TOXICITY OF VOLATILE ORGANIC COMPOUNDS PRESENT INDOORS*

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Cave dwellers were perhaps the first to be concerned with the quality of indoor air, when they built fires inside their caves. By cooking and heating over open flames, they probably exposed themselves to toxic vapors from various chemicals, including formaldehyde. They may have partially solved this problem simply by building the fire at the entrance to the cave.

Modern man confronts problems of indoor air quality that resemble those of cave dwellers. People now build well-sealed homes and install insulation and other materials to conserve energy. This reduces movement of air through a building and increases the concentration of many indoor pollutants.[1] Our problems of indoor air pollution are more complex than were those faced by our ancestors. This paper sheds little light on solutions to these problems, but may provide insight into some health effects associated with exposure to toxic organic vapors inside the home (or cave, depending upon one's life style). Many products used in our homes produce toxic vapors; more than 40 organic vapors have been found in homes or office buildings (Table I).[2] A given vapor may come from many home products (Table II). For example, particle board, plywood, glue, textiles, and urea-formaldehyde foam all yield formaldehyde.[3-6] This

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TABLE I

ORGANIC GASES AND VAPORS IN HEADSPACE OVER BUILDING MATERIALS

Compound	*Average conc mg./m.³*	*Compound*	*Average conc mg./m.³*	*Compound*	*Average conc mg./m.³*
Toluene	36.0	$C_{10}H_{16}$	31.0	Heptane	7.3
n-Decane	1.45	Δ3 Carene	0.07	Heptene-1	1.90
3-Xylene	30.0	Styrene	0.61	3-Methyl heptane	3.7
n-Undecane	0.58	Alkane C7-13	0.36	Freon	0.18
n-Propylbenzene	0.11	n-Propanol	0.15	1,2 Dichhoroethane	3.3
2-Xylene	5.8	2-Butanone	0.16	Pentanol	0.25
Ethylbenzene	4.1	Acetone	0.56	Ethylacetate	0.11
Alkane C_{10}	2.4	Diethylbenzene	0.25	Octane	0.29
C3-Benzene	0.45	Hexanol	1.45	Decene-1	0.26
n-Nonane	0.92	Limonene	0.55	Methyl 2-Butanone	0.04
αPinene	2.8	Butanol	29.0	Ketone C5	0.07
Mesitylene	0.04	Isooctane	0.11	Ketone C8	0.05
n-Hexane	8.7	Isopropylbenzene	0.06		
4-Xylene	7.6	Alkane C9	0.97		

Modified from Molhave (1980).[2]

TABLE II

SOURCES OF VOLATILE ORGANIC POLLUTANTS IN THE HOME

A. Structural materials (particle board, plywood, panelling, insulation)
B. Furnishings (carpet, clothes, drapes, furniture)
C. Combustion (fireplaces, furnaces, unvented heaters, stoves)
D. Consumer products (aerosols, deodorizers, cleansers, coatings)
E. Pesticides
F. Activities (cooking, smoking, arts, and crafts)

review surveys the toxicity of many chemicals found indoors, and uses formaldehyde to illustrate aspects of indoor air pollution caused by organic gases.

SOLVENTS

Volatile organic solvents commonly pollute indoor air. Exposure occurs when using spot removers, paint removers, cleaning products, paints, and numerous other household products. The lipid solubility of organic vapors assures that they are rapidly absorbed through the lungs and enter organs containing high concentrations of lipid. They rapidly cross the blood-brain barrier and commonly depress central nervous system and cardiac functions. Organic solvents cause many other health effects. In order to facilitate our presentation, these solvents have been placed in seven classes. The first, aliphatic hydrocarbons, is simplest.

Aliphatic hydrocarbons (such as propane, butane, and isobutane) with fewer than five carbon atoms are gases. Their most common use indoors is for cooking and heating, and they are often aerosol propellants. These gases do not apparently induce chronic health effects, such as cancer, but may cause asphyxia by displacing oxygen from a closed environment.

