92

Sick Building Syndrome and Building-related Illness

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Since the late 1970s, consultants and public health agencies at the local, state, and federal levels have been barraged with requests for investigative assistance to determine the origins of and solutions to complaints of office workers regarding their indoor environments. The most frequent constellation of building-associated complaints is called *sick building syndrome*. It consists of mucous membrane irritation of eyes, nose, and throat; headache; unusual tiredness or fatigue; and, less frequently, dry or itchy skin. The hallmark of these symptoms is their tight temporal association with building occupancy and their rapid resolution, within minutes to hours, when affected office workers leave implicated buildings. Sick building syndrome is distinguished from more medically serious building-related illness by its subjective nature, reversibility, and high prevalence within implicated buildings and across the nonindustrial building stock in North America and Europe. Building-related illnesses include asthma, hypersensitivity pneumonitis, inhalation fever, rhinosinusitis, and infection. In contrast to sick building syndrome, these building-related illnesses are less common and may result in substantial medical morbidity. Building-related asthma, hypersensitivity pneumonitis, and rhinosinusitis are usually accompanied by sick building syndrome symptoms among coworkers. Whether similar etiologies contribute to sick building syndrome and these building-related illnesses is still speculative.

[1]The findings and conclusion in this chapter are those of the author and do not necessarily represent the views of the National Institute for Occupational Safety and Health.

EPIDEMIOLOGY OF BUILDING-RELATED RISK FACTORS

Despite nearly three decades of public health investigation of sick building syndrome, scientific research regarding cause and effective intervention or prevention has been meager. The historical origins of this inattention from the scientific community are relevant to other occupational and environmental problems of uncertain etiology.

The initial approach to building complaints was dominated by an industrial hygiene conceptual framework with applicability to the industrial environment. Since the late 1970s and even currently, building investigators typically measure air concentrations of pollutants of building material origin, such as formaldehyde or volatile organic compounds. Finding individual chemicals in low concentrations, in comparison to permissible exposure limits, frequently led to allegations that building occupants had no verifiable basis for complaint and therefore had mass psychogenic illness. Mass psychogenic illness, however, is not a diagnosis of exclusion and has criteria for diagnosis (1). The endemic nature of sick building syndrome within implicated buildings, its high prevalence in "nonproblem" buildings, and its symptom constellation are not explicable by hysteria resulting from hyperventilation and a visible person-to-person chain of transmission. However, building occupants whose complaints about indoor environmental quality have been ignored or for whom investigation has not resulted in effective remediation are often anxious and turn to nonscientific explanations of their symptoms.

The industrial hygiene conceptual approach to problem building investigation resulted in measurement of carbon dioxide (CO_2) concentration and the guidance that levels should be kept below 1,000 ppm. Of course, CO_2 could not cause the symptoms composing sick building syndrome even at the highest levels found in office buildings. However, CO_2, a product of human metabolism, served as a marker of ventilation rate in relation to occupancy, with increases above the 350-ppm level found in outdoor air being typical of indoor environments. The underlying assumption of this ventilation hypothesis was that human occupants were the source of the deterioration of indoor environmental quality. Indeed, this assumption was the basis of the earliest ventilation standards, which sought to ameliorate body odor from assembled groups indoors in the decades before current hygiene practices, indoor plumbing, and personal deodorants. The popularity of this approach to problem building investigation was derived from the observation that building-related complaints surfaced after the energy crisis in the 1970s. The American Society of Heating, Refrigerating, and Air-Conditioning Engineers had lowered its consensus standard for ventilation rate in occupied spaces from 20 cubic feet of outdoor air per minute (cfm) per person to 5 cfm per person in 1975. CO_2 concentration is often still used as an indication of ventilation adequacy for removing general indoor air pollutants, although relationships between CO_2 and actual ventilation rates are complex (2,3).

