TABLE 13-8. (continued)

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

TABLE 13-8. (continued)

Unadjusted Exposure Index for Hepatic Variables by Occupation

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

TABLE 13-8. (continued)

Unadjusted Exposure Index for Hepatic Variables by Occupation

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

TABLE 13-8. (continued)

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

[a]Transformed from natural logarithm scale.

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

[b]Transformed from natural logarithm (X + 0.1) scale.

[c]Relative risk/confidence interval not given due to a cell with zero frequency.

TABLE 13-9.

Adjusted Exposure Index for Hepatic Variables by Occupation

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

TABLE 13-9. (continued)

Adjusted Exposure Index for Hepatic Variables by Occupation

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

TABLE 13-9. (continued)

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

TABLE 13-9. (continued)

Adjusted Exposure Index for Hepatic Variables by Occupation

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

TABLE 13-9. (continued)

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

TABLE 13-9. (continued)

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

TABLE 13-9. (continued)

Adjusted Exposure Index for Hepatic Variables by Occupation

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

TABLE 13-9. (continued)

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

TABLE 13-9. (continued)

Adjusted Exposure Index for Hepatic Variables by Occupation

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

TABLE 13-9. (continued)

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

TABLE 13-9. (continued)

Adjusted Exposure Index for Hepatic Variables by Occupation

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

TABLE 13-9. (continued)

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

TABLE 13-9. (continued)

Adjusted Exposure Index for Hepatic Variables by Occupation

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

[a]Transformed from natural logarithm scale.

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

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

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

[b]Transformed from natural logarithm (X + 0.1) scale.

TABLE 13-10.

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

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

TABLE 13-10. (continued)

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

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

*Refer to Table J-4 for a further investigation of these interactions.
C: Continuous Analysis.
D: Discrete Analysis.

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

AST

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

ALT

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

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

GGT

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

Alkaline Phosphatase

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

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

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

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

Total Bilirubin

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

Direct Bilirubin

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

LDH

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

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

Cholesterol

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

HDL

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

Cholesterol-HDL Ratio

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

Triglycerides

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

Creatine Kinase

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

Fasting Glucose

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

Longitudinal Analysis

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

Mortality Count Data

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

TABLE 13-11.

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

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

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

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

TABLE 13-12.

Group Cumulative Site-Specific Digestive System Mortality

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

DISCUSSION

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

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

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

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

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

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

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

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

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

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

Significant ($p<0.001$) race-related differences in two serum enzymes (GGT and creatine kinase) were documented and, in the case of the creatine kinase, the mean for Blacks was almost twice that for nonblacks. These data are consistent with observations first reported by H.Y. Meltzer[54] and subsequently confirmed in a small number of studies over the past decade. The elevation, not yet explained, appears to be race- and gender-specific and is limited to Black males.

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

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

SUMMARY

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

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

TABLE 13-13.

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

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

TABLE 13-13. (continued)

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

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

--Analysis not performed or not applicable.

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

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

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

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

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

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

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

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

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

CHAPTER 13

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CHAPTER 14

DERMATOLOGIC EVALUATION

INTRODUCTION

Background

The skin is a major target organ following heavy exposure to chlorophenols and dioxin and, therefore, is a primary focus of the Air Force Health Study (AFHS) clinical examination.

Since the association between chlorinated chemicals and chloracne was first noted in 1957,[1,2] a variety of animal experiments have shown the dermal sensitivity of rabbits, monkeys, and hairless mice to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), 2,4,5-T (contaminated with TCDD), and other chlorinated dibenzo compounds, furans, or their brominated analogs.[1-9] Chloracne is not associated with exposure to 2,4-D.[8] Studies in animals have found the development of severe skin lesions in rats from 2,4-D exposure,[9] chloracne in hairless mice from TCDD that also causes an increase in synthesis of keratins,[10] and squamous cell carcinomas on the skin of the facial region in hamsters that had ingested TCDD.[11] One study in rats investigating testosterone interaction with TCDD has indicated that chloracne, hirsutism, and skin hyperpigmentation may result from the involvement of the endocrine system.[12] Accidental exposure to waste oils containing TCDD has caused significant dermal symptoms, including loss of hair, ulcerative dermatitis, and inflamed mucous membranes in horses, dogs, cats, and mice.[13,14] Studies have suggested that the chloracnegens induce a series of pathological skin changes in target cells of the epithelial lining of sebaceous glands via the Ah receptor.[15] Hyperkeratinization of these cells eventually leads to the formation of the comedone characteristic of acne.