Higher molecular weight aliphatic hydrocarbons (such as hexane, heptane, and octane) are liquid and are often solvents in aerosol products, glues, thinners, paints, and fuels. Many are toxic. For example, human exposure to n-hexane causes demyelination and degeneration of peripheral nerves.[7,8] This most probably results from the toxicity of the 2,5-dione metabolic products of hexane. Animal studies confirm this effect and show that other hydrocarbons (and ketones) which are metabolized to 2,5-diones also cause peripheral neuropathy.

Halogenated hydrocarbons such as methyl chloroform and methylene chloride are excellent solvents used widely in home products. Many have multiple uses. For example, methylene chloride is used as a paint stripper, an aerosol solvent, and a degreasing agent. Acute exposure to halogenated hydrocarbons typically causes central nervous system and myocardial depression. In animals, greater exposure may cause hepatotoxicity and cancer.[9] Halogenated hydrocarbons which cause cancer in animals include 1,1,2-trichloroethane, hexachloroethane, 1,2-dichloroethane, vinyl chloride, vinylidene, and tetrachloroethylene.[10-12] At least one, vinyl chloride, causes cancer in humans.[13] Exposure to some of these chemicals still occurs, either by contamination of products or during dry cleaning operations. Metabolic products of halogenated hydrocarbons may produce additional toxicity. For example, many mammalian species metabolize methylene chloride to carbon monoxide. Consequently, its toxicity includes that caused by carbon monoxide in addition to that caused by methylene chloride.[14] Some of their effects are additive; both cause central nervous system and cardiac depression. In addition, methylene chloride causes many toxic effects similar to those produced by other chlorinated hyrocarbons.

Aromatic hydrocarbons are also used as solvents. Most aromatic hydrocarbons in home products lack halogens, but chlorinated aromatics are in some products intended for home use. For example, some moth balls contain paradichlorobenzene, which is being tested for its carcinogenic potential by the National Cancer Institute. Toluene is a good example of a nonhalogenated aromatic hydrocarbon commonly used. It is chloride in paints, varnishes, glues, enamels, and lacquers. One study revealed that toluene was present in more than 50% of the samples taken of indoor air.[1] Toluene causes fatigue, muscle weakness, and confusion in humans exposed for eight hours to atmospheric concentrations of 200 to 300 ppm.[15,16] When its vapors are inhaled, toluene causes central nervous system depression, psychosis, and liver and kidney damage.[17,18] Some have suggested that it may also cause birth defects.[19,20] "Glue sniffers" desire toluene's psychological effects and unwittingly use it as a recreational chemical.[21] The chemical structure of benzene is similar to that of toluene. Benzene causes some acute effects similar to those of other organic aromatic solvents, including toluene and the xylenes. For example, it causes local irritation, intoxication, central nervous system depression, and death. Benzene elicits unusual chronic effects. It damages the hematopoietic system, causing first a decrease in the number of white blood cells. This may be followed by aplastic or hyperplastic changes which manifest themselves as anemia, leukopenia, thrombocytopenia, and leukemia.

Alcohols are used in such products as aerosols, window cleaners, paints, paint thinners, cosmetics, and adhesives. Alcohols irritate mucous membranes and produce depression of the central nervous system. Symptoms produced by alcohols include excitation, ataxia, drowsiness, and narcosis at higher concentrations. Excitation precedes the other effects and results from depression of inhibitory centers in the brain. Ethanol exemplifies alcohols which have these properties. Methanol has many toxic properties similar to those of ethanol, [23] and in addition affects the retina at higher concentrations, causing blindness.[24] This effect is likely due to formate and/or formic acid, which are metabolites of methanol.[24]

Ketones such as acetone, methyl ethyl ketone, and methyl isobutyl ketone are present in lacquers, varnishes, polish removers, and adhesives. These cause central nervous system depression and pulmonary vascular dilation.[25] Methyl-n-butyl ketone, which may contaminate some household products, strongly chelates certain metals in important enzymes.[25] As mentioned earlier, certain ketones that convert to 2,5-diones produce peripheral neuropathy.[7,8] Methyl-n-butyl ketone is one of these chemicals. The concomitant presence of methyl ethyl ketone enhances the toxicity of methyl-n-butyl ketone.[8] The effects of these two chemicals illustrate synergistic toxicity.

