Environmental Medicine, Part 2 – Health Effects of and Protection from Ubiquitous Airborne Solvent Exposure

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Abstract
Chemicals known as solvents are part of a broad class of chemicals called volatile organic compounds. These compounds are used in a variety of settings, are ubiquitous, and off-gas readily into the atmosphere. As a result of their overuse, they can be found in detectable levels in virtually all samples of both indoor and outdoor air. Certain of these compounds are detectable in adipose samples of all U.S. residents. Once in the body they can lead to a variety of neurological, immunological, endocrinological, genitourinary, and hematopoietic problems. Some individuals also have metabolic defects that diminish the liver's clearing capacity for these compounds. Supplementation may be of benefit to help clear these compounds from the body and to prevent adverse health effects.
(*Altern Med Rev* 2000;5(2):133-143)

Indoor Air – Home

In 1985, the Total Exposure Assessment Methodology (TEAM) study by the U.S. Environmental Protection Agency (EPA) changed the way indoor air quality was viewed. This study showed the greatest personal exposure to volatile organic compounds (VOCs) occurs from air in the home and not from outside air as had previously been thought. EPA looked for the presence of 20 VOCs, commonly known as solvents, in indoor air, outdoor air, respired air, and personal air in a total of 780 people. Personal air was sampled by attaching sampling cartridges to clothing. Personal air samples revealed very high exposure to eleven VOCs (see Table 1), in levels much higher than would have been predicted by outdoor air levels. The biggest source of personal exposures came from indoor air, which showed much higher levels of VOCs, especially at night, than what was measurable in the back yard of the same home during the same time frame.[1,2]

The compounds found most commonly were: paradichlorobenzene (mothballs and room deodorizers), styrene (plastics, foam rubber, and insulation), tetrachloroethylene (dry cleaning), vinylidene chloride (plastics), xylene (paints), and benzene and ethylbenzene from gasoline. Higher levels were found in the respired air of smokers than in non-smokers, confirming earlier work that showed smoking increased the alveolar retention of inhaled chemicals. Higher levels of benzene, xylene, and tetrachloroethylene in personal sample cartridges after the individual visited a gas station or a dry cleaning establishment were also reported. Individuals working in dry cleaning businesses obviously have much higher exposures than their patrons;

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however, the dry cleaner staff also bring tetrachloroethylene (also known as perchloroethylene) home with them, presumably on clothing, hair, and in the lungs. Significantly higher levels of tetrachloroethylene are found in the indoor air of the homes of dry cleaner workers than in selected control homes, leading to increased family exposure as well.[3]

Studies conducted prior to and reviewed in the TEAM study showed fairly consistent results in more than 800 homes. All reported that every one of the 40 or more VOCs studied were found in higher levels indoors than outdoors, often 10 times higher. The sources for these compounds were numerous, and included: building materials, furnishings, dry-cleaned clothes, cigarettes, gasoline, cleansers, moth crystals, hot showers, and printed materials. These studies also found the ranges of concentration were great, often with two or more orders of magnitude difference. Not only have repeated studies shown the amount of solvents the entire population is exposed to, they have also shown those who are exposed must pass these solvents through their bodies. As mentioned earlier, dichlorobenzene, from mothballs and room deodorizers, was one of the solvents found in high concentrations in indoor air. The metabolite of dichlorobenzene has been found in the urine of 96 percent of all children in Arkansas and in 98 percent of 1,000 selected adults from across the United States.[4]

The elevated levels of these compounds in household air can be attributed to two factors. First, as a result of the "oil shortage" in the 1970s, building techniques were changed to emphasize airtight, energy-efficient homes. New building methods emphasized a reduction in incidental exchange of inside and outside air so the internal home climate would not diffuse, and therefore less energy would be needed to maintain temperature. As a consequence of reducing inside air exchange, newer homes retain off-gassed VOCs in higher levels than older, less airtight homes.

Second, during the same time frame a tremendous increase began in the use of VOC-containing compounds in building materials, fabrics, and home furnishings. The use of standard plywood gave way to less-costly chipboard with higher formaldehyde and VOC content. Plywood laminate beams with not insignificant formaldehyde content replaced solid wood beams. Flooring changed from hardwood to plywood with pad and carpeting, all of which off-gas VOCs. The 1970s also saw changes in home-furnishing materials that put VOCs into indoor air. Polyurethane foam and polyester fiberfill replaced traditional upholstery fillers in sofas and chairs, and synthetic fabrics replaced cotton, rayon, and silk in draperies and upholstery. Upholstery fabrics contain formaldehyde to prevent them from wrinkling when sat upon. Plastic items, off-gassing phthalates, are now found throughout the home. The prevalence of home offices, with computers, fax machines, and copiers, has increased the amount of ozone, plastic fumes, and VOCs present in homes. These items, in addition to paint, glue, gas heating, gas appliances, attached garages with storage of paints, paint thinner, gasoline, pesticides, and herbicides, as well as biological contaminants of molds and bacteria all contribute to a toxic home environment. Table 2 lists the categories of indoor air pollutants.

