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Indoor Air Quality

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The focus of occupational health has been transformed in many ways by the increasing proportion of the workforce employed in offices and other kinds of public facilities, merging in many respects with the concerns of environmental health. Once considered safe by crude comparison with industrial settings such as construction, mining, and agriculture, experience has proven that these indoor environments are not free of significant health hazards. Moreover, the workers engaged in these sectors are neither experienced with environmental risks, nor as well prepared in general to think about hazards of work as their industrial counterparts were even long before the modern regulatory era. Because almost all previous attention has focused on the kinds of conditions and hazards that arise in more traditionally dangerous settings, the regulatory framework has not evolved forms of controls that ensure, at least in law, that work will be safe.

This chapter is divided into two sections. The first deals with the spectrum of problems that occur indoors in nonindustrial buildings, focusing on common features of implicated facilities. The second deals with the spectrum of clinical complaints related to low-dose chemical exposures (relative to doses that occur in industry), which have received increasing attention. Although these problems of chemical sensitivity most often occur in association with indoor nonindustrial environments, they may also be seen in a range of other work settings as well as in the non-work environment. Their distinguishing feature is the occurrence of symptoms or other clinical problems at levels that are far below those at which knowledge of toxicology would predict effects, and typically far below accepted standards in industry for human exposures. These somewhat vexing problems have challenged many of the cherished paradigms of occupational and environmental health about what is safe and what is not, and they pose a special challenge for physicians whose patients may complain about chemicals at levels deemed "safe."

BUILDING-RELATED CONDITIONS

Nonspecific Building-Related Illness

Since the 1970s, office workers worldwide have frequently complained of mucous membrane irritation, fatigue, and headache when working in specific buildings, with improvement within minutes to an hour of leaving the building. This constellation of symptoms, with tight temporal association to building occupancy, is called sick building syndrome, or, more recently, nonspecific building-related illness. It is the most

frequent of the building-associated health complaints in industrialized countries, which also include diseases caused by infection, allergic hypersensitivity, and specific toxins. Up to 30% of office workers surveyed may report symptoms attributed to poor air quality, and workers in buildings not known to have indoor air-quality problems have many complaints attributed to the indoor work environment.

Despite the impacts on productivity and employee morale when many workers in a building have building-related symptoms, the causes of these symptoms are incompletely understood. Early investigations of this phenomenon sometimes concluded that symptoms were caused by mass psychogenic illness because no specific contaminants were measured in concentrations that could account for symptoms. However, the endemic nature of complaints in specific buildings and the consistency of complaints from workers in tight buildings across the world did not satisfy diagnostic criteria for mass psychogenic illness. Fortunately, such attribution to psychological cause is no longer common or acceptable, although work stress is associated with reporting of symptoms among occupants of specific buildings (see Chapters 14 and 19). Occupants of buildings with high levels of complaints are often angry and fearful, in no small part due to resistance of managers to investigation of the cause(s) of their problems, inconclusive results of investigations that are conducted, or ineffectual remediation.

The recognition of building-related complaints by public health workers in the United States followed an energy crisis in the 1970s, during which ventilation standards were lowered to supplying 5 cubic feet of outdoor air per person per minute. This observation led to the hypothesis that building-related symptoms were attributable to lower rates of ventilation in relation to indoor contaminant sources. In some studies, ventilation rates are related to the prevalence of nonspecific building-related complaints, especially for ventilation supplying outdoor air at less than 30 cubic feet per person per minute. Indoor air-quality consultants commonly measure carbon dioxide levels as a marker for inadequate fresh air in buildings with high complaint rates. However, carbon dioxide level is not predictive of nonspecific building-related complaints.

The American Society of Heating, Refrigerating, and Air-Conditioning Engineers (ASHRAE) publishes consensus standards for ventilation of various types of buildings that are frequently adopted into building codes. These standards are not health based, and they are not performance standards for operating ventilation systems. Rather, they stipulate ventilation rates for design purposes and are based on occupant comfort. The latest ASHRAE Standard (62.1-2007) recommends 5 cubic feet per minute of outdoor air per occupant and an additional 0.06 cubic feet per minute for every square foot in office buildings, in the absence of cigarette smoking. Measuring effective ventilation is technically difficult, expensive, and rarely done apart from research settings. Indoor air consultants examine ventilation systems for possible entrainment of contaminants in the outdoor air source; design and operation of air flow; filter condition and maintenance schedules; cleanliness of the cooling coils and drip pans, which commonly support microbial growth because of moisture and dirt; condition of the duct lining, which commonly supports microbial growth if wet; and postdesign changes in occupancy, activities, and layout that may impact air quality.[1]

Studies suggest that certain building features and occupant characteristics are related to symptom prevalence. Variation in prevalence of building-related complaints among buildings suggests remediable causes.[2] Occupants of buildings with air conditioning have higher rates of building-related symptoms than occupants of naturally ventilated buildings or buildings with mechanical ventilation that does not alter air temperature or humidity, suggesting that the ventilation system may be the source of poor air quality in some buildings. In one study, ultraviolet germicidal irradiation in office ventilation systems reduced microbial contamination of cooling coils and drip pans, and also reduced work-related respiratory and mucosal symptoms.[3] Building dampness, associated with bioaerosols, is also frequently accompanied by nonspecific building-related illness. Measurable indices of bioaerosols are being studied as correlates of building-related illness; some evidence implicates endotoxin, β-1,3-glucan, ergosterol, and culturable hydrophilic fungi in dust samples. Other environmental correlates include carpeting,

high occupancy, and video display terminal use. Personal factors associated with building-related symptoms include female gender, allergies, and job stress or dissatisfaction.