The findings with animals have led to a number of studies with human epidermal cells to investigate the exact nature of TCDD skin effects in man. Skin effects generally recognized and investigated in man include: acanthosis (thickening of the epidermis), hyperkeratosis, and squamous metaplasia of the epithelial lining of the sebaceous glands.[16] Two studies found that TCDD produced hyperkeratinization, probably due to action in the epidermal basal cells to enhance terminal differention through the mechanisms regulated partly by Ah receptors.[16,17] (Another study in mice found that physiological factors beyond the epidermal cells may be involved in epidermal responses.[18,19]) Chloracne is believed to develop as hair follicles dilate and fill with keratin and the sebaceous glands become cystic.[20]

In humans, development of the hallmark rash, chloracne, is generally acknowledged to represent substantial topical or systemic exposure to one or more chloracnegens.[1,5,6,21-27] Acute fulminant chloracne is characterized by a maculopapular rash of active comedones, conforming to an eyeglass or facial butterfly distribution, often accompanied by chest, back, or eyelid lesions.[3,27] Since these lesions are seen in other skin diseases, the clinical diagnosis of chloracne is often based on a history of exposure to known acnegenic chemicals; however, the only definitive method of diagnosis is by histologic examination of biopsy material.[27]

Chronic chloracne has been clinically observed more than 30 years after onset,[25] but a biopsy is often necessary to confirm these cases.[27] Mild or transient cases of chloracne may be confused with persistent adolescent acne or other skin conditions.

The severity of the chloracne appears to be generally dose related, but may also depend on the route of administration, age, genetic predisposition, and the existence of acne vulgaris or other skin disorders.[5,24,27] Occasionally, exposure, via contaminated clothes of an industrial worker, has been associated with chloracne in family members.[28] Sequelae from severe chloracne include actinic elastosis, acne scars, disfigurement, excessive hair growth, and Peyronie's disease.[5,25] Severe chloracne is often accompanied by acute effects in other organ systems. In contrast, low to moderate exposure to chloracnegens generally produces mild chloracne with few, if any, attendant systemic signs and symptoms.

As noted in the AFHS Baseline Morbidity Report, over one-half of the veteran complaints in the Veterans Administration Herbicide Registry involved dermatologic conditions, a fact sometimes alluded to as "evidence" of exposure to Agent Orange. In actuality, skin disease was a major medical problem among American troops serving in Vietnam. Forty-seven percent of the combat-days lost in the 9th Infantry Division from July 1968 to June 1969 were due to dermatologic conditions.[29] These diseases were directly related to the tropical climate and terrain. Only in rare cases has the Veterans Administration made a diagnosis of chloracne in a Vietnam combat veteran. The natural history of chloracne suggests that most cases should have been diagnosed while in Vietnam, but a dermatologic survey failed to reveal any cases.[29] In a study of members of the American Legion, investigators found an increase in reports of skin rashes with blisters and changes in skin color among 102 men who reported having worked with herbicides in Vietnam.[30] Medical examinations to substantiate these reported problems were not conducted.

Most recognized chloracne cases have been diagnosed in chemical plant workers or in victims of industrial accidents. Thousands of cases were recorded in the 1930-1940 era, and earlier descriptions of chloracne-like disease were found between 1897 and 1901.[31] Industrial exposure to chloracnegens has been generally characterized as moderate-prolonged or severe-acute. In the setting of casual-sporadic exposure, as in the typical cases of the contaminated housing areas in Times Beach, Missouri, and the Quail Run Trailer Park, chloracne is virtually unknown.[32-34]

