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Hypotheses to Explain the Higher Symptom Rates Observed around Hazardous Waste Sites

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Five studies were carried out around hazardous waste sites in California in which the main route of exposure was to low-level parts per billion concentrations of either gaseous emissions or airborne dust particles. Although there was no evidence suggesting excesses in cancer or birth defects, the total number and the prevalence of many of subjective symptoms were higher in areas near the site than in control neighborboods. We discuss a number of causal processes that could explain these results. We conclude that a classical toxicological response and mass psychogenic illness are not valid explanations. Recall bias may explain part of the pattern. We present data from situations where stress alone from environmental anxiety has produced a similar magnitude of excess symptoms in populations. The fact that excess symptoms in waste site neighbors is found primarily in those who complain of odors or who are worried about environmental chemicals suggests the possibility that autonomic, stress-mediated mechanisms or behavioral sensitization are active in the genesis of these symptoms. A variety of confounders were controlled for. The hypothesis that chemically "acquired immune deficiency" can cause subtle symptomatology as a prodrome to subsequent serious disease has been raised in testimony at several toxic tort trials about waste sites. Although this hypothesis seems unlikely, particularly at sites such as the ones we studied with low airborne exposures, if true it would have profound regulatory implications.

Introduction

Over the decade that has elapsed since the Love Canal first drew the public's attention to the problems of hazardous waste, there have been may community demands to study alleged excesses of cancer, birth defects, and a variety of symptom complaints in association with real or perceived environmental pollution. The California Department of Health Services has carried out four studies in which symptoms have been assessed (*1–4*) and was responsible for seeing that a fifth (*5,6*) was carried out under contract. In these five studies, community residents expressed a high degree of concern regarding local environmental hazards and fears with regard to alleged dramatic increases in birth defects and cancer. These health concerns were not borne out by careful study, but without exception, one or more bothersome symptoms were more prevalent near the waste site than in the control communities chosen for comparison. Table 1 indicates the symptoms with increased prevalence that reached statistical significance in these studies. These are odds ratios adjusted for important confounders that varied from study to study. For those studies where the waste site neighbors were divided into "near" and "far" groups, both odds ratios (in comparison to the control group) are shown.

Since the complaints were most often subjective in nature and were not accompanied by an excess of hospitalization for more serious conditions, researchers at the California Department of Health Services do not believe that serious health problems are occurring. All the communities studied have been the subject of intense media scrutiny and many community members have been involved in litigation against responsible parties. The possibility of some kind of reporting bias has always seemed a credible hypothesis to explain the higher symptom rates.

A second hypothesis to explain the higher rates, one at the other extreme of etiological thinking, comes from the legal testimony of expert witnesses for the plaintiffs in some of the hazardous waste site lawsuits. They have testified that they believe low-level exposure to hazardous chemicals may result in a kind of chemical "acquired immune deficiency," which is alleged to produce a variety of symptoms whose immunological origin may thus have a grave prognostic significance (*7*).

In addition to these two very different hypotheses, it is perhaps worthwhile to consider the full range of causal processes that could be at work in a concerned or worried community residing next to a hazardous waste site and that could conceivable cause the pattern so often observed. To accomplish this we present data illustrating the magnitude of effects that can be produced by each of these respective processes. Table 2 displays the eight causal

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Table 1. Crude odds ratios for symptom incidence: exposed compared with control populations.

