



EDWARD P. HORVATH, MD, MPH

Dr. Horvath is director of occupational health in the Department of General Internal Medicine at the Cleveland Clinic. He is coeditor of the textbook *Occupational Medicine*.

Building-related illness and sick building syndrome: from the specific to the vague

■ KEY POINTS:

Building-related illness, in which an identifiable factor causes a specific illness, is much less common than sick building syndrome, in which there is no identifiable cause for nonspecific symptoms.

Microbes growing in the heating, ventilation, and air-conditioning system can cause hypersensitivity pneumonitis, humidifier fever, rhinitis, sinusitis, asthma, and Legionnaire's disease. Chemicals and other substances can also cause a range of disorders.

Sick building syndrome may be multifactorial and have psychosocial aspects.

■ **ABSTRACT:** When a primary-care physician encounters a patient with a possible building-related illness, common sense applies. Does the patient have a potentially serious condition? Does he or she need a referral to a specialist? This paper explores the topics of building-related illness and sick building syndrome.

The energy crisis of the 1970s led to various attempts to reduce the amount of fuel used in heating and cooling indoor air. As buildings became “tighter” and ventilation rates became lower, more people began to complain about the quality of indoor air.

Media coverage of indoor air quality has heightened public anxiety. Growing employee dissatisfaction with the demands of modern work has increased the number of complaints of all kinds, including those related to indoor air quality. And primary care physicians are encountering a growing number of patients who believe their health problems are caused by indoor air pollution.

This article provides practical information to the primary care physician about evaluating and managing such patients. Although a generalist would probably not become involved in investigating a problem building, he or she should nonetheless know how to initiate the medical evaluation and when to refer patients to appropriate specialists.

■ TERMINOLOGY

“Building-related illness” applies to well-defined medical condi-



TABLE 1

BUILDING-RELATED ILLNESSES WITH KNOWN CAUSES

Allergic and immunologic disease

Hypersensitivity pneumonitis
Humidifier fever
Rhinitis
Sinusitis
Asthma

Infections

Legionnaire's disease
Pontiac fever
Viral infections
Influenza
Common cold
Rubella
Varicella
Bacterial pneumonia
Mycobacterial (tuberculosis)

Chemicals and other substances

Man-made mineral fibers (fibrous glass)
Detergent residues (carpet shampoos)
Carbon monoxide
Carbonless copy paper
Formaldehyde
Pesticides
Volatile organic compounds
Carcinogens (radon, asbestos)

Look for
pneumonitis,
asthma,
carbon
monoxide
poisoning

tions for which a specific cause can be found. Examples include asthma, hypersensitivity pneumonitis, and respiratory infections such as Legionnaire's disease. Unfortunately, such clear-cut situations account for only a small percentage of cases.

“Sick building syndrome” is much more common: a collection of symptoms reported by workers in a given building for which no cause is apparent. Such symptoms may resolve when away from work and may include irritation of the mucous membranes and skin, central nervous system complaints (headache, fatigue, difficulty with concentration), chest tightness, and unpleasant odors or tastes.

Older terms such as “tight building syndrome” or “toxic carpet syndrome” are vague, confusing, and misleading. However, even “sick building syndrome” leaves much to be desired. Does it apply to the patient or to the building? Does a single sick employee warrant the designation of sick building syndrome, or

do several have to be afflicted? Moreover, a case of sick building syndrome may later be properly designated as a building-related illness if a specific cause can be identified.

Accurate prevalence estimates are not available because of variable terminology and lack of standard case definitions. However, the Occupational Safety and Health Administration estimates that the sick building syndrome affects 30 to 70 million US workers¹—from 19% to 80% of workers in studies from North America and Europe.²⁻⁴ The World Health Organization estimates that 30% of new buildings have poor air quality.⁵

■ BUILDING-RELATED ILLNESS

Causes of building-related illness fall into three main categories: allergic and immunologic disease, infections, and exposure to chemicals and other substances (TABLE 1). The clinician's primary role is to assure that potentially serious building-related illnesses (eg, hypersensitivity pneumonitis, asthma, carbon monoxide poisoning) are promptly diagnosed and treated.

Allergic and immunologic disease

Hypersensitivity pneumonitis. Most physicians are familiar with farmer's lung, the classic form of hypersensitivity pneumonitis resulting from inhalation of mold spores in agricultural environments. Fewer are aware that hypersensitivity pneumonitis and a related disorder, humidifier fever, can also occur as building-related illnesses. However, numerous cases and outbreaks have been documented.⁶

Many fungi, bacteria, and protozoa can cause hypersensitivity pneumonitis. In most cases, a malfunction of some component of the heating, ventilation, and air conditioning (HVAC) system allows the organisms to grow and be disseminated; organisms can grow in spray-water air washers, air filters, poorly maintained cooling coils, and water leaking into air ducts.