Table 1: Volatile Organic Compounds Found Consistently in Breath Samples in the TEAM Study

Chloroform
1,1,1-Trichloroethane
Benzene
Carbon Tetrachloride
Trichloroethylene
Tetrachloroethylene
Styrene
m,p-Dichlorobenzene
Ethylbenzene
o-Xylene
m,p-Xylene

Table 2: Categories of Indoor Air Pollutants

1. Combustion by-products
2. Volatile organic compounds
3. Respirable dusts and particulates:
   - Molds
   - Cigarette smoke
   - Infectious agents
   - Animal dander
4. Bioaerosols
5. Contaminants generated by human activity

The unfortunate truth is, whether outdoors or indoors, at work or at home, solvents are being inhaled. The two worst places to have high solvent content in the air is the home, the place where people usually spend at least half of the day, and the workplace, where they spend at least eight hours.

Indoor Air – The Workplace

In office buildings the operational cost of quantity of ventilation has been given higher priority than quality of ventilation. The result has been more recycling of air, rather than a greater exchange of indoor air with outdoor air. Throughout the 1980s and 1990s there have been numerous instances of poorly-conceived and poorly-operated heating, ventilation, and air conditioning (HVAC) systems. HVAC systems almost uniformly have condensers, which provide a fertile place for proliferation of biological agents that contaminate air. This was first noted in the Legionnaire's disease outbreak, when 221 attendees at a 1976 American Legion conference in Philadelphia became ill from an airborne biological agent (later named *Legionella pneumophila*). The author knows of two office buildings of his patients in which the fresh air intake was in direct line with the heating system exhaust in one, and the underground garage in the other, both piping high levels of polycyclic aromatic hydrocarbons directly into the respective HVAC systems. With modular/cubicle office landscapes, containing carpeted floors and partitions, computers, fax machines, copiers, and laminated pressboard furniture, the level of formaldehyde, ozone, and VOCs is high in many office buildings. Often the levels of these compounds are within the threshold values industry has set for itself, but these levels can and do cause problems for certain individuals.

New or newly remodeled buildings have a substantial amount of chemical off-gassing and can easily become "sick buildings," with many workers getting "sick building syndrome" (SBS).[5,6] The most common presenting symptoms of SBS are: headache, dizziness, disorientation, difficulty concentrating, fatigue, and eye, nose and throat irritation.[7] When complaints of SBS first surfaced, complaining workers were often treated with disdain by building owners. Upon repeated complaints, building owners often hired air quality consultants who would test for the presence of a single compound, such as carbon monoxide. Quite often the individual compound would be well within the standard for air quality set by the EPA. In fact, this happened at EPA after completion of its new headquarters building in Washington, D.C., in 1988. Many EPA staffers began to complain of adverse health symptoms; the air was tested but no single agent was found to be out of range. However, when 71 ill employees evacuated the building claiming health problems – that went away when they were not in the building – and began picketing, the EPA realized the issue was real. The EPA's awakening resulted in the booklet entitled: The Inside Story, A Guide to Indoor Air Quality (September 1988, EPA/400/1-88/004). Table 3 lists the common VOCs emitted by standard building materials.[8]

Table 3: Volatile Organic Compounds Emitted from Building Materials and Interior Furnishings [8]

Source	Pollutant Emitted
Adhesives	Alcohols Amines Benzene Formaldehyde Terpenes
Caulking Compounds	Xylenes Alcohols Alkanes Amines Benzene Formaldehyde Methylketone Xylenes
Carpeting	Alcohols Alkanes Formaldehyde 4-Methylbenzene Styrene
Particle Board	Alcohols Alkanes Amines Benzene 3-Carene Formaldehyde Terpenes Toluene
Tile and linoleum Floor coverings Wall coverings	Acetates Alcohols Alkanes Amines Benzene Formaldehyde Methyl styrene Xylenes
Paints, stains, varnishes	Acetates Acrylates Alcohols Alkanes Amines Benzenes Formaldehyde

Carpet As a Major Source of Indoor Air Chemicals

Carpeting can be a significant factor in the emission of VOCs and retention of pesticide residues. When EPA finally investigated the cause of its toxic headquarters in 1988, they discovered the elevated VOC levels were attributable to new carpet, and eventually removed 27,000 square yards of carpet to make the building a more healthful place. A partial list of chemicals present in carpeting is presented in Table 4. It should be noted that these chemicals are the same as those EPA found in high levels in indoor air in the TEAM study, and which are also implicated in the Swedish SBS studies. Many of the compounds, including 4-phenylcyclohexene, TCE, benzene, xylene, toluene, styrene, the methylbenzenes, and others are known neurotoxins.