Ethers, including methyl, ethyl, and butyl ethers of ethylene glycol, dimethylether, tetrahydrofuran, and dioxane, are employed widely in solvent systems of oil-water combinations. Ethers are present in resins, paints, varnishes, lacquers, dyes, soaps, and cosmetics. Exposure to them often occurs in combination with other organic solvents. Exposure to ethers causes headaches, weakness, drowsiness, disorientation, and lethargy. Their potent central nervous system depressing properties led to the use of certain ethers as medical anesthetics. Dioxane (1,2,4), an ether which received much public attention, produces skin and eye irritation, liver and kidney damage, and cancer in animals.[26]

Esters such as ethyl acetate, butyl acetate, and ethyl butyrate are used in plastics, resins, plasticizers, and lacquer solvents. Many emit pleasant odors and are used in flavors and perfumes. In higher concentrations, esters irritate the eyes, nose, and throat; some cause central nervous system depression.[27] Some pesticides are toxic esters and will be discussed later. The alkyl phthalates, some of which cause cancer in animals, are also important esters and are presented in the following section.

POLYMER COMPONENTS

Polymer components are interesting and important indoor air pollutants. Polymers literally surround us. Our clothes, furniture, packages, cookware, and food contain them. Many are used for medical purposes, for example, in blood transfusion bags and disposable syringes. Fortunately, most polymers are relatively nontoxic. Unfortunately, polymers contain unreacted monomers, plasticizers, stabilizers, fillers, colorants, and antistatic agents, some of which are toxic. These chemicals diffuse from polymers into air. They attract attention as indoor air pollutants because they affect human health. Let us review three groups of these chemicals.

Monomers such as acrylic acid esters, toluene-diisocyanate, epichlorohydrin, styrene, and vinyl chloride may escape from polymers composed of them.[28,29] These monomers are toxic. Acrylic acid esters, used to produce plastics, can irritate skin, eyes, and mucous membranes.[12,30] Epichlorohydrin, used in such epoxy resins as those in tile floors, likewise irritates most tissues. When inhaled, its vapors corrode the mucous membranes in the respiratory tract.[31] Like many other chemicals, it damages DNA and may cause cancer.[31,32] Toluene diisocyanate, used in the synthesis of polyurethane, irritates the skin, eyes, and respiratory tract.[33] It is also a strong sensitizer. Chronic repeated exposures may eventually cause asthmatic attacks. At high concentrations it causes neurological and cerebral effects.[33] Chronic exposure of humans to vinyl chloride causes even greater concern; it causes cancer in man.[13]

Plasticizers increase flexibility of plastics. Alkyl phthalates are the most common plasticizers in the United States. Others include esters of citric acid. Few data exist concerning the toxicity of these chemicals. Generally, plasticizers do not elicit excessive acute toxicity unless exposure to them is great.[30] Some phthalate esters cause chromosomal and teratogenic effects in animals.[30] Two alkyl phthalates, di-(2-ethylhexyl) phthalate (DEHP) and di-(2-ethylhexyl) adipate, cause cancer in both rats and mice. In the same study, the carcinogenic potential of butylbenzyl phthalate in rats or mice was undetermined.[34] DEHP accounts for more than 20% of all plasticizers produced in the United States. It is in soft vinyl plastic products, such as baby mattresses, shower curtains, and toys. Physicians may appreciate that blood storage and transfusion bags contain DEHP, which leaches into blood during storage and enters patients during transfusion.[35]

Other chemicals in plastics that pollute indoor air may be important in the future. For example, organotin compounds (which preserve vinyl plastics) irritate tissues and cause neurological changes.[29] Other examples of potential polluters include curing agents like diethyltetramine, mercaptobenzothiazole, or tetramethylthiuram and antioxidants like monobenzylether or hydroquinone and phenylbeta naphthylamine.

