

## The health effects of nonindustrial indoor air pollution

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**Background:** There is growing public awareness regarding the risk associated with poor indoor air quality in the home and workplace. Because Americans spend approximately 22 hours every day indoors, susceptible individuals are at much greater risk of adverse health effects from chronic low levels of exposure to indoor air pollutants over time. Along with particulate matter, gases such as ozone, nitrogen dioxide, carbon monoxide, and sulfur dioxide; microbial and chemical volatile organic compounds; passive smoke; and outdoor ambient air are the most common types of air pollutants encountered indoors.

**Objective:** To provide the allergists with necessary information that will assist them in making useful recommendations to patients seeking advice regarding indoor environmental triggers beyond traditional perennial allergens.

**Methods:** Review of the literature pertaining to indoor exposure and health effects of gaseous and particular matter.

**Results:** Indoor pollutants act as respiratory irritants, toxicants, and adjuvants or carriers of allergens.

**Conclusion:** The allergist should be prepared to evaluate patient exposure to allergic and nonallergic triggers and understand how outdoor air pollution is affecting indoor environments. This requires being familiar with methodologies for monitoring and interpreting indoor air quality and interpreting results in the context of the patients exposure history and advising patients

about rational environmental control interventions. (*J Allergy Clin Immunol* 2008;121:585-91.)

**Key words:** Indoor air pollutants, ozone, particulate matter, nitrogen dioxide, carbon monoxide, sulfur dioxide, health effects, volatile organic compounds, tobacco smoke, passive smoke exposure, cotinine, fungal allergens

Recently the health effects of outdoor air pollution were reviewed in detail.<sup>1</sup> There is growing public awareness regarding the risk associated with poor indoor air quality (IAQ) in the home and workplace. Because Americans spend approximately 22 hours every day indoors, susceptible individuals are at much greater risk of adverse health effects from chronic low levels of exposure to indoor air pollutants over time. Along with particulate matter (PM), gases such as ozone (O<sub>3</sub>), nitrogen dioxide (NO<sub>2</sub>), carbon monoxide (CO), and sulfur dioxide (SO<sub>2</sub>); microbial and chemical volatile organic compounds (VOCs); and passive smoke are the most common types of air pollutants encountered indoors. A major limitation of understanding the adverse health effects of these specific air pollutants is the inability directly to equate measurable ambient air concentrations to personal exposure. To complicate matters, in the nonoccupational indoor setting, environmental exposures are often more subtle and not readily recognized. In the most extreme cases, controversial terms like *sick building syndrome* (SBS), *toxic mold syndrome*, and *multiple chemical sensitivity* have been coined for lack of a better way to characterize unexplained constellation of symptoms that are attributed to some exposure in the home or nonindustrial occupational setting. Furthermore, very little information is available regarding permissible exposure levels for the home or nonindustrial workplace for known indoor air pollutants. Many experts recommend indoor air pollutant levels be maintained at 50% or less than the National Ambient Air Quality Standards for outdoor air pollutants established by the Environmental Protection Agency (Table I). This review attempts to provide allergists with necessary information that will assist them in making useful recommendations to patients seeking advice regarding indoor environmental triggers beyond traditional perennial allergens.

### SPECIFIC INDOOR AIR POLLUTANTS

#### O<sub>3</sub>

Acute exposure to O<sub>3</sub> produces decrements in pulmonary function and exercise capacity and induces airways inflammation in both healthy individuals and those with pre-existing airways disease (ie, asthma, chronic obstructive pulmonary disease).<sup>2-4</sup>

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**Abbreviations used**

ETS: Environmental tobacco smoke  
IAQ: Indoor air quality  
mVOC: Microbial volatile organic compound  
PM: Particulate matter  
SBS: Sick building syndrome  
TVOC: Total volatile organic compound  
VOC: Volatile organic compound

