Livestock Odors: Implications for Human Health and Well-Being[1]

Susan S. Schiffman

Duke University Medical School, Durham, NC 27710

ABSTRACT: The purpose of this paper is to examine the potential effects of livestock odors on the health and well-being of neighbors. Complaints of odor nuisance have become more frequent in communities surrounding areas with high concentrations of livestock. This increase in complaints from livestock odors parallels increased complaints of odor in general, including ammonia, diesel exhaust, beauty products, cleaners, and paints. Persons who report symptoms from odors generally find problems with many different types of odorous compounds. A review of recent studies suggests that the main complaints of health symptoms from odors are eye, nose, and throat irritation, headache, and drowsiness. Sensory irritation (pungency) can be produced by a broad range of odorous volatile organic compounds from trees, flowers, foods (pepper and ginger) as well as emissions from livestock operations. Odors can also potentially affect mood and memory. Further research is required to assess fully the health impact of odors in order to establish recommendations for air quality guidelines based on scientific data.

Key Words: Odors, Senses, Health, Livestock, Pigs

 J. Anim. Sci. 1998. 76:1343–1355

Introduction

The purpose of this paper is to examine whether odorous compounds from agricultural operations could potentially alter health status in humans. With the move on a nationwide scale to greater concentrations of livestock in confined areas, complaints of odor nuisance by surrounding communities have become more frequent (Bundy, 1992). Smell sensations are induced by inhalation of volatile organic compounds (**VOC**). There are four main ways that odors could potentially affect human health. First, the VOC themselves could produce toxicological effects. Shusterman (1992), however, suggested that any health symptoms from odors are probably caused by nontoxicological mechanisms. Second, odorant compounds could cause sensory irritation in the eye, nose, and throat. Third, the VOC could stimulate sensory nerves to cause neurochemical changes that potentially influence health. Fourth, health effects from agricultural odors could be due to cognitive and emotional factors such as stored mental experience with similar odors or attitudes toward unpleasant odors. Complaints of health effects from odors associated with livestock operations probably derive from a combination of physiological and psychogenic sources. Human and animal studies suggest that expression of health symptoms involves a complex interplay between biological and behavioral/psychosocial influences (Engel, 1977; Schwartz, 1982; Kaplan, 1990; Baltrusch et al., 1991; Friedman et al., 1995).

Discussion: Potential Effects of Odors on Health and Well-Being

The experimental data on the effect of unpleasant odors on human health will be addressed in this paper in a question-and-answer format. Each question will examine whether unpleasant odors from livestock operations could have a negative impact on physical or mental health status.

Question 1: What Health Symptoms Do Persons Exposed to Odors Complain About?

A review of recent studies suggests that the main complaints of health symptoms from odors are eye, nose, and throat irritation, headache, and drowsiness. Persons who report symptoms from odors generally find problems with a broad array of compounds. Thus, any scientific studies of putative effects of odors from livestock operations must also examine other odors in the rural environment that do not arise from livestock operations.

Hudnell et al. (1992) at the Environmental Protection Agency (EPA) studied health symptoms in 66

[1]Presented at a symposium titled "The Biology of Livestock Odor" at the ASAS/ADSA Midwestern Mtg., March 18, 1997, Des Moines, IA.

Received May 21, 1997.

Accepted December 18, 1997.

healthy males who, during separate sessions, were exposed to clean air and to a mixture of VOC for 2.75-h exposure periods. The mixture contained 22 VOC (25 mg/m^3 total concentration) of commonly found airborne compounds. Subjects rated the intensity of perceived odor, irritation, and other variables before and during exposure. During exposure to VOC, eye and throat irritation, headache, and drowsiness increased or showed no evidence of adaptation while odor intensity decreased by 30%. Hudnell et al. (1992) concluded that the symptoms were not psychosomatic responses but rather were caused by stimulation of free nerve endings in the nose and throat by subthreshold levels of VOC that interacted additively or hyperadditively.

Schiffman (unpublished data) administered the Environmental Exposures and Health Questionnaire, which is used at the Health Effects Research Laboratory, U.S. Environmental Protection Agency (Research Triangle Park, NC), to residents of North Carolina who do not live near agricultural operations. None of the residents surveyed suffered from putative illnesses such as Multiple Chemical Sensitivity or Gulf War Syndrome or had sought medical advice regarding symptoms from odors.

Several items on the EPA Questionnaire were the following. First, respondents were asked whether they considered themselves unusually sensitive to everyday chemicals such as those in household cleaning products, paints, perfumes, detergents, and insect sprays. They were asked to respond by rating one of the following answers: Not at all more sensitive, A little more sensitive, Moderately more sensitive, or Much more sensitive. Second, they were asked to rate how much certain chemicals and odors would bother them if they were exposed for up to 30 min. They selected one of the following scales: 0 = Not bothered at all, 1 = Mildly bothered or ill, 2 = Moderately bothered or ill, 3 = Severely bothered or ill. Third, they were asked to indicate the symptoms they had and rate the severity of the symptoms as follows: 0 = Don't have symptom at all, 1 = Mildly affected, 2 = Moderately affected, 3 = Severely affected.

The results indicated that large differences occur in ratings of odors among individuals. For the purpose of analysis, subjects who rated themselves a little, moderately, or much more sensitive to odors were grouped together as "sensitive" subjects. Subjects who rated themselves as "not at all more sensitive" were considered the "less-sensitive" control group. The "sensitive" and "less-sensitive" subjects were analyzed separately for their ratings on odors that bothered them as well as their symptoms.

The results are given in Tables 1 and 2 for 50 sensitive subjects and 50 less-sensitive subjects matched for age, race, and sex. The information in Table 1 is limited to chemicals and odors that bothered 60% or more of the respondents. (Cigarette smoke is not included on this particular EPA questionnaire.) Self-reported "sensitive" persons in Table 1 were bothered by significantly more items than persons who considered themselves "less-sensitive." Animal odors constituted 1 of the 12 items that 60% of the subjects in the "sensitive" and "less-sensitive" groups reported would make them ill if exposed for 30 min or more. The percentage of subjects in the "less-sensitive" group that rated certain odors as problematic was surprising, however. This may be due to several reasons. Persons willing to complete the lengthy EPA questionnaire may be more environmentally concerned than the average citizen. Second, many people in both groups commented that a single sniff doesn't bother them but exposure over time does cause some symptoms. The most frequent symptoms shown in Table 2 for the "sensitive" group were tearing eyes (i.e., ocular irritation), sinus headache, sinus/nasal congestion, and nasal irritation/burning. Tearing eyes (i.e., ocular irritation) was the most frequent symptom for the "less-sensitive" group. It is noteworthy that 34 of the 50 "sensitive" subjects reported that they had allergies, compared with only 7 of their matched "less-sensitive" controls. These data are consistent with other studies that have found a fairly large proportion of persons with symptoms to odors (Bell, 1993a,b).

An additional study was performed in which subjects were again asked how sensitive they were to odors. Then they were asked to fill out a single page "Odor Questionnaire" that did not mention the environment or length of exposure. Again, the sensitive subjects rated many items as problematic. However, the "less-sensitive" group rated only a few items as problematic (mainly cigarette, cigar, and pipe smoke, ammonia, and diesel exhaust), and no more than 32% of the "less-sensitive" individuals reported a problem with any item. This finding illustrates that the responses to surveys about odors can be affected by the perceived purpose of the questionnaire as well as the duration of exposure.

Question 2: What Causes Sensory Irritation?

In order to understand the role of odors in sensory irritation, it is important to understand the anatomy that is affected by odorous VOC. Odorous VOC can activate at least five different cranial nerves: 1) the olfactory nerve, 2) the trigeminal nerve, 3) the chorda tympani nerve, 4) the glossopharyngeal nerve, and 5) the vagus nerve. The olfactory nerve has receptors at the top of the nasal cavity and transmits odor signals to the brain. The trigeminal nerve transmits information on pungency or irritation and is activated by stimulation of free nerve endings in the nose, eye, and mouth (Silver, 1992; Spit et al., 1993; Sekizawa and Tsubone, 1994). Free nerve endings in the oral cavity from the chorda tympani nerve, the glossopharyngeal nerve, and the vagus nerve can be also be stimulated by irritant VOC during mouth breathing or when VOC

Table 1. Chemicals or odors that 60% or more "sensitive" and "less-sensitive" subjects rated as ones that would make them ill if exposed for 30 minutes or more. Ratings of how much they are bothered on a strength scale from 0 to 3 points are also given