In the case of population exposures in Seveso, Italy, chloracne has been found in both children and adults.[35-37] A study comparing body burdens of the exposed adults in Seveso with dermally exposed prisoners who developed severe chloracne indicated body burdens in the Seveso population at 180 times that of the normal unexposed population and body burdens in the prisoners at 38 times that of the exposed Seveso population.[38] Another study of six factory workers with chloracne found adipose tissue levels of TCDD 15 times higher than normal population levels.[39] A study of farmers dermally exposed to 2,4-D pesticides found indications of dermal uptake but no skin effects, indicating that 2,4-D does not act the same as TCDD on the skin in man.[40] Workers at a 2,4,5-T (trichlorophenoxyacetic acid) plant were monitored for many years after their exposures; TCDD is a contaminant of 2,4,5-T.[41]

Eighty-six percent of the persons exposed during both normal operations and following an accident developed chloracne, and 52.7 percent still had it 20 to 30 years after the initial exposure. No other effects were found.

The use of chloracne as an indicator of TCDD exposure is still controversial.[38,42-44] Yet many population studies use it without comment.[37-42] Others have used it with qualifiers as to the possible existence of other initiators.[37-42] Based on chloracne data an exposure limit of 200 pg/m^3 has been recommended; this level has been proposed to prevent chloracne from repeated acute exposures as well as chronic exposures.[45] In the recommendation, it is believed that control of chloracne will prevent all other exposure effects.

A number of dioxin morbidity studies have shown a clustering of abnormal laboratory tests in individuals with chloracne.[22,24-26,46-49] This has led some investigators to believe that long-term sequelae to dioxin exposure will be found only in people with chloracne.[27] Other investigators feel that this belief is not consistent with normal spectrum-of-illness concepts and that effects may occur in the absence of chloracne.[50]

Baseline Summary Results

The 1982 Baseline clinical examination revealed an unexpected significant excess ($p=0.03$) of basal cell carcinoma in the Ranch Hand group. Risk factor data (e.g., sun exposure, host factors of tannability, complexion) were not collected in 1982.

The 1982 examination focused on the diagnosis of chloracne both in historical terms by a detailed questionnaire and in contemporary terms via a comprehensive clinical assessment. The questionnaire data did not demonstrate anatomic, incidence, or onset-time patterns of acne in the Ranch Hand group that might support an inference of past chloracne, nor did the physical examination detect a single case. Fourteen biopsies from 11 participants also failed to document a chloracne diagnosis. A dermatology index (the number of clinically detected skin abnormalities per individual) was virtually identical between the Ranch Hand and Comparison groups, and was associated with the history of past acne in both groups. No exposure level associations were noted in any occupational category of the Ranch Hand group. The comprehensive dermatologic assessment did not reveal evidence of past or current chloracne in the Ranch Hand group.

1985 Followup Study Summary Results

Questionnaire data recaptured many of the acne parameters of the 1982 questionnaire, and the physical examination parameters were similar to the 1982 Baseline examination. Particular emphasis was given to the diagnosis of basal cell carcinoma and to the collection of risk factor data, e.g., skin color, reaction to sun, ethnicity (see Chapter 10, Malignancy).

Interval questionnaire data on the occurrence, time, and location of acne were analyzed to assess the possible historical diagnosis of chloracne. No significant difference was observed between groups for reported occurrence of acne, although the Ranch Hand cohort reported slightly more acne. The

occurrence of acne relative to 1961 was comparable between groups. A marginally significant difference in the occurrence of post-1961 acne was found, with more Ranch Hands than Comparisons reporting acne strictly post-Southeast Asia (SEA). The duration of post-1961 acne was not significantly different between the two groups.

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

Analyses of the 1985 followup physical examination data, as with the Baseline examination, placed primary emphasis on six dermatologic disorders: comedones, acneiform lesions, acneiform scars, inclusion cysts, depigmentation, and hyperpigmentation. Secondary emphasis was given to 16 other minor conditions (generally not associated with chloracne) recorded at the physical examination.

No significant difference was found for any of these variables in the unadjusted analyses. The variable consisting of the 16 secondary conditions, labeled "other abnormalities," had the largest difference in the prevalence of abnormalities for the Ranch Hand cohort over the Comparison group, but the difference was nonsignificant. The covariate effects of age, race, occupation, and the presence of pre-SEA acne were often profound with respect to the recorded dermatologic conditions.