PESTICIDES

As with other chemicals mentioned, volumes have been written about pesticides. These highly toxic chemicals are designed to kill. Frequently people "bomb" their homes with pesticides. One report indicates 90.7% of American households used pesticides in the home, garden, or lawn. The same report reveals that many people become ill after using pesticides around the home.[36] Warning labels and instructions for use could substantially reduce adverse health effects if people read them, but they don't.[36] Exposure to pesticides continues, sometimes with serious consequences. By monitoring air in homes in North Carolina, the Environmental Protection Agency found that five pesticides are commonly present: chlordane 0.1 to 10; ronnel 0.2 to 2; dichlorvos 0.5 to 10; malathion 0.2 to 2; diazinon 0.2 to 2; and dursban 0.2 to 2 (atmospheric concentrations as $\mu g./m.^3$)[37] Except for chlordane, these are organophosphate pesticides. Although these are relatively safe compared to other pesticides, they are still quite toxic.

The efficacy and toxicity of the organophosphate pesticides result from their anticholinesterase activity. These chemicals bind with acetylcholine esterase to decrease its activity and to increase the serum concentration of acetylcholine which competes less successfully for the binding sites. Toxicity results from both events.

In humans, symptoms of toxicity following exposure to acetylcholinesterase-inhibiting pesticides include wheezing, lacrimation, nausea, bradycardia, constriction of pupils, fatigue, headaches, and tremors. Atropine is often used to treat acute organophosphate poisoning. Some pesticides used in homes cause cancer in animals. These include captan, lindane, and chlordane. Interestingly, captan has structural similarities to thalidomide and like thalidomide causes birth defects in animals.[38] Many pesticides also cause behavioral and neurotoxicologic damage.[39]

The pesticide pentachlorophenol (PCP) preserves wood, wood products, starches, dextrins, and glues. A 5% solution is used to preserve logs and redwood in wooden homes.[40] In California and Kentucky, occupants of PCP-treated homes became ill.[40,41] Measurements of PCP in these homes reveal concentrations ranging up to 142 mcg./ft.^{3} (5 mg./m.^{3}).[40] The widespread use and slow degradation of this pesticide raises concerns about other effects in humans.[42] To address one such concern, the National Toxicology Program is testing the carcinogenic potential of PCP.

ALDEHYDES

The aldehydes form another important group of organic indoor pollutants. In general, aldehydes react quickly with other chemicals. They cause considerable irritation and evoke sensitization reactions. Some cause cancer in animals. One review listed 16 aldehydes that produced tumors in animals, often following dermal application or subcutaneous injection.[43] For example, proprionaldehyde, glycidaldehyde, and malondialdehyde are all irritants and tumorogens in animals. Three examples are presented to illustrate the toxicity of aldehydes.

Acetaldehyde is used in glues, deodorants, fuels, and to prevent mold growth on leathers. It is a component of tobacco smoke. At low concentrations, acetaldehyde irritates the skin, nose, and throat. Animal studies indicate that acetaldehyde is carcinogenic and mutagenic.[44,45] Although acetaldehyde may also cause cancer in humans, this has not been established conclusively.[46]

Acrolein is a volatile component of oak wood and a byproduct of the combustion of wood, kerosene, and cotton. The heating of oils and fats that contain glycerol (such as cooking oil) produces acrolein vapors. To date, there is no evidence of illness due to inhalation of these vapors. Smoking a cigarette produces from 51 to 102 μg. of acrolein.[47] It is used in making plastics, textile finishes, synthetic fibers, and perfumes. It irritates the eyes and respiratory tract. Acute exposure to high levels causes bronchitis or pulmonary edema, and its irritating properties are sufficiently strong to cause serious injury.[42] Acrolein possesses potent cytotoxic and ciliotoxic properties.[48] It can impair mitochondrial function and DNA replication.[48,49] It is mutagenic, but apparently not carcinogenic.[50,51]

Formaldehyde, a recently publicized aldehyde, unquestionably pollutes indoor air. Its toxicity and use typify many aspects of indoor air pollution. For this reason, it is reviewed in the most detail of all chemicals presented today.

