Chapter XV

DERMATOLOGIC EVALUATION

A thorough dermatologic assessment was deemed essential because chloracne is the only recognized definitive clinical end point following exposure to chlorophenols and dioxin. Over one-half of all veteran complaints recorded in the Veterans Administration Herbicide Registry cited dermatologic symptoms. These facts, coupled with the knowledge that chloracne is transient following a single point exposure (Homberger, 1979), suggested that there is a significant potential to misclassify adolescent acne and chloracne. While the issue of correct diagnosis could be resolved by biopsies and histopathologic characterizations in all participants, this approach was rejected on ethical grounds, as well as concern for the adverse impact of biopsy procedures on future study participation. Consequently, the dermatologic assessment was carefully planned to collect historical and distributional dermatologic data by questionnaire, followed by a detailed corroborative physical examination, supplemented by voluntary biopsies when indicated. Most data reported in this chapter are from the 1045 Ranch Handers and the 773 originally selected comparison individuals enrolled in the study. Minor fluctuations from these denominators reflect missing dependent variable or covariate data. Relative risks and confidence intervals are shown for all dependent variables in Appendix XVIII.

1. Questionnaire Data

The in-home study questionnaire collected detailed medical histories on the occurrence of acne. These data are displayed in Table XV-1 and show that the Ranch Handers reported slightly more acne than their comparisons.

Table XV-1

REPORTED OCCURRENCE OF ACNE BY GROUP

	No Acne		Reported Acne		Total	
Group	Number	Percent	Number	Percent	Number	Percent
Ranch Hand	659	63.3	382	36.7	1041	100
Comparison	498	64.8	271	35.2	769	100

Reported acne group contrast: P = 0.52

Beginning and end dates of up to three sustained periods of acne activity were recorded for each individual on the questionnaire. Since only acne after 1961 could be possibly induced by herbicide exposure, cases of post-1961 acne were placed in time reference to each individual's RVN tour(s). This temporal distribution was not statistically different with respect to group membership. These data are reflected in Table XV-2.

Table XV-2

REPORTED POST-1961 ACNE BY TIME OF THE SOUTHEAST ASIA [SEA] TOUR(S) BY GROUP

	Pre-SEA Only		Post-SEA Only		Pre- and Post-SEA*	
Group	Number	Percent	Number	Percent	Number	Percent
Ranch Hand N = 179	62	34.6	31	17.3	86	48.0
Comparison N = 116	51	44.0	17	14.7	48	41.4

Reported acne by group by pre/post SEA: P = 0.27
Reported acne (Post SEA) relative risk: 1.18, 95% Conf. int. (.67, 2.18)

*Such acne could have been separate cases or the same case starting before his RVN tour and ending afterwards.

Durations of the cumulative acne episodes were distributed by 5-year intervals and contrasted by group and SEA category. These data are shown in Table XV-3.

Table XV-3

DURATION OF ACNE IN 5-YEAR CATEGORIES BY SEA TOUR AND GROUP MEMBERSHIP

	Duration in Years				
Pre-SEA ONLY	≤5	5 <Yr ≤10	10 <Yr ≤15	15 <Yr ≤20	Total
Ranch Hand	44	15	2	1	62
Comparison	38	12	0	1	51
			P = 0.63		
Post-SEA ONLY					
Ranch Hander	15	4	11	1	31
Comparison	9	2	4	2	17
			P = 0.61		