Health care providers faced with the challenge of responding to indoor air-quality complaints must proceed without the benefit of a complete scientific understanding of what may be a multifactorial syndrome.[1] No single measurement can determine the adequacy of indoor air quality; determination of the acceptability of indoor air quality rests with the occupants—not a laboratory. In response to complaints about indoor air quality, a multidisciplinary approach allows attention to design and maintenance of air-conditioning systems, exclusion of obvious contaminant sources or water damage in the occupied space, and reassurance of occupants that nonspecific building-related symptoms (unlike building-related respiratory symptoms, described later) are self-limited. Indoor air-quality investigations customarily assess the ventilation in relation to occupant load by *(a)* measuring carbon dioxide, *(b)* identifying remediable deficiencies in ventilation system maintenance and cleanliness, *(c)* assessing water damage and moisture incursion, and *(d)* examining smoking policies. Health care providers, on a multidisciplinary team alongside industrial hygienists and ventilation engineers, have an important role to play in ruling out the possibility of less common, but more serious, building-related diseases, such as asthma and hypersensitivity pneumonitis, that frequently occur with a background of nonspecific building-related complaints among other workers.

Building-Related Allergic Disease

A 48-year-old social services eligibility technician began working in an office building in October. She had a history of sinus symptoms and 15 pack-year history of cigarette smoking, having been an ex-smoker for 10 years. Three months later, in January, she began to have insidious onset of dry cough, which, in March, was diagnosed as asthma. Skin-prick tests were negative to common aeroallergens. She was referred to an occupational medicine clinic in August, when she noted worsening symptoms during the workday (requiring use of inhaled bronchodilators) and recovery in the evenings and on weekends (when she did not need to use them). Her asthma became much worse when she handled dusty records while her desk was being moved. Self-monitoring of peak-flow showed reproducible, striking air-flow limitation shortly after entering the building, with partial recovery during lunch breaks outside the building and full recovery on weekends (Fig. 7-1). Methacholine challenge testing in September and November, before a 16-day vacation, found the provocative concentrations (PC20) for a 20% decrement in forced expiratory volume in 1 second (FEV_1) to be 0.29, and after the vacation to be 0.47 mg/mL (normal PC20 >15 mg/mL). These results confirmed a diagnosis of asthma

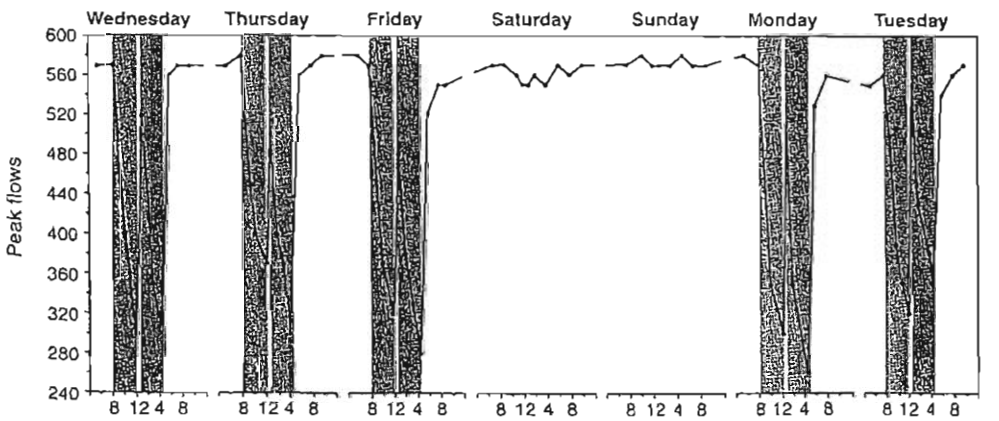

Figure 7-1. Peak-expiratory flow measurements by hour and day in a case of office building–related asthma. Stippled columns indicate time at work.

and suggested slight improvement in airway hyperreactivity with a short absence from work. Although she had notified her employer, her relocation to another building was delayed until late February, after her third course of prednisone treatment. After this relocation, her symptoms cleared, her work-related airflow limitation (documented by peak-flow measurements) resolved, and her need for asthma medications ended. Three months after her relocation, her PC20 normalized to above 25 mg/mL.

Nine months later, she was moved back to the original building into a set of offices that shared no ventilation system with the offices that she had previously occupied. Over the next 6 weeks, she experienced increasing symptoms and airflow limitation, once again requiring daily medication, and her PC20 fell to 0.22 mg/mL. She was medically restricted from the implicated building, with resolution of her work-related decrements in peak flow, decrease of her medication requirements, and increase in her PC20 to 5.19 mg/mL over the following 6 weeks. She has had no further difficulty with clinical asthma since then.

This building was built into an earthen bank, and workers reported musty odors and visible mold growth on the interior wall that abutted the bank. Aspergillus species of fungi were detected in the interior air but not in simultaneous measurements of outdoor air, suggesting amplification and dissemination of this fungus indoors. The presumed source of the woman's asthma was fungal bioaerosols associated with moisture coming in from the earthen bank.

