chemical brain injury

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5

Hydrogen Sulfide Exposure from Refineries in Cities

Death by asphyxiation from hydrogen sulfide (H_2S) has been recognized for over 200 years (1). Christison described fatalities from working in sewers and with animal excreta in 1845 (2). Hydrogen sulfide poisons metallo-enzymes, particularly cytochrome oxidase, and paralyzes the human respiratory center (3). It also causes hyperpnea by stimulating the carotid body, similarly to cyanide (1). In fatal poisoning the cerebral cortices, basal nuclei, lentiform body, and putamen showed greenish discoloration (4). Computerized tomography has demonstrated abnormal low density of the basal ganglia and surrounding white matter in chronic H_2S poisoning (5), and after fatal exposure (6), but clinical neurological examinations have been normal after "recovery" (3, 7). Thirteen subjects died, and unconsciousness was reported in 75% of 221 subjects made ill by H_2S exposure in Alberta, Canada from 1969 to 1973 (8). Nearly all of them had headaches, altered behavior, confusion, and vertigo. Agitation or somnolence were noted in 28%, nausea and/or vomiting in 22%, and disequilibrium in 17%. The completeness of recovery, that is, whether the survivors had long-term impairment, is unknown because neurological testing was not done.

Persistent neurobehavioral impairment after H_2S induced unconsciousness has been described recently. Six workers rendered unconscious by H_2S and mercaptans from sewage, manure, decaying fish in fishing boats, a tannery, and an oil drilling platform had neurobehavioral testing after two to six years (9). Five men had abnormal balance, impaired dexterity (slowed placement of pegs in a pegboard) and slow trail making B performance, poor verbal and visual recall on Wechsler's memory scale, and reduced scores on block design, digit symbol, similarities, picture completion, and vocabulary from the Wechsler Adult Intelligence Scale (WAIS) (10). The sixth ex-worker was demented and bedfast. After three men had been overcome by H_2S, they had similar impairment and abnormal auditory evoked potentials (P-300 latency) (11).

Several case reports had added clues about the effects of H_2S, which are briefly reviewed. Thirty-nine months after an offshore oil worker was overcome by H_2S (12), he showed profound impairment of balance, slow simple and choice reaction times,

impaired verbal and visual recall, prolonged trail making A and B, and reduced Culture Fair, block design, and digit symbol scores. His profile of mood states (POMS) score was greatly elevated with a low vigor score. A 20-month-old child was exposed for a year to 0.6 ppm H_2S downwind from a burning tip gas ignition point for a colliery. The H_2S levels exceeded the World Health Organization community standards of 0.003 to 0.01 ppm. Computerized tomography (5) showed subacute necrotizing encephalopathy in the basal ganglia and white matter. He had improved ten weeks after exposure ceased, but his final status was not described. A 45-year-old man showed similar bilateral symmetrical lucent lesions in the lentiform nucleus and basal ganglia on computerized tomography after unconsciousness due to H_2S (6). Acute coma due to H_2S has also been followed by periventricular leukomalacia (6).

Hydrogen sulfide and reduced sulfur gases from oil refineries in Canada (13) and from paper making in Finland (14) produced symptoms and impaired pulmonary function in residents downwind, but no neurological or psychological testing was done. Low level environmental exposure to H_2S has been ignored because mortality does not rise (15), or it is thought to trigger only mass psychogenic illness or "crowd disease" (16, 17). Before dismissing these gases as only nuisances, it would be prudent to examine exposed populations. The adverse CNS findings in 11 patients exposed to H_2S strongly supported the idea of permanent impairment from H_2S. The complaints of 9 workers triggered an epidemiological investigation of workers from a desulfurization unit of a California coastal oil refinery. Workers had shortness of breath, wheezing, eye and nose irritation and cough, skin rashes, depression, and headache and showed small airway obstruction on spirometry. Downwind neighbors of the refinery also had many symptoms, and 22 of them were studied with 13 former workers. Our hypothesis was that these symptoms were accompanied by impaired performance. Neurobehavioral impairment from chronic low-dose H_2S exposure has not been reported.

This chapter describes and analyzes patients and populations exposed to H_2S, which add strength to the hypothesis that H_2S causes chronic brain damage as shown by neurobehavioral dysfunction. As described in the following pages, there were several sources for these subjects. First were the H_2S-exposed patients seen in consultation from 1987 to 1995. The second group was from a pilot study in 1996 of 68 subjects who were exposed downwind from a Los Angeles area oil refinery explosion and gas leak in 1992. The third group included workers and downwind neighbors of an oil refinery near San Luis Obispo. The fourth group consisted of people in two communities with oil refineries who were studied as "unexposed" subjects for other chemical exposure groups but showed impairment most plausibly associated with being neighbors of oil refineries. The fifth and last group came from a study for balance and reaction time in Los Angeles oil refinery workers during their evaluation for asbestos exposure.

THE 16 PATIENTS

The 16 patients had been referred for evaluation of the effects of H_2S exposure (Table 5.1). They comprised nearly 10 percent of 160 consecutively examined chemically exposed patients. Five worked in oil fields, crude oil refining, and products shipping areas in Louisiana. Four were exposed downwind from oil fields in Kentucky and Texas, two were barge men hauling asphalt, two worked in a chemical plant downwind, one worked in sewage treatment, one was exposed to H_2S generated in a tank truck, and one was a dishwasher in a chemical process laboratory. Comparison and analysis was made to an unexposed group studied as the match for a chemical exposure group.

TABLE 5.1 Demographic and exposure data, H_2S exposure

Yr	Age	Sex	Ed Lev	Occupation	State	Exposure: Conditions	Exposure: Duration	Smoke	Major Symptoms
90	27	M	12	Oil field laborer	LA	Tank top oil depot	5–10 min	Never	Cognitive symptoms
91	62	M	0	Truck deliveries	LA	Next-door to H_2S release from well flameout	1 hr	Ex	Syncope
93	22	M	12	Tank cleaner	NV	Sodium hyposulfite and acid	2 hrs	Ex	Excess fatigue
93	21	M	13	Bargeman Miss. R.	LA	Pumping asphalt from oil refinery into barge	11/2 hrs	Ex	Headache
93	37	M	12	Bargeman Miss. R.	LA	Pumping asphalt from oil refinery into barge	5–6 hrs	Never	Pain in chest and back
94	62	M	18	Insurance business	KY	Downwind of crude oil pumping, with and without flare burning	2 yrs	Ex	Chest tightness
94	57	F	8	Farmer, homemaker	KY	Downwind of crude oil pumping, with and without flare burning	2 yrs	Never	Memory loss, asthma
92	42	M	16	Minister	TX	Downwind of refinery	12 yrs	Never	Memory loss
94	52	M	12	Water treatment worker	NV	Generated in sewage and "gray water" treatment	11 yrs	Ex 29 yrs	Extreme fatigue
94	35	F	12	Chemical plant process control 11 yrs	LA	Escape of H_2S and methyl mercapoproprionate into control room	1 day	Never	Unconsciousness
94	39	F	14	Chemical plant process control 10 yrs	LA	Loading area of plant as above	1 day	Never	Odor–headache
95	27	M	14	Contractor refinery	TX	Dug out pipeline leak	10 min	Never	Unconsciousness, recall memory loss
95	39	M	0	Contractor refinery	TX	Dug out pipeline leak	10 min	Ex	Unconsciousness, swelling legs and body
95	61	M	0	Contractor refinery	TX	Dug out pipeline leak	10 min	Ex	Unconsciousness, dizziness, fatigue
95	68	M	12	Contractor refinery	TX	Dug out pipeline leak	10 min	Ex	Unconsciousness, productive cough
95	63	F	9	Process laboratory	MO	Laboratory exposure	13 yrs	Never	Dizziness

The exposure, which rendered the first patient semiconscious, was monitored by his H_2S meter, which read to full scale at 10,000 parts per million (ppm). All the others smelled "rotten eggs" (H_2S); so their exposures are estimated to have been between 1 and 10 parts per million (ppm), that is, beneath the threshold for olfactory fatigue. However, exposure of the two barge men who were pumping asphalt from an oil refinery was probably 25 to 50 ppm, as they had headache and chest and back pain, and could not smell H_2S after an hour or more of exposure. One patient was delivering chicken feed for one to two hours downwind from H_2S released after the flame on an oil well vent pipe flared out. Exposure of another man, a tank cleaner, was to H_2S generated from sodium hyposulfite and acid within a tanker truck. A married couple, who lived downwind from wells pumping crude oil in Kentucky, associated the H_2S odor with an unlit vent flare and with memory loss and difficulty in concentrating. With the flame they noted a sharp pungent odor, and they had chest pain and tightness with asthma. Hydrogen sulfide escaped during the no-flame periods, and sulfur dioxide was released when the flare was lit. The sixth was a minister exposed to H_2S in Odessa, Texas, in his church and rectory immediately downwind from two H_2S-emitting oil refineries. When the wind shifted during church services, he had noted that numerous members of his congregation became nauseated and rushed outside to vomit. Chronic exposure to sewer gas in an aeration field for 20 years affected the sewerage treatment worker.

Exposed subjects ranged in age from 21 to 68 years with a mean of 44.7 years and had educational levels ranging from 0 to 18 years with a mean of 10.0 years, which was significantly below the unexposed subjects' mean because of three men without formal education (Table 5.1). Durations of H_2S exposures ranged from a few minutes in patients 1 and 13 through 16, who were most impaired, to 12 years in the minister. At the time of exposure 8 patients had never smoked and 8 were ex-smokers. Clinical physical and neurological examinations were essentially as expected for this age range of patients except for poor recall and diminished vibration sense. Data were analyzed by prevalence of abnormality and by comparison of means to the Arizona unexposed subjects. The prevalences of abnormality, as defined by test scores 1.5 standard deviations ($\pm$) from those of unexposed subjects (Chapter 3), were described for the 16 patients. In a second analysis, mean values of the 16 exposed patients were compared to unexposed subjects' means. Memory loss, excessive fatigue, and dizziness were the most common and most frequent symptoms, followed by difficulty in concentrating and chest pain and tightness (Table 5.2). Other symptoms included headache and memory loss, disorientation, nausea, decreased libido, and loss of strength. The woman with cough and asthma had also been exposed to sulfur dioxide intermittently when the flare above the upwind collection tank was burning.

Neurobehavioral testing showed that balance was impaired in 75% of subjects with eyes closed, as mean sway speed of the group was 2.95 cm/s compared to 1.18 cm/s in unexposed ($p < .0001$), and it was impaired in 56% of patients with eyes open, with mean 1.28 cm/s vs. 0.82 cm/s in unexposed ($p < .0001$) (see Tables 5.3 and 5.4). Choice reaction time was also prolonged in 63% of patients and the mean of the group was prolonged ($p < .0001$), whereas 44% had prolonged simple reaction time and the mean differences was significant ($p < .001$). Blink reflex latency (R-1) was lengthened in 75% of patients, but there were three with faster than average responses; so the mean was not different from the unexposed. Color discrimination was abnormal in 70% and visual fields were abnormal in 50% of those examined. Vibration sense was reduced in 82% of subjects tested.

Fingertip writing errors were the most common abnormality of psychological tests,

95	61	M	0	Contractor refinery	TX	Dug out pipeline leak	10 min	Ex	Unconsciousness, dizziness, fatigue, swelling legs and body
95	68	M	12	Contractor refinery	TX	Dug out pipeline leak	10 min	Ex	Unconsciousness, productive cough
95	63	F	9	Printex laboratory	MO	Laboratory exposure	13 yrs	Never	Dizziness

TABLE 5.2 Major complaints with frequencies greater than weekly, in H_2S-exposed patients

Symptom	Prevalence
Memory loss	11
Excessive fatigue	9
Dizziness	9
Headache	8
Decreased libido	8
Difficulty concentrating	5
Chest pain/tightness	5
Disorientation	5
Loss of strength	5
Nausea	4
Shortness of breath	4
Somnolence	2
Asthma	2
Cough	2
Sleep disturbed/dreams	2
Depression, severe	2
Blurred vision	2
Diarrhea	1
Syncope	1
Palpitations	1
Loss of appetite	1
Tinnitus	1
Body swelling and pain	1

and these errors were elevated in 75% with a significant difference in means ($p < .003$). Sixty-three percent had prolonged trail making B with a significant difference from unexposed; so the perceptual motor domain was impaired ($p < .0001$). Culture Fair and block design scores were each reduced in 69%, and means were significantly different from those of unexposed. Vocabulary score was diminished in 58%, and the means were significantly different. Immediate verbal recall was impaired in 63% and visual reproduction was impaired in 44%; neither difference was significant. Tests of long-term memory showed minimal impairment.

POMS score was elevated in 63% of patients, and the mean was significantly elevated (Table 5.3). Frequencies of 35 symptoms were elevated significantly above unexposed subjects' levels, as highlighted by the prevalence list of Table 5.2. Extensive questionnaires for medical and neurological diseases and for home and occupational chemical exposures did not show any pattern or combinations of confounding medical, neurological, or psychiatric diagnoses or exposure to other neurotoxins. All of these symptoms were rare, except that depression after H_2S exposures was frequent and needed treatment. These patients' symptoms are different from patterns identified for post-traumatic-stress syndrome, minimal head injury, or chronic fatigue syndrome.