Advances in scientific understanding of indoor environmental quality complaints were made by European investigators beginning in the 1980s (4–6). Taking an epidemiologic approach, they showed that building-associated symptoms were common in buildings not recognized as having indoor environmental problems. Symptom rates varied substantially from building to building and were associated with building types and characteristics. Most interesting from the point of view of etiology and prevention was the finding that ventilation system type was important in determining risk of occupant symptoms, with mechanical ventilation and/or air-conditioning conferring a several-fold risk in comparison to buildings with natural ventilation (7–9). This finding shifted the research emphasis from characteristics of affected persons to ventilation engineering and building design concerns. The association of air-conditioning with symptom prevalence also dovetailed nicely with the findings of human panel studies that evaluated subjective air quality, odor, and stuffiness of buildings in relation to ventilation system activity and occupancy (10,11). In some buildings, operation of the ventilation system resulted in deterioration of subjective air quality, suggesting that ventilation systems could be sources of symptoms rather than the solution to them.

These findings called into question the simple guidance, now increasingly recognized as obsolete, that CO_2 levels be maintained below 1,000 ppm. Today, we know that building materials, furnishings, equipment, and ventilation systems produce irritant pollutants that can interact to produce even more irritating chemicals (12). Controlling nonhuman pollutant levels requires ventilation without regard to control of human bioeffluents, as indicated by CO_2 levels. Experimental studies evaluating symptom prevalence rates in relation to ventilation rate have mixed results with regard to level of ventilation. At ventilation rates substantially above 20 cfm per person, increases in ventilation sometimes have no effect on the symptoms of sick building syndrome (13). However, starting with ventilation rates of about 20 cfm per person or less, several experimental studies have documented statistically significant improvement in symptom prevalence with increases in ventilation rate (3,14). In summary, minimum ventilation levels are likely important for dilution of the suspected indoor pollutants resulting in sick building syndrome, as long as the ventilation system is not itself the source of the pollutants (15). In cross-sectional studies, ventilation rates above 30 cfm per person are associated with further reduction of occupant symptoms (16), suggesting that the current ventilation and CO_2 guidelines may not be health protective.

The association of air-cooling and/or humidification with occupant symptoms spawned the hypothesis that moisture in the ventilation system could support microbial amplification and dissemination in the indoor environment. Air-cooling may chill the air stream below the dew point within duct work. Humidification obviously increases the moisture available for saprophytic fungi. Modern duct work is commonly lined with sound-dampening materials, such as fibrous glass, which can support microbial growth when damp and which collect dirt, providing additional carbon sources for microbial proliferation.

Despite many attempts to demonstrate associations between microbial concentrations in indoor air and sick building syndrome symptom prevalence, the evidence is still inconclusive. Available methods of measuring microbial pollution in buildings are limited. No correlations have been consistently found for total viable bacteria or fungi in air and symptom rates (14), but sampling times of minutes, used in quantitative sampling methods, are unrepresentative. A Dutch study reported that Gram-negative bacilli had several times higher concentration in supply air in mechanically ventilated buildings characterized by higher symptom rates when compared to mechanically ventilated buildings in which occupants had symptom rates typical of naturally ventilated buildings (17). Similarly, Gram-negative bacteria in carpet dust have been shown in one study to be related to symptom prevalence (18). Viable fungi in carpet dust were associated with symptom prevalence in a water-damaged building (19) and among adolescent students (20).

Viability of microbes may not be important for biologic effect of an allergic, toxic, or inflammatory nature. Endotoxin, a constituent of the cell walls of Gram-negative bacteria, has potent biologic effects. Contradictory data exist for the association of airborne endotoxin with symptom prevalence (21); two reports document an association (17,22). Endotoxin activity in floor dust was not shown to be correlated with symptoms in one study that showed strong correlations with viable Gram-negative organisms in that dust (18). Endotoxin measurement in floor dust has been correlated with symptom prevalence in water-damaged buildings (19,23). Fungal spore counts are independent of viability, but typical short-duration sampling may not be representative. Methods for measuring mycotoxin biomarkers and mycotoxin concentration in air are not yet available to assess their potential role in building-related symptoms (24). Newer approaches for assessing fungal biomass with ergosterol and β-1,3-glucans, which are constituents of fungal membranes and cell walls, respectively, may be promising as a means of assessing fungal microbial contamination in relation to symptom prevalence (25,26). Phthalates and dampness-associated chemical deterioration of plastic floor coverings may play a role in building-associated symptoms (27,28).

