TABLE 17-1.

Statistical Analysis for the Renal Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
History of Kidney Disease/Stones	Q-SR	D	Yes No	AGE RACE OCC DIAB	UC:FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Urinary Protein (mg/dl)	LAB	D	Absent Present	AGE RACE OCC DIAB	UC:FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Urinary Occult Blood (RBC/HPF)	LAB	D	Normal: Absent Abnormal: ≥1	AGE RACE OCC DIAB	UC:FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Urinary White Blood Cell Count (WBC/HPF)	LAB	D	Normal: ≤2 Abnormal: ≥2	AGE RACE OCC DIAB	UC:FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Blood Urea Nitrogen (BUN)(mg/dl)	LAB	C	--	AGE RACE OCC DIAB	UC:TT AC:GLM CA:CC,GLM,TT UE:GLM,TT AE:GLM L:RM
Urine Specific Gravity	LAB	C	--	AGE RACE OCC DIAB	UC:TT AC:GLM CA:CC,GLM,TT UE:GLM,TT AE:GLM

TABLE 17-1. (continued)

Statistical Analysis for the Renal Assessment

Covariates

Variable (Abbreviation)	Data Source	Data Form	Cutpoints
Age (AGE)	MIL	D/C	Born ≥1942 Born 1923-1941 Born ≤1922
Race (RACE)	MIL	D	Nonblack Black
Occupation (OCC)	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Diabetic Class (DIAB)	LAB/Q-V	D	Diabetic: past history or ≥200 mg/dl glucose Impaired: ≥140-<200 mg/dl glucose Normal: <140 mg/dl glucose

Abbreviations:

Data Source:
LAB--1987 SCRF laboratory results
MIL--Air Force military records
Q-SR--1987 Family and Personal History questionnaire (self-reported)
Q-V--1987 NORC questionnaire (verified)

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

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

TABLE 17-1. (continued)

Statistical Analysis for the Renal Assessment

Abbreviations (continued):

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

TABLE 17-2.

Number of Participants With Missing Data for the Renal Assessment by Group

Variable	Analysis Use	Group: Ranch Hand	Group: Comparison	Total
History of Kidney Disease/Stones	DEP	0	2	2
Urinary Protein	DEP	0	1	1
Urinary Occult Blood	DEP	0	1	1
Urinary White Blood Cell Count	DEP	0	1	1
Blood Urea Nitrogen	DEP	1	2	3
Urine Specific Gravity	DEP	0	1	1
Diabetic Class	COV	5	7	12

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

TABLE 17-3.

Unadjusted Analysis for Renal Variables by Group

Variable	Statistic	Group: Ranch Hand		Group: Comparison		Est. Relative Risk (95% C.I.)	p-Value
History of Kidney Disease/ Stones	n	995		1,297			
	Number/%						
	Yes	108	10.9%	143	11.0%	0.98 (0.75,1.28)	0.952
	No	887	89.1%	1,154	89.0%		
Urinary Protein	n	995		1,298			
	Number/%						
	Present	47	4.7%	60	4.6%	1.02 (0.69,1.51)	0.986
	Absent	948	95.3%	1,238	95.4%		
Urinary Occult Blood	n	995		1,298			
	Number/%						
	Abnormal	83	8.3%	94	7.2%	1.17 (0.86,1.59)	0.368
	Normal	912	91.7%	1,204	92.8%		
Urinary White Blood Cell Count	n	995		1,298			
	Number/%						
	Abnormal	71	7.1%	92	7.1%	1.01 (0.73,1.39)	0.999
	Normal	924	92.9%	1,206	92.9%		
Blood Urea Nitrogen	n	994		1,297			
	Mean[a]	14.6		14.7		--	0.339
	95% C.I.[a]	(14.4,14.8)		(14.5,14.9)			
Urine Specific Gravity	n	995		1,298			
	Mean	1.0198		1.0200		--	0.477
	95% C.I.	(1.0194,1.0202)		(1.0197,1.0203)			

[a]Transformed from square root scale.

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

TABLE 17-4.

Adjusted Analysis for Renal Variables by Group

Variable	Statistic	Group: Ranch Hand	Group: Comparison	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
History of Kidney Disease/ Stones	n	995	1,297	0.98 (0.75,1.27)	0.853	AGE (p<0.001)
Urinary Protein	n	990	1,292	1.02 (0.68,1.52)**	0.928**	GRP*OCC (p=0.027) AGE (p=0.001) DIAB (p<0.001)
Urinary Occult Blood	n	995	1,298	1.17 (0.86,1.59)**	0.321**	GRP*RACE (p=0.016) OCC (p=0.039)
Urinary White Blood Cell Count	n	995	1,298	1.01 (0.73,1.39)	0.966	AGE (p=0.010) RACE (p=0.002)
Blood Urea Nitrogen	n Adj. Mean**[a] 95% C.I.**[a]	990 14.1 (13.7,14.5)	1,292 14.3 (13.9,14.7)	--	0.229**	GRP*RACE (p=0.040) AGE*RACE (p=0.014) AGE*OCC (p=0.023) AGE*DIAB (p=0.007)
Urine Specific Gravity	n Adj. Mean 95% C.I.	995 1.0198 (1.0194, 1.0201)	1,298 1.0196 (1.0192, 1.0200)	--	0.497	AGE*OCC (p=0.035)

GRP: Group (Ranch Hand, Comparison).
**Group-by-covariate interaction (0.01<p≤0.05)--adjusted relative risk/mean, confidence interval, and p-value derived from a model fitted after deletion of this interaction.
[a]Transformed from square root scale.
--Adjusted relative risk not applicable for continuous analysis of a variable.

Questionnaire Variable

History of Kidney Disease/Stones

As shown in Table 17-3, the unadjusted analysis of history of kidney disease/stones did not reveal a significant difference between the Ranch Hand and Comparison groups (p=0.952).

Based on the pooled group data, the covariate test of association with age was statistically significant (p<0.001). There was a history of kidney disease/stones reported for 7.7 percent of the participants born in or after 1942, 13.1 percent of those born between 1923 and 1941, and 15.5 percent of those born in or before 1922.

In the adjusted analysis of history of kidney disease/stones, no significant difference between the Ranch Hands and the Comparisons was detected (p=0.853). Age was a significant covariate in this analysis (p<0.001).

Laboratory Examination Variables

Urinary Protein

In the unadjusted analysis of urinary protein, no significant difference was identified between the Ranch Hand and Comparison groups (p=0.986).

As shown in Table N-1 of Appendix N, covariate tests of associations showed that age, race, and diabetic class were statistically significant (p=0.030, p=0.047, and p<0.001, respectively). The percentage of participants with urinary protein present increased with age (3.5% for those born in or after 1942, 5.4% for those born between 1923 and 1941, and 8.3% for those born in or before 1922). The percentage of abnormalities in Blacks was 8.8 compared to 4.4 in nonblacks. The analysis of diabetic class showed that 12.8 percent of the diabetic participants had urinary protein present compared to 4.7 percent and 3.6 percent in the glucose-impaired and normal classes, respectively.

In the adjusted analysis of urinary protein, there was a significant group-by-occupation interaction (p=0.027). Age and diabetic class were significant effects in the model (p=0.001 and p<0.001, respectively). Stratifying by occupation, there was a significant group difference for enlisted flyers with a higher percentage of abnormalities in the Comparisons (Adj. RR: 0.30, 95% C.I.: [0.10,0.93], p=0.036). No significant differences were detected for the officer and enlisted groundcrew categories (p=0.182 and p=0.670, respectively). No significant group difference was revealed when the group-by-occupation interaction was deleted from the model (p=0.928).

Urinary Occult Blood

The unadjusted analysis of urinary occult blood showed no statistically significant difference between the two groups (p=0.368).

The results of the covariate associations suggested no age or diabetic class effects, but significant associations for race (p=0.015) and occupation (p=0.022) were noted. Blacks had a higher percentage of abnormalities than nonblacks (13.9% vs. 7.3%). For occupation, the highest percentage of abnormalities was for enlisted flyers (10.2%). There were 6.0 percent and 8.3 percent abnormalities in the officer and enlisted groundcrew categories, respectively.

There was a significant group-by-race interaction in the adjusted analysis (p=0.016). Occupation was a significant covariate in the model (p=0.039). The Black Ranch Hands had a significantly higher percentage of abnormalities than Black Comparisons (Adj. RR: 3.75, 95% C.I.: [1.33,10.60], p=0.013). No group difference was detected for nonblacks (p=0.858). Without the group-by-race interaction in the model, there was no significant difference between the Ranch Hands and Comparisons (p=0.321).

Urinary White Blood Cell Count

No significant difference was detected between the Ranch Hands and Comparisons in the unadjusted analysis of urinary white blood cell count (p=0.999).

Based on pooled group data, race was statistically significant (p=0.006), and diabetic class was borderline significant (p=0.073). Blacks had 13.9 percent abnormalities as compared to 6.7 percent abnormalities in nonblacks. For diabetic class, there were 9.4 percent abnormalities in the impaired class and 9.1 percent among diabetic participants. The percentage of abnormalities in the normal diabetic class was 6.4.

No significant group difference in urinary white blood cell count was detected in the adjusted analysis (p=0.966). Age and race were significant factors in the analysis (p=0.010 and p=0.002, respectively).

Blood Urea Nitrogen

In the unadjusted analysis of blood urea nitrogen, there was no significant difference between the two groups (p=0.339).

The covariate associations with blood urea nitrogen revealed that age (p<0.001), race (p=0.003), and occupation (p<0.001) were significant. Diabetic class was borderline significant (p=0.057). There was a positive correlation with age (r=0.195). The mean for nonblacks (14.8 mg/dl) was higher than for Blacks (13.5 mg/dl). For occupation, the officers had the highest mean (15.3 mg/dl), followed by the enlisted groundcrew (14.3 mg/dl) and enlisted flyers (14.2 mg/dl). The diabetic participants had a mean of 15.2 mg/dl as compared with means of 14.6 mg/dl and 14.5 mg/dl for the normal and glucose-impaired classes, respectively.

There were four significant interactions in the adjusted analysis of blood urea nitrogen: group-by-race (p=0.040), age-by-race (p=0.014), age-by-occupation (p=0.023), and age-by-diabetic class (p=0.007). Investigating the group-by-race interaction further, no significant group difference was detected for nonblacks (p=0.506); however, the Black Comparisons had a statistically significant higher adjusted mean than the Black Ranch Hands (14.5 mg/dl vs. 13.1 mg/dl, p=0.022). Without the group-by-race interaction in the model, no significant group difference was found (p=0.229).

