne relative to the time of duty in SEA was analyzed for three strata of participants: (1) all participants of the 1992 examination, (2) participants of the 1992 examination without pre-SEA acne, and (3) participants of the 1992 examination with pre-SEA acne.

Location of acne was analyzed twice. The first analysis was limited to the participants who had all their acne after the start of the first duty in SEA (post-SEA). The second analysis was based on participants who had all their acne after the start of the first duty in SEA or who had multiple occurrences—both before and after the start of the first duty in SEA, or a case of acne that began before the start of the first duty in SEA and ended after starting duty in SEA (post-SEA combined with pre- and post-SEA). No participants were excluded for medical reasons from the analyses of these variables.

Physical Examination Data

Two composite variables from the physical examination data were analyzed in the dermatologic assessment: a dermatology index and a variable labeled "other abnormalities." The dermatology index was formed by examining the following conditions: comedones, acneiform lesions, acneiform scars, inclusion cysts, depigmentation, and hyperpigmentation. Depigmentation and hyperpigmentation are defined as areas of skin that are less or more pigmented relative to the rest of the skin. A participant was defined to be "abnormal" for this dermatology index if any of these conditions were present and defined as "normal" if none were present. The variable other abnormalities was coded as abnormal or normal. A participant was considered to be abnormal for this variable if any of the following disorders were detected in the physical examination: vitiligo, jaundice, spider angiomas, palmar erythema, palmar keratoses, actinic keratoses, petechiae, ecchymoses, conjunctival abnormality, oral mucosal abnormality, fingernail abnormality, toenail abnormality, dermatographia, cutis rhomboidalis, nevus, or other nonspecific abnormalities. Abnormalities relating to skin malignancies are discussed in Chapter 10, Neoplasia Assessment. No participants were excluded for medical reasons from the analyses of these variables.

Covariates

The covariates age, race, and military occupation were used in adjusted statistical analyses of the occurrence of acne and location of acne. Presence of pre-SEA acne (yes, no) was a stratification variable in the analysis of acne relative to time of duty in SEA. Time reference to SEA (pre- and post-SEA and post-SEA) was a stratification variable in the analysis of location of acne. The covariates age, race, occupation, and presence of pre-SEA acne were used in adjusted statistical analyses of both physical examination variables in the dermatologic assessment. Age was used in its continuous form for modeling purposes for all dependent variables and dichotomized for interaction summaries.

Statistical Methods

Chapter 7, Statistical Methods, describes basic statistical methods used throughout this report. Table 14-1 summarizes the statistical analyses performed for the Dermatologic Assessment. The first part of this table describes the dependent variables and identifies the candidate covariates and the statistical methods. The second part of this table further describes the candidate covariates. Abbreviations used in the body of the table are defined at the end of the table. Dependent variable data were missing for some participants. The number of participants with missing data are summarized in Table 14-2.

Analyses of data collected at the 1987 followup study indicated that dioxin was associated with military occupation. In general, enlisted personnel had higher levels of dioxin than officers, with enlisted groundcrew having higher levels than enlisted flyers. Consequently, adjustment for military occupation in statistical models using dioxin as a measure of exposure may improperly mask an actual dioxin effect. However, occupation also can be a surrogate for socioeconomic effects. Failure to adjust for occupation could overlook important risk factors related to lifestyle. If occupation was found to be significantly associated with a dependent variable in the 1992 followup analyses and was retained in the final statistical models using dioxin as a measure of exposure, the dioxin effect was evaluated in the context of two models. Analyses were performed with and without occupation in the final models to investigate whether conclusions regarding the association between the health endpoint and dioxin differed.

The results of the analyses without occupation are presented in Appendix J-3 and are only discussed in the text if the level of significance differs from the original final adjusted model (significant versus nonsignificant).

RESULTS

Dependent Variable-Covariate Associations

Table J-1-1 in Appendix J presents the results of the following tests of association between the dermatology dependent variables and covariates.

Using pooled group data, the covariate tests of association detected a high association between the occurrence of acne and age ($p < 0.001$). The percentage of participants with at least one occurrence of acne in their lifetime increased with age (81.7% for those participants born in or after 1942 and 89.0% for those participants born before 1942).

The association between the covariates and acne relative to time of duty in SEA for the primary stratum of pre- and post-SEA and post-SEA acne versus pre-SEA acne and none revealed highly significant associations with age ($p < 0.001$) and presence of pre-SEA acne ($p < 0.001$). Younger participants had a lower percentage of acne relative to time of duty in SEA than older participants (81.1% vs. 88.8%). Participants with a history of pre-SEA acne had a higher percentage of post-SEA acne (96.4%) than those with no pre-SEA acne (84.3%).

**Table 14-1.
Statistical Analyses for the Dermatologic Assessment**

Dependent Variables

Variable	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analysis
Occurrence of Acne (Lifetime)	MR-V	D	Yes No	AGE,RACE, OCC	U:LR,CS A:LR
Acne Relative to Time of Duty in SEA	MR-V and MIL	D	Pre-SEA Pre- & Post-SEA Post-SEA None	AGE,RACE, OCC,PRESEA	U:LR,CS A:LR
Location of Acne	MR-V	D	Temples Eyes Ears Other Sites	AGE,RACE, OCC,TIMESEA	U:LR,CS A:LR
Other Abnormalities	PE	D	Abnormal Normal	AGE,RACE, OCC,PRESEA	U:LR,CS A:LR
Dermatology Index	PE	D	Abnormal Normal	AGE,RACE, OCC,PRESEA	U:LR,CS A:LR

Covariates

Variable (Abbreviation)	Data Source	Data Form	Cutpoints
Age (AGE)	MIL	D/C	Born ≥ 1942 Born < 1942
Race (RACE)	MIL	D	Black Non-Black
Occupation (OCC)	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Time Reference to SEA (TIMESEA)	MR-V and MIL	D	Pre- & Post-SEA Post-SEA
Presence of Pre-SEA Acne (PRESEA)	MR-V and MIL	D	Yes No

**Table 14-1. (Continued)
Statistical Analyses for the Dermatologic Assessment**

Abbreviations

Data Source:	MIL	=	Air Force military records
	MR-V	=	Medical records (verified)
	PE	=	1992 physical examination
Data Form:	D	=	Discrete analysis only
	D/C	=	Appropriate form for analysis (either discrete or continuous)
Statistical Analyses:	U	=	Unadjusted analyses
	A	=	Adjusted analyses
Statistical Methods:	CS	=	Continuity-adjusted chi-square statistic
	LR	=	Logistic regression analysis

**Table 14-2.
Number of Participants with Missing Data for the Dermatologic Assessment**

Variable	Variable Use	Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
		Ranch Hand	Comparison	Initial	Current	Ranch Hand	Comparison
Location of Acne	DEP	2	1	2	2	2	1
Other Abnormalities	DEP	0	2	0	0	0	2
Dermatology Index	DEP	0	1	0	0	0	1

Abbreviations: DEP = Dependent variable.

Note: 952 Ranch Hands and 1,281 Comparisons;
520 Ranch Hands for initial dioxin; 894 Ranch Hands for current dioxin;
894 Ranch Hands and 1,063 Comparisons for categorized dioxin.

One Ranch Hand missing total lipids for current dioxin.

Investigation of the relationship between location of acne for participants with pre- and post-SEA and post-SEA acne and the covariates revealed highly significant associations with age ($p < 0.001$) and race ($p < 0.001$). Younger participants had a lower percentage of acne on the temples, eyes, and ears than older participants (38.7% vs. 51.1%). Blacks had a lower percentage of acne on the temples, eyes, and ears than non-Blacks (25.7% vs. 47.3%).

Statistically significant associations were found between the composite variable containing all other dermatologic abnormalities and age ($p < 0.001$), occupation ($p = 0.007$), race ($p = 0.002$), and presence of pre-SEA acne ($p = 0.001$). The percentage of other abnormalities increased with age. Of the younger participants, 74.0 percent had other abnormalities, while 89.2 percent of the older participants had abnormalities. The number of participants with other abnormalities was higher for the enlisted flyers (85.7%) than for the officers (84.6%) and enlisted groundcrew (79.9%). A higher percentage of non-Blacks than Blacks had other abnormalities (83.3% vs. 72.5%). Also, participants without pre-SEA acne had a higher percentage of other abnormalities (83.5%) than did those participants with pre-SEA acne (74.7%).

The dermatology index showed highly significant associations with the covariates occupation ($p < 0.001$), race ($p < 0.001$), and presence of pre-SEA acne ($p < 0.001$). The percentage of participants with at least one abnormality was higher for enlisted flyers (49.5%) than for enlisted groundcrew (47.7%) and officers (39.1%). More Blacks had at least one abnormality than non-Blacks (64.1% vs. 43.5%). More participants with pre-SEA acne had at least one abnormality (59.1%) than those without pre-SEA acne (43.0%).

Exposure Analysis

The following section presents results of the statistical analyses of the dependent variables shown in Table 14-1. Dependent variables are grouped into two sections: those derived and verified from a review of medical records and data obtained during the 1992 physical examination.

Unadjusted and adjusted analyses of six models are presented for each variable. Model 1 examines the relationship between the dependent variable and group (Ranch Hand or Comparison). Model 2 explores the relationship 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, a 1992 level was used. A statistical adjustment for the percent of body fat at the participant's time of duty in SEA and the change in the percent of body fat from the time of duty in SEA to the date of the blood draw for dioxin is included in this model to account for body-fat-related differences in elimination rate (45). Model 3 dichotomizes the Ranch Hands in Model 2 based on their initial dioxin measures; these two categories of Ranch Hands are referred to as the "low Ranch Hand" category and the "high Ranch Hand" category. These participants are added to Ranch Hands and Comparisons with current serum dioxin levels (1987, if available; 1992, if the 1987 level was not available) at or below 10 ppt to create a total of four categories. Ranch Hands with current serum dioxin levels at or below 10 ppt are referred to as the "background Ranch Hand" category. The relationship between the dependent variable in each of the three Ranch Hand categories and the dependent variable in the "Comparison"

category is examined. A fourth contrast, exploring the relationship of the dependent variable in the low Ranch Hand category and the high Ranch Hand category combined, also is conducted. This combination is referred to in the text and tables as the “low plus high Ranch Hand” category. As in Model 2, a statistical adjustment is made for the percent of body fat at the participant’s time of duty in SEA and the change in the percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

Models 4, 5, and 6 examine the relationship between the dependent variable and 1987 dioxin levels in all Ranch Hands with a dioxin measurement. If a participant did not have a 1987 dioxin measurement, a 1992 measurement was utilized in determining the current dioxin level. The measure of dioxin in Model 4 is lipid-adjusted, whereas whole-weight dioxin is used in Models 5 and 6. Model 6 differs from Model 5 in that a statistical adjustment for total lipids is included in Model 6. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7 respectively.