A DISASTROUS INCIDENT IN TORRANCE, CALIFORNIA

On October 10, 1992, at 9:45 P.M. residents of the Los Angeles harbor area and north were shaken by two explosions at the TRM1 refinery hydrocracker, which registered

TABLE 5.3 Neurobehavioral performance of H_2S-exposed patients compared to unexposed means

	Unexposed		Exposed			Abnormal	
	Mean	Sd	Mean	Sd	*p* Value	Total	% Abnormal
Age yrs	42.4	15.4	44.7	16.7	NS		
Ed Level yrs	13.2	2.1	10.0	5.4	.004		
Balance cm/sec							
Eyes Open	0.82	0.21	1.28	0.47	.0001	9/16	56
Closed	1.18	0.41	2.95	1.54	.0001	12/16	75
Simple Reaction Time ms	285	64	422	192	.001	7/16	44
Choice Reaction Time ms	528	85	691	182	.0001	10/16	63
Blink Reflex Latency							
Supraorbital Tap ms							
Right	14.5	1.9	14.7	2.0	NS	9/12	38
Left	15.1	1.8	14.7	2.3	NS		75
Color Vision							70
Visual Fields						7/14	50
Vibration						9/11	82
Culture Fair sc	29.7	7.5	22.3	8.8	.001	11/16	69
Block Design sc	31.3	9.7	20.9	11.6	.0001	11/16	69
Digit Symbol sc	58.7	11.7	38.5	17.6	.001	9/16	56
Pegboard s	71.0	18.1	89.8	32.7	NS	6/16	38
Trails A sc	31.0	8.8	58.6	47.1	NS	5/16	31
Trails B sc	71.0	25.7	147.3	103.8	.0001	10/16	63
Fingertip Writing errors	3.9	1.9	10.8	8.7	.003	12/16	75
Recall							
Verbal, Immediate	23.3	4.2	15.6	10.0	NS	10/16	63
Visual, Immediate	35.4	3.9	24.6	8.5	NS	7/16	44
Vocabulary	24.2	9.2	12.3	5.7	.001	7/12	58
Information	17.9	5.6	14.6	7.0	NS	5/16	31
Picture Completion	14.4	3.0	13.3	4.5	NS	5/16	31
Similarities	19.8	4.6	16.5	6.1	NS	4/16	25
POMS Score	19.1	32.8	83.2	36.5	.0001	10/16	63
Symptom Freq sc	0.7	0.6	4.8	2.5	.001	10/16	63
Depression			23.9			9/15	60

ms = milliseconds NS = normal
s = seconds (I/D) = immediate/30 min. delay)
sc = score

3.0 on the Richter scale (see Figure 5.1). Broken windows and blown-down walls caused hundreds of injuries, which were only a portent of the damage to lungs, skin (including hair loss), and brains that followed 6 to 8 days of sour gas leaks—hydrogen sulfide and related sulfur-containing gases—from this petroleum refinery. In high concentrations these gases kill, but at lower levels they damage exposed persons' brains to disturb and disorder balance, vision, memory recall, and ability to concentrate. Ammonia, chlorine, gasoline, phenols, and other refinery gases were also released. Exposure caused profound depression in many people, as well as asthma and progressively severe airway obstructive disease. Many persons were hospitalized for traumatic injuries, including those to the head, and for respiratory distress and insufficiency. OSHA cited Texaco for 28 serious violations and levied civil penalties of $147,500 (citation of May 21, 1993). Fries Avenue Elementary School and Wilmington Junior High School

TABLE 5.4 Neurobehavioral performance of H_2S-exposed patients

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Age/Ed Level yrs	27/12	39/0	68/12	61/0	27/14	62/0	21/13	27/12	37/12	39/14	35/12	62/18	57/8	52/12	42/16	63/9
Balance cm/sec																
Eyes Open	1.57*	0.49	1.18*	2.17*	1.73*	1.55*	0.84	1.19*	1.11	1.39*	0.76	1.26	1.01	0.76	1.91*	1.62
Eyes Closed	6.39*	1.40	3.36*	3.94*	2.83*	4.00*	1.12	1.80*	2.11*	5.73*	2.39*	1.26	2.35	1.37	2.73*	4.38
Simple Reaction Time ms	560*	575*	320*	249*	375*	550*	226	293*	423*	990*	421*	318	333	287	227	603*
Choice Reaction Time ms	676*	871*	699*	675*	600*	990*	467	558*	768*	1081*	549	615*	715*	500	416	875*
Blink Reflex Latency ms																
Right	18†	14.1	13.5	NR	12.6	18*	12.5	17*	16*	14.6	15.3*	13.5	13	15.4*	14	13.7
Left	18*	13.0	13.3	14.8*	11.8	20*	12.5	17*	16*	14.9	17*	13.5	13.6	13	14	
Color Vision sc	—	Ab	Ab	Ab	N	—	Ab	N	Ab*	Ab†	Ab*	—	Ab	Ab	—	Ab
Visual Fields	—	Ab	Ab	Ab	Ab	—	N	N	Ab	Ab	Ab(c)	Ab	Ab	N	—	Ab
Vibration	—	Ab	Ab	Ab	Ab	—	N	N	—	Ab	Ab	—	Ab	Ab	—	Ab
Culture Fair sc	20*	12*	19*	5*	24	18*	30	28	29	17*	34	21*	20*	24	41	14*
Block Design sc	25	2*	22	11*	22	13*	6*	45	28	10	29	16*	22*	21	41	21*
Digit Symbol sc	42	8*	36	14*	57	15*	49*	74	55	21*	42	41*	34*	40	52	36*
Pegboard sc	65	191*	99	88	67	112*	76	56	67	109*	76	92*	64	88*	61	136*
Trails A sc	43*	132*	91	129*	31	68	32	18	33	180*	23	38	37	37	21	54
Trails B sc	94*	—	238*	221*	50	335*	74	49	118*	180(e)*	55	111*	127*	94*	67	144*
Fingertip Writing errors	33*	16*	11*	7	2	19*	10*	5	0	16*	11*	15*	0	0	12*	16*
Recall immed/del																
Verbal	9*	0*	6*	7*	12	15/8*	33	22/1*	33	15/0*	14/14*	9*	18/12*	15/13*	33/13*	9*
Visual	15*	10*	24*	14*	16*	19/0*	34	35/32	36	30/0*	33/33	31	28/26	20/17	30/26	18*
Vocabulary sc	—	5	7*	2*	10*	—	15	—	16	13*	12*	20	10*	20	—	17
Information sc	21	3	15	9*	5*	6*	15	15	15	12*	17	24	12	23	26	16
Picture Completion sc	17	3	12	6*	15	10*	47	15	14	15	18	15	11*	15	20	10*
Similarities sc	16	0	18	6*	15	5*	23	19	19	23	22	21	13*	20	25	19
POMS sc	91*	137*	69*	96*	82	57	62*	48	155*	87	89	57	101*	34	31	138*
Depression	13	36*	20*	32*	24*	19*	12	17	54*	17	23*	18*	34*	6	2	40*
Symptom Freq. score	4.7*	9.9*	6.5*	5.4*	7.5*	—	3.1	2.1	3.4*	7.3*	3.7*	3.2	1.8	3.9*	1.9	7.9*

Ab = abnormal
N = normal
— = not measured
cm/s = centimeters per second
ms = milliseconds
sc = score
* = $p < .05$

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FIGURE 5.1.

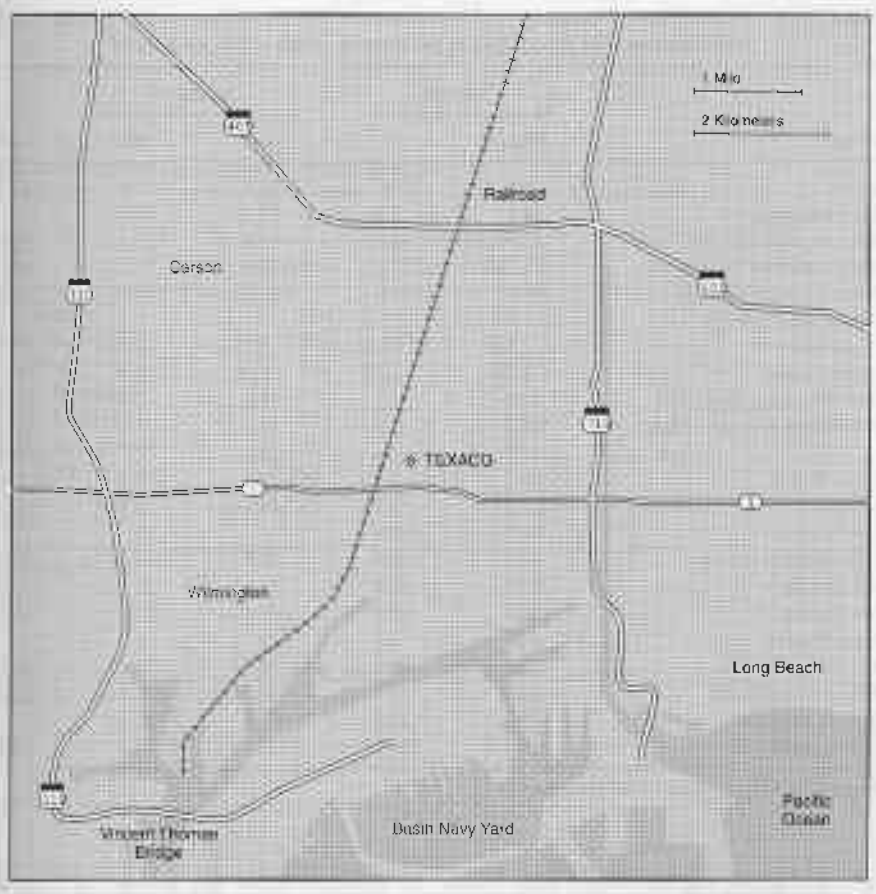

FIGURE 5.1. Wilmington, California, harbor area.

were primary and secondary evacuation sites, followed by Harbor College. The civil penalties were later raised to $231,000 (State $83,500; OSHA $147,500).

Subjects were divided on the basis of an examining physician's clinical judgment into four groups of ascending severity. Of the 68 pilot subjects, 25% were in Group 1, 21% in Group 2, 32% in Group 3, and 21% in Group 4. They included 24 African Americans and 20 Latino adults. Thirteen of the 20 children were Latino. Ethnically discrete comparisons were made to 20 African-American reference subjects from Oklahoma City and to 36 Latino unexposed subjects from Houston.

The ages of exposed African-Americans and unexposed were not different (Table 5.5, Figure 5.2). The figures were scaled by dividing the expected maximum for each test by 1,000 to create a scale factor. Because for some tests, for example, Culture Fair

TABLE 5.5a Comparison of unexposed African-American adults, 24 exposed at Torrance and 21 at Oklahoma City by analysis of variance; p values <0.05 underlined

Variable	Exposed		Unexposed		p value
	Mean	Sd	Mean	Sd	
Age yrs	46.9	17.0	42.4	7.4	.273
Education Level yrs	11.0	2.2	13.3	2.3	.001
Profile of Mood States	62.9	44.4	−0.4	15.6	.0001
Simple Reaction Time ms	491.0	274.0	278.5	53.2	.002
Choice Reaction Time ms	688.0	159.0	503.4	78.3	.0001
Sway–Balance cm/sec					
Eyes Open	1.06	0.73	0.75	0.20	.074
Eyes Closed	1.79	1.29	1.23	0.36	.057
Color Vision Lanthony Hue	13.4	1.5	12.1	1.1	.002
Blink Reflex R-1 ms Right	11.7	1.5	13.3	1.6	.005*
Left	11.1	1.4	13.4	1.7	.0005*
Culture Fair A	20.1	7.3	22.3	6.6	.300
Vocabulary	2.5	5.1	14.1	7.4	.0001
Digit Symbol	42.7	16.9			
Pegboard dominant sec	79.4	11.9	72.7	10.8	.056
Trail Making A	53.0	32.5	36.0	10.3	.027
Trail Making B	120.6	46.9	95.4	41.7	.066
Finger Writing	11.8	3.3			
FVC % of predicted	70.5	12.8	90.7	14.0	.0001
FEV_1 % of predicted	70.4	13.7	90.0	12.8	.0001
F_{25} % of predicted	80.0	35.2	97.6	21.5	.057
F_{75} % of predicted	80.0	38.0	95.1	30.1	.158

* Exposed are normal; unexposed are abnormal

and vocabulary, higher scores were better, the exposed score was subtracted from the unexposed. In other tests, such as balance and reaction time, lower scores were better; thus unexposed were subtracted from exposed. In both cases the result was multiplied by the scale factor. Statistically significant differences ($p < 0.05$) were shown by hatched bars and insignificant results by clear bars. Educational level was two years lower in exposed subjects than in unexposed (significantly different), but this difference had no effect on physiological tests, nor would it decrease the substantial difference for vocabulary to change the interpretation. Reaction times, both simple and choice, and color discrimination were different in exposed vs. unexposed. Balance sway speed was nearly statistically significantly faster (more) abnormal and highly variable in exposed subjects. Perceptual motor speed tests, pegboard, trail making A and B and fingertip number writing, were worse and approached statistical significance in exposed subjects. Unexposed subjects had not been tested with recall or memory tests, or for visual fields. Compared to other unexposed groups, many of the visual fields were highly abnormal in exposed subjects, usually for both eyes, and nearly 50% showed arcuate scotomata or concentric field losses. Vital capacity and forced expiratory volume in 1 second, FEV_1, were 20% below the predicted and thus greatly different in exposed subjects, and midflow differences approached significance at $p < 0.057$. Blink reflex latency R-1 was abnormal in Oklahoma City subjects, presumably because of TCE, and was normal in the Torrance subjects, who were unexposed to chlorinated solvents.