Urine Specific Gravity

No significant difference was detected between the Ranch Hands and Comparisons in the unadjusted analysis of urine specific gravity (p=0.477).

Using the Ranch Hand and Comparison data combined, age (p<0.001), race (p=0.045), and occupation (p<0.001) were found to be statistically significant. The analysis showed that urine specific gravity was negatively correlated with age (r=-0.100). The mean urine specific gravity for Blacks and nonblacks was 1.0209 and 1.0198, respectively. The mean of the enlisted groundcrew was 1.0209 as compared to means of 1.0196 and 1.0189 for enlisted flyers and officers, respectively.

In the adjusted analysis of urine specific gravity, no difference between the Ranch Hands and Comparisons was identified (p=0.497). Age-by-occupation was a significant interaction in the model (p=0.035).

Exposure Index Analysis

The unadjusted and adjusted results of the exposure index analyses of the Ranch Hands are presented in Tables 17-5 and 17-6, respectively. An overall summary of exposure index-by-covariate interactions is provided in Table 17-7; detailed results are contained in Table N-3 of Appendix N. The final interpretation of these exposure index data must await the reanalysis of the clinical data using the results of the serum dioxin assay. This report is expected in 1991.

Questionnaire Variable

History of Kidney Disease/Stones

The unadjusted and adjusted analyses identified no statistically significant results. However, in the unadjusted analyses, the high versus low exposure contrast for the officers and the medium versus low contrast for enlisted groundcrew were borderline significant (p=0.098 and p=0.076, respectively). For the officers, 16.0 percent of the high exposure category reported a history of kidney disease/stones as compared to 8.5 percent of the low exposure category (Est. RR: 2.06, 95% C.I.: [0.94,4.50]). Within the enlisted groundcrew cohort, 12.9 percent of the low exposure category and 6.3 percent of the medium exposure category reported a history of kidney disease/stones (Est. RR: 0.46, 95% C.I.: [0.20,1.02]).

TABLE 17-5.

Unadjusted Exposure Index for Renal Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low		Medium		High		Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
History of Kidney Disease/ Stones	Officer	n	130		124		125		Overall		0.128
		Number/%									
		Yes	11	8.5%	12	9.7%	20	16.0%	M vs. L	1.16 (0.49,2.73)	0.904
		No	119	91.5%	112	90.3%	105	84.0%	H vs. L	2.06 (0.94,4.50)	0.098
	Enlisted Flyer	n	55		63		53		Overall		0.140
		Number/%									
		Yes	6	10.9%	11	17.5%	3	5.7%	M vs. L	1.73 (0.59,5.03)	0.456
		No	49	89.1%	52	82.5%	50	94.3%	H vs. L	0.49 (0.12,2.07)	0.526
	Enlisted Groundcrew	n	147		158		140		Overall		0.133
		Number/%									
		Yes	19	12.9%	10	6.3%	16	11.4%	M vs. L	0.46 (0.20,1.02)	0.076
		No	128	87.1%	148	93.7%	124	88.6%	H vs. L	0.87 (0.43,1.77)	0.838
Urinary Protein	Officer	n	130		124		125		Overall		0.498
		Number/%									
		Present	6	4.6%	4	3.2%	8	6.4%	M vs. L	0.69 (0.19,2.50)	0.808
		Absent	124	95.4%	120	96.8%	117	93.6%	H vs. L	1.41 (0.48,4.20)	0.726
	Enlisted Flyer	n	55		63		53		Overall		0.738
		Number/%									
		Present	2	3.6%	1	1.6%	1	1.9%	M vs. L	0.43 (0.04,4.85)	0.898
		Absent	53	96.4%	62	98.4%	52	98.1%	H vs. L	0.51 (0.05,5.79)	0.999
	Enlisted Groundcrew	n	147		158		140		Overall		0.355
		Number/%									
		Present	6	4.1%	8	5.1%	11	7.9%	M vs. L	1.25 (0.42,3.70)	0.896
		Absent	141	95.9%	150	94.9%	129	92.1%	H vs. L	2.00 (0.72,5.57)	0.270

TABLE 17-5. (continued)

Unadjusted Exposure Index for Renal Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low		Medium		High		Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
Urinary Occult Blood	Officer	n	130		124		125		Overall		0.589
		Number/%									
		Abnormal	8	6.2%	6	4.8%	10	8.0%	M vs. L	0.78 (0.26,2.30)	0.856
		Normal	122	93.8%	118	95.2%	115	92.0%	H vs. L	1.33 (0.51,3.48)	0.740
	Enlisted Flyer	n	55		63		53		Overall		0.828
		Number/%									
		Abnormal	6	10.9%	9	14.3%	6	11.3%	M vs. L	1.36 (0.45,4.10)	0.790
		Normal	49	89.1%	54	85.7%	47	88.7%	H vs. L	1.04 (0.31,3.46)	0.999
	Enlisted Groundcrew	n	147		158		140		Overall		0.243
		Number/%									
		Abnormal	9	6.1%	18	11.4%	11	7.9%	M vs. L	1.97 (0.86,4.54)	0.155
		Normal	138	93.9%	140	88.6%	129	92.1%	H vs. L	1.31 (0.53,3.26)	0.730
Urinary White Blood Cell Count	Officer	n	130		124		125		Overall		0.294
		Number/%									
		Abnormal	6	4.6%	6	4.8%	11	8.8%	M vs. L	1.05 (0.33,3.35)	0.999
		Normal	124	95.4%	118	95.2%	114	91.2%	H vs. L	1.99 (0.71,5.57)	0.276
	Enlisted Flyer	n	55		63		53		Overall		0.161
		Number/%									
		Abnormal	6	10.9%	4	6.3%	1	1.9%	M vs. L	0.55 (0.15,2.07)	0.578
		Normal	49	89.1%	59	93.7%	52	98.1%	H vs. L	0.16 (0.02,1.35)	0.125
	Enlisted Groundcrew	n	147		158		140		Overall		0.272
		Number/%									
		Abnormal	10	6.8%	11	7.0%	16	11.4%	M vs. L	1.03 (0.42,2.49)	0.999
		Normal	137	93.2%	147	93.0%	124	88.6%	H vs. L	1.77 (0.77,4.04)	0.246

TABLE 17-5. (continued)

Unadjusted Exposure Index for Renal Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low	Exposure Index: Medium	Exposure Index: High	Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
Blood Urea Nitrogen	Officer	n	130	124	124	Overall		0.654
		Mean[a]	15.0	15.5	15.3	M vs. L	--	0.356
		95% C.I.[a]	(14.4,15.7)	(14.8,16.1)	(14.6,16.0)	H vs. L	--	0.587
	Enlisted Flyer	n	55	63	53	Overall		0.491
		Mean[a]	13.5	14.0	14.2	M vs. L	--	0.418
		95% C.I.[a]	(12.5,14.5)	(13.2,14.8)	(13.3,15.1)	H vs. L	--	0.260
	Enlisted Groundcrew	n	147	158	140	Overall		0.114
		Mean[a]	14.7	14.4	13.8	M vs. L	--	0.470
		95% C.I.[a]	(14.1,15.3)	(13.8,15.0)	(13.3,14.3)	H vs. L	--	0.033
Urine Specific Gravity	Officer	n	130	124	125	Overall		0.064
		Mean	1.0187	1.0183	1.0200	M vs. L	--	0.609
		95% C.I.	(1.0177, 1.0198)	(1.0172, 1.0195)	(1.0191, 1.0210)	H vs. L	--	0.072
	Enlisted Flyer	n	55	63	53	Overall		0.197
		Mean	1.0182	1.0200	1.0184	M vs. L	--	0.093
		95% C.I.	(1.0168, 1.0197)	(1.0186, 1.0213)	(1.0167, 1.0201)	H vs. L	--	0.889
	Enlisted Groundcrew	n	147	158	140	Overall		0.051
		Mean	1.0217	1.0205	1.0202	M vs. L	--	0.052
		95% C.I.	(1.0209, 1.0226)	(1.0196, 1.0214)	(1.0193, 1.0212)	H vs. L	--	0.023

[a]Transformed from square root scale.

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

TABLE 17-6.

Adjusted Exposure Index for Renal Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low	Medium	High	Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
History of Kidney Disease/ Stones	Officer	n	130	124	123	Overall		0.156
						M vs. L	0.98 (0.40,2.36)	0.960
						H vs. L	1.89 (0.86,4.18)	0.115
	Enlisted Flyer	n	55	63	53	Overall		0.128
						M vs. L	1.74 (0.57,5.29)	0.331
						H vs. L	0.47 (0.11,2.02)	0.313
	Enlisted Groundcrew	n	146	156	140	Overall		0.283
						M vs. L	0.53 (0.23,1.20)	0.129
						H vs. L	0.87 (0.42,1.79)	0.699
Urinary Protein	Officer	n	130	124	123	Overall		0.626
						M vs. L	0.76 (0.20,2.92)	0.689
						H vs. L	1.39 (0.44,4.35)	0.574
	Enlisted Flyer	n	55	63	53	Overall		0.212
						M vs. L	0.06 (0.002,1.99)	0.117
						H vs. L	0.45 (0.03,6.84)	0.562
	Enlisted Groundcrew	n	146	156	140	Overall		0.537
						M vs. L	1.36 (0.45,4.06)	0.588
						H vs. L	1.79 (0.63,5.05)	0.274

TABLE 17-6. (continued)

Adjusted Exposure Index for Renal Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low	Medium	High	Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
Urinary Occult Blood	Officer	n	130	124	123	Overall		0.501
						M vs. L	0.67 (0.22,2.05)	0.485
						H vs. L	1.25 (0.47,3.32)	0.650
	Enlisted Flyer	n	55	63	53	Overall		0.830
						M vs. L	1.38 (0.44,4.34)	0.578
						H vs. L	1.05 (0.31,3.53)	0.939
	Enlisted Groundcrew	n	146	156	140	Overall		0.144
						M vs. L	2.26 (0.96,5.35)	0.063
						H vs. L	1.32 (0.52,3.36)	0.560
Urinary White Blood Cell Count	Officer	n	130	124	123	Overall		0.395
						M vs. L	1.06 (0.32,3.51)	0.923
						H vs. L	1.89 (0.66,5.41)	0.238
	Enlisted Flyer	n	55	63	53	Overall		****
						M vs. L	****	****
						H vs. L	****	****
	Enlisted Groundcrew	n	146	156	140	Overall		****
						M vs. L	****	****
						H vs. L	****	****