The adjusted analyses closely mirrored the unadjusted analyses, with no significance noted between groups for any variable. Only one group-by-covariate interaction was observed in the adjusted analysis of the dermatology index, with a group-by-presence of pre-SEA acne interaction noted. However, further analysis of this interaction did not show an adverse effect in the Ranch Hand group.

Exposure index analyses did support dose-response relationships for some of the variables in certain occupational strata, but did not reveal a strong pattern of results suggesting a relationship between skin disease and herbicide exposure.

Overall, the 1985 followup examination results paralleled the Baseline findings. Although the followup examination detected more dermatologic abnormalities than those present at Baseline, slightly more abnormalities were found in the Comparisons, and most relative risks approached unity. The longitudinal analysis for the dermatology index showed no statistically significant differences between groups in the change in results from the Baseline to the 1985 followup examination.

In conclusion, none of the questionnaire results disclosed an increased likelihood of past chloracne in the Ranch Hands. The physical examination did not diagnose a current case of chloracne. The dermatologic data were similar between the Ranch Hand and Comparison groups, and the longitudinal analysis of the dermatology index suggested equivalence between the Baseline and 1985 followup examination results.

Parameters of the 1987 Dermatologic Evaluation

Dependent Variables

The dermatologic evaluation was based on questionnaire and physical examination data.

Questionnaire Data

During the face-to-face health interview, each study participant was asked about the occurrences of acne since the date of the last health interview. This self-reported information was used to update the reported acne data through the 1985 followup, which include date of occurrence, length of occurrence, and location for each occurrence. The variables defined below were constructed from the self-reported acne data and analyzed in the dermatologic evaluation.

- Occurrence of Acne (Lifetime):

  Yes: at least one occurrence of acne

  No: no occurrences of acne

- Occurrence of Acne (Relative to SEA Tour of Duty):

  Post-SEA: all occurrences after the start of the first SEA tour

  Pre- and post-SEA: multiple occurrences, both before and after the start of the first SEA tour, or a case of acne that began before the start of the first SEA tour and that ended after starting the SEA tour

  Pre-SEA: last occurrence before the start of the first SEA tour

  None: no occurrences of acne

- Duration of Acne: for (a) participants with all occurrences after the start of the first SEA tour (post-SEA) and (b) participants with all occurrences after the start of the first SEA tour or with multiple occurrences, both before and after the start of the first SEA tour, or a case of acne that began before the start of the first SEA tour and that ended after starting the SEA tour (post-SEA combined with pre- and post-SEA)

  Computed as the sum of the length of occurrences in years; time periods were only counted once in the case of occurrences in overlapping time periods; occurrences of less than a month were counted as 1 month

- Location of Acne: for (a) participants with all occurrences after the start of the first SEA tour (post-SEA) and (b) participants with all occurrences after the start of the first SEA tour or with multiple occurrences, both before and after the start of the first

SEA tour, or a case of acne that began before the start of the first SEA tour and that ended after starting the SEA tour (post-SEA combined with pre- and post-SEA)

Locations: temples; eyes/eyelids; ears; temples and eyes; eyes and ears; temples and ears; temples, eyes, and ears; and other sites (cheeks, nose, forehead, jaw/chin, chest, back)

If more than one episode of acne occurred, cases involving the temples, eyes, or ears took precedence; multiple-site involvement took precedence over single-site involvement.

The analysis of occurrence of acne was based on responses from all of the participants of the 1987 followup. The occurrence of acne relative to SEA tour of duty was analyzed using all of the participants of the 1987 followup, all participants excluding those with both pre- and post-SEA acne, and all participants of the 1987 followup stratified by pre-SEA occurrence (yes/no) of acne. Duration of acne and location of acne were both analyzed twice. In one case, the location of acne was limited to the participants who had all occurrences after the start of the first SEA tour (post-SEA). The second analysis was based on the participants who had all occurrences after the start of the first SEA tour or who had multiple occurrences, both before and after the start of the first SEA tour, or a case of acne that began before the start of the first SEA tour and that ended after starting the SEA tour (post-SEA combined with pre- and post-SEA).