Building-related asthma is infrequently recognized by physicians, although, unlike nonspecific building-related illness, it can lead to chronic irreversible illness. Early recognition and removal from the building, as in this woman's case, can result in cure of asthma. Permanent asthma can result when recognition of occupational etiology is delayed and asthma becomes severe before the patient leaves the implicated exposure. Such sentinel cases of asthma imply risk for other workers. In this case, public health investigation after two sentinel cases showed that co-workers had nearly five times the prevalence of physician-diagnosed asthma with onset or exacerbation since building occupancy, compared with workers in another social service agency.[5]

Building-related asthma occurs in water-damaged buildings and in relation to microbially contaminated humidifiers used in them.[6] Biologic aerosols containing mold spores and possibly bacteria are the sensitizing and irritant agents. No air measurement of viable fungi or spore count has been shown to predict hazard in the nonindustrial environment. An indoor source of microbial amplification and dissemination can be inferred from looking at the rank order of mold species concentrations indoors compared to outdoors, but no quantitative standards exist or are likely to be developed based on air exposure–response studies. Visible mold (Fig. 7-2) and moldy smells should be remediated without demonstrating specific mold air levels by culture or air sampling. Despite the difficulty in characterizing the exposure, the affected individual's symptom history and peak-flow measurements can be valuable in documenting the occupational nature of building-related asthma. Cases of building-related asthma may occur along with cases of hypersensitivity pneumonitis in water-damaged buildings.

A 46-year-old pediatrician had been followed by an allergist for 10 years for upper respiratory and chest complaints after moving into an office suite. At first, he complained of sinus drainage and a sore feeling in his nose and throat. Over the years, he had acquired achiness in his chest associated with fever, productive cough, chest tightness, wheezing, fatigue to exhaustion, and shortness of breath on exertion. His forced vital capacity (FVC) fell within 3 years of building occupancy, consistent with a restrictive pattern. Without ever receiving a diagnosis, he had been treated with nasal cromolyn, inhaled steroids, bronchodilators, theophylline, antibiotics, and intermittent oral corticosteroids. A year before his referral to an occupational medicine specialist, he had noted exacerbation of his chest symptoms when he returned to his office suite after a week away from work. He then began to suspect an office-related cause to his symptoms, with increased cough, chest tightness, and achiness when he entered his suite, and resolution within hours after leaving and improvement on weekends. He noted a musty smell and fungal discoloration of wall board in the suite bathroom, which resulted from leaking pipes.

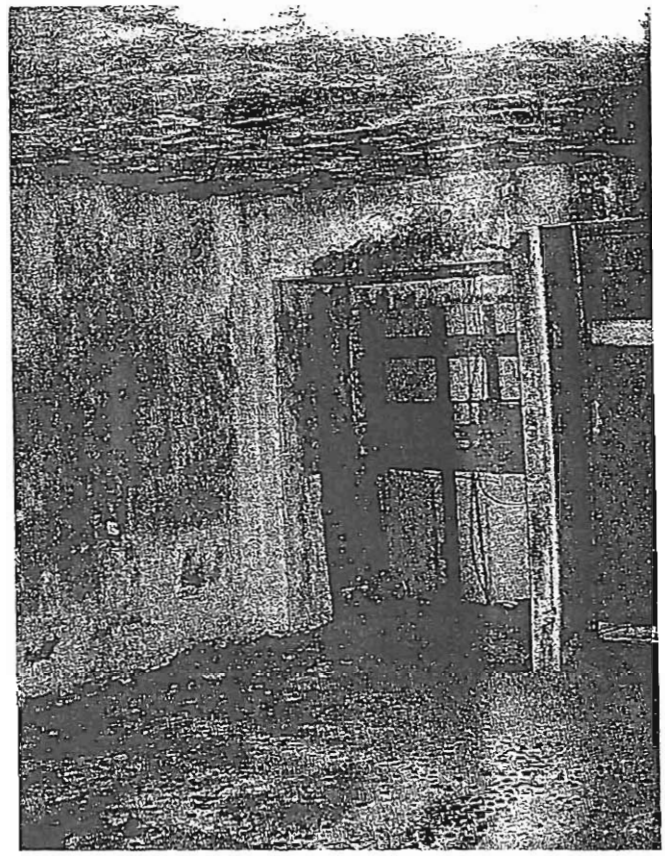

Figure 7-2. Extensive mold growth in a room of a former hotel in New Orleans, years before Hurricane Katrina struck New Orleans in 2005. (Photograph courtesy of Michael R. Gray.)

On referral, he was found to have basilar rales, bronchial hyperreactivity on histamine challenge testing, and reduced exercise tolerance with an excessive respiratory rate at rest and excessive minute ventilation for oxygen consumption. Chest X-ray was normal, but a high-resolution computed tomography (CT) scan showed fine centrilobular nodules. Bronchoalveolar lavage showed a lymphocytic alveolitis compatible with hypersensitivity pneumonitis. A transbronchial lung biopsy showed a mild, patchy lymphocytic interstitial pneumonitis. His symptoms resolved with prednisone and removal from the office suite.

However, 2 months later, chest aching, exertional shortness of breath, profound fatigue, and chilly feelings recurred within 45 minutes of using a musty restaurant bathroom that had been water-damaged from recurrent roof leaks. He had a prolonged recovery time, requiring systemic steroids for 7 months. A year after this acute exacerbation, he again had a recurrence of chest symptoms, within hours of handling medical records from his previous office suite that had become wet while stored in his basement (because of a hot water heater leak). He again required months of prednisone use and did not fully recover his health until 1 year later.