TABLE 17-6. (continued)

Adjusted Exposure Index for Renal Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low	Exposure Index: Medium	Exposure Index: High	Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
Blood Urea Nitrogen	Officer	n	130	124	123	Overall		0.977**
		Adj. Mean**[a]	14.2	14.3	14.2	M vs. L	--	0.860**
		95% C.I.**[a]	(12.8,15.8)	(12.9,15.8)	(12.8,15.7)	H vs. L	--	0.983**
	Enlisted Flyer	n	55	63	53	Overall		0.462
		Adj. Mean[a]	13.0	13.6	13.8	M vs. L	--	0.367
		95% C.I.[a]	(11.4,14.6)	(12.2,15.0)	(12.2,15.4)	H vs. L	--	0.234
	Enlisted Groundcrew	n	146	156	140	Overall		****
		Adj. Mean	****	****	****	M vs. L	--	****
		95% C.I.	****	****	****	H vs. L	--	****
Urine Specific Gravity	Officer	n	130	124	123	Overall		0.064
		Adj. Mean	1.0183	1.0180	1.0197	M vs. L	--	0.691
		95% C.I.	(1.0157, 1.0209)	(1.0154, 1.0206)	(1.0171, 1.0223)	H vs. L	--	0.071
	Enlisted Flyer	n	55	63	53	Overall		0.272
		Adj. Mean	1.0188	1.0204	1.0189	M vs. L	--	0.150
		95% C.I.	(1.0160, 1.0216)	(1.0180, 1.0228)	(1.0163, 1.0215)	H vs. L	--	0.924
	Enlisted Groundcrew	n	146	156	140	Overall		0.059
		Adj. Mean	1.0214	1.0201	1.0201	M vs. L	--	0.042
		95% C.I.	(1.0202, 1.0227)	(1.0189, 1.0214)	(1.0188, 1.0213)	H vs. L	--	0.038

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

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

[a]Transformed from square root scale.

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

TABLE 17-7.

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

Variable	Occupation	Covariate	p-Value
Urinary White Blood Cell Count	Enlisted Flyer	Age	0.004
Urinary White Blood Cell Count	Enlisted Flyer	Diabetic Class	0.033
Urinary White Blood Cell Count	Enlisted Groundcrew	Race	0.005
Urinary White Blood Cell Count	Enlisted Groundcrew	Diabetic Class	0.014
Blood Urea Nitrogen	Officer	Age	0.024
Blood Urea Nitrogen	Enlisted Groundcrew	Age	0.006

*Refer to Table N-3 for a further investigation of these interactions.

Laboratory Examination Variables

Urinary Protein

There were no significant differences detected in the unadjusted and adjusted analyses of urinary protein.

Urinary Occult Blood

In the unadjusted analyses, no significant differences were identified. Based on the adjusted analyses, the medium versus low exposure contrast within the enlisted groundcrew cohort was borderline significant (p=0.063). For this contrast, the adjusted relative risk was 2.26 (95% C.I.: [0.96,5.35]).

Urinary White Blood Cell Count

The unadjusted analyses revealed no significant differences among the exposure categories for urinary white blood cell count. A similar non-significant finding was seen in the adjusted analysis for the officer cohort. There were two significant exposure index-by-covariate interactions in both the enlisted flyer and enlisted groundcrew cohorts. Sparse numbers of abnormalities resulted when the interactions were investigated by stratifying by the covariates.

For the enlisted flyer cohort, the exposure index-by-age and exposure index-by-diabetic class interactions were significant (p=0.004 and p=0.033, respectively). Stratifying by age and diabetic class with this cohort, the overall analysis for the Ranch Hands in the normal diabetic class who were born in or after 1942 and for those in the normal diabetic class born between 1923 and 1941 were borderline significant (p=0.099 for both). Both of the abnormalities in the normal diabetic class for the Ranch Hands born in or after 1942 were in the low exposure category. For the Ranch Hands in the normal diabetic class who were born between 1923 and 1941, there were 12.9 percent abnormalities in the low exposure category as compared to 14.8 percent in the medium exposure category and 0.0 percent in the high exposure category.

There were significant exposure index-by-covariate interactions for race and diabetic class in the enlisted groundcrew cohort (p=0.005 and p=0.014, respectively). The overall exposure level relationship for nonblack Ranch Hands in the normal diabetic class detected a borderline significant dose-response relationship with 3.0 percent, 6.2 percent, and 11.7 percent abnormalities in the low, medium, and high exposure categories, respectively (p=0.053). The high versus low exposure contrast was significant (p=0.036). The overall exposure level analysis for nonblacks classified as diabetic was significant (27.3% low, 30.8% medium, and 0.0% high; p=0.049). Within this stratum, the high versus low exposure contrast was borderline significant (p=0.100). Among the Black Ranch Hands classified as diabetic, there was only one abnormality, which was in the high exposure level (p=0.050).

Blood Urea Nitrogen

There was no evidence of a significant dose-response relationship for blood urea nitrogen for the enlisted flyer cohort in both unadjusted and adjusted analyses. In the officer cohort, there was a significant exposure index-by-age interaction (p=0.024); stratifying by age revealed no significant differences. The unadjusted analysis and the adjusted analysis without the interaction for the officer cohort also did not support a dose-response relationship.

For the enlisted groundcrew cohort, the means for the low, medium, and high exposure categories were 14.7 mg/dl, 14.4 mg/dl, and 13.8 mg/dl, respectively. In the unadjusted analysis, the high versus low exposure contrast was significant (p=0.033). There was a significant exposure index-by-age interaction in the adjusted analysis (p=0.006). Stratifying by age, two contrasts were found to be borderline significant (p=0.074 high vs. low for those born in or after 1942 and p=0.084 medium vs. low for those born in or before 1922). However, neither result supported a relationship of abnormal mean levels increasing as the level of exposure increases.

Urine Specific Gravity

Within the officer cohort, the highest mean was in the high exposure category, and the lowest mean was in the medium exposure category (unadjusted means: 1.0187 low, 1.0183 medium, and 1.0200 high). The unadjusted and adjusted analyses for the officer cohort were borderline significant (p=0.064 for both). The high versus low exposure contrasts were also borderline significant (p=0.072 unadjusted and p=0.071 adjusted).

In the enlisted flyer cohort, the highest mean level was in the medium exposure category. Although the overall exposure relationships were not found to be significant, the unadjusted analysis of the medium versus low exposure contrast was borderline significant (means: 1.0182 low, 1.0200 medium, and 1.0184 high; p=0.093).

The overall exposure level relationships for the enlisted groundcrew cohort were borderline significant (p=0.051 unadjusted and p=0.059 adjusted). In the unadjusted analysis, the means were 1.0217, 1.0205, and 1.0202 for the low, medium, and high exposure categories, respectively. The high versus low exposure contrast was found to be significant (p=0.023), and the medium versus low contrast was marginally significant (p=0.052). In the adjusted analysis, both contrasts were significant (p=0.042 medium vs. low and p=0.038 high vs. low).

Longitudinal Analysis

Of the renal variables, blood urea nitrogen was investigated to assess longitudinal differences between the 1982 Baseline examination and the 1987 followup examination. As shown in Table 17-8, no significant difference in the change over time was detected (p=0.553). A slight increase in the blood urea nitrogen mean levels from 1982 to 1987 was observed for both groups.

DISCUSSION

In clinical practice, the presence of renal or urinary tract disease can be determined with confidence based on the medical history, physical examination, and the five laboratory indices included in the present study.

Though subject to some day-to-day variation related to diet and state of hydration, the blood urea nitrogen is considered a reliable index of glomerular filtration, while the integrity and concentrating ability of the renal tubular system are reflected in the urinary specific gravity. In documenting the presence of red or white blood cells in significant numbers, the examination of the urinary sediment can provide valuable clues to the presence of a broad range of infectious, inflammatory, and neoplastic conditions intrinsic to the upper and lower urinary tracts.

The frequent finding in ambulatory medicine of isolated abnormalities in the routine urinalysis of healthy individuals who in fact have no disease of the genitourinary system is pertinent to interpretation of the renal assessment data. With normal fluid balance, the healthy kidneys can excrete up to 100-150 mg of total protein in 24 hours. The qualitative dipstick test used in the current study is sensitive to protein concentrations as low as 10-15 mg per deciliter and, particularly in specimens collected after overnight fasting, will often give a trace to 1+ positive reaction in the absence of parenchymal renal disease.

TABLE 17-8.

Longitudinal Analysis of Blood Urea Nitrogen:
A Contrast of 1982 Baseline and 1987 Followup Examination Means

	Group Means[a]		p-Value[a]
Examination	Ranch Hand	Comparison	(Equality of Differences)
1982 Baseline	13.7	14.0	0.553
1985 Followup	14.2	14.4	
1987 Followup	14.5	14.7	

Note: Summary statistics for the 1982 Baseline and 1987 followup are based on 943 Ranch Hands and 1,110 Comparisons who participated in 1982 Baseline and 1987 followup examinations. The p-value given is in reference to ahypothesis test involving 1982 Baseline and 1987 followup results. Summary statistics on 923 of these Ranch Hands and 1,093 of these Comparisons who also participated in the 1985 followup are also included for reference purposes only.

[a]Means transformed from the square root scale; hypothesis test performed on the square root scale.

Similarly, on microscopic examination of the urinary sediment, it is not uncommon to intermittently find a few red or white blood cells in the absence of definable neoplastic or inflammatory cause, trauma, or kidney stones. When documented as an isolated finding in the absence of symptoms or other signs, such intermittent microcyturia can usually be considered benign.

With reference to the current study, no significant group differences in the renal indices were found between the Ranch Hands and Comparisons in the unadjusted analyses. In the dependent variable-covariate analysis, several associations were defined that are consistent with established clinical observations.

In the adjusted analyses, significant covariate associations with age were documented. The twofold increased historical incidence of genitourinary disease would be expected with aging in this all male population with the development of benign prostatic hypertrophy and bladder outlet obstruction.

In association with benign nephrosclerosis of the normally aging kidney, there is a gradual reduction in renal mass (from an average of 260 grams in the young adult to 190 grams in the eighth decade) and a 50 percent reduction in renal plasma flow (from 600 cc/min to 300 cc/min). An age-related increase in blood urea nitrogen and proteinuria would be expected findings and were documented in the current study.

