
We investigated the effects of a combined exposure to restraint stress and low doses of chemicals pyridostigmine bromide (PB), N, N-diethyl-m-toluamide (DEET), and permethrin in adult male rats, a model of Gulf-War syndrome. Animals were exposed daily to one of the following for 28 days: (i) a combination of stress and chemicals (PB, 1.3 mg/kg/day; DEET, 40 mg/kg/day; and permethrin, 0.13 mg/kg/day); (ii) stress and vehicle; (iii) chemicals alone; and (iv) vehicle alone. All animals were evaluated for: (i) the disruption of the blood-brain barrier (BBB) using intravenous horseradish peroxidase (HRP) injections and endothelial barrier antigen (EBA) immunostaining; (ii) neuronal cell death using H&E staining, silver staining, and glial fibrillary acidic protein (GFAP) immunostaining; and (iii) acetylcholinesterase (AChE) activity and m2-muscarinic acetylcholine receptors (m2-AChR). Animals subjected to stress and chemicals exhibited both disruption of the BBB and neuronal cell death in the cingulate cortex, the dentate gyrus, the thalamus, and the hypothalamus. Other regions of the brain, although they demonstrated some neuronal cell death, did not exhibit disruption of the BBB. The neuropathological changes in the above four brain regions were highly conspicuous and revealed by a large number of HRP-positive neurons (21-40% of total neurons), a decreased EBA immunostaining (42-51% reduction), a decreased number of surviving neurons (27-40% reduction), the presence of dying neurons (4-10% of total neurons), and an increased GFAP immunostaining (45-51% increase). These changes were also associated with decreased forebrain AChE activity and m2-AchR (19-25% reduction). In contrast, in animals exposed to stress and vehicle or chemicals alone, the above indices were mostly comparable to that of animals exposed to vehicle alone. Thus, a combined exposure to stress and low doses of PB, DEET, and permethrin leads to significant brain injury. The various neurological symptoms reported by Gulf-War veterans could be linked to this kind of brain injury incurred during the war.

Exposure to a combination of stress and low doses of the chemicals pyridostigmine bromide (PB), DEET, and permethrin in adult rats, a model of Gulf War exposure, produces blood-brain barrier (BBB) disruption and neuronal cell death in the cingulate cortex, dentate gyrus, thalamus, and hypothalamus. In this study, neuropathological alterations in other areas of the brain where no apparent BBB disruption was observed was studied following such exposure. Animals exposed to both stress and chemical exhibited decreased brain acetylcholinesterase (AChE) activity in the midbrain, brainstem, and cerebellum and decreased m2 muscarinic acetylcholine (ACh) receptor ligand binding in the midbrain and cerebellum. These alterations were associated with significant neuronal cell death, reduced microtubule-associated protein (MAP-2) expression, and increased glial fibrillary acidic protein (GFAP) expression in the cerebral cortex and the hippocampal subfields CA1 and CA3. In the cerebellum, the neurochemical alterations were associated with Purkinje cell loss and increased GFAP immunoreactivity in the white matter. However, animals subjected to either stress or chemicals alone did not show any of these changes in comparison to vehicle-treated controls. Collectively, these results suggest that prolonged exposure to a combination of stress and the chemicals PB, DEET, and permethrin can produce significant damage to the cerebral cortex, hippocampus, and cerebellum, even in the absence of apparent BBB damage. As these areas of the brain are respectively important for the maintenance of motor and sensory functions, learning and memory, and gait and coordination of movements, such alterations could lead to many physiological, pharmacological, and behavioral abnormalities, particularly motor deficits and learning and memory dysfunction.


Malathion (O,O-dimethyl-S-[1,2-carbethoxyethyl]phosphorodithionate), DEET (N,N-diethyl-m-toluamide), and permethrin [(+/-)-cis/trans-3-(2,2-dichloroethyl)-2,2-dimethylcyclopropane carboxylic acid (3-phenoxypyphenyl) methyl ester] are commonly used pesticides. To determine the effects of the dermal application of these chemicals, alone or in combination, the sensorimotor behavior, central cholinergic system, and histopathological alterations were studied in adult male Sprague-Dawley rats following a daily dermal dose of 44.4 mg/kg malathion, 40 mg/kg DEET, and 0.13 mg/kg permethrin, alone and in combination for 30 d. Neurobehavioral evaluations of sensorimotor functions included beam-walking score, beam walk time, inclined plane, and grip response assessments. Twenty-four hours after the last treatment with each chemical alone or in combination all behavioral measures were impaired. The combination of DEET and permethrin, malathion and permethrin, or the three chemicals together resulted in greater impairments in inclined performance than permethrin alone. Only animals treated with a combination of DEET and malathion or with DEET and permethrin exhibited significant increases in plasma butyrylcholinesterase (BChE) activity. Treatment with DEET or permethrin alone, malathion and permethrin, or DEET and permethrin produced significant increases in cortical acetylcholinesterase (AChE) activity. Combinations of malathion and permethrin or of DEET and permethrin produced significant decreases in midbrain AChE activity. Animals treated with DEET alone exhibited a significant increase in cortical m2 muscarinic ACh receptor binding. Quantification of neuron density in the dentate gyrus, CA1 and CA3 subfields of the hippocampus, midbrain, brainstem, and cerebellum revealed significant reductions in the density
of surviving neurons with various treatments. These results suggest that exposure to real-life doses of malathion, DEET, and permethrin, alone or in combination, produce no overt signs of neurotoxicity but induce significant neurobehavioral deficits and neuronal degeneration in brain.


Organophosphorus compounds are potent neurotoxic chemicals that are widely used in medicine, industry, and agriculture. The neurotoxicity of these chemicals has been documented in accidental human poisoning, epidemiological studies, and animal models. Organophosphorus compounds have 3 distinct neurotoxic actions. The primary action is the irreversible inhibition of acetylcholinesterase, resulting in the accumulation of acetylcholine and subsequent overstimulation of the nicotinic and muscarinic acetylcholine receptors, resulting in cholinergic effects. Another action of some of these compounds, arising from single or repeated exposure, is a delayed onset of ataxia, accompanied by a Wallerian-type degeneration of the axon and myelin in the most distal portion of the longest tracts in both the central and peripheral nervous systems, and is known as organophosphorus ester-induced delayed neurotoxicity (OPIDN). In addition, since the introduction and extensive use of synthetic organophosphorus compounds in agriculture and industry half a century ago, many studies have reported long-term, persistent, chronic neurotoxicity symptoms in individuals as a result of acute exposure to high doses that cause acute cholinergic toxicity, or from long-term, low-level, subclinical doses of these chemicals. The author attempts to define the neuronal disorder that results from organophosphorus ester-induced chronic neurotoxicity (OPICN), which leads to long-term neurological and neurobehavioral deficits. Although the mechanisms of this neurodegenerative disorder have yet to be established, the sparse available data suggest that large toxic doses of organophosphorus compounds cause acute necrotic neuronal cell death in the brain, whereas sublethal or subclinical doses produce apoptotic neuronal cell death and involve oxidative stress degeneration in brain.


The operating environment of the service personnel during the Persian Gulf War involved psychological, biological, and chemical elements including exposure to pesticides such as the insect repellent DEET (N,N-diethyl-m-toluamide) and the insecticide chlorpyrifos (O,O-diethylO-3,5,6-trichloropyridinyl phosphorothioate) and to pyridostigmine bromide (PB, 3-dimethylaminocarboxyloxy-N-methylpyridinium bromide) that was administered as a prophylactic agent against possible nerve gas attack. The present study was designed to determine the toxicity produced by individual or coexposure of hens 5 days/week for 2 months to 5 mg PB/kg/day in water, by gavage; 500 mg DEET/kg/day, neat, sc; and 10 mg chlorpyrifos kg/day in corn oil, sc. Coexposure to various binary treatments produced greater neurotoxicity than that caused by individual exposures and was characterized by severe neurologic deficit and neuropathological alterations. Also, neurotoxicity was further enhanced following concurrent administration of the three chemicals. Severe inhibition of plasma butyrylcholinesterase (BuChE) activity was produced in hens treated with PB (activity 17% of control) compared to those treated with chlorpyrifos (activity 51% of control) or DEET (activity 83% of control).
BuChE inhibition was further increased in binary and tertiary treatment groups compared to individual treatment groups. In contrast, a significant inhibition of brain acetylcholinesterase (AChE) was produced in hens administered chlorpyrifos alone (activity 67% of control), while those given chlorpyrifos in combination with other compounds exhibited a significant inhibition of brain AChE activity ranging from 43 to 76%. Brain neurotoxicity target esterase (NTE) was not inhibited in any of the individual treatment groups or PB/DEET, but was significantly inhibited and had activity expressed as a percentage of control in groups administered combined chlorpyrifos with PB of 73% or DEET of 74% and in the tertiary treatment group of 71%. We hypothesize that test compounds may compete for xenobiotic metabolizing enzymes in the liver and blood and may also compromise the integrity of the blood–brain barrier, leading to an increase in their “effective concentrations” in the nervous system to levels equivalent to the toxic doses of individual compounds. This is consistent with the present observation of increases in (1) the inhibition of brain AChE and NTE, (2) the extent of neurologic dysfunction, and (3) the severity and frequency of neuropathologic lesions in the combined treatment groups compared to those administered individual compounds.