This case of building-related hypersensitivity pneumonitis illustrates the typical medical delay in suspecting and diagnosing a building-related etiology for symptoms. Few physicians are aware that office settings can be associated with diseases related to organic antigens. In contrast to building-related asthma, however, there are many published case reports and epidemic investigations of hypersensitivity pneumonitis and humidifier fever. Typically, people with hypersensitivity lung diseases may not be able to reoccupy a building in which they were sensitized to biologic aerosols from humidifiers, ventilation systems, or water-damaged materials on which fungal growth

has occurred. Even after remediation of the conditions that led to sensitization and disease, low levels of exposure can trigger recurrent symptoms. Because hypersensitivity pneumonitis can lead to irreversible lung fibrosis after recurrent acute episodes or prolonged exposure, early recognition and restriction of affected people from the implicated building are the best measures for preventing progression. Remediation is warranted to prevent cases in co-workers who are not yet sensitized. Occupational medicine physicians can encourage specialists to proceed with diagnostic tests before the affected individuals develop classic late-stage abnormalities, such as those evident on chest X-rays. The aforementioned case suggests that this pediatrician was sensitized to an antigen that was not unique to his water-damaged office setting.

Cases of hypersensitivity pneumonitis are often accompanied by systemic symptoms of myalgia, fever, and profound fatigue. These symptoms are not usually present in asthma, although both diseases commonly share chest symptoms, such as cough, chest tightness, and wheezing. In contrast to asthma and hypersensitivity pneumonitis, sick building syndrome alone is not accompanied by chest symptoms. When indoor air-quality complaints exist, health care providers should evaluate occupants for building-related asthma and hypersensitivity pneumonitis. The occurrence of building-related chest disease dictates evaluation for sources of fungal and bacterial growth and means of dissemination from areas of water damage or from the ventilation system.[7] The presence of chest disease also requires more aggressive medical restriction from the building to prevent irreversibility of the condition.

Many patients report that they have building-related nose and sinus symptoms. Allergic rhinosinusitis can occur, in a way analogous to the response of airways and lung tissue to building-related antigen exposure. Little research has been done on this common clinical complaint to determine its epidemiology, to distinguish it from nonimmunologic mucous membrane complaints in sick building syndrome, or to link it to exposures in implicated buildings.[7] Unfortunately, there are no practical ways of measuring antigens related to indoor microbial bioaerosols, although research is underway on antigen identification, measurement, and size differentiation. However, rhinitis may precede or exacerbate asthma. If the temporal association suggests that the nasal or sinus symptoms are building related, the same attention to identifying and removing sources of water damage and attending to the maintenance of the heating, ventilation, and air-conditioning system is needed as for building-related chest diseases.

In residential environments, allergic disease commonly occurs in relation to indoor allergens, which are more diverse than those in office settings. Antigens from dust mites, cockroaches, and animal danders are implicated in asthma beginning in childhood. Environmental intervention to lower these antigen exposures, such as by using antigen-impermeable mattress covers, vacuum cleaners equipped with high-efficiency particulate air (HEPA) filters, HEPA air purifiers, and professional pest control, can reduce childhood asthma morbidity when it is tailored to the sensitizers affecting an asthmatic child.

Building-Related Infection

In 1976, a total of 182 cases of a mysterious pneumonia occurred among members of the American Legion attending a convention in Philadelphia. After months of laboratory investigation, a newly discovered bacterial organism, *Legionella pneumophila*, was found to be the responsible agent. We now know that, in the absence of vigorous attempts to eradicate it, this common environmental organism frequently grows in the warm water of building cooling towers. When contaminated cooling tower mists are entrained in air intakes of large buildings, cases of infection with this organism (legionellosis) can occur. Outbreaks have also been recognized as a result of contaminated industrial water sprays, hospital shower heads, and hot tubs. Legionella pneumonia is not spread by person-to-person transmission.

When legionellosis occurs, molecular biology techniques are now used to identify specific strains by DNA fingerprinting. Possible sources can be tested for the same strain in environmental reservoirs. This matching of aerosol source with clinical cases can help prioritize environmental controls through disinfection of hot water systems and avoidance of entrainment of contaminated aerosols.

In addition to pneumonia, Legionella organisms have been associated with another building-related disease called Pontiac fever, which is self-limited and characterized by fever, chills, headache, and myalgia. It was first described in 1968, in a building-related epidemic of 144 cases in a county health department in Michigan. The attack rate was nearly 100%, with an average incubation period of 36 hours.

Building ventilation characteristics are important factors affecting the spread of contagious infections, such as those due to respiratory viruses. Types of housing with different ventilation characteristics, such as air-conditioned buildings (as compared with tents or naturally ventilated barracks), are associated with increased incidence of respiratory symptoms and signs of communicable disease in military troops. Other airborne infectious diseases, such as tuberculosis, pneumococcal disease, varicella, and measles, may be affected by rates of building ventilation. A major concern in hospitals, prisons, and shelters is control of tuberculosis, for which ventilation and air disinfection techniques are critical. (See also Chapter 13.)