Symptom	McColl (*1*)	OII[a] (*2*)	Del Amo (*3*)	Montrose (*3*)	Stringfellow (*5*)	Purity (*4*)
Nervousness	1.6–5.5*	—	—	—	—	—
Headache	1.6–7.1*	1.8–4.6[b]	2.2[b]	1.2	1.1, 1.2	1.05
Sleeplessness	1.7–7.9*	1.9–5.3[b]	2.2[b]	1.1	—	—
Fatigue	2.6–7.0*	1.8–3.1[b]	3.0[b]	1.2	1.3, 1.2	—
Dizziness	2.4–8.0*	1.0–2.2[b]	3.3[b]	1.5	1.7, 1.4	—
Nausea	2.1–24.5*	2.1[b]–3.9[b]	2.9[b]	1.6	2.2[b], 1.9[b]	—
Loss of appetite	1.5–17.3*	2.2[a]–5.1[b]	1.5	1.0	—	—
Stomachache	1.1–10.2*	—	—	—	—	—
Sinus congestion	1.4–4.4*	1.4–2.7[b]	3.3[b]	2.1[b]	1.1, 1.1	—
Blurred vision	—	—	—	—	1.6, 2.2[b]	—
Eye irritation	1.6–4.8*	1.4–3.7[b]	3.3[b]	1.8[b]	1.2, 1.3	—
Nose irritation	2.0–7.5*	—	—	—	—	—
Runny nose	2.8–5.6*	—	—	—	—	—
Sore throat	1.8–5.9*	1.7–2.9[b]	3.5[b]	2.1[b]	—	—
Cough	1.6–4.0*	—	—	—	1.2, 2.1[b]	—
Asthma	—	1.3–2.8[b]	1.9	1.8	—	—
Allergies	1.4–4.2*	—	1.9	1.8	—	—
Wheezing	2.8–15.5*	—	—	—	1.2, 0.9	—
Skin irritation	1.1–5.0*	2.2[b]–3.1[b]	3.4[b]	2.3[b]	—	1.7
Chest pains	1.7–4.4*	—	—	—	1.2, 1.3	—
Earaches	1.4–3.8*	1.5–3.1[b]	3.5[b]	1.6	1.6, 2.2	—
Frequent urination	—	—	—	—	1.7, 1.7[b]	—
Difficulty breathing	—	1.7–3.3[b]	1.7[b]	1.2	—	0.8
Toothache	—	1.5–2.3[b]	2.3[b]	1.4	—	1.0
Muscle aches	—	2.1–3.7[b]	1.9[b]	1.4	—	1.1
Weak in extremities	—	—	—	—	1.9[b], 1.5	—
Numbness in limbs	—	1.3–2.9[b]	2.2[b]	1.4	1.8, 1.1	—
High environmental worry	9%	32%	18%	18%	—	—
Worry followed illness[c]	0.5%	7%	8%	8%	—	—
Number in control area	354	928	212	194	203	1801
Total number in "exposed" areas	703	1349	444	430	402	157

[a]OII, Operating Industries Inc.
[b]Lower 95% confidence limit was > 1.
[c]Worry arose because of illness.
*χ^2 trend $p < 0.05$.

Table 2. Potential causes for higher symptom rates near hazardous waste sites.

Classical, toxicological reaction
Immunological or other physiogenic "hazardous waste syndrome"
Behavioral sensitization
Psychosomatic reaction to stress
Mass psychogenic illness
Reporting bias
Confounding factors
Odor, the effect modifier

processes we wish to consider; they are not necessarily listed in order of their plausability. It should be noted that the excess prevalence of symptoms at any one site might be due to one or more of these processes.

Classical Toxicological Reaction

There are few instances in which there is scientific consensus that discharged hazardous waste has achieved a dose in human beings sufficient to produce the kind of health effects expected on the basis of prior toxicological knowledge. One such example is the episode in Hardemann County, Tennessee (*8*). From the mid-1960s to the early 1970s, 20 million gallons of chlorinated solvents and pesticides were deposited in buried barrels. In mid-1977, nearby residents complained of chemical odor and strange tastes in their water. They complained as well of skin and eye irritation, weakness, nausea, vomiting, and diarrhea. The effects extended to well water users 1 mile away. In mid-1978, chlorinated solvents including perchlorethylene were found in well water. By the end of that year, EPA advised against the ingestion of that water, and a clinical study of 36 individuals was conducted showing higher symptom rates. In January of the next year, a follow-up study, this time including a control group was conducted (*8*). The study showed elevations in alkaline-phosphatase and serum glutamate oxalate transaminase and lowered levels of serum albumin. The levels of contamination were in the part-per-million range, and the effects observed were compatible with prior toxicological knowledge.

In the studies conducted by the California Department of Health Services mentioned above, the principal or sole route of exposure has been airborne, and the exposure to the major chemical substances, aromatic and chlorinated solvents, has been believed to be at the low part-per-billion level. One would not expect traditional clinical laboratory tests to be abnormal under such circumstances, and indeed in the one study (*5*) (Stringfellow) in which children were tested for liver function and other standard clinical parameters, the exposed children did not differ from the controls. For these reasons, we believe the excess prevalence of symptoms in California studies can probably not be attributed to a classical toxicological process.

Immunological or Other Physiogenic "Hazardous Waste Syndrome"

Physicians who have been grouped into a school of thought called "clinical ecology" claim that they identified a subgroup of patients who are affected by very low doses of environmental chemicals and react to a wide range of these chemicals with symptoms varying from classical asthmatic responses to subtle psychological disturbances (*9*). A universal or standardized definition of this syndrome has yet to be formalized.