Classic cases of acute hypersensitivity pneumonitis present with recurrent fever, cough, myalgia, and shortness of breath. In the

chronic form, there is insidious progression of cough, shortness of breath, and fatigue. The diagnosis is based on:

- A typical history of symptoms that occur after exposure.
- Abnormalities on pulmonary function testing, particularly a decreased carbon monoxide diffusion capacity.
- Radiographic findings, particularly interstitial reticulonodular densities.
- Precipitating antibodies to the suspected causative organism. Standard screening panels for hypersensitivity pneumonitis are routinely available and test for antibodies to the most commonly encountered antigens.

In difficult cases, bronchoalveolar lavage or lung biopsy may be necessary. Occasionally, a specific microbial source may not be identified.

Humidifier fever, although related to hypersensitivity pneumonitis, is probably a distinct entity. Outbreaks are characterized by flu-like symptoms of fever, chills, headache, chest tightness, and dyspnea, which occur on Monday evening (or the night after starting the work week). Symptoms subside over 12 hours but recur each Monday. In one outbreak, multiple organisms were detected in a humidifier reservoir; after the humidifier was removed, no further episodes occurred.⁷ Features that distinguish humidifier fever from hypersensitivity pneumonitis include typical recurring Monday symptoms, occasional asthmatic symptoms, minimal radiographic findings, and higher attack rates.

Rhinitis and sinusitis are common and are usually vaguely described by the patient. Allergic rhinitis can be aggravated by exposure to allergens such as mites and fungi, both of which increase with higher relative humidity. Inadequate maintenance of ventilation units can allow materials that support microbial growth to accumulate. This may explain why atopic persons have more frequent nasal complaints in buildings with air conditioning than under conditions of natural ventilation. On the other hand, low ambient humidity, which occurs during winter, can dry the nasal mucosa and predispose to infection.

Asthma, although relatively common in the general population, is uncommonly attributed to building contaminants. However, conditions that allow fungi to increase (eg, excessive ambient humidity, standing water, and malfunctioning HVAC equipment) can lead to allergic asthmatic reactions. One outbreak of “humidifier asthma” occurred in 35

employees in a building with a contaminated humidifier system.⁸ Damp carpeting, leaks in the roof or into air ducts, and repair and remodeling work also lead to increases in airborne fungi. It is sometimes difficult to determine whether a person’s asthmatic episode was caused de novo by exposure to a specific chemical or was due to nonspecific exacerbation of preexisting airway hyperactivity by an irritant such as formaldehyde.

Infections

Legionnaire’s disease, first described among attendees of the American Legion convention in Philadelphia in 1976, remains the best-known and most serious infection associated with contaminated indoor air. In this epidemic, 29 of 182 patients died, a fatality rate of 16%.⁹

Legionella pneumophila is a ubiquitous organism. Its most common reservoir is water, and epidemics have been traced to contaminated aerosols from cooling towers, evaporative condensers, and humidifiers in industrial cooling systems. In a patient with pneumonitis, the diagnosis is made by:

- *Legionella* antibody measurements—a fourfold rise in titer or a single titer greater than 1:256.
- Documentation of the organism by direct fluorescent immune stains in body tissues.
- Culture of the organism from body tissues or fluids.

Individual risk factors include age greater than 50, cigarette smoking, immune suppression, excessive alcohol consumption, and pre-existing chronic lung disease.

Pontiac fever is a self-limited, nonpneumonic form of legionellosis characterized by fever, chills, and mild headache. Its name comes from an epidemic that occurred in a hospital in Pontiac, Michigan in 1968, in which at least 144 persons were infected. This disorder has not caused any known deaths or permanent sequelae. Because of the nonspecific nature of the illness, the diagnosis is likely to be made only in epidemic situations. Dissemination from ventilation systems is controlled by treating the cooling tower water with biocidal solutions.

Other infectious diseases that can be transmitted indoors include influenza, the common cold, measles, rubella, varicella, and tuberculosis. However, unlike legionellosis, these diseases are transmitted from person to person. Coughing or sneezing produces large

Acute hypersensitivity pneumonitis presents with recurrent fever, cough, myalgia, and shortness of breath



droplets that evaporate rapidly, forming small droplet nuclei capable of remaining airborne for long periods. Person-to-person transmission can occur in confined indoor spaces with low ventilation rates. Low relative humidity has also been suggested to contribute to respiratory infections by causing rhinitis sicca and reduced capacity to resist viral infectivity.¹⁰

Except in epidemics in which a point source can be identified (eg, a tuberculosis outbreak), it is often impossible to distinguish between work-related and nonwork-related episodes of common illnesses such as influenza.

Chemicals and other substances

Fibrous glass and other man-made mineral fibers that are used to insulate air ducts can become airborne, especially when damaged by age or moisture. Although unlikely to cause any significant respiratory disease, such fibers can irritate the skin, leading to pruritus, an evanescent rash, or nonspecific dermatitis.¹¹ Eye irritation may also occur, particularly among contact lens wearers. Symptoms often diminish markedly after showering. Samples taken from horizontal surfaces, either using cellophane tape or by wiping, may confirm the source of the problem.