Building-Related Complaints Due to Specific Toxic Agents

Health professionals responding to building-related complaints must also consider specific toxic exposures as a possible explanation. This is particularly important when complaints differ from those of nonspecific building-related illness or occur in epidemic—rather than endemic—fashion. For example, complaints of headache and nausea dictate consideration of carbon monoxide poisoning, which can occur when internal combustion sources are not exhausted to the outdoors or when air intakes entrain fumes from loading docks, parking garages, or boiler-stack emissions. Building-related itching without rash can occur with fibrous glass exposure, which can result when air-duct lining is entrained in the airstream entering the occupied space. Epidemic coughing, dry throat, and eye irritation can result from detergent residues after the misapplication of carpet cleaning products. In instances of building-related complaints associated with specific exposures, a careful evaluation of types of symptoms, their distribution among building occupants by location or job, and their temporal onset may point investigators to the cause and to remediation resources.

INDOOR CARCINOGEN EXPOSURE

Environmental tobacco smoke has been the most common indoor carcinogen, but public tolerance of this exposure is decreasing across the United States, as reflected in state and municipality ordinances prohibiting smoking in workplaces, restaurants, and bars. (See Box 7-1 and Fig. 7-3.) Sadly this is not yet true in many parts of the developing world, where tobacco smoke is still commonly encountered, posing risks for cancer and respiratory disease. Also widely encountered are poorly exhausted combustion products of available and cheap biomass fuels used for heating and cooking. (See Box 7-2.) Even as their precise contribution to cancer risk and respiratory disease burden in children and adults remains under study, there is little controversy that these indoor exposures constitute one of the most prevalent and serious environmental problems in the world.

Sometimes building-related exposures to carcinogens do not cause symptoms in occupants, but still pose a health risk. For example, radon gas emitted from building materials, water, and soil surrounding foundations increases the risk of cancer. Radon exposures can be measured with simple devices. The Environmental Protection Agency (EPA) has issued guidelines for elevated exposures and effective remediation, such as sealing of foundations and subsurface ventilation. Similarly, asbestos in insulation and some building materials in older buildings poses risks of cancer of the lung and other sites (as well as nonmalignant lung disease) if it is disturbed during occupant activities or renovation. Because of latency and dose–response considerations, health professionals are often called to help communicate risks of asbestos exposure to building occupants or the public during removal of asbestos from older buildings. Most states license asbestos-abatement professionals, who are trained to protect remediation workers with respirators and other personal protective equipment, while maintaining negative pressure in asbestos removal areas to prevent asbestos

Box 7-1. Environmental Tobacco Smoke

Kathleen Kreiss

Environmental tobacco smoke (ETS), or secondhand tobacco smoke, contains more than 4,000 compounds, which demonstrate their biologic properties through different mechanisms. Environmental tobacco smoke exposure is associated with increased risks of lung cancer, heart disease, and nonmalignant respiratory disease in people who have never smoked. An estimated 46,000 deaths (range: 22,700 to 69,600) from heart disease and more than 3,400 deaths (range: 3,423 to 8,866) from lung cancer attributable to ETS occur annually in the United States.[1] No risk-free level of exposure has been determined. The only way to fully protect nonsmokers from exposure to ETS is to eliminate smoking in indoor spaces. There are no occupational exposure limits for ETS. Other methods to reduce exposure, such as separating smokers from nonsmokers, cleaning the air, and increasing ventilation in buildings, cannot eliminate ETS exposures of nonsmokers. Homes and personal vehicles remain major venues of exposure to involuntary ETS exposure.

Environmental tobacco smoke exposure, in utero and during the neonatal period and childhood, causes substantial respiratory effects in children. Maternal smoking during pregnancy is associated with lower birthweight, reduced lung growth, and adverse effects on lung function shortly after birth that can persist throughout childhood. Postnatal exposure causes a lower level of lung function during childhood; increased respiratory illnesses in infants and children; middle ear disease (acute and recurrent otitis media and chronic effusion); symptoms of cough, phlegm, wheeze, and breathlessness among school-age children; risk of ever having asthma in schoolchildren; and onset of wheeze-related illnesses in early childhood. ETS exposure is causally related to sudden infant death syndrome. The causal effects of parental smoking are stronger for younger children and for maternal smoking; however, paternal smoking is associated with some of these outcomes even in homes where the mother does not smoke.[2]

Asthmatic adults exposed to ETS have increased acute respiratory symptoms, including cough, chest tightness, and difficulty breathing. Healthy adults also may complain of these acute and chronic symptoms as a result of ETS exposure. There is suggestive evidence that short-term ETS exposure can cause an acute decline in lung function in persons with asthma and that chronic exposure may cause a small decrement in lung function in the general population. Similarly, there is suggestive, but not sufficient, evidence to infer a causal relationship between ETS exposure and adult-onset asthma, worsening of asthma control, risk of chronic obstructive pulmonary disease, and morbidity in persons with chronic obstructive pulmonary disease.

Environmental tobacco smoke also leads to annoyance from odors and sensory irritation of the nose and throat, which accounts for most nonsmokers finding air quality unacceptable in indoor spaces where ETS is present. The odor threshold for respirable suspended particles in environments with cigarette smoking is about 1 $\mu g/m^3$.

In studying exposures to ETS, one often monitors "marker" substances and uses them as indices of exposure. Selection of these compounds is based on their ease of measurement and not their toxicity. They include nicotine, respirable suspended particles, volatile organic compounds, particulate polynuclear aromatic hydrocarbons (PAHs), and aldehydes.

Levels of biomarkers can be measured to determine how much ETS a person has absorbed or metabolized. These biomarkers commonly include carboxyhemoglobin; urinary or serum cotinine, a major metabolite of nicotine; and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol, the major metabolite of the tobacco-specific carcinogen 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone. Urinary cotinine levels are commonly adjusted for creatinine. The biological half-life of cotinine is approximately 16 to 20 hours; therefore, urinary cotinine is an indicator of ETS exposures from the previous 1 to 2 days. The half-life of the tobacco-specific carcinogen is 40 days, and its urinary metabolite, 45 days.