In individuals with allergy, O<sub>3</sub> acts as an adjuvant, enhancing the allergic response to inhaled allergen.<sup>5</sup> Interactions between ozone and particulate matter in office settings has also been reported.<sup>6</sup> O<sub>3</sub>-induced health effects are dependent on the dose and concentration of O<sub>3</sub> deposited in the lung and the individuals ventilation rate and duration of exposure. Main sources of indoor O<sub>3</sub> are from outdoor O<sub>3</sub> resources as well as air purifiers (electrostatic precipitators, negative ion generators, and ozone generators), which are marketed to the public to provide relief from numerous respiratory ailments as well as to reduce odors and destroy microbes. These devices have been shown to increase indoor O<sub>3</sub> concentrations in the range of 16 to 453 ppb.<sup>7,8</sup>

**NO<sub>2</sub>**

Because more than half of all households in the United States use gas, the primary source of indoor NO<sub>2</sub> is gas-fueled cooking and heating appliances. An extensive literature has examined the link between NO<sub>2</sub> exposure and duration causing adverse respiratory effects in susceptible populations, but results are inconclusive. There is recent good evidence suggesting that children with atopy or asthma, infants who are at risk of developing asthma, and female adults are more sensitive to the respiratory effects of NO<sub>2</sub> exposure.<sup>9,10</sup> Indoor NO<sub>2</sub> exposure may also enhance asthmatic reactions to inhaled allergens.<sup>11</sup> In the United States, elevated indoor NO<sub>2</sub> levels are more prevalent in lower-income housing developments because of poor ventilation, small apartment size, and frequent use of gas stoves for supplemental heating.<sup>12</sup> Nitrous acid, a product of primary combustion formed as a secondary product of NO<sub>2</sub> and other nitrogen oxides and water, is also found on indoor surfaces. Nitrous oxides acidic nature makes it capable of causing respiratory damage leading to respiratory symptoms in patients with asthma at concentrations of 650 ppb over 3 hours.<sup>10,13</sup>

**SO<sub>2</sub>**

Sulfur dioxide is a primary combustion product of fossil fuels that can be grouped together with acid aerosols and particles to form a complex group of distinct air pollutants associated with a wide array of adverse health effects, including short-term respiratory morbidity and mortality.<sup>14</sup> Chamber studies have determined that kerosene heaters are the major source of sulfate aerosols and indoor SO<sub>2</sub>.<sup>15</sup> Some early controlled chamber studies have demonstrated that SO<sub>2</sub> can cause bronchoconstriction in healthy adults and adults with asthma, but a more recent study found that SO<sub>2</sub> (200 ppb) and its reaction products (sulfuric acid 200 μg/m<sup>3</sup> and ammonium bisulfate 2000 μg/m<sup>3</sup>) caused no significant change in spirometry or symptoms in healthy subjects and subjects with asthma.<sup>16,17</sup> However, a recently published report examining the effect of indoor heating sources on respiratory

**TABLE I.** National Ambient Air Quality Standards (adapted from <http://www.epa.gov/air/criteria.html>)\*

Pollutant	Primary standards	Averaging times		Secondary standards
CO	9 ppm (10 mg/m <sup>3</sup> )	8-Hour†		None
	35 ppm (40 mg/m <sup>3</sup> )	1-Hour†		None
NO <sub>2</sub>	0.053 ppm (100 μg/m <sup>3</sup> )	Annual (arithmetic mean)		Same as primary
PM <sub>10</sub>	Revoked‡	Annual‡ (arithmetic mean)		Revoked‡
	150 μg/m <sup>3</sup>	24-Hour§		Same as primary
PM <sub>2.5</sub>	15.0 μg/m <sup>3</sup>	Annual   (arithmetic mean)		Same as primary
	35 μg/m <sup>3</sup>	24-Hour¶		Same as primary
O <sub>3</sub>	0.08 ppm	8-Hour#		Same as primary
	0.12 ppm	1-Hour** (applies only in limited areas)		Same as primary
Sulfur oxides	0.03 ppm	Annual (arithmetic mean)		—
	0.14 ppm	24-hour†		—
		3-hour†		0.5 ppm (1300 μg/m <sup>3</sup> )

\*Primary standards, limits set to protect public health, especially sensitive subpopulations such as patients with asthma, the elderly, and children. Secondary standards, limits set to protect public welfare such as visibility and damage to crops, animals, and buildings. Levels for VOCs have not been established.