	"More Sensitive"		"Less Sensitive"	
Odor	% of Subjects	Mean strength[a]	% of Subjects	Mean strength[b]
Ammonia	100	2.27	84	2.18
Diesel exhaust	100	2.27	84	2.18
Perfume or cologne	94	2.54	—	—
Bathroom tile cleaners	92	2.15	70	1.78
Bleach	92	2.15	84	1.45
Fresh latex paint	92	2.03	—	—
Pumping gasoline	92	2.09	—	—
Fresh oil-based paint	90	2.18	—	—
Bug or insect repellent	86	1.94	76	1.70
Magic marker	86	1.72	—	—
Nail polish remover	86	1.97	70	1.78
Bathroom cleaners	84	2.03	—	—
General traffic exhaust	84	2.10	76	1.80
Insecticide treatment	84	2.32	70	1.78
Mothballs	84	1.90	70	1.67
Turpentine	84	2.06	70	2.00
Fresh road tar	82	1.97	70	1.67
Restroom deodorizer	82	1.87	—	—
Detergent aisle	78	1.90	—	—
Beauty salon	76	1.71	—	—
Hair spray	76	2.00	—	—
Potpourri	70	2.04	—	—
Animal odors	68	2.08	62	1.13
Burning leaves	68	1.84	—	—
Dry cleaners	68	1.48	—	—
Garden store	68	1.72	—	—
New carpeting	68	2.00	—	—
Swimming pool	68	1.32	—	—
Nail polish	64	2.04	—	—
Fabric store	62	1.87	—	—
Scented candles	62	1.78	—	—
Gas stove/oven	60	1.73	—	—

[a]Standard errors for strength for "More Sensitive" subjects ranged from .12 to .33.
[b]Standard errors for strength for "Less Sensitive" subjects ranged from .11 to .36.

contact the throat and enter the oral cavity during nasal breathing or inhalation.

Nasal irritation has repeatedly been shown to reduce respiratory volume (Warren et al., 1992, 1994). Irritant effects of VOC can serve as warning properties for potential health effects (Dick, 1988). Airborne chemicals can stimulate all mucosae of the body, including ocular, nasal, and respiratory mucosae, to produce pungent sensations such as irritation, stinging, burning, piquancy, prickling, freshness, and tingling (Cometto-Muniz and Cain, 1992, 1994). They can be delivered to the mucosa in gaseous form or on particles/dust. Sensory irritation (also called pungency) can be produced by volatile compounds in many environmental settings. A broad array of compounds can cause pungency, including VOC from trees, flowers, foods (pepper and ginger), as well as emissions from livestock operations. Nasal and(or) respiratory irritation have also been associated with animal feed (Smid et al., 1994), solvents (Dick, 1988), aliphatic amines (Gagnaire et al., 1989), acetic acid (Warren et al., 1994), alkylbenzenes (Cometto-Muniz and Cain, 1994), ketones, alcohols, and acetates (Cometto-Muniz and Cain, 1991, 1993), vapor phase of cigarette smoke including formaldehyde and acrolein (Feron and Kruysse, 1978; Ayer and Yeager, 1982; Lundblad and Lundberg, 1984), alkali dust (Gomez et al., 1992), chrome plating (Lindberg and Hedenstierna, 1983), acetaldehyde (Kruysse et al., 1975), diesel exhaust (Rudell et al., 1994), methanol vapor (Kawai et al., 1991), cotton and synthetic textile fiber mills (Fishwick et al., 1994), methyl bromide (Kishi et al., 1991), and sulfur trioxide (Stueven et al., 1993).

The same compound can induce both odor and pungency, but the concentration necessary to elicit pungency is often higher than that needed to elicit odor. Irritant sensations from mixtures of compounds can be hyperadditive in that the pungency of the mixture may be greater than the sum of the individual

components. In addition, subthreshold levels of individual VOC can add their sensory impacts when delivered in a mixture to produce noticeable sensory irritation. Pungency, unlike odor, is resistant to adaptation.

When VOC are inhaled at a concentration that produces pungency, this can cause respiratory symptoms (Ware et al., 1993) and reflex, transitory apnea. There seems to be a reflex mechanism that is responsible for the increase in airway resistance and bronchoconstriction that results from irritant stimuli in the nasal cavity (Nolte and Berger, 1983). Muscular contraction of bronchial tubes upon irritation restricts airflow and minimizes intake. Hoarseness of

Table 2. Percentage of persons with specific symptoms and symptom severity on a scale from 0 to 3

	"More Sensitive"		"Less Sensitive"	
Symptom	% of Subjects	Mean strength[a]	% of Subjects	Mean strength[b]
Tearing eyes	82	1.60	62	1.25
Sinus headache	76	2.07	24	1.33
Sinus/nasal congestion	76	2.18	8	1.00
Nasal irritation, burning	76	1.93	38	1.40
Other headache	68	1.96	46	1.17
Throat sore, irritated	64	1.67	24	1.67
Throat itching inside	62	1.83	—	—
Nasal secretions	62	1.91	24	1.00
Cough	62	1.65	30	1.25
Eyes dry, irritated	56	1.62	38	1.60
Difficulty breathing	56	1.48	38	1.20
Nausea	56	1.67	22	1.33
Hives, itching skin	44	1.69	—	—
Migraine headache	44	2.13	—	—
Spacy feeling	44	2.00	30	1.00
Shortness of breath	44	1.38	16	2.00
Skin redness, flushing	40	1.73	—	—
Ears itching inside	40	1.87	—	—
Difficulty concentrating	36	1.62	38	1.00
Feeling angry, irritable	32	1.67	8	1.00
Wheeze, chest tightness	32	1.58	16	1.00
Skin rash	30	1.64	8	1.00
Brain fog	28	1.70	24	1.00
Feeling anxious, panicky	28	1.60	—	—
Hoarseness	28	1.60	—	—
Undue fatigue	24	1.44	16	1.00
Heart racing, pounding	24	1.22	—	—
Blurred vision	22	1.88	8	1.00
Abdominal bloating, pain	22	1.88	—	—
Muscle aches, joint pain	18	1.86	—	—
Feeling depressed	18	1.86	—	—
Memory problems	18	1.57	—	—
Daytime sleepiness	18	1.71	8	1.00
Chest pain	18	1.43	—	—
Feeling feverish or chills	16	1.50	—	—
Coordination problems	16	1.50	8	1.00
Ear redness, flushing	16	2.33	—	—
Cough up sputum, phlegm	16	1.50	—	—
Heartburn	16	1.67	—	—
Trembling, body shaking	14	1.80	—	—
Vomiting	14	1.60	—	—
Muscle weakness	10	1.75	—	—
Inappropriate emotions	10	2.00	—	—
Diarrhea	10	1.75	—	—
Constipation	10	2.00	—	—
Numbness of legs, arms	8	1.67	—	—
Pelvic pain	6	2.50	—	—
Cold hands or feet	2	1.75	—	—

[a]Standard errors for strength for "More Sensitive" subjects ranged from .08 to .39.
[b]Standard errors for strength for "Less Sensitive" subjects ranged from 0 to .36.

voice can also occur and can be measured using spectral frequencies of the voice (Wolfe et al., 1991). However, there are individual differences in the concentrations of VOC that produce these symptoms as well as individual differences in the degree to which persons find these symptoms bothersome.

Question 3: Can Odors From Livestock Operations Cause Rhinitis, Asthma, Bronchitis, or Other Immunological Irregularities?

Irritants can set up a low-grade neurogenic inflammation with leukocyte recruitment that predispose to hyperreactivity and allergy (see Levin and Byers, 1987; Marshall and Bienenstock, 1994; Eccles, 1995; Samet, 1995). Inflammatory responses in the upper airways have been monitored by nasal lavage to monitor neutrophil (PMN) influx into the nasal passages following exposure to VOC (Koren and Devlin, 1992; Koren et al., 1992). Donham et al. (1990) found that 87% of swine confinement workers reported work-related cough due to exposure inside livestock buildings. Bronchitis and chest tightness symptoms were reported as more severe when workers returned to work after an absence of 7 d or more. In addition, 34% of workers reported episodes of organic dust toxic syndrome. Total dust and ammonia are two primary environmental predictors of pulmonary function decrements over a work period. Reynolds et al. (1996) suggested that levels of 2.5 mg/m^3 (total dust) and 7.5 ppm (ammonia) are reasonable guidelines for occupational exposure limits for swine workers. These levels of odor and dust are higher, in general, than those that would be experienced downwind from a swine operation in many instances. However, Thu et al. (1997) have recently found that neighbors of a large-scale swine operation reported experiencing more symptoms associated with respiratory inflammation than demographically similar control subjects living near minimal livestock production.

An overview of the literature on respiratory symptoms indicates that there has been a general increased incidence of rhinitis, especially in urban areas, which has been linked to chronic nasal irritation from industrial pollution (Eccles, 1995). There is also an increased prevalence of asthma in the last 15 to 20 years, which is attributed in part to pollutants, including volatile organic compounds (Koren, 1995; Leikauf et al., 1995; Utell and Looney, 1995). The prevalence of asthma in children is especially striking in urban and rural areas (Bloomberg and Strunk, 1992; Weeke, 1992; Powell, 1993; Rusznak et al., 1994; Bates, 1995; Crockett et al., 1995; Koren, 1995). For example, the incidence of asthma in schoolchildren from Aberdeen, Scotland aged 8 to 13 yr rose from 4.1% to 10.2% from 1964 to 1989 (Rusznak et al., 1994). Occupational asthma has long been associated with agriculture workers, such as those exposed to flour or wheat (Burge, 1992).