Formaldehyde is a highly reactive gas with a pungent odor. In 1978 16 corporations produced about 9 *billion* lbs. per year of formaldehyde. Sixty percent of that went into producing resins for use in such items as particle board, plywood, and insulation.[52] That year, an estimated 6.4 *billion* pounds of formaldehyde were used to produce consumer goods in America.[52] Little is known about the concentrations of formaldehyde to which most people are chronically exposed. Single measurements of concentrations in homes vary significantly with the season of year and time of day.[53] Concentration measurements obtained in the same home over two weeks vary by a factor of up to 30 because of changes in atmospheric conditions, household ventilation, and outdoor concentrations.[54] Many factors affect outdoor concentrations, including weather, location, traffic patterns, and time of day.[55] Typical outdoor concentrations may be 10.0 ppb. or less. [4,53,55] In urban areas they may exceed 30 ppb.[53] Concentrations of formaldehyde indoors almost always exceed those outdoors, when both measurements are made simultaneously.[53]

A few studies compared the atmospheric concentration of formaldehyde in homes insulated with urea formaldehyde foam (UFF) with that in homes lacking UFF. According to one review, homes lacking UFF had 0.01 to 0.1 ppm. of formaldehyde and homes containing UFF averaged 0.35 ppm.[53] The data about homes containing UFF were obtained primarily from owners who complained to the local or federal agencies about its effects. A comprehensive analysis of air in homes injected with UFF revealed an average concentration of 0.13 ppm. of formaldehyde, as compared to 0.03 ppm. in homes lacking UFF.[56] Data from the Franklin Institute show that all UFF emits formaldehyde gas, even when the temperature, humidity, and installation procedures assure minimal offgassing.[6] In their study, offgassing continued through five months of observation. Similar offgassing occurs from particle boards containing formaldehyde resin. Table III shows some of the factors that may affect the offgassing of formaldehyde from wood products. Indoor air pollution by formaldehyde from particle board is a significant problem in mobile homes.[53]

TABLE III

FACTORS INFLUENCING THE LIBERATION OF FORMALDEHYDE FROM PARTICLE BOARD, PRESSBOARD, AND PLYWOOD

1) Free formaldehyde content in the adhesive
2) Moisture content of the glued wood chips or wood
3) Amount and type of hardener added
4) The amount of adhesive resin applied
5) Presence of other chemicals in the resin and product
6) The compression time and temperature used during the curing of the product
7) The exposed surface area of the panel in relation to the space and ventilation available in that enclosed space
8) Temperature and humidity of the product in relation to those of the immediate environment

Modified from: Bardana, E.: *Immunology and Allergy Practice*, vol. 2, No.3, p. 11, 1980.

Why are so many people concerned about formaldehyde? One reason is that formaldehyde is a strong irritant and sensitizer in humans.[4,56,58] Symptoms of ill-health depend partly on the mode, duration, and concentration of exposure. Short-term exposure to limited amounts produces many symptoms including eye, nose, throat, and skin irritation. Concentrations of 0.25 ppm. or less irritate the eyes, nose, and throat. For comparison, cigarette smoke contains about 30 ppm. of formaldehyde.[4] Longer exposures of people to formaldehyde alter the structure and function of the respiratory system.[59,60] With time, formaldehyde may cause chronic respiratory disease.[59] Minuscule amounts of formaldehyde can initiate severe reactions in sensitized individuals, who constitute about 4% of the population with dermal problems.[44,59] Some reports claim that even the limited amount of formaldehyde in tissue paper causes dermatitis.[3] The National Academy of Sciences reviewed the acute effects of formaldehyde and determined that a "population threshold" for its toxicity does not exist.[4]