†Not to be exceeded more than once per year.

‡Because of a lack of evidence linking health problems to long-term exposure to coarse particle pollution, the agency revoked the annual PM<sub>10</sub> standard in 2006 (effective December 17, 2006).

§Not to be exceeded more than once per year on average over a period of 3 years.

||To attain this standard, the 3-year average of the weighted annual mean PM<sub>2.5</sub> concentrations from single or multiple community-oriented monitors must not exceed 15.0 μg/m<sup>3</sup>.

¶To attain this standard, the 3-year average of the 98th percentile of 24-hour concentrations at each population-oriented monitor within an area must not exceed 35 μg/m<sup>3</sup> (effective December 17, 2006).

#To attain this standard, the 3-year average of the fourth-highest daily maximum 8-hour average O<sub>3</sub> concentrations measured at each monitor within an area over each year must not exceed 0.08 ppm.

\*\* (1) The standard is attained when the expected number of days per calendar year with maximum hourly average concentrations above 0.12 ppm is ≤1. (2) As of June 15, 2005, the Environmental Protection Agency revoked the 1-hour O<sub>3</sub> standard in all areas except the fourteen 8-hour O<sub>3</sub> nonattainment Early Action Compact (EAC) areas.

symptoms in nonsmoking women reported that a 10-ppb increase in SO<sub>2</sub> was associated with increased wheezing and chest tightness.<sup>18</sup>

**CO**

Carbon monoxide is a tasteless, odorless, colorless, and nonirritating gas produced by incomplete combustion of organic material and is the leading cause of poisoning in the United States.<sup>19</sup> The main sources of indoor CO are gas appliances, unvented kerosene heaters, and environmental tobacco smoke (ETS). The main health effect of CO is a result of its ability to impair the oxygen binding capacity of hemoglobin, which can cause headaches, nausea, dizziness, breathlessness, and fatigue, and with high exposures can lead to coma and death.<sup>19</sup> The severity of CO poisoning is dependent on concentration, length of exposure, and the general underlying health status of the exposed individual. Because carboxy-hemoglobin concentrations in blood are cumulative over time, prolonged exposure to low

TABLE II. VOCs and their sources

Source	VOCs	Source	VOCs
Adhesives/ sealants	Formaldehyde, butyl ether, vinyl cyclohexane, 2-propenoic acid, propylene glycol	Paints	Toluene, propylene glycol, ethylene glycol, butyl propionate, methyl propanol
Carpet	4-Phenylcyclohexene, vinyl acetate, styrene, dodecanol, acetaldehyde	Printers/copiers	Styrene, ethylbenzene, xylenes, benzene, 2-ethyl-1-hexanol
Cleaning chemicals	Limonene, isopentane, isopropanol, butoxyethanol, 1,4 dichlorobenzene	Resilient/rubber flooring	Styrene, dodecane, benzothiazole, vinyl acetate, cyclohexane
Linoleum	Acetic acid, hexanal, hexanoic acid, pentanoic acid, decane	Textiles	Formaldehyde, acrylonitrile, acetaldehyde, decane, tetradecane
Millwork	formaldehyde, 2-pentylfuran, benzaldehyde, hexanal, pentanal	Wall covering	Naphthalene, methyl pyrrolidinone, styrene, phenol, ethyl hexanoic acid
Office furniture	formaldehyde, acetaldehyde, butylacetate, hexanal, cyclohexanone	Window shades	Ethyl hexanoic acid, decanol, dodecene, ethyl hexanol, naphthalene
Building occupants	Benzene from tobacco smoke (ETS) and attached garages, limonene (a terpene) and various siloxane compounds (eg, decamethylcyclopentasiloxane) from personal care products including antiperspirants and deodorants, tetrachloroethylene from dry-cleaned clothing, and C <sub>12</sub> to C <sub>16</sub> alkanes from hand and body lotion, moisturizing soaps, and cosmetics		

concentrations can result in considerable health effects.<sup>19</sup> Burnett et al<sup>20</sup> found that CO, compared with the other major indoor gaseous pollutants, NO<sub>2</sub>, SO<sub>2</sub>, and O<sub>3</sub>, was the strongest predictor of elderly patients being hospitalized for congestive heart failure.