Odors and vapors have been implicated in allergic disorders (Taub, 1967) as well as headaches (Speer, 1976). One compound that occurs in hog odor (formaldehyde, HCHO) has been studied extensively because it is commonly found in occupational and residential environments. Formaldehyde can cause asthma-like symptoms in some individuals that are more severe when adsorbed on respirable particles than as gaseous HCHO alone. Green et al. (1989) found that nasal irritation and other symptoms can occur in normal, nonsmoking, non-allergic subjects during exposure to 3 ppm HCHO for 2 h. Importantly, the levels of formaldehyde downwind from swine operations are in the parts per billion or parts per trillion range, which is 3 to 6 orders of magnitude lower than those that cause irritation as a single VOC.

Persons with respiratory vulnerabilities may be more likely to complain about odors (Horesh, 1966). Doty et al. (1988) found that persons who complained about environmental odors seem to experience an increase in nasal resistance, respiration rates, and heart rate after exposure to odors. They also suggested that persons who report problems with odors may also be more aware of the irritant effects of volatile compounds as they interact with the trigeminal nerve endings in the nasal cavity. Airborne compounds with odors may also decrease beat frequency of cilia in the nose (Riechelmann et al., 1994) or modify mucociliary clearance (Singh et al., 1994; Bascom et al., 1995). Saunders et al. (1995) reported anaphylaxis could be triggered by chemical odors.

Question 4: Are Any of the Compounds in Hog Odors Toxic? Can Any of the Compounds in a Plume Get into the Body?

High levels of VOC can have profound toxic effects when they affect the olfactory system directly (Schiffman and Nagle, 1992). Volatile compounds can also be absorbed through the lungs, gastrointestinal tract, and skin and may affect metabolic or other physiological processes. Volatile organic compounds with low water solubility but high fat solubility can pass through the alveolar lining into the bloodstream and be distributed to fat stores and organ sites for which they have special affinity. However, it is unlikely that the concentrations of individual VOC from livestock operations are toxic to neighbors downwind from swine operations according to the rules of classical neurotoxicology because the concentrations are too low. On the other hand, it is not yet known whether the mixtures of low levels of VOC have potential toxicity. Although small and large molecules can be transported to the brain in the olfactory and trigeminal nerves (Baringer, 1976; Jackson et al., 1979; Shipley, 1985; Roberts, 1986; Lach and Atack, 1988; Barnett et al., 1994; Becker, 1995), there is an active detoxification system in the nose that adequately deals with low levels of most odorous VOC.

Question 5: Do Unpleasant Odors Alter Brain Activity?

For many years, odors differing in hedonic properties, including those of low-level exposure, have been shown to have differential effects on electrical brain activity as measured by electro-olfactograms and electroencephalograms (Lorig and Roberts, 1990; Durand-Lagarde and Kobal, 1991; Kobal and Hummel, 1991; Lorig, 1994). Lorig et al. (1990, 1991) found that odorous compounds below the olfactory threshold (i.e., those that are consciously undetectable) also can produce distinct electroencephalogram responses as well as impairment of mood and performance.

Recent studies have used noninvasive neuroimaging techniques to visualize and localize activity in discrete regions of the brain in response to odor stimulation (Wexler et al., 1995; Zald and Pardo, 1997; Yousem et al., 1997). These studies suggest that there are specific physiological neural markers for olfactory hedonics. Zald and Pardo (1997) reported alterations of activity in the amygdala (a brain center that is involved in emotional processing) during aversive olfactory stimulation. The amygdala is a conglomerate of related nuclei, each nucleus having specific anatomical connections and functions. The amygdala receives input from the olfactory nerve with only two intervening synapses. Zald and Pardo (1997) measured regional cortical blood flow (**rCBF**) using positron emission tomography in 12 healthy women who were exposed to highly aversive (sulfides), moderately aversive (garlic breath, natural gas, and motor oil), and pleasant smells (fruits, flowers, and spices). Highly aversive stimuli such as sulfides produced peak rCBF maxima in the amygdala bilaterally and in the left posterior orbitofrontal cortex. Activity to unpleasant stimuli was localized laterally in the amygdala. Pleasant odorants increased activity in the right anterior/medial amygdala relative to neutral odorants. Zald and Pardo (1997) concluded that amygdalar activity depends on the hedonic properties of odorants, and that unpleasant odor increases rCBF in the left amygdala. These findings are interesting in light of anatomical and electrophysiological studies that have shown olfactory projections and electrophysiological activity in the anterior/medial amygdala but less in the basolateral nuclei (Hughes and Andy, 1979; Price, 1991). The basolateral nuclei have been shown to mediate hedonic coding and aversive emotional conditioning (Aggleton, 1992). Wexler (1995) has also shown lateral amygdalar activity to unpleasant odors using functional magnetic resonance imaging (**fMRI**). Thus, distinct neurochemical changes occur as a result of exposure to unpleasant odors, but their health effects are unknown.

Bell (1994) and Bell et al. (1993a,b, 1995, 1996) suggested that olfactory pathway kindling and long-term potentiation (**LTP**) may account for physical symptoms from chemical exposures. Kindling is a phenomenon that occurs when repetitions of subthreshold stimuli summate, triggering seizure activity in brain cells that had previously functioned normally. Long-term potentiation refers to the persisting enhancement of synaptic responses resulting from high-frequency stimulation of excitatory pathways. She hypothesized that kindling and LTP registers information about past high dose and(or) cumulative low dose chemical exposures, increasing the likelihood of limbic responsivity to subsequent low dose exposures. Limbic dysregulation could then produce a range of behavioral, autonomic, and endocrine dysfunctions that are under limbic control or influence. The propensity for kindling may be increased by chronic low level exposure to environmental toxicants such as pesticides that can alter the functional properties of the CNS (Gilbert, 1992). However, there are no definitive data to support this hypothesis regarding odors from swine operations.

Question 6: Can Odors Affect Memory?

Odors can have an effect on memory (Herz and Engen, 1996). The presentation of an odor often prompts retrieval of early memories. When odors are experienced in a range of situations, the memory of the situation is retrieved more easily if the odor is presented again because it reinstates the context (Cann and Ross, 1989; Herz and Engen, 1996). In addition, memories that are linked to odor cues have been shown to be more emotionally laden, especially in women. This is probably due to the anatomical overlap of the olfactory and limbic (emotional) systems in the brain.

There are no data to determine whether persons with early childhood memories of odors from agricultural operations seem to be less bothered by the odors as adults. Associative-odor-learning is known to occur prenatally in utero, perinatally, and throughout the lifespan (van Toller and Kendal-Reed, 1995).

Question 7: Can Odors Produce Stress or Alter Mood?

The perception of odor is dominated by the pleasantness-unpleasantness dimension (Schiffman, 1974). Pleasant aromas such as cookies baking in the oven beckon us, whereas unpleasant odors such as those from a garbage dump repel us. This strong hedonic aspect of odor can affect mood due to the anatomical overlap of the olfactory and limbic (emotional) systems in the brain.

Schiffman et al. (1995a) studied the effect of environmental odors emanating from large-scale hog operations on the mood of nearby residents. Measurements of mood were determined using the Profile of Mood States (**POMS**). The scores for six POMS

factors and the total mood disturbance score (**TMD**) for 44 persons living near swine operations were compared to those of 44 control subjects who were matched according to gender, race, age, and years of education. The results indicated a significant difference in mood between persons exposed to swine odors and control subjects for all six POMS factors and the TMD. Persons living near the intensive swine operations who experienced the odors had significantly more tension, more depression, more anger, less vigor, more fatigue, and more confusion than control subjects. Persons exposed to the odors also had more total mood disturbance than controls as determined by their ratings on the POMS. Both innate physiological responses and learned responses may contribute to the impairment of mood.

Because unpleasant odors can produce impaired mood and stress, they may influence health via biological mechanisms that include immune changes (Shavit et al., 1984) or hippocampal damage (Sapolsky et al., 1990). Shavit et al. (1984) found that stress produced opioid peptides that suppressed natural killer activity. Hippocampal damage occurs with prolonged glucocorticoid exposure in stress (Sapolsky et al., 1990). King (1981) found that exposure to allergens can induce cognitive and emotional symptoms as well as somatic symptoms in susceptible individuals.

Persons who are depressed may be more likely to make complaints about unpleasant odors. Doty et al. (1988) reported that persons who claim that odors bother them had higher scores on the Beck Depression scale than control subjects.