The second principal reason for concern is that formaldehyde is a potential carcinogen in humans.[60,61] Metabolic, mutagenic, and carcinogenic evidence supports this statement. Formaldehyde reacts easily with other chemicals, including protein and nucleic acids. Reactions with biochemicals occur almost as soon as formaldehyde contacts tissue. This helps to explain why formalin fixes tissues so effectively. During metabolism, formaldehyde enters the 1-carbon metabolic pool and is converted to formic acid, which is excreted in urine as a sodium salt. Some is catabolized to carbon dioxide. These reactions are similar in laboratory animals and in man, but reaction rates may differ among species.[60]

Many *in vitro* studies reveal formaldehyde's mutagenic properties and ability to damage DNA.[4,60] Studies in mammals are needed to determine if these effects occur *in vivo.* Many studies of formaldehyde's carcinogenic potential have been done. Some failed to reveal a carcinogenic response.[60,61] This commonly occurred when formaldehyde was given with feed where its rapid reaction with the feed or the gastrointestinal contents may prevent its interaction with tissue. Other routes of exposure (e.g., inhalation) are more appropriate for toxicity studies of formaldehyde because human exposure commonly occurs by this route.

Most studies wherein rats and mice received formaldehyde by injection or by inhalation reveal tumor development.[60,61] Perhaps research by the Chemical Industries Institute of Toxicology sparked the greatest concern.[62] In this study, rats and mice inhaled formaldehyde gas for 24 months. By 11 months, rats given 15 ppm. developed squamous cell carcinoma, appearing in some instances as large lumps in the nose. By 12 months, hyperplastic and metaplastic changes developed in the rats exposed to 2.0 and 6.0 ppm. of formaldehyde.[61] At 24 months, two mice receiving 15 ppm. of formaldehyde developed similar nasal cancers, as did three rats which were exposed to 6 ppm. A total of 95 rats exposed to 15 ppm. developed nasal carcinomas.[63] These limited data suggest that rats reponded more extensively to formaldehyde than did mice. Possibly, differences in response between rats and mice result from differences in respiratory minute volume and in the surface area of the nasal turbinates. The dose-response profiles for rats and for mice seem similar when exposures are expressed as micrograms of formaldehyde per square centimeter of nasal turbinate and adjusted to constant minute volumes.[64] However, more information is needed accurately to determine the response of mice.

In 1980 the Consumer Product Safety Commission convened an expert Federal Panel on Formaldehyde to assess possible health affects associated with chronic exposure to formaldehyde. This panel limited its concern to hazards of chronic exposure because the National Academy of Science reported hazards associated with acute exposure earlier that year.[4,60]

After reviewing the literature and studies in progress the panel concluded that:

1. The metabolic pathways for formaldehyde in various animal species

and man are qualitatively the same but differ in rate, with formaldehyde or a formaldehyde adduct likely to be the carcinogenic agent.
2. Most of the studies available on the possible teratogenicity or reproductive effects of formaldehyde are inadequate for evaluation and none are adequate for inhalation exposure.
3. Formaldehyde is mutagenic in a variety of test systems including bacteria, yeasts, fungi, insects and mammalian cells and causes mutations and chromosome aberrations.
4. By inhalation, formaldehyde is carcinogenic to the Fischer 344 rat (data from mice were not available when the report was completed), producing nasal tumors at dose levels that are within the same order of magnitude as those to which humans are exposed.
5. Formaldehyde may be carcinogenic to species other than the rat and to tissues other than nasal.
6. Formaldehyde should be presumed to pose a carcinogenic risk to humans.
7. No information is presently available on whether (a) certain individuals may be at greater risk of cancer from formaldehyde exposure, (b) tumors may be expected to arise at non-respiratory sites as a result of inhalation of formaldehyde by humans, or (c) the effects of formaldehyde exposure may contribute in an additive or synergistic way to the effects of other carcinogens or tumor promoters."[60]