## VOCs

**Chemical.** Primary product sources of VOCs in buildings include office furniture, cabinetry, carpet tile, vinyl wall coverings, paints, and adhesives. Primary formaldehyde emitters are paints, adhesives, insulations, cabinetry, workstations, ceiling tile, and wallboard. Building occupants and activities are also major sources of these indoor chemicals. Table II lists some of these common building sources and their associated VOCs. The combination of these chemical sources in buildings can result in the occupant being exposed to anywhere from 50 to 300 different individual VOCs, each present in a microgram per cubic meter concentration range ( $\mu\text{g}/\text{m}^3$ ). This complex “chemical soup” frequently results in odors that lead to complaints by occupants in these nonindustrial indoor environments.

Adverse health responses attributed but not proven to be caused by VOCs in nonindustrial indoor environments include (1) irritant effects resulting from mucous membrane irritation, (2) systemic effects such as fatigue and difficulty concentrating, and (3) toxic effects such as carcinogenicity.<sup>21-23</sup> The strongest association has been with VOCs causing mucous membrane irritation.<sup>22,23</sup>

Formaldehyde is the VOC most familiar to the general public that has been associated with indoor air pollution. The major sources of formaldehyde are from indoor construction materials such as particleboard, fiberboard, and plywood. Formaldehyde concentrations are higher in residential buildings compared with office buildings because of the relatively large ratio of pressed wood products to air volume in homes.<sup>24</sup>

The sum of all individual VOCs, referred to as TVOCs (total volatile organic compounds), measured in  $\mu\text{g}/\text{m}^3$ , are often used as a guide to determine whether chemical levels are elevated in air samples. These levels often reflect the potential for occupant irritation and discomfort.<sup>24</sup> In new office buildings, the TVOC concentration at the time of initial occupancy is often 50 to 100 times higher than outdoor air. Occupants almost always complain

when TVOC levels are 3000  $\mu\text{g}/\text{m}^3$  or higher.<sup>24</sup> IAQ guidelines have been incorporated into the design and construction specifications for new buildings and to a lesser extent homes to reduce VOCs to allowable levels on the basis of current toxicologic information on health, irritation, and odor hazards.

**Microbial.** More than 200 microbial VOCs (mVOCs) have been associated with different fungi including alcohols, aldehydes, ketones, terpenes, esters, amines, and aromatic compounds as well as sulfur-containing and nitrogen-containing compounds.<sup>25</sup> Moisture problems with molds located behind surfaces or inside building materials can lead to increased release of mVOCs manifested as mildew/musty odors. It has been suggested that mVOCs could be used as tracers for suspected microbial contamination in building materials when occupants complain of moldy/mildew odors and/or indoor air-related symptoms.<sup>26</sup> In water-damaged buildings, both the microbial species and the growth substrate (building materials) affect the mVOC profile in indoor air.<sup>27</sup> However, use of mVOCs as tracers of microbial contamination can be problematic if other sources of these compounds originating from traffic, human activities, or normal building materials are not taken into account.

Indoor microbial VOCs have been associated with eye, nose, and throat irritation; cough and wheezing; fatigue; headache; dizziness; and nausea.<sup>28</sup> Limited mVOC challenge studies have been conducted. Nasal provocation studies in a healthy individual using a relatively high concentration of the mVOC, 1-octen-3-ol (10  $\text{mg}/\text{m}^3$ ), caused eye irritation and headache associated with an increase in lysozyme, myeloperoxidase, and eosinophilic cationic protein (ECP) in nasal lavage fluid obtained post-challenge.<sup>29</sup> More recently, a 3-methylfuran (1  $\text{mg}/\text{m}^3$ ) nasal provocation challenge caused an increase in myeloperoxidase and lysozyme in nasal lavage associated with a decrease in forced vital capacity.<sup>30</sup> *In vitro* studies using bronchoalveolar lavage cells incubated with mVOCs (2-methyl-1-propanol, 3-methyl-1-butanol, 2-methyl-1-butanol and 1-pentanol) resulted in increased histamine release.<sup>31</sup> Finally, in a mold-sensitized individual, inhalational challenge to 3-methylfuran (1  $\text{mg}/\text{m}^3$ ) was demonstrated to induce both an early and a late airway response.<sup>32</sup> Although these limited studies are intriguing, these findings are inconclusive and require further investigation in larger populations to determine their significance.