Odors that are hedonically positive, conversely, have been reported to improve emotional and physical health. Pleasant odors have been used therapeutically to improve mood, reduce stress and anxiety, increase alertness and performance, and have a beneficial effect on sleep patterns (Badia et al., 1990; Schiffman and Siebert, 1991; Badia, 1995; Dember et al., 1995; Ehrlichman, 1995; Redd and Manne, 1995; Schiffman et al., 1995b,c). Pleasant food odors including bacon and ham have even been associated with improved immune status (Schiffman and Warwick, 1993).

Question 8: Can Health Symptoms Associated with Odors Be Learned?

Conditioning or learned associations can play a role in symptoms induced by odors (Bolla-Wilson et al., 1988; Simon et al., 1990). For example, Shusterman et al. (1988) reported two cases in which recurrent panic and hyperventilation symptoms occurred after acute overexposure to chemicals with irritant and odorant properties. The odor of the offending chemical was tolerated before the acute overexposure. They suggest that the panic and hyperventilation symptoms after the overexposure were produced by Pavlovian conditioning. Russell et al. (1984) showed that histamine can be released as a learned response to presentation of an odor. Meggs (1993) suggested that inflammation in the nose and respiratory tract can be triggered by the nervous system, which implies that learned responses transmitted to the nose from the brain could produce symptoms.

Question 9: Do Environmental Concerns or Attitudes About Safety Affect Health Symptoms?

The American public is constantly exposed to information in the media about toxic compounds in the environment. This has led to outbreaks of putative "environmental illness" that cannot be explained by the concentration of chemicals to which the workers are exposed (e.g., Sparks et al., 1990). Sparks et al. (1990) evaluated a case series of 53 composite-materials workers in a large aircraft manufacturing facility who filed workers' compensation claims for illness labeled by the media as the "aerospace syndrome." The authors concluded that psychosocial factors played a major role in the high prevalence of illness in this group.

Dalton (1996, 1997) has also reported that beliefs about the safety of an odor can have an effect on its perception. In Dalton's studies, cognitive factors were found to modulate overall sensory ratings resulting from odor exposure in a small but statistically significant manner. She infused two different odors at different times into a chamber for 20 minutes at a constant steady state concentration. One-third of the subjects, the "positive" group, was told that the odor was a natural extract used by aromatherapists. Another third of the subjects, the "negative" group, was told that the odorant was an industrial chemical which purportedly caused health effects after long exposure. The remaining third, the "neutral" group, was told that the stimulus was a common, approved stimulus for olfactory experiments. The "positive" group showed normal adaptation over the test period, that is, the perceived intensity decreased over time. The "negative" group, however, rated the strength of the odor as increasingly greater after an exposure of 10 min, which was illusory because it actually remained constant over time. The "neutral group" separated between the "positive" and "negative" groups. The negative bias group found the odors to be more irritating and had the greatest number and intensity of health symptoms, including nose, throat, and eye irritation as well as light-headedness.

In a separate experiment (Dalton, 1997), subjects received implied information (not directly stated) about odors by viewing pictures of people with positive, negative, and neutral expressions depicted in either a positive or negative odorous environment. Implicit bias, like direct instructions about potential hazards of an odor, were effective in inducing subjects to rate odor and irritation as more intense.

Negative psychological states and health symptoms can also occur if someone thinks that there is an odor

and one is not present. Knasko et al. (1990) studied the behavior, physical well-being, and emotional state of persons in a room that supposedly contained an odor but really did not. People who were given the suggestion that the room contained a malodor reported a more negative mood and more symptoms of discomfort than persons given the suggestion that the feigned odor was pleasant. This study, like those of Dalton, show that people's cognitive expectations about odor and irritation can influence sensory perception.

Question 10: How Does Chronic Exposure to Odors Affect Perception?

In order to better comprehend the nature of odor complaints it is helpful to understand two concepts that occur in all sensory systems: adaptation and sensitization. Adaptation is the reduction in responsiveness (i.e., a rapid decrease in intensity) during or following repetitive exposure. Sensitization, conversely, is the increased responsiveness during or following exposure. Sensitization is also called priming (Wachs et al., 1989). Adaptation to odors can occur on either a short-term or a long-term basis. During short-term adaptation there is a transient reduction in response to odors during or immediately after exposure. This is generally due to the fact that the activation of receptors by VOC induces a short refractory period during which further stimulation cannot occur. During long-term adaptation, there is a more persistent reduction in response that can be measured hours or even days following exposure. Long-term adaptation to animal odors occurs in persons who work daily in highly odorous environments (Schiffman, unpublished data). This chronic exposure to an odor over a long time can modify a person's perceptual world. It accounts for the finding that persons who work with livestock cannot fully understand the complaints from neighbors who only receive odors intermittently.

Wysocki et al. (1997) found that the perception of odor and irritation for acetone varied with exposure history. That is, there was a difference in the perceptual worlds of acetone-exposed workers and matched unexposed subjects. The acetone-exposed workers tested had an average age of 38.3 yr with an average exposure of 500 ppm acetone over a 10-yr period. Two different threshold assessments were performed: 1) odor detection thresholds and 2) lateralization thresholds. A detection threshold is the lowest concentration that can be reliably detected and is a measure of odor sensitivity. A lateralization threshold is the lowest concentration that can be localized to the stimulated nostril when a compound plus diluent is sprayed into one nostril and the diluent alone in the other nostril. Some researchers consider lateralization thresholds to be a measure of nasal trigeminal activation (i.e., nasal irritation). (Nasal irritation is only one kind of irritation; others include eye or throat irritation.)

Table 3. Thresholds (median) for acetone and butanol in acetone-exposed workers and unexposed subjects[a]

Threshold type	Acetone	Butanol
Odor detection threshold, ppm		
Workers	855	3.17
Unexposed	41	.16
Laterization threshold, ppm		
Workers	36,669	2,538
Unexposed	15,758	2,300

[a]The threshold limit value (generally accepted as safe) for acetone is 750 ppm. Data are from Wysocki et al. (1997).

The results shown in Table 3 indicate that workers exposed to acetone require higher concentrations to detect the odor and irritating sensory properties of acetone. Two possible reasons for this persistent reduction in odor and irritation of acetone in acetone-exposed workers are the following. First, inhaled VOC (in this case, acetone) can enter the blood stream from the lungs and dissolve in fat stores. After exposure, VOC are slowly released from body stores back into the blood and lungs and can cause constant adaptation at olfactory receptors as they are exhaled. Odorous compounds have been measured in the blood and brain after a 3-h exposure (Benignus et al., 1984), and olfactory receptors have been shown to respond to blood-borne odorants (Maruniak et al., 1983). Another possibility is that a cognitive factor also contributes to a person's perceptual world and that acetone-exposed workers learn to tune out the smell of acetone at a cognitive level. There does not seem to be a striking general loss of olfactory perception at threshold levels; acetone-exposed workers and unexposed persons had similar thresholds to butanol.

Dalton et al. (1997) tested the perception of acetone-exposed workers and unexposed control subjects to suprathreshold concentrations of acetone and phenyl ethyl alcohol (**PEA**) in an environmental chamber. They asked them to judge both the odor and irritation intensities of suprathreshold concentrations on the following scale: strongest imaginable, very strong, strong, moderate, weak, barely detectable, and no sensation. They found that unexposed subjects rated the odor of the acetone concentration to be very strong or strong whereas the acetone-exposed subjects rated it moderate in intensity. There were no differences in ratings of suprathreshold odor intensity for PEA between the acetone workers and unexposed controls. They also found that unexposed subjects rated the irritation of the acetone concentration to be strong but the acetone-exposed subjects rated it as weak to barely detectable. There were no differences in ratings of suprathreshold irritation intensity for PEA between the acetone workers and unexposed

controls. More unexposed subjects than exposed acetone workers had health symptoms from the suprathreshold concentrations of both acetone and PEA. The symptoms included nasal irritation, eye irritation, throat irritation, light-headedness, nausea, and drowsiness.

More work needs to be done to determine whether any of the effects (either adaptation or sensitization) from environmental odor exposures are permanent. Dalton and Wysocki (1996) performed a 35-d study in which thresholds for an odorant were determined seven times. Baseline threshold values to the odor were taken on d 1 and 8. Then the subjects were exposed continuously to the odor at night (from a fragrance dispenser) for 1 to 2 wk with threshold measures for the odor taken on d 15 and 22. Twenty-four hours after the fragrance dispenser was removed, thresholds were again assessed. Finally, thresholds were determined during a 1- to 2-week recovery period on d 29 and 35. The main findings were that thresholds were higher to the adapting odor during the period that subjects were exposed at night (i.e., subjects were less sensitive); thresholds to the adapting odor returned to baseline levels during recovery. However, thresholds determined at the end of the recovery period for a control odor (which was different from the adapting odor) were even lower (far more sensitive) than at baseline. These lower thresholds suggest that sensitization occurred as a result of exposure or that subjects learned to discriminate odors better from the background.