Several of the race-dependent variable associations can be explained on the basis of established clinical correlations. The increased incidence of hypertension with hypertensive nephropathy in Blacks is well recognized and might account for the increased incidence of proteinuria, hematuria, and elevated blood urea nitrogen in this population. Though the numbers are small, microinfarction of the renal medulla in sickle cell trait (8-10% incidence in Blacks) might have been a minor contributing factor in the incidence of hematuria. The cause of the twofold increased incidence of leukocyturia in Blacks is uncertain and the very slight difference in mean specific gravity (1.0209 vs. 1.0198) is not clinically significant.

In the diabetic class, the increased incidence of hypertensive and arteriosclerotic vascular disease and of urinary tract infections related to glycosuria provide reasonable explanation for the significant covariate association of proteinuria, leukocyturia, and elevated blood urea nitrogen in this population.

In summary, the renal assessment data revealed abnormalities in five laboratory indices at a prevalence that is common in ambulatory practice. There were no significant overall differences between the Ranch Hand and Comparison cohorts. Most of the covariate associations can be explained on the basis of established clinical correlations. Finally, when documented as isolated findings, the benign nature of these abnormalities should be emphasized.

SUMMARY

The 1987 renal assessment was based on six variables. The results of the Ranch Hand and Comparison contrasts are summarized in Table 17-9.

The historical assessment of kidney disease/stones based on self-reported data showed no significant differences between the Ranch Hand and Comparison groups. These results are consistent with the results of the 1985 followup but appear to be in marked contrast to the Baseline findings. The Comparison cohort is different between the Baseline report and the 1987 followup study (Original Comparisons vs. all Comparisons), and the definition of kidney disease has been expanded from the Baseline study to include kidney stones. However, when the analysis of the 1987 followup data was restricted to the Original Comparisons and kidney stones were not included in the definition of kidney disease, the prevalence rate of kidney disease was comparable between the two examinations, but the difference between groups was still nonsignificant ($p=0.952$).

The current renal function was evaluated by five laboratory variables: urine protein, urinary occult blood, urinary white blood cell count, blood urea nitrogen, and urine specific gravity.

There was no significant difference detected between the two groups based on the unadjusted analysis of urinary protein. In the adjusted analysis, there was a significant interaction between group and occupation. Stratifying by occupation revealed that the Comparison enlisted flyers had a higher percentage of abnormalities than the Ranch Hand enlisted flyers ($p=0.036$). After deleting the group-by-occupation interaction, no difference between the two groups was observed. This result differed from the twofold increase of proteinuria observed in Comparisons at Baseline.

TABLE 17-9.

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

Variable	Type of Analysis	Unadjusted	Adjusted
Questionnaire			
History of Kidney Disease/Stones	D	NS	NS
Laboratory			
Urinary Protein	D	NS	** (NS)
Urinary Occult Blood	D	NS	** (NS)
Urinary White Blood Cell Count	D	NS	NS
Blood Urea Nitrogen	C	NS	** (NS)
Urine Specific Gravity	C	NS	NS

D: Discrete analysis performed.
C: Continuous analysis performed.
NS: Not significant ($p>0.10$).
** (NS): Group-by-covariate interaction ($0.01<p\leq0.05$); not significant when interaction is deleted; refer to Table N-2 for a detailed description of this interaction.

No difference was identified between the Ranch Hands and the Comparisons based on the analysis of urinary occult blood without adjustments for covariates. However, after stratifying by race due to a significant group-by-race interaction, the estimated prevalence rate for the Black Ranch Hands was noted as being statistically higher than the corresponding rate for the Black Comparisons ($p=0.013$). The estimated prevalence rates were not detected as being different based on an adjusted model without the group-by-race interaction.

Based on the analyses of urinary white blood cell count, no differences were detected between the two groups in either the unadjusted or adjusted analyses.

The mean blood urea nitrogen levels of the Ranch Hands and Comparisons did not vary significantly when compared without adjustments. The adjusted analysis detected a significant group-by-race interaction. Stratifying by race revealed that the mean of the Black Comparisons was statistically higher than the mean of the Black Ranch Hands ($p=0.022$). The adjusted means were also not significantly different when estimated without the group-by-race interaction in the model.

There was no evidence that the mean urine specific gravity was different between the Ranch Hands and Comparisons in either the unadjusted or adjusted analysis.

The exposure index analyses showed very little evidence of a dose-response relationship at the 1987 followup examination. No pattern in the relationship of abnormality rates or mean levels was seen within occupational cohort.

The longitudinal analysis was based solely upon the contrast of blood urea nitrogen levels between the 1982 and 1987 examinations. The unadjusted mean levels increased slightly from 1982 to 1987, but the change between the Ranch Hands and Comparisons over time was not significantly different.

In conclusion, none of the six variables of the renal assessment showed a significant difference based on the unadjusted analyses. For three of the variables, the adjusted results supported the findings of the unadjusted analyses; there were significant group-by-covariate interactions for the other variables. Further examination by strata revealed that in one case the Ranch Hand prevalence rate was higher than the Comparison rate and that the opposite relationship existed for another case. In the third instance, the Comparison mean was higher than the mean of the Ranch Hands; however, both means were within the normal range. The adjusted analyses without the group-by-covariate interactions supported the findings of the unadjusted analyses; the renal status of the Ranch Hands and Comparisons was generally similar.

CHAPTER 17

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CHAPTER 18

ENDOCRINE ASSESSMENT

INTRODUCTION

Background

The human endocrine system is not considered to be a major target of chlorophenol or 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) exposure. This is not so in animals, however. A wide range of endocrine abnormalities in many animal species has been induced experimentally by TCDD and includes hypoglycemia,[1] hypothyroxinemia,[1,2] reduced progesterone levels,[3] and increased testosterone levels, the latter presumably reflecting decreased liver catabolism due to parenchymal liver damage or an inhibition of the cytochrome P-450 system.[4]

Extensive studies have been conducted on the interaction of TCDD with thyroid hormones in experimental animals. The exact nature of the interaction is still a matter of some discussion, but it is known that TCDD depresses the production and/or interaction of various thyroid hormones.[5-12] The effect on thyroid hormone-mediated metabolism of various compounds may be dependent on multiple hormones and may be the result of the alteration of receptor coupling or the number of receptors.[12-13] Hypoinsulinemia and hypoglycemia have been found to occur together in rats and may be an internal attempt to alter the toxic effects of TCDD.[14,15] The hypothalmus has been recently shown to also be a site of TCDD action in studies of dopamine.[16]

Extensive work with androgen levels in experimental animals has also been done. Studies consistently have shown a pronounced decrease in uterine estrogen (nuclear and cytosolic), progesterone (nuclear and cytosolic), and plasma testosterone and dihydrotestosterone following exposure to dioxin.[17-20] Hepatic and uterine estrogen receptor levels have shown a decrease after TCDD administration, and animals that do not maintain estrogen levels successfully (guinea pig and horse) show a much higher sensitivity to TCDD.[21,22] TCDD may alter the synthesis and release rate for androgens.[17]

Cholesterol metabolism suppression has also been shown with inhibition of cholesterol side-chain cleavage.[23,24] Further, thymic atrophy, one of the most sensitive indicators of TCDD toxicity in animals, has been shown not to be mediated by the pituitary-adrenal axis.[25] Comparable animal data for the isolated effects of 2,4-D and 2,4,5-T have been noticeably meager.

Other animal studies have emphasized the endocrine system, and thyroid function in particular, as important in causing or ameliorating TCDD toxicity, and not simply as an endpoint response.[26,27] Mounting experimental evidence suggests that both natural and radiation-induced hypothyroidism protect against TCDD lethality and that this favorable process can be quickly reversed by treatments with thyroxine (T_4).[28,29]

If the protective reaction of hypothyroidism in animals can be extrapolated to humans, it suggests that cases of hypothyroidism or altered patterns of thyroid hormones may aggregate in groups of highly exposed workers (particularly in those with chloracne) and, alternatively, that severe sequelae of TCDD exposure may be associated with hyperthyroidism. In fact, such thyroid findings have not been commonly reported in dioxin morbidity studies. Occasional cases of hypothyroidism and thyromegaly have been linked to exposures to polybrominated biphenyls and hexachlorobenzene, but the data were too sparse and oblique to support a causal relationship for hypothyroidism and TCDD exposure.[30,31] An assessment of the Times Beach, Missouri, residents, whose community was contaminated with TCDD, did not reveal thyroid stimulating hormone (TSH) or T_4 differences between the high- and low-risk groups.[32]

Temporary glycosuria and impaired glucose tolerance tests were noted in two studies of industrial workers exposed to TCDD.[33,34] However, neither abnormal glucose metabolism nor frank diabetes was specifically noted in other comparable studies.[35-38]

Overall, dioxin morbidity studies of humans have not rigorously assessed the clinical or biochemical parameters of the endocrine system. Detailed evaluations of endocrine function following TCDD exposure were included in the Air Force Health Study Baseline Morbidity Report and the 1985 followup report. Both reports are summarized below.

Baseline Summary Results

A comprehensive biochemical assessment of the endocrine system was used for analysis in the Baseline examination in 1982.

Five measures of endocrine status were assessed: triiodothyronine percent (T_3 %) uptake, T_4, free thyroxine index (FTI), testosterone, and 2-hour postprandial glucose.

Results showed significant group differences for T_3 % uptake, predominantly in Ranch Hands 40 years old or less, and abnormally low T_3 % uptake values; the highest percentage of abnormalities was in those with high percent body fat. No group difference was noted for elevated 2-hour postprandial glucose values, and as expected, the prevalence of abnormal values was associated with older ages and higher percent body fat. Similarly, low testosterone levels were identical in both groups and were associated with increasing age and increasing percent body fat. Higher mean testosterone values (although still within normal range) were significantly more prevalent in the Ranch Hand group. Significant mean shifts were not noted for the T_3 % uptake, T_4, and FTI variables, although the T_3 % uptake was associated with a group-by-age interaction.

The exposure index analyses were essentially negative for the T_3 % uptake and T_4 variables. FTI, postprandial glucose, and testosterone analyses were marked by a series of covariate interactions in varying occupational categories. Of some note were the significant percent body fat-by-exposure interactions in two occupational strata in the glucose determination.

In summary, the endocrine system, as measured by five biochemical assays in 1982, did not reveal clinically apparent abnormalities that could be attributed to Herbicide Orange exposure. However, significant mean shifts in several values (although still in the normal range) presented trends, some of which were consistent with a herbicide etiology and others were counter to such an effort.

These data, coupled with the animal literature on the profound influence of the endocrine system on lethality and body fat metabolism following TCDD exposure, clearly underscored the importance of evaluating the endocrine system more comprehensively, as was done in the subsequent followup examinations.