Results of investigations for group-by-covariate and dioxin-by-covariate interactions are referenced in the text, and tabular results are presented in Appendix J-2. As described previously, additional analyses are performed when occupation was retained in the final models for Models 2 through 6. Results excluding occupation from these models are tabled in Appendix J-3, and dioxin-by-covariate interactions with occupation excluded from these models are presented in Appendix J-4. Results from analyses excluding occupation are discussed in the text only if a meaningful change in the results occurred (that is, changes between significant results, marginally significant results, and nonsignificant results).

Verified Medical Records Variables

Occurrence of Acne (Lifetime)

Analysis of lifetime occurrence of acne did not find a significant difference between Ranch Hands and Comparisons in the unadjusted and adjusted analyses for Model 1 (Table 14-3(a,b): $p > 0.13$ for unadjusted and adjusted results). The final model in the adjusted analysis contained the covariate age. Stratifying the Model 1 analyses by occupation displayed a marginally significant association between group and occurrence of acne for enlisted groundcrew. In the unadjusted analysis, the percentage of enlisted groundcrew Ranch Hands with abnormalities (87.2%) was significantly greater than the percentage of enlisted groundcrew Comparisons with abnormalities (82.8%) (Table 14-3(a): $p = 0.067$, Est. RR = 1.42). The relative risk for the adjusted analysis of enlisted groundcrew was also marginally significant (Table 14-3(b): $p = 0.051$, Adj. RR = 1.43).

Models 2 and 3 did not find a significant association between initial or categorized dioxin and occurrence of acne for the unadjusted and adjusted analyses (Table 14-3(c-f): $p > 0.18$ for all analyses). The final adjusted model for Model 2 included age and occupation. Model 3 accounted for age in the adjusted analysis.

The unadjusted and adjusted analyses for Models 4 through 6 did not show significant associations between occurrence of acne and current dioxin (Table 14-3(g,h): $p > 0.51$ for all

Table 14-3.
Analysis of Occurrence of Acne (Lifetime)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	Group	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
<i>All</i>	<i>Ranch Hand</i>	<i>952</i>	<i>87.2</i>	<i>1.21 (0.95,1.55)</i>	<i>0.134</i>
	<i>Comparison</i>	<i>1,281</i>	<i>84.9</i>		
Officer	Ranch Hand	367	88.0	1.21 (0.81,1.81)	0.410
	Comparison	502	85.9		
Enlisted Flyer	Ranch Hand	162	85.2	0.77 (0.42,1.42)	0.494
	Comparison	203	88.2		
Enlisted Groundcrew	Ranch Hand	423	87.2	1.42 (0.99,2.03)	0.067
	Comparison	576	82.8		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks^a
<i>All</i>	<i>1.21 (0.94,1.54)</i>	<i>0.135</i>	AGE (p < 0.001)
Officer	1.18 (0.79,1.77)	0.428	
Enlisted Flyer	0.75 (0.41,1.39)	0.364	
Enlisted Groundcrew	1.43 (1.00,2.05)	0.051	

^a Covariates and associated p-values correspond to final model based on all participants with available data.

**Table 14-3. (Continued)
Analysis of Occurrence of Acne (Lifetime)**

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log₂ (Initial Dioxin)^a	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)^b	p-Value
Low	174	87.9	0.93 (0.77,1.13)	0.487
Medium	173	87.9		
High	173	84.4		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log₂ (Initial Dioxin)^c			
n	Adj. Relative Risk (95% C.I.)^b	p-Value	Covariate Remarks
520	0.93 (0.74,1.18)	0.559	AGE (p<0.001) OCC (p=0.010)

^a Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

^b Relative risk for a twofold increase in initial dioxin.

^c Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

**Table 14-3. (Continued)
Analysis of Occurrence of Acne (Lifetime)**

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)^{ab}	p-Value
Comparison	1,063	86.1		
Background RH	374	88.2	1.28 (0.89,1.84)	0.180
Low RH	260	88.1	1.15 (0.76,1.74)	0.507
High RH	260	85.4	0.91 (0.62,1.35)	0.643
Low plus High RH	520	86.7	1.02 (0.75,1.39)	0.900

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)^c	p-Value	Covariate Remarks
Comparison	1,063			AGE (p < 0.001)
Background RH	374	1.19 (0.83,1.72)	0.349	
Low RH	260	1.09 (0.72,1.66)	0.683	
High RH	260	1.04 (0.70,1.55)	0.829	
Low plus High RH	520	1.07 (0.78,1.46)	0.688	

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

^c Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.

Comparison: Current Dioxin ≤ 10 ppt.

Background (Ranch Hand): Current Dioxin ≤ 10 ppt.

Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.

High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 14-3. (Continued)
Analysis of Occurrence of Acne (Lifetime)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
Model^a	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log₂ (Current Dioxin + 1)	
	Low	Medium	High	Est. Relative Risk (95% C.I.)^b	p-Value
4	87.1 (295)	88.7 (300)	86.3 (299)	0.96 (0.84,1.10)	0.577
5	87.7 (300)	88.6 (297)	85.9 (297)	0.98 (0.87,1.10)	0.691
6 ^c	87.6 (299)	88.6 (297)	85.9 (297)	0.96 (0.85,1.09)	0.514

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
Model^a	Analysis Results for Log₂ (Current Dioxin + 1)			
	n	Adj. Relative Risk (95% C.I.)^b	p-Value	Covariate Remarks
4	894	0.97 (0.83,1.13)	0.687	AGE (p<0.001) OCC (p=0.043)
5	894	0.98 (0.86,1.12)	0.752	AGE (p<0.001) OCC (p=0.045)
6 ^d	893	0.97 (0.84,1.12)	0.676	AGE (p<0.001) OCC (p=0.043)

^a Model 4: Log₂ (lipid-adjusted current dioxin + 1).
 Model 5: Log₂ (whole-weight current dioxin + 1).
 Model 6: Log₂ (whole-weight current dioxin + 1), adjusted for log₂ total lipids.

^b Relative risk for a twofold increase in current dioxin.

^c Adjusted for log₂ total lipids.

^d Adjusted for log₂ total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
 Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

analyses). Each of the adjusted analyses for Models 4 through 6 accounted for age and occupation.

Acne Relative to SEA Time of Duty in SEA (Pre- and Post-SEA and Post-SEA vs. Pre-SEA and None)

The Model 1 unadjusted and adjusted analyses of acne relative to time of duty in SEA revealed no significant overall differences in the history of post-SEA acne between groups (Table 14-4(a,b): $p > 0.14$ for unadjusted and adjusted analyses). However, after stratifying the Model 1 analyses by occupation, the association between group and acne was significant for the enlisted groundcrew. For the unadjusted analysis, the enlisted groundcrew Ranch Hands had a significantly higher prevalence of post- and pre- and post-SEA acne (87.2%) than the enlisted groundcrew Comparisons (82.3%) (Table 14-4(a): $p = 0.042$, Est. RR=1.47). Similarly, the adjusted analysis displayed a significant relative risk for enlisted groundcrew (Table 14-4(b): $p = 0.025$, Adj. RR=1.51). The Model 1 analysis was adjusted for age and presence of pre-SEA acne.

Examination of the unadjusted and adjusted results for Models 2 and 3 for acne relative to time of duty in SEA did not show a significant association with initial or categorized dioxin (Table 14-4(c-f): $p > 0.16$ for all analyses). The final models for both Models 2 and 3 were adjusted for age, occupation, and presence of pre-SEA acne.

The unadjusted and adjusted analyses for Models 4 through 6 did not display any significant associations between acne relative to time of duty in SEA and current dioxin (Table 14-4(g,h): $p > 0.47$ for all analyses) when Ranch Hands with acne before and after the start of their first duty in SEA (pre- and post-SEA) and Ranch Hands with acne only after the start of their first duty in SEA (post-SEA) were contrasted with Ranch Hands who did not have acne after the start of their duty in SEA (pre-SEA and none). Similar to Models 2 and 3, Models 4 through 6 accounted for the significant covariates of age, occupation, and presence of pre-SEA acne.

Acne Relative to Time of Duty in SEA (Post-SEA vs. None)

The Model 1 unadjusted and adjusted analyses of acne relative to time of duty in SEA for participants with no pre-SEA acne revealed no significant differences between groups combining all occupations (Table 14-5(a,b): $p > 0.11$ for unadjusted and adjusted analyses). However, stratifying by occupation revealed a difference between Ranch Hands and Comparisons for enlisted groundcrew. The unadjusted analysis showed a marginally significant higher percentage of post-SEA acne for Ranch Hands (85.8%) than for Comparisons (80.7%) (Table 14-5(a): $p = 0.059$, Est. RR=1.44). The adjusted analysis also revealed a significant relative risk for enlisted groundcrew (Table 14-5(b): $p = 0.041$, Adj. RR=1.47). Age was the only significant covariate for Model 1.

The unadjusted and adjusted analyses of acne relative to time of duty in SEA for participants with no pre-SEA acne for Models 2 and 3 were not statistically significant (Table 14-5(c-f): $p > 0.15$ for all analyses). The adjusted analysis of Model 2 accounted for the

Table 14-4.
Analysis of Acne Relative to Time of Duty in SEA
(Pre- and Post-SEA and Post-SEA vs. Pre-SEA and None)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	Group	n	Percent Pre-/Post-SEA & Post-SEA	Est. Relative Risk (95% C.I.)	p-Value
<i>All</i>	<i>Ranch Hand</i>	<i>952</i>	<i>86.8</i>	<i>1.20 (0.94,1.53)</i>	<i>0.158</i>
	<i>Comparison</i>	<i>1,281</i>	<i>84.5</i>		
Officer	Ranch Hand	367	87.5	1.17 (0.79,1.74)	0.504
	Comparison	502	85.7		
Enlisted Flyer	Ranch Hand	162	84.0	0.70 (0.39,1.28)	0.311
	Comparison	203	88.2		
Enlisted Groundcrew	Ranch Hand	423	87.2	1.47 (1.03,2.10)	0.042
	Comparison	576	82.3		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks^a
<i>All</i>	<i>1.20 (0.94,1.53)</i>	<i>0.145</i>	AGE (p<0.001) PRESEA (p<0.001)
Officer	1.15 (0.77,1.72)	0.507	
Enlisted Flyer	0.67 (0.36,1.23)	0.196	
Enlisted Groundcrew	1.51 (1.05,2.17)	0.025	

^a Covariates and associated p-values correspond to final model based on all participants with available data.

Note: Pre-/Post-SEA = multiple occurrences of acne, both before and after the start of the first duty in SEA, or a case of acne that began before the start of the first duty in SEA and ended after starting duty in SEA.