Question 11: How Does Intermittent Exposure to Odors Affect People?

There may be a subset of people who feel "ill" from intermittent exposure to the odor of xenobiotic chemicals (i.e., suffer from cacosmia) (Bell et al., 1996). Cacosmia occurs in "a population subset, with or without occupational xenobiotic exposures or disability, that has distress and symptom amplification and neuropsychiatric and somatic symptoms, none of which are explained fully by psychological measures." Bell and colleagues (1996) concluded that the data were consistent with a time-dependent sensitization model (i.e., progressive response amplification to repeated, intermittent stimuli over time) for illness from low-level chemical exposures.

Intermittent exposure to the odor of androstenone (a boar taint odor) in humans (Wysocki et al., 1989) and animals (Wang et al., 1993) has been shown to induce a highly significant increase in odor sensitivity to androstenone in previously insensitive individuals. Induction of elevated sensitivity to isovaleric acid (a component of swine odor) after intermittent exposure to isovaleric acid has also been found in animals (Wang et al., 1993). Wysocki et al. (1989) and Wang et al. (1993) proposed that the increase in sensitivity to androstenone and isovaleric acid from intermittent exposure is due to clonal expansion of olfactory receptors with high affinity for these compounds in the olfactory epithelium.

Question 12: Is It Possible to Treat Persons Who Claim to Have Health Effects from Livestock Odors?

If it is impossible for neighbors to avoid odors from swine operations that they fear impair their health, use of behavioral techniques such as relaxation therapy may be helpful in reducing symptoms. Behavioral concepts are currently integrated into the diagnosis and treatment of a broad range of medical conditions (Carlson and Hoyle, 1993), including diabetes (Jenkins, 1990), coronary heart disease exacerbated by anger (Cottraux, 1993; Emmelkamp and van Oppen, 1993; Verrier and Mittleman, 1996), cancer (Emmelkamp and van Oppen, 1993), headaches (Cottraux, 1993; Emmelkamp and van Oppen, 1993), pain (Cottraux, 1993; Emmelkamp and van Oppen, 1993), stuttering (Cottraux, 1993), alcoholism (Cottraux, 1993), bulimia nervosa (Cottraux, 1993; Emmelkamp and van Oppen, 1993), asthma (Emmelkamp and van Oppen, 1993), obesity (Emmelkamp and van Oppen, 1993), gastrointestinal disorders (Whitehead, 1992), as well as AIDS and HIV prevention and treatment (Kelly and Murphy, 1992). Sanderson et al. (1989) showed that anxiety induced by the irritant carbon dioxide can be reduced by giving patients an illusion of control over the procedure. Reduction of symptoms in several persons living near swine operations were achieved by behavioral changes that included exercise, biofeedback, systematic desensitization, and progressive muscle relaxation training to relieve stress (Schiffman, unpublished data). Cognitive therapeutic intervention leading to behavioral changes was helpful as well.

Question 13: Do Present Air Quality Guidelines Protect Persons Exposed to Livestock Odors?

Risk levels or standards called threshold limit values (**TLV**) have been established for some VOC in ambient air, taking into account concentrations thought to cause health effects based on the length of exposure. Threshold limit values are generally based on animal bioassays (Alarie, 1966, 1973, 1981), although recently mathematical models have been used to predict the irritating properties of chemicals (Abraham et al., 1990, 1996; Alarie et al., 1995). Threshold limit values have not been established for most of the compounds in livestock odors. However, concentrations of VOC given in air quality guidelines that have been established may be too high for the segment of the population that is susceptible to respiratory illness (Ziem and Davidoff, 1992; Wardlaw, 1993). They base this conclusion on mathemati-

cal treatment of animal studies. In addition, low concentrations of mixtures of numerous VOC may induce health consequences whereas a single low level VOC does not. Enforcement of TLV is presently cumbersome but new technologies (e.g., Carey, 1996) will make it easier in years to come.

Development of emissions standards for VOC from livestock operations presents many scientific challenges, mainly because volatile compounds emitted from livestock facilities also arise from other sources. For example, aldehydes such as formaldehyde and acetaldehyde are not only produced by livestock facilities, but also by incomplete combustion of fossil fuels (Marnett, 1988). Thus, the source of formaldehyde and acetaldehyde downwind from a livestock facility could also be due to combustion of gasoline and diesel fuels produced by on-road motor vehicles in the neighborhood. Aldehydes have been an active target of environmental research because acute exposures are known to cause eye and throat irritation as well as more serious neurotoxic and reproductive effects (Leikauf, 1992).

Other VOC that have been targeted as research priorities for mobile air toxics by the Health Effects Institute (Goldstein, 1993) and are also found in odor plumes from swine facilities include 1,3-butadiene, methanol, benzene, and polycyclic organic matter. The presence of these VOC downwind may not derive from a livestock facility, however, but rather from other sources in the ambient environment. The largest source of 1,3-butadiene is not livestock facilities but rather incomplete combustion from on-road vehicles as well as internal combustion engine-driven machinery. Eighty-five percent of all benzene emissions originate from motor vehicles. Use of methanol as an alternative fuel can be the source of methanol in ambient air. Polycyclic organic matter compounds occur in combustion products such as tobacco, wood, and fossil fuels and are also encountered in the normal diet. To further compound the problem, it is difficult to determine how outdoor air quality affects air quality indoors, where most people spend 80 to 90% of their time (Shah and Singh, 1988). There are no federal exposure guidelines for residential exposures, although many risk-assessors use .1 or .01 of the TLV.

Question 14: What Studies Should Be Performed to Determine Health Effects of Odors?

A core database of demographic and psychological/medical variables should be obtained, including immunologic, neurologic, endocrinologic, psychologic, and social markers for persons exposed to livestock odors. Exposure could be in a natural setting or in an environmental chamber that would allow for controlled exposures to challenge subjects in a well-defined environment. Dose-response relationships should be obtained. Prospective longitudinal studies of exposure to odors in the usual environment in which individuals are evaluated over time should be performed. Animal models should also be developed that mimic the human exposures. Tissues from animals could be obtained by biopsy and necropsy for evaluation of pathological changes. Epidemiological studies are crucial as well (Eisen et al., 1991). These studies are consistent with the suggestion of Morse (1995) that environmental regulations for livestock producers be based on sound scientific data.

A variety of tests should be performed on persons downwind from swine operations to evaluate more fully the health effects of VOC from swine operations. Ventilatory measurements could include vital capacity (the largest volume of air measured on complete expiration after the deepest inspiration without rapid or forced effort), forced vital capacity (vital capacity with the most forceful, rapid expiration possible), one-second forced expiratory volume (volume of air forcibly exhaled in the first second), one-second forced expiratory volume expressed as a percentage of forced vital capacity, and peak expiratory flow rate (the rate of maximal expiratory flow). Small portable devices are available to measure peak expiratory flow rate and would be appropriate for an epidemiological study of exposure to VOC from swine operations.

Implications

The main complaints of health symptoms from odors in general are eye, nose, and throat irritation as well as headache and drowsiness. It is not known at the present time whether the low concentrations of volatile organic compounds in odorous plumes are high enough to cause these or other health symptoms in neighbors of livestock operations. Further research is required to establish recommendations for air quality guidelines based on scientific data of potential health effects.

Literature Cited

Abraham, M. H., J. Andonian-Haftvan, J. E. Cometto-Muniz, and W. S. Cain. 1996. An analysis of nasal irritation thresholds using a new solvation equation. Fundam. Appl. Toxicol. 31:71–76.

Abraham, M. H., G. S. Whiting, Y. Alarie, J. J. Morris, P. J. Taylor, R. M. Doherty, R. W. Taft, and G. D. Nielsen. 1990. Hydrogen bonding 12. A new QSAR for upper respiratory tract irritation by airborne chemicals in mice. Quant. Struct-Act. Relat. 9:6–10.

Aggleton, J. P. (Ed.). 1992. The Amygdala: Neurobiological Aspects of Emotion, Memory and Mental Dysfunction. Wiley-Liss, New York.

Alarie, Y. 1966. Irritating properties of airborne materials to the upper respiratory tract. Arch. Environ. Health 13:433–449.

Alarie, Y. 1973. Sensory irritation of the upper airways by airborne chemicals. Toxicol. Appl. Pharmacol. 24:279–297.

Alarie, Y. 1981. Dose-response analysis in animal studies: prediction of human responses. Environ. Health Perspect. 42:9–13.

Alarie, Y., G. D. Nielsen, J. Andonian-Haftvan, and M. H. Abraham. 1995. Physicochemical properties of nonreactive volatile organic chemicals to estimate RD50: alternatives to animal studies. Toxicol. Appl. Pharmacol. 134:92–99.

Ayer, H. E., and D. W. Yeager. 1982. Irritants in cigarette smoke plumes. Am. J. Public Health 72:1283–1285.