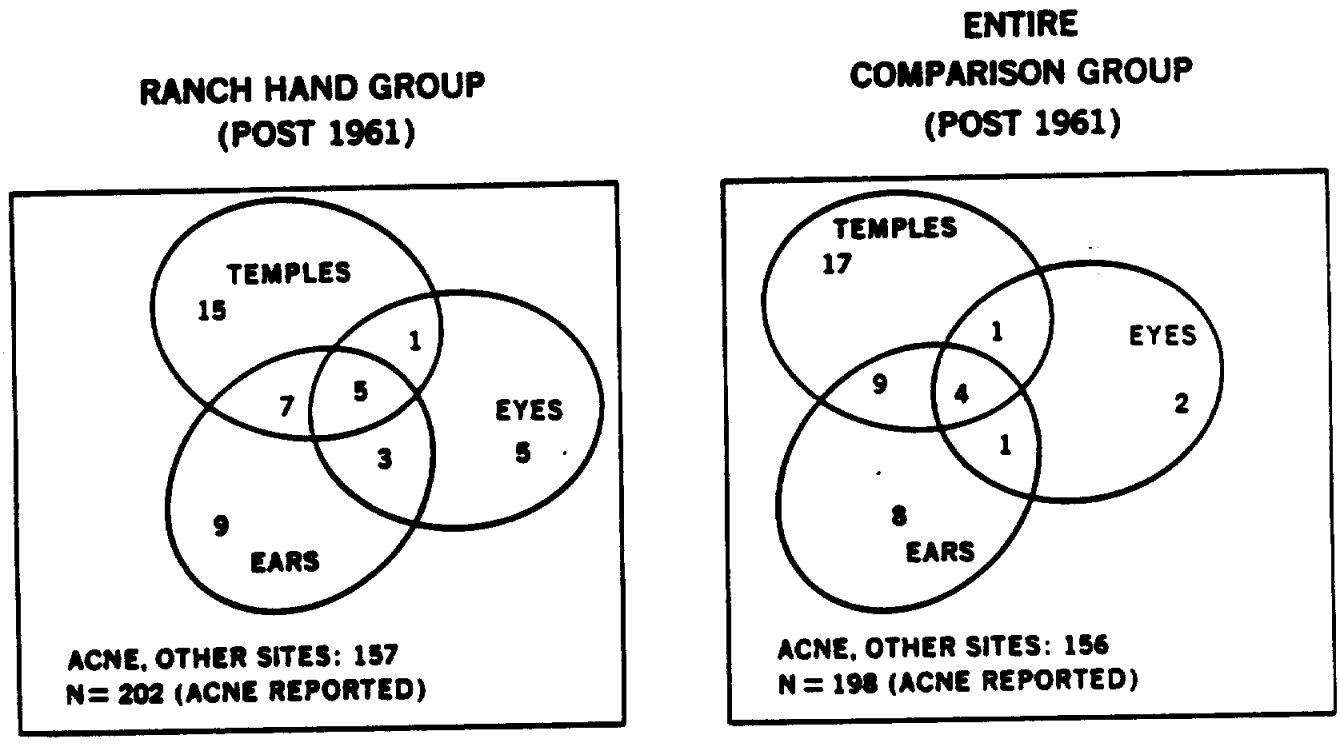
Thus, these SEA tour categories suggested that there were no group differences for the pre-SEA or post-SEA acne. Questionnaire information on whether the participant consulted a physician for his acne was used as an indirect measure of the clinical severity of the acne. Of 70 Ranch Handers with acne post-1961 who were asked this question, 29 (41.4%) responded as having visited a physician as contrasted to 15 of the 45 (33.3%) comparisons (P = 0.38), suggesting that there was not a statistically significant difference in the clinical severity of their acne.

Since chloracne, following mild to moderate exposures, is classically found in skin areas on the temples, eyes/eyelids, and ears (eyeglass distribution), questions on rash locations and combinations of locations were presented to each participant reporting acne. Of the 117 post-SEA plus pre- and post-SEA cases of acne in Ranch Handers after SEA duty, 75 (64%) reported no acne at any of these locations, while 36 (55%) of the 65 post-SEA plus pre- and post-SEA comparisons reported none. These proportions are not significantly different (P = 0.25), and the occurrence of skin disease which could potentially be chloracne does not differ in the two groups. There were only four individuals, two in each group, with acne confined exclusively to the classical chloracne areas.