Restrictions on tobacco smoking indoors are now the norm in the United States in most commercial and government buildings, as well as public transportation facilities and conveyances. The passage of local ordinances has been facilitated by the increasing prevalence of nonsmokers in the population, the quantification of risk from their estimated ETS exposures, and energy savings on ventilation rates in the absence of cigarette smoking.

Some public spaces still permit smoking, especially entertainment and hospitality facilities. Casinos have often remained exempt from laws and regulations mandating smoke-free workplaces. The estimated number of annual deaths from ETS-induced heart disease and lung cancer in Pennsylvania casino workers is five-fold those due to Pennsylvania mining disasters, and the number far exceeds the Occupational Safety and Health Administration (OSHA) level indicating significant risk of health impairment.[3]

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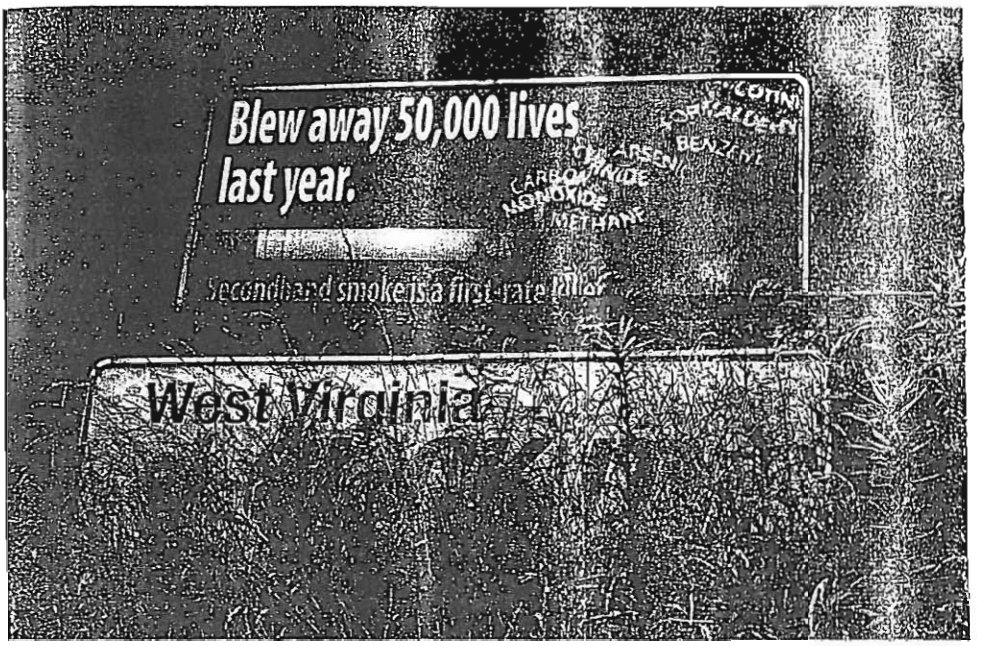

Figure 7-3. Billboard warning the public about the dangers of environmental (secondhand) tobacco smoke. (Photograph by Earl Dotter.)

fibers from entering occupied spaces. For all of these carcinogens, primary prevention is through identification and management.

MULTIPLE CHEMICAL SENSITIVITY

Since the 1980s, a new clinical syndrome—now most widely referred to as multiple chemical sensitivity (MCS)—has been recognized, characterized by symptoms in multiple systems after exposure to low levels of synthetic chemicals.[8] Despite research efforts, its pathophysiologic basis remains uncertain and controversial. Unlike any other building-related illness, it recurs in affected people in a diverse array of environmental situations and cannot be readily reversed by attention to any single exposure situation. The following is a representative example:

A 46-year-old library worker was in good health until the onset of eye, nose, and throat irritation and recurrent headache associated with renovation of the library where she worked. She and many co-workers complained primarily of dust and paint fume exposures, which were poorly controlled initially. After several weeks of effort, the employer succeeded in establishing temporary ventilation for the work area and performing most of the renovation at night. Almost all of the patient's co-workers improved dramatically after these changes were made. She, however, felt no better and began experiencing similar symptoms in her car, at various stores, whenever she was around anything she termed "scented," and especially in the office. She believed she was experiencing effects from the small residual levels of construction-related exposures, but temporary transfer to another part of the library brought no relief. New symptoms, including difficulty breathing, muscle and joint aches, and confusion occurred both at work and at home, triggered by an increasing number of offensive odors, irritants, and products. Efforts to clean her house of such materials, as well as a trial leave of absence from work (without the benefit of workers' compensation), resulted in only minimal improvement.

On clinical evaluation, the patient appeared well and had no abnormal physical findings. Laboratory tests, including a work-up for respiratory and central nervous system abnormalities, were unrevealing. Consultations in pulmonary medicine, rheumatology, and neurology were unhelpful. Attempts at empirical

Box 7-2. Exposure to Biomass Fuel Fumes

John R. Balmes

Half of all people still rely for their daily energy requirements on solid fuels, with even a higher fraction—up to 80%—in rural areas of some countries. These solid fuels are mainly biomass: wood, dung, and crop wastes. Because biomass is typically burned in inefficient, poorly vented stoves indoors—and often in open fires—women and young children are intensely exposed to indoor air pollution (IAP). Levels of exposure to particulate matter (PM) in such homes are often at least an order of magnitude higher than the highest concentrations that occur in the ambient air of developed countries.[1] In addition to PM, carbon monoxide, nitrogen oxides, formaldehyde, and toxic organic compounds, such as benzene; 1,3-butadiene, and benzo(a)pyrene, are present in smoke from biomass combustion, depending on the type of fuel that is burned.[2] In terms of emissions of PM and gases, the combustion of wood and other biomass is qualitatively similar to the burning of tobacco, although without the nicotine.