In addition to air-conditioning and low ventilation rates, epidemiologic approaches have identified several other workspace risk factors for sick building syndrome. Carpets, textile wall materials, and increased numbers of workers in an office space are supported as risk factors in most studies (14,29). The most important risk factor may be building dampness, and an Institute of Medicine review concluded that nasal and throat symptoms are associated with mold and other exposures in damp indoor environments (30). In systematic investigations by the National Institute for Occupational Safety and Health of 2,435 respondents in 80 buildings with perceived problems, the relative risk of having multiple symptoms of sneezing, eye irritation, and other nasal symptoms was increased in the presence of maintenance deficiencies of heating, ventilation, and air-conditioning (HVAC) systems, in the presence of suspended ceiling panels, by daily surface dusting, and by interior pesticide application (31). Apart from measuring ventilation rates, no quantitative measurements of indoor environmental quality have been consistently shown to be associated with some symptom of the sick building syndrome. Measurements consistently shown not to be associated with symptom rates include carbon monoxide, formaldehyde, total particles, viable fungi, air velocity, and noise. In a large study of U.S. office buildings, elevated CO_2 measurements, adjusted for many covariates, had some exposure-dependent association with mucous membrane symptoms and wheeze (32), but the resulting guidance was to provide sufficient per person ventilation and to reduce indoor air pollutant sources. Measurements remaining open to further investigation because of sparse evidence or inconsistent findings among studies include total volatile organic hydrocarbons, respirable particulates, floor dust measurements, endotoxins, β-1,3-glucan, low negative ions, high temperature, low humidity, and light intensity and glare (14).

Although specific measurements are not available to determine the likelihood that building occupants will avoid the sick building syndrome, the epidemiologic findings to date do lay a foundation for experimental and intervention studies. The risk factors of air-conditioning, carpet, respirable particulates, floor dust, office and HVAC maintenance, and dampness incursion may all be related as affecting sources or reservoirs of biologically active agents from micro-organisms or building fabric. Intervention studies have been conducted, some with blind and crossover designs, to evaluate lowering respirable particulates (33,34), irradiating HVAC coils with ultraviolet germicidal light (35), remediating dampness (36–38), increasing ventilation (39,40), and removing contaminated furnishings and filters (41,42).

EPIDEMIOLOGY OF PERSONAL AND JOB RISK FACTORS

The study of sick building syndrome is challenging because of the psychosocial milieu in which symptoms arise. Although the body of epidemiologic research clearly documents environmental risk factors for the syndrome, investigators of problem buildings commonly experience polarization, suspicion, and controversy surrounding their efforts. Job stress or dissatisfaction has been consistently demonstrated to be related to sick building syndrome in investigations of occupants in buildings not known to have indoor air symptoms (14). It remains uncertain whether this association is a cause or an effect of sick building syndrome.

Researchers have documented an invariable female gender predisposition to report building-associated symptoms (4,6,13–15,43). Whether this female predominance reflects overexposure to unknown etiologic agents in building microenvironments, higher susceptibility, job dissatisfaction, or lower threshold for observation or reporting remains disputed. Smokers have inconsistently shown increased risk of sick building syndrome (14).

Respondent reports of asthma or allergies are consistently associated with sick building syndrome (13–15,43), but no prospective studies exist to establish whether this personal factor is an outcome, a confounder, or a predisposing factor for reports of mucous membrane symptoms in relation to building occupancy. Among occupants of problem buildings, physician diagnosis of asthma since building occupancy was statistically associated with outdoor air intake within 25

feet of vehicular traffic, dirty HVAC filters, debris inside the air intake, presence of cloth-covered partitions, and renovation (especially the installation of new drywall in the preceding 3 months) (31). These environmental associations with the development of asthma during building occupancy suggest that asthma may be a result of exposures predictive of sick building syndrome.

The job-related risk factor consistently demonstrated to be associated with sick building syndrome has been video display terminal use. Inconsistent associations have been found with clerical jobs, use of carbonless copy paper, and photocopier use (14).

The study of sick building syndrome has been complicated by the subjective nature of the complaints. In the face of associations with job stress and dissatisfaction, investigators have feared that classification of cases was unreliable. For eye irritation symptoms, however, breakup time of the tear film, eye epithelial damage, and blink frequency have been shown to correlate with symptoms and with experimental manipulations of the environment (44,45). Other research methods, such as nasal resistance, acoustic rhinometry, and nasal lavage, are being evaluated for their utility in corroborating sick building syndrome symptoms and environmental associations (46,47). The consistency of building-related symptoms across nations and their similar environmental associations make the effort to find objective measures less of a concern than formerly, when a substantial portion of the indoor air scientific community wondered whether the complaints were of purely psychosocial origin.