Table 14-4. (Continued)
Analysis of Acne Relative to Time of Duty in SEA
(Pre- and Post-SEA and Post-SEA vs. Pre-SEA and None)

c) MODEL 2: RANCH HANDS -- INITIAL DIOXIN -- UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log₂ (Initial Dioxin)^a	
Initial Dioxin	n	Percent Pre-/Post-SEA & Post-SEA	Estimated Relative Risk (95% C.I.)^b	p-Value
Low	174	86.8	0.94 (0.78,1.13)	0.497
Medium	173	87.9		
High	173	83.8		

d) MODEL 2: RANCH HANDS -- INITIAL DIOXIN -- ADJUSTED			
Analysis Results for Log₂ (Initial Dioxin)^c			
n	Adj. Relative Risk (95% C.I.)^b	p-Value	Covariate Remarks
520	0.92 (0.73,1.16)	0.470	AGE (p<0.001) OCC (p=0.001) PRESEA (p=0.014)

^a Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

^b Relative risk for a twofold increase in initial dioxin.

^c Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Pre-/Post-SEA = multiple occurrences of acne, both before and after the start of the first duty in SEA, or a case of acne that began before the start of the first duty in SEA and ended after starting duty in SEA.

Table 14-4. (Continued)
Analysis of Acne Relative to Time of Duty in SEA
(Pre- and Post-SEA and Post-SEA vs. Pre-SEA and None)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Pre-/ Post-SEA & Post-SEA	Est. Relative Risk (95% C.I.)^{ab}	p-Value
Comparison	1,063	85.7		
Background RH	374	88.0	1.29 (0.90,1.84)	0.168
Low RH	260	87.3	1.11 (0.74,1.66)	0.615
High RH	260	85.0	0.91 (0.62,1.34)	0.638
Low plus High RH	520	86.2	1.00 (0.74,1.36)	0.985

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	n	Adj. Relative Risk (95% C.I.)^{ac}		p-Value	Covariate Remarks
Comparison	1,063				AGE (p<0.001) OCC (p=0.119) PRESEA (p<0.001)
Background RH	374	1.26 (0.87,1.84)		0.219	
Low RH	260	1.07 (0.71,1.61)		0.761	
High RH	260	1.00 (0.67,1.50)		0.995	
Low plus High RH	520	1.03 (0.75,1.41)		0.841	

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

^c Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.

Comparison: Current Dioxin \leq 10 ppt.

Background (Ranch Hand): Current Dioxin \leq 10 ppt.

Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin \leq 143 ppt.

High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Pre-/Post-SEA = multiple occurrences of acne, both before and after the start of the first duty in SEA, or a case of acne that began before the start of the first duty in SEA and ended after starting duty in SEA.

Table 14-4. (Continued)
Analysis of Acne Relative to Time of Duty in SEA
(Pre- and Post-SEA and Post-SEA vs. Pre-SEA and None)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
Model^a	Current Dioxin Category			Analysis Results for Log₂ (Current Dioxin + 1)	
	Percent Pre-/Post-SEA & Post-SEA/(n)			Est. Relative Risk (95% C.I.)^b	p-Value
	Low	Medium	High		
4	86.8 (295)	88.0 (300)	86.0 (299)	0.96 (0.84,1.09)	0.520
5	87.3 (300)	87.9 (297)	85.5 (297)	0.97 (0.87,1.09)	0.619
6 ^c	87.3 (299)	87.9 (297)	85.5 (297)	0.96 (0.84,1.08)	0.470

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
Model^a	Analysis Results for Log₂ (Current Dioxin + 1)			
	n	Adj. Relative Risk (95% C.I.)^b	p-Value	Covariate Remarks
4	894	0.95 (0.81,1.11)	0.513	AGE (p<0.001) OCC (p=0.005) PRESEA (p=0.001)
5	894	0.96 (0.84,1.10)	0.558	AGE (p<0.001) OCC (p=0.005) PRESEA (p=0.001)
6 ^d	893	0.95 (0.82,1.11)	0.527	AGE (p<0.001) OCC (p=0.005) PRESEA (p=0.001)

^a Model 4: Log₂ (lipid-adjusted current dioxin + 1).
 Model 5: Log₂ (whole-weight current dioxin + 1).
 Model 6: Log₂ (whole-weight current dioxin + 1), adjusted for log₂ total lipids.

^b Relative risk for a twofold increase in current dioxin.

^c Adjusted for log₂ total lipids.

^d Adjusted for log₂ total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
 Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.
 Pre-/Post-SEA = multiple occurrences of acne, both before and after the start of the first duty in SEA, or a case of acne that began before the start of the first duty in SEA and ended after starting duty in SEA.

Table 14-5.
Analysis of Acne Relative to Time of Duty in SEA
(Post-SEA vs. None)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	Group	n	Percent Post-SEA	Est. Relative Risk (95% C.I.)	p-Value
<i>All</i>	<i>Ranch Hand</i>	<i>859</i>	<i>85.8</i>	<i>1.23 (0.96,1.57)</i>	<i>0.116</i>
	<i>Comparison</i>	<i>1,149</i>	<i>83.1</i>		
Officer	Ranch Hand	335	86.9	1.24 (0.83,1.86)	0.350
	Comparison	450	84.2		
Enlisted Flyer	Ranch Hand	145	83.4	0.75 (0.41,1.38)	0.437
	Comparison	186	87.1		
Enlisted Groundcrew	Ranch Hand	379	85.8	1.44 (1.00,2.07)	0.059
	Comparison	513	80.7		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks^a
<i>All</i>	<i>1.22 (0.95,1.56)</i>	<i>0.116</i>	AGE (p < 0.001)
Officer	1.19 (0.79,1.80)	0.401	
Enlisted Flyer	0.74 (0.40,1.37)	0.331	
Enlisted Groundcrew	1.47 (1.02,2.12)	0.041	

^a Covariates and associated p-values correspond to final model based on all participants with available data.

Table 14-5. (Continued)
Analysis of Acne Relative to Time of Duty in SEA
(Post-SEA vs. None)

c) MODEL 2: RANCH HANDS -- INITIAL DIOXIN -- UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log₂ (Initial Dioxin)^a	
Initial Dioxin	n	Percent Post-SEA	Estimated Relative Risk (95% C.I.)^b	p-Value
Low	159	86.8	0.92 (0.76,1.12)	0.430
Medium	154	86.4		
High	157	82.8		

d) MODEL 2: RANCH HANDS -- INITIAL DIOXIN -- ADJUSTED				
Analysis Results for Log₂ (Initial Dioxin)^c				
n	Adj. Relative Risk (95% C.I.)^b	p-Value	Covariate Remarks	
470	0.93 (0.73,1.17)	0.525	AGE (p < 0.001) OCC (p = 0.007)	

^a Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

^b Relative risk for a twofold increase in initial dioxin.

^c Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 14-5. (Continued)
Analysis of Acne Relative to Time of Duty in SEA
(Post-SEA vs. None)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Post-SEA	Est. Relative Risk (95% C.I.)^{ab}	p-Value
Comparison	946	84.4		
Background RH	337	86.9	1.31 (0.91,1.89)	0.150
Low RH	237	86.9	1.18 (0.77,1.79)	0.447
High RH	233	83.7	0.91 (0.62,1.35)	0.650
Low plus High RH	470	85.3	1.03 (0.76,1.41)	0.845

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)^{ac}	p-Value	Covariate Remarks
Comparison	946			AGE (p < 0.001)
Background RH	337	1.21 (0.83,1.75)	0.317	
Low RH	237	1.11 (0.73,1.70)	0.622	
High RH	233	1.07 (0.72,1.60)	0.735	
Low plus High RH	470	1.09 (0.80,1.50)	0.592	

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

^c Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.

Comparison: Current Dioxin ≤ 10 ppt.

Background (Ranch Hand): Current Dioxin ≤ 10 ppt.

Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.

High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 14-5. (Continued)
Analysis of Acne Relative to Time of Duty in SEA
(Post-SEA vs. None)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
Model^a	Current Dioxin Category Percent Post-SEA/(n)			Analysis Results for Log₂ (Current Dioxin + 1)	
	Low	Medium	High	Est. Relative Risk (95% C.I.)^b	p-Value
4	85.7 (266)	87.5 (273)	84.7 (268)	0.96 (0.84,1.10)	0.563
5	86.3 (271)	87.4 (270)	84.2 (266)	0.98 (0.87,1.10)	0.695
6 ^c	86.3 (271)	87.4 (270)	84.1 (266)	0.96 (0.84,1.09)	0.498

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED					
Model^a	n	Analysis Results for Log₂ (Current Dioxin + 1)			Covariate Remarks
		Adj. Relative Risk (95% C.I.)^b	p-Value		
4	807	0.97 (0.82,1.14)	0.677	AGE (p<0.001) OCC (p=0.030)	
5	807	0.98 (0.85,1.12)	0.734	AGE (p<0.001) OCC (p=0.031)	
6 ^d	807	0.97 (0.83,1.12)	0.670	AGE (p<0.001) OCC (p=0.030)	

^a Model 4: Log₂ (lipid-adjusted current dioxin + 1).
 Model 5: Log₂ (whole-weight current dioxin + 1).
 Model 6: Log₂ (whole-weight current dioxin + 1), adjusted for log₂ total lipids.

^b Relative risk for a twofold increase in current dioxin.

^c Adjusted for log₂ total lipids.

^d Adjusted for log₂ total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
 Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

significant covariates of age and occupation. The final adjusted analysis for Model 3 revealed age as the only significant covariate.

For Models 4 through 6, the adjusted and unadjusted analyses did not show any significant associations between current dioxin and post-SEA acne for participants with no pre-SEA acne (Table 14-5(g,h): $p > 0.49$ for all analyses). The adjusted analysis of Models 4 through 6 each contained the significant covariates of age and occupation.

Acne Relative to Time of Duty in SEA (Pre- and Post-SEA vs. Pre-SEA)

The unadjusted analyses of acne relative to time of duty in SEA for participants with pre-SEA acne did not reveal a significant association between post-SEA acne and group (Table 14-6(a): $p > 0.38$ for all analyses). The adjusted analyses led to highly significant group-by-age and group-by-occupation interactions (Table 14-6(b): $p = 0.002$ and $p = 0.001$). Stratified results of these interactions are presented in Appendix Table J-2-1; the sparse number of individuals with pre-SEA acne only ($n = 8$) precluded meaningful analysis; therefore, the relative risks, confidence intervals, and p-values are not presented in Appendix Table J-2-1.

The unadjusted and adjusted analyses of Models 2 and 3 did not find a significant relationship between initial or categorized dioxin and post-SEA acne for participants with pre-SEA acne (Table 14-6(c-f): $p > 0.22$ for all analyses). For the Model 2 adjusted analyses, the sparse number of Ranch Hands with pre-SEA acne only ($n = 3$) precluded meaningful analysis; therefore, results are not presented. No covariates were retained in the final adjusted analyses for Model 3, therefore, the adjusted results are equivalent to the unadjusted results for this model.