The panel's conclusions about the carcinogenic potential of formaldehyde were subsequently substantiated by two other independent reviews.[52,61] One of these reviewing groups recently published research results which confirm the carinogenic potential of formaldehyde.[61]

In summary, concern is growing that indoor air pollutants may adversely affect health. As this cursory review indicates, many household products contain potentially toxic chemicals. These chemicals usually benefit society and cause few problems. Occasionally, they cause serious health problems. Research is needed to elucidate the full extent and nature of indoor air pollutants and their effects on health. By being aware of these chemicals and their toxicity, physicians can better serve society.

SUMMARY

Today Americans use various means, including storm windows and insulation, to conserve energy in their homes and new homes are also built tightly. These factors reduce movement of air through the home and increase the atmospheric concentration of certain toxic chemicals. Extensive use of organic chemicals inside buildings creates opportunities for indoor air to become polluted. One study showed that more than 40 chemical vapors polluted indoor air. In some instances, these chemicals cause serious health problems. In many instances, the effect of chronic exposure to small amounts of these chemicals is unknown. Formaldehyde is a toxic chemical that illustrates problems of indoor air pollution: used in resins that are a part of many home products, including particle board, plywood and urea formaldehyde foam insulation, it causes adverse health effects when it "offgasses" from these products into a tightly-sealed, occupied building. Most noticeably, formaldehyde irritates eyes, skin, and respiratory tract and causes allergic reactions, but these may not be its most serious effects. Formaldehyde also causes mutagenic and carcinogenic changes in test animals, and may cause these effects in humans. Research is under way better to understand these chronic changes and to evaluate other potential effects. Physicians aware of indoor air pollutants can provide their patients with better medical care.

Questions and Answers

MISS YVONNE LUMSDEN (ASARCO, Inc.): You talked about individual solvents being harmful and a combination of two or more being even more toxic. Earlier, someone spoke about the possible harmful effects of cooking odors and the need to differentiate between discomfort and health effects. Has anyone studied the degree of toxicity and the possible harmful health effects in the home where a woman is using a combination of cleaning solvents such as Clorox, Pine-Sol, Ajax, etc. This is not just one dose or a random dose here and there, but a repeated weekly exposure to that kind of toxic combination.

DR. BEALL: There are about 4.5 million chemicals in the environment with which humans may come in contact. To study the interaction of those chemicals would involve astronomical numbers of possible studies that exceed the realm of the possible. From time to time, toxicologists do get involved in such studies where there is a likelihood of two chemicals coming together. This is done most commonly with drugs, to see whether the synergy of two chemicals can be beneficial.

We know a little about chemical interactions in toxicology, but what we know, relative to what needs to be known, is almost nonexistent. In response to your specific question about housewives working with multiple chemicals, one could study a given question of that nature, spend a few months on it, and possibly come up with a reasonable answer to one set of commonly used chemicals.

MISS LUMSDEN: I understand that it is impossible to create a risk-free society. However, when a woman is exposed to glue, just fumes from glue, and this has an effect on the fetus, then it makes one think about repeated exposure.

DR. BEALL: That woman put the glue in the bottom of a bag, stuck her nose over the other end, and inhaled deeply for many, many hours. So one must bear exposure in mind, and that is what I tried to indicate when I discussed the complexity of multiple exposures. We do not know the effects of many of these chemicals at the concentrations present in the home under normal kinds of living conditions. All we can say is that the chemical is present at some concentration, and that it is toxic at a given concentration in animals or humans. We really do not know what is happening at the specific exposures found in the home. I think that is part of the purpose of this conference, to define our state of ignorance at this point.

DR. EISENBUD: Your list did not include one chlorinated hydrocarbon that used to be very common in the home. That was carbon tetrachloride, which was the original composition of Carbona. Carbona, which is very common now, no longer contains any chlorinated hydrocarbons. The use of Carbona in the homes back in the 1930s and up to the mid-1940s, I would guess, was responsible for many deaths, several of which I investigated myself.