Duration of acne was analyzed as a continuous variable. The other variables are discrete.

No participants were excluded for medical reasons from the analysis of these variables.

The information on biopsies was tabulated. Further description on the analysis of the biopsy data is presented in Chapter 10, Malignancy.

Physical Examination Data

Eight variables from the physical examination data were analyzed in the dermatologic evaluation. The variables were comedones, acneiform lesions, acneiform scars, depigmentation, inclusion cysts, hyperpigmentation, other abnormalities, and dermatology index. The variable, other abnormalities, was coded as normal/abnormal. A participant was considered as abnormal for this variable if any of the following disorders were detected in the physical examination: jaundice, spider angiomata, palmar erythema, suspected melanoma, palmar keratoses, actinic keratoses, petechiae, ecchymoses, conjunctival abnormality, oral mucosal abnormality, fingernail abnormality, toenail abnormality, dermatographia, cutis rhomboidalis, suspected basal cell carcinoma, suspected squamous cell carcinoma, nevus, or other abnormalities. The dermatology index was formed by counting the number of abnormalities present for the following conditions: comedones, acneiform lesions, acneiform scars, and inclusion cysts. All other variables were coded as yes/no.

No participants were excluded for medical reasons from the analysis of these variables.

Covariates

No adjustments were made in the analysis of occurrence of acne. Presence of pre-SEA acne (yes/no) was a stratification variable in an analysis of occurrence of acne relative to SEA tour. Time reference to SEA (pre- and post-SEA/post-SEA) was a stratification variable in the analysis of duration of acne and location of acne. The covariates age, race, and presence of pre-SEA acne were used in adjusted statistical analyses of all physical examination variables in the dermatologic evaluation. Age was used in its continuous form for modeling purposes for all dependent variables except comedones, where age was trichotomized. Age was also trichotomized for presentation purposes for dependent variable-covariate associations and interaction summaries.

Relation to Baseline and 1985 Followup Studies

The same variables analyzed in the 1985 followup were analyzed in the 1987 followup. Except for depigmentation, which was a refinement in the analysis of the 1985 followup, the same variables were analyzed in the Baseline study.

The longitudinal analysis for the dermatologic evaluation was based on the dermatology index. For this analysis, the dermatology index was dichotomized as no abnormalities and at least one abnormality.

Statistical Methods

Table 14-1 summarizes the statistical analyses that were performed for the dermatologic evaluation. The first part of this table describes the dependent variables analyzed and identifies the candidate covariates and the statistical methods used. The basic statistical analysis methods are described in Chapter 7. The second part of this table provides a further description of candidate covariates. Abbreviations are used extensively in the body of the table and are defined in footnotes.

Although no participants were excluded for medical reasons in the dermatologic assessment as stated above, some dependent variable and covariate data were missing. The number of participants with missing data is provided in Table 14-2 by group and variable.

TABLE 14-1.

Statistical Analysis for the Dermatologic Evaluation

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Occurrence of Acne (Lifetime)	Q-SR	D	Yes No	--	UC:FT
Occurrence of Acne (Relative to SEA Tour)	Q-SR/ MIL	D	Pre-SEA Pre- and Post-SEA Post-SEA None	SEAACNE	UC:FT
Duration of Acne (years)	Q-SR	C	--	TIMESEA	UC:TT
Location of Acne	Q-SR	D	Temples Eyes Ears Other Sites	TIMESEA	UC:CS
Comedones	PE	D	Yes No	AGE RACE OCC SEAACNE	UC:FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Acneiform Lesions	PE	D	Yes No	AGE RACE OCC SEAACNE	UC:FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Acneiform Scars	PE	D	Yes No	AGE RACE OCC SEAACNE	UC:FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Depigmentation	PE	D	Yes No	AGE RACE OCC SEAACNE	UC:FT AC:LR CA:CS,FT UE:CS,FT AE:LR

TABLE 14-1. (continued)