We investigated the effects of uranyl acetate on sensorimotor behavior, generation of nitric oxide and the central cholinergic system of rats. Male Sprague-Dawley rats were treated with intramuscular injection of 0.1 and 1 mg/kg uranyl acetate in water, daily for 7 days. Control animals received equivalent amount of water. The treatment was stopped after the seventh injection because the animals in the 1-mg/kg group appeared lethargic. The animals were maintained for an additional observation period of 30 days. The study was initiated as a dose-finding study that covered doses of 10 and 100 mg/kg, as well. However, all the animals in the 100-mg/kg treatment group died after the third and fourth injections, and all animals given 10 mg/kg died after the fifth and sixth injections. On day 30 following the cessation of treatment, the sensorimotor functions of the animals in the 0.1- and 1-mg/kg treatment groups were evaluated using a battery of tests that included measurements of postural reflexes, limb placing, orientation to vibrissae touch, grip time, beam walking and inclined plane performance. The animals were sacrificed the same day and the cerebral cortex, brainstem, cerebellum and midbrain were dissected. The levels of nitric oxide as marker for increased oxidative stress, and the integrity of the cholinergic system as reflected in acetylcholinesterase (AChE) activity and m2 muscarinic acetylcholine receptors ligand binding, were determined. The data from behavioral observations show that there was a dose-related deficit at the 0.1- and 1-mg/kg treatment groups for inclined plane performance. Both doses reduced grip time, but there was no significant difference between the two doses. Similarly, both beam-walk score and beam-walk time were impaired at both doses as compared with the controls. A significant increase in nitric oxide was seen at 0.1 mg/kg dose in cortex and midbrain, whereas brainstem and cerebellum showed an insignificant decrease at both the doses. Similarly, there was no significant change in nitric oxide levels in kidneys and liver of the treated animals as compared with the controls. There was a significant increase in AChE activity in the cortex of the animals treated with 1 mg/kg uranyl acetate, but not in other brain regions. Ligand binding densities for the m2 muscarinic receptor did not show any change. These results show that low-dose, multiple
exposure to uranyl acetate caused prolonged neurobehavioral deficits after the initial exposure has ceased.


Military personnel deployed in the Persian Gulf War (PGW) were exposed to a combination of chemicals, including pyridostigmine bromide (PB), DEET, and permethrin. We investigated the dose-response effects of these chemicals, alone or in combination, on the sensorimotor performance and cholinergic system of male Sprague-Dawley rats. Animals were treated with a daily dermal dose of DEET and/or permethrin for 60 days and/or PB (gavage) during the last 15 days. Neurobehavioral performance was assessed on day 60 following the beginning of the treatment with DEET and permethrin. The rats were sacrificed 24 h after the last treatment for biochemical evaluations. PB alone, or in combination with DEET, or DEET and permethrin resulted in deficits in beam-walk score and longer beam-walk times compared to controls. PB alone, or in combination with DEET, permethrin, or DEET and permethrin caused impairment in incline plane performance and forepaw grip strength. PB alone at all doses slightly inhibited plasma butyrylcholinesterase activity, whereas combination of PB with DEET or permethrin increased its activity. Brainstem acetylcholinesterase (AChE) activity significantly increased following treatment with combinations of either DEET or permethrin at all doses, whereas the cerebellum showed a significant increase in AChE activity following treatment with a combination of PB/DEET/permethrin. Co-exposure to PB, DEET, and permethrin resulted in significant inhibition in AChE in midbrain. PB alone or in combination with DEET and permethrin at all doses increased ligand binding for m2 muscarinic acetylcholine receptor in the cortex. In addition, PB and DEET together or a combination of PB, DEET, and permethrin significantly increased ligand binding for nicotinic acetylcholine receptor. These results suggest that exposure to various doses of PB, alone and in combination with DEET and permethrin, leads to sensorimotor deficits and differential alterations of the cholinergic system in the CNS.


In this study concentrations of markers of oxidative stress 3-nitrotyrosine and 8-hydroxy-2′-deoxyguanosine (8-OhdG) were determined in rat urine following a single oral dose of pyridostigmine bromide (PB) 13 mg/kg and a single intramuscular dose of sarin 80 microg/kg alone or in combination. Urine samples were collected 16, 24, 48, 72, and 96 h following dosing. Control urine samples of five rats treated with normal saline were also collected at the same time intervals. A combined dose of PB and sarin significantly increased levels of 3-nitrotyrosine and (8-OhdG) starting 48 h after dosing. An increase in the concentration of these markers was not detected following a single dose of PB or sarin alone. Maximal increase in 3-nitrotyrosine and 8-OhdG was detected 48 h after administration of a combination PB and sarin. The results indicate that concurrent exposure to PB and sarin could generate free radical species that may cause oxidative stress in rats. The results may have significant impact if veterans were exposed to sarin following an oral dose of PB.

Biomarkers rely on biochemical, histological, morphological, and physiological changes in whole organisms. Their use is becoming an important tool to examine changes at cellular and molecular levels, especially in nucleic acids and proteins. Biomarkers are used to measure exposure to a toxic agent, to detect severity of any toxic response, and to predict the possible outcome. Information on the mechanisms of action of toxicants can allow the development of potential biomarkers of effect and thus improvement of the risk assessment processes. Use of biomarkers as a tool to predict induction of apoptosis allows identification of biological signs that may indicate increased risk for disease. In cells undergoing apoptosis, the release of cytochrome c from the mitochondria to the cytoplasm and the activation of caspase-3, a key enzyme to execution stage of apoptotic pathway, have been studied as biomarkers of cell death (apoptosis). Products of DNA fragmentation that either accumulate in the cellular tissues or are excreted in the urine are useful markers of DNA damage. The induction level of urinary or cellular level of 8-hydroxy-2-deoxyguanosine and 3-nitrotyrosine has been used as a marker to measure extent of DNA oxidative damage. Furthermore, alteration or overexpression of the p53 gene was considered an indication of apoptosis. This article reviews some of the aspects of biomarkers of apoptosis, indicating relevance of their uses to predict apoptosis following exposure to environmental toxicants.


The *in vitro* human plasma activity and liver microsomal metabolism of pyridostigmine bromide (PB), a prophylactic treatment against organophosphate nerve agent attack, N,N-diethyl-m-toluamide (DEET), an insect repellent, and permethrin, a pyrethroid insecticide, either alone or in combination were investigated. 2. The three chemicals disappeared from plasma in the following order: permethrin > PB > DEET. The combined incubation of DEET with either permethrin or PB had no effect on permethrin or PB. Binary incubation with permethrin decreased the metabolism of PB and its disappearance from plasma and binary incubation with PB decreased the metabolism of permethrin and its clearance from plasma. Incubation with PB and/or permethrin shortened the DEET terminal half-life in plasma. These agents behaved similarly when studied in liver microsomal assays. The combined incubation of DEET with PB or permethrin (alone or in combination) diminished DEET metabolism in microsomal systems. 3. The present study evidences that PB and permethrin are metabolized by both human plasma and liver microsomal enzymes and that DEET is mainly metabolized by liver oxidase enzymes. Combined exposure to test chemicals increases their neurotoxicity by impeding the body's ability to eliminate them because of the competition for detoxifying enzymes.

Many of the symptoms described in Sick Building Syndrome (SBS) and multiple chemical sensitivity (MCS) resemble those known to be elicited by airborne irritant chemicals. Irritation of the eye, nose, and throat is common to SBS, MCS, and sensory irritation (SI). Difficulty of breathing is often seen with SBS, MCS, and pulmonary irritation (PI). We therefore asked the question: can indoor air pollutants cause SI and/or PI? In laboratory testing in which mice breathed the dilute volatile emissions of air fresheners, fabric softeners, colognes, and mattresses for 1 h, we measured various combinations of SI and PI as well as airflow decreases (analogous to asthma attacks). Air samples taken from sites associated with repeated human complaints of poor air quality also caused SI, PI, and airflow limitation (AFL) in the mice. In previous publications, we have documented numerous behavior changes in mice (which we formally studied with a functional observational battery) after exposure to product emissions or complaint site air; neurological complaints are a prominent part of SBS and MCS. All together, these data suggest that many symptoms of SBS and MCS can be described as SI, PI, AFL, and neurotoxicity. All these problems can be caused by airborne irritant chemicals such as those emitted by common commercial products and found in polluted indoor air. With some chemical mixtures (e.g., emissions of some fabric softeners, disposable diapers, and vinyl mattress covers) but not others (e.g., emissions of a solid air freshener), the SI response became larger (2- to 4-fold) when we administered a series of two or three 1-h exposures over a 24-h period. Since with each exposure the intensity of the stimulus was constant yet the magnitude of the response increased, we concluded that there was a change in the sensitivity of the mice to these chemicals. The response was not a generalized stress response because it occurred with only some mixtures of irritants and not others; it is a specific response to certain mixtures of airborne chemicals. This is one of the few times in MCS research that one can actually measure both the intensity of the stimulus and the magnitude of the response and thus be allowed to discuss sensitivity changes. The changing SI response of the mice might serve as a model of how people develop increasing sensitivity to environmental pollutants. Intensive study of this system should teach us much about how people respond to and change sensitivity to airborne irritant chemicals.


There is increasing evidence that human exposure to levels of chemicals once thought to be safe—or presenting insignificant risk—are, in fact, harmful. So-called low-level exposures are now known to be associated with adverse biological effects including cancer, endocrine disruption, and chemical sensitivity. This requires that we change both (1) the way we design research linking chemicals and health, and (2) the solutions we devise to address chemically caused injury. The new and emerging science of low-level exposure to chemicals requires appropriate social policy responses which include regulation of toxic substances, notification of those exposed, and compensation and reasonable accommodation to those affected. Research and social policy need to be focused towards two distinct groups: (1) those individuals who could become chemically intolerant as a result of an initiating exposure, and (2) those individuals who have already become chemically intolerant and are now sensitive to chemicals at low levels.