Models 4 through 6 unadjusted analyses did not show any significant associations between current dioxin and post-SEA acne for participants with pre-SEA acne (Table 14-6(g): $p > 0.62$ for all unadjusted analyses). Similar to Model 2, the sparse number of Ranch Hands with pre-SEA acne only ($n = 4$) precluded meaningful adjusted analyses of these models.

Location of Acne (Post-SEA only)

The location of acne was analyzed for the participants with post-SEA acne only. Table 14-7 presents the spatial distribution of acne with primary emphasis on the temples, around the eyes, or on the ears. Due to the sparse number at individual sites, the analyses contrasted participants with acne on the temples, eyes, and ears, or a combination of these sites with participants with acne on other sites.

The Model 1 analysis of location of acne—temples, eyes, and ears versus other locations—for those participants with post-SEA acne did not uncover any statistically significant results (Table 14-8(a,b): $p > 0.13$ for all analyses). Covariate adjustment for Model 1 accounted for age and race.

Table 14-6.
Analysis of Acne Relative to Time of Duty in SEA
(Pre- and Post-SEA vs. Pre-SEA)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	Group	n	Percent Pre-/Post-SEA	Est. Relative Risk (95% C.I.)	p-Value
<i>All</i>	<i>Ranch Hand</i>	93	95.7	0.70 (0.17,2.85)	0.888
	<i>Comparison</i>	132	97.0		
Officer	Ranch Hand	32	93.8	0.29 (0.03,3.38)	0.665
	Comparison	52	98.1		
Enlisted Flyer	Ranch Hand	17	88.2	0.18 (0.01,3.98)	0.466
	Comparison	17	100.0		
Enlisted Groundcrew	Ranch Hand	44	100.0	5.15 (0.26,102.22)	0.383
	Comparison	63	95.2		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks^a
<i>All</i>	****	****	GROUP*AGE (p=0.002) GROUP*OCC (p=0.001)
Officer	****	****	
Enlisted Flyer	****	****	
Enlisted Groundcrew	****	****	

^a Covariates and associated p-values correspond to final model based on all participants with available data.

**** Group-by-covariate interaction ($p \leq 0.01$); adjusted relative risk, confidence interval, and p-value not presented; refer to Appendix Table J-2-1 for further analysis of this interaction.

Note: Pre-/Post-SEA = multiple occurrences of acne, both before and after the start of the first duty in SEA, or a case of acne that began before the start of the first duty in SEA and ended after starting duty in SEA.

Table 14-6. (Continued)
Analysis of Acne Relative to Time of Duty in SEA
(Pre- and Post-SEA vs. Pre-SEA)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log₂ (Initial Dioxin)^a	
Initial Dioxin	n	Percent Pre-/ & Post-SEA	Estimated Relative Risk (95% C.I.)^b	p-Value
Low	15	86.7	1.20 (0.44,3.29)	0.705
Medium	19	100.0		
High	16	93.8		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log₂ (Initial Dioxin)			
n	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
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^a Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

--: Analysis not performed due to the sparse number of pre-SEA only occurrences of acne.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Pre-/Post-SEA = multiple occurrences of acne, both before and after the start of the first duty in SEA, or a case of acne that began before the start of the first duty in SEA and ended after starting duty in SEA.

Table 14-6. (Continued)
Analysis of Acne Relative to Time of Duty in SEA
(Pre- and Post-SEA vs. Pre-SEA)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Pre-/Post-SEA	Est. Relative Risk (95% C.I.)^{ab}	p-Value
Comparison	117	96.6		
Background RH	37	97.3	1.37 (0.14,13.90)	0.786
Low RH	23	91.3	0.32 (0.05,1.99)	0.222
High RH	27	96.3	0.82 (0.08,8.19)	0.865
Low plus High RH	50	94.0	0.48 (0.10,2.36)	0.367

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)^b	p-Value	Covariate Remarks
Comparison	117			
Background RH	37	1.37 (0.14,13.90)	0.786	
Low RH	23	0.32 (0.05,1.99)	0.222	
High RH	27	0.82 (0.08,8.19)	0.865	
Low plus High RH	50	0.48 (0.10,2.36)	0.367	

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

Note: RH = Ranch Hand.

Comparison: Current Dioxin ≤ 10 ppt.

Background (Ranch Hand): Current Dioxin ≤ 10 ppt.

Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.

High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Pre-/Post-SEA = multiple occurrences of acne, both before and after the start of the first duty in SEA, or a case of acne that began before the start of the first duty in SEA and ended after starting duty in SEA.

Table 14-6. (Continued)
Analysis of Acne Relative to Time of Duty in SEA
(Pre- and Post-SEA vs. Pre-SEA)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
Model^a	Current Dioxin Category Percent Pre-/Post-SEA/(n)			Analysis Results for Log₂ (Current Dioxin + 1)	
	Low	Medium	High	Est. Relative Risk (95% C.I.)^b	p-Value
4	96.6 (29)	92.6 (27)	96.8 (31)	0.88 (0.48,1.61)	0.671
5	96.6 (29)	92.6 (27)	96.8 (31)	0.88 (0.52,1.48)	0.625
6 ^c	96.4 (28)	92.6 (27)	96.8 (31)	0.91 (0.50,1.66)	0.757

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
Model	Analysis Results for Log₂ (Current Dioxin + 1)			
	n	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
4	--	--	--	
5	--	--	--	
6	--	--	--	

^a Model 4: Log₂ (lipid-adjusted current dioxin + 1).
 Model 5: Log₂ (whole-weight current dioxin + 1).
 Model 6: Log₂ (whole-weight current dioxin + 1), adjusted for log₂ total lipids.

^b Relative risk for a twofold increase in current dioxin.

^c Adjusted for log₂ total lipids.

--: Analysis not performed due to the sparse number of pre-SEA only occurrences of acne.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
 Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.
 Pre-/Post-SEA = multiple occurrences of acne, both before and after the start of the first duty in SEA,
 or a case of acne that began before the start of the first duty in SEA and ended after starting duty in SEA.

Table 14-7.
Number of Participants with, and Location of, Post-SEA Acne

Location	Group	
	Ranch Hand	Comparison
Temples Only	222	271
Eyes Only	9	21
Ears Only	38	50
Temples and Eyes	19	15
Temples and Ears	43	53
Eyes and Ears	3	4
Temples, Eyes, and Ears	5	7
Other Sites	396	533

Location	Initial Dioxin	Current Dioxin
Temples Only	124	210
Eyes Only	4	9
Ears Only	14	31
Temples and Eyes	8	19
Temples and Ears	22	41
Eyes and Ears	0	3
Temples, Eyes, and Ears	5	5
Other Sites	222	374

Location	Current Dioxin Category				
	Comparison	Background RH	Low RH	High RH	Low plus High RH
Temples Only	233	86	67	57	124
Eyes Only	17	5	3	1	4
Ears Only	40	17	7	7	14
Temples and Eyes	12	11	4	4	8
Temples and Ears	45	19	12	10	22
Eyes and Ears	3	3	0	0	0
Temples, Eyes, and Ears	6	0	1	4	5
Other Sites	441	152	111	111	222

**Table 14-8.
Analysis of Location of Acne (Post-SEA)**

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	Group	n	Percent Temples/Eyes/Ears	Est. Relative Risk (95% C.I.)	p-Value
<i>All</i>	<i>Ranch Hand</i>	735	46.1	1.08 (0.89,1.32)	0.443
	<i>Comparison</i>	954	44.1		
Officer	Ranch Hand	291	48.1	1.06 (0.78,1.44)	0.777
	Comparison	379	46.7		
Enlisted Flyer	Ranch Hand	121	43.8	0.82 (0.51,1.31)	0.479
	Comparison	162	48.8		
Enlisted Groundcrew	Ranch Hand	323	45.2	1.24 (0.92,1.67)	0.175
	Comparison	413	40.0		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks^a
<i>All</i>	1.07 (0.88,1.31)	0.474	AGE (p<0.001) RACE (p<0.001)
Officer	1.04 (0.76,1.41)	0.821	
Enlisted Flyer	0.79 (0.49,1.27)	0.326	
Enlisted Groundcrew	1.26 (0.93,1.70)	0.139	

^a Covariates and associated p-values correspond to final model based on all participants with available data.

Note: Temples/Eyes/Ears = Temples, eyes, ears, temples and eyes, temples and ears, eyes and ears, or temples, eyes, and ears.

**Table 14-8. (Continued)
Analysis of Location of Acne (Post-SEA)**

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log₂ (Initial Dioxin)^a	
Initial Dioxin	n	Percent Temples/Eyes/Ears	Estimated Relative Risk (95% C.I.)^b	p-Value
Low	137	48.9	0.96 (0.82,1.11)	0.551
Medium	133	42.9		
High	129	41.1		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log₂ (Initial Dioxin)^c			
n	Adj. Relative Risk (95% C.I.)^b	p-Value	Covariate Remarks
399	1.00 (0.86,1.18)	0.961	AGE (p=0.012) RACE (p=0.059)

^a Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

^b Relative risk for a twofold increase in initial dioxin.

^c Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Temples/Eyes/Ears = Temples, eyes, ears, temples and eyes, temples and ears, eyes and ears, or temples, eyes, and ears.

**Table 14-8. (Continued)
Analysis of Location of Acne (Post-SEA)**

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Temples/Eyes/Ears	Est. Relative Risk (95% C.I.)^{ab}	p-Value
Comparison	797	44.7		
Background RH	293	48.1	1.17 (0.90,1.54)	0.246
Low RH	205	45.9	1.02 (0.75,1.39)	0.906
High RH	194	42.8	0.91 (0.66,1.26)	0.574
Low plus High RH	399	44.4	0.97 (0.76,1.23)	0.781

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	n	Adj. Relative Risk (95% C.I.)^c		p-Value	Covariate Remarks
Comparison	797				AGE (p<0.001) RACE (p<0.001)
Background RH	293	1.11 (0.84,1.46)		0.472	
Low RH	205	1.00 (0.73,1.37)		0.984	
High RH	194	1.01 (0.73,1.40)		0.936	
Low plus High RH	399	1.00 (0.78,1.29)		0.970	

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

^c Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.

Comparison: Current Dioxin ≤ 10 ppt.

Background (Ranch Hand): Current Dioxin ≤ 10 ppt.

Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.

High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Temples/Eyes/Ears = Temples, eyes, ears, temples and eyes, temples and ears, eyes and ears, or temples, eyes, and ears.