## TOBACCO SMOKE: PASSIVE AND SIDESTREAM EXPOSURE

Tobacco is the leading cause of preventable death. Tobacco smoke contains more than 4000 chemicals in the form of particles and gases, many of which are known or suspected carcinogens.<sup>33</sup>

The 2001 European Community Respiratory Health Survey reported that 65% of respondents identified at least 1 smoking parent during their childhood, and 39% currently were being exposed to ETS.<sup>34</sup> In the United States, 37% of adult nontobacco users reported ETS exposure at home or work, yet 88% demonstrated detectable serum cotinine levels.<sup>35</sup> Young children in particular who spend most of their time in the home are at increased risk for even greater exposures to tobacco smoke if their mothers smoke.

Several studies in adults have shown a dose-response relationship between ETS exposure and chronic respiratory tract symptoms in the home and workplace.<sup>36</sup> A meta-analysis of 7 studies in infancy and early childhood reported an odds ratio of 1.98 for an increased risk of wheezing with ETS exposure. Jaakkola et al<sup>37</sup> reported that school-age children were 1.24 to 1.40 more likely to experience increased lower respiratory tract symptoms if they had ETS exposure. More studies are needed to determine whether ETS can cause or exacerbate asthma. Studies thus far have found that ETS exposure in the home can increase the risk of developing asthma from 40% to 200%. Although currently there are no longitudinal studies in adults demonstrating that ETS can reduce lung function, several longitudinal studies in children have demonstrated this effect.<sup>38</sup> Additional longitudinal studies are needed to define better the relationship between ETS and other adverse health effects in susceptible subpopulations such as children and the elderly. These studies require methodology that can better measure the cumulative effect of ETS exposure on subjects. However, the currently available evidence supports a concerted public health policy directed at reducing or preventing ETS exposure in public settings and in the home.

## INDOOR PARTICULATE MATTER

### Classification

The regulation of ambient PM and the implementation of enforcement laws for emissions by the US Environment Protection Agency have made a significant step in improving outdoor air quality. However, there has been growing concern about the adverse health effects of indoor particulate matter and its associated chemical or biological agents. In industrialized countries, people spend approximately 22 hours of their time indoors. Recent studies have demonstrated an association between indoor PM and respiratory illness including asthma.<sup>39,40</sup>

The adverse effects of indoor PM are dependent on deposition in the respiratory tract and the ability of the respiratory tree to remove them, which is directly related to particle size and chemical composition. For example, coarse PM generated indoors (2.5-10  $\mu\text{m}$ ) tends to deposit in the nasal, pharyngeal, and laryngeal regions of the respiratory system, whereas fine (0.1-2.5  $\mu\text{m}$ ) and ultrafine (<0.1  $\mu\text{m}$ ) PM generated indoors and outdoors tends to deposit in the tracheobronchial region and alveoli. Organic pollutants can adsorb onto the surface of these particles, contributing to important adverse health effects. The large surface area of smaller PM (ie, ultrafine PM) allows these particles to carry greater amounts of air toxics (ie, polycyclic aromatic

hydrocarbons [PAH], metals, and quinones) that can deposit in the lower respiratory tract, thereby having a greater effect on causing or aggravating respiratory diseases, such as asthma.<sup>40-42</sup>

Indoor PM can also be classified according to its sources, which include ETS, cooking, heating, consumer products, building materials, house dust, particle resuspension from human activity such as vacuuming and foot traffic, outdoor particle infiltration, and secondary organic aerosols.<sup>43,44</sup>