The explanation for this postulated condition varies depending on the practitioner and includes immunological and nutritional theories. Interviews with colleagues who have been involved in lawsuits settled out of court with relation to several different hazardous waste sites have revealed that in some cases, laboratory tests of subtle immunological and neurological functioning have been abnormal in selected residents near hazardous waste sites when compared to normal controls. At this point in time, these findings, the reliability of the laboratory tests used, and the theories which underlie the findings are highly controversial.

Behavioral Sensitization

Occupational physicians report the existence of patients who after an initial challenge by a high-dose (i.e., irritant) exposure to a chemical substance may subsequently experience high-dosage-type symptomatology when exposed to odors of the same chemical at exceedingly low dosages. Tabershaw et al. reported this for pesticides in 1966 (*10*). Schottenfield and Cullen (*11*) refer to it as a form of "a typical post traumatic stress disorder." More recently, Shusterman et al. (*12*) have reported several cases of recurrent paniclike symptoms that seem to illustrate this pattern. He has coined the term "behavioral sensitization to an odorant" to describe the phenomenon. At this time it is thought that the reaction is a type of involuntary conditioned reflex and in many cases that the only remedy is either to abate the exposure to subodorant levels or to remove the patients from their occupational exposure. Bolla-Wilson et al. (*13*) suggest deconditioning or desensitization as a treatment.

In all but one of the California studies mentioned above, odor was a prominent complaint in the community, and many of the symptoms were excessive primarily in those who complained of odor. The total number of newly acquired symptoms reported was excessive only in those who complained of odor. To our knowledge, however, none of the community residents had ever been exposed to high (ppm) doses of chemicals from the dump-site as an initiating episode. It seems possible, however, that stress-related symptoms might be conditioned to an odor stimulus.

Psychosomatic Reaction to Stress

One could well imagine that the continuous state of arousal and anxiety that many hazardous waste site neighbors feel and express could lead to chronic muscular tension, headaches, sleep disturbance, and the like. One might be able to observe these effects in situations where the public believes that it is exposed to a hazard and is anxious about it, while in fact, no hazard is present capable of producing symptoms by a toxicological mechanism.

The prime example of this occurred in the year or so following the Three-Mile Island nuclear accident. Although there are some who would argue that the low levels of radiation released at Three-Mile Island might conceivably cause carcinogenic or reproductive effects, we know of no one who believes that the low level of radiation delivered could in and of itself cause headaches, sleeplessness, and other anxiety symptoms. Indeed, the public itself did not link any such symptoms to the effects of radiation. Thus, the most likely explanation of any excess, if it were to be observed, would be with relation to anxiety and stress and not to radiation or reporting bias. In 1981, a study by Houts et al. (*14*) reported the level of self-reported anxiety to be quite high in residents near the plant but near zero beyond 16 miles from the site. The prevalence of either one or more "physical symptom" or one or more "behavioral stress symptom" displayed an absolute drop of about 10 percentage points as one moved beyond 16 miles from the site. Even more suggestive was a study carried out by Baum et al. (*15*) a year and a half after the original accident. He and his colleagues collected urinary samples for norepinephrine levels and carried out psychological tests, including a proofreading task that aimed at detecting stress. A group of volunteers near the Three-Mile Island plant showed higher levels of norepinephrine and a lower ability to carry out proofreading tasks than groups living near another nuclear plant, near a coal fire plant, and in an area with no energy plant at all. The results are presented in Table 3. We interpret these findings to suggest that there are physiological and psychological objective measures of stress that are manifested during an environmental crisis, while at the same time there can also be an absolute increased prevalence of certain kinds of symptoms, of about ten percentage points.

Investigations (*16*) by the California Department of Health Services during the Mediterranean fruit fly (Medfly) crisis in the early 1980s provided the opportunity to observe a natural experiment for evaluating the role of anxiety in the generation of symptoms. When the Federal government preempted the then Governor of California, Jerry Brown, and announced that community-wide aerial spraying with malathion protein bait was about to begin, there was a high degree of anxiety in the population of Santa Clara County where the spraying was to be done. An ad hoc health advisory committee to the director of the department suggested that surveillance for pesticide-related acute illness be carried out and that a baseline study be conducted a few days before the spraying was to begin. A study carried out several days into the spraying would allow the department to identify any increased prevalence of cholinergic symptoms, if they were to occur. The protein bait delivered such a low dose of malathion that no such symptoms were expected by the department's toxicologists. The results of a survey of 238 individuals taken both before and after spraying are shown in Table 4. Much to the department's surprise, the prevalence of a large number of symptoms

Table 3. Objective signs of stress at Three-Mile Island (TMI).