As further corroboration of these anatomically categorized data, a Venn diagram was constructed for post-1961 acne lesions on the temples, ears, and eyes for the Ranch Hand group and the entire comparison group. These data are shown in Figure XV-I and display remarkable visual concordance.

Figure XV-1

VENN DIAGRAM OF POST-1961 TEMPLE, EAR, AND EYE ACNE BY GROUP



2. Physical Examination Data

All physical examination data were described using a diagnostic checklist, and abnormalities were annotated on a full body diagram. Color photographs were obtained at the dermatologist's discretion, and 14 lesions were biopsied. Of the 14 biopsies collected from 11 patients, none were suggestive of chloracne. No cases of chloracne were diagnosed. Histologic descriptions of these biopsies are presented in Table XV-4.

Table XV-4

BIOPSY RESULTS

Number	Histologic Description
3	Active degeneration
2	Inclusion cysts
2	Epidermal cysts
1	Basal cell carcinoma
1	Intradermal melanosis
1	Seborrheic keratosis
1	Pigmented nevus
1	Psoriasiform dermatitis
1	Chronic inflammation
1	Insect bite

The five most common diagnoses and the P value for group differences are shown in Table XV-5. Abnormal skin findings were prevalent but almost identical in both groups (i.e., 45.0% in Ranch Handers, and 44.9% in the comparisons; P = 0.97). Only for the miscellaneous diagnoses of "Other Abnormalities" (which included 15 diagnostic categories) was there a statistically significant group difference, with the comparisons having more disease than the Ranch Handers.

Table XV-5

PREVALENCE OF DERMATOLOGIC DIAGNOSES IN PERCENT

Diagnoses	Ranch Hand N = 1045	Comparison N = 773	P Value	Relative Risk	95% Conf int
Comedones	21.7	20.7	0.60	1.05	(.87,1.26)
Acneiform lesions	18.3	17.5	0.66	1.05	(.85,1.29)
Acneiform scars	11.2	10.4	0.57	1.08	(.82,1.43)
Cysts	11.6	10.5	0.46	1.10	(.84,1.46)
Hyperpigmentation	8.3	7.1	0.35	1.17	(.84,1.65)
Other abnormalities	12.6	16.3	0.03	.77	(.81, .98)
Any abnormality	45.0	44.9	0.97	1.00	(.90,1.11)

Based upon the four most prevalent diagnoses in Table XV-5 (comedones, acneiform lesions, acneiform scars, and dermal cysts), all of which should encompass the diagnostic possibility of chloracne, a dermatologic index was constructed for each study participant. A score of zero was given if none of the four lesions were noted, and a score of 1 was assigned if one lesion was diagnosed, etc. These data are displayed in Table XV-6.

Table XV-6

DERMATOLOGIC INDEX SCORE BY GROUP

Group	Scores 0 Number	0 %	1 Number	1 %	2 Number	2 %	3 Number	3 %	4 Number	4 %
Ranch Hand (N = 1045)	633	60.6	234	22.4	124	11.9	42	4.0	12	1.1
Comparison (N = 773)	487	63.0	157	20.3	95	12.3	27	3.5	7	0.9

P = 0.74

The distributions of these scores did not differ significantly, suggesting a similar crude clinical severity between the groups.

3. Questionnaire - Examination Correlations

The dermatologic index was contrasted to the historical occurrence of acne by group. These data are shown in Table XV-7.

Table XV-7

DERMATOLOGIC INDEX IN PERCENT BY QUESTIONNAIRE HISTORY OF ACNE BY GROUP

History	Group	Score 0	1	2	3	4	P Value
No Acne	Ranch Hand	66.3	21.4	9.4	2.4	0.5	0.72
	Comparison	69.1	18.1	9.6	2.6	0.6	
Acne ≤1961	Ranch Hand	55.3	25.1	13.4	4.5	1.7	0.84
	Comparison	55.1	21.8	17.7	4.1	1.4	
Acne >1961	Ranch Hand	47.3	23.2	17.7	8.9	3.0	0.82
	Comparison	48.4	26.6	16.9	6.4	1.6	

These data show that the dermatologic index does not differ significantly by group for any historical subset. And, as can be observed in Table XV-7, there is a positive association between the history (and time) of acne and the dermatologic index, regardless of group membership. An additional analysis of the dermatologic index for each individual who reported acne after his SEA tour (post-SEA only) did not reveal significant Ranch Hand-comparison differences ($P = 0.50$).