Because carpeting can have a profound neurotoxic effect via emission of these compounds, Anderson Labs began testing carpet for its effect on the immune system. They exposed mice to air that was blown over carpet samples and observed the resulting effects. In testing over 400 samples, they found neurotoxins present in more than 90 percent of the samples, including some that caused death.[9]

Carpeting and house dust both act as sinks for pesticides. In 1993, the EPA-sponsored "Non-Occupational Pesticide Exposure Study" (NOPES) was published.[11] This study confirmed the results of previous studies i.e., that indoor air is, indeed, more toxic than outdoor air. EPA's NOPES study, however, did not look at solvent levels but at pesticide levels. The EPA researchers found that concentrations of pesticides in indoor air were highest in summer and lowest in winter, corresponding with the seasonal patterns of pesticide use. In addition, they looked at dietary exposure to these compounds and exposure levels via dust and carpet fabric. Table 5 lists the pesticides that were found most frequently in the carpet.

Table 4: A partial list of chemicals present in carpet[10]

Formaldehyde	Azulene	Phthalic acid esters
TCE	Benzene	Xylene
Toluene	Methyl methacrylate	Methacrylic acid
Acetonitrile	Styrene	1-Chloronaphthalene
1-Ethyl-3-methylbenzene	Ethylzylene	1,2,3-Trimethylbenzene
1,2,4-Trimethylbenzene	Biphenyl	1-Methyl-3-Propylbenzene
4-Phenylcyclohexane	Isocyanates	Cyclopentadiene-ethenyl-2-ethylene
2-Butyloctanol-1	Diphenyl ether	Undecane, 2,6-Dimethyl
1,3,5-Cycloheptatriene	Butadiene	1,4-Dihydroxyacenophthene
Dodecane	Hexadecanol	Hexamethylene Triamine
1-Methylnaphthalaene	1-H-indene	2-Methylnaphthalene
1-Methyl-4-Tridecene	Polyacrylates	5-Methyltridecane
Octadecenyl Amine	Oxarium	Tetradecene
2,3,7-Trimethyldecane		

The carpet samples contained an average of 12 pesticide residues (of the pesticides being specifically tested for), while the air samples averaged 7.5 pesticides. Thirteen pesticides were found in dust that were not detected in air; these were less volatile compounds and therefore tended to stay where they landed.

The populations at greatest potential risk for exposure to carpet and dust-bonded pesticides are toddlers and infants. They spend the most time in contact with carpet and constantly put things from the carpet into their mouths. According to the NOPES study, this route of exposure likely provides infants and toddlers with nearly all of non-dietary exposure to DDT, aldrin, atrazine, and carbaryl. Knowing these compounds are recognized immunotoxins should encourage parents to take measures to reduce the level of these compounds in the home. Such measures would include removing carpeting, cleaning heater ducts, installing an air purifier, removing shoes before entering the house, and avoiding pesticide use in the home or garden.

Table 5: Pesticides Detected Most Frequently in Carpet Dust in NOPES Study

Heptachlor	DDT
Chlorpyrifos	ortho-Phenylphenol
Aldrin	Propoxur
Dieldrin	Diazinon
Chlordane	Carbaryl
Atrazine	

Outdoor Air

Many people who feel the air in the home or workplace is toxic may want to go outside for "some fresh air." Such individuals will ultimately be disappointed with what they might possibly inhale. Despite the "Clean Air Act," outdoor air is far from clean. Most of the available data on outdoor air pollution comes from emission rates disclosed by industry. While industry data may not provide the