Sign	TMI	No plant	Coal[a]	Nuclear[b]
Proofreading efficiency	44.0%	73.0%	74.0%	70.0%
Urinary epinephrine, mg/mL	12.3%	8.9%	6.2%	7.5%

[a]An area adjacent to a coal-fired electrical generating plant.

[b]An area adjacent to a nuclear generating plant with no history of problem or overt community concern. From Baum et al. (*14*).

Table 4. Prevalence of self-reported symptoms just before and just after aerial malathion application, Santa Clara County, 1981.[a]

Symptom	Prevalence, %		Decrease in prevalence, %
	Before spraying	After spraying	
Headache	20.6	10.9	9.7
Watering eyes	13.9	7.1	6.8
Blurring vision	6.7	1.7	5.0
Difficulty sleeping	16.4	7.6	8.8
Muscle aches or pains	13.4	6.3	7.1
Change of appetite	7.6	2.9	4.7
Difficulty remembering things	8.0	3.8	4.2
Dizziness or feeling faint	8.4	3.0	5.4
Tense or anxious	15.7	8.8	6.8

[a]All differences are significant at $p = 0.05$ level; $n = 238$.

decreased by four to ten percentage points even though the personal interview survey was conducted in exactly the same way, in the same randomly selected group of individuals in the population. Similar results were seen in a briefer phone survey of a sprayed and nonsprayed area. Both showed a decrease in anxiety and symptoms after spraying began. Since malathion is not promoted by its manufacturer as an effective nerve tonic, the dosage of malathion to human beings must have been infinitesimally small, and as an unsprayed area in the same county showed a decrease in anxiety and symptoms after spraying began in other parts of the county, one must look for a nonpharmacological explanation for this change. One factor that had changed dramatically was the attitude of the public. Within a day or so of the spraying, it became clear that the emergency room visits had not increased and that there were no obvious subjective effects from the spraying. Both the public and the newspapers lost interest. The number of anxious telephone calls to the health department decreased dramatically. This and the 7% drop in self-reported anxiety strongly suggests that the level of anxiety in the community was significantly abated.

Our interpretation of these data is that the level of stress decreased in the population, and the prevalence of stress-associated symptoms decreased concomitantly. Once again we have a situation in which no chemical agent was present during the time of high symptom prevalence and, indeed, the public knew that no chemical was present and had no reason to anxiously scan themselves for symptoms during the preaerial-spraying time period. Given these circumstances, it is unlikely that the higher level of symptoms reported in the prespraying period was due to reporting bias. Thus we have two different episodes in which anxiety and stress seem to be associated with about a four to ten percentage point increase in prevalence of a variety of symptoms. It is beyond the scope of this paper to consider the long-term prognosis for communities with chronic anxiety-induced stress reactions, but it is a research topic that must be considered in any long-term follow-up of such communities.

Mass Psychogenic Illness

Although public officials are given to describing anxious communities as "hysterical," the situations we have seen in California would not meet the technical criteria for true mass psychogenic illness. The latter is characterized by acute onset, is of short duration, displays propagation from a small number of index cases to a larger group, and is usually characterized by fainting, seizures, and trances. It more characteristically occurs in schools, factories, institutions, and small towns. The literature has been reviewed by Culligan and Pennebaker (*17*).

Reporting Bias

If we compare a population near a hazardous waste site that believes it is exposed to unknown amounts of a mixture of chemicals with a distant population that has no such belief, it is not unreasonable that the hazardous waste site neighbors would have a lowered threshold for noticing mild symptoms and for reporting them. In one California study by Baker et al. (*5*), questionnaire reports of skin cancer were validated by contacting the patients' physicians. Table 5 shows the number of self-reported skin cancers from this study in the "exposed" and control areas, as well as the proportion of the self-reported cases near the dumpsite that withstood the test of confirmation. Apparently the hazardous waste site neighbors were more likely to remember skin lesions that had been investigated for carcinogenicity as if they were really cancers. The residents of the control area had a less "value-laden" recollection. The same process might well be operating with regard to more subjective symptoms. In the more recent California studies, the symptom "toothache" has been included as a dummy question to gauge the degree of recall bias. As can bee seen in Table 1, there was a 1.5- to 2-fold excess reporting in two of the three studies in which toothache status was ascertained.