Statistical Analysis for the Dermatologic Evaluation

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Inclusion Cysts	PE	D	Yes No	AGE RACE OCC SEAACNE	UC:FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Hyperpigmentation	PE	D	Yes No	AGE RACE OCC SEAACNE	UC:FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Other Abnormalities	PE	D	Normal: 0 Abnormal: $\geq$1	AGE RACE OCC SEAACNE	UC:FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Dermatology Index	PE	D	0 1 2 3 4	AGE RACE OCC SEAACNE	UC:FT AC:LL CA:CS
			Normal: 0 Abnormal: $\geq$1	AGE RACE OCC SEAACNE	UE:CS,FT AE:LR L:OR

TABLE 14-1. (continued)

Statistical Analysis for the Dermatologic Evaluation

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
Time Reference of Acne Relative to SEA (TIMESEA)	Q-SR/ MIL	D	Pre- and Post-SEA Post-SEA
Presence of Pre-SEA Acne (SEAACNE)	Q-SR/ MIL	D	Yes No

Abbreviations:

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

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

Statistical Methods:
CS--Chi-square contingency table test
FT--Fisher's exact test
LL--Log-linear models analysis
LR--Logistic regression analysis
OR--Chi-square test on the odds ratio
TT--Two-sample t-test

TABLE 14-2.

Number of Participants With Missing Data for Dermatology Evaluation by Group

Variable	Analysis Use	Group: Ranch Hand	Group: Comparison	Total
Occurrence/Time Reference of Acne Relative to SEA	DEP/ COV	11	13	24
Presence of Pre-SEA Acne	COV	8	10	18

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

Note: Six participants (three Ranch Hand and three Comparison) had acne before the start of their first SEA tour. These participants were not able to be classified distinctly as pre-SEA or pre- and post-SEA, however, which explains the difference in the number of missing participants for the two variables given above.