Table 6: Steps to Avoid Voluntary Solvent Exposure

Avoid	Replace With
Dry-cleaned clothing	Clothing that doesn't need dry cleaning or wash them in Woolite
Fresh Paint	Low or no VOC paint (Benjamin Moore, or Best Paint)
Pumping your own gas	Carry a charcoal mask to wear when filling up
Household cleaners with solvents	Vinegar, Bon Ami, etc.
Cigarette smoke	Avoidance
New Carpeting	Hardwood floors with throw-rugs or used carpeting that has already off gassed
Solvent containing glues	Water based glues
Liquid paper	Spell check
Acrylic nails	Go without
Pesticide use in home or garden (All have inert ingredients that are usually solvents)	Organic pest control methods

entire emission picture, this data has been analyzed with dispersion models, wind speed, wind direction, meteorological conditions, and atmospheric stability. The results indicated that outdoor air concentrations of benzene, formaldehyde, and 1,3-butadiene were greater than cancer benchmark concentrations in over 90 percent of all the census tract areas in the contiguous United States. Approximately 10 percent of all the census tracts (mostly on the east coast) had estimated concentrations of one or more carcinogenic air pollutants at greater than a 1-in-10,000 risk level.[12]

Once it is understood that no matter where a person goes in a day they are likely to inhale solvents, proper action can be taken to help prevent the heath effects of inhaling such compounds.

Adverse Health Effects of Solvents

Solvents have a variety of adverse health effects. Part One of this series reviewed EPA's National Human Adipose Tissue survey that showed four solvents were present in 100 percent of tissue samples tested across the country: xylene, dichlorobenzene, ethylphenol, and styrene (listed in decreasing order).[13] For these solvents to be in the adipose tissue of every U.S. citizen tested that year confirms long-term, regular exposure to VOCs

for the entire population, and that these compounds are stored in the body's adipose tissue.

VOCs primarily act in the body as both peripheral and central nervous system neurotoxins.[14,15] When the central nervous system is primarily affected the symptoms can include diminished cognition, memory, reaction time, and hand-eye and foot-eye coordination, and balance and gait disturbances. Exposure can also lead to mood disorders, with depression, irritability, and fatigue being common symptoms. Peripheral neurotoxicity usually results in paresthesias, tremors, and diminished fine and gross motor movements.

VOCs have been implicated in kidney damage.[16-18] They have been associated with immunological problems, including increased cancer rates and immunotoxicity.[19] Solvents have been found to lower testosterone and LH,[20] and increase insulin and sex hormone binding globulin.[21,22] They have been associated with infertility,[23] decreased sperm count,[24] increased rates of spontaneous abortion,[25] and increased rates of fetal malformation.[26] They have also been associated with hematological disorders[27] and increased cardiovascular death rates.[28] Indoor air levels of solvents and formaldehyde are closely associated with increased rates of asthma and chronic bronchitis, especially in children.[29] The typical presentation of low-dose formaldehyde exposure includes upper respiratory irritations (rhinitis, sinusitis, pharyngitis), lower respiratory symptoms of wheezing, and persistent flu-like symptoms.[10]

Prevention and Treatment Options

It is abundantly clear that all persons are exposed to solvents on an everyday basis. Therefore, limiting such exposure must be achieved wherever possible. The first step in limiting exposure is avoidance of all voluntary exposures. See Table 6.

In addition to avoiding exposure to solvents as much as possible, air cleaners can be utilized to remove VOCs from indoor air. Several good indoor air filters work well for this purpose. Some indoor house plants may also be used to accomplish this goal. In 1989, Wolverton, Johnson and Bounds published their work for the U.S. National Aeronautics and Space Administration which examined what plants could clean indoor air. They found that several plants (Table 7) could reduce ambient levels of benzene, trichloroethylene, and formaldehyde.[30]

The next step after avoidance of unnecessary exposure and reduction of indoor levels by air purification is to assist the metabolism of the solvents once they are in the body. Some individuals clear solvents from the bloodstream better than others. Several factors that can reduce the efficiency with which solvents are cleared from the body include: deficiency of nutrients needed by the body to metabolize solvents, the presence of alcohol, aspirin, and other solvents,[15] low protein or high

Table 7: Plants effective in removing benzene, formaldehyde and trichlorethylene from indoor air

Gerbera jamesonii (Gerbera daisy)
Chrysanthemum morifolium (Pot or florists mum)
Hedera helix (English Ivy)
Sansevieria trifasciata (Mother-in-law's tongue)
Dracaena deremensis (variety "Warneckei", "Janet Craig", "Bausei", "Longii")
Dracaena marginata
Spathiphyllum araceae (Peace Lily)
Aglaonema modestum (Chinese evergreen)
Chamaedorea seifrizii (Bamboo palm)

sugar intake,[31] genetic metabolic defects such as GSTTI,[32] the presence of heavy metals reducing available glutathione,[33] and suppression of emotions.[34]