The exposed Latino adults were well matched to Houston unexposed for age and

TABLE 5.5b T

Information	
Picture Completion	
Similarities	
Stories Immediat	
Delayed	
Visual Design Rec	
Visual Field Righ	
Left	
Smell	

* No comparison data

FIGURE 5.2. Co
(Oklahoma City) sul
and unexposed (U) g
× 100

TABLE 5.5b Tests of exposed Torrance subjects

	Exposed		Unexposed*	
	Mean	Sd	Mean	Sd
Information	11.4	3.5		
Picture Completion	10.6	3.2		
Similarities	12.2	7.7		
Stories Immediate	17.3	3.5		
Delayed	13.5	3.1		
Visual Design Recall	21.6	7.7		
Visual Field Right	323	148		
Left	336	132		
Smell	3.3	0.9		

* No comparison data

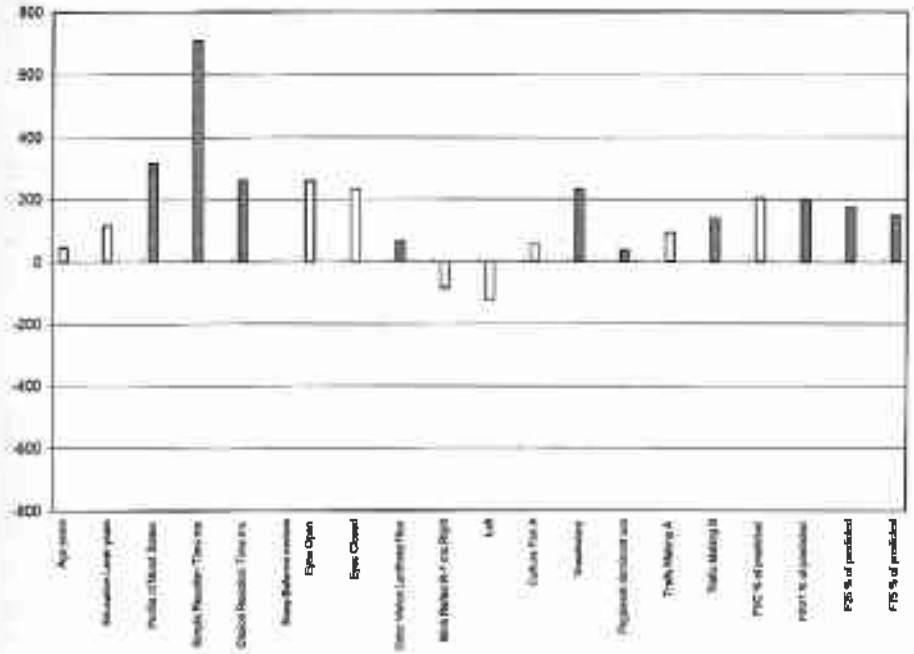

FIGURE 5.2. Comparison of African-American adults, 24 exposed to H_2S and 21 unexposed (Oklahoma City) subjects by ANOVA. Hatched bars are statistically significant. Scores for exposed (E) and unexposed (U) groups were divided by predicted values and the results expressed as a ratio E/U × 100.

TABLE 5.6 Comparison of Latino adults, 20 exposed at Torrance and 103 unexposed in Houston, by analysis of variance; p values <0.05 underlined

	Exposed		Unexposed		p
	Mean	Sd	Mean	Sd	Value
Age years	37.4	12.5	33.7	10.9	.176
Education Level years	10.1	2.7	11.0	2.8	.149
Simple Reaction Time min	403	149	323	106	.005
Choice Reaction Time min	569	131	537	112	.255
Sway–Balance Eyes Open	0.86	0.24	0.77	0.17	.059
Closed	1.40	0.56	1.15	0.35	.01
Blink Reflex R-1 ms Right	11.5	2.1	14.9*	2.3	.0001
Left	11.1	0.9	14.7*	2.3	.0001
Grip Strength Right	35.4	10.9	40.8	13.1	.01
Left	31.0	12.1	38.4	12.1	.0005
Visual Fields Right	447	96			
Left	424	99			
Color score	13.6	1.3	11.7	1.3	.0001
Contrast Sensitivity					
Smell	3.4	0.6			
Cognitive Function Domain					
Culture Fair A	20.9	8.3	25.1	7.8	.029
Digit Symbol	46.1	17.0	51.5	14.6	.05
Vocabulary	12.2	4.8	16.9	7.0	.005
Perceptual Motor Speed					
Pegboard	72.8	11.0	73.6	32.7	.908
Trail Making A	40.7	12.7	42.5	21.0	.713
Trail Making B	104.6	40.8	96.3	43.2	.430
Recall Domain					
Story Immediate	8.7	4.1	18.8	7.2	.0001
Story Delayed	6.8	4.8	15.6	7.4	.0001
Visual Design Recall	24.2	7.5	27.2	8.1	.122
Finger Writing Errors	7.8	3.8	5.06	6.6	.084
Long-Term Memory Domain					
Picture Completion	11.2	4.3	12.5	4.0	.183
Similarities	13.9	6.5	16.5	6.4	.103
Information	9.2	4.6	12.6	6.0	.02
Profile of Mood States	53	41	29.7	40.3	.02
Pulmonary Function Tests					
FVC % of pred	90.7	14.0	101.2	12.1	.0008
FEV_1 % of pred	90.0	12.8	96.9	12.4	.025
FEF_{25-75} % of pred	97.6	21.5	98.0	25.7	.956
$FEF_{75\ 85}$ % of pred	95.1	30.1	87.5	43.4	.455

* Abnormal "control" values

education (Table 5.6, Figures 5.3a, b). The exposed had slower simple reaction times, and choice reaction times, balance sway speed was significantly faster in the exposed with eyes closed and almost significant with eyes open. Blink reflex latency R-1 was faster (normal) in exposed vs. abnormal in Houston subjects, which is a seeming paradox. Grip strength and color vision were abnormal in the exposed. Cognitive functions, Culture Fair, digit symbol, and vocabulary were much lower in the exposed. Similarly, verbal recall, immediate and delayed, was much lower in exposed, but the long-term memory tests were not different, a finding consistent with the equivalent ability in the

FIGURE 5.3a.
(Houston) by ANC

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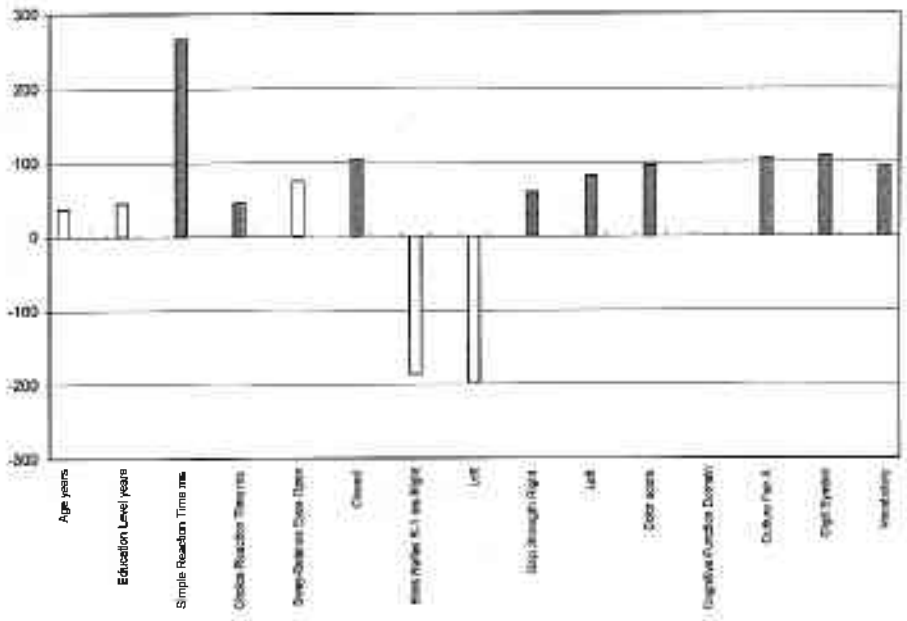

FIGURE 5.3a. Comparison of Latino adults, 20 exposed to H_2S (Torrance) and 103 unexposed (Houston) by ANOVA. Hatched bars are statistically significant.

groups before exposure. Perceptual motor speed tests were not different, but those values of the unexposed subjects were higher (more abnormal) than expected. In Latinos the vital capacity and FEV_1 were abnormal, although not low as in the African Americans, corrected for ethnic difference.

The 20 exposed children were mainly Latino and matched well for age and educational level to Houston children (Table 5.7, Figures 5.4a, b). Exposed children showed abnormal balance with eyes open but not eyes closed and more abnormal color vision. Reaction times were not increased in the exposed, and blink reflex latency R-1 was normal. Digit symbol score was lower in the exposed, perceptual motor speed was equivocal because of exceptionally high and probably abnormal trail making B scores in the unexposed, and recall was not different. Exposed children's vital capacities were lower, as were values for terminal flow (FEF_{75-85}).

Symptom frequency scores in adults compared to our standard unexposed group were elevated except for decreased alcohol tolerance (Table 5.8, Figures 5.5a, b). These frequencies of complaints elevations were consistent with the results of neurobehavioral tests.

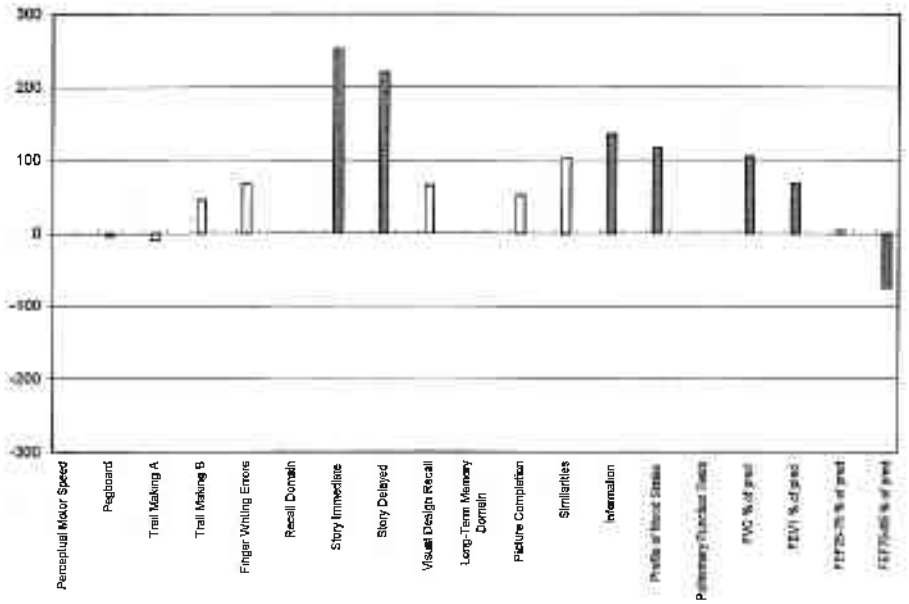

FIGURE 5.3b. Comparison of Latino adults, 20 exposed to H_2S (Torrance) and 103 unexposed (Houston) by ANOVA. Hatched bars are statistically significant.

No correlations were found between the clinical categories of ascending injury graded from 1 least to 4 greatest and any of these test results. The caveat is that when they were divided by ethnicity and the children were considered separately, the groups were small. As we also looked at the distributions of ethnicity and age within the groups and found no notable imbalances, we based this conclusion on the entire sample of 68 subjects.

THE UNOCAL REFINERY EXPOSURE

Unocal refinery workers and downwind neighbors had symptoms of asthma, depression, and dermatitis. We tested 13 former workers from the refinery and 22 downwind neighbors in Nipoma, California, before and after they filed suit against the refinery. When the 13 ex-workers were studied, the small airways obstruction, dermatitis, and depression had cleared.