### Health effects of indoor PM

Indoor PM has been associated with increased respiratory symptoms.<sup>45</sup> A study conducted in 421 houses in northern-central Italy showed a positive correlation between indoor PM<sub>2.5</sub> exposure and the presence of bronchitis and asthmatic symptoms, especially during the winter season.<sup>45</sup> A study conducted in Oslo homes showed that indoor suspended PM contained a large amount of potential allergen carriers (ie, soot particles <1  $\mu\text{m}$ ).<sup>46</sup> The presence of organic pollutants together with these allergens or endotoxin may exert a proinflammatory effect, leading to the exacerbation of allergic diseases such as asthma.<sup>46,47</sup> Several studies have reported that children living within 100 meters of the freeway experienced more respiratory symptoms than those living further away, suggesting that adverse health effects can be attributed to both outdoor PM exposure and exposure to PM that permeates inside from the outdoors, causing poor IAQ.<sup>48</sup>

### Potential mechanisms of indoor PM-related respiratory illness

Mechanisms by which PM exerts its adverse respiratory effects by acting as a possible adjuvant have been reviewed previously.<sup>1,49</sup> Indoor PM may carry toxic pollutants and reaction products into the airway, generating oxidative stress.<sup>46</sup> Many organic chemicals (eg, PAH and quinones) associated with ambient PM are redox active and have been shown to induce proinflammatory responses through the generation of oxidative stress.<sup>50,51</sup> Finally, reactive compounds, such as radicals and organic compounds, generated from the interactions between indoor PM, O<sub>3</sub>, or NO<sub>2</sub> can also have proinflammatory effects.<sup>6,11,12,49</sup>

## BUILDING-RELATED ILLNESSES ASSOCIATED WITH INDOOR AIR POLLUTANTS

### SBS

*Sick building* is a term first used to describe workplaces with poor ventilation where an excess above the expected numbers of occupants report symptoms of fatigue, headache, nasal, eye or skin irritation, sore throat, and cough that temporally occur with being in the building and improve away from the building. SBS has been defined as having 3 or more symptoms including dry or irritated eyes, sore or dry throat, stuffy or runny nose, unusual fatigue, and weekly headaches that improve away from work.<sup>52</sup> However, although this definition may be useful for epidemiologic studies, it has limited clinical utility because the symptoms are nonspecific. The diagnosis of SBS remains very controversial because of the lack of objective biomarkers relating symptoms with indoor environmental exposures.

Multiple epidemiologic studies have been inconsistent in identifying specific associated factors. Putative factors that may be involved include problems with temperature, humidity control,

lighting (glare), sound/vibration, overcrowding, job stress, and job dissatisfaction. Air quality factors may involve inadequate ventilation, poor building maintenance, increased dust, volatile organic compounds (eg, new furnishings, photocopy machines), bioaerosols, endotoxin, and fungal contamination. The lack of consistent findings in these studies suggests that several factors may be responsible for the symptomatic complaints by inhabitants. In 1 study, an attempt was made to look at symptomatic relief using UV germicidal lights to reduce bioaerosol in a putative sick building.<sup>53</sup> In this double-blind multiple crossover study design, installed UV irradiation units resulted in a 99% reduction of microbial and endotoxin concentrations on irradiated surfaces. This was associated with an overall mean 20% reduction in work symptoms, 30% reduction in mucosal symptoms, and 40% reduction in respiratory symptoms.<sup>53</sup> However, the health benefits of central UV systems in homes or office buildings require further investigation.

Regardless, whether or not one believes that SBS exists, it is imperative that the allergist/clinical immunologist have a practical approach for evaluating these cases when they present in the outpatient setting. A careful environmental history should be obtained to ascertain details of their exposure and whether other workers are also experiencing similar symptoms. Objective diagnostic tests such as allergy skin testing, pulmonary function testing, methacholine provocation, and appropriate blood work should be performed to exclude more prevalent and diagnostically accurate conditions such as chronic allergic or nonallergic rhinitis and/or asthma. Finally, other controversial idiopathic syndromes often manifest simultaneously with SBS such as chronic fatigue syndrome and idiopathic environmental intolerance (also known as *multiple chemical sensitivity*). These individuals frequently complain of upper and lower respiratory symptoms in addition to neurocognitive problems after exposure to chemical odors and irritants in and out of the workplace. However, similar to SBS, there are no objective biomarkers available that link environmental exposures with clinical symptoms associated with these syndromes.