1985 Followup Study Summary Results

Questionnaire and review-of-systems data for past thyroid disease were essentially equivalent in both the Ranch Hand and Comparison groups. These historical data were confirmed by medical record reviews. Physical examination findings were necessarily limited to data from palpation of thyroid glands and testicles; the unadjusted results showed no significant group differences.

Evaluation of the endocrine system was conducted primarily by laboratory testing of hormone levels. The thyroid test battery consisted of T_3 % uptake and TSH, as determined by radioimmunoassay (RIA) techniques. Testosterone, initial cortisol, differential cortisol (the difference between the initial and 2-hour cortisol levels), and 2-hour postprandial glucose levels were also analyzed. The T_3 % uptake data showed no group differences for either mean values or frequency of abnormally low or high values. Occupation was a significant covariate. TSH results revealed a significantly higher mean level in the Ranch Hand group, but this difference was not found by discrete analysis of the proportions of abnormally high TSH results.

The mean level of testosterone remained significantly elevated among Ranch Hands as contrasted with Comparisons in the 10 to 25 percent body fat category, but this was not reflected by the discrete analyses. For the few participants with less than 10 percent body fat (six Ranch Hands, four Comparisons), mean testosterone levels were lower for Ranch Hands than for Comparisons. Age, occupation, and percent body fat were significant adjusting variables.

Two timed cortisol specimens showed no significant group differences in mean values and percent abnormalities. The difference between the timed cortisol results, termed the differential cortisol, showed no significant group differences for nonblacks or Blacks born before 1942, but Black Ranch Hands born in or after 1942 had a lower mean differential cortisol level than did their Comparisons. Age, percent body fat, and personality type were significant covariates in these analyses.

Group means of 2-hour postprandial glucose levels were not statistically different, but discrete analyses revealed that there was a significantly higher frequency of glucose-impaired (at least 140 but less than 200 mg/dl) Comparisons than Ranch Hands. A constructed variable comprised of known diabetics and individuals classified as diabetic by the glucose tolerance test showed no difference between the Ranch Hand and Comparison groups. As expected, past and current diabetes were highly influenced by the covariates age, race, and percent body fat.

Exposure index analyses did not reveal any pattern consistent with a dose-response relationship. Enlisted flyers in the medium exposure level were significantly different from those in the low exposure level for 2-hour cortisol, differential cortisol, and 2-hour postprandial glucose. However, the corresponding high versus low contrasts were not statistically significant.

Longitudinal analyses of T_3 % uptake, TSH, and testosterone levels on all individuals attending both the Baseline and 1985 followup examinations revealed only symmetrical and nonsignificant changes in the Ranch Hand and Comparison groups in the interval between examinations.

In conclusion, both limited historical and physical examination data, seven endocrinologic laboratory variables, and a composite indicator of diabetes did not demonstrate consistent patterns indicating a herbicide effect. TSH and testosterone means tests were statistically significant, and in the expected direction of a herbicide effect. There was a significant interaction between group and percent body fat for testosterone that could be interpreted as a herbicide effect. These results were not confirmed by the discrete analyses. Also significant was the impaired category of the glucose tolerance test, which showed an excess in the Comparison group. The expected effects of age, race, occupation, and percent body fat on appropriate endocrine variables were consistently demonstrated. Overall, the endocrine health status was comparable in both groups.

Parameters of the 1987 Endocrine Assessment

Dependent Variables

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

Questionnaire Data

In both the review-of-systems questionnaire and the health interval questionnaire, general screening questions on thyroid function and disease were posed to each participant. The review-of-systems questionnaire contained five questions on current thyroid function: thyroid or goiter trouble, high thyroid level, low thyroid level, lump in throat, and taking thyroid medication. Responses to these five questions were combined into a single item, which was coded as yes if there was a positive response to any question. During the face-to-face health interview, each study participant was asked, "Since the date of the last interview, has a doctor told you for the first time that you had thyroid problems?" A self-reported affirmative response to the interviewer-administered question was verified by medical record review and added to previously reported and verified information on the thyroid function for each participant. Based on the verified data, history of thyroid disease (interviewer-administered) was classified as yes/no. Responses from both the self-administered and interviewer-administered questions were analyzed as measures of the endocrine function.

Participants with a pre-Southeast Asia (SEA) history of thyroid disease, as determined by inteviewer-administered information, were excluded from the analysis of this variable.

Physical Examination Data

The physical examination of the endocrine function was limited to manual palpation of the thyroid gland and the testes. Thyroid abnormalities consisted of enlarged gland, tenderness, or presence of nodules. The results of the testicular examination were coded as abnormal if atrophy was noted by the examiner.

Participants with thyroidectomies were excluded from the analysis of the thyroid gland. For the analysis of the testes, participants with orchiectomies were excluded.

Laboratory Examination Data

The endocrine assessment from laboratory data consisted of the analysis of T_3 % uptake, TSH (µIU/ml), follicle stimulating hormone (FSH in µU/ml), testosterone (ng/dl), 2-hour postprandial glucose (mg/dl), and the composite diabetes indicator. The 100-gram glucose load for the postprandial assay was standardized by the use of Glucola®. The composite diabetes indicator was coded as yes for a verified history of diabetes or a 2-hour postprandial glucose greater than or equal to 200 mg/dl.

Except for the composite diabetes indicator, all laboratory variables were analyzed in both discrete and continuous forms. Continuous analyses for T_3 % uptake, TSH, FSH, and 2-hour postprandial glucose were done after transforming the data to the natural logarithm scale. A square root transformation was applied for all continuous analyses of testosterone. The cutpoints for the discrete analyses were based on Scripps Clinic and Research Foundation (SCRF) reference values. For the discrete analyses, T_3 % uptake and testosterone were initially to be coded as abnormal low, normal, and abnormal high. However, examination of the frequencies revealed sparse data for the abnormal low T_3 % uptake category and the abnormal high testosterone grouping. Only 22 participants had T_3 % uptake less than 25 percent (11 Ranch Hands, 11 Comparisons), and only 2 Ranch Hands and 3 Comparisons had testosterone levels greater than 1,250 ng/dl. Because of these sparse frequencies, the categories were collapsed with the respective normal classification for analysis. TSH was classified as normal/abnormal high. In the discrete analysis of 2-hour postprandial glucose, the results were coded as normal, impaired, and diabetic.

Participants with thyroidectomies or those taking thyroid medication were excluded from the analysis of T_3 % uptake and TSH. For testosterone, participants with orchiectomies or taking testosterone medication were excluded. Known diabetics (verified history) were excluded from the analysis of 2-hour postprandial glucose. Participants with a pre-SEA history of diabetes were excluded from the analyses of the composite diabetes indicator. No participants were excluded from the analyses of FSH.

Covariates

The effects of the covariates age, race, occupation, and personality type were examined in the assessment of the endocrine function, both in pairwise associations with the dependent variables and in adjusted statistical analyses. Personality type was not used for the adjusted analysis of FSH. In the adjusted analyses of testosterone, 2-hour postprandial glucose, and the composite diabetes indicator, percent body fat was also a candidate covariate. Age and percent body fat were treated as continuous variables for all adjusted analyses. These variables were categorized for presentation of the covariate tests of association in Table 0-1 and for interaction exploration.

Personality type was determined from the Jenkins Activity Survey administered at the 1985 followup examination. This variable was derived from a discriminant function equation based on questions that best discriminate men judged to be Type A from those judged as Type B. Positive scores reflect the Type A direction and negative scores the Type B direction. This variable was dichotomized into Type A and Type B for all analyses. Participants at the 1987 followup examination who did not attend the 1985 followup examination had missing information for this covariate, as well as a few participants who could not be classified in 1985.

Percent body fat, a measure of the relative body mass[39] of an individual derived from height and weight recorded at the physical examination, was computed by the following formula:

$$\text{Percent Body Fat} = \frac{\text{Weight (kg)}}{[\text{Height (m)}]^2} \cdot 1.264 - 13.305.$$

In its discrete form, this variable was dichotomized as lean/normal ($\leq$25%) and obese (>25%).

Relation to Baseline and 1985 Followup Studies

All variables analyzed in the 1987 followup study except FSH were analyzed in the 1985 followup study. Of the variables analyzed in the 1987 followup, only T_3 % uptake, 2-hour postprandial glucose, and testosterone were analyzed at Baseline.

Three variables were analyzed in the longitudinal analysis of the endocrine function: T_3 % uptake, TSH, and testosterone.

Statistical Methods

The basic statistical analysis methods used in the assessment of the endocrine function are described in Chapter 7. Table 18-1 lists the dependent variables, data source, data form(s) (discrete and/or continuous), cutpoints, candidate covariates, and statistical methods used in the evaluation of the endocrine system. Additional information on the candidate covariates is provided in the second part of the table. Abbreviations are used extensively in the body of the table and are defined in footnotes.

TABLE 18-1.

Statistical Analysis for the Endocrine Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Current Thyroid Function (Self-Administered)	Q-SR	D	Normal Abnormal	--	UC:FT
History of Thyroid Disease (Interviewer-Administered)	Q-V	D	Yes No	--	UC:FT
Thyroid Gland	PE	D	Normal Abnormal	--	UC:FT
Testes	PE	D	Normal Abnormal	--	UC:FT
T_3 % Uptake	LAB	D/C	Normal: ≤35% Abnormal High: >35%	AGE RACE OCC PERS	UC:FT,TT AC:LR,GLM CA:CC,TT,GLM, CS,FT UE:GLM,TT AE:GLM L:RM
Thyroid Stimulating Hormone (TSH) (μIU/ml)	LAB	D/C	Normal: ≤3 Abnormal: >3	AGE RACE OCC PERS	UC:FT,TT AC:LR,GLM CA:CC,TT,GLM, CS,FT UE:GLM,TT AE:GLM L:OR
Follicle Stimulating Hormone (FSH) (μU/ml)	LAB	D/C	Abnormal Low: <3 Normal: 3-18 Abnormal High: >18	AGE RACE OCC	UC:CS,FT,TT AC:LL,GLM CA:CC,TT,GLM,CS UE:GLM,TT AE:GLM
Testosterone (ng/dl)	LAB	D/C	Abnormal Low: <260 Normal: ≥260	AGE RACE OCC PERS %BFAT	UC:FT,TT AC:LR,GLM CA:CC,TT,GLM, CS,FT UE:GLM,TT AE:GLM L:RM

TABLE 18-1. (continued)