4. Exposure Index Analyses

Several comparisons were made using the exposure index and both historical and examination findings in the Ranch Hand group. Two historical parameters (incidence of acne and severity of acne) and the dermatologic examination findings were contrasted to the exposure index after stratifying for occupational categories by log-linear models. The historical-exposure analyses were essentially negative. Major dermatologic lesions from the examination were contrasted to the exposure index by occupational category. This analysis is presented in Table XV-8.

Table XV-8

PERCENTAGE OF SPECIFIC SKIN LESIONS IN RANCH HANDERS
BY EXPOSURE LEVEL BY OCCUPATIONAL CATEGORY
(POST 1961 DATA ONLY)

Condition	Occupational Group	Exposure Level Low %	Medium %	High %	P Value
All skin abnormalities	Officers	57.1	22.2	21.4	0.20
	Enlisted Flying	14.3	16.7	60.0	0.17
	Enlisted Ground	39.5	35.8	25.0	0.40
Comedones	Officers	14.3	22.2	21.4	0.91
	Enlisted Flying	57.1	50.0	20.0	0.42
	Enlisted Ground	18.6	24.5	31.2	0.45
Acneiform Lesions	Officers	0	33.3	50.0	0.08
	Enlisted Flying	57.1	16.7	20.0	0.23
	Enlisted Ground	37.2	22.6	37.5	0.21
Acneiform Scars	Officers	28.6	11.1	21.4	0.68
	Enlisted Flying	71.4	50.0	40.0	0.53
	Enlisted Ground	10.9	28.3	31.2	0.57
Inclusion Cysts	Officers	14.3	0	14.3	0.49
	Enlisted Flying	14.3	50.0	20.0	0.32
	Enlisted Ground	18.6	18.6	27.1	0.53
Hyperpigmentation	Officers	0	11.1	7.1	0.72
	Enlisted Flying	14.3	16.7	0	0.64
	Enlisted Ground	9.3	15.1	3.1	0.20

Thus, of the 18 exposure analyses, none were statistically significant (although based upon small sample sizes). Similarly, the relationship between the dermatologic index and exposure index was explored. For all three occupational categories, the dermatologic index showed no significant correlation to the exposure index, as reflected in Table XV-9.

Table XV-9

RANCH HAND DERMATOLOGIC INDEX IN ALL OCCUPATIONAL CATEGORIES
BY THE EXPOSURE INDEX
(POST 1961 DATA ONLY)

	Dermatologic Index			
	0		≥ 1	
Exposure Level	Number	Percent	Number	Percent
Low	26	45.6	31	54.4
Medium	28	41.2	40	58.8
High	20	39.2	31	60.8

P = 0.78

5. Summary

A comprehensive dermatologic assessment was conducted by questionnaire and physical examination. The questionnaire data revealed that the incidence of past acne, its time of occurrence relative to the individual's SEA tour(s), its severity and duration, and its anatomic location did not significantly differ between the Ranch Hand and comparison groups. No cases of chloracne were diagnosed at physical examination or by biopsy. No group differences were noted for the five most prevalent dermatologic diagnoses. The category, other abnormalities (containing 15 dermatologic conditions), was significantly larger for the comparison group than for the Ranch Hand group. However, when all skin abnormalities were considered, the group rates were essentially identical. A dermatologic index was constructed to account for the number of skin abnormalities per individual (severity index) that might encompass a diagnosis of chloracne. The index was not associated with group membership but showed some correlation with a total history of past acne in both groups. There were no associations between historical or dermatological examination findings and exposure level in any occupational category of the Ranch Hand group.