This is a community-based study of odor sensitivity and respiratory complaints for persons reporting asthma (n=14/141), hay fever (n=72/140), and chemical odor intolerance (CI) (n=41/181). CI, a symptom of multiple chemical sensitivity (MCS), was determined from self-ratings of feeling `moderately' to `severely' ill using the Chemical Odor Intolerance Index (CII). Index odors included perfume, pesticide, drying paint, new carpet odor, and car exhaust. Six additional odors [natural gas, disinfectants, chlorinated water, room deodorizers, and environmental tobacco smoke (ETS)] were also assessed in the health and environment survey. Asthmatics reported feeling `frequently' to `almost always' ill from the CII index odors of drying paint, new carpet odor, perfume, and cleaning agents compared to nonasthmatics. People with hay fever documented feeling `frequently' to `almost always' ill from pesticides, drying paint, and car exhaust compared to individuals without hay fever. The CI cited illness from air freshener, natural gas and chlorinated water, in addition to the index odors of perfume, paint, pesticides, new carpeting and auto exhaust. All three groups were significantly more likely to report feeling ill from ETS. People with asthma were significantly more likely to report lower lung complaints, such as wheeze and dyspnea. People with hay fever cited more chest tightness. The CI were significantly more likely to report upper and lower respiratory symptoms. Given this overlap in respiratory complaints, it could be that CI may serve to amplify these traditional immune-related disorders and/or suggest that having asthma or hay fever could make one more vulnerable to CI.


The Working Group on Neurogenic Inflammation proposed 11 testable hypotheses in the three domains of neurogenic inflammation, perceptual and central integration, and nonneurogenic inflammation. The working group selected the term people reporting chemical sensitivity (PRCS) to identify the primary subject group. In the domain of neurogenic inflammation, testable hypotheses included: PRCS have an increased density of c-fiber neurons in symptomatic tissues; PRCS produce greater quantities of neuropeptides and prostanoids than nonsensitive subjects in response to exposure to low-level capsaicin or irritant chemicals; PRCS have an increased and prolonged response to exogenously administered c-fiber activators such as capsaicin; PRCS demonstrate augmentation of central autonomic reflexes following exposure to agents that produce c-fiber stimulation; PRCS have decreased quantities of neutral endopeptidase in their mucosa; exogenous neuropeptide challenge reproduces symptoms of PRCS. In the domain of perceptual and central integration, testable hypotheses included: PRCS have alterations in adaptation, habituation, cortical representation, perception, cognition, and hedonics compared to controls; the qualitative and quantitative interactions between trigeminal and olfactory systems are altered in PRCS; higher integration of sensory inputs is altered in PRCS. In the domain of nonneurogenic inflammation, testable hypotheses included: increased inflammation is present in PRCS in symptomatic tissues and is associated with a heightened neurosensory response; PRCS show an augmented inflammatory response to chemical exposure. The working group recommended that studies be initiated in these areas.

The current principles of toxicology, immunology and allergy do not provide a coherent explanation of a chemical sensitivity lacking reproducible and measurable physiologic or biochemical changes. A new paradigm is needed as a scientific model for multiple chemical sensitivities.


Two individuals developed an asthma-like illness after a single exposure to high levels of an irritating aerosol, vapor, fume, or smoke. Symptoms developed within a few hours. A consistent physiologic accompaniment was airways hyperreactivity, with the two subjects showing positive methacholine challenge tests. No documented preexisting respiratory illness was identified, nor did subjects relate past respiratory complaints. Respiratory symptoms and airways hyperreactivity persisted for at least four years after the incident. The incriminated etiologic agents all shared a common characteristic of being irritant in nature. Bronchial biopsy specimens showed an airways inflammatory response. This report suggests that acute high-level irritant exposures may produce an asthma-like syndrome in some individuals, with long-term sequelae and chronic airways disease. Nonimmunologic mechanisms seems to be operative in the pathogenesis of this syndrome.


The article presents information on the findings of a telephone survey conducted to find the prevalence of hypersensitivity to low levels of common chemicals in the American population. Chemical hypersensitivity--often called multiple chemical sensitivity (MCS)--is also referred to as toxicant-induced loss of tolerance or environmental illness. It is typically acknowledged to be a condition characterized by acute reactions that occur after exposure to even low levels of common chemical products such as fragrances, household cleaners, fresh paints, newsprint, pesticides and other products that contain petrochemicals. MCS can produce a wide range of symptoms, and individuals with the hypersensitivity can encounter great difficulty functioning in normal working and living environments. Although a limited number of epidemiological studies have investigated the regional prevalence of chemical hypersensitivity in the U.S., its national prevalence is speculative. The National Academy of Sciences estimated that up to 15% of the U.S. population experiences some degree of hypersensitivity to common chemicals.


Objective: The objective of this study was to investigate the linkage between asthma and chemical hypersensitivity.

Methods: The authors conducted a population study with a random sample of 1057 geographically weighted cases to determine the prevalence of both asthma and chemical hypersensitivity in the American population and to explore their co-occurrence.
Results: A total of 14.1% of the respondents reported being diagnosed with asthma and 11.2% reported a hypersensitivity to chemicals. Of those with asthma, 27.2% also reported being hypersensitive to chemicals and 7.4% reported also being diagnosed with multiple chemical sensitivities (MCS). Of those diagnosed with MCS, 42% reported also being diagnosed with asthma. Additionally, 29.7% of those with asthma said air fresheners caused breathing difficulties, and 37.2% found scented products irritating.

Conclusions: The results indicate that there is significant overlap between some forms of asthma and chemical hypersensitivity.


A questionnaire was administered to individuals who had reported a hypersensitivity to common chemical products in an earlier epidemiological study in the Atlanta, Georgia, metropolitan area. The questionnaire investigated the nature of the symptoms and factors that potentially initiated hypersensitivity and subsequently triggered reactions. Also examined were associated lifestyle modifications and the relationships of hypersensitivity with other illnesses. The authors found that a majority of hypersensitive individuals (52.2%) experienced either "severe" or "somewhat severe" symptoms. The most common triggers of symptoms were cleaning products (88.4%), tobacco smoke (82.6%), perfume (81.2%), pesticides (81.2%), and car exhaust (72.5%). Only 1.4% of the subjects had a prior history of emotional problems, whereas 37.7% developed such problems after the emergence of their hypersensitivity. Lifestyle modifications varied; 76.8% changed their household cleaning/personal hygiene products, 47.8% began using water and/or air filtration systems, and 13% found it necessary to change residence. Although hypersensitivity was more common in females than males, the condition affects individuals in all categories of race/ethnicity, age, household income, and educational level.


In the United States, some 80,000 commercial and industrial chemicals are now in use of which over 30,000 are produced or used in the Great Lakes region. Thus, the environmental quality within the Great Lakes basin has been compromised particularly with respect to persistent toxic substances (PTS). Information derived from wildlife studies, prospective epidemiological and toxicological studies, databases, demographics, and Geographical Information Systems (GIS) demonstrate significant public health implications. Studies of human populations indicate: (a) elevated body burden levels of PTSs, (b) decrease in gestational age, (c) low birth weight (LBW), (d) greater risk of male children with birth defects (OR = 3.01), (e) developmental and neurological deficits, (f) increased risk of infertility, (g) changes in sex ratio, and (h) fluctuations in thyroid hormones. These findings have been identified in vulnerable populations, such as the developing fetus, children, minorities, and men and women of reproductive age who are more susceptible because of their physiologic sensitivity and/or elevated exposure to toxic chemicals. Typically such health effects are assessed on a chemical specific basis; however, most human populations are exposed to hazardous chemicals as mixtures in air, water, soil, and biota. In this article we present an assessment of the potential for joint toxic action of these substances in
combinations in which they are typically found. These evaluations represent an integration of all available scientific evidence in accordance with the "NAS paradigm" for risk assessment. In aggregate, our evaluations have demonstrated a need for community-based frameworks and computational techniques to track patterns of environmentally related exposures and associated health effects.


Background: Exposure to perfume and fragrance products may, in some individuals, cause symptoms from the eyes and airways. The localization, character and risk factors of such symptoms in the general population are unknown.

Objective: To investigate both the localization and character of symptoms from the eyes and airways elicited by fragrance products, and the associations between such symptoms and skin prick test reactivity (atopy), methacholine bronchial hyper-reactivity (BHR), allergic rhinitis and asthma.

Methods: A questionnaire on mucosal symptoms elicited by fragrance products was posted to 1189 persons who had participated in a Danish population-based study of allergic diseases in 1997/1998. The study included measurement of BHR, atopy, forced expiratory volume in 1 s (FEV1), and serum eosinophilic cationic protein (serum ECP).

Results: The response rate was 79.6%. Symptoms from the eyes or airways elicited by fragrance products were reported by 42%. BHR (adjusted odds ratio 2.3, 95% confidence interval 1.5–3.5) was independently associated with symptoms from the eyes and airways elicited by fragrance products. There were no significant associations between these symptoms and atopy, FEV1 or serum ECP.

Conclusions: Mucosal symptoms from the eyes and airways were common in this population. BHR was a significant and independent predictor of these symptoms. The lack of association with atopy suggested that IgE-mediated allergic mechanisms do not play a major role in the development of these symptoms.


The authors sought to determine whether reported symptoms of mothers and infants were associated significantly with the use of household products that raised indoor levels of total volatile organic compounds (TVOC\textsubscript{\text{a}}). Data collected from 170 homes within the Avon Longitudinal Study of Parents and Children (ALSPAC: a large birth cohort of more than 10,000) had determined which household products were associated with the highest levels of TVOC\textsubscript{\text{a}}. The latter data were collected over a period that approximated 6 mo of pregnancy and the infants' first 6 mo of life. This paper presents (a) the mothers' self-reports of the use of these products in their homes and (b) self-reported medical symptoms of mothers and infants postnatally. Higher TVOC levels were associated with air freshener and aerosol use. Infant diarrhea and earache were statistically significantly associated with air freshener use, and diarrhea and vomiting were significantly associated with aerosol use. Headache experienced by mothers 8 mo after birth was
significantly associated with the use of air fresheners and aerosols; maternal depression was significantly associated with the use of air fresheners. The results of the study suggest a link between the use of products that raise indoor levels of TVOCs and an increased risk of certain symptoms among infants and their mothers.