Statistical Analysis for the Endocrine Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
2-Hour Post-prandial Glucose (mg/dl)	LAB	D/C	Normal: <140 Impaired: 140-<200 Diabetic: ≥200	AGE RACE OCC PERS %BFAT	UC:CS,FT,TT AC:LL,GLM CA:CC,TT,GLM,CS UE:GLM,TT AE:GLM
Composite Diabetes Indicator	LAB	D	Yes: Verified History or glucose ≥200 mg/dl No: Otherwise	AGE RACE OCC PERS %BFAT	UC:FT AC:LR CA:CS,FT UE:CS,FT AE:LR

Covariates

Variable (Abbreviation)	Data Source	Data Form	Cutpoints
Age (AGE)	MIL	D/C	Born ≥1942 Born 1923-1941 Born ≤1922
Race (RACE)	MIL	D	Nonblack Black
Occupation (OCC)	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Personality Type (PERS)	PE (1985)	D	A Direction B Direction
Percent Body Fat (%BFAT)	PE	D/C	Lean/Normal: ≤25% Obese: >25%

TABLE 18-1. (continued)

Statistical Analysis for the Endocrine Assessment

Abbreviations:

Data Source:	LAB--1987 SCRF laboratory results MIL--Air Force military records PE--1987 SCRF physical examination PE (1985)--1985 SCRF physical examination Q-SR--1987 Family and Personal History questionnaire (self-reported) Q-V--1987 NORC questionnaire (verified)
Data Form:	D--Discrete analysis only D/C--Discrete and continuous analyses for dependent variables; appropriate form for analysis (either discrete or continuous) for covariates
Statistical Analyses:	UC--Unadjusted core analyses AC--Adjusted core analyses CA--Dependent variable-covariate associations UE--Unadjusted exposure index analyses AE--Adjusted exposure index analyses L--Longitudinal analyses
Statistical Methods:	CC--Pearson's product moment correlation coefficient CS--Chi-square contingency table test FT--Fisher's exact test GLM--General linear models analysis LL--Log-linear models analysis LR--Logistic regression analysis OR--Chi-square tests on the odds ratio RM--Repeated measures analysis TT--Two-sample t-test

In addition to the medical exclusions discussed previously, some dependent variable and covariate data were missing. Table 18-2 summarizes missing and exclusionary data by group and variable.

RESULTS

Ranch Hand and Comparison Group Contrast

Unadjusted results for questionnaire and physical examination variables are presented in Table 18-3. Tables 18-4 and 18-5 summarize unadjusted and adjusted analysis results, respectively, for the laboratory examination variables. Pairwise associations between the laboratory examination variables and the candidate covariates are detailed in Appendix O, Table O-1. Table O-2 provides stratified results for analyses in which group-by-covariate interactions were found.

Questionnaire Variables

Current Thyroid Function

As shown in Table 18-3, the response to self-administered questions relating to thyroid problems was not significantly different between groups (p=0.990 without adjustment for covariates).

History of Thyroid Disease

The percentage of participants who had a verified history of thyroid disease did not differ between groups in the unadjusted analysis (p=0.999).

Physical Examination Variables

Thyroid Gland

The percentage of thyroid abnormalities was not significantly different between groups in the unadjusted analysis (p=0.914).

Testes

No significant unadjusted group difference was found for the testicular examination (p=0.999).

TABLE 18-2.

Number of Participants Excluded or With Missing Data for the Endocrine Assessment

Variable	Analysis Use	Group: Ranch Hand	Group: Comparison	Total
Current Thyroid Function (Self-Administered)	DEP	4	2	6
T_3 % Uptake	DEP	1	2	3
TSH	DEP	1	2	3
FSH	DEP	1	2	3
Testosterone	DEP	1	2	3
2-Hour Postprandial Glucose	DEP	27	28	55
Composite Diabetes Indicator	DEP	5	7	12
Personality Type (1985)	COV	39	78	117
Thyroidectomy	EXC	11	11	22
Currently Taking Thyroid Medication	EXC	12	17	29
Pre-SEA History of Thyroid Disease	EXC	7	6	13
Orchiectomy	EXC	7	2	9
Currently Taking Testosterone Medication	EXC	1	0	1
Verified History of Diabetes	EXC	75	94	169
Pre-SEA History of Diabetes	EXC	3	3	6

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

TABLE 18-3.

Unadjusted Analysis for Endocrinologic Questionnaire and Physical Examination Variables by Group

Variable	Statistic	Group				Est. Relative Risk (95% C.I.)	p-Value
		Ranch Hand		Comparison			
Current Thyroid Function (Self-Administered)	n	991		1,297			
	Number/%						
	Abnormal	41	4.1%	55	4.2%	0.98 (0.65,1.47)	0.990
	Normal	950	95.9%	1,242	95.8%		
History of Thyroid Disease (Interviewer-Administered)	n	988		1,293			
	Number/%						
	Yes	45	4.5%	58	4.5%	1.02 (0.68,1.51)	0.999
	No	943	95.5%	1,235	95.5%		
Thyroid Gland	n	984		1,288			
	Number/%						
	Abnormal	258	26.2%	334	25.9%	1.02 (0.84,1.23)	0.914
	Normal	726	73.8%	954	74.1%		
Testes	n	988		1,297			
	Number/%						
	Abnormal	33	3.3%	44	3.4%	0.98 (0.62,1.56)	0.999
	Normal	955	96.7%	1,253	96.6%		

TABLE 18-4.

Unadjusted Analysis for Endocrinologic Laboratory Examination Variables by Group

Variable	Statistic	Group: Ranch Hand	Group: Comparison	Contrast	Est. Relative Risk (95% C.I.)	p-Value
T_3 % Uptake	n	975	1,273			
	Mean[a]	30.5	30.5		--	0.930
	95% C.I.[a]	(30.3,30.6)	(30.4,30.6)			
	Number/%					
	High	39 4.0%	45 3.5%		1.14 (0.73,1.76)	0.640
	Normal	936 96.0%	1,228 96.5%			
TSH (continuous)	n[b]	813	1,051			
	Mean[b]	1.01	0.97		--	0.099
	95% C.I.[b]	(0.98,1.04)	(0.95,1.00)			
(below detection limit)	n	975	1,273			
	Number/%					
	ADL*	813 83.4%	1,051 82.6%		--[c]	0.648
	BDL*	162 16.6%	222 17.4%			
(discrete)	n	975	1,273			
	Number/%					
	High	20 2.1%	24 1.9%		1.09 (0.60,1.99)	0.894
	Normal	955 97.9%	1,249 98.1%			
FSH	n	994	1,297			
	Mean[a]	7.85	7.60		--	0.289
	95% C.I.[a]	(7.49,8.22)	(7.31,7.90)			
	Number/%					
	Low	84 8.5%	103 7.9%	Overall		0.192
	Normal	793 79.8%	1,070 82.5%	Low vs. Normal/High	1.07 (0.79,1.45)	0.714
	High	117 11.8%	124 9.6%	High vs. Normal/Low	1.26 (0.97,1.65)	0.102

TABLE 18-4. (continued)

Unadjusted Analysis for Endocrinologic Laboratory Examination Variables by Group

Variable	Statistic	Group: Ranch Hand	Group: Comparison	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Testosterone	n	986	1,295			
	Mean[d]	533.1	526.1		--	0.304
	95% C.I.[d]	(522.9,543.4)	(517.4,534.9)			
	Number/%					
	Low	19 1.9%	20 1.5%		1.25 (0.67,2.36)	0.590
	Normal	967 98.1%	1,275 98.5%			
2-Hour Post-prandial Glucose	n	915	1,198			
	Mean[a]	110.7	110.3		--	0.758
	95% C.I.[a]	(108.7,112.6)	(108.6,111.9)			
	Number/%					
	Normal	750 82.0%	995 83.1%	Overall		0.795
	Impaired	142 15.5%	176 14.7%	Impaired vs. Normal	1.07 (0.84,1.36)	0.622
	Diabetic	23 2.5%	27 2.3%	Diabetic vs. Normal	1.13 (0.64,1.99)	0.774
Composite Diabetes Indicator	n	987	1,288			
	Number/%					
	Yes	92 9.3%	113 8.8%		1.07 (0.80,1.43)	0.704
	No	895 90.7%	1,175 91.2%			

[a]Transformed from natural logarithm (log) scale.

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

[b]Transformed from log (X-0.4) scale; statistics based only on TSH values at or above detection limit of 0.5 μIU/ml.

*: ADL--Above detection limit; BDL--Below detection limit.

--[c]Analysis not done.

[d]Transformed from square root scale.

TABLE 18-5.

Adjusted Analysis for Endocrinologic Laboratory Examination Variables by Group

Variable	Statistic	Group: Ranch Hand	Group: Comparison	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
T_3 % Uptake	n Adj. Mean[a] 95% C.I.[a]	937 30.6 (30.4,30.9)	1,198 30.6 (30.4,30.9)		—	0.941	AGE (p=0.012) OCC (p<0.001) RACE*PERS (p=0.047)
	n	975	1,273	High vs. Normal	1.14 (0.73,1.77)	0.561	AGE*RACE (p=0.011)
TSH	n[b] Adj. Mean[b] 95% C.I.[b]	813 0.96 (0.92,1.01)	1,051 0.93 (0.89,0.97)		—	0.092	AGE (p<0.001) RACE (p=0.014)
	n	975	1,273	High vs. Normal	1.09 (0.60,1.98)	0.779	—
FSH	n Adj. Mean[a] 95% C.I.[a]	994 7.82 (7.49,8.17)	1,297 7.62 (7.33,7.91)		—	0.290	AGE (p<0.001)
	n	994	1,297	Low vs. Normal/High High vs. Normal/Low	1.10 (0.81,1.51) 1.23 (0.92,1.64)	0.523 0.164	AGE (p<0.001)
Testosterone	n Adj. Mean[c] 95% C.I.[c]	986 532.4 (523.4,541.5)	1,295 526.6 (518.8,534.5)		—	0.345	AGE (p<0.001) %BFAT (p<0.001)
	n	947	1,217	Low vs. Normal	****	****	GRP*AGE (p=0.019) GRP*RACE (p=0.031) GRP*OCC (p=0.012) GRP*PERS(p=0.003) AGE*OCC (p=0.006) AGE*PERS (p=0.036) OCC*PERS (p<0.001) %BFAT (p<0.001)

TABLE 18-5. (continued)

Adjusted Analysis for Endocrinologic Laboratory Examination Variables by Group

Variable	Statistic	Group: Ranch Hand	Group: Comparison	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
2-Hour Post-prandial Glucose	n Adj. Mean[a] 95% C.I.[a]	878 111.1 (109.2,113.0)	1,122 110.5 (108.8,112.3)		—	0.643	AGE (p<0.001) OCC (p=0.001) %BFAT (p<0.001) PERS (p=0.042)
	n	915	1,198	Overall Impaired vs. Normal Diabetic vs. Normal	 1.09 (0.85,1.39) 1.19 (0.64,2.22)	0.679 0.493 0.575	AGE (p<0.001) OCC (p=0.002) %BFAT (p<0.001)
Composite Diabetes Indicator	n	987	1,288		1.10 (0.81,1.49)**	0.533**	GRP*%BFAT (p=0.019) AGE*RACE (p=0.006) AGE*%BFAT (p=0.037) OCC*RACE (p=0.046)

[a]Transformed from natural logarithm (log) scale.