**Table 14-8. (Continued)
Analysis of Location of Acne (Post-SEA)**

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
Model^a	Current Dioxin Category Percent Temples/Eyes/Ears / (n)			Analysis Results for Log₂ (Current Dioxin + 1)	
	Low	Medium	High	Est. Relative Risk (95% C.I.)^b	p-Value
4	47.4 (228)	49.2 (238)	41.2 (226)	0.94 (0.84,1.04)	0.207
5	48.3 (234)	48.1 (235)	41.3 (223)	0.94 (0.86,1.03)	0.186
6 ^c	48.3 (234)	48.1 (235)	41.3 (223)	0.93 (0.84,1.03)	0.144

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
Model^a	Analysis Results for Log₂ (Current Dioxin + 1)			
	n	Adj. Relative Risk (95% C.I.)^b	p-Value	Covariate Remarks
4	692	0.97 (0.87,1.08)	0.607	AGE (p=0.001) RACE (p=0.005)
5	692	0.94 (0.84,1.04)	0.202	AGE (p<0.001) RACE (p=0.002) OCC (p=0.142)
6 ^d	692	0.94 (0.84,1.05)	0.236	AGE (p<0.001) RACE (p=0.002) OCC (p=0.142)

^a Model 4: Log₂ (lipid-adjusted current dioxin + 1).
 Model 5: Log₂ (whole-weight current dioxin + 1).
 Model 6: Log₂ (whole-weight current dioxin + 1), adjusted for log₂ total lipids.

^b Relative risk for a twofold increase in current dioxin.

^c Adjusted for log₂ total lipids.

^d Adjusted for log₂ total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
 Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.
 Temples/Eyes/Ears = Temples, eyes, ears, temples and eyes, temples and ears, eyes and ears, or temples, eyes, and ears.

analyses of both Models 2 and 3 accounted for age and race. As presented in Table 14-8(g,h), the analyses for Models 4 through 6 did not detect a significant association between current dioxin and location of acne for participants with post-SEA acne ($p > 0.14$ for all analyses). The Model 4 adjusted analysis included the significant covariates of age and race. Models 5 and 6 each accounted for the covariates age, race, and occupation.

Location of Acne (Pre- and Post-SEA and Post-SEA)

The location of acne was also analyzed for participants with pre- and post-SEA and post-SEA acne. Table 14-9 presents the spatial distribution of acne for these participants with primary emphasis on the temples, around the eyes, or on the ears. Due to the sparse numbers at individual sites, the analyses contrasted participants with acne on the temples, eyes, and ears, or any combination of these sites, with participants with acne on other sites.

The analysis of location of acne on the eyes, ears, and temples versus other locations for those participants with pre- and post-SEA and post-SEA acne did not show a significant association with group (Table 14-10(a,b): $p > 0.18$ for all analyses). The covariates age and race were significant in the adjusted analysis.

Examination of the unadjusted and adjusted results for Models 2 and 3 of location of acne also did not disclose a statistically significant association with initial or categorized dioxin (Table 14-10(c-f): $p > 0.25$ for all analyses). After adjusting for covariates, Model 2 accounted for age, and Model 3 accounted for age and race.

The unadjusted and adjusted analyses for Models 4 through 6 showed no significant relationship between current dioxin and location of acne (Table 14-10(g,h): $p > 0.17$ for all analyses) for participants with pre- and post-SEA and post-SEA acne. The adjusted analyses for Models 4 through 6 each accounted for age, race, and occupation.

Physical Examination Variables

Other Abnormalities

The analyses performed in Model 1 found no significant difference between the composite variable containing all other dermatologic abnormalities and group (Table 14-11(a,b): $p > 0.31$ for all contrasts). The covariates age, race, occupation, and presence of pre-SEA acne were included in the final adjusted model.

The unadjusted analysis for Model 2 showed no significant relationship between other abnormalities and initial dioxin (Table 14-11(c): $p = 0.216$); however, the adjusted analysis detected a highly significant initial dioxin-by-presence of pre-SEA acne interaction (Table 14-11(d): $p = 0.001$) as well as the following interactions: presence of pre-SEA acne and age, presence of pre-SEA acne and race, presence of pre-SEA acne and occupation, and race and occupation. Further examination of the interaction with initial dioxin is presented in Appendix Table J-2-2. The association between initial dioxin and the occurrence of other abnormalities was positive and significant ($p = 0.012$) for Ranch Hands with pre-SEA acne and negative but nonsignificant for Ranch Hands with no history of pre-SEA acne. In Model

Table 14-9.
Number of Participants with, and Location of, Pre- and Post-SEA and Post-SEA Acne

Location	Group	
	Ranch Hand	Comparison
Temples Only	253	314
Eyes Only	10	27
Ears Only	41	52
Temples and Eyes	19	16
Temples and Ears	48	67
Eyes and Ears	4	6
Temples, Eyes, and Ears	9	12
Other Sites	440	588

Location	Initial Dioxin	Current Dioxin
Temples Only	138	238
Eyes Only	5	10
Ears Only	16	34
Temples and Eyes	8	19
Temples and Ears	24	46
Eyes and Ears	0	4
Temples, Eyes, and Ears	8	9
Other Sites	247	415

Location	Current Dioxin Category				
	Comparison	Background RH	Low RH	High RH	Low plus High RH
Temples Only	271	100	72	66	138
Eyes Only	23	5	3	2	5
Ears Only	42	18	7	9	16
Temples and Eyes	13	11	4	4	8
Temples and Ears	58	22	13	11	24
Eyes and Ears	5	4	0	0	0
Temples, Eyes, and Ears	11	1	2	6	8
Other Sites	487	168	125	122	247

Table 14-10.
Analysis of Location of Acne (Pre- and Post-SEA and Post-SEA)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	Group	n	Percent Temples/Eyes/Ears	Est. Relative Risk (95% C.I.)	p-Value
<i>All</i>	<i>Ranch Hand</i>	824	46.6	1.04 (0.87,1.25)	0.716
	<i>Comparison</i>	1,082	45.7		
Officer	Ranch Hand	321	47.4	0.93 (0.70,1.25)	0.695
	Comparison	430	49.1		
Enlisted Flyer	Ranch Hand	136	44.9	0.92 (0.59,1.44)	0.801
	Comparison	179	46.9		
Enlisted Groundcrew	Ranch Hand	367	46.6	1.20 (0.91,1.58)	0.215
	Comparison	473	42.1		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks^a
<i>All</i>	1.03 (0.86,1.24)	0.753	AGE (p < 0.001) RACE (p < 0.001)
Officer	0.92 (0.69,1.23)	0.575	
Enlisted Flyer	0.88 (0.56,1.38)	0.577	
Enlisted Groundcrew	1.21 (0.91,1.59)	0.184	

^a Covariates and associated p-values correspond to final model based on all participants with available data.

Note: Temples/Eyes/Ears = Temples, eyes, ears, temples and eyes, temples and ears, eyes and ears, or temples, eyes, and ears.

Table 14-10. (Continued)
Analysis of Location of Acne (Pre- and Post-SEA and Post-SEA)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log₂ (Initial Dioxin)^a	
Initial Dioxin	n	Percent Temples/Eyes/Ears	Estimated Relative Risk (95% C.I.)^b	p-Value
Low	150	46.7	1.02 (0.88,1.17)	0.804
Medium	152	43.4		
High	144	43.8		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log₂ (Initial Dioxin)^c			
n	Adj. Relative Risk (95% C.I.)^b	p-Value	Covariate Remarks
446	1.09 (0.94,1.27)	0.252	AGE (p=0.002)

^a Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

^b Relative risk for a twofold increase in initial dioxin.

^c Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Temples/Eyes/Ears = Temples, eyes, ears, temples and eyes, temples and ears, eyes and ears, or temples, eyes, and ears.

Table 14-10. (Continued)
Analysis of Location of Acne (Pre- and Post-SEA and Post-SEA)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Temples/Eyes/Ears	Est. Relative Risk (95% C.I.)^{ab}	p-Value
Comparison	910	46.5		
Background RH	329	48.9	1.12 (0.87,1.44)	0.392
Low RH	226	44.7	0.91 (0.68,1.22)	0.537
High RH	220	44.5	0.92 (0.68,1.24)	0.594
Low plus High RH	446	44.6	0.92 (0.73,1.15)	0.457

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)^{ac}	p-Value	Covariate Remarks
Comparison	910			AGE (p<0.001) RACE (p<0.001)
Background RH	329	1.06 (0.82,1.37)	0.665	
Low RH	226	0.89 (0.66,1.20)	0.446	
High RH	220	1.01 (0.75,1.37)	0.950	
Low plus High RH	446	0.95 (0.75,1.19)	0.646	

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

^c Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.

Comparison: Current Dioxin ≤ 10 ppt.

Background (Ranch Hand): Current Dioxin ≤ 10 ppt.

Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.

High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Temples/Eyes/Ears = Temples, eyes, ears, temples and eyes, temples and ears, eyes and ears, or temples, eyes, and ears.

Table 14-10. (Continued)
Analysis of Location of Acne (Pre- and Post-SEA and Post-SEA)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
Model^a	Current Dioxin Category Percent Temples/Eyes/Ears /(n)			Analysis Results for Log₂ (Current Dioxin + 1)	
	Low	Medium	High	Est. Relative Risk (95% C.I.)^b	p-Value
4	47.7 (256)	49.0 (263)	42.6 (256)	0.95 (0.86,1.05)	0.321
5	48.9 (262)	47.3 (260)	43.1 (253)	0.95 (0.88,1.04)	0.265
6 ^c	48.7 (261)	47.3 (260)	43.1 (253)	0.95 (0.86,1.04)	0.226

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
Model^a	Analysis Results for Log₂ (Current Dioxin + 1)			
	n	Adj. Relative Risk (95% C.I.)^b	p-Value	Covariate Remarks
4	775	0.94 (0.84,1.05)	0.265	AGE (p<0.001) RACE (p=0.005) OCC (p=0.076)
5	775	0.94 (0.85,1.03)	0.178	AGE (p<0.001) RACE (p=0.005) OCC (p=0.063)
6 ^d	774	0.94 (0.85,1.04)	0.222	AGE (p<0.001) RACE (p=0.006) OCC (p=0.067)

^a Model 4: Log₂ (lipid-adjusted current dioxin + 1).
 Model 5: Log₂ (whole-weight current dioxin + 1).
 Model 6: Log₂ (whole-weight current dioxin + 1), adjusted for log₂ total lipids.

^b Relative risk for a twofold increase in current dioxin.

^c Adjusted for log₂ total lipids.

^d Adjusted for log₂ total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
 Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.
 Temples/Eyes/Ears = Temples, eyes, ears, temples and eyes, temples and ears, eyes and ears, or temples, eyes, and ears.