Ten male ex-workers, mean age 38 years, who had worked in the desulfurization unit of the refinery for 1.5 to 3 years, and eight male and nine female neighbors of the

unexposed

TABLE 5.7 20 exposed children vs. 44 Houston Latino children, means and standard deviations

	Unexposed		Exposed		*p*
	Mean	Sd	Mean	Sd	Value
Age yrs	10.9	3.0	12.5	3.0	.057
Education Level yrs	4.9	2.9	6.2	2.8	.118
Physiological Domain					
Simple Reaction Time ms	390	175	459	170	.137
Choice Reaction Time ms	613	192	650	173	.437
Sway-Balance cm/sec					
Eyes Open	1.12	0.42	0.87	0.30	.023
Eyes Closed	1.58	0.51	1.44	0.63	.338
Blink Reflex R-1 ms					
Right	14.6	1.7	11.0*	1.5	.0001*
Left	14.8	2.0	10.5*	1.1	.0001*
Color Vision (Lanthony Hue)	12.1		13.3		.017
Visual Fields Automated Perimetry					
Right			451		
Left			450		
Smell			3.4		
Cognitive Domain					
Culture Fair A score	22.9	8.0	23.4	7.1	.823
Digit Symbol	47.1	17.1	35.8	13.4	.007
Vocabulary	8.6	3.8	11.7	4.5	.224
Profile of Mood States	35.9	34.4	43.9	34.4	.388
Verbal Recall (Stories)					
Story 1 Immediate	7.7	4.4	8.6	4.1	.462
Story 2 Delayed	6.2	4.9	5.9	4.2	.819
Visual Recall			26.9	6.8	
Remote Memory					
Information	5.9	4.7	6.3	3.7	.711
Picture Completion	9.3	5.1	11.4	4.1	.114
Similarities	10.5	7.1	11.2	6.3	.724
Perceptual Motor Speed					
Pegboard	89.2	31.4	77.1	10.9	.10
Trail Making A	64.5	35.9	42.9	19.8	.015*
Trail Making B	124.6	46.6	95.9	47.7	.029*
Fingertip Number Writing	13.5	9.2	10.5	8.3	.223
Profile of Mood States Sc	35.0	37.0	53.0	41.4	
Pulmonary Function Tests					
FVC	87.4	21.4	74.8	14.2	.02
FEV_1	72.8	15.4	71.4	17.4	.743
FEF_{25-75}	60.3	23.5	71.3	29.0	.116
FEF_{75-85}	52.8	33.7	69.9	27.7	.053

* Exposed had better scores.

ms = millisecond

cm = centimeter

sec = second

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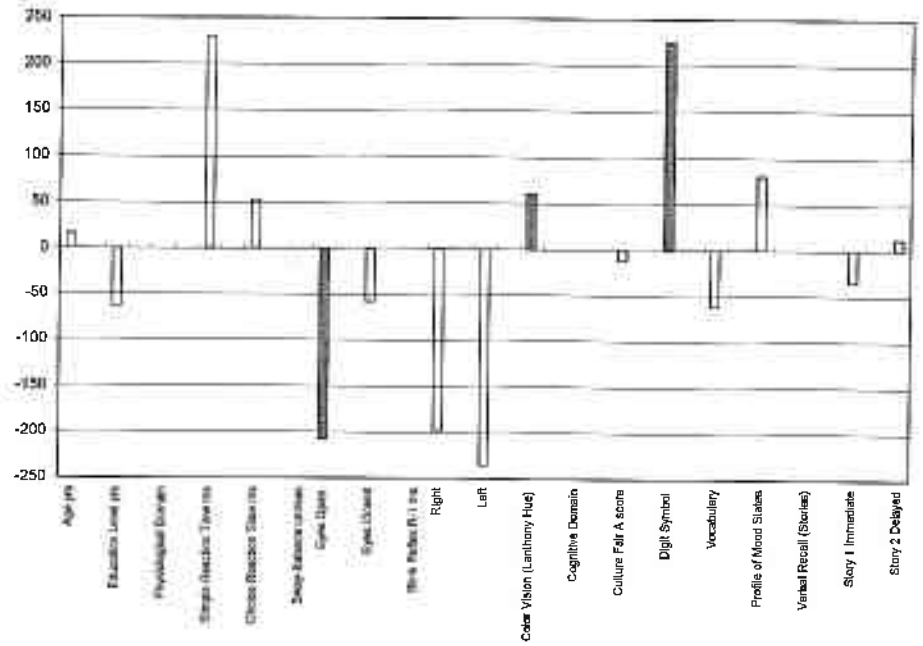

FIGURE 5.4a. Comparison of Latino children, 20 exposed to H_2S (Torrance) and 44 unexposed (Houston) by ANOVA. Hatched bars are statistically significant.

FIGURE 5.4b.
(Houston) by ANO

refinery, mean age 38.5 years, were studied in January 1989 and restudied in June 1991. In June we studied three additional ex-workers from oil refinery desulfurization and five additional neighbors (total 35 ex-workers and neighbors), and 32 unexposed (17 men and 15 women). The ex-workers had been pipe fitters, painters, laborers, and process handlers in the vanadium pentoxide (V_2O_5) desulfurization unit after its installation in 1986. None had ever been overcome by H_2S. Twelve workers studied had left the refinery by October 1988; one left in July 1989. One worker was lost to follow-up in 1991. These ex-workers and neighbors were plaintiffs in a class action lawsuit. Reference subjects were chosen from friends and relatives of the exposed subjects who had not worked at the refinery or resided in the downwind zone and were close matches for age, sex, and educational level.

Exposure Conditions and Air Monitoring Data

Residents lived within 1,200 meters east–northeast and at a lower elevation than the refinery and were within 2,400 meters of the sulfur plant and coking units (Figure 5.6).

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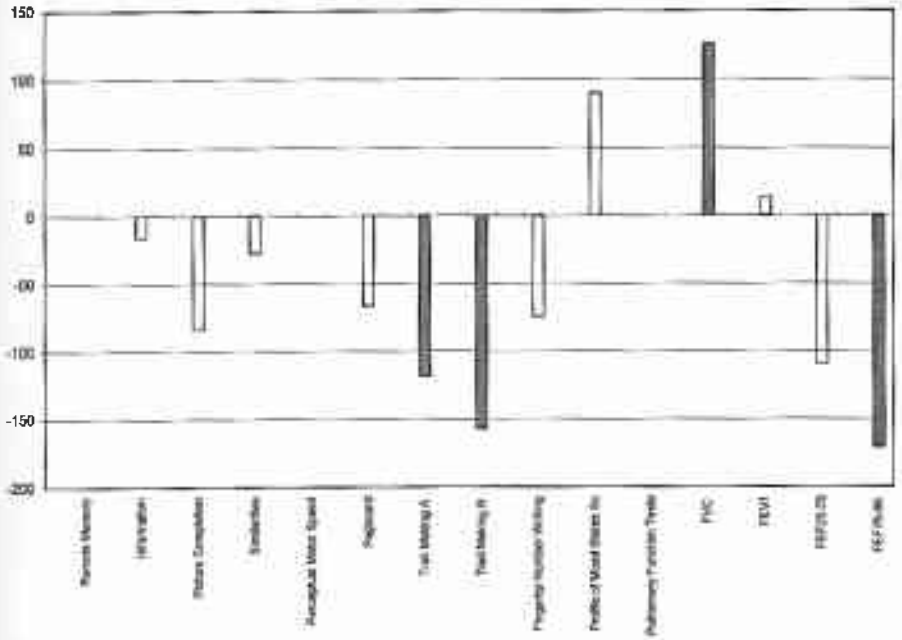

FIGURE 5.4b. Comparison of Latino children, 20 exposed to H_2S (Torrance) and 44 unexposed (Houston) by ANOVA. Hatched bars are statistically significant.

Almost daily coastal air inversions held the refinery's odorous stack gases close to the ground. These reduced sulfur gases are heavier than air. Air monitoring at street level on Calle Bendita near the center of the subjects' homes for one week in July 1990 showed H_2S at 10 parts per billion (ppb) with periodic peaks of 100 ppb, as well as dimethylsulfide 4 ppb, mercaptans 2 ppb, ethane 500 ppb, and propane 500 ppb. Also vanadium, as V_2O_5, and thiodiglycolic acid were detected by air and soil monitoring. Reduced sulfur gases outside the desulfurization unit between April 1987 and January 1991 showed 24-hour averages for mercaptans from 0.1 to 21.1 parts per million (ppm), hydrogen sulfide from 0.0 to 8.8 ppm, carbon oxide sulfide (COS) from 2.6 to 52.1 ppm, and total reduced sulfur from 6.1 to 70.7 ppm. Workers' exposures within this unit were not measured. The refinery's 24-hour emissions averaged 0 to 8.8 ppm for H_2S and 1.13 to 70.7 ppm for total reduced sulfur gases from 1987 to 1991. The regional air pollution monitoring station, located east of the refinery and south of the subjects' homes (Figure 5.6), often had the nation's highest ambient air SO_2 levels.

The mean test scores were pooled for the 35 ex-workers and neighbors and for men and women, as their ages, educational levels, and test scores showed only small

TABLE 5.8 Comparison of symptom frequencies in Torrance exposed subjects and the Wickenburg unexposed group (scale 1–11)

	Exposed	Unexposed
Skin itching	4.5	3.3
Deformed fingernails	2.3	1.6
Chest tightness	3.3	2.2
Palpitations	2.8	2.2
Pain or burning chest	3.4	2.1
Shortness of breath	4.0	2.5
Dry cough	4.5	2.6
Cough with mucus	4.3	2.8
Cough with blood in mucus	1.9	1.2
Dry mouth	4.7	3.2
Throat irritation	4.2	2.6
Eye irritation	6.0	2.8
Decreased sense of smell	3.6	2.1
Headache	6.1	4.4
Nausea	3.9	2.4
Dizziness	4.1	2.4
Lightheadedness	4.1	2.5
Unusual exhilaration	2.5	1.5
Loss of balance	3.3	2.0
Loss of consciousness	1.9	1.2
Extreme fatigue	5.1	3.4
Somnolence	3.8	2.6
Insomnia	4.4	2.9
Wake frequently	4.4	2.9
Sleep only a few hours	4.2	2.9
Irritability	5.4	3.4
Lack of concentration	5.7	3.2
Recent memory loss	5.1	3.1
Long-term memory loss	4.1	2.2
Mood swings	4.3	2.5
Loss of libido	3.6	3.1
Decreased alcohol tolerance	2.0	2.4
Indigestion	3.6	3.2
Loss of appetite	3.5	2.6
Stomach swollen	3.3	2.9

differences which were not statistically significant (Table 5.9 and 5.10, Figures 5.7a–c). Values of the entire exposed group were compared to unexposed in the first probability column, p, and scores of the 22 neighbors alone were compared in the p^* column.

Neurophysiological Domain

The simple reaction time of the exposed group was significantly longer than that of the unexposed, and the choice reaction time of the exposed subjects was also slower, by 71 ms ($p < 0.003$). Sway speed with eyes open was significantly faster in exposed subjects than unexposed, and with eyes closed the difference was also significant ($p < 0.04$). Color discrimination (Lanthony 15 hue test; 18) was significantly reduced in exposed compared to unexposed. In exposed subjects blink reflex latency (R-1) was

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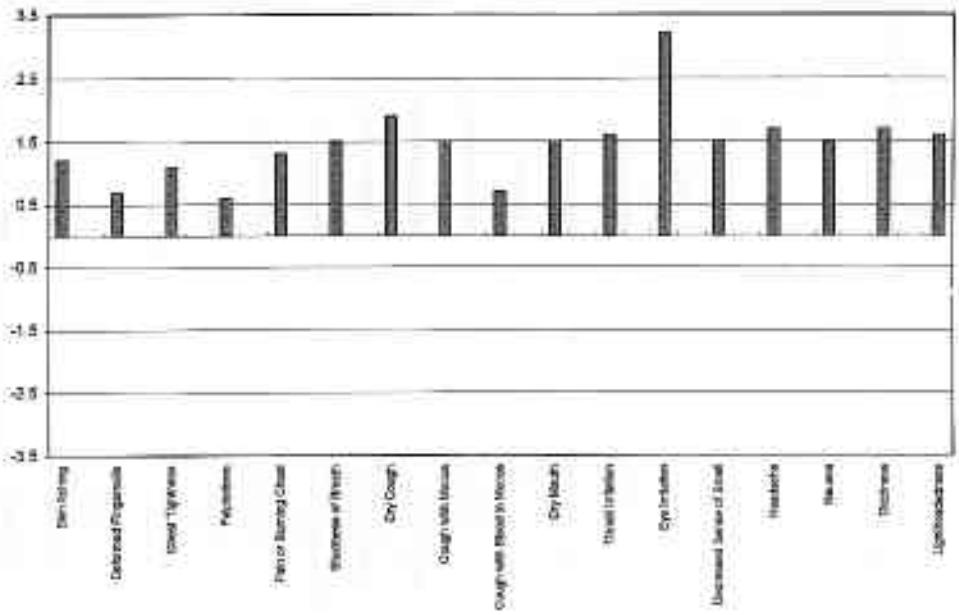

FIGURE 5.5a. Comparisons of symptom frequencies for H_2S-exposed adults (Torrance) and controls (Wickenburg), frequency scale 1–11. Hatched bars are statistically significant.

nearly identical on the right and the left, and neither result was significantly different from that for the unexposed. Thus exposed subjects, workers, and neighbors were significantly impaired compared to unexposed for three of four neurophysiological functions.