Multiple chemical sensitivity (MCS) is a phenomenon whereby individuals report an increased sensitivity to low levels of chemicals in the environment. Kindling is a model of synaptic plasticity whereby repeated low-level electrical stimulation to a number of brain sites leads to permanent increases in seizure susceptibility. Stimulation that is initially subthreshold for subclinical seizure provocation comes, over time, to elicit full-blown motor seizures. Kindling can also be induced by chemical stimulation, and repeated exposures to some pesticides have been shown to induce signs of behavioral seizure, facilitate subsequent electrical kindling, and induce subclinical electrographic signs of hyperexcitability in the amygdala. Many of the symptoms of MCS suggest that CNS limbic pathways involved in anxiety are altered in individuals reporting MCS. Limbic structures are among the most susceptible to kindling-induced seizures, and persistent cognitive and emotional sequelae have been associated with temporal lobe epilepsy (TLE) in humans and kindling in animals. Thus, a number of parallels exist between kindling and MCS phenomena, leading to initial speculations that MCS may occur via a kindling-like mechanism. However, kindling requires the activation of electrographic seizure discharge and has thus been primarily examined as a model for TLE. Events leading to the initial evocation of a subclinical electrographic seizure have been much less well studied. It is perhaps these events that may serve as a more appropriate model for the enhanced chemical responsiveness characteristic of MCS. Alternatively, kindling may be useful as a tool to selectively increase sensitivity in subcomponents of the neural fear circuit to address questions relating the role of anxiety in the development and expression of MCS.


Environmental exposures to very low levels of airborne chemicals are associated with adverse symptoms, often affecting multiple organ systems, in the phenomenon of chemical sensitivity (CS). Recent surveys suggest a significant prevalence of chemically sensitive subjects in the United States, but the mechanism linking exposure to symptoms remains unclear, despite the advancement of a variety of theoretical models. In many of these models, exposure of the nasal respiratory system to an airborne agent is the first step in the pathway leading to symptoms. In this article, we advance the hypothesis that interactions between environmental chemicals and the vomeronasal organ (VNO) may play a role in the etiology of CS. The VNO, a bilateral, tubular organ located in the nose, serves in animals as part of a sensitive chemosensory system; however, evidence suggesting that the VNO retains a functional role in the adult human is controversial. Reported characteristics of the human VNO relevant to CS, including location, prevalence, selective sensitivity to airborne chemical exposure, and capacity to produce systemic effects, are discussed within the context of this ongoing debate. Beyond relevance to CS, the demonstration of an active, adult VNO could have significant impact on environmental toxicology.

Previously Haley et al. described six possible syndromes identified by factor analysis of symptoms in Gulf War veterans and demonstrated that veterans with these symptom complexes were more neurologically impaired than age-sex-education-matched well controls. They also uncovered strong associations (relative risks 4-8) suggesting that these symptom complexes were related to wartime exposure to combinations of organophosphate pesticides, chemical nerve agents, high concentration DEET insect repellant, and symptoms of advanced acute toxicity after taking pyridostigmine. Here we have shown that compared to controls, ill veterans with the neurologic symptom complexes were more likely to have the R allele (heterozygous QR or homozygous R) than to be homozygous Q for the paraoxonase/arylesterase 1 (PON1) gene. Moreover, low activity of the PON1 type Q (Gln192, formerly designated type A) arylesterase allozyme distinguished ill veterans from controls better than just the PON1 genotype or the activity levels of the type R (Arg192, formerly designated type B) arylesterase allozyme, total arylesterase, total paraoxonase, or butyrylcholinesterase. A history of advanced acute toxicity after taking pyridostigmine was also correlated with low PON1 type Q arylesterase activity. Type Q is the allozyme of paraoxonase/arylesterase that most efficiently hydrolyzes several organophosphates including sarin, soman, and diazinon. These findings further support the proposal that neurologic symptoms in some Gulf War veterans were caused by environmental chemical exposures.


The authors studied the association between long-term exposure (i.e., > 10 y) to outdoor air pollution and the severity of obstructive pulmonary disease and prevalence of bronchial hyperreactivity to Beta 2 agonists in two groups of adult patients who were of similar ages and who had similar smoking habits. The subjects lived in downtown districts or in the outer suburbs of Marseilles, the neighborhood that contained air samplers. The regions were similar with respect to sulfur dioxide levels, but levels of nitric oxides and particulate matter (10 millimeters or less) were higher in the downtown area than the suburbs. The authors assessed airway obstruction, as determined by a decrease in forced expiratory volume in 1 s, mean forced expiratory flow measured between 25% and 75% of vital capacity, and an elevated value of central airway resistance. The authors tested the changes in these variables induced by inhalation of a Beta 2 agonist. Baseline lung function was altered more significantly in both male and female patients who lived in downtown Marseilles than in those who resided in the suburbs, and the differences persisted regardless of the season during which the study occurred. Prevalence of bronchial hyperreactivity and symptoms of asthma (but not of rhinitis) were higher in the downtown than suburban male subjects. The results of this study suggest that an association exists between actual environmental exposure to outdoor air pollution (i.e., nitrogen oxides and/or particulate matter of 10 millimeters or less) and respiratory effects in sensitive adults represented by patients with chronic obstructive pulmonary disease or asthma.
Patients with upper and lower airway symptoms and with pronounced sensitivity to chemical odours, such as perfumes, flower scents and tobacco smoke, have been suggested to have sensory hyperreactivity (SHR). The symptoms have been difficult to identify with physiological measurements and the effects of various medications are doubtful. However, these patients have been found to be more sensitive to inhalation of capsaicin than healthy people. The aim of this study was to establish limit values with the capsaicin inhalation test in patients with SHR.

**METHODS:** Ninety-five consecutive patients with upper and lower airway problems, who were admitted for allergy testing, underwent a capsaicin inhalation test with three different concentrations. The number of coughs was registered during each challenge. Score systems were used for symptoms and influence on social life of sensitivity to odours. In relation to scored symptoms, the patients were grouped as SHR or not, and compared with 73 healthy controls.

**RESULTS:** All patients and controls coughed on capsaicin in a dose-dependent manner. Symptom score of odour sensitivity in patients was positively correlated to the response of the test. Out of 95 patients, 15 (16%) were scored to SHR. Patients with SHR reacted more to the capsaicin inhalation test than the other patients and the healthy controls. The limit values for a positive capsaicin inhalation test for the SHR were determined to be 10, 35 and 55 coughs at 0.4, 2.0 and 10 microM capsaicin, respectively. **CONCLUSION:** The capsaicin inhalation test well reflects the degree of airway sensitivity to chemicals and to what extent the social life is influenced. The cut-off values of the test can distinguish patients with pronounced sensitivity to odours.


**We conducted a pilot study using a randomized, single-blind, placebo-controlled exposure among 10 individuals with and 7 without reported chemical sensitivities in a dedicated testing chamber. Objectives of the study were to explore the length of the adaptation period to obtain stable readings, evaluate responses to different substances, and measure the level and type of symptomatic and physiologic reactions to low-level exposures. Reported and observed symptoms, electrodermal response, heart rate, skin temperature, surface electromyogram, respiratory rate, contrast sensitivity, and the Brown-Peterson cognitive test were used and compared between cases and controls and between test substances (glue, body wash solution, dryer sheet) and control substances (unscented shampoo and clean air). Subjects with chemical sensitivities (cases) took longer to adapt to baseline protocols than did controls. After adaptation, despite small study numbers, cases displayed statistically significant responses (all measures, \( p < 0.02 \)) in tonic electrodermal response to test substances compared with controls and compared with the control substance. Symptoms were also higher in cases than in controls for the body wash solution \( (p = 0.05) \) and dryer sheets \( (p = 0.02) \). Test-retest showed good agreement for both symptoms and tonic electrodermal responses (McNemar's test, \( p = 0.32 \) and \( p = 0.33 \), respectively). Outside of skin conductance, other measures had no consistent patterns between test and control substances and between cases and controls. This study shows the importance of using an adaptation period in testing individuals with reported chemical sensitivities and, despite
small numbers, raises questions about underlying mechanisms and level of reactivity to low-level chemical exposures in sensitive individuals.


Background: The collapse of the World Trade Center (WTC) on September 11, 2001 created a large-scale disaster site in a dense urban environment. In the days and months thereafter, thousands of rescue/recovery workers, volunteers, and residents were exposed to a complex mixture of airborne pollutants.

Methods: We review current knowledge of aerodigestive inhalation lung injuries resulting from this complex exposure and present new data on the persistence of nonspecific bronchial hyperreactivity (methacholine PC20 ≤8 mg/mL) in a representative sample of 179 Fire Department of the City of New York (FDNY) rescue workers stratified by exposure intensity (according to arrival time) who underwent challenge testing at 1, 3, 6, and 12 months post-collapse.

Results: Aerodigestive tract inflammatory injuries, such as declines in pulmonary function, reactive airways dysfunction syndrome (RADS), asthma, reactive upper airways dysfunction syndrome (RUDS), gastroesophageal reflux disease (GERD), and rare cases of inflammatory pulmonary parenchymal diseases, have been documented in WTC rescue/recovery workers and volunteers. In FDNY rescue workers, we found persistent hyperreactivity associated with exposure intensity, independent of airflow obstruction. One year post-collapse, 23% of highly exposed subjects were hyperreactive as compared with only 11% of moderately exposed and 4% of controls. At 1 yr, 16% met the criteria for RADS.