DR. BEALL: Yes, carbon tetrachloride, for those who may not know, causes liver damage in humans, and it causes tumors of the liver in animals.

DR. PETER PREUSS (Consumer Product Safety Commission): We are looking at about half of the products that Dr. Beall discussed to try to determine the levels that we might encounter in the home. After we do that, we come up against the problem that, in most cases, there are essentially no data to allow us to understand whether a health effect may or may not be possible or whether a problem may exist.

The case of n-hexane, which is one that we have been looking at for a long time now, is very typical. There are many data on the central and peripheral distal axonopathy following exposure to n-hexane as well as data on a number of other effects. These are, however, almost entirely data from occupational settings, where we see that exposure to 300, 400, 500 parts per million has an observable effect. When we look at the home, we are generally one, two, or three orders of magnitude below those levels and so, again, we have difficulties in judging possible health effects that may result regardless of whether we are talking about n-hexane or benzene or methylene chloride or any of the volatile chemicals.

Conversely, we have now demonstrated that the levels one might observe in a home during the time that a product containing a volatile substance is in use can be 10 or even 100 times the levels generally observed in occupational settings. Using a paint stripper or a glue, for example, one may observe several hundred or several thousand parts per million of a specific compound for the time that a person is working with it.

Again, the effects of high-level, short-duration exposures have not been well documented. Therefore, at both ends of that spectrum (i.e., high-level short duration and low-level long duration) that we have been discussing, there is a great need to start experiments at those exposure levels so that we can get some idea of the kind of health effects that are occurring. The problem is so severe that even for such classical pollutants as carbon monoxide that have been extensively studied I am not sure that we really understand at this point what the toxicology or the health effects really are at levels such as 5 or 10 parts per million. Therefore, in all of these areas, it is very difficult at this point to discuss the health effects really based on data rather than supposition.

DR. EISENBUD: Isn't it significant, Dr. Preuss, that you can make that statement 20 years after people began examining the effects of low levels of carbon monoxide? It all started probably with the West Coast papers on the effects of carbon monoxide on the central nervous system. It surely must have been 15 or 20 years ago, and there has been a lot of work done since. While it is hard to prove a negative, I think it significant that after all of the research you can say that we still don't know. The question is, how hard is one obliged to look?

DR. PREUSS: The problem is that although we do have data for carbon monoxide, unfortunately it has been contradictory in nature. We have indications, I believe, that health effects may indeed be observed at low levels, but I do not know to what extent one can actually use those as a basis for regulatory decisions or personal decisions, for that matter. The problem with all the others, though, is that we do not even have that jump from the occupational setting to the home setting, or we do not even have it for the occupational setting.

MR. BERNERD BURBANK (McGraw-Hill): I just saw something in the *New York Times*' Science Questions and Answers section last week. Science is getting very smart. The question is, why do onions make us cry? The answer given is that onions, when attacked, give off a volatile gas which dissolves in the fluid in the eye and forms sulfuric acid. That goes along with cooking odors and all. At least that was a surprise to me.

DR. EISENBUD: After I made the comment about carbon tetrachloride, I recalled that Alice Hamilton's first volume on industrial toxicology, which is a classic that was written about 1933, dealt only with about 50 industrial chemicals, and yet it pretty well covered the field at that time. Do you want to comment on some of the older uses of toxic substances?

DR. CRAIG HOLLOWELL (University of California-Berkeley): A few years ago, a mortality study was done of chemists. Chemists generally like to whiff everything to determine what it is, or they stick their finger in it. They determined that chemists lived, on the average about five years less than other people. While that list may have included 35 to 50 chemicals, and a lot of chemists may have died to provide us with that list, the reality is that there are more than 700 chemicals now identified by the Occupational Safety and Health Agency as posing sufficient problems within occupational settings to have limits placed on them, and the list is growing.

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