A study by Roth et al. of a Louisiana hazardous waste site (*18*) attempted to control for recall bias by stratifying on measures of hypochondriasis and the opinion that environmental exposure to hazardous waste is dangerous to one's health. They found that the prevalence of hypochondria was the same in these living near and remotely from the site and that hypochondria was neither a confounder nor an effect modifier. Strong opinion on environmental hazards was a different matter. It was held more frequently by waste-site neighbors than by controls and was a strong effect modifier. The prevalence of symptoms was only in excess among those dumpsite neighbors who thought hazardous waste was dangerous. Since the authors did not determine whether the environmental opinion resulted from an illness experience, they were not sure if the opinion caused the symptoms or vice versa. In California, we have more recently been asking about "environmental worry" and whether it resulted from illness or other sources. The majority of worry does not originate in illness, as can be seen from Table 1. As will be seen in the next section, environmental worry is a powerful predictor of symptoms even in control individuals who claim that illness did not cause this environmental worry. Thus, environmental worry is a potential confounder and, in addition, would appear as an effect modifier if worriers near the site had a lower threshold for noticing and reporting symptoms than worriers in the control area. This phenomenon may explain all of the overall differences in the Louisiana Study. In the California studies, there was some confounding and some effect modification, but not enough to explain all the differences between site neighborhood and their respective control groups.

Table 5. Bias in self-reporting of "skin cancer" (*5*).

Area	Cases	Confirmed	Benign lesions	No information
Waste site	27	30%	33%	38%
Comparison area	7	57%	14%	29%

Confounding Factors

When one compares rates of cancer in one area to another, it is taken for granted that we control for the powerful confounders of race, sex, and age. But what additional confounders are relevant when we compare rates of headache, difficulty sleeping, and the like? To address this issue, Lipscomb, while working with the department, did a systematic review of the factors that predict symptoms among the control groups of the four studies for which the department was directly responsible (*19*).

Analysis of data from three of these studies included responses from adults only in the Operating Industries, Inc. (OII), Del Amo, and McColl, control populations containing 928, 1063, and 354 respondents, respectively. The first two studies were conducted by either the phone or in-person interviews using the same questionnaires, while the third study was conducted using a slightly different mailed self-administered. The type of questionnaire, either interview or self-administered, was controlled for in a logistic regression analysis. This analysis focused on symptoms that were worded most similarly across all studies.

Because we believed that individuals who were particularly concerned about environmental chemicals might be more likely to report disease or to report symptoms, we decided in several of the studies to ask individuals directly about the degree of their concern for environmental chemicals. If they expressed any concern, we asked them if it had arisen because of illness in themselves or because of hearing about them in the paper. The idea here was to identify and eliminate those persons for whom symptoms had caused the environmental concern. From 0.5 to 8.0% of "worriers" were so excluded.

We were interested to see if the number of symptoms an individual reported had a different distribution for those who were worried and for those who were not. Figure 1 shows the two distributions for the control group used in our study of the OII waste site in Los Angeles. One can see that worried individuals were much more likely to report four or more symptoms and less likely to report zero symptoms. The other control groups showed a similar if not quite so dramatic difference in distributions.

We wondered also if worry affected the prevalence of different symptoms in different ways, and particulary if symptoms that were more subjective in nature were more likely to be affected. Figure 2 shows the odds of reporting a variety of symptoms among those who are very worried relative to those who are not worried. The confidence limits around these relative odds are also shown. The figures were obtained by calculating a Mantel-Haenszel summary odds ratio across several studies. None of the chi square tests for heterogeneity were significant, so it was appropriate to pool across the studies. In all, 13 symptoms were present in comparable ways in the questionnaires of the three studies for which both symptoms and worry were asked. The presence of worry increased the odds of reporting each of these symptoms in a statistically significant way. There was nearly a 5-fold difference for sinus congestion and a 2-fold difference for sleep disturbance, with other symptoms ranging in between. We see