Detergent residues left in carpets after cleaning sometimes cause eye and respiratory irritation.¹² Cough and dry throat are common symptoms. Formation of suds when an air sampling filter is shaken in distilled water supports the diagnosis. The sulfate content of dust can also be determined.

Carbon monoxide poisoning is uncommon in commercial buildings, although it is a potentially serious problem in private homes and certain industries. Carbon monoxide may enter the air intake of a building from nearby parking garages or boiler stacks. The odor of other combustion products may be evident.¹³ Symptoms of mild poisoning include headache, dizziness, fatigue, and nausea. Determination of blood carboxyhemoglobin is diagnostic.

Carbonless copy paper has been linked to multiple symptoms: upper respiratory congestion, upper airway obstruction, contact urticaria, acute systemic reactions (eg, laryngeal

edema) and allergic contact dermatitis.¹⁴⁻¹⁷

Formaldehyde gas is emitted from such products as plywood, particle board, foam insulation, and office furnishings. This ubiquitous gas irritates the eyes and mucous membranes even at relatively low exposure levels, and irritation increases with dose.¹⁸ Measurements of formaldehyde levels may be helpful in buildings in which the aforementioned products have recently been installed, particularly in new construction or after the remodelling of enclosed spaces.

Pesticides applied within office buildings rarely lead to clinical toxicity.¹⁹ However, the odor of most formulations, combined with the reputation of this class of chemicals, often leads to anxiety-related symptoms that may persist long after the initial exposure.

Volatile organic compounds comprise four major classes: aliphatic, aromatic, halogenated, and oxygenated. Specific chemicals commonly encountered include benzene, toluene, methanol, methyl ethyl ketone, and acetone. These compounds are present in maintenance products and building materials, or evolve from combustion processes, particularly tobacco smoking. In sufficiently high concentrations, they can irritate the eyes, skin, and mucous membranes, and cause central nervous system effects. Such levels are only infrequently encountered indoors. Nonetheless, strong solvent odors should alert occupants to the possibility that gasoline or other fuel from leaking underground storage tanks has seeped into basements or sewers.²⁰ Low-level exposure to volatile organic compounds, including those in tobacco smoke, has been proposed as an explanation for sick building syndrome.²¹

Asbestos and radon in office buildings, homes, and schools raise concern, not about acute effects, but rather about the possible role of these substances as environmental carcinogens. The risk from airborne asbestos in such buildings has probably been overstated. Air sampling has generally not shown asbestos fiber counts greater than background levels; therefore, the risk in most public buildings can be considered negligible.

The Environmental Protection Agency

Carbon monoxide may enter the air intake of a building from nearby parking garages or boiler stacks

TABLE 2

SYMPTOMS OF SICK BUILDING SYNDROME

Irritation of the eyes, nose, and throat

Dryness
Stinging
Hoarseness

Skin irritation

Reddening
Stinging
Dryness

Neurotoxic

Fatigue
Lethargy
Reduced memory or concentration
Headache
Dizziness
Nausea

Odor or taste complaints

Unpleasant odor or taste
Changed sensitivity

Nonspecific reactions

Chest sounds
Asthma-like symptoms

(EPA) recommends remedial action if radon levels exceed 4 pCi/L. The actual risk from long-term exposure in houses is unknown.

■ SICK BUILDING SYNDROME

Unfortunately, in most cases, a specific etiologic agent cannot be identified to explain employee symptoms. In such circumstances, the term “sick building syndrome” has been used, in spite of continued misgivings about its vagueness.

Symptoms are nonspecific, signs are lacking

Affected building occupants usually have multiple, nonspecific symptoms, which have been grouped into five major categories (TABLE 2).²¹ Most have some symptoms compatible with central nervous system or psychiatric disorders, including fatigue, memory impairment, or diminished concentration. Objective findings are generally absent on physical examination, and the usual laboratory studies are not helpful except to uncover coincidental medical conditions (eg, thyroid disease) that may be contributing to the symptom complex in individual cases.

Possible causes of sick building syndrome

A variety of hypotheses have been advanced to explain sick building syndrome, including

TABLE 3

CAUSES OF INDOOR AIR QUALITY PROBLEMS (NIOSH HEALTH HAZARD EVALUATIONS, 1971 TO 1988)

Primary problems	Percent
Inadequate ventilation (eg, HVAC malfunction)	53
Contaminants inside building (eg, volatile organic compounds)	15
Contaminants outside building (eg, vehicle exhaust)	10
Microbes (eg, molds)	5
Building materials, fabrics (eg, formaldehyde)	4

Data from Seitz, reference 31

inadequate ventilation