Table 14-11.
Analysis of Other Abnormalities

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	Group	n	Percent Abnormal	Est. Relative Risk (95% C.I.)	p-Value
<i>All</i>	<i>Ranch Hand</i>	<i>952</i>	<i>83.6</i>	<i>1.13 (0.90,1.41)</i>	<i>0.329</i>
	<i>Comparison</i>	<i>1,279</i>	<i>81.9</i>		
Officer	Ranch Hand	367	85.8	1.19 (0.81,1.73)	0.429
	Comparison	501	83.6		
Enlisted Flyer	Ranch Hand	162	84.6	0.85 (0.47,1.52)	0.683
	Comparison	202	86.6		
Enlisted Groundcrew	Ranch Hand	423	81.3	1.17 (0.85,1.61)	0.370
	Comparison	576	78.8		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks^a
<i>All</i>	<i>1.10 (0.88,1.39)</i>	<i>0.400</i>	AGE (p<0.001) RACE (p=0.006)
Officer	1.14 (0.77,1.68)	0.516	OCC (p=0.017)
Enlisted Flyer	0.81 (0.44,1.47)	0.482	PRESEA (p=0.076)
Enlisted Groundcrew	1.18 (0.85,1.64)	0.310	

^a Covariates and associated p-values correspond to final model based on all participants with available data.

**Table 14-11. (Continued)
Analysis of Other Abnormalities**

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log₂ (Initial Dioxin)^a	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)^b	p-Value
Low	174	83.9	0.90 (0.75,1.07)	0.216
Medium	173	82.7		
High	173	80.9		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log₂ (Initial Dioxin)^c			
n	Adj. Relative Risk (95% C.I.)^b	p-Value	Covariate Remarks
520	****	****	INIT*PRESEA (p=0.001) AGE*PRESEA (p=0.025) RACE*PRESEA (p=0.007) OCC*PRESEA (p=0.003) RACE*OCC (p=0.031)

^a Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

^b Relative risk for a twofold increase in initial dioxin.

^c Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

**** Log₂ (initial dioxin) by-covariate interaction (p ≤ 0.01); relative risk, confidence interval, and p-value not presented; refer to Appendix Table J-2-2 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
INIT = Log₂ (initial dioxin).

**Table 14-11. (Continued)
Analysis of Other Abnormalities**

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)^{ab}	p-Value
Comparison	1,061	81.3		
Background RH	374	85.3	1.44 (1.04,2.01)	0.029
Low RH	260	84.6	1.20 (0.83,1.74)	0.342
High RH	260	80.4	0.89 (0.63,1.26)	0.519
Low plus High RH	520	82.5	1.03 (0.78,1.35)	0.849

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)^{ac}	p-Value	Covariate Remarks
Comparison	1,061			AGE (p<0.001) OCC (p=0.005) RACE (p=0.002) PRESEA (p=0.037)
Background RH	374	1.41 (1.00,1.99)	0.052	
Low RH	260	1.13 (0.77,1.68)	0.525	
High RH	260	0.98 (0.67,1.41)	0.896	
Low plus High RH	520	1.05 (0.78,1.40)	0.749	

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

^c Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.

Comparison: Current Dioxin ≤ 10 ppt.

Background (Ranch Hand): Current Dioxin ≤ 10 ppt.

Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.

High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 14-11. (Continued)
Analysis of Other Abnormalities

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
Model^a	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log₂ (Current Dioxin + 1)	
	Low	Medium	High	Est. Relative Risk (95% C.I.)^b	p-Value
4	86.4 (295)	83.7 (300)	80.9 (299)	0.89 (0.79,1.01)	0.062
5	85.7 (300)	83.5 (297)	81.8 (297)	0.93 (0.84,1.03)	0.180
6 ^c	85.6 (299)	83.5 (297)	81.8 (297)	0.89 (0.79,0.99)	0.038

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
Model^a	Analysis Results for Log₂ (Current Dioxin + 1)			
	n	Adj. Relative Risk (95% C.I.)^b	p-Value	Covariate Remarks
4	894	0.93 (0.81,1.07)	0.318	AGE (p<0.001) PRESEA (p=0.104) RACE*OCC (p=0.032)
5	894	0.97 (0.86,1.09)	0.566	AGE (p<0.001) PRESEA (p=0.105) RACE*OCC (p=0.029)
6 ^d	893	0.93 (0.81,1.06)	0.264	AGE (p<0.001) PRESEA (p=0.084) RACE*OCC (p=0.0228)

^a Model 4: Log₂ (lipid-adjusted current dioxin + 1).
 Model 5: Log₂ (whole-weight current dioxin + 1).
 Model 6: Log₂ (whole-weight current dioxin + 1), adjusted for log₂ total lipids.

^b Relative risk for a twofold increase in current dioxin.

^c Adjusted for log₂ total lipids.

^d Adjusted for log₂ total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
 Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Appendix Table J-2-2. The association between initial dioxin and the occurrence of other abnormalities was positive and significant ($p=0.012$) for Ranch Hands with pre-SEA acne and negative but nonsignificant for Ranch Hands with no history of pre-SEA acne. In Model 3, the unadjusted analysis exhibited a significantly higher percentage of other abnormalities in the background Ranch Hand category (85.3%) than in the Comparison category (81.3%) (Table 14-11(e): $p=0.029$, Est. RR=1.44) but no significant difference in the other dioxin categories. Similarly, the adjusted analysis showed a marginally significant difference between background Ranch Hands and Comparisons (Table 14-11(f): $p=0.052$, Adj. RR=1.41). The adjusted analysis for Model 3 contained the significant covariates age, occupation, race, and presence of pre-SEA acne.

The unadjusted analysis for Model 4 showed a marginally significant inverse association between other abnormalities and current lipid-adjusted dioxin (Table 14-11(g): $p=0.062$, Est. RR=0.89). The percentages of Ranch Hands with at least one other abnormality were 86.4 percent, 83.7 percent, and 80.9 percent for low, medium, and high current lipid-adjusted dioxin categories respectively. In the adjusted analysis for Model 4, no significant relationship was found between current dioxin and other abnormalities. Examination of the unadjusted and adjusted analyses of other abnormalities for Model 5 did not show any statistically significant results (Table 14-11(g,h): $p \geq 0.18$ for unadjusted and adjusted analyses). The unadjusted analysis for Model 6 revealed a statistically significant inverse association between current whole-weight dioxin and other abnormalities (Table 14-11(g): $p=0.038$, Est. RR=0.89). The percentage of Ranch Hands with at least one other dermatologic abnormality index decreased over the low, medium, and high current whole-weight dioxin categories (85.6%, 83.5%, and 81.8%). The adjusted analysis for Model 6 did not detect any statistically significant results. Models 4, 5, and 6 accounted for age, presence of pre-SEA acne, and a race-by-occupation interaction in the adjusted final model.

Dermatology Index

Analysis of the dermatology index did not reveal a significant difference between Ranch Hands and Comparisons in the unadjusted analysis for Model 1 (Table 14-12(a): $p > 0.10$ for all analyses). However, a highly significant group-by-age interaction was detected in the adjusted analysis (Table 14-12(b): $p=0.005$). Stratified results of the interaction are presented in Appendix Table J-2-3. There was not a significant association between group and the dermatology index for younger participants; however older Comparisons had a marginally significant higher percentage of an abnormal dermatology index than older Ranch Hands (Adj. RR=0.80, $p=0.58$). After further stratifying by occupation, there were still no significant differences between younger Ranch Hands and younger Comparisons for the dermatology index. For older participants, there was a significant difference between Ranch Hands and Comparisons for the enlisted flyer stratum ($p=0.034$). For this stratum, older enlisted flyer Ranch Hands had fewer occurrences of an abnormal dermatology index (45.2%) than older enlisted flyer Comparisons (53.8%). In addition to the group-by-age interaction, race, occupation, and presence of pre-SEA acne were significant in the final adjusted model.

The unadjusted analyses for Models 2 and 3 did not disclose a significant relationship between initial or categorized dioxin and the dermatology index (Table 14-12(c,e): $p > 0.11$).

Table 14-12.
Analysis of Dermatology Index

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	Group	n	Percent Abnormal	Est. Relative Risk (95% C.I.)	p-Value
<i>All</i>	<i>Ranch Hand</i>	952	43.8	0.94 (0.80,1.11)	0.505
	<i>Comparison</i>	1,280	45.3		
Officer	Ranch Hand	367	38.1	0.93 (0.71,1.23)	0.664
	Comparison	502	39.8		
Enlisted Flyer	Ranch Hand	162	44.4	0.70 (0.46,1.06)	0.108
	Comparison	202	53.5		
Enlisted Groundcrew	Ranch Hand	423	48.5	1.05 (0.82,1.35)	0.746
	Comparison	576	47.2		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks^a
<i>All</i>	****	****	GROUP*AGE (p=0.005) RACE (p<0.001) OCC (p<0.001) PRESEA (p<0.001)
Officer	****	****	
Enlisted Flyer	****	****	
Enlisted Groundcrew	****	****	

^a Covariates and associated p-values correspond to final model based on all participants with available data.

**** Group-by-covariate interaction (p≤0.01); relative risk, confidence interval, and p-value not presented; refer to Appendix Table J-2-3 for further analysis of this interaction.

**Table 14-12. (Continued)
Analysis of Dermatology Index**

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log₂ (Initial Dioxin)^a	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)^b	p-Value
Low	174	37.9	1.03 (0.90,1.18)	0.673
Medium	173	45.7		
High	173	39.9		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED				
Analysis Results for Log₂ (Initial Dioxin)^c				
n	Adj. Relative Risk (95% C.I.)^b	p-Value	Covariate Remarks	
520	0.92 (0.79,1.07)	0.282	RACE (p=0.082) OCC (p=0.005) PRESEA (p=0.063)	

^a Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

^b Relative risk for a twofold increase in initial dioxin.

^c Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 14-12. (Continued)
Analysis of Dermatology Index

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY -- UNADJUSTED				
Dioxin Category	n	Percent Abnormal	Est. Relative Risk (95% C.I.)^{ab}	p-Value
Comparison	1,062	44.8		
Background RH	374	46.8	1.13 (0.89,1.43)	0.332
Low RH	260	40.4	0.83 (0.63,1.09)	0.180
High RH	260	41.9	0.86 (0.65,1.13)	0.271
Low plus High RH	520	41.2	0.84 (0.68,1.04)	0.114

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY -- ADJUSTED					
Dioxin Category	n	Adj. Relative Risk (95% C.I.)^c		p-Value	Covariate Remarks
Comparison	1,062				DXCAT*AGE (p=0.013) OCC (p<0.001) RACE (p=0.001) PRESEA (p<0.001)
Background RH	374	1.26 (0.98,1.61)**		0.070**	
Low RH	260	0.80 (0.60,1.06)**		0.124**	
High RH	260	0.77 (0.58,1.03)**		0.075**	
Low plus High RH	520	0.79 (0.63,0.98)**		0.031**	

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

^c Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table J-2-4 for further analysis of this interaction.