Badia, P., M. R. Boecker, and K. P. Wright, Jr. 1995. Some effects of fragrances on sleep. In: A. N. Gilbert (Ed.) Compendium of Olfactory Research. pp 31–37. Kendall/Hunt, Dubuque, IA.

Badia, P., N. Wesensten, W. Lammers, J. Culpepper, and J. Harsh. 1990. Responsiveness to olfactory stimuli presented in sleep. Physiol. Behav. 48:87–90.

Baltrusch, H. J., W. Stangel, and I. Titze. 1991. Stress, cancer and immunity. New developments in biopsychosocial and psychoneuroimmunologic research. Acta Neurol. (Naples) 13: 315–327.

Baringer, J. R. 1976. The biology of herpes simplex virus infection in humans. Surv. Ophthalmol. 21:171–174.

Barnett, E. M., G. Jacobsen, G. Evans, M. Cassell, and S. Perlman. 1994. Herpes simplex encephalitis in the temporal cortex and limbic system after trigeminal nerve inoculation. J. Infect. Dis. 169:782–786.

Bascom, R., J. Kesavanathan, T. K. Fitzgerald, K. H. Cheng, and D. L. Swift. 1995. Sidestream tobacco smoke exposure acutely alters human nasal mucociliary clearance. Environ. Health Perspect. 103:1026–1030.

Bates, D. V. 1995. Observations on asthma. Environ. Health Perspect. 103(Suppl. 6):243–247.

Becker, Y. 1995. HSV-1 brain infection by the olfactory nerve route and virus latency and reactivation may cause learning and behavioral deficiencies and violence in children and adults: A point of view. Virus Genes 10:217–226.

Bell, I. R. 1994. White paper: Neuropsychiatric aspects of sensitivity to low-level chemicals: A neural sensitization model. Toxicol. Ind. Health 10:277–312.

Bell, I. R., E. E. Hardin, C. M. Baldwin, and G. E. Schwartz. 1995. Increased limbic system symptomatology and sensitizability of young adults with chemical and noise sensitivities. Environ. Res. 70:84–97.

Bell, I. R., C. S. Miller, G. E. Schwartz, J. M. Peterson, and D. Amend. 1996. Neuropsychiatric and somatic characteristics of young adults with and without self-reported chemical odor intolerance and chemical sensitivity. Arch. Environ. Health 51: 9–21.

Bell, I. R., G. E. Schwartz, J. M. Peterson, and D. Amend. 1993a. Self-reported illness from chemical odors in young adults without clinical syndromes or occupational exposures. Arch. Environ. Health. 48:6–13.

Bell, I. R., G. E. Schwartz, J. M. Peterson, D. Amend, and W. A. Stini. 1993b. Possible time-dependent sensitization to xenobiotics: Self-reported illness from chemical odors, foods, and opiate drugs in an older adult population. Arch. Environ. Health 48: 315–327.

Benignus, V. A., K. E. Muller, J. A. Graham, and C. N. Barton. 1984. Toluene levels in blood and brain of rats as a function of toluene level in inspired air. Environ. Res. 33:39–46.

Bloomberg, G. R., and R. C. Strunk. 1992. Crisis in asthma care. Pediatr. Clin. North Am. 39:1225–1241.

Bolla-Wilson, K., R. J. Wilson, and M. L. Bleecker. 1988. Conditioning of physical symptoms after neurotoxic exposure. J. Occup. Med. 30:684–686.

Bundy, D. S. 1992. Odor issues with wastes. In: National Livestock, Poultry and Aquaculture Waste Management. ASAE Publ. 03-92. pp 288–292. American Society of Agricultural Engineers, St. Joseph, Michigan.

Burge, P. S. 1992. New developments in occupational asthma. Br. Med. Bull. 48:221–230.

Cann, A., and D. Ross. 1989. Olfactory stimuli as context cues in human memory. Am. J. Psychol. 102:91–102.

Carey, J. 1996. Building a "canary on a chip." Business Week December:130.

Carlson, C. R., and R. H. Hoyle. 1993. Efficacy of abbreviated progressive muscle relaxation training: A quantitative review of behavioral medicine research. J. Consult. Clin. Psychol. 61: 1059–1067.

Cometto-Muniz, J. E., and W. S. Cain. 1991. Nasal pungency, odor, and eye irritation thresholds for homologous acetates. Pharmacol. Biochem. Behav. 39:983–989.

Cometto-Muniz, J. E., and W. S. Cain. 1992. Sensory irritation. Relation to indoor air pollution. Ann. N.Y. Acad. Sci. 641: 137–151.

Cometto-Muniz, J. E., and W. S. Cain. 1993. Efficacy of volatile organic compounds in evoking nasal pungency and odor. Arch. Environ. Health 48:309–314.

Cometto-Muniz, J. E., and W. S. Cain. 1994. Sensory reactions of nasal pungency and odor to volatile organic compounds: The alkylbenzenes. Am. Ind. Hyg. Assoc. J. 55:811–817.

Cottraux, J. 1993. Behavioral psychotherapy applications in the medically ill. Psychother. Psychosom. 60:116–128.

Crockett, A. J., J. M. Cranston, and J. H. Alpers. 1995. The changing prevalence of asthma-like respiratory symptoms in South Australian rural schoolchildren. J Paediatr. Child Health 31: 213–217.

Dalton, P. 1996. Odor perception and beliefs about risk. Chem. Senses 21:447–458.

Dalton, P. 1997. Cognitive influence on odor perception. Aroma-Chol. Rev. 6:2–9.

Dalton, P., and C. J. Wysocki. 1996. The nature and duration of adaptation following long-term odor exposure. Percept. Psychophys. 58:781–792.

Dalton, P., C. J. Wysocki, M. J. Brody, and H. J. Lawley. 1997. Perceived odor, irritation, and health symptoms following short-term exposure to acetone. Am. J. Ind. Med. 31:558–569.

Dember, W. N., J. S. Warm, and R. Parasuraman. 1995. Olfactory stimulation and sustained attention. In: A. N. Gilbert (Ed.) Compendium of Olfactory Research. pp 39–46. Kendall/Hunt Publ. Co., Dubuque, IA.

Dick, R. B. 1988. Short duration exposures to organic solvents: the relationship between neurobehavioral test results and other indicators. Neurotoxicol. Teratol. 10:39–50.

Donham, K. J., J. A. Merchant, D. Lassise, W. J. Popendorf, and L. F. Burmeister. 1990. Preventing respiratory disease in swine confinement workers: Intervention through applied epidemiology, education, and consultation. Am. J. Ind. Med. 18:241–261.

Doty, R. L., D. A. Deems, R. E. Frye, R. Pelberg, and A. Shapiro. 1988. Olfactory sensitivity, nasal resistance, and autonomic function in patients with multiple chemical sensitivities. Arch. Otolaryngol. Head Neck Surg. 114:1422–1427.

Durand-Lagarde, M., and G. Kobal. 1991. P300: A new technique of recording a cognitive component in olfactory evoked potential. Chem. Senses 16:379.

Eccles, R. 1995. Rhinitis as a mechanism of respiratory defense. Eur. Arch. Oto-Rhino-Laryngol. Suppl. 1:S2–S7.

Ehrlichman, H. 1995. Influence of odors on mood-related behavior. In: A. N. Gilbert (Ed.) Compendium of Olfactory Research. pp 91–96. Kendall/Hunt, Dubuque, IA.

Eisen, E. A., D. H. Wegman, D. Kriebel, S. R. Woskie, and X. Hu. 1991. An epidemiologic approach to the study of acute reversible health effects in the workplace. Epidemiology 2:263–270.

Emmelkamp, P. M., and P. van Oppen. 1993. Cognitive interventions in behavioral medicine. Psychother. Psychosom. 59: 116–130.

Engel, G. L. 1977. The need for a new medical model: A challenge for biomedicine. Science (Wash., DC) 196:129–136.

EPA. The Environmental Exposures and Health Questionnaire. Obtained from Dr. Howard Kerhl at the Environmental Protection Agency, U.S. EPA Chapel Hill, NC.

Feron, V. J., and A. Kruysse. 1978. Til HP. Immel HR. Repeated exposure to acrolein vapour: subacute studies in hamsters, rats and rabbits. Toxicology 9:47–57.

Fishwick, D., A. M. Fletcher, C. A. Pickering, R. M. Niven, and E. B. Faragher. 1994. Ocular and nasal irritation in operatives in Lancashire cotton and synthetic fibre mills. Occup. Environ. Med. 51:744–748.

Friedman, R., D. Sobel, P. Myers, M. Caudill, and H. Benson. 1995. Behavioral medicine, clinical health psychology, and cost offset. Health Psychol. 14:509–518.