Neuropsychological Domain

Peg placement with the dominant hand was not significantly longer in exposed subjects than in unexposed, but trail making A and B times were significantly different between the exposed and unexposed groups when 22 exposed residents, excluding the ex-workers, were compared to unexposed. Differences between the groups for recall were equivocal. Thus the exposed group's verbal recall for story 1, immediate and delayed, was not significantly different from that of the unexposed, while the exposed group's immediate recall of story 2 was significantly less (Table 5.10, Figure 5.7b). Recall of

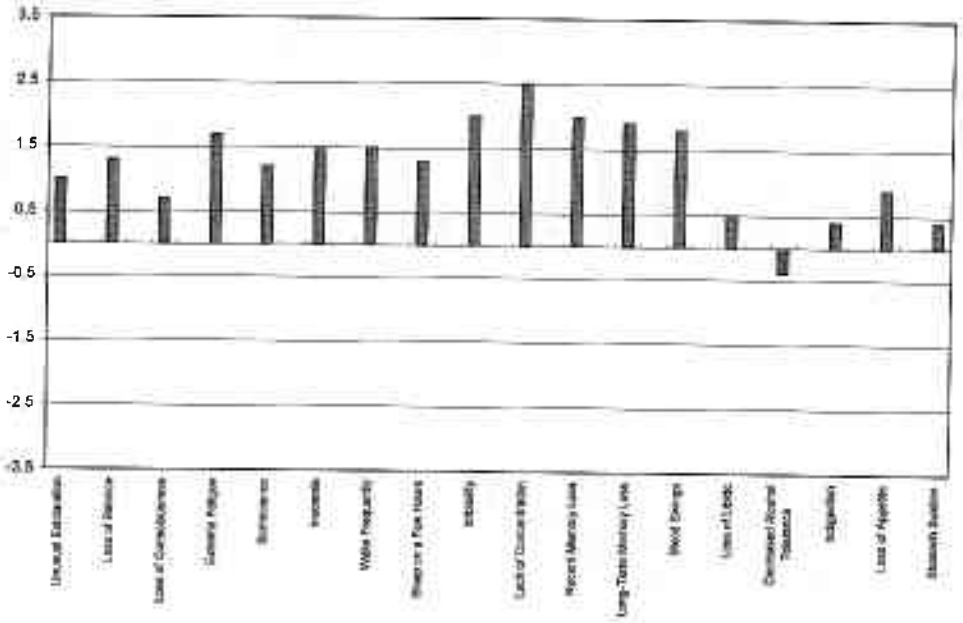

FIGURE 5.5b. Comparisons of symptom frequencies for H_2S-exposed adults (Torrance) and controls (Wickenburg), frequency scale 1–11. Hatched bars are statistically significant.

drawings and recall of numbers were not different for exposed compared to unexposed, but exposed residents scored significantly lower on immediate and delayed recall of drawings. The exposed group's scores for overlearned memory were not different from those of the unexposed group. Scores for Culture Fair, block design, and embedded figures were not significantly different in exposed and unexposed groups. Errors in recognition of numbers written on the fingertips were not different for the groups. Thus, although digit symbol scores were significantly lower, this domain appeared unaffected by exposure.

Affective Domain

The POMS score for the exposed group mean was seven times that of the unexposed (Table 5.11, Figure 5.8), whose scores equaled published normal values (19). Anger, confusion, depression, tension–anxiety, and fatigue scores were significantly elevated

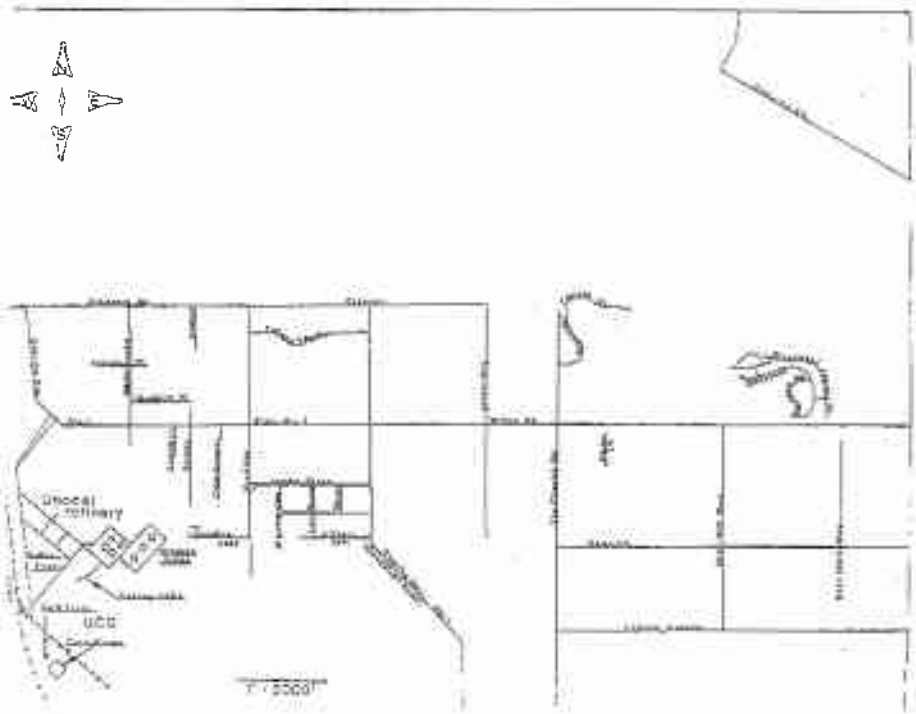

FIGURE 5.6. Unocal facility and vicinity.

TABLE 5.9 Neurophysiological functions in exposed and unexposed subjects (means and standard deviations with *p* values by t-test)

	35 Exp mean s.dev.	32 Ref mean s.dev.	*p*	*p**
Age yrs	39.7 ± 12.0	38.9 ± 12.5	NS	NS
Educ Level yrs	11.3 ± 2.2	12.2 ± 2.4	NS	NS
Reaction Time				
Simple ms	336 ± 145	268 ± 50	0.01	0.01
Choice ms	593 ± 106	522 ± 89	0.004	0.004
Sway Speed cm/s				
Eyes Open	0.92 ± 0.28	0.79 ± 0.19	0.037	0.000
Eyes Closed	1.47 ± 0.81	1.15 ± 0.31	0.04	0.000
Color Vision (Lanthony Hue Test)				
errors	12.1 ± 5.4	11.4 ± 4.3	0.005	0.000
Blink				
Glabellar Tap R-1				
Right ms	13.9 ± 1.7	13.8 ± 1.8	NS	NS
Left ms	14.1 ± 1.9	13.5 ± 2.0	NS	NS

* In 22 residents compared to unexposed

ms = millisecond, cm/s centimeters per second

NS = not significant

TABLE 5.10 Comparison of immediate and 30-minute delayed recall, overlearned memory, and cognitive and psychomotor functions for exposed and unexposed subjects (means and standard deviations with p values by t-test)

	35 Exposed mean s. dev.	32 Unexposed mean s. dev.	p	p*
Perceptual Motor				
Trail Making A	35.4 ± 15.4	28.8 ± 8.0	.033	.012
Trail Making B	87.8 ± 29.8	71.4 ± 35.8	.04	.01
Pegboard Dom. Hand	74.8 ± 21.3	69.7 ± 10.3	NS	NS (.09)
Recall				
Story 1 Immediate	9.6 ± 3.7	10.8 ± 3.8	NS	NS
Delayed	7.9 ± 5.6	8.3 ± 4.0	NS	NS
Story 2 Immediate	9.4 ± 3.9	11.8 ± 4.3	.023	.0285
Delayed	8.6 ± 4.7	9.9 ± 4.2	NS	NS
Visual Immediate	29.6 ± 6.7	31.4 ± 4.6	NS	.016
Delayed	23.2 ± 8.9	26.5 ± 7.0	NS	.021
Digit Forward	6.4 ± 1.7	6.5 ± 1.4	NS	NS
Backward	4.3 ± 1.3	4.7 ± 1.3	NS	NS
Overlearned Memory				
Information	16.8 ± 5.7	18.9 ± 6.2	NS	NS
Similarities	19.6 ± 5.0	20.1 ± 5.8	NS	NS
Picture Complet.	15.4 ± 2.3	14.7 ± 3.2	NS	NS
Cognitive				
Culture Fair	28.6 ± 6.5	30.7 ± 6.9	NS	NS (.08)
Block Design	30.8 ± 9.2	30.5 ± 11.5	NS	NS
Digit Symbol	50.6 ± 13.3	57.4 ± 13.7	.04	.03
Digit Symbol Recall	5.4 ± 2.4	5.7 ± 2.3	NS	NS
Embedded Figures	31.7 ± 4.1	32.2 ± 4.6	NS	NS
Fingertip Number Writing				
Errors Right	2.8 ± 2.9	3.0 ± 3.4	NS	NS
Errors Left	2.2 ± 2.8	2.4 ± 3.2	NS	NS

* 22 residents compared to unexposed

in exposed residents and in former workers, who were nearly identical. POMS score had significant coefficients in linear regression models for many symptom frequencies. However, POMS scores as independent variables, whether separately or together with age, sex, and educational level, had *no significant coefficients with the abnormal test scores*, including CRT, sway speed, color recognition, and trail making A and B.

Symptoms

Frequencies of 31 of 33 symptoms were significantly higher for exposed subjects than unexposed (Table 5.12, Figures 5.9a, b) when compared by t-test. Only a rare complaint, loss of consciousness, and loss of appetite were not significantly different. Respiratory and mucous membrane irritation were 10 to 30 times as frequent in exposed compared to unexposed, as were neurological symptoms, sleep disturbances, and general symptoms including headache. Skin complaints were three to six times higher in exposed subjects compared to unexposed.

Confounding Factors

The most frequent possible confounding factor was surgical anesthesia, which had been experienced by 50% of exposed subjects. Some of their test results were different from

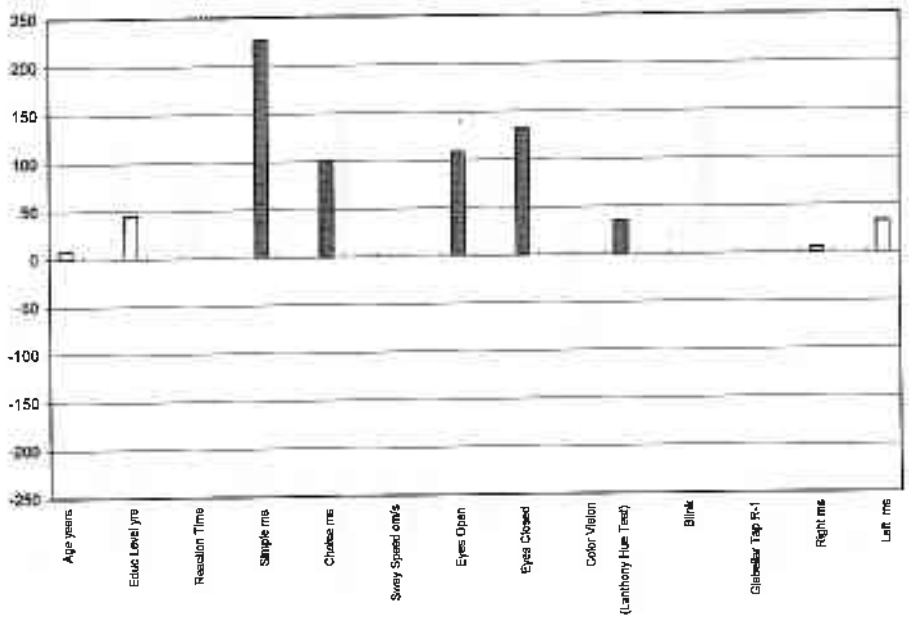

FIGURE 5.7a. Comparisons of 35 H_2S-exposed (Nipoma) and 32 unexposed (San Luis Obispo). Hatched bars are statistically significant.

those of subjects who had not received anesthesia. However, minutes of anesthesia as an independent variable had no significant coefficients in linear regression models for any neurophysiological test score. All of the ex-workers had been exposed to solvents; one was a painter. Half of them had used vibrating tools. Nine of the exposed residents had confounding factors, three used solvents at home, two used vibrating tools, one had received anesthesia numerous times, one had seizures and was on medication, and two had pesticide and herbicide exposures from their nursery. Excluding these nine subjects from analysis for each test category, in turn, did not change the outcomes significantly; so all subjects were retained. Alcohol use was not a confounding factor, as no subject had an elevated alveolar (air) alcohol on the day of testing, and only one neighbor and three ex-workers reported that they had ever been inebriated from alcohol.

Bias

As testers did not know the exposure status of the subjects, bias from this source is unlikely. Scores from testing the exposed group before and after they became clients

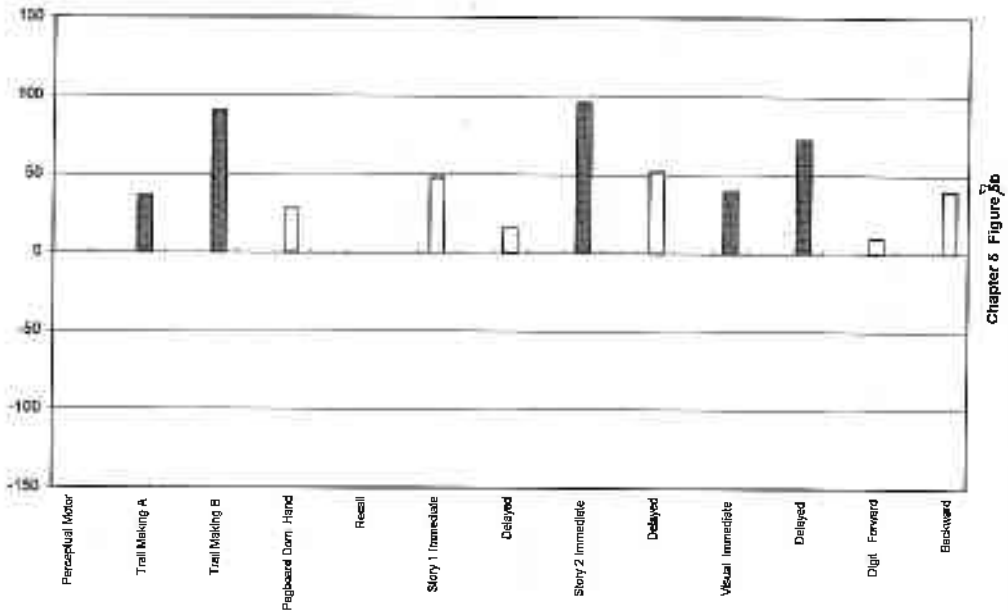

FIGURE 5.7b. Comparisons of 35 H_2S-exposed (Nipoma) and 32 unexposed (San Luis Obispo). Hatched bars are statistically significant.

did not vary, showing that becoming clients was not a bias. Groupwide bias in selection of a comparison subject is possible but unlikely, as subjects did not have insight into how to select better performers on the tests.