Conclusions: While it is too early to ascertain all of the long-term effects of WTC exposures, continued medical monitoring and treatment is needed to help those exposed and to improve our prevention, diagnosis, and treatment protocols for future disasters.


In the 19th century, deaths from acute exposure to hydrogen sulfide (H2S) portended permanent brain injury from nonlethal doses. The neurobehavioral effects of H2S exposures lasting from moments to years were compared in 16 subjects, 2 years to 22 years afterward. METHODS: Neurophysiologic and psychologic tests were used to appraise mood status and frequencies of 35 symptoms. Functions and frequencies, described as percent predicted adjusted for age, sex, educational achievement, and other factors, were compared with those in an unexposed population. RESULTS: Frequencies were elevated for 31 of 33 symptoms. Balance was impaired (246% predicted with eyes closed, 159% predicted with eyes open), and simple and choice reaction times were prolonged (151% and 130% predicted, respectively). Visual fields performance was decreased to 72% predicted (right) and 55% predicted (left), color discrimination was abnormal, and hearing was decreased. Psychologic domains showed cognitive disability, reduced perceptual motor speed, impaired verbal recall and remote memory, and abnormal mood status. CONCLUSIONS: Exposure to H2S must be avoided.

(Editorial) Discusses issues on the effects of chemicals on the brain. Result of the comparison measurements of group of individuals who had been exposed to chemicals; Implication of the widespread use of chemicals and the repetitive patterns of exposure; Practical and safe strategy of preventing the effects of chemicals on the brain.


In this study, the authors describe a new “reactive syndrome,” Reactive Intestinal Dysfunction Syndrome (RIDS), which has similarities to the previously described clinical syndromes Reactive Airway Dysfunction Syndrome (RADS) and Reactive Upper Airway Dysfunction Syndrome (RUDS). Given that at least 5 neuropeptides are common to both the respiratory tract and digestive tract, the authors propose that the abnormal secretion of these neuropeptides or the abnormal numbers of their receptors play a role in what is perceived clinically as RADS, RUDS, and RIDS. The relatively large surface areas of both the lungs and gut render them especially vulnerable to the environment to which they are exposed constantly.


Intentional hydrocarbon inhalation can be fatal. Death can be secondary to hydrocarbon's cardiopulmonary effects. We present a case of a patient who survived ventricular fibrillation after inhalation of Glade Air Freshener(TM), which contains short chain aliphatic hydrocarbons (butane and isobutane). Unlike our case, myocardial sensitization and hypoxia are more commonly described with aromatic, halogenated or longer chain hydrocarbons.


Exposure to organophosphate (OP's) insecticides and nerve gases during the Persian Gulf War has been implicated in the development of Gulf War Syndrome. Paraoxonase (PON1) present in human serum detoxifies OP's. We determined the levels of PON1 in the serum of Gulf War Veterans and compared these to those found in a control population. One hundred fifty-two Gulf War Veterans from the UK who self-reported the presence of Gulf War Syndrome via a questionnaire and 152 age and gender matched controls were studied. PON1 activity, concentration, and genotype were determined. In the Gulf War Veterans, paraoxon hydrolysis was less than 50% of that found in the controls (100.3 (14.8-233.8) vs 214.6 (50.3-516.2) nmol/min/ml, P < 0.001). This low activity was independent of the effect of PON1 genotype. The serum PON1 concentration was also lower in the Gulf War Veterans (75.7 (18.1-351.3) vs 88.2 (34.5-527.4) microg/ml, P < 0.00025), which was again independent of PON1 genotype. There was no difference in the rate of diazoxon hydrolysis between the groups (10. 2 +/- 4.1 micromol/min/ml vs 9.86 +/- 4.4, P = NS). A decreased capacity to detoxify OP insecticides
resulting from low serum PON1 activity may have contributed to the development of Gulf War Syndrome.


Episodic exposures refer to intermittent acute exposures to chemicals that ordinarily have a rapid onset and short duration of effect. There has been a long tradition in preclinical behavioral pharmacology of using episodic-exposure paradigms in order to establish dose-response functions in individual organisms. In these experiments, stable baselines of behavior are first established and then followed by administering varying doses of a drug intermittently, for example, once or twice a week. The power of this approach is well established; the within-subjects design reduces error variance, allows exploration of the entire range of effective doses, and can be used to identify individual differences in drug sensitivity. Of course, the approach is only applicable to reversibly acting compounds, and checks need to be included to insure effects of one dose are not influenced by prior exposure to another dose. We have used baseline approaches to evaluate the effects of pesticides and solvents on the behavior of adult male rats and mice. Moreover, a novel probabilistic dose-tolerance analysis applied to the data suggests substantial individual differences in chemical sensitivity, often spanning orders of magnitude. These results suggest that individual differences in chemical sensitivity may be much greater than previously acknowledged.


We report exacerbation of symptoms and chemical intolerances in three of four self-described chemically sensitive women following relocation to a newly constructed office building. Levels of total volatile organic compounds (TVOCs) in this building prior to occupancy were approximately 200 µg/m³ (toluene equivalent units) with a myriad of individual components present. By day 50 after occupancy, the concentration of TVOCs in the building dropped to approximately 50 µg/m³. Nevertheless, three women reported significant worsening of their symptoms with spreading of their sensitivities to previously tolerated chemical exposures. One woman relocated to another building, while the other two managed their symptoms by reducing time spent in the building or by using a room air cleaner. By day 600 following occupancy, although TVOCs had increased significantly (perhaps due to cleaning agents), there were fewer individual VOCs present in the air, and some of the women were able to tolerate the air in the building. We conclude that complex mixtures of VOCs at very low levels tolerated by the majority of building occupants may pose problems for persons who report pre-existing chemical sensitivities. TVOC measurements may not correlate with symptoms in these individuals. Reasonable accommodations by an employer can reduce problem exposures, making it possible for some affected individuals to continue productive employment.

In earlier studies, we have shown that patients with a history of sensory hyperreactivity develop asthma-like symptoms when exposed to strong scents, even if they cannot smell any scent. METHODS: For study of possible pathophysiologic mechanisms behind sensory hyperreactivity, the patients' airways and eyes were separately exposed to a common inducing factor, perfume. Eleven patients with a history of hyperreactivity to chemical trigger factors, such as perfume, were provoked single-blindly in a placebo-controlled, randomized study. During airway exposure, the eyes were covered and, during the eye exposure, the patients inhaled fresh air. A special face mask or a nose clip was used to avoid any smell. RESULTS: During the 30-min exposure to perfume, there was a gradual increase in three main symptoms; i.e., eye irritation, cough, and dyspnea, after both the airway and eye exposures. The increases were significant compared with placebo. CONCLUSIONS: Asthma-like and other symptoms, such as irritation of the eyes, may be induced by exposure of both the airways and the eyes in patients with sensory hyperreactivity. This points to the importance of studying the sensory nervous system, not only in the airways, but also in other organs.


Patients complaining of upper and lower airway symptoms caused by scents and chemicals have previously been shown to have increased cough sensitivity to inhaled capsaicin, but the precise mechanisms behind this reaction are unknown. Hypothesizing that a neurochemical alteration related to sensory hyperreactivity (SHR) of the airway mucosa occurs, we measured levels of nerve growth factor (NGF) in nasal lavage fluid (NAL) before and after capsaicin inhalation provocations and related the capsaicin cough sensitivity to the NGF levels. Thirteen patients with SHR and 14 control subjects were provoked with capsaicin inhalation at three different doses. We measured NGF in NAL before and after provocation and recorded cough and capsaicin-induced symptoms. All subjects demonstrated a dose-dependent cough response to capsaicin inhalation, with a more pronounced effect in patients than in controls. Basal levels of NGF were significantly lower in the patient group than in the control subjects (p < 0.01). After capsaicin provocation, the patients showed a significant increase in NGF (p < 0.01), which was related to capsaicin cough sensitivity. The findings demonstrate that, in patients with airway symptoms induced by scents and chemicals, SHR is real and measurable, demonstrating a pathophysiology in the airways of these patients compared to healthy subjects.


Newlin's [Newlin D.B. Evolutionary game theory of tolerance and sensitization in substance abuse. Paper presented to the Research Society on Alcoholism, Hilton Head, SC, 1998] evolutionary game theory of addictive behavior specifies how evolutionarily stable strategies for survival and reproduction may lead to addiction. The game theory of multiple chemical sensitivity (MCS) assumes that: (1) the MCS patient responds to low-level toxicants as stressors or as direct threats to their survival and reproductive fitness, (2) this activates the cortico-mesolimbic dopamine system, (3) this system is a survival motivation center—not a `reward center', (4) the subject emits a counter-response that is in the same direction as the naive response to the chemicals, (5) previously neutral stimuli associated with chemicals also trigger conditioned
responses that mimic those to the chemicals, (6) these counter-responses further activate the dopaminergic survival motivation system, and (7) this produces a positive feedback loop that leads to strong neural sensitization in these structures and in behavior controlled by this system, despite a small initial response. Psychologically, the MCS patient with a sensitized cortico-mesolimbic dopamine system is behaving as though his/her survival is directly threatened by these chemicals. Non-MCS subjects have counter-responses opposite in direction to those of the chemicals and show tolerance. An autoshaping/sign-tracking model of this game is discussed. This evolutionary game makes several specific, testable predictions about differences between MCS subjects, non-MCS controls, and substance abusers in laboratory experiments, and between sensitized and nonsensitized animals.


As surgeons, otolaryngologists tend to most be interested in operative procedures and leave the hospital environment to the care of administrators and the nursing staff. Given the dangers that are present, it would seem prudent to spend some time considering the agents that are used in patient care and in operating suites, to minimize the risk to patients and co-workers.