Cooking with biomass fuels is generally done on unvented stoves, typically consisting of such simple arrangements as three rocks, a U-shaped hole in a block of clay, or a pit in the ground. Combustion under such conditions leads to high emission factors that can lead to extremely high pollutant concentrations near the stove. Pollutant concentrations are further exacerbated by the lack of ventilation that characterizes many kitchens in rural areas of developing countries. Since households in rural areas of these countries often require cooking for many hours daily, exposure to biomass smoke is considerable, especially for women and children. Infants and young children are often carried on their mothers' backs while they cook, so from early infancy children spend hours breathing smoke from cooking or heating fires. In temperate climates and highland areas, people spend more time indoors, and the cold temperatures that characterize these areas require fires that burn over extended periods and tighter house construction for space heating. Therefore, both pollution levels and exposure times increase.

There is great public health impact of the relatively high exposures to PM in homes where cooking is done with inefficient, poorly ventilated stoves using biomass fuels. IAP from solid fuel use is responsible for *(a)* 2.6% of the total global burden of disease in terms of disability-adjusted life years (DALYs), and *(b)* between 1.5 and 2.0 million deaths annually.[3] Indoor air pollution is the second most important environmental risk factor, after poor water, sanitation, and hygiene.

The greatest burden of IAP-related premature deaths is in children with pneumonia. A recent meta-analysis showed a significantly increased overall pooled odds ratio (1.78) for acute lower respiratory tract infection (ALRI) in children exposed to unprocessed solid fuel smoke.[4] This finding is biologically plausible because smoke from biomass impairs respiratory tract defense mechanisms, such as mucociliary clearance and alveolar macrophage function.

While cigarette smoking is the leading preventable cause of chronic obstructive pulmonary disease (COPD) in developed countries, IAP exposure from inefficient burning of solid fuels may be the leading preventable cause of COPD among women in developing countries. Since almost 3 billion people use biomass or coal as their main cooking and heating fuel, the resultant population at risk for COPD (including men) is huge. (In addition, people in developed countries exposed to wood burning in fireplaces and stoves in their homes are at increased risk of COPD.) Cooking with biomass fuel has been associated with both chronic bronchitis and chronic airflow obstruction. A recent intervention trial found a slower rate of decline in lung function in women who used an improved chimney stove.[5]

Given that IAP exposure from solid fuel used for cooking and heating remains common worldwide and that the health impacts of this exposure are substantial, reducing this exposure needs to be a high public health priority.

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therapy with various inhalers, nonsteroidal anti-inflammatory agents, and migraine therapies also failed to relieve her symptoms. Because of the disparity between complaints and findings, she was referred to a psychiatrist who confirmed some depressive features but could not explain her symptoms. She began a trial of selective serotonin reuptake inhibitor (SSRI) antidepressants, but she could not tolerate them and discontinued them after 3 days.

Finally, frustrated by unsympathetic physicians and her employer, she sought evaluation from a nonstandard environmental medicine physician, who advised (a) total avoidance of all chemical exposures, including quitting her job, and (b) nontraditional remedies, based on results of

blood and hair tests in an alternative laboratory, which reported measurable levels of organic chemicals and heavy metals as well as immunologic responses to a range of common chemicals. She continues to have many symptoms.

Although this case occurred in the setting of building-related illness, MCS may develop in occupational and nonoccupational settings, and in people who have experienced one or more episodes of chemically induced illnesses due to solvents, pesticides, or other chemicals. Once MCS begins, however, affected individuals experience symptoms they associate with many types of environmental contaminants in air, food, or water at doses well below those that clinically affect others.[9] Although there is typically no measurable impairment of specific organs, complaints are associated with dysfunction and disability.[10] While MCS as severe as in the aforementioned case is not common, milder variants of chemical intolerance are very prevalent among adults.

There is no general consensus on a definition for MCS, but certain features are sufficiently characteristic to raise suspicion and differentiate it from other occupational and nonoccupational health problems. Its major features are as follows:

- Symptoms usually occur after a single or recurrent occupational or environmental inhalational exposure.
- Symptoms resembling those associated with the preceding exposure begin to occur after exposures to surprisingly lower levels of other common work and household substances, especially irritants and those with a pungent odor.
- Symptoms appear referable to many organ systems, especially the central nervous system.
- Chronic symptoms often make it difficult to discover any relationship between exposures and effects.
- Objective organ impairment is typically absent.
- No other diagnosis easily explains the range of responses or symptoms.

Not every patient meets these criteria precisely. But because the diagnosis of MCS is, in the end, based on subjective information, each point should be carefully considered. Each serves to rule out other clinical disorders that MCS may resemble, such as generalized anxiety disorder, classic sensitization to environmental antigens (such as occupational asthma), late sequelae of organ system damage (such as reactive airways dysfunction syndrome after a toxic inhalation), or systemic disease (such as systemic lupus erythematosus). On the other hand, the diagnosis of MCS does not require the exclusion of all other possibilities, and exhaustive testing is not required in most cases.