### Microbial contamination in damp buildings

Moisture damage and consequent mold contamination have been commonly reported in homes, schools, offices, and hospitals. In addition to mold, yeasts, wood-rotting fungi, and bacteria can grow in moist building materials.<sup>54</sup> Furthermore, dampness can damage building materials and furnishings, leading to off-gassing of chemicals (eg, formaldehyde) and release of nonbiological particles.

Numerous studies conducted worldwide have reported an association between dampness or mold and adverse health effects.<sup>55-57</sup> Moisture and microorganisms in buildings can affect human health by a variety of biological mechanisms, including infections, allergic or hypersensitivity reactions, and irritant reactions. Allergens, (1-3)- $\beta$ -D-glucan, mVOCs, and mycotoxins are among the proposed components that may contribute to some these adverse health effects. Fungal allergens are typically proteins or glycoproteins that can be structural components of the cell or produced by the cell such as enzymes and metabolic byproducts that are released into the environment.<sup>58</sup> The release of allergen from spores has been shown to increase during spore germination.<sup>58</sup> (1-3)- $\beta$ -D-glucan is a biologically active polyglucose molecule composing as much as 60% of the mold cell wall,

some soil bacteria, and plants.<sup>59</sup> Mycotoxins are nonvolatile secondary metabolites.<sup>60</sup> Their production may be triggered by competition with other microorganisms or by unfavorable environmental growth conditions, such as nutritional starvation. Allergens, (1-3)- $\beta$ -D-glucan, and mycotoxins may be dispersed into the air in fungal spores and mycelial cells. Recently it has been shown that these fungal components may also be carried by smaller ultrafine and even nanosize particles called *fragments*, which have been shown to contain allergens, mycotoxins, and (1-3)- $\beta$ -D-glucan.<sup>61-63</sup> Because of their small size, fungal fragments can stay in the air longer than larger spores with the potential to penetrate deep into the alveolar region when inhaled.<sup>63</sup> However, studies that demonstrate the relationship between inhaled fungal fragments and clinical disease in humans are lacking.<sup>55</sup>

Allergic reactions caused by microbial agents have been well described.<sup>60</sup> The most common allergic disorders secondary to fungi are allergic rhinitis and asthma.<sup>56,57</sup> However, sensitization to molds as a result of chronic indoor exposure may not be as common as for other indoor allergens. One study reported only about 5% of students in moisture-damaged schools were allergic to mold.<sup>64</sup> A more recent study evaluating subjects with suspected mold-related health effects also demonstrated that the majority of the individuals were nonatopic; however, the subjects who were sensitized to mold were more likely to be exposed to the specific molds in their indoor environment on the basis of mold sampling reports by certified industrial hygienists.<sup>65</sup>

Glucans can have proinflammatory capabilities and have been suggested to be involved in adverse nonallergic respiratory health effects. Interestingly, 2 recent studies in school children (5-13 years old) and infants have shown a possible protective effect on atopic wheeze in relation to high (1-3)- $\beta$ -D-glucan concentrations in house dust.<sup>59,66</sup>

The health effects of fungal toxins in human beings remain highly controversial. Most of the knowledge on the health effects of fungal toxins is gained from agricultural settings and ingestion of contaminated feed by livestock. There are increasing number of case studies that are attempting to establish a possible role of airborne exposure to mycotoxins in mold-contaminated buildings.<sup>62,67-69</sup> Mycotoxins produced by *Stachybotrys chartarum* were implicated in a cluster of acute pulmonary hemorrhage (diffuse bleeding or hemorrhage in the alveoli) cases in infants in Cleveland.<sup>68,70</sup> The role of *S chartarum* in these cases has been extensively debated in the literature and still remains highly controversial because these studies did not directly measure mycotoxins in the air.<sup>71</sup> Acute effects, such as lung inflammation and hemorrhagic exudates in the alveolar lumina, have been shown in animal studies using high doses of mycotoxin-containing spores.<sup>72</sup> Although a recent review by the United States Institute of Medicine concluded that *in vitro* and *in vivo* studies suggest biological plausibility between *S chartarum* exposure and health effects, more extensive research is needed to clarify this highly controversial area.<sup>55</sup>