Some individuals report that, following either a single high-level or repeated lower-level exposures to chemicals (initiation), subsequent exposure to very low concentrations of chemicals (triggering) produces a variety of adverse effects, including disruption of cognitive processes. Our objective was to model this two-step process in a laboratory animal. Two groups of 16 rats, eight male and eight female, received whole-body inhalation exposure to toluene, either at 80 ppm for 6 h/day for 4 weeks (Repeat group) or to 1600 ppm for 6 h/day on one day only (Acute group). Two other groups (Trigger group and Clean group) of 16 were sham-exposed. After 17 days without toluene exposure, the Acute, Repeat and Trigger groups began a series of daily toluene 'trigger' exposures (10 ppm for 1 h) followed immediately by testing on an operant repeated-acquisitions task requiring learning within and across sessions. The Clean group was sham-exposed prior to operant testing. Trigger or sham exposures and operant testing continued 5 days/week for 17 sessions. Analysis of variance revealed a variety of statistically significant ($P<0.05$) differences between treatment groups. Furthermore, the patterns of differences between groups differed ($P<0.05$) for female and male rats. For example, male rats of the Trigger group made the most responses, and female rats of the Repeat group responded most slowly. The observation of important changes in the operant behavior of female and male rats previously exposed to toluene, at relatively low concentrations (80 or 1600 ppm) and then later re-exposed at very low concentrations (10 ppm), is consistent with the experiences of humans reporting cognitive difficulties following acute or chronic exposures to chemicals.

The subset of patients reporting chemical sensitivity with neurocognitive complaints usually exhibits specific abnormalities of brain metabolism consistent with neurotoxicity, on imaging with single photon emission computed tomography (SPECT). These recurrent neurotoxic patterns are characterized by a mismatch in tracer uptake between early-and late-phase imaging, multiple hot and cold foci throughout the cortex, temporal asymmetry and increased tracer uptake into the soft tissues and, sometimes, the basal ganglia. Previous studies confirm these neurotoxic findings in patients with neurotoxic chemical exposures and breast implants. Affective processes such as depression do not, alone, show this pattern. These abnormalities in SPECT images correlate with documented neurocognitive impairment. Controlled challenges to ambient chemicals can induce profound neurotoxic changes seen on SPECT imaging in chemically sensitive patients. Detoxification treatment techniques frequently produce significant improvement on brain SPECT brain imaging in these patients. Neurotoxicity appears to be characteristic in many cases of chemical sensitivity.


A case history of the induction of asthma and chemical sensitivity in a 42-year-old registered nurse illustrates several of the characteristic features of multiple chemical sensitivity (MCS). This patient's problems started shortly after moving into a new home under construction, with associated chemical exposures. Other MCS patients report the onset of the condition with other chemical exposures such as those encountered at their places of work or use of pesticides at their residences. Patients often describe a spreading phenomenon of increasing intolerance to commonly encountered chemicals at concentrations well tolerated by other people. Symptoms usually wax and wane with exposures, and are more likely to occur in patients or families with preexisting histories of migraine or with classical allergies. Idiosyncratic medication reactions (especially to preservative chemicals) are common in MCS patients, as are dysautonomia symptoms (such as vascular instability) and poor temperature regulation. Myalgia and joint pains and food intolerance are common features as well. Contamination with xenobiotic chemicals is frequently found in these patients when they are tested. Reactive airways dysfunction syndrome is a recently identified condition that exhibits features of both asthma and chemical sensitivity. MCS patients frequently have patterns of neurotoxic brain metabolism that can be confirmed on single photo emission computed tomography imaging.


It has been suggested that the neurobehavioral dysfunction observed in persons presenting with symptoms of Multiple Chemical Sensitivity (MCS) syndrome involves sensitization of neural circuits. Two hypotheses for the route of exposure in induction of neural sensitization in MCS are: (a) direct chemical stimulation of olfactory processes, or (b) general systemic response to inhaled chemicals. In either case, the mechanism of action may involve chemical kindling or kindling-related phenomena. A neural sensitization mechanism based on kindling or kindling-related phenomena is attractive and has been previously demonstrated in both in vitro and in vivo animal models. Without a testable animal model for chemically mediated induction of MCS, however, any argument that MCS is mediated by kindling or kindling-related phenomena is reduced to the circular argument "the mechanism of sensitization is sensitization." The present
survey provides an overview of the experimental paradigms that result in sensitization, differentiated on the basis of probable neurophysiological and neurochemical mechanisms. Neurophysiological potentiation, electrical kindling, chemical kindling and behavioral sensitization are evaluated and discussed in relationship to MCS.


The central nervous, immune, and endocrine systems communicate through multiple common messengers. Over evolutionary time, what may be termed integrated defense system(s) (IDS) have developed to coordinate these communications for specific contexts; these include the stress response, acute-phase response, nonspecific immune response, immune response to antigen, kindling, tolerance, time-dependent sensitization, neurogenic switching, and traumatic dissociation (TD). These IDSs are described and their overlap is examined. Three models of disease production are generated: damage, in which IDSs function incorrectly; inadequate/inappropriate, in which IDS response is outstripped by a changing context; and evolving/learning, in which the IDS learned response to a context is deemed pathologic. Mechanisms of multiple chemical sensitivity (MCS) are developed from several IDS disease models. Model 1A is pesticide damage to the central nervous system, overlapping with body chemical burdens, TD, and chronic zinc deficiency; model 1B is benzene disruption of interleukin-1, overlapping with childhood developmental windows and hapten-antigenic spreading; and model 1C is autoimmunity to immunoglobulin-G (IgG), overlapping with spreading to other IgG-inducers, sudden spreading of inciters, and food-contaminating chemicals. Model 2A is chemical and stress overload, including comparison with the susceptibility/sensitization/triggering/spreading model; model 2B is genetic mercury allergy, overlapping with: heavy metals/zinc displacement and childhood/gestational mercury exposures; and model 3 is MCS as evolution and learning. Remarks are offered on current MCS research. Problems with clinical measurement are suggested on the basis of IDS models. Large-sample patient self-report epidemiology is described as an alternative or addition to clinical biomarker and animal testing.


Objective: To examine analytically the question of whether the characterization of somatoform disorders (SFDs) in Diagnostic and Statistical Manual, Fourth Edition (DSM-IV) provides adequate grounds for classifying them as mental disorders rather than as physical disorders.

Methods: Analytical examination.

Results: There are prima facie grounds for classifying SFDs as physical disorders since they are characterized by physical symptoms. The characterization of SFDs in DSM-IV does not provide adequate grounds for classifying them as mental disorders.

Conclusion: The spectrum of SFDs is drawn too widely in DSM-IV. At least some of the conditions now listed as SFDs in DSM-IV should be either given a dual diagnosis or classified simply as physical disorders.
Multiple chemical sensitivity (MCS) is characterized by chemically induced symptoms from multiple organ systems. No consistent physical findings or laboratory abnormalities have been determined for the associated symptoms. Twelve patients with chemically induced airway symptoms, who satisfied Cullen’s criteria for MCS, were provoked double-blind, randomized with saline and three increments of inhaled capsaicin. The recordings were compared with those of a control group of healthy individuals. The results found that the patients coughed more than the control subjects at each dose of capsaicin (P < 0.05 for 0.4 _mol/L capsaicin and P < 0.005 for 2 _mol/L and 10 _mol/L). The capsaicin provocation also induced significantly more symptoms in patients with MCS. We conclude that airway sensory reactivity is increased in patients with MCS, a finding which suggests that neurogenic factors may be of importance in this condition.


The health effects of low-dose occupational exposure to organic solvents remains unclear. A cross-sectional survey was conducted among 762 male printing workers to assess the impacts of exposure to mixtures of n-hexane, toluene, isopropyl alcohol, and benzene on neurological and other symptoms. After controlling for age, smoking, alcohol drinking, past exposure history, working hours and shift work, current exposure to solvent mixtures was significantly associated with the total number of neurological symptoms and with the prevalence of specific symptoms of the nervous system and mucous membrane irritation. The adjusted odds ratio of neurovegetative lability (1.7–5.9), abnormal or reduced smell (1.6–4.1), memory loss (1.8), and mucous membrane irritation symptoms (1.5– 4.6) significantly increased in the exposed group, especially when the summation index of exposure exceeded one.


BACKGROUND: Published epidemiological information relating the effects of occupational exposure to organic solvents (OS) to olfaction is limited. AIMS: The objectives of this pilot study were to measure the chemosensory abilities of medical laboratory employees occupationally exposed to OS mixtures, to compare these with control workers employed within the same occupational setting and to correlate chemosensory performance with OS exposure history and with employees' hedonic (pleasantness) perceptions about workplace OS odors. METHODS: Twenty-four medical laboratory employees (OS-exposed technicians plus control workers minimally exposed to OS) completed a health-related questionnaire, a test of pyridine odor detection threshold, along with a gustatory detection threshold test involving aqueous quinine solutions. Estimates of cumulative hours of OS exposure (CSI) were calculated from self-reports. RESULTS: OS-exposed laboratory technicians detected weaker concentrations of pyridine odor. Positive correlations were detected between CSI estimates to both pyridine
detection and the degree that participants reported that OS odors were present in the workplace. However, no association was detected between pyridine detection and how unpleasant workplace OS odors were perceived. The OS-exposed participants were able to detect weaker concentrations of quinine. Compared to controls, OS-exposed workers complained more of experiencing several symptoms while working, including headaches, nasal irritation and mild cognitive impairment. CONCLUSIONS: The results of this cross-sectional pilot study indicated that, compared to controls, medical laboratory technicians exposed to low-level OS mixtures displayed evidence of elevated olfactory sensitivity (hyperosmia) to pyridine odor. The relation of this study's results to chemical intolerance warrants further investigation.