MAGNITUDE OF SICK BUILDING SYNDROME

Investigators surveying buildings not known to have indoor environmental complaints have found a substantial subset with symptom rates similar to those demonstrable in buildings being investigated for complaints (4–6,8,17,32,43). A random sample telephone survey of the U.S. population documented that about one fourth of office workers perceived indoor air quality problems to exist in their office environments, and 20% of all respondents reported their work performance to be hampered by the air quality (48).

Although sick building syndrome is not considered medically serious by most physicians, the comfort of a substantial sector of nonindustrial workers is compromised by the office building stock. Cost estimates of productivity loss related to discomfort and illness are substantial in comparison to the energy cost savings of decreasing ventilation or savings on ventilation system capacity and maintenance and housekeeping (41,49). The solution of this common problem will likely depend on many disciplines, including architects, general contractors, ventilation engineers, building operations personnel, physicians, industrial hygienists, epidemiologists, and microbiologists. Although existing science does not support standard setting for specific measurable etiologies, the epidemiologic findings to date suggest the effectiveness of some interventions in some buildings, such as remediating water damage, lowering respirable particulates, maintaining an immaculate ventilation system and duct work, using ultraviolet germicidal light on cooling coils, increasing ventilation, and fastidious housekeeping.

BUILDING-RELATED ILLNESSES

Building-related illnesses, such as hypersensitivity pneumonitis and asthma, occur against a backdrop of sick building syndrome symptoms among other building occupants. Their recognition is important because they are often medically serious, require cessation of exposure to improve prognosis, and serve as sentinel events for others at risk. When building occupants report building-related chest symptoms such as shortness of breath with exertion, cough, and wheezing or chest tightness, asthma or hypersensitivity pneumonitis should be suspected. These chest symptoms are not typical of sick building syndrome, although cough can be of either sinus or chest origin. Profound malaise and sick fatigue are characteristic of granulomatous lung disease, such as hypersensitivity pneumonitis, and are not characteristic of asthma or sick building syndrome. Physician recognition of building-related asthma and hypersensitivity pneumonitis may be poor, and the building investigator may need to suggest referral of building occupants with building-related chest symptoms to specialists with an interest in early diagnosis of disease from building-associated etiologies. Persons with building-related asthma or hypersensitivity pneumonitis may have symptom exacerbation with re-entry into an implicated environment even after environmental remediation (50–53), presumably because of the immunologic potentiation of response to even low levels of antigen exposure.

Outbreaks of building-related hypersensitivity pneumonitis have been reported in association with contaminated spray-water humidification systems and contaminated air-conditioning systems (51,54–57), including duct work (58). Hypersensitivity pneumonitis also can occur endemically in water-damaged buildings (30,38,50,59,60) in which wet furnishings or structural components support microbial growth. In contrast to the frequency of water damage to buildings from roof and window leaks, plumbing mishaps, and basement flooding, reports of hypersensitivity pneumonitis are infrequent. This may indicate low-risk, reversible disease or poor recognition of building-related granulomatous or interstitial lung disease by clinicians who seldom inquire about building risk factors for these lung diseases

in sporadic cases. In industrial settings, outbreaks of interstitial lung disease are more likely to be recognized in relation to water-spray processes, humidification systems, or air-conditioning systems. These have been reported from the stationery industry (61), printing works (62), photographic film industry (63), swimming pools with water-spray features (64), and textile industry (65).