Repeat Testing

After 30 months, 21 residents and 9 workers showed statistically insignificant variation across the interval without a trend of improvement (see Chapter 16, Table 16.5.)

CASPER AND HOUSTON SUBJECTS

Casper, Wyoming Exposed and Unexposed Subjects

In 1991 approximately 100 residents of the Brookhurst section of northwest Casper, Wyoming brought suit against six chemical companies for causing adverse health effects

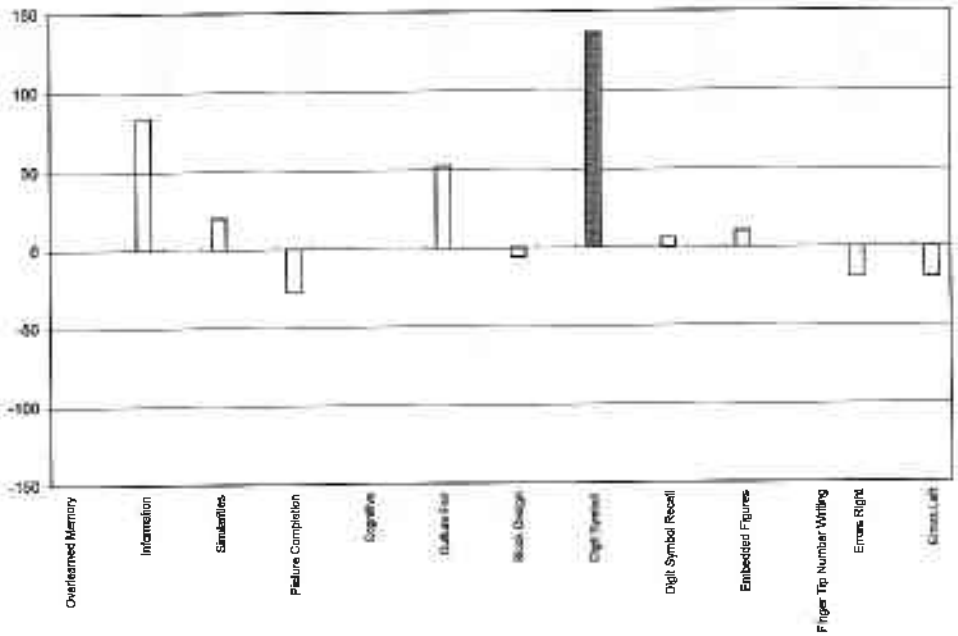

FIGURE 5.7c. Comparisons of 35 H_2S-exposed (Nipoma) and 32 unexposed (San Luis Obispo). Hatched bars are statistically significant.

TABLE 5.11 Profile of mood states, total score and components

	35 Exposed mean s.dev.	32 Unexposed mean s.dev.	p^*
Total	70.9 ± 40.7	10.3 ± 20.0	.0001
Anger	16.8 ± 11.3	5.6 ± 5.7	.0001
Depression	18.8 ± 11.7	5.1 ± 6.4	.0001
Tension	18.3 ± 7.3	7.8 ± 4.0	.0001
Confusion	13.3 ± 5.7	4.9 ± 2.8	.0001
Fatigue	15.5 ± 7.3	5.3 ± 3.7	.0001
Vigor	11.8 ± 7.0	18.5 ± 4.4	.0001

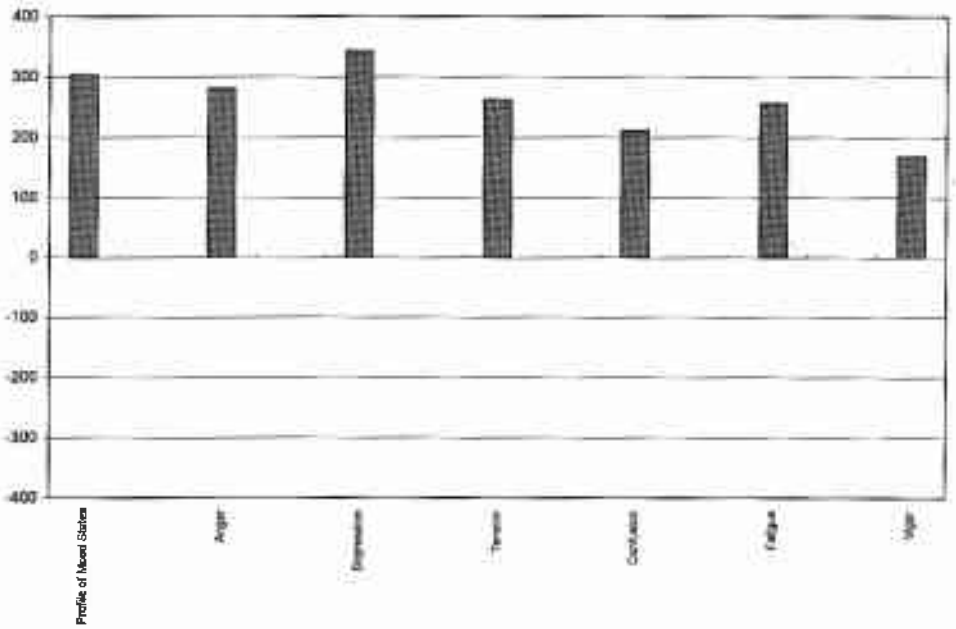

FIGURE 5.8. Comparisons of profile of mood states, H_2S-exposed and unexposed. Hatched bars are statistically significant.

and decreasing property values. They had lived in the subdivision for over ten years and contended that the plume of odorous fumes, together with surface and subsurface drainage of solvent-smelling chemicals, contaminated their yards and wells and was responsible for their numerous health complaints, cancers, and birth defects. Casper is a city of 51,000 located on the Platt River in central Wyoming. It is in an oil-producing area, and a refinery is located near the center of town. Six chemical companies were part of a corridor between Brookhurst and the city.

Eighty-four exposed individuals, whose ages ranged from 10 to 77 years, with a mean age of 38 and an educational level of 11 years, were compared with 50 unexposed subjects from the city of Casper with an average age of 50 years, range 14 to 82 years, and an educational level of 12.8 years. Although the strategy was for an exposed individual to nominate and contact a comparison person, this approach did not yield enough unexposed subjects; so we appealed to local organizations, including the Elks Lodge and the local hospital and medical center, to augment the comparison group.

TABLE 5.12

Respiratory
Chest tightness
Palpitations
Chest pain
Dry cough
Cough with blo
Dry mouth, nos
Throat irritation
Eye irritation
Reduced smell
Neurological
Dizziness
Lightheadness
Loss of balance
Loss of conscio
Lack of concent
Recent memory
Long-term mem
Mood unstable
Irritability
Exhilaration
Sleep
Somnolence
Insomnia
Can't fall asl
Wake freque
Sleep few ho
General
Headache
Nausea
Libido decrease
Excess fatigue
Alcohol toleran
Indigestion
Loss of appetite
Skin
Itching
Dryness
Redness

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TABLE 5.12 Frequencies of 33 respiratory, neurological, general, and skin complaints in exposed and unexposed subjects in 1991

	Exposed (35)		Unexposed (32)		
	mean	Sd	mean	Sd	p
Respiratory					
Chest tightness	91.7	± 78.0	8.6	± 18.9	.0000
Palpitations	68.5	± 70.8	19.9	± 54.6	.0022
Chest pain	69.7	± 76.6	2.8	± 8.9	.0000
Dry cough	82.4	± 79.3	6.4	± 18.3	.0000
Cough with blood	28.4	± 51.4	1.0	± 6.0	.0030
Dry mouth, nose, throat	97.1	± 82.2	3.7	± 9.9	.0000
Throat irritation	105.7	± 78.0	11.1	± 24.0	.0000
Eye irritation	125.1	± 79.4	6.0	± 21.6	.0000
Reduced smell	78.4	± 80.7	7.7	± 24.6	.0000
Neurological					
Dizziness	80.7	± 75.5	4.2	± 12.0	.0000
Lightheadness	93.6	± 74.5	10.3	± 17.7	.0000
Loss of balance	66.9	± 66.8	5.4	± 17.4	.0000
Loss of consciousness	2.5	± 9.2	0		—
Lack of concentration	138.2	± 86.1	8.3	± 16.1	.0000
Recent memory loss	137.5	± 90.7	8.3	± 21.5	.0000
Long-term memory loss	84.4	± 90.2	4.7	± 13.4	.0000
Mood unstable	137.3	± 93.3	2.4	± 8.6	.0000
Irritability	131.3	± 92.4	22.4	± 36.7	.0000
Exhilaration	32.6	± 60.3	1.9	± 8.1	.0000
Sleep					
Somnolence	89.3	± 101.4	1.4	± 8.4	.0000
Insomnia					
Can't fall asleep	101.3	± 88.5	17.0	± 45.9	.0000
Wake frequently	126.9	± 91.9	16.4	± 46.9	.0000
Sleep few hours	121.4	± 94.1	21.6	± 57.4	.0000
General					
Headache	145.5	± 76.6	31.3	± 47.1	.0000
Nausea	90.5	± 74.4	8.4	± 17.7	.0000
Libido decreased	79.8	± 89.2	17.6	± 45.9	.0000
Excess fatigue	136.9	± 88.2	18.1	± 37.4	.0000
Alcohol tolerance decreased	32.3	± 76.7	4.3	± 21.8	.044
Indigestion	94.9	± 105.7	9.2	± 21.5	.0000
Loss of appetite	48.2	± 76.4	20.6	± 52.8	.086
Skin					
Itching	72.7	± 81.8	19.0	± 55.4	.002
Dryness	93.2	± 93.1	16.2	± 46.8	.0001
Redness	76.4	± 72.9	21.4	± 55.5	.0008

This effort resulted in a somewhat older and better-educated unexposed group than the exposed individuals. Age would reduce the difference between the exposed and unexposed, but in some tests this effect would be offset by the greater educational level in the unexposed.

The methods used for evaluating neurophysiological and neuropsychological performance are those outlined in Chapter 3. In brief we tested the simple and two-choice visual reaction time, color vision using the Lanthony desaturated hue test, balance as sway speed with eyes open and with eyes closed, blink reflex, and latency of R-1

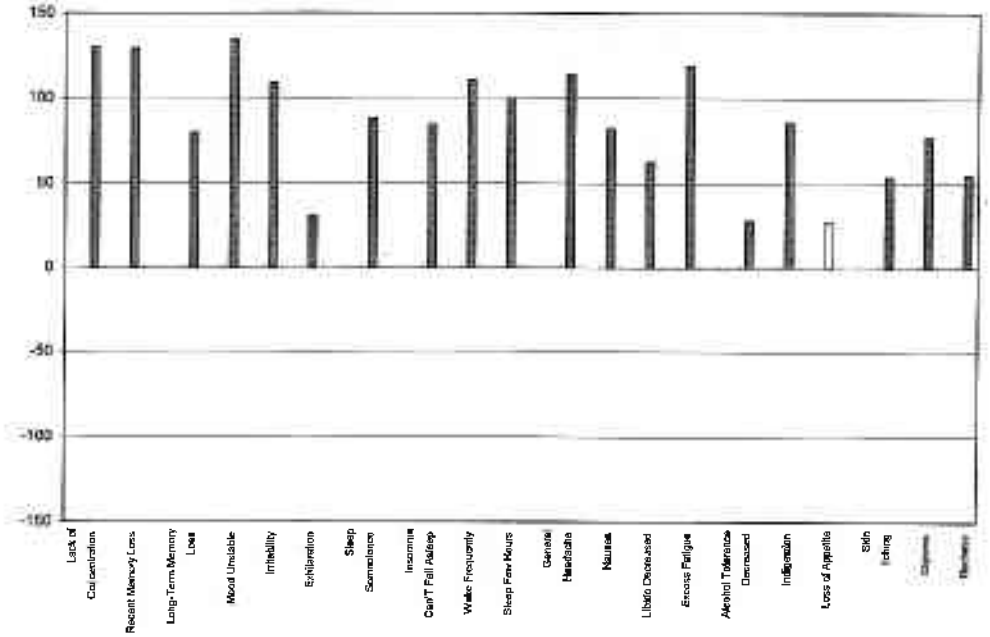

FIGURE 5.9a. Comparisons of symptom frequencies for 35 H_2S-exposed (Nipoma) and 32 unexposed (San Luis Obispo). Hatched bars are statistically significant.

FIGURE 5.9b.
unexposed (San

stimulated by glabellar tap. Cognitive tests included Culture Fair 2A, a nonverbal and nonarithmetic design-solving test of constructional and cognitive performance, block design, and digit symbol from the WAIS. Perceptual motor speed was tested with a pegboard using slotted pegs, trail making A and B, and fingertip number writing errors from the Halstead-Reitan battery. Recall was tested with story 1 and story 2, visual reproduction, and digits forward and backward from the Wechsler memory scale. Embedded memory was evaluated with information, picture completion, and similarities from the WAIS.