Phase 1 Biotransformation

Phase 1 biotransformation is the first step in clearing these compounds from the blood. Solvents are oxidized by the cytochrome P450 class of enzymes. Some solvents, such as toluene and xylene, are oxidized to benzoic acid. Styrene can be oxidized to benzoic, mandelic, or phenylglyoxylic acid. Hexane is oxidized to 2,5-hexanediol. There is clear evidence of genetic polymorphism, leading to differences of function of the various cyclooxygenase enzymes.[35] Such genetic differences, if present in the enzymes needed for solvent oxidation, can lead to certain individuals being less able to initiate the process of clearing solvents from the blood.

Diet can have an effect on clearing xenobiotics from the blood. Protein deprivation has been shown to decrease the liver content of several of the cytochrome P450 enzymes.[36] Protein quality also plays a role, as it was found that Asian vegetarians with incomplete amino acid intake have reduced clearing of xenobiotics.[37] Both hypochlorhydria and achlorhydria, neither of which are uncommon findings in a chemically-compromised patient, have an adverse impact on the availability of dietary amino acids, even in a high protein diet. This makes the use of partially hydrolyzed whey protein a reasonable and prudent addition to the nutritional protocol for an exposed person. Not only will whey provide the complete protein needed for metabolization of xenobiotics, it has also been shown to increase glutathione content in the liver.[38,39]

In addition to adequate complete protein, sugar content should be kept to a minimum. Dietary carbohydrates have been shown to reduce drug clearing effectiveness in animal models. In a human trial, a high protein, low carbohydrate diet was compared to a low protein, high carbohydrate diet. The researchers found greater xenobiotic clearance with the high protein, low carbohydrate diet and diminished clearance when the ratio was reversed.[40] The fact that the average U.S. resident consumes 150 grams of sugar daily in the face of daily chemical exposure is very probably a factor in our apparent national toxicity. On the other hand, the consumption of cruciferous vegetables, high in indol-3-carbinol, has been shown to enhance xenobiotic clearance.[41]

Certain micronutrients have also been shown to be beneficial in phase 1 clearing of compounds. Many of the B vitamins are necessary for the proper functioning of the cyclooxygenase systems, including thiamine, riboflavin, niacin, pyridoxine, and choline. Deficiency of these vitamins has been shown to decrease the efficiency of phase 1 clearing. Vitamins E and C, and the minerals magnesium and selenium, also have a great impact on this pathway.[36]

Phase 2 Biotransformation

After VOCs are oxidized during phase 1 detoxification they are conjugated with amino acids in phase 2 biotransformation. This is referred to as the acylation or amino acid conjugation pathway. The amino acids most commonly used for conjugation are glycine (for toluene and xylene), taurine, and glutamine. Taurine also assists the sulfation pathway, through which several VOC metabolites are cleared. Some VOCs pass through the glutathione conjugation pathway instead. Deficiency of this conjugating amino acid can reduce the clearance of solvents from the bloodstream. Support of glutathione levels can be accomplished by additional vitamin C, whey protein, milk thistle, alpha lipoic acid, selenium, and N-acetylcysteine, all of which have been shown to increase body glutathione levels. The single study on oral intake of glutathione, while small, failed to show any detectable increase in glutathione as a result of supplementation. The researchers in this study

felt the hydrolysis of glutathione by intestinal and hepatic gamma-glutamyltransferase effectively neutralized the potential benefit of oral reduced-glutathione supplementation.[42] In addition to increasing glutathione content in the body, alpha lipoic acid helps to mobilize mercury, preventing further glutathione depletion.[43] Alpha lipoic acid has been shown to provide protection against hexane-induced neuropathy.[44]

Clinically, the author has found the supplementation of vitamin C, selenium, glycine, glutamine, taurine, N-acetylcysteine, and alpha lipoic acid of great benefit for VOC-exposed patients, especially when body cleansing was undertaken contemporaneously.[45]

Conclusion

Daily exposure to solvents takes place with each unconscious inspiration of ambient air. Some individuals are exposed to higher levels of solvents depending on where they work or live. These compounds can lead to serious health problems in certain cases and certainly are never conducive to the health of any individual. Conscious avoidance of high sources of VOC out-gassing is the most prudent first step for preventive health. The second step involves supplementation with basic nutrients needed to assist phase 1 biotransformation, with the addition of specific nutrients to assist solvent-clearing phase 2 pathways. Individuals with more serious health problems resulting from solvent overload may need to do intensive body cleansing.

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