The sequence of pathologic events that leads from apparently self-limited episodes of an environmental exposure to the development of MCS in certain people is not known. Most available data are descriptive. And debate over the etiology of MCS has been heavily dominated by dogma.

Detailed information about the epidemiology of MCS is not available. Estimates of prevalence in the U.S. population range as high as 6%; the rate found in military "controls" for veterans of the Persian Gulf War was about 2.5%, while veterans of this war suffered MCS-like symptoms twice as frequently.[11] Although many people find chemicals and other odors objectionable and report life modifications to avoid exposure to them, MCS in the clinically overt form remains uncommon. Other observations include the following:

- Multiple chemical sensitivity syndrome occurs most commonly in midlife.
- Women are more frequently affected than men.
- Some host factor or susceptibility is important because mass outbreaks have been uncommon, and only a small fraction of victims of chemical overexposures acquire MCS or a similar disorder.
- Several classes of chemicals have been commonly implicated in the initial presentation of MCS, specifically organic solvents, pesticides, and respiratory irritants. In a "sick building" situation, some patients evolve from nonspecific building-related illness into MCS.

Natural History

Multiple chemical sensitivity syndrome has not yet been studied enough to delineate its clinical

course completely. But there is little evidence that it is progressive, and it is not lethal. Complete remissions are equally unlikely. There is no established treatment for MCS.

Primary prevention strategies cannot be developed without knowledge of the pathogenesis of the disorder or the host risk factors that predispose some people to become affected.

Secondary prevention would appear to offer some greater control opportunities, although no specific interventions have been studied. Because psychological factors may play a role in victims of occupational overexposures, careful and early management of people seeking care after acute toxic exposures or symptoms related to buildings is advisable even when the prognosis from the exposure itself is good. Patients seen in clinics or emergency departments immediately after acute exposures should be assessed for their reactions to the events and should probably receive very close follow-up when undue concerns of long-term effects or persistent symptoms are noted. Efforts should be made for such patients to prevent recurrences of symptomatic exposures, which may be precipitants of MCS by whatever mechanism is causal. Aggressive interventions or those that lead to unnecessary limitation of activity should be avoided.

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FURTHER READING

Black DW, Doebbling BN, Voelker MD, et al. Multiple chemical sensitivity syndrome: symptom prevalence and risk factors in a military population. Archives of Internal Medicine 2000; 160: 1169–1176.
This study concluded that self-reported symptoms suggestive of multiple chemical sensitivity syndrome are relatively frequent in a military population and are more common among Persian Gulf War veterans than comparable controls.

Fisk WJ, Lei-Gomez Q, Mendell MJ. Meta-analyses of the associations of respiratory health effects with dampness and mold in homes. Indoor Air 2007; 17: 284–296.
Based on meta-analyses, the authors concluded that building dampness and mold are associated with approximately 30% to 50% increases in a variety of respiratory and asthma-related health outcomes.

Gibson PR, Elms AN, Ruding LA. Perceived treatment efficacy for conventional and alternative therapies reported by persons with

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This study found that results for most therapies for people with multiple chemical sensitivity were mixed. Participants had consulted a mean of 12 health care providers and spent over one-third of their annual income on health care costs.

Institute of Medicine. Damp indoor spaces and health. Washington, DC: National Academies Press, 2004.
This interdisciplinary review of the scientific evidence on associations between exposure to "dampness" in buildings and health effects concluded that cough, wheeze, asthma, airways infections, tiredness, and headache are caused by dampness but that the mechanisms and environmental measurements predicting risk are unknown.

Mendell MJ, Cozen M, Lei-Gomez Q, et al. Indicators of moisture and ventilation system contamination in U.S. office buildings as risk factors for respiratory and mucous membrane symptoms: analyses of the EPA BASE data. Journal of Occupational and Environmental Hygiene 2006; 3: 225–233.
Even in non-compliant office buildings, symptoms are associated with remediable building environmental conditions.

Sparks PJ, Daniell W, Black DW, et al. Multiple chemical sensitivity: a clinical perspective. I. Case definition, theories of pathogenesis, and research needs. Journal of Occupational Medicine 1994; 36: 718–730.
This paper and the one that follows comprise a refereed review of multiple chemical sensitivity syndrome. This review article explores four theories of causation of MCS syndrome and suggests areas for further research. Although published in 1994, these two papers still comprise the best and most balanced review in this format of this complex subject.

Sparks PJ, Daniell W, Black DW, et al. Multiple chemical sensitivity: a clinical perspective. II. Evaluation, diagnostic testing, treatment, and social considerations. Journal of Occupational Medicine 1994; 36: 731–737.
This review article proposes strategies for clinical evaluation and management of patients with MCS using a biopsychosocial model of illness.

Saito M, Kumano H, Yoshiuchi K, et al. Symptom profile of multiple chemical sensitivity in actual life. Psychosomatic Medicine 2005; 67: 318–325.
This study, which examined real-time, self-reported experiences of MCS patients coupled with real-time assessment of the environments that triggered symptoms, concluded that patients with multiple chemical sensitivity do not have either somatic or psychological symptoms under chemical-free conditions, and that symptoms may be provoked only when exposed to chemicals.

The findings and conclusions in this chapter are those of the authors and do not necessarily represent the views of the National Institute for Occupational Safety and Health.