Building-related asthma is likely much more common than hypersensitivity pneumonitis, but it has been investigated less frequently. Outbreak investigations and case reports document water incursion (38,50,60,66,67), moisture in the air-conditioning system (68), cool mist vaporizers (51,69), and humidifiers (70,71) as factors in etiology. As with hypersensitivity pneumonitis, recognition of possible environmental or occupational cause may be lacking by clinicians evaluating asthma patients who work in nonindustrial indoor environments. A robust set of population-based studies implicate residential dampness, mold, and associated exposures as risk factors for respiratory symptoms and asthma exacerbation (30). Since the 2004 Institute of Medicine review of dampness and human health, *new-onset* asthma excess has been reported in the context of specific water-damaged buildings and in relation to fungal measurements in floor dust (19,60,67). Follow-up of remediation workers and residents of New Orleans following hurricane-related flooding may provide additional insight regarding dampness- and mold-related risks of asthma, rhinosinusitis, and hypersensitivity pneumonitis. Building-related rhinosinusitis deserves investigation. Occupational nasal disease is a risk factor for asthma (72,73), and dampness is related to nasal symptoms (30,46,66,74). In France, a national sample of professional women demonstrated that air-conditioning at work was a risk factor for otorhinolaryngologist attendance and sickness absence, with adjusted odds ratios of 2.3 and 1.7, respectively, in comparison to the natural ventilation group (75).

Building-related illnesses include inhalation fevers. Pontiac fever is a self-limited illness with high attack rate associated with serologic immunity to *Legionella* antigen (76). Humidifier fever has been attributed to endotoxins (77), *Bacillus subtilis* (78), and amoebae (79–82).

INFECTION

From a public health viewpoint, the most important condition influenced by buildings is communicable respiratory infection, such as the common cold, influenza, and tuberculosis (49). Compelling evidence exists that infection transmission for respiratory disease is affected by ventilation characteristics. A landmark study in this regard was the observation that military recruits housed in energy-efficient barracks had a 51% increase in incidence of febrile respiratory disease when compared to recruits housed in old barracks, presumably with greater air infiltration (83). Higher increases to 250% were documented in epidemic years when trainees were not immunized against adenovirus. Military troops housed in air-conditioned buildings in Saudi Arabia had excess symptoms of sore throat and cough compared to troops housed in outdoor environments, and this was attributed to increased infection transmission indoors (84). Similarly, epidemic pneumococcal disease has been documented in an overcrowded jail, in which median ventilation was only 6.1 cfm per inmate (85). Risk of short-term sick leave in office workers, largely due to upper respiratory infection, has been associated with outdoor air supply rate, independent of indoor air quality complaints (86). Tuberculosis transmission has long been known to be affected by ventilation patterns and rates (87). Despite the considerable burden of preventable infection associated with building environments, insufficient research exists in this area to support major educational efforts for architects and ventilation engineers. Established microbial etiology in the case of infection has put this set of diseases in the purview of infectious disease specialists, with scant consideration by the many disciplines required to pursue preventive strategies of an environmental nature.

Apart from building ventilation characteristics enhancing transmission of communicable disease, building structures have been implicated as sources of noncommunicable infections. The classic example of building-related infection is *Legionella* pneumonia from entrainment of cooling tower aerosols, construction dusts, and potable water aerosols in buildings. Infection of immunocompromised patients with *Mycobacterium avium* complex has been shown to be associated with this organism in potable water supplies (88) and indoor swimming pools (89). Systemic fungal infections in immunocompromised hosts have occurred in hospital settings with saprophytic fungi colonizing ventilation duct work and water-damaged structures or disseminated in construction and renovation dusts (90,91). Laboratory techniques and molecular epidemiology allow us to understand the implications of building environments as risk factors for both common and new agents of infection, including bioterrorism agents such as anthrax (85,88).

SUMMARY

Occupational and environmental health professionals have a unique contribution to make in the assessment of indoor environmental problems. Careful assessment of the nature of health complaints can result in the recognition of building-related asthma or hypersensitivity pneumonitis. These diseases require a different clinical management and public health investigation than sick building syndrome alone. Recognition of dampness

as a public health problem dictates remedial action to protect occupants in buildings with structural water incursion, water damage, and ventilation-related bioaerosol sources.

Sufficient scientific basis does not yet exist to recommend specific concentrations of air contaminants below which the health of building occupants can be assured, prospectively or in response to intervention in a problem building. Nevertheless, the epidemiology of building-related symptoms offers promising leads to pursue research using new methods for assessment of the indoor environment, including microbial burden. Also, useful intervention studies can be conducted without knowing specific measurable etiologies. The science of indoor environmental quality does not support the uncritical application of either ventilation rates specified in building codes or CO_2 measurements as criteria for determining whether a building is acceptable to occupants. Finally, results of several studies point toward potential opportunities to lower morbidity from infections that are impacted by ventilation rates, building operation practices, and bioterrorism.

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