Compared to the 50 Casper reference people, the exposed group had almost identical values for reaction time and for blink although fewer of the exposed had a delayed BRL R-1 on glabellar tap and considerably fewer responded to supraorbital tap stimulation (see Table 5.13, Figures 5.10a–d). Although sway speed appeared faster in the exposed group, particularly with eyes closed, this difference was not statistically significant. Similarly, the cognitive functions, although favoring the performance of the com-

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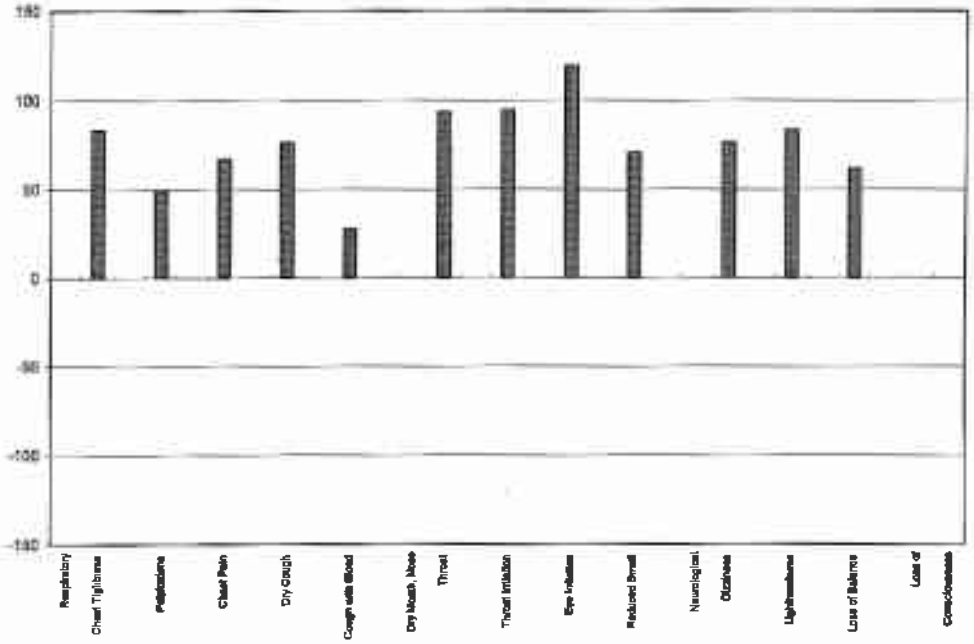


FIGURE 5.9b. Comparisons of symptom frequencies for 35 H_2S-exposed (Nipoma) and 32 unexposed (San Luis Obispo). Hatched bars are statistically significant.

parison group most times, actually showed a reversal, with more impairment for perceptual motor functions, pegboard, and trails A and trails B in unexposed controls, although these differences between the groups were not statistically significant. For recall functions the comparison group did slightly better, again without statistical significance, and this was also seen to be true for the embedded memory functions.

However, when the overall function was compared with the national predicted group based on Louisiana and California unexposed groups, there was a statistically significant slowing of choice reaction time in the exposed, and, most outstandingly, differences—both with eyes open and with eyes closed—for sway speed as a measure of balance (Figures 5.10c, d). Trail making B took longer in both exposed and unexposed Casper groups than in the national unexposed, whereas trail making A was prolonged in the comparison group only.

The interpretation of these differences, namely, that both the exposed and the comparison group had abnormalities of sway speed, choice reaction time, and trails B,

TABLE 5.13 Casper exposed compared to local unexposed and national unexposed, showing the intermediate scores for Casper unexposed

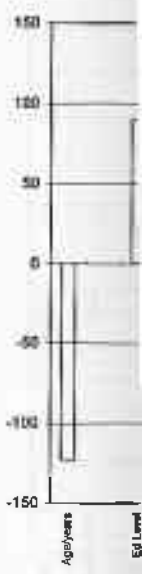
	Comparison (50)		Exposed (84)		National (66)		
	Mean	Sd	Mean	Sd	Mean	Sd	p
Age/years	50.4	20.1	38.1	17.5	38.0	12.8	
Ed Level	12.8	2.4	11.0	3.1	12.5	2.1	
POMS Score	18.1	27.9	56.6	51.5	16.0	28.4	
Physiological							
Simple Reaction Time	280	59.7	288	74	281	85	
Choice Reac. Time 1	542	107	553	115	519	88	
2	533	85	551	107	514	81	
3	539	94	559	94	524	88	.0067*
Color Score	12.1	7.06	12.3	6.6			
Blink Glabellar R ms	15.0	1.8 (92)	14.6	1.9 (67)			
L ms	15.5	1.8 (78)	15.4	1.9 (53)			
Supraorbital R ms	14.5	1.7 (94)	14.6	1.7 (39)			
L ms	14.4	1.9 (98)	14.2	1.6 (40)			
Sway Speed cm/sec							
Eyes Open	0.94	0.22	0.99	0.30	0.87	0.22	.0014*
Eyes Closed	1.40	0.41*	1.52	0.58	1.31	0.66	.01*
Cognitive							
Culture Fair A	27.6	7.9	29.3	7.3	30.6	6.1	
Block Design Score	28.7	10.6	31.0	9.2	31.0	10.3	
Digit Symbol	54.4	16.0	51.2	15.3	56.8	14.9	
Perceptual Motor							
Finger Writing Right	2.6	2.7	2.9	3.4	2.5	3.2	
Left	2.3	2.7	2.4	3.1	2.1	2.7	
Pegboard	82.7	25.8*	72.9	19.7	68.9	4.5	
Trails A	39.8	17.3*	34.6	13.0	33.8	14.1	
B	83.8	49.7*	79.2	45.1*	74.9	44.3	
Recall							
Story 1	11.7	4.4	10.6	4.2	10.5	3.8	
Story 2	11.4	4.5	9.8	4.4	9.7	4.1	
Visual Recall	11.7	4.3*	10.5	3.2	10.1	3.1	
Digits Forward	6.7	1.3	6.6	1.3	6.8	1.5	
Backward	4.5	1.1	4.4	1.4	4.7	1.2	
Embedded Memory							
Information	18.4	6.0	16.7	5.8	16.9	5.3	
Picture Completion	14.2	3.3	14.6	3.4	15.3	3.1	
Similarities	19.4	4.8	20.8	6.5	20.2	5.3	

* $p = < .05$

r = range

suggested a citywide exposure. There was a large oil refinery practically at the crossroads of the main east–west and north–south streets of Casper, which refined high sulfur crude from the basin fields in the Casper vicinity. There was gas flaring, with a perceptible odor of hydrogen sulfide. This observation suggested that the generalized effects observed were from the oil refinery exposure, which extended into the comparison group.

Certainly other interpretations should be considered, including the possibility that we are simply observing oddities due to the age deterioration factor and the physiologi-



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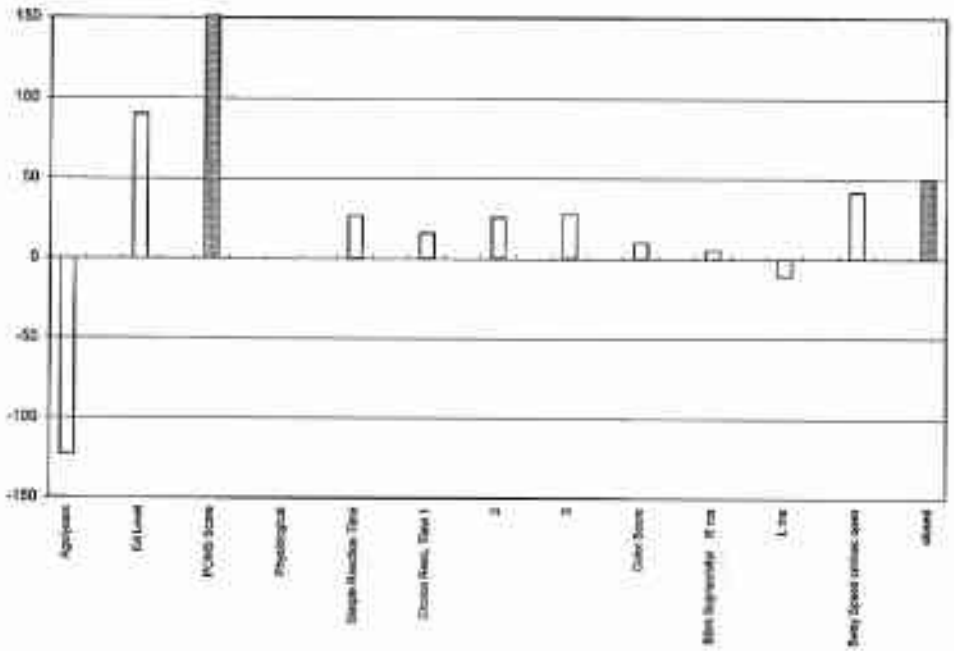

FIGURE 5.10a. Comparison of 80 exposed (Brookhurst) and 50 unexposed (Casper).

cal and perceptual motor responses. We reasoned that if further experience with the physiological tests shows that their sensitivity can be relied upon, then when they individually show differences of this magnitude, confounding exposure should be sought or some other factor that could explain the differences. Such differences do not seem to be methodological or site-specific, as we now have similar reference values from five different states in the United States.

The POMS score was more than three times as high in the exposed as the unexposed (56 compared to 18), and increased by component scores for anger, confusion, and depression. Objective tests showed a "Casper effect," which overlay both groups and did not distinguish them. Symptom frequencies and profile of mood states score (self-appraisal) were different, which may reflect concern or a sense of injury. This finding would tend to support, at least in a small way, the differences in objective tests compared to the national group.

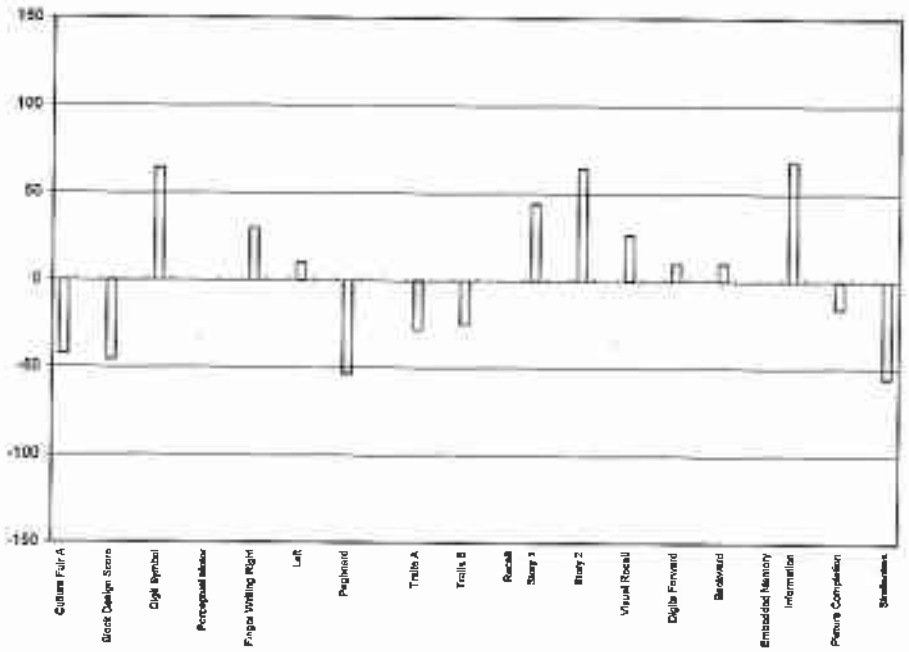

FIGURE 5.10b. Comparison of 80 exposed (Brookhurst) and 50 unexposed (Casper).

Houston Petroleum Refineries—Circumstantial Exposure

The Houston–Wickenburg comparison suggests abnormality for the Houston unexposed, who differ from Wickenburg unexposed for blink, recall, reaction time, vocabulary, and perhaps trails A and B. These differences are despite their being 10 years younger than the Wickenburg group with slightly higher POMS scores. Are Houston unexposed TCE-exposed? Blink abnormalities suggest that they are chemically affected, with chlorinated solvents as the prime possibility.

Consideration of children showed again a significant lengthening of blink reflex latency R-1 of 1.4 to 2.0 ms in all three ethnic groups (Caucasians, African-Americans, and Latinos), an increased sway speed, an impaired reaction time of 70 to 94 ms, and a general impairment of cognition (CFA, vocabulary, and digit symbol), recall, and long-term memory, despite a near match for age (Wickenburg 11.5 years, Caucasians 12 years, and Latino 11.4 years). Thus either living near the oil refinery–chemical region or being economically impoverished, unable to escape, was associated with impaired function scores.