Note: RH = Ranch Hand.

Comparison: Current Dioxin \leq 10 ppt.

Background (Ranch Hand): Current Dioxin \leq 10 ppt.

Low (Ranch Hand): Current Dioxin $>$ 10 ppt, ppt $<$ Initial Dioxin \leq 143 ppt.

High (Ranch Hand): Current Dioxin $>$ 10 ppt, Initial Dioxin $>$ 143 ppt.

DXCAT=Categorized Dioxin.

**Table 14-12. (Continued)
Analysis of Dermatology Index**

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
Model^a	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log₂ (Current Dioxin + 1)	
	Low	Medium	High	Est. Relative Risk (95% C.I.)^b	p-Value
4	48.1 (295)	39.7 (300)	42.8 (299)	0.94 (0.86,1.03)	0.167
5	46.7 (300)	42.4 (297)	41.4 (297)	0.94 (0.87,1.01)	0.099
6 ^c	46.5 (299)	42.4 (297)	41.4 (297)	0.95 (0.88,1.04)	0.253

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED					
Model^a	n	Analysis Results for Log₂ (Current Dioxin + 1)			Covariate Remarks
		Adj. Relative Risk (95% C.I.)^b	p-Value		
4	894	0.85 (0.77,0.95)	0.003	RACE (p=0.028) OCC (p=0.002) PRESEA (p=0.008)	
5	894	0.87 (0.79,0.95)	0.002	RACE (p=0.030) OCC (p=0.002) PRESEA (p=0.009)	
6 ^d	893	0.87 (0.79,0.96)	0.006	RACE (p=0.031) OCC (p=0.002) PRESEA (p=0.010)	

^a Model 4: Log₂ (lipid-adjusted current dioxin + 1).
 Model 5: Log₂ (whole-weight current dioxin + 1).
 Model 6: Log₂ (whole-weight current dioxin + 1), adjusted for log₂ total lipids.

^b Relative risk for a twofold increase in current dioxin.

^c Adjusted for log₂ total lipids.

^d Adjusted for log₂ total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
 Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

The results of the adjusted analysis for Model 2, which accounted for race, occupation, and presence of pre-SEA acne in the final model, were also nonsignificant (Table 14-12(d): $p=0.282$). However, the adjusted analysis of Model 3 showed a significant categorized dioxin-by-age interaction (Table 14-12(f): $p=0.013$). The covariates occupation, race, and presence of pre-SEA acne were also significant in the final adjusted model. Stratified results of the dioxin-by-age interaction are displayed in Appendix Table J-2-3. Removing the interaction from the model revealed significant relative risks for the following contrasts: background Ranch Hands versus Comparisons ($p=0.070$, Adj. RR=1.26), high Ranch Hands versus Comparisons ($p=0.075$, Adj. RR=0.77), and low plus high Ranch Hands versus Comparisons ($p=0.031$, Adj. RR=0.79). After removing occupation from the model, none of the above contrasts were significant (Appendix Table J-3-7: $p>0.10$).

The unadjusted analyses for Models 4 and 6 did not detect a significant association between the dermatology index and current dioxin. However, the unadjusted analysis for Model 5 displayed a marginally significant inverse association between current whole-weight dioxin and the dermatology index (Table 14-12(g): $p=0.099$, Est. RR=0.94). The percentages of Ranch Hands with an abnormal dermatology index in the low, medium, and high current whole-weight dioxin categories for Model 5 were 46.7, 42.4, and 41.4 respectively. The adjusted analyses for Models 4, 5, and 6 all displayed a highly significant inverse relationship between the dermatology index and current dioxin (Table 14-12(h): $p=0.003$, Adj. RR=0.85; $p=0.002$, Adj. RR=0.87; $p=0.006$, Adj. RR=0.87). The covariates of race, occupation, and presence of pre-SEA acne were significant in the final adjusted model for Models 4, 5, and 6. However, after excluding occupation from the final models, the results for Models 4, 5, and 6 were no longer significant (Appendix Table J-3-7: $p>0.10$).

DISCUSSION

In the study of biological effects of herbicides in humans, the dermatologic examination assumes special importance. Of the organ systems analyzed in this report, only the skin has a clinical endpoint (chloracne) that has been related conclusively to dioxin exposure. Although the intact skin is an effective protective barrier to a wide range of industrial chemicals, it also can serve as a portal of entry across which other internal organ systems can be placed at risk for toxicity.

In dermatologic practice particularly, the history can be more important to accurate diagnosis than the physical examination findings. Chloracne, for example, apart from the characteristic cutaneous distribution, has no hallmark features that distinguish it from other more common acneiform eruptions. In the current study, examiners were strictly forbidden from taking any occupational history, a restriction considered essential to the elimination of observer bias. As in previous examination cycles, skin lesions felt to be suspicious for skin cancer were biopsied. Although blind to the participants' status, examiners performed a similar number of biopsies in the Ranch Hand (20 out of 952) and Comparison (34 out of 1,281) cohorts.

Because chloracne is rare, few dermatologists will encounter even a single case in a lifetime of clinical practice. Experimental dose-response studies in animals and humans have

confirmed that the topical concentrations of TCDD required to produce overt lesions are far greater than the concentrations to which participants in the current study were likely to have been exposed during service in SEA. It is therefore not surprising that, in the four examination cycles to date, no cases of chloracne have been detected. Recognizing the remote possibility that acute cases of chloracne might have occurred and resolved, several chronic complications of all forms of acne (scarring and hyperpigmentation) were included in the dermatology index as dependent variables in the comparative analyses. The prevalence of these complications of acne were similar in the two groups.

Most of the dependent variable-covariate associations documented would be expected in clinical practice. Age-related changes in the epidermis, stratum corneum, and corium layers of the skin are associated with thinning of the skin, an increase in capillary fragility, hyperkeratinization, dyshydrosis with wrinkling and scaling, and loss of elasticity. Hyperplasia of the epidermis is associated typically with keratoses (seborrheic and senile) and basal cell carcinomas. With the exception of typical acne, which is more common at an early age, an increase in most other forms of skin disease would be expected over time and were documented in the current study.

Several of the highly significant covariate associations can be explained on race-specific variations well established in dermatologic practice. Many of the components of the dermatology index, for example, occur far more commonly in Blacks than non-Blacks. Pseudofolliculitis barbae, a cutaneous inflammatory reaction to ingrown hair, occurs almost exclusively in Black males who shave. This highly prevalent condition, associated with hyperpigmentation, no doubt contributed to the highly significant association of an abnormal index in Blacks versus non-Blacks (64.1% vs. 43.5%, $p < 0.001$). In contrast, the prevalence of the composite other abnormalities was significantly greater in non-Blacks (83.3% vs. 72.5%, $p = 0.002$) and includes the components of dermatosis and actinic keratoses, which are rare in Blacks.

Although the lifetime occurrence of acne as self-reported by questionnaire was similar in both groups, Ranch Hand enlisted groundcrew, those most heavily exposed to TCDD, appeared to be at increased risk for the development of acne subsequent to time of duty in SEA. The possibility of bias associated with self-reporting is raised, however, in that on physical examination no group differences were defined.

In the analyses relating other abnormalities to the current and extrapolated initial body burden of dioxin, Ranch Hands with background levels of serum dioxin had a higher prevalence of certain dermatoses than Comparisons (85.3% vs. 81.3%, $p = 0.029$). However, in all models employing current serum dioxin data, Ranch Hands with the highest levels of serum dioxin had fewer abnormalities on physical examination than those with medium and low levels (see Table 14-11). Although the differences were not statistically significant, these results provide evidence against a dose-response effect, as does the lower occurrence of an abnormal dermatology index in Ranch Hands with low and high levels of serum dioxin relative to Comparisons (41.9% vs. 44.8%, $p = 0.031$).

In summary, consistent with prior examinations, there was no evidence to suggest a dioxin effect on the skin.

SUMMARY

The Dermatologic Assessment was based on the following health endpoints: occurrence of acne (lifetime and relative to time of duty in SEA); location of acne; other abnormalities (a composite of 16 dermatologic conditions); and a dermatology index based on the presence of comedones, acneiform lesions, acneiform scars, and inclusion cysts, depigmentation, and hyperpigmentation. Each of these variables was analyzed for associations with group (Model 1), initial dioxin (Model 2), categorized dioxin (Model 3), current lipid-adjusted dioxin (Model 4), and current whole-weight dioxin (Models 5 and 6). Tables 14-13, 14-14, 14-15, and 14-16 summarize the results. A summary of group-by-covariate and dioxin-by-covariate interactions is provided in Table 14-17.

Model 1: Group Analysis

In the unadjusted analyses of Model 1, none of the dermatology variables showed a significant relationship with group except for acne relative to time of duty in SEA. When enlisted groundcrew with post-SEA acne only or those who had acne both before and after the start of their time of duty in SEA (pre- and post-SEA) were contrasted with enlisted groundcrew who did not have acne after the start of their duty in SEA (pre-SEA and none), a significant direct association between group and post-SEA acne was found ($p=0.042$). This association exhibits an increased risk of post-SEA acne for the Ranch Hand enlisted groundcrew.

In the adjusted analysis of acne relative to time of duty in SEA, an association with group was found for the enlisted groundcrew for the pre- and post-SEA and post-SEA versus pre-SEA and none contrast ($p=0.025$, Adj. RR=1.51) and for the post-SEA acne versus none contrast ($p=0.041$, Adj. RR=1.47). Also, for the subset of participants with pre-SEA acne, there were significant interactions between group and age and between group and occupation. These interactions could have been caused by or affected by the small number of participants with only pre-SEA acne in each stratum. The dermatology index variable also showed a significant interaction between group and age in the adjusted analysis. For older participants, Ranch Hands in the low and high initial dioxin categories had significantly lower percentages of an abnormal dermatology index than Comparisons.

Model 2: Initial Dioxin Analysis

The unadjusted analyses of Model 2 did not find a significant association between any of the dependent variables and the continuous measure of initial dioxin in Ranch Hands. The adjusted analysis for other abnormalities detected a significant interaction between initial dioxin and presence of pre-SEA acne.