### CURRENT METHODS FOR MONITORING IAQ

Diagnostic techniques used for IAQ evaluations are usually divided into a qualitative and a quantitative phase.<sup>73</sup> Instrumentation used during the qualitative IAQ evaluation is limited and is intended primarily to supplement the investigators visual observations. Direct-reading instruments are used to measure relative

humidity, room temperature, O<sub>3</sub>, CO, CO<sub>2</sub>, and particulate concentrations. The qualitative evaluation for microbial contaminants includes an assessment of the building and heating, ventilating, and air-conditioning (HVAC) system for water damage and moisture problems, including condensation and the presence of visible mold or musty odors indicative of mVOCs.<sup>26</sup> The qualitative evaluation for VOCs includes an observance of odors, building renovation, specialized office equipment, pressed wood products, and cleaning products used. Methodologies for collecting and culturing dust, bulk, and air sampling are discussed in more detail elsewhere.<sup>73,74</sup> Environmental testing should be restricted to specific situations that warrant further assessment of the relationship between IAQ and clinical symptoms.

## HOW TO CREATE A HEALTHIER INDOOR ENVIRONMENT

### Building procedures

The allergy specialist should have some familiarity with building a healthy home because patients are frequently presenting with health complaints related to poor IAQ attributed to their home or workplace. The 3 primary considerations in improving IAQ are (1) evaluation of construction failures that allow moisture into the walls of a building, (2) poor ventilation causing excessive humidity and accumulation of gaseous and/or chemical exposure from materials in the living space, and (3) poorly designed or failing HVAC systems that contribute to poor air circulation. An extensive overview of building sciences and the guidelines for new home construction can be found at <http://www.healthhouse.org>. Building a healthy home should take into account costs versus energy savings and improved health outcomes. Further studies are needed to confirm the health benefits of healthy home construction.

### IAQ standards

In contrast with the industrial workplace setting, quantitative standards for chemical, biological, and particulate exposures as well as ventilation requirements have not been well established and are not routinely monitored. Although some government entities provide guidelines related to IAQ concerns, these generally take the form of recommendations for the control or elimination of sources and strategies for exposure reduction, rather than for achieving pollutant levels below some specific air concentration (Table I). Legislation such as Clean Indoor Air acts ban or restrict smoking in workplaces and in public places and reduce exposures to ETS for workers and patrons.<sup>75</sup> The Environmental Protection Agency's IAQ Tools for Schools program addresses IAQ management in schools by providing guidance for those aspects of building maintenance, housekeeping, and daily school operations that can influence IAQ, such as the importance of preventing water intrusion; carefully selecting, using, and storing cleaning and pesticide products; and ensuring proper ventilation. This program also provides resources and strategies for remediation of allergen and irritant-induced IAQ problems and strategies to maintain good IAQ over time.<sup>76</sup> These voluntary programs are gaining widespread acceptance.<sup>76</sup>

### Conclusion

This review was prepared with the goal of providing allergists with a balanced perception of indoor pollution and how to apply

this information in the evaluation of individual patients who present with suspected symptoms arising from poor IAQ. As the patients foremost advocate, the allergy consultant should be prepared to acquire and maintain expertise in environmental factors that directly affect genetic susceptibilities inherent in allergic diseases. Evaluation of an individual patient's exposure also requires that the allergist be familiar with methodologies for monitoring IAQ and interpreting results in the context of the patient's exposure history. Finally, the allergist should be informed about existing indoor and outdoor air quality standards with the goal of advising patients about rational environmental control interventions.

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