RESULTS

Ranch Hand and Comparison Group Contrast

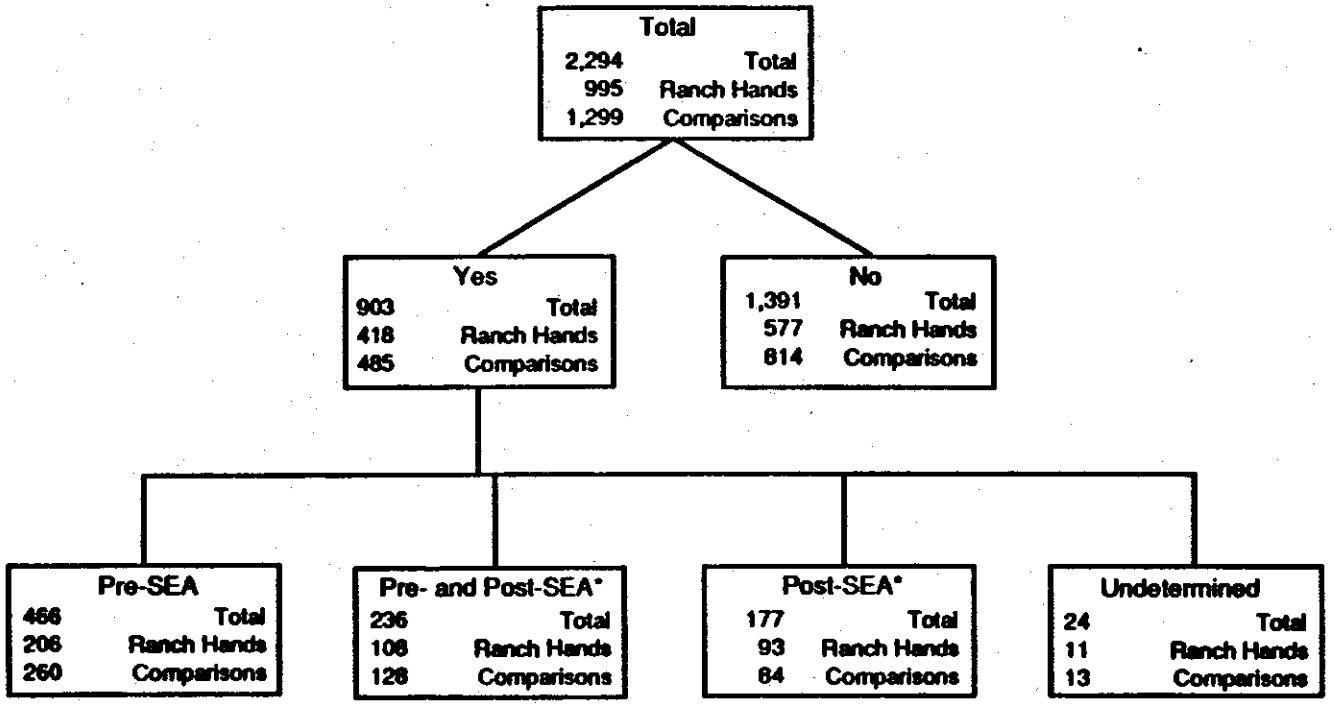
Questionnaire Variables

The occurrence of acne by time for the 2,294 participants in the 1987 followup is presented in Figure 14-1. The results of the analyses of the reported historical occurrence and duration of acne by group are provided in Table 14-3.

Occurrence of Acne

Lifetime

Of the 2,294 participants in the 1987 followup, 903 participants reported having experienced at least one occurrence of acne in their lifetime, and



Yes to Acne – Reported acne on Baseline and/or 1985 followup study and/or 1987 followup study.

No to Acne – Never had acne.

Pre-SEA Acne – Participants with acne who had all occurrences of acne before the start of first SEA tour (as determined from military records).

Pre- and Post-SEA Acne – Participants with acne who had multiple occurrences, both before and after the start of first SEA tour, or a case of acne that began before the start of first SEA tour and that ended after starting SEA tour.

Post-SEA Acne – Participants with acne who had all occurrences of acne after the start of first SEA tour.

Undetermined – Time reference not determinable from date information available.

*: Analysis of duration and location of acne performed for these participants.

Figure 14-1.
Occurrence of Acne by Time for 1987 Followup Participants

TABLE 14-3.

Analysis of Reported Historical Occurrence and Duration of Acne by Group

Variable	Statistic	Group: Ranch Hand		Group: Comparison		Est. Relative Risk (95% C.I.)	p-Value
Occurrence of Acne (Lifetime)	n	995		1,299			
	Number/%						
	Yes	418	42.0%	485	37.3%	1.22 (1.03,1.44)	0.026
	No	577	58.0%	814	62.7%		
Occurrence of Acne (Relative to SEA Tour)	n[a]	876		1,158			
	Number/%						
	Post-SEA vs. Pre-SEA/None	93	10.6%	84	7.3%	1.52 (1.12,2.07)	0.010
		783	89.4%	1,074	92.7%		
	n	984		1,286			
	Number/%						
	Post-SEA/Pre and Post-SEA vs. Pre-SEA/None	201	20.4%	212	16.5%	1.30 (1.05,1.61)	0.019
		783	79.6%	1,074	83.5%		
	n[b]	670		898			
	Number/%						
	Post-SEA vs. None	93	13.9%	84	9.4%	1.56 (1.14,2.14)	0.007
		577	86.1%	814	90.6%		

TABLE 14-3. (continued)

Analysis of Reported Historical Occurrence and Duration of Acne by Group

Variable	Statistic	Group: Ranch Hand	Group: Comparison	Est. Relative Risk (95% C.I.)	p-Value
	n[c]	314	388		
	Number/%				
	Pre- and Post-SEA vs.	108 34.4%	128 33.0%	1.07 (0.78,1.46)	0.754
	Pre-SEA	206 65.6%	260 67.0%		
Duration of Acne	n[d]	92	2		
	Mean[d]	3.85	3.39	--	0.451
	95% C.I.[d]	(3.04,4.75)	(2.59,4.29)		
	n[e]	199	209		
	Mean[e]	9.17	9.69	--	0.611
	95% C.I.[e]	(7.82,10.64)	(8.33,11.17)		

[a]Participants with pre- and post-SEA acne excluded.

[b]Participants with no history of acne before the start of their first SEA tour.

[c]Participants with a prior occurrence of acne before the start of their first SEA tour.

[d]Transformed from square root scale; analysis based on participants with acne in the post-SEA category only.

[e]Transformed from square root scale; analysis based on participants with acne in the post-SEA category combined with participants in the pre- and post-SEA category.