—Adjusted relative risk not applicable for continuous analysis of a variable; no covariates significant in final model.
[b]Transformed from log (X-0.4) scale; statistics based only on TSH values at or above detection limit of 0.5 μIU/ml.

[c]Transformed from square root scale.

GRP: (Ranch Hand, Comparison).

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

**Group-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.

Laboratory Examination Variables

T_3 % Uptake

For the T_3 % uptake unadjusted analyses there was no statistically significant difference between Ranch Hand and Comparison group means (p=0.930) or the percentage of abnormal high values (p=0.640).

Using pooled group data, the covariate tests of association showed a highly significant relationship between T_3 % uptake and occupation (p<0.001). Table O-1 of Appendix O shows that the T_3 % uptake mean was highest for officers (30.9%), less for enlisted groundcrew (30.3%), and lowest for enlisted flyers (30.1%). None of the other covariates was significantly associated with T_3 % uptake.

Both the adjusted continuous and the discrete analysis did not detect a significant group difference (p=0.941, p=0.561, respectively). Significant covariates in the adjusted continuous model were a race-by-personality type interaction (p=0.047), and the main effects of age (p=0.012) and occupation (p<0.001). For the adjusted discrete model, the only significant term was an age-by-race interaction (p=0.011).

TSH

The unadjusted continuous analysis for TSH consisted of two analyses because only TSH levels of 0.5 μIU/ml or more (82.9% of participants) could be accurately measured. First, the percentage of individuals with TSH levels less than the detection limit of 0.5 μIU/ml was compared between groups. This difference was not significant (p=0.648). Second, the group means for participants with values equal to and above the detection limit were compared. This difference approached statistical significance (p=0.099). The Ranch Hand group mean was 1.01 μIU/ml versus the Comparison group mean of 0.97 μIU/ml. The results of the unadjusted discrete analysis did not show a significant group difference (p=0.894).

Treating TSH as a continuous variable and pooling over groups, significant associations with age (p<0.001) and race (p=0.001) were found, along with a marginally significant association with occupation (p=0.062). These results are based only on participants with TSH values above the detection limit. The correlation with age was 0.173. The mean for nonblacks (1.00 μIU/ml) was higher than the mean for Blacks (0.87 μIU/ml). The means were 1.02 μIU/ml, 0.99 μIU/ml, and 0.96 μIU/ml for officers, enlisted flyers, and enlisted groundcrew, respectively.

Using data only from participants with TSH levels above the detection limit, the group difference based on the adjusted continuous analysis was marginally significant (p=0.092). The adjusted means were 0.96 μIU/ml and 0.93 μIU/ml for the Ranch Hands and Comparisons, respectively. Age (p<0.001) and race (p=0.014) were used for adjustment. No significant group difference was found for the adjusted discrete analysis (p=0.779). None of the candidate covariates or pairwise interactions between the covariates was included in the final adjusting model.

FSH

For the unadjusted analyses of FSH, there were no statistically significant differences between Ranch Hand and Comparison group means (p=0.289), the percentage of abnormally low values (p=0.714), or the percentage of abnormally high values (p=0.102).

Using pooled group data, the covariate tests of association showed a highly significant relationship between FSH in its continuous form and age (p<0.001), between the percentage of participants having abnormally low FSH values and age (p<0.001), and between the percentage of participants having abnormally high FSH values and age (p<0.001). The correlation between FSH and age was 0.281. The percentages of participants having abnormally low FSH values among those born in or after 1942, between 1923 and 1941, and in or before 1922 were 11.1 percent, 6.3 percent, and 2.4 percent, respectively. The corresponding percentages of participants having abnormally high FSH values were 4.7 percent, 13.4 percent, and 33.3 percent, respectively.

There was a significant change in the FSH means due to race (p=0.016). The mean FSH levels for Blacks and nonblacks were 6.67 mU/ml and 7.78 mU/ml, respectively.

FSH means changed significantly with occupation (p<0.001); the means for officers, enlisted flyers, and enlisted groundcrew were 8.25 mU/ml, 7.99 mU/ml, and 7.18 mU/ml, respectively. There was a marginally significant association between the percentage of participants with abnormally low FSH values and occupation (p=0.056); the percentages for officers, enlisted flyers, and enlisted groundcrew were 6.8 percent, 7.3 percent, and 9.7 percent, respectively. There was a significant association between the percentage of participants having abnormally high FSH values and occupation (p<0.001); the percentages for officers, enlisted flyers, and enlisted groundcrew were 13.3 percent, 11.8 percent, and 7.7 percent, respectively.

In adjusted analyses of FSH, there was no significant group difference in means (p=0.290), the percentage of participants with abnormally high versus normal FSH levels (p=0.164), or the percentage of participants with abnormally low versus normal FSH levels (p=0.523). The only significant covariate in both the continuous and discrete analyses was age (p<0.001) for all analyses.

Testosterone

No significant group difference was present for testosterone in either the unadjusted continuous (p=0.304) or discrete (p=0.590) analyses.

Covariate tests of association treating testosterone as a continuous variable revealed statistically significant or marginally significant relationships with all the candidate covariates. After discretizing testosterone, the only significant associations were with age (p<0.001) and percent body fat (p<0.001). A negative correlation with age was seen (r=-0.293, p<0.001). Correspondingly, the percentage of abnormally low values increased with age (1.3% for participants born in or after 1942, 1.7% for those born between 1923 and 1941, 7.1% for those born in or before 1922).

The testosterone means were 504.4 ng/dl, 529.6 ng/dl, and 550.3 ng/dl, for the officer, enlisted flyer, and enlisted groundcrew cohort, respectively ($p<0.001$). The correlation between testosterone and percent body fat was -0.366 ($p<0.001$); a much higher percentage of abnormally low levels was found for obese participants (4.2%) than for normal/lean participants (1.1%). The mean for personality Type B individuals (522.5 ng/dl) was lower than the mean for Type A participants (537.6 ng/dl, $p=0.031$). Nonblacks had a marginally lower mean than Blacks (527.6 ng/dl and 553.2 ng/dl, respectively; $p=0.078$).

For the adjusted continuous analysis, the Ranch Hand group mean was not significantly different from the Comparison group mean ($p=0.345$). Significant covariates included in the adjusted model were age ($p<0.001$) and percent body fat ($p<0.001$).

The results for the adjusted discrete analysis were not nearly as straightforward. Here, four group-by-covariate interactions were encountered (group-by-age, $p=0.019$; group-by-race, $p=0.031$; group-by-occupation, $p=0.012$; and group-by-personality type, $p=0.003$). To interpret these findings, the data were reanalyzed fitting separate adjusted models for each occupational cohort. No significant group difference was found for either officers ($p=0.765$) or enlisted flyers ($p=0.234$). The model for officers was adjusted for age ($p=0.010$) and percent body fat ($p<0.001$); the enlisted flyer model was adjusted for percent body fat ($p<0.001$) and personality type ($p=0.008$). For the enlisted groundcrew analysis, a group-by-age interaction ($p=0.009$) and a group-by-personality type interaction ($p=0.037$) existed. Categorizing age, unadjusted relative risks were derived for each of the six covariate combinations of age and personality type within the enlisted groundcrew cohort. Overall, there were 14 abnormally low enlisted groundcrew (7 Ranch Hands, 7 Comparisons). The basis of the interaction was partially attributable to the circumstance that the only three Type B Ranch Hand abnormals were all in the oldest age category. This contrasts with the Comparison group in which the five Type B abnormals were all found in the two younger age categories.

2-Hour Postprandial Glucose

Unadjusted group differences in 2-hour postprandial levels were not significant for the continuous and discrete analyses ($p=0.758$ and $p=0.795$, respectively).

Covariate tests of association using pooled group data revealed significant relationships between 2-hour postprandial glucose and age, occupation, percent body fat, and personality type. A positive correlation with age was found ($r=0.191$, $p<0.001$). This association was also highly significant after categorizing glucose levels ($p<0.001$). The highest percentage of participants with diabetic glucose levels was found for the middle age category (2.8%, born between 1923 and 1941); the highest percentage of participants with impaired glucose levels was found for the oldest age category (30.0%, born in or before 1922); and the highest percentage of participants with normal glucose levels was found for the youngest category (88.9%, born in or after 1942).

Of the occupational cohorts, the glucose mean was highest for the enlisted flyers (114.4 mg/dl). The means for the enlisted groundcrew and officers were 109.8 mg/dl and 109.5 mg/dl, respectively (p=0.024). Examination of the discrete test of association with occupation (p=0.004) showed the highest percentage of diabetic glucose level individuals in the enlisted groundcrew (3.3%), followed by enlisted flyers (2.0%) and officers (1.5%). The highest percentage of impaired glucose level individuals was found for the enlisted flyers (20.3%), followed by officers (14.1%), and enlisted groundcrew (13.9%).

The correlation between 2-hour postprandial glucose and percent body fat was 0.303 (p<0.001). Correspondingly, the percentage of diabetic glucose level participants was higher for obese men (6.7%) than normal/lean men (1.4%), as was the percentage of impaired individuals (24.4% and 12.8%, respectively; p<0.001). The mean for personality Type B participants was higher than the mean for Type A individuals (112.3 mg/dl and 108.4 mg/dl, respectively; p=0.004). Also, analysis of trichotomized 2-hour postprandial glucose revealed a marginally significant association (p=0.051). The percentage of Type B individuals with impaired glucose levels (17.0%) was higher than the corresponding percentage of Type A participants (13.1%); the percentages of diabetic participants were roughly equal (2.3% and 2.4% for Type A and Type B, respectively).

No significant group difference was found for both the adjusted continuous analysis (p=0.643) and the discrete analysis (p=0.679). The group difference in the continuous model was adjusted for age (p<0.001), occupation (p=0.001), percent body fat (p<0.001), and personality type (p=0.042). Age (p<0.001), occupation (p=0.002), and percent body fat (p<0.001) were used for adjustment in the final discrete model.