Exposures which can induce multiple chemical sensitivity (MCS) involve symptomatic, usually repeated, exposures to pesticides, solvents, combustion products, remodeling, sick buildings, carbonless copy paper (occupational heavy use) and other irritants and petrochemicals. Accompanying toxic injury often involves the immune, endocrine and nervous systems as well as impairments in detoxification, energy and neurotransmitter metabolism, protein, mineral, and other nutrient deficiencies and gastrointestinal changes such as candida, parasites, reduced chymotrypsin (marker enzyme for reduced pancreatic enzyme function), gluten intolerance, and reduced Secretory IgA. Chronic cortisol elevation leading to adrenal insufficiency if not corrected is common. Such elevation can lead to protein and mineral deficiencies with increased osteoporosis and reduced steroid precursors for normal estrogen and testosterone production. Detoxification changes often involve reduction in one or more Phase II pathways which causes excess free radical production. Impaired digestive enzymes can reduce breakdown of foods, with larger more antigenic molecules being absorbed and consequent food intolerances. Many of these conditions are treatable. There is extensive overlap of MCS with Chronic Fatigue Syndrome and Fibromyalgia which may be one condition in many cases. Current occupational exposure limits are not health based and thus may not prevent MCS and are totally inadequate to accommodate sensitive persons. Warning symptoms indicating increased risk for MCS onset include repeated headache, eye and respiratory irritation and fatigue. Eliminating exposures which cause repeated symptoms is a critical strategy for preventing sensitization and MCS. It also significantly reduces the degree of disability in persons with MCS, the single most important factor from the literature. Affected persons with disability can utilize the Americans With Disability Act to request reasonable accommodations for work, home (condo, apartment), and school.
Appendix: Related Articles


To evaluate whether emissions of a commercial air freshener produced acute toxic effects in a mammalian species, the authors allowed male Swiss-Webster mice to breathe the emissions of one commercial-brand solid air freshener for 1 h. Sensory irritation and pulmonary irritation were evaluated with the ASTM-E-981 test. A computerized version of this test measured the duration of the break at the end of inspiration and the duration of the pause at the end of expiration--two parameters subject to alteration via respiratory effects of airborne toxins. Measurements of expiratory flow velocity indicated changes in airflow limitation. The authors then subjected mice to a functional observational battery, the purpose of which was to probe for changes in nervous system function. Emissions of this air freshener at several concentrations (including concentrations to which many individuals are actually exposed) caused increases in sensory and pulmonary irritation, decreases in airflow velocity, and abnormalities of behavior measured by the functional observational battery score. The test atmosphere was subjected to gas chromatography/mass spectroscopy, and the authors noted the presence of chemicals with known irritant and neurotoxic properties. The Material Safety Data Sheet for the air freshener indicated that there was a potential for toxic effects in humans. The air freshener used in the study did not diminish the effect of other pollutants tested in combination. The results demonstrated that the air freshener may have actually exacerbated indoor air pollution via addition of toxic chemicals to the atmosphere.


To evaluate whether fragrance products can produce acute toxic effects in mammals, we allowed groups of male Swiss-Webster mice to breathe the emissions of five commercial colognes or toilet water for 1 h. We used the ASTM-E-981 test method to evaluate sensory irritation and pulmonary irritation. We used a computerized version of this test to measure the duration of the break at the end of inspiration and the duration of the pause at the end of expiration. Decreases in expiratory flow velocity indicated airflow limitation. We subjected the mice to a functional observational battery to probe for changes in nervous system function. The emissions of these fragrance products caused various combinations of sensory irritation, pulmonary irritation, decreases in expiratory airflow velocity, as well as alterations of the functional observational battery indicative of neurotoxicity. Neurotoxicity was more severe after mice were repeatedly exposed to the fragrance products. Evaluation of one of the test atmospheres with gas chromatography/mass spectrometry revealed the presence of chemicals for which irritant and neurotoxic properties had been documented previously. In summary, some fragrance products emitted chemicals that caused a variety of acute toxicities in mice.

To determine whether there is any biological basis for complaints that fabric softener emissions can cause acute adverse effects in certain individuals, screening tests were performed in which groups of mice were exposed to the emissions of 5 commercial fabric softener products (antistatic pads used in laundry dryers) for 90 min. Pneumotachographs and a computerized version of ASTM test method E-981 were used to measure acute changes in several respiratory cycle parameters, especially the pause after inspiration, the pause after expiration, and the midexpiratory airflow velocity. From these changes, sensory irritation (SI), pulmonary irritation (PI), and airflow limitation (AFL) of differing intensities were measured with each of the five brands tested. At the peak effect, SI ranged from 21 to 58% of the breaths, PI ranged from 4 to 23% of the breaths, and AFL ranged from 6 to 32% of the breaths. After three exposures, histopathology revealed mild inflammation of interalveolar septae of the lungs. Gas chromatography/ mass spectroscopy (GC/MS) analysis of the emissions of one pad identified several known irritants (isopropylbenzene, styrene, trimethylbenzene, phenol, and thymol). Laundry that had been dryed with one the fabric softener pads emitted sufficient chemicals to elicit SI in 49% of breaths at the peak effect. Placing one fabric softener pad in a small room overnight resulted in an atmosphere that caused marked SI (61% of breaths). These results demonstrate that some commercial fabric softeners emit mixtures of chemicals that can cause SI, PI, and reduce midexpiratory airflow velocity in normal mice. The results provide a toxicological basis to explain some of the human complaints of adverse reactions to fabric softener emissions.


Mice were monitored with pneumotachographs while they breathed emissions of three brands of disposable diapers (described herein as brands A, B, and C) and one brand of cloth diapers for 1 hr. The authors used a computerized version of the ASTM-E-981 test method to measure changes in the pattern and frequency of respiration. In response to two brands of disposable diapers, many mice exhibited reduced mid-expiratory airflow velocity, sensory irritation, and pulmonary irritation. During the peak effects, brand A caused sensory irritation in 47% of the breaths and reduced mid-expiratory airflow velocity in 17% of the breaths (n = 39 mice), whereas the respective percentages noted for brand B were 20% and 15% of the breaths (n = 28 mice). The effects were generally larger during repeat exposures to these emissions, with up to 89% of breaths showing sensory irritation in response to brand A and up to 35% of breaths showing reduced mid-expiratory airflow velocity with brand B. A third brand of disposable diapers caused increases in respiratory rate, tidal volume, and mid-expiratory airflow velocity. The emissions of cloth diapers produced only slight SI and slight PI. Chemical analysis of the emissions revealed several chemicals with documented respiratory toxicity. The results demonstrate that some types of disposable diapers emit mixtures of chemicals that are toxic to the respiratory tract. Disposable diapers should be considered as one of the factors that might cause or exacerbate asthmatic conditions.

To evaluate complaints of adverse reactions to marking pen emissions, groups of mice were exposed for 1 h to the emissions of 8 brands of felt-tip markers or white-board cleaner. Pneumotachographs and a computerized version of ASTM E-981 test method were used to measure changes in respiration. Sensory irritation (SI), pulmonary irritation (PI), and/or air flow limitation (AFL) of differing intensities were documented with each of the eight brands tested. At the peak of the effects, the largest SI was observed with pen F (72% of the breaths); the largest PI occurred with pen D (13% of the breaths), and the largest AFL was seen with pen F (25% of the breaths). Pens G and H produced minimal SI, PI, or AFL. A functional observational battery was used to screen for signs of neurotoxicity. Emissions from all eight of the pens produced behavioral abnormalities such as altered posture and gait, tremors, falling, and hyperactivity. The exposure concentrations were similar to the total volatile organic compounds (TVOC) values near marking pens in actual use. Gas chromatography identified mixtures of alcohols, acetates, and/or ketones. Exposures to white-board cleaner solution resulted in similar toxicity (SI, PI, AFL, and neurotoxicity). These results document that some marking pens and white-board cleaner emit mixtures of chemicals that can produce acute respiratory toxicity and acute behavioral abnormalities in normal mice. These results provide a toxicological explanation for some of the human complaints concerning respiratory and neurological reactions to marking pen emissions.


Groups of male Swiss-Webster mice breathed emissions of several brands of crib mattresses for two 1-hr periods. The authors used a computerized version of ASTM-E-981 test method to monitor respiratory frequency, pattern, and airflow velocity and to diagnose abnormalities when statistically significant changes appeared. The emissions of four mattresses caused various combinations of upper-airways irritation (i.e., sensory irritation), lower-airways irritation (pulmonary irritation), and decreases in mid-expiratory airflow velocity. At the peak effect, a traditional mattress (wire springs with fiber padding) caused sensory irritation in 57% of breaths, pulmonary irritation in 23% of breaths, and airflow decrease in 11% of breaths. All mattresses caused pulmonary irritation, as shown by 17-23% of breaths at peak. The largest airflow decrease (i.e., affecting 26% of the breaths) occurred with a polyurethane foam pad covered with vinyl. Sham exposures produced less than 6% sensory irritation, pulmonary irritation, or airflow limitation. Organic cotton padding caused very different effects, evidenced by increases in both respiratory rate and tidal volume. The authors used gas chromatography/mass spectrometry to identify respiratory irritants (e.g., styrene, isopropylbenzene, limonene) in the emissions of one of the polyurethane foam mattresses. Some mattresses emitted mixtures of volatile chemicals that had the potential to cause respiratory-tract irritation and decrease airflow velocity in mice.