Model 3: Categorized Dioxin Analysis

In Model 3, the unadjusted analyses for categorized dioxin exhibited a significantly higher percentage of other abnormalities in the background Ranch Hands category than in the Comparisons category ($p=0.029$). Similarly, the adjusted analyses for other abnormalities detected a marginally significant higher occurrence of other abnormalities in the background

Table 14-13.
Summary of Group Analyses (Model 1) for Dermatology Variables
(Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Questionnaire				
Occurrence of Acne (Lifetime)	NS	NS	ns	NS*
<u>Acne Relative to Time of Duty in SEA</u>				
Pre- & Post-SEA and Post-SEA vs. Pre-SEA and None	NS	NS	ns	+0.042
Post-SEA vs. None	NS	NS	ns	NS*
Pre- & Post-SEA vs. Pre-SEA	ns	ns	ns	NS
Location of Acne (Post-SEA)	NS	NS	ns	NS
Location of Acne (Pre- & Post-SEA and Post-SEA)	NS	ns	ns	NS
Physical Examination				
Other Abnormalities	NS	NS	ns	NS
Dermatology Index	ns	ns	ns	NS

+: Relative risk ≥ 1.00 .

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

NS*: Marginally significant ($0.05 < p \leq 0.10$).

Note: P-value given if $p \leq 0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater. A lower case "ns" denotes relative risk less than 1.00.

Table 14-13. (Continued)
Summary of Group Analyses (Model 1) for Dermatology Variables
(Ranch Hands vs. Comparisons)

Variable	ADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Questionnaire				
Occurrence of Acne (Lifetime)	NS	NS	ns	NS*
<u>Acne Relative to Time of Duty in SEA</u>				
Pre- & Post-SEA and Post-SEA vs. Pre-SEA and None	NS	NS	ns	+0.025
Post-SEA vs. None	NS	NS	ns	+0.041
Pre- & Post-SEA vs. Pre-SEA	****	****	****	****
Location of Acne (Post-SEA)	NS	NS	ns	NS
Location of Acne (Pre- & Post-SEA and Post-SEA)	NS	ns	ns	NS
Physical Examination				
Other Abnormalities	NS	NS	ns	NS
Dermatology Index	****	****	****	****

+: Relative risk ≥ 1.00 .

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

NS*: Marginally significant ($0.05 < p \leq 0.10$).

**** Group-by-covariate interaction ($p \leq 0.01$); refer to Appendix J-2 for further analysis of this interaction.

Note: P-value given if $p \leq 0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater. A lower case "ns" denotes relative risk less than 1.00.

Table 14-14.
Summary of Initial Dioxin Analyses (Model 2) for Dermatology Variables
(Ranch Hands Only)

Variable	Unadjusted	Adjusted
Questionnaire		
Occurrence of Acne (Lifetime)	ns	ns
Acne Relative to Time of Duty in SEA		
Pre- & Post-SEA and Post-SEA vs. Pre-SEA and None	ns	ns
Post-SEA vs. None	ns	ns
Pre- & Post-SEA vs. Pre-SEA	NS	--
Location of Acne (Post-SEA)	ns	NS
Location of Acne (Pre- & Post-SEA and Post-SEA)	NS	NS
Physical Examination		
Other Abnormalities	ns	****
Dermatology Index	NS	ns

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

--: Adjusted analysis not performed due to sparseness of pre-SEA only occurrences of acne.

**** Log_2 (initial dioxin)-by-covariate interaction ($p \leq 0.01$); refer to Appendix J-2 for further analysis of this interaction.

Note: A capital "NS" denotes a relative risk of 1.00 or greater. A lower case "ns" denotes relative risk less than 1.00.

Table 14-15.
Summary of Categorized Dioxin Analyses (Model 3) for Dermatology Variables
(Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Questionnaire				
Occurrence of Acne (Lifetime)	NS	NS	ns	NS
Acne Relative to Time of Duty in SEA				
Pre- & Post-SEA and Post-SEA vs. Pre-SEA and None	NS	NS	ns	NS
Post-SEA vs. None	NS	NS	ns	NS
Pre- & Post-SEA vs. Pre-SEA	NS	ns	ns	ns
Location of Acne (Post-SEA)	NS	NS	ns	ns
Location of Acne (Pre- & Post-SEA and Post-SEA)	NS	ns	ns	ns
Physical Examination				
Other Abnormalities	+0.029	NS	ns	NS
Dermatology Index	NS	ns	ns	ns

+: Relative risk ≥ 1.00 .

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

Note: P-value given if $p \leq 0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater. A lower case "ns" denotes relative risk less than 1.00.

Table 14-15. (Continued)
Summary of Categorized Dioxin (Model 3) for Dermatology Variables
(Ranch Hands vs. Comparisons)

Variable	ADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Questionnaire				
Occurrence of Acne (Lifetime)	NS	NS	NS	NS
Acne Relative to Time of Duty in SEA				
Pre- & Post-SEA and Post-SEA vs. Pre-SEA and None	NS	NS	NS	NS
Post-SEA vs. None	NS	NS	NS	NS
Pre- & Post-SEA vs. Pre-SEA	NS	ns	ns	ns
Location of Acne (Post-SEA)	NS	NS	NS	NS
Location of Acne (Pre- & Post-SEA and Post-SEA)	NS	ns	NS	ns
Physical Examination				
Other Abnormalities	NS*	NS	ns	NS
Dermatology Index	** (NS*)	** (ns)	** (ns*)	** (-0.031)

-: Relative risk < 1.00.

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

NS* or ns*: Marginally significant ($0.05 < p \leq 0.10$).

** (ns): Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); not significant when interaction is deleted; refer to Appendix J-2 for further analysis of this interaction.

** (NS*) or ** (ns*): Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); marginally significant when interaction is deleted; refer to Appendix J-2 for further analysis of this interaction.

** (-0.031): Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); significant ($p = 0.031$) when interaction is deleted; refer to Appendix J-2 for further analysis of this interaction.

Note: P-value given if $p \leq 0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater. A lower case "ns" denotes relative risk less than 1.00.

Table 14-16.
Summary of Group Analyses (Models 4, 5, and 6) for Dermatology Variables
(Ranch Hands Only)

Variable	UNADJUSTED		
	Model 4: Lipid-Adjusted Current Dioxin	Model 5: Whole-Weight Current Dioxin	Model 6: Whole-Weight Current Dioxin Adjusted for Total Lipids
Questionnaire			
Occurrence of Acne (Lifetime)	ns	ns	ns
Acne Relative to Time of Duty in SEA			
Pre- & Post-SEA and Post-SEA vs. Pre-SEA and None	ns	ns	ns
Post-SEA VS. None	ns	ns	ns
Pre- & Post-SEA vs. Pre-SEA	ns	ns	ns
Location of Acne (Post-SEA)	ns	ns	ns
Location of Acne (Pre- & Post-SEA and Post-SEA)	ns	ns	ns
Physical Examination			
Other Abnormalities	ns*	ns	-0.038
Dermatology Index	ns	ns*	ns

-.: Relative risk < 1.00.

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

ns*: Marginally significant ($0.05 < p \leq 0.10$).

Note: P-value given if $p \leq 0.05$.

A lower case "ns" denotes relative risk less than 1.00.

Table 14-16. (Continued)
Summary of Group Analyses (Models 4, 5, and 6) for Dermatology Variables
(Ranch Hands Only)

Variable	ADJUSTED		
	Model 4: Lipid-Adjusted Current Dioxin	Model 5: Whole-Weight Current Dioxin	Model 6: Whole-Weight Current Dioxin Adjusted for Total Lipids
Questionnaire			
Occurrence of Acne (Lifetime)	ns	ns	ns
Acne Relative to Time of Duty in SEA			
Pre- & Post-SEA and Post-SEA vs. Pre-SEA and None	ns	ns	ns
Post-SEA vs. None	ns	ns	ns
Pre- & Post-SEA vs. Pre-SEA	--	--	--
Location of Acne (Post-SEA)	ns	ns	ns
Location of Acne (Pre- & Post-SEA and Post-SEA)	ns	ns	ns
Physical Examination			
Other Abnormalities	ns	ns	ns
Dermatology Index	-0.003	-0.002	-0.006

-: Relative risk < 1.00.

ns: Not significant (p > 0.10).

--: Adjusted analysis not performed due to sparseness of pre-SEA only occurrences of acne.

Note: P-value given if p ≤ 0.05.

A lower case "ns" denotes relative risk less than 1.00.

Table 14-17.
Summary Table of Group-by-Covariate and Dioxin-by-Covariate Interactions
from Adjusted Analyses of Dermatology Variables

Model	Variable	Covariate
1 ^a	Acne Relative to Time of Duty in SEA (Pre- & Post- SEA vs. Pre-SEA)	Age, Occupation
	Dermatology Index	Age
2 ^b	Other Abnormalities	Presence of Pre-SEA Acne
3 ^c	Dermatology Index	Age

^a Group analysis (Ranch Hand vs. Comparison).

^b Ranch Hands - Log₂ (Initial Dioxin).

^c Categorized Dioxin.

Ranch Hands than in Comparisons. The dermatology index variable showed a significant interaction between categorized dioxin and age in the adjusted analysis. When this interaction was removed from the adjusted model, the background Ranch Hands showed a marginally significant higher occurrence of an abnormal dermatology index than Comparisons ($p=0.070$), while the high Ranch Hands showed a marginally lower occurrence of an abnormal dermatology index. When Ranch Hands in the low and high initial dioxin categories were combined and contrasted with Comparisons, Ranch Hands displayed a significantly lower occurrence of an abnormal dermatology index ($p=0.031$).

Models 4, 5, and 6: Current Dioxin Analysis

The unadjusted analyses of both Models 4 and 6 showed marginal and significant inverse associations between other abnormalities and current dioxin ($p=0.062$ and $p=0.038$ respectively). However, after adjusting for age, occupation, and presence of pre-SEA acne, these associations were no longer significant. In addition, the unadjusted analysis of Model 5 detected a marginally significant inverse relationship between current whole-weight dioxin and the dermatology index ($p=0.099$). In Models 4, 5, and 6, the adjusted analyses also detected a highly significant inverse association between current dioxin and the dermatology index ($p=0.003$, $p=0.002$, $p=0.006$, respectively; Adj. RR < 0.88 for all analyses).

CONCLUSION

In general, the dermatology variables showed no significant differences between Ranch Hands and Comparisons except for a few significant results for acne for enlisted groundcrew participants. In these significant analyses, Ranch Hands had higher occurrences of acne than Comparisons.

The analyses of categorized initial dioxin indicated a marginally significant positive difference between background Ranch Hands and Comparisons for the composite variable other abnormalities. The analyses of categorized initial dioxin also indicated a significantly lower occurrence of dermatology index abnormalities for Ranch Hands in the low plus high category than for Comparisons. However, the background Ranch Hands showed a marginally significant higher occurrence of dermatology index abnormalities than Comparisons.

The analysis of dermatology index exhibited a significant negative association with current dioxin in Models 4, 5, and 6. Also, all other results for Models 4, 5, and 6, although nonsignificant, displayed a negative association between current dioxin and the dermatology variables.

In summary, there is no consistent evidence in these data to suggest an adverse dioxin effect on the dermatologic system at doses received by U.S. military personnel in SEA.

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