Composite Diabetes Indicator

The percentage of Ranch Hands with a verified history of diabetes or a 2-hour postprandial glucose level greater than or equal to 200 mg/dl was not significantly different from the corresponding percentage of Comparisons in the unadjusted analysis (p=0.704).

Covariate tests of association showed highly significant relationships with age (p<0.001) and percent body fat (p<0.001). The percentage of diabetics increased with age (4.8%, 11.8%, and 14.5% for participants born in or after 1942, born between 1923 and 1941, and born in or before 1922, respectively). Obese individuals were much more likely to be diabetic than normal/lean individuals (20.3% and 6.0%, respectively).

The results of the adjusted analysis revealed a significant group-by-percent body fat interaction (p=0.019). Other significant covariates included in the model were interactions between age and race (p=0.006), age and percent body fat (p=0.037), and occupation and race (p=0.046). Stratified results showed a group relative risk marginally greater than 1 for normal/lean participants (Adj. RR: 1.40, p=0.093), in contrast to a relative risk less than 1 for obese participants (Adj. RR: 0.82, p=0.405). A second adjusted analysis was done ignoring the group-by-percent body fat interaction. The group difference was not significant for this analysis (p=0.533). Significant covariates used for adjustment in this analysis were an age-by-race interaction (p=0.033), an age-by-percent body fat interaction (p=0.044), and occupation (p=0.009).

Exposure Index Analysis

Laboratory Examination Variables

The exposure index analysis was done for the six laboratory examination variables. Except for the composite diabetes indicator, each was analyzed in its continuous form. Unadjusted and adjusted results are presented in Tables 18-6 and 18-7, respectively. Table 18-8 lists the exposure index-by-covariate interactions that were noted. Stratified results for these interactions are summarized in Table 0-3.

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

T_3 % Uptake

For each of the occupational cohorts, the unadjusted results of the T_3 % uptake were not significant. A significant exposure index-by-race interaction (p=0.022) was found for officers after covariate adjustment. Stratifying by race showed no significant differences among exposure categories for nonblack officers. For Black officers, the mean for the low exposure category was significantly less than the mean for the medium exposure category (p=0.008), and marginally less than the mean for the high exposure category (p=0.055). After excluding the interaction, the adjusted results were not significant. Adjusted results for the enlisted cohorts were not significant.

TSH

To account for the TSH detection limit problem discussed earlier, two sets of unadjusted exposure index analyses, comparable to the unadjusted core analysis, were done. The first analysis assessed the relationship between the proportion of detected values and the exposure index categories. For the officer cohort, a marginally significant difference between categories was seen (p=0.067). The percentage of undetectable observations (less than 0.5 μIU/ml) was highest for the low exposure group (20.2%), and lower for the other categories (11.2% and 11.5%, medium and high exposure, respectively). The medium versus low and high versus low contrasts were also marginally significant (p=0.071 and p=0.087, respectively). The results of this analysis were not significant for the enlisted cohorts. Using data only above or equal to the detection limit, the unadjusted means were not significantly different for any of the occupational cohorts. After covariate adjustment, a marginally significant difference was noted for the officer cohort (p=0.084). The adjusted means were 1.14 μIU/ml, 1.01 μIU/ml, and 1.17 μIU/ml for the low, medium, and high exposure categories, respectively. The medium versus low contrast was marginally significant (p=0.089).

TABLE 18-6.

Unadjusted Exposure Index for Endocrine Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low	Medium	High	Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
T_3 % Uptake	Officer	n	129	118	122	Overall		0.363
		Mean[a]	30.9	31.1	30.6	M vs. L	--	0.710
		95% C.I.[a]	(30.5,31.4)	(30.6,31.5)	(30.2,31.1)	H vs. L	--	0.306
	Enlisted Flyer	n	55	63	50	Overall		0.671
		Mean[a]	30.2	30.0	30.5	M vs. L	--	0.792
		95% C.I.[a]	(29.3,31.0)	(29.5,30.6)	(29.8,31.1)	H vs. L	--	0.547
	Enlisted Groundcrew	n	146	153	139	Overall		0.605
		Mean[a]	30.5	30.2	30.2	M vs. L	--	0.426
		95% C.I.[a]	(30.1,30.9)	(29.9,30.6)	(29.8,30.6)	H vs. L	--	0.354

TABLE 18-6. (continued)

Unadjusted Exposure Index for Endocrine Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low		Medium		High		Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
TSH	Officer	n[b]	103		105		108		Overall		0.208
		Mean[b]	1.05		1.01		1.13		M vs. L	--	0.510
		95% C.I.[b]	(0.96,1.16)		(0.93,1.10)		(1.03,1.26)		H vs. L	--	0.279
		n	129		118		122		Overall		0.067
		Number/%									
		ADL*	103	79.8%	105	89.0%	108	88.5%	M vs. L	--[c]	0.071
		BDL*	26	20.2%	13	11.0%	14	11.5%	H vs. L	--[c]	0.087
	Enlisted Flyer	n[b]	43		49		44		Overall		0.652
		Mean[b]	0.93		1.02		0.97		M vs. L	--	0.357
		95% C.I.[b]	(0.84,1.04)		(0.90,1.15)		(0.84,1.15)		H vs. L	--	0.659
		n	55		63		50		Overall		0.317
		Number/%									
		ADL*	43	78.2%	49	77.8%	44	88.0%	M vs. L	--[c]	0.999
		BDL*	12	21.8%	14	22.2%	6	12.0%	H vs. L	--[c]	0.282
	Enlisted Groundcrew	n[b]	120		122		119		Overall		0.471
		Mean[b]	0.98		0.94		1.01		M vs. L	--	0.526
		95% C.I.[b]	(0.90,1.06)		(0.88,1.02)		(0.93,1.12)		H vs. L	--	0.554
		n	146		153		139		Overall		0.419
		Number/%									
		ADL*	120	82.2%	122	79.7%	119	85.6%	M vs. L	--[c]	0.696
		BDL*	26	17.8%	31	20.3%	20	14.4%	H vs. L	--[c]	0.534

TABLE 18-6. (continued)

Unadjusted Exposure Index for Endocrine Variables by Occupation

			Exposure Index			Exposure Index	Est. Relative	
Variable	Occupation	Statistic	Low	Medium	High	Contrast	Risk (95% C.I.)	p-Value
FSH	Officer	n	130	124	124	Overall		0.270
		Mean[a]	8.25	9.49	8.46	M vs. L	--	0.128
		95% C.I.[a]	(7.28,9.35)	(8.28,10.86)	(7.44,9.61)	H vs. L	--	0.789
	Enlisted Flyer	n	55	63	53	Overall		0.319
		Mean[a]	7.10	8.59	8.60	M vs. L	--	0.182
		95% C.I.[a]	(5.75,8.76)	(7.10,10.39)	(6.95,10.66)	H vs. L	--	0.196
	Enlisted Groundcrew	n	147	158	140	Overall		0.226
		Mean[a]	6.74	6.92	7.73	M vs. L	--	0.747
		95% C.I.[a]	(6.01,7.56)	(6.26,7.65)	(6.73,8.87)	H vs. L	--	0.104
Testos-terone	Officer	n	129	123	122	Overall		0.032
		Mean[d]	536.8	496.5	494.7	M vs. L	--	0.024
		95% C.I.[d]	(508.5, 565.8)	(474.0, 519.6)	(469.2, 520.9)	H vs. L	--	0.023
	Enlisted Flyer	n	55	62	53	Overall		0.152
		Mean[d]	531.7	550.5	491.5	M vs. L	--	0.544
		95% C.I.[d]	(490.3, 574.8)	(507.1, 595.8)	(451.0, 533.8)	H vs. L	--	0.201
	Enlisted Groundcrew	n	146	157	139	Overall		0.218
		Mean[d]	547.5	576.7	542.8	M vs. L	--	0.168
		95% C.I.[d]	(519.0, 576.8)	(550.9, 603.2)	(513.8, 572.6)	H vs. L	--	0.818

TABLE 18-6. (continued)

Unadjusted Exposure Index for Endocrine Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low	Exposure Index: Medium	Exposure Index: High	Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
2-Hour Postprandial Glucose	Officer	n	119	116	108	Overall		0.639
		Mean[a]	108.3	111.6	110.3	M vs. L	--	0.350
		95% C.I.[a]	(103.8, 112.9)	(106.5, 116.9)	(105.2, 115.7)	H vs. L	--	0.564
	Enlisted Flyer	n	54	56	51	Overall		0.550
		Mean[a]	109.5	114.6	116.0	M vs. L	--	0.401
		95% C.I.[a]	(101.8, 117.8)	(105.9, 124.2)	(107.5, 125.1)	H vs. L	--	0.306
	Enlisted Groundcrew	n	137	144	130	Overall		0.875
		Mean[a]	111.1	110.1	109.2	M vs. L	--	0.782
		95% C.I.[a]	(106.6, 115.9)	(105.0, 115.4)	(103.6, 115.1)	H vs. L	--	0.606

TABLE 18-6. (continued)

Unadjusted Exposure Index for Endocrine Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low		Medium		High		Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
Composite Diabetes Indicator	Officer	n	130		124		121		Overall		0.699
		Number/%									
		Yes	10	7.7%	11	8.9%	13	10.7%	M vs. L	1.17 (0.48,2.86)	0.910
		No	120	92.3%	113	91.1%	108	89.3%	H vs. L	1.44 (0.61,3.43)	0.536
	Enlisted Flyer	n	55		63		53		Overall		0.007
		Number/%									
		Yes	1	1.8%	10	15.9%	2	3.8%	M vs. L	10.19 (1.26,82.40)	0.015
		No	54	98.2%	53	84.1%	51	96.2%	H vs. L	2.12 (0.19,24.07)	0.972
	Enlisted Groundcrew	n	145		156		140		Overall		0.340
		Number/%									
		Yes	11	7.6%	16	10.3%	18	12.9%	M vs. L	1.39 (0.62,3.11)	0.544
		No	134	92.4%	140	89.7%	122	87.1%	H vs. L	1.80 (0.82,3.96)	0.202

[a]Transformed from natural logarithm scale.

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

[b]Transformed from log (X-0.4) scale; statistics based on TSH values at or above detection limit of 0.5 µIU/ml.

*: ADL--Above detection limit; BDL--Below detection limit.

--[c]Analysis not done.

[d]Transformed from square root scale.