Gagnaire, F., S. Azim, P. Bonnet, P. Simon, J. P. Guenier, and J. de Ceaurriz. 1989. Nasal irritation and pulmonary toxicity of aliphatic amines in mice. J. Appl. Toxicol. 9:301–304.

Gilbert, M. E. 1992. Neurotoxicants and limbic kindling. In: R. L. Isaacson and K. F. Jensen (Ed.) The Vulnerable Brain and Environmental Risks. Vol. 1. Malnutrition and Hazard Assessment. Plenum Press, New York.

Goldstein, B. D. (Workshop Chair). 1993. Research Priorities for Mobile Air Toxics. Health Effects Institute, Cambridge, MA.

Gomez, S. R., R. A. Parker, J. A. Dosman, and H. H. McDuffie. 1992. Respiratory health effects of alkali dust in residents near desiccated Old Wives Lake. Arch. Environ. Health 47:364–369.

Green, D. J., R. Bascom, E. M. Healey, J. R. Hebel, L. R. Sauder, and T. J. Kulle. 1989. Acute pulmonary response in healthy, nonsmoking adults to inhalation of formaldehyde and carbon. J. Toxicol. Environ. Health 28:261–275.

Herz, R. S., and T. Engen. 1996. Odor memory: Review and analysis. Psycho. Bull. Rev. 3:300–313.

Horesh, A. J. 1966. The role of odors and vapors in allergic disease. J. Asthma Res. 4:125–136.

Hudnell, H. K., D. A. Otto, D. E. House, and L. Molhave. 1992. Exposure of humans to a volatile organic mixture. II. Sensory. Arch. Environ. Health. 47:31–38.

Hughes, J. R., and O. J. Andy. 1979. The human amygdala. I. Electrophysiological responses to odorants. Electroencephalogr. Clin. Neurophysiol. 46:428–443.

Jackson, R. T., J. Tigges, and W. Arnold. 1979. Subarachnoid space of the CNS, nasal mucosa, and lymphatic system. Arch. Otolaryngol. 105:180–184.

Jenkins, C. D. 1990. An integrated behavioral medicine approach to improving care of patients with diabetes mellitus. Behav. Med. 21:53–68.

Kaplan, R. M. 1990. Behavior as the central outcome in health care. Am. Psychol. 45:1211–1220.

Kawai, T., T. Yasugi, K. Mizunuma, S. Horiguchi, Y. Hirase, Y. Uchida, and M. Ikeda. 1991. Methanol in urine as a biological indicator of occupational exposure to methanol vapor. Int. Arch. Occup. Environ. Health 63:311–318.

Kelly, J. A., and D. A. Murphy. 1992. Psychological interventions with AIDS and HIV: prevention and treatment. J. Consult. Clin. Psychol. 60:576–585.

King, D. S. 1981. Can allergic exposure provoke psychological symptoms? A double-blind test. Biol. Psychiatry 16:3–19.

Kishi, R., I. Itoh, S. Ishizu, I. Harabuchi, and H. Miyake. 1991. Symptoms among workers with long-term exposure to methyl bromide. An epidemiological study. Sangyo Igaku 33:241–250.

Knasko, S. C., A. N. Gilbert, and J. Sabini. 1990. Emotional state, physical well-being, and performance in the presence of feigned ambient odor. J. Appl. Soc. Psychol. 20:1345–1357.

Kobal, G., and T. Hummel. 1991. Human electro-olfactograms and brain responses to olfactory stimulation. In: D. F. Laing, R. L. Doty, and W. Breipohl (Ed.) The Human Sense of Smell. pp 199–215. Springer, Berlin.

Koren, H. S. 1995. Associations between criteria air pollutants and asthma. Environ. Health Perspect. 103(Suppl. 6):235–242.

Koren, H. S., and R. B. Devlin. 1992. Human upper respiratory tract responses to inhaled pollutants with emphasis on nasal lavage. Ann. NY Acad. Sci. 641:215–224.

Koren, H. S., D. E. Graham, and R. B. Devlin. 1992. Exposure of humans to a volatile organic mixture. III. Inflammatory response. Arch. Environ. Health 47:39–44.

Kruysse, A., V. J. Feron, and H. P. Til. 1975. Repeated exposure to acetaldehyde vapor. Studies in Syrian golden hamsters. Arch. Environ. Health 30:449–452.

Lach, B., and E. Atack. 1988. Disseminated hemorrhagic leukoencephalomyelitis with localized herpes simplex brain stem infection. Acta Neuropathol. (Berl.). 75:354–361.

Leikauf, G. D. 1992. Formaldehyde and other aldehydes. In: M. Lippmann (Ed.) Environmental Toxicants: Human Exposures and Their Health Effects. pp 299–330. Van Nostrand Reinhold, New York.

Leikauf, G. D., S. Kline, R. E. Albert, C. S. Baxter, D. I. Bernstein, and C. R. Buncher. 1995. Evaluation of a possible association of urban air toxics and asthma. Environ. Health Perspect. 103(Suppl. 6):253–271.

Levin, A. S., and V. S. Byers. 1987. Environmental illness: A disorder of immune regulation. Occup. Med. 2:669–681.

Lindberg, E., and G. Hedenstierna. 1983. Chrome plating: Symptoms, findings in the upper airways, and effects on lung function. Arch. Environ. Health. 38:367–374.

Lorig, T. S. 1994. EEG and ERP studies of low-level odor exposure in normal subjects. Toxicol. Ind. Health 10:579–586.

Lorig, T. S., K. B. Herman, G. E.Schwartz, and W. S. Cain. 1990. EEG activity during administration of low-concentration odors. Bull. Psychonom. Soc. 28:405–408.

Lorig, T. S., E. Huffman, A. DeMartino, and J. DeMarco. 1991. The effects of low concentration odors on EEG activity and behavior. J. Psychophysiol. 5:69–77.

Lorig, T. S., and M. Roberts. 1990. Odor and cognitive alteration of the contingent negative variation. Chem. Senses 15:537–545.

Lundblad, L., and J. M. Lundberg. 1984. Capsaicin sensitive sensory neurons mediate the response to nasal irritation induced by the vapour phase of cigarette smoke. Toxicology 33:1–7.

Marnett, L. J. 1988. Health effects of aldehydes and alcohols in mobile source emissions. In: A. Y. Watson, R. R. Bates, and D. Kennedy (Ed.) Air Pollution, The Automobile, and Public Health. National Academy Press, Washington, DC.

Marshall, J. S., and J. Bienenstock. 1994. The role of mast cells in inflammatory reactions of the airways, skin and intestine. Curr. Opin. Immunol. 6:853–859.

Maruniak, J. A., W. L. Silver, and D. G. Moulton. 1983. Olfactory receptors respond to blood-borne odorants. Brain Res. 265: 312–316.

Meggs, W. J. 1993. Neurogenic inflammation and sensitivity to environmental chemicals. Environ. Health Perspect. 101: 234–238.

Morse, D. 1995. Environmental considerations of livestock producers. J. Anim. Sci. 73:2733–2740.

Nolte, D., and D. Berger. 1983. On vagal bronchoconstriction in asthmatic patients by nasal irritation. Eur. J. Respir. Dis. Suppl. 128:110–115.

Powell, C. V. 1993. Asthma in childhood. Br. J. Hosp. Med. 49: 127–130.

Price, J. L. 1991. The olfactory system. In: G. Paxinos (Ed.) The Human Nervous System. pp 979–998. Academic Press, San Diego, CA.

Redd, W. H., and S. Manne. 1995. Using aroma to reduce distress during magnetic resonance imaging. In: A. N. Gilbert (Ed.) Compendium of Olfactory Research. pp 47–52. Kendall/Hunt, Dubuque, IA.

Reynolds, S. J., K. J. Donham, P. Whitten, J. A. Merchant, L. F. Burmeister, and W. J. Popendorf. 1996. Longitudinal evaluation of dose-response relationships for environmental exposures and pulmonary function in swine production workers. Am. J. Ind. Med. 29:33–40.

Riechelmann, H., K. Kienast, J. Schellenberg, and W. J. Mann. 1994. An in vitro model to study effects of airborne pollutants on human ciliary activity. Rhinology 32:105–108.

Roberts, E. 1986. Alzheimer's disease may begin in the nose and may be caused by aluminosilicates. Neurobiol. Aging 7: 561–567.

Rudell, B., T. Sandstrom, U. Hammarstrom, M. L. Ledin, P. Horstedt, and N. Stjernberg. 1994. Evaluation of an exposure setup for studying effects of diesel exhaust in humans. Int. Arch. Occup. Environ. Health. 66:77–83.

Russell, M., K. A. Dark, R. W. Cummins, G. Ellman, E. Callaway, and H. V. Peeke. 1984. Learned histamine release. Science (Wash., DC) 225:733–734.

Rusznak, C., J. L. Devalia, and R. J. Davies. 1994. The impact of pollution on allergic disease. Allergy 49(Suppl. 18):21–27.