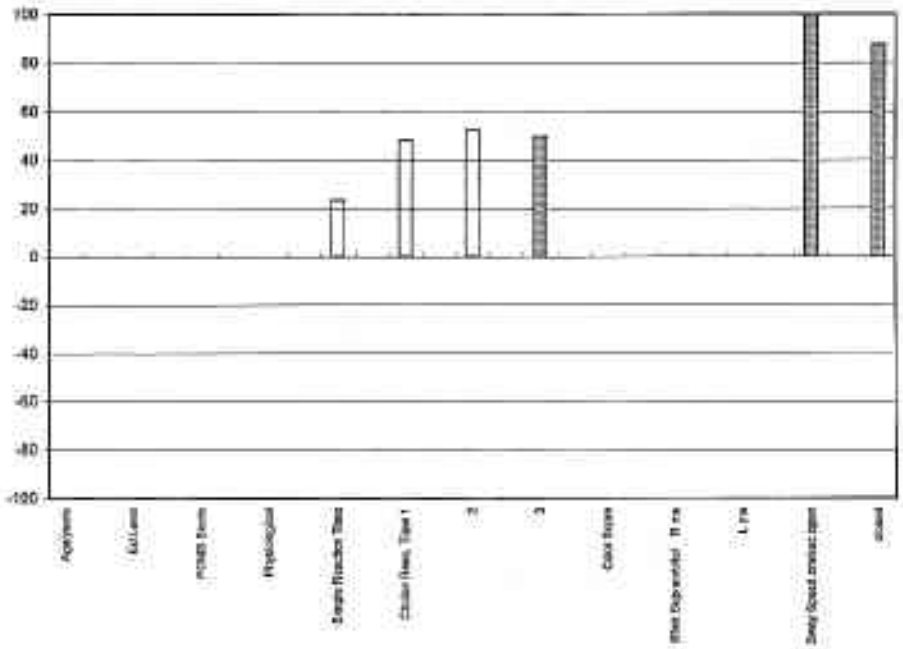

FIGURE 5.10c. Comparison of 80 exposed (Brookhurst) and national predicted groups.

Obviously, these differences could be reflecting ability, but that is unlikely for blink and balance. Thus, it is hypothesized that maladaptive performance has resulted from living near refineries and a major chemical manufacturing center where H_2S is the principal chemical exposure.

BALANCE FUNCTION AND REACTION TIMES IN REFINERY WORKERS EXPOSED TO H_2S

Balance function as sway speed and two-choice visual reaction time were measured in 38 refinery workers recruited from a group of 75 being examined for asbestos-related disease. The mean age was 42.7 ± 11.4 years, with a range from 22 to 63 years. Methods were the standard ones just described. Balance with eyes closed was abnormal, with sway speed 1.48 ± 78 cm/sec compared to 1.17 ± .32 cm/sec ($p < .0043$) in 68 unexposed subjects of mean age 37.6 years. Age means were not significantly different ($p < .06$). Sway speed with eyes open was also abnormal at 1.06 ± .44

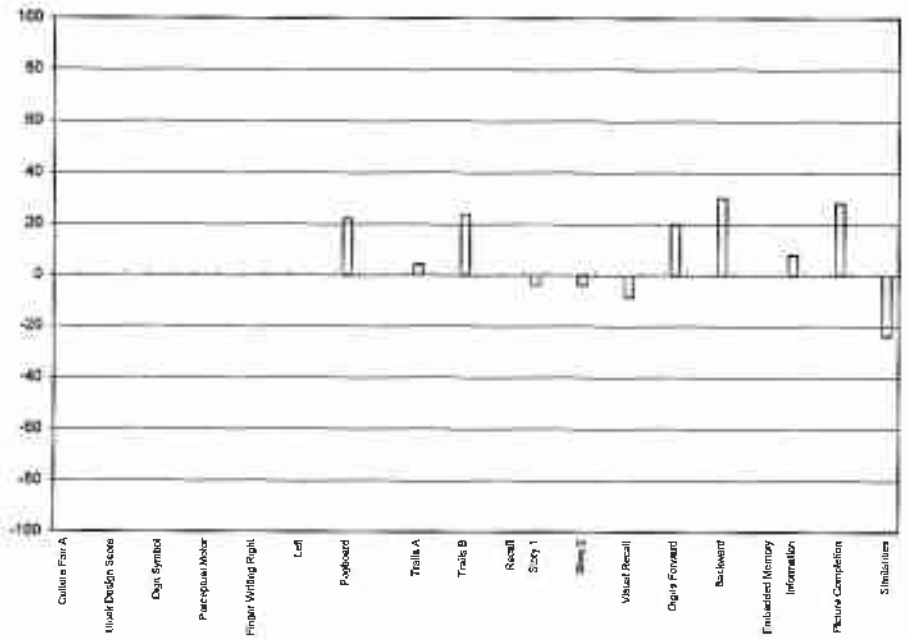

FIGURE 5.10d. Comparison of 80 exposed (Brookhurst) and national predicted groups.

cm/sec as compared to 0.81 ± .20 cm/sec ($p < .0001$) in unexposed subjects. Six subjects had sway speed with eyes closed greater than 2.0 cm/sec and should be considered to be an abnormal subgroup. One of these men has tinnitus, and another was in a spill of hydrogen chloride or hydrogen fluoride and had suffered lung damage. Otherwise, their other exposures and past medical disorders were not pertinent to balance abnormality. Choice reaction time was 537 ± 71 msec compared to 513 ± 79 msec, a difference that was not significant. Based on the previous study of ex-workers and downwind neighbors of a refinery processing Santa Barbara, California, channel crude oil rich in reduced sulfur gases, who had abnormal sway speed and abnormal choice reaction time at 593 ± 106 msec, the new data support the suggestion of toxic effects from these gases. Other exposures to hydrocarbons, sulfur oxides, hydrogen chloride, and fluoride included known neurotoxins. Stack emissions include manganese, chromium, mercury, lead, and vanadium, which are neurotoxic; so careful characterization of tank and stack emissions by environmental sampling is needed to establish which associations are causal. Of the metals, manganese and mercury should be accorded the highest index of suspicion because in occupational concentrations, as in mining and refining, they produce adverse effects on balance. Nevertheless, with our present insight

into levels of exposure, mechanisms of action, and similarity to clinical poisoning, hydrogen sulfide is the most likely toxicant.

DISCUSSION

The 16 patients provide a scouting examination of the spectrum of H_2S effects. These ranged from serious neurobehavioral impairment, including balance and reaction time impairment from near fatal exposures, to insidious function loss from long-term exposure doses around refinery operations, gas flares, asphalt loading, and, most important, simple proximity to refineries. Skepticism about this novel interpretation seemingly was abolished by the observations of severe impairment, including visual field loss, in subjects around and downwind of the Torrance refinery explosion. Less intense impairment characterized the population exposed downwind and at work to the desulfurization plant oil refinery at San Luis Obispo. Probably refineries cannot be made safe for nearby residents or even those some miles away.

The downwind effect plus observations from other studies of chemical effects at Casper and Houston and in refinery workers has strengthened the social implications of these findings. In light of the adverse effects at Torrance and Nipoma, brain damage is implied at Casper and Houston, as populations unexposed to chemical manufacturing in Casper and to chlordane in Houston showed patterns of impairment consistent with the effects of reduced sulfur gases.

The most common neurophysiological impairment was for balance, followed by blink. In the neuropsychological testing, choice reaction time, fingertip number writing, and verbal recall were most commonly impaired, followed by trail making and Culture Fair. Thus, integrative functions with multiple inputs were impaired by H_2S exposure. Statistical certainty is a difficult problem in analyzing small groups of patients. Two available methods were used. One is to consider H_2S exposure as the definer of the group despite many differences in patients' exposure and previous status, so as to compare their average scores to those of an unexposed group. The other method is to use the 95% confidence limits of expected performance and determine prevalence of abnormality for each test score. The first analysis showed decreased performance for balance, reaction time, and cognitive and perceptual motor skills. The second, based on counting the prevalence, although more crude, showed that the same functions were impaired.

There are three conclusions. The first is that sensitive testing in subjects who were not made unconscious by H_2S or whose exposure was even lower showed protracted impairment when the subjects were tested at intervals from months to years after exposure. The second conclusion is that exposures causing impairment occurred in environmental situations, downwind as well as in the workplace, and the third is that the exposure did not have to be sublethal to cause permanent ill effects. A few hours of occupational H_2S exposure without unconsciousness or respiratory distress impaired neurobehavioral function, an effect that appeared to be permanent. Although alternative explanations may be possible in each individual, the composite experience suggests that well-planned epidemiological studies with sensitive methods should be performed on subjects environmentally exposed as well as on those occupationally exposed.

Occupational and downwind residential exposures to a California coastal refinery processing high sulfur crude oil and emitting reduced sulfur gases, rich in H_2S, were associated with abnormal objective physiological tests: slower simple and choice reaction times, excessive speed of sway with eyes open and with eyes closed, and reduced

color discrimination. Thus the automatic (subconscious) parts of the neuroaxis except for blink showed impairment. The impaired performance was accompanied by reduced perceptual motor speed and perhaps recall. Impairment was less severe than in subjects who had recovered from H_2S-induced unconsciousness (9, 11, 12). Most of the psychometric differences were small and not significant, which implied that these tests were less sensitive than the physiological ones, or that the subjects studied had less damage to the cerebral cortex than did our groups. There was a sevenfold greater affective disturbance as shown by mood states and an excessive frequency of 31 of 33 symptoms.

The objective and subjective abnormalities followed activation of a petroleum desulfurization unit in the nearby refinery. Reduced sulfur gases exemplified by H_2S are the most plausible explanation of the neurotoxic effects, but mercury, manganese, and vanadium pentoxide, as potent inhibitors of signal transduction pathways conveyed in airborne dust, may have contributed. It is unclear whether the desulfurization plant had a specific causal role in the health disorders above that of the refinery. Clearly it added more irritative complaints, which made the burden of being downwind "unbearable" to the subjects. Because ex-workers had greater proximity to the source, one might have expected them to be more severely affected than the downwind neighbors. Because they were not, workers may have recovered somewhat in the interval of nearly a year between leaving work and being tested. Alternately they may have had better initial performance than the neighbors but lost more, so as to average with them. Finally, it is possible that intermittent exposure, for 40 hours per week for 3 or 4 years, at the refinery was not equivalent to neighbors exposed at presumably lower doses for up to 168 hours per week for 10 to 15 years. Exploration of the dose–response relationships needs more subjects and continuous monitoring of concentrations of reduced sulfur gases and other neurotoxins. Ex-workers had minimal changes during the 1989 to 1991 interval although their balance improved slightly, whereas the residents, all of whom continued to be exposed, remained impaired.

Alternate Explanations

Clients in environmental chemical lawsuits have been viewed as seeking personal gain and thus as unreliable and undeserving as "whiplash" or "back strain" plaintiffs. In checking the group scores for possible evidences of bias from poor performance, poor attention, or early termination of effort was not observed. Being party to a lawsuit could have motivated them to raise their symptom frequencies and conceivably could even influence scores on psychological tests, but this seems unlikely because a majority of exposed subjects would have to do this in a consistent pattern without rehearsal, and they were all naive concerning these tests. Furthermore, scores were nearly identical on retesting after two years, which also argues against this explanation (see Chapter 16, Table 16.5). Balance by sway speed, choice reaction time, and blink reflex are multiple-trial tests in which the subjects' scores improve and become stable. If the exposed were test-wise subjects, poor performance would be anticipated in all tests in the battery, not just in the most sensitive ones. Moreover, the pattern of abnormality was similar to but less severe than that in workers overcome by H_2S (9, 11, 12).

Inappropriate Comparison Group

If comparison subjects were "supranormals" they could bias interpretation of average results wrongly, causing investigators to consider them abnormal. However, comparison

of the mean scores of these 32 reference subjects to those of three reference groups showed virtual identity in the neurophysiological and neuropsychological domains (20–22). Thus the choice of the comparison group seems appropriate.

Somatization disorder or chronic post-traumatic stress (DSM III, 1980) triggered by odors and health fears might elevate POMS scores and symptom frequencies, but this seems unlikely in these subjects because POMS scores had no significant coefficients in linear regression models for any abnormal physiological or psychological test score. It is more probable that the exposed subjects' elevated POMS scores and excess frequency of symptoms were neuropsychological consequences of chemicals acting on the brain. Moreover, stress does not impair balance and choice reaction time, but improves them (23).

Attribution of Effects

The desulfurization workers' complaints that initiated the study, mainly dermatitis, depression, and asthma, gradually disappeared when they were away from the refinery. Asthma and dermatitis but not depression were attributed to sulfur dioxide (SO_2) and vanadium pentoxide. In contrast, the neighbors' symptoms did not improve as they continued exposure downwind of reduced sulfur gases. Workers and neighbors developed airway and skin irritation shortly after the installation of a vanadium pentoxide desulfurization unit. However, H_2S and carbon oxide sulfide (COS) were measured in the residential area for 5 years, and this refinery had processed "sour" crude oil, with reduced sulfur gases, for nearly 40 years. Hydrogen sulfide, COS, and mercaptans are heavier than air, collect in low places such as sewers and holds of ships from decomposition of sulfur compounds under hypoxic conditions (7, 9, 14), and have caused deaths (8, 9).

Mechanisms

Reduced sulfur gases cause death quickly by respiratory paralysis at exposures above 500 ppm of H_2S. Levels between 100 and 500 ppm irritate the eyes and respiratory tract, and unconsciousness and death have been reported from prolonged breathing of 50 ppm. Fortunately, the odor threshold is 25 ppb. The mechanism of brain damage from low doses of H_2S is unclear, but soluble sulfides may interfere with cellular utilization of oxygen by combining with iron in the cytochrome oxidase respiratory enzyme in mitochondria (3). Primates exposed to 500 ppm of H_2S for 22 minutes showed cerebral cortical necrosis, reduction in Purkinje cells of the cerebellar cortex, and focal gliosis. Repeated exposures of mice to H_2S reduced brain RNA and inhibited cytochrome oxidase activity (3).

CONCLUSIONS

It would be prudent to assess the neurobehavioral performance of workers before their employment in oil fields and refineries (23) and periodically thereafter. By coupling the results with careful measurements of reduced sulfur gases and "trace" components, dose–response relationships would emerge. Meanwhile refineries with H_2S desulfurization should be viewed with caution.

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