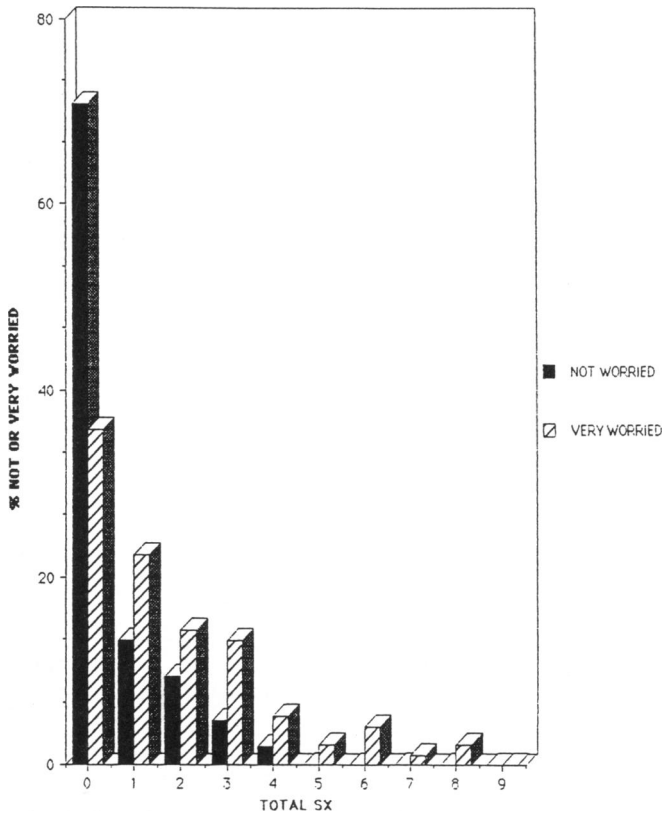

FIGURE 1. Even in a control neighborhood, those who worry about environmental chemicals report a greater number of symptoms than those who are not worried.

no predictable pattern for predicting the symptoms whose prevalence is most affected by worry.

We carried out a logistic regression to predict a subjective and emotional symptom (sleep disturbance) and a more objective symptom (skin irritation). The variables of the model included whether a mailed or telephone questionnaire was used, if the patient was female, greater than 45 years of age, Asian, Hispanic or other ethnicity, was a smoker, the number of years of high school education, the exposure to home pesticides, and the degree to which they were worried. We display the antilogs of the regression coefficients as odds ratios in Figure 3. For skin irritation we can see that there is a slightly greater prevalence for mailed questionnaires than for telephone questionnaires; that females are considerably more likely to report skin irritation than males; older people are less likely to do so than younger people. Asians report more skin irritations than Hispanics, who in turn report more than Anglos; smokers are more likely to skin conditions than nonsmokers. Skin conditions are less common in those with education that extends beyond high school and are more common among those who said they use pesticides in their home. As noted before, worried individuals have a more than 2-fold relative odds for reporting skin conditions. The predictors of sleep disturbance are not the same. For example, Asians are less likely to report sleep disturbance, although more likely to report skin conditions. But worry persists as an important predictor.

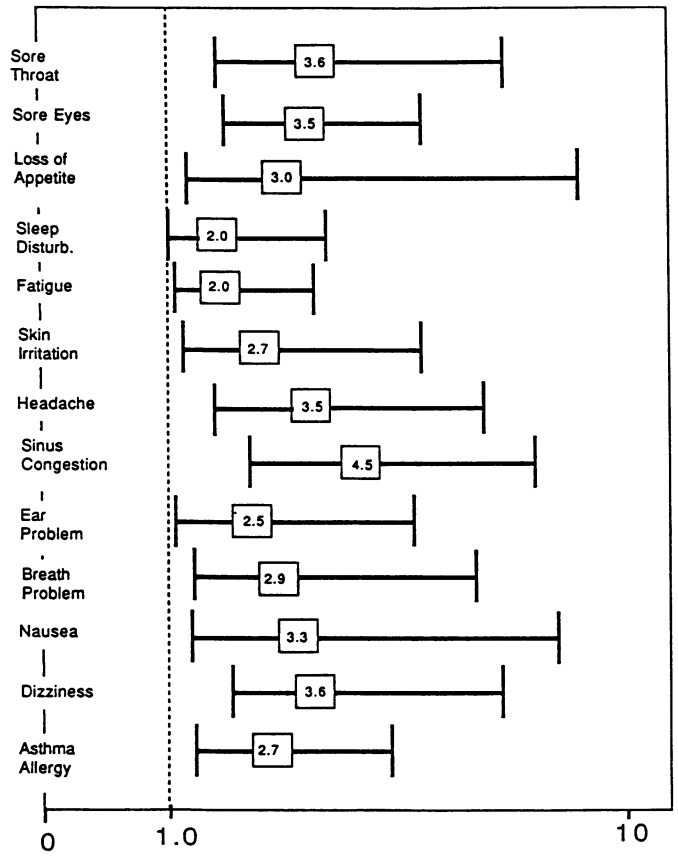

FIGURE 2. Control neighborhood residents report from two to five times higher prevalences of a variety of symptoms if they are worried about environmental chemicals. Because waste site neighbors tend to worry more about chemicals, worry is an important potential confounder of the effect of waste sites.

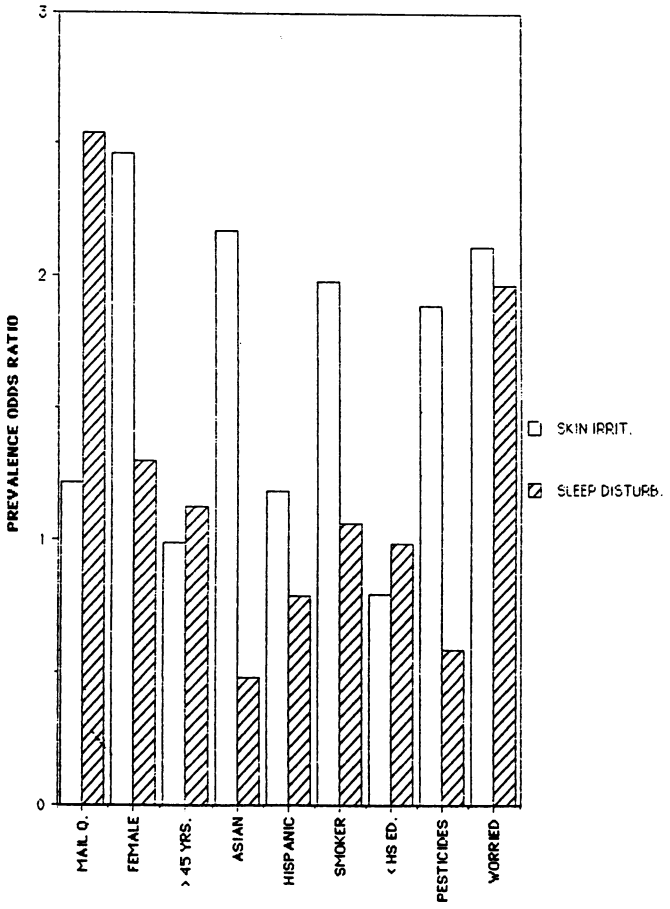

FIGURE 3. A number of demographic and lifestyle factors influence the prevalence of symptoms even in control neighborhoods.

In short, there are a number of potential factors that could be confounded between dumpsite neighbors and controls. Certainly worry about environmental hazards is more prevalent among the residents near a hazardous waste site; however, in all of these California studies, worry was controlled for in the analysis. Despite the fact that it was both a confounder and an effect modifier, the differences in symptom prevalence did not go away after control for these factors in the analysis.

It should be noted that the strong association between worry and symptoms has an alternative explanation than that of reporting bias. If worrying about environmental chemicals is a sign of chemically induced depression, it could easily be correlated with other induced symptoms. Alternatively, worry about the dumpsite, particularly when triggered by odor perception (*20*), could lead to stress, immunological change, and a variety of symptoms.

Odor, the Powerful Effect Modifier

In four of the sites we studied, odor perception modified the effect of dumpsite proximity on number of symptoms. For example, the distribution of symptoms was virtually identical for the 34% of Del Amo meighbors and the 75% of controls who did-not complain of environmental odors. For them, proximity to the site did not increase the number of symptoms.

In the control area, odor perception brought with it a somewhat greater number of symptoms, but at Del Amo the odor-complaining distribution acquired a tail of subjects with more than nine symptoms. Indeed, the overall difference in the number of symptoms experienced by Del Amo neighbors is contributed only by those who complain of odor.

One may well ask if this pattern is seen for all of the 16 symptoms that were investigated in this study. The answer is that in odor nonperceivers only eye irritation had a higher prevalence in the Del Amo neighborhood when compared to the control area. All the other 15 symptoms had similar prevalences for the two areas in odor nonperceivers. Ten of the 16 symptoms in frequent odor perceivers were more prevalent near the site than in the control area. The difference between Del Amo prevalences and control prevalences, with one exception, is restricted to those who notice odor. Table 6 shows the results for selected symptoms. Similar patterns have been seen at other odoriferous waste sites in California. At the McColl site we were able to use odorometric techniques to independently define several odor zones as a surrogate for chemical airborne exposure. For each zone it was the group complaining of odors who reported more symptoms. For this reason we do not think that the pattern we are seeing is just a reflection of exposure.

How then, are we to explain this striking finding? One could

Table 6. Prevalence of new onset symptoms (per 100 adults) by frequency of odor detection (3).

Symptom	Prevalence, %		
	Del Amo	Control	χ^2 *p*-value
Eye irritation			
Never	6.5	1.2	0.006
Rare, < 4/month	8.4	2.2	0.149
> 4/month	18.8	2.2	0.000
Throat soreness[a]			
Never	1.5	1.8	0.744
Rare, < 4/month	7.8	1.9	0.001
> 4/month	13.4	2.6	0.000
Sneezing/sinus congestion[a]			
Never	1.0	1.5	0.814
Rare, < 4/month	3.9	3.4	0.392
> 4/month	16.0	4.3	0.000
Headaches[a]			
Never	3.0	3.7	0.954
Rare, < 4/month	2.6	2.9	0.959
> 4/month	11.3	3.4	0.000
Sleep difficulties[a]			
Never	0.0	2.7	0.069
Rare, < 4/month	4.8	2.4	0.151
> 4/month	11.3	5.1	0.003
Toothache			
Never	2.5	1.2	0.459
Rare, < 4/month	6.1	2.7	0.037
> 4/month	5.1	3.0	0.313

[a] χ^2 for heterogeneity at $p < 0.05$.

use it as evidence for recall bias. But our dummy question "toothache" in Table 6 shows a weak excess prevalence in all odor categories not just in the odor perceivers. The majority of the symptoms show a pattern distinct from the toothache pattern. This is compatible with behavioral sensitization, with an odor-worry-stress process, or some odor-physiological process. It is a pattern not suggestive of a pharmacological process because chemicals should act equally well in nonodor perceivers, as was indeed the case for the symptom eye irritation.

The hypothesis that the symptom complaints and the subsequent lack of a sense of well-being are due to stress and behavioral sensitization is not put forward to minimize the importance of these symptoms to waste site neighbors. The odor-triggered symptoms are not easily removed except by dealing with the source of the odors. Indeed, in many parts of California there are strictly enforced regulations against odor exposures to the general populations.

Second-Generation Hazardous Waste Site Studies

The first-generation studies show that populations of a few hundred individuals living near waste sites often report more subjective symptoms than control subjects do. The prevalence of people with one or more symptoms is often around 10 percentage points higher near the site than in the control areas.

We have presented evidence suggesting that stress, recall bias, confounding, and something associated with the perception of odor can in some cases account for much of this difference. We believe that classical toxicological effects and mass psychogenic illness are unlikely explanations. The possibility of physiological effects related to odors, odor-related behavioral sensitization, and finally, an immunological "hazardous waste syndrome" are alternative explanations.

The last explanation has been advanced during toxic tort proceedings, with the claim that there is an ominous prognostic linkage between symptoms and more serious conditions such as cancer and birth defects. If this were true, it would have profound regulatory implications.

Having worked directly with individuals in a number of communities and having carried out the above described studies, we believe that the "hazardous waste syndrome" hypothesis to explain the greater number of symptoms around waste sites with low-level airborne exposures is a very improbable hypothesis because *a*) it invokes biological mechanisms that are not generally recognized; *b*) it ignores other more likely explanations; and *c*) it has usually been justified on the basis of data from unrepresentative samples of ill patients with post hoc interpretations of physical and laboratory findings.

Nontheless, one can propose protocols to test the hypothesis that symptoms associated with low-level chemical exposures are early warnings of serious immunological or neurological dysfunction. These protocols would involve sophisticated exposure assessment, the use of validated laboratory tests, and physical examinations. They would need to simultaneously evaluate the physiological parameters of stress, neurological, and immune status. They are million dollar studies and since they test paradigm-breaking hypotheses, they would need to be replicated several times to be believed (*21*). Should they be done at all? It can be argued that the hypothesis is so far-fetched and the replicate studies so expensive that the matter should be dropped. On the other hand, one can argue that the potential protection of the public health and the clarification of tort liability which often runs into millions of dollars make such studies a bargain.

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