Samet, J. M. 1995. Asthma and the environment: do environmental factors affect the incidence and prognosis of asthma? Toxicol. Lett. 82–83:33–38.

Sanderson, W. C., R. M. Rapee, and D. H. Barlow. 1989. The influence of an illusion of control on panic attacks induced via inhalation of 5.5% carbon dioxide-enriched air. Arch. Gen. Psychiatry 46:157–162.

Sapolsky, R. M., H. Uno, C. S. Rebert, and C. E. Finch. 1990. Hippocampal damage associated with prolonged glucocorticoid exposure in primates. J. Neurosci. 10:2897–2902.

Saunders, R. L, Jr., G. M. Halpern, and M. E. Gershwin. 1995. Odor-associated idiopathic anaphylaxis. A case report. Allergol. Immunopathol. (Madr.) 23:35–37.

Schiffman, S. S. 1974. Physicochemical correlates of olfactory quality. Science (Wash., DC) 185:112–117.

Schiffman, S. S., and H. T. Nagle. 1992. Effect of environmental pollutants on taste and smell. Otolaryngol. Head Neck Surg. 106:693–700.

Schiffman, S. S., E. A. Sattely-Miller, M. S. Suggs, and B. G. Graham. 1995a. The effect of environmental odors emanating from commercial swine operations on the mood of nearby residents. Brain Res. Bull. 37:369–375.

Schiffman, S. S., E. A. Sattely-Miller, M. S. Suggs, and B. G. Graham. 1995b. The effect of pleasant odors and hormone status on mood of women at midlife. Brain Res. Bull. 36:19–29.

Schiffman, S. S., and J. M. Siebert. 1991. New frontiers in fragrance use. Cosmet. Toiletries 106:39–45.

Schiffman, S. S., M. S. Suggs, and E. A. Sattely-Miller. 1995c. Effect of pleasant odors on mood of males at midlife: Comparison of African-American and European-American men. Brain Res. Bull. 36:31–37.

Schiffman, S. S., and Z. S. Warwick. 1993. Effect of flavor enhancement of foods for the elderly on nutritional status: Food intake, biochemical indices and anthropometric measures. Physiol. Behav. 53:395–402.

Schwartz, G. E. 1982. Testing the biopsychosocial model: The ultimate challenge facing behavioral medicine?. J. Consult. Clin. Psychol. 50:1040–1053.

Sekizawa, S. I., and H. Tsubone. 1994. Nasal receptors responding to noxious chemical irritants. Respir. Physiol. 96:37–48.

Shah, J. J., and H. B. Singh. 1988. Distribution of volatile organic chemicals in outdoor and indoor air. Environ. Sci. Technol. 22: 1381–1388.

Shavit, Y., J. W. Lewis, G. W. Terman, R. P. Gale, and J. C. Liebeskind. 1984. Opioid peptides mediate the suppressive effect of stress on natural killer cell cytotoxicity. Science (Wash., DC) 223:188–190.

Shipley, M. T. 1985. Transport of molecules from nose to brain: Transneuronal anterograde and retrograde labeling in the rat olfactory system by wheat germ agglutinin-horseradish peroxidase applied to the nasal epithelium. Brain Res. Bull. 15: 129–142.

Shusterman, D. 1992. Critical review: The health significance of environmental odor pollution. Arch. Environ. Health 47:76–87.

Shusterman, D., J. Balmes, and J. Cone. 1988. Behavioral sensitization to irritants/odorants after acute overexposures. J. Occup. Med. 30:565–567.

Silver, W. L. 1992. Neural and pharmacological basis for nasal irritation. Ann. NY Acad. Sci. 641:152–163.

Simon, G. E., W. J. Katon, and P. J. Sparks. 1990. Allergic to life: psychological factors in environmental illness. Am. J. Psychiatry 147:901–906.

Singh, I., M. Mehta, J. Singh, and J. Yadav. 1994. Nasal mucus clearance in chronic smokers. Indian J. Chest Dis. Allied Sci. 36:133–136.

Smid, T., D. Heederik, R. Houba, and P. H. Quanjer. 1994. Dust- and endotoxin-related acute lung function changes and work-related symptoms in workers in the animal feed industry. Am. J. Ind. Med. 25:877–888.

Sparks, P. J., G. E. Simon, W. J. Katon, L. C. Altman, G. H. Ayars, and R. L. Johnson. 1990. An outbreak of illness among aerospace workers. West. J. Med. 153:28–33.

Speer, F. 1976. Allergic headache. Compr. Ther. 2:45–50.

Spit, B. J., F. Bretschneider, E. G. Hendriksen, and C. F. Kuper. 1993. Ultrastructure of free nerve endings in respiratory and squamous epithelium on the rat nasal septum. Cell Tissue Res. 274:329–335.

Stueven, H. A., P. Coogan, and V. Valley. 1993. A hazardous material episode: Sulfur trioxide. Vet. Hum. Toxicol. 35:37–38.

Taub, S. J. 1967. The role of odors and vapors in allergic disorders. Eye Ear Nose Throat Mon. 46:779–780.

Thu, K., K. Donham, R. Ziegenhorn, S. Reynolds, P. S. Thorne, P. Subramanian, P. Whitten, and J. Stookesberry. 1997. A control study of the physical and mental health of residents living near a large-scale swine operation. J. Agric. Safety Health 3:13–26.

Utell, M. J., and R. J. Looney. 1995. Environmentally induced asthma. Toxicol. Lett. 82–83:47–53.

van Toller, S., and M. Kendal-Reed. 1995. A possible protocognitive role for odor in human infant development. Brain Cognition 29: 275–293.

Verrier, R. L., and M. A. Mittleman. 1996. Life-threatening cardiovascular consequences of anger in patients with coronary heart disease. Cardiol. Clin. 14:289–307.

Wachs, M., D. Proud, L. M. Lichtenstein, A. Kagey-Sobotka, P. S. Norman, and R. M. Naclerio. 1989. Observations on the pathogenesis of nasal priming. J. Allergy Clin. Immunol. 84:492–501.

Wang, H. W., C. J. Wysocki, and G. H. Gold. 1993. Induction of olfactory receptor sensitivity in mice. Science (Wash., DC) 260: 998–1000.

Wardlaw, A. J. 1993. The role of air pollution in asthma. Clin. Exp. Allergy 23:81–96.

Ware, J. H., J. D. Spengler, L. M. Neas, J. M. Samet, G. R. Wagner, D. Coultas, H. Ozkaynak, and M. Schwab. 1993. Respiratory and irritant health effects of ambient volatile organic compounds. The Kanawha County Health Study. Am. J. Epidemiol. 137:1287–1301.

Warren, D. W., J. C. Walker, A. F. Drake, and R. W. Lutz. 1992. Assessing the effects of odorants on nasal airway size and breathing. Physiol. Behav. 51:425–430.

Warren, D. W., J. C. Walker, A. F. Drake, and R. W. Lutz. 1994. Effects of odorants and irritants on respiratory behavior. Laryngoscope 104:623–626.

Weeke, E. R. 1992. Epidemiology of allergic diseases in children. Rhinol. Suppl. 13:5–12.

Wexler, B. E., R. F. Fulbright, C. Greer, G. M. Shepherd, A. Bowers, C. Lacdie, and J. C. Gore. 1995. An fMRI study of human brain responses to attractant and aversive odors. Chem. Senses 20: 801.

Whitehead, W. E. 1992. Behavioral medicine approaches to gastrointestinal disorders. J. Consult. Clin. Psychol. 60:605–612.

Wolfe, V., R. Cornell, and C. Palmer. 1991. Acoustic correlates of pathologic voice types. J. Speech Hear. Res. 34:509–516.

Wysocki, C. J., P. Dalton, M. J. Brody, and H. J. Lawley. 1997. Acetone odor and irritation thresholds obtained from acetone-exposed factory workers and from control (occupationally unexposed) subjects. Am. Ind. Hyg. Assoc. J. 58:704–712.

Wysocki, C. J., K. M. Dorries, and G. K. Beauchamp. 1989. Ability to perceive androstenone can be acquired by ostensibly anosmic people. Proc. Natl. Acad. Sci. USA 86:7976–7978.

Yousem, D. M., S. C. Williams, R. O. Howard, C. Andrew, A. Simmons, M. Allin, R. J. Geckle, D. Suskind, E. T. Bullmore, M. J. Brammer, and R. L. Doty 1997. Functional MR imaging during odor stimulation: Preliminary data. Radiology 204: 833–838.

Zald, D. H., and J. V. Pardo. 1997. Emotion, olfaction and the human amygdala: Amygdala activation during aversive olfactory stimulation. Proc. Natl. Acad. Sci. USA 94:4119–4124.

Ziem, G. E., and L. L. Davidoff. 1992. Illness from chemical “odors”: is the health significance understood? Arch. Environ. Health 47:88–91.