To evaluate factors that might contribute to the rise in prevalence of childhood asthma, we allowed groups of male Swiss-Webster mice to breath the emissions of six brands of waterproof crib mattress covers for 1 h. We used a computerized version of ASTM-E-981 test method to monitor respiratory frequency, pattern, and airflow velocity. Single exposure to the emissions of
these mattress covers caused various combinations of sensory irritation, pulmonary irritation, and decreases in mid-expiratory airflow velocity. At the peak effects of these emissions, sensory irritation ranged from 9% to 51% of the breaths, pulmonary irritation ranged from 4% to 16% of the breaths, and airflow limitation ranged from 9% to 38% of the breaths. Three brands caused airflow limitation that persisted for at least 24 h after a single 1-h exposure of naive mice to these emissions. Repeat exposures to the emissions of four brands caused more marked effects (i.e., up to 96% of the breaths showing sensory irritation, up to 44% of the breaths showing pulmonary irritation, and up to 75% of the breaths showing airflow limitation). Histological evaluation of the lungs revealed a mild inflammatory response, with focal collections of polymorphonuclear leukocytes and edema, but there were no eosinophils and no bronchial mucosa changes. We used gas chromatography/mass spectrometry to evaluate one of the test atmospheres, and there was evidence of chemicals for which toxic properties have been documented previously. The results of our study demonstrated that some mattress covers emit mixtures of chemicals that can cause a variety of acute toxic effects in mice, including asthma-like reactions.


Products containing scent are a part of daily life. The majority of cosmetics, toiletries, household and laundry products contain fragrance. In addition, there is exposure to fragrance from products that are used to scent the air, such as air fresheners and fragranced candles. In spite of this widespread use and exposure, there is little information available on the materials used in fragrance. Fragrance formulas are considered trade secrets and components that make up the fragrance portion of the product are not revealed on labels. Fragrance is increasingly cited as a trigger in health conditions such as asthma, allergies and migraine headaches. In addition, some fragrance materials have been found to accumulate in adipose tissue and are present in breast milk. Other materials are suspected of being hormone disruptors. The implications are not fully known, as there has been little evaluation of systemic effects. There are environmental concerns as well, as fragrances are volatile compounds, which add to both indoor and outdoor air pollution. Synthetic musk compounds are persistent in the environment and contaminate waterways and aquatic wildlife. At present there is little governmental regulation of fragrance. The fragrance industry has in place a system of self-regulation. However, the present system has failed to address many of the emerging concerns. Industry needs to responsibly address concerns and ensure that scented products are safe for users, those inadvertently exposed and the environment. It is essential that an industry that is, and wishes to continue to be, self-regulated should identify and address concerns in a forthright and responsible manner.


Exposure to volatile organic compounds (VOCs) in the indoor environment has received substantial research attention in the past several years, with the goal of better understanding the impact of such exposures on human health and well-being. Many VOCs can arise from consumer products used within the indoor environment. The VOCs emitted from five representative consumer products were collected onto Tenax-GC and subjected to thermal desorption and
analysis by gas chromatography, in combination with low-resolution mass spectrometry (MS), high-resolution MS, and matrix-isolation Fourier transform infrared spectroscopy for structural characterization. An emphasis was placed on the polar organic compounds often used to provide fragrance in these products. The structures of a number of these compounds were confirmed, and an electronic literature search was carried out on them to determine any known toxic properties. The search revealed that many of the VOCs possess toxic properties when studied at acute, relatively high-level exposures. In addition, toxic effects were reported for a few of the chemicals, such as benzaldehyde, alpha-terpineol, benzyl acetate, and ethanol, at relatively low dose levels of 9-14 mg/kg. In general, the data were unclear as to the effect of chronic, low-level exposures. The widespread use of such chemicals suggests that the health effects of chronic exposures need to be determined. Validated analytical methods for the quantitative characterization of polar organic compounds at low concentrations will be required to make such work possible.


Ozone-driven chemistry is a source of indoor secondary pollutants of potential health concern. This study investigates secondary air pollutants formed from reactions between constituents of household products and ozone. Gas-phase product emissions were introduced along with ozone at constant rates into a 198-L Teflon-lined reaction chamber. Gas-phase concentrations of reactive terpenoids and oxidation products were measured. Formaldehyde was a predominant oxidation byproduct for the three studied products, with yields for most conditions of 20-30% with respect to ozone consumed. Acetaldehyde, acetone, glycolaldehyde, formic acid, and acetic acid were each also detected for two or three of the products. Immediately upon mixing of reactants, a scanning mobility particle sizer detected particle nucleation events that were followed by a significant degree of secondary particle growth. The production of secondary gaseous pollutants and particles depended primarily on the ozone level and was influenced by other parameters such as the air-exchange rate. Hydroxyl radical concentrations in the range 0.04-200 x 10(5) molecules cm(-3) were determined by an indirect method. OH concentrations were observed to vary strongly with residual ozone level in the chamber, which was in the range 1-25 ppb, as is consistent with expectations from a simplified kinetic model. In a separate chamber study, we exposed the dry residue of two products to ozone and observed the formation of gas-phase and particle-phase secondary oxidation products.


Phthalates are multifunctional chemicals used in a variety of applications, including personal care products. The present study explored the relationship between patterns of personal care product use and urinary levels of several phthalate metabolites. Subjects include 406 men who participated in an ongoing semen quality study at the Massachusetts General Hospital Andrology Laboratory between January 2000 and February 2003. A nurse-administered questionnaire was
used to determine use of personal care products, including cologne, aftershave, lotions, hair products, and deodorants. Phthalate monoester concentrations were measured in a single spot urine sample by isotope dilution-high-performance liquid chromatography coupled to tandem mass spectrometry. Men who used cologne or aftershave within 48 hr before urine collection had higher median levels of monoethyl phthalate (MEP) (265 and 266 ng/mL, respectively) than those who did not use cologne or aftershave (108 and 133 ng/mL, respectively). For each additional type of product used, MEP increased 33% (95% confidence interval, 14-53%). The use of lotion was associated with lower urinary levels of monobutyl phthalate (MBP) (14.9 ng/mL), monobenzyl phthalate (MBzP) (6.1 ng/mL), and mono(2-ethylhexyl) phthalate (MEHP) (4.4 ng/mL) compared with men who did not use lotion (MBP, 16.8 ng/mL; MBzP, 8.6 ng/mL; MEHP, 7.2 ng/mL). The identification of personal care products as contributors to phthalate body burden is an important step in exposure characterization. Further work in this area is needed to identify other predictors of phthalate exposure.


Four outcomes that evidence suggests are candidates for "environmental causation" were chosen for analysis: diabetes, Parkinson's disease (PD), neurodevelopmental effects and hypothyroidism, and deficits in intelligence quotient (IQ). These are an enormous burden in the United States, Canada, and other industrial countries. We review findings on actual social and economic costs, construct estimates of some of the costs from pertinent sources, and provide several hypothetical examples consistent with published evidence. Many detailed costs are estimated, but these are fragmented and missing in coverage and jurisdiction. Nonetheless, the cumulative costs identified are very large, totaling $568 billion to $793 billion per year for Canada and the United States combined. Partial Canadian costs alone are $46 billion to $52 billion per year. Specifics include diabetes (United States and Canada), $128 billion per year; PD in the United States, $13 billion to $28.5 billion per year; neurodevelopmental deficits and hypothyroidism are endemic and, including estimates of costs of childhood disorders that evidence suggests are linked, amount to $81.5 billion to $167 billion per year for the United States and $2 billion per year in Ontario; loss of 5 IQ points cost $30 billion per year in Canada and $275 billion to $326 billion per year in the United States; and hypothetical dynamic economic impacts cost another $19 billion to $92 billion per year for the United States and Canada combined. Reasoned arguments based on the weight of evidence can support the hypothesis that at least 10%, up to 50% of these costs are environmentally induced--between $57 billion and $397 billion per year.


Fragranced consumer products—such as air fresheners, laundry supplies, personal care products, and cleaners—are widely used in homes, businesses, institutions, and public places. While prevalent, these products can contain chemicals that are not disclosed to the public through product labels or material safety data sheets (MSDSs). What are some of these chemicals and what limits their disclosure? This article investigates these questions, and brings new pieces of evidence to the science, health, and policy puzzle. Results from a regulatory analysis, coupled
with a chemical analysis of six best-selling products (three air fresheners and three laundry supplies), provide several findings. First, no law in the U.S. requires disclosure of all chemical ingredients in consumer products or in fragrances. Second, in these six products, nearly 100 volatile organic compounds (VOCs) were identified, but none of the VOCs were listed on any product label, and one was listed on one MSDS. Third, of these identified VOCs, ten are regulated as toxic or hazardous under federal laws, with three (acetaldehyde, chloromethane, and 1,4-dioxane) classified as Hazardous Air Pollutants (HAPs). Results point to a need for improved understanding of product constituents and mechanisms between exposures and effects.


United States environmental regulations, intended to protect human health, generally fail to address major sources of pollutants that endanger human health. These sources are surprisingly close to us and within our control, such as consumer products and building materials that we use within our homes, workplaces, schools, and other indoor environments. Even though these indoor sources account for nearly 90% of our pollutant exposure, they are virtually unregulated by existing laws. Even pollutant levels found in typical homes, if found outdoors, would often violate federal environmental standards. This article examines the importance of human exposure as a way to understand and reduce effects of pollutants on human health. Results from exposure studies challenge traditional thinking about pollutant hazards, and reveal deficiencies in our patchwork of laws. And results from epidemiological studies, showing increases in exposure-related diseases, underscore the need for new protections. Because we cannot rely solely on regulations to protect us, and because health effects from exposures can develop insidiously, greater efforts are needed to reduce and prevent significant exposures before they occur. Recommendations include the development and use of safer alternatives to common products, public education on ways to reduce exposure, systematic monitoring of human exposure to pollutants, and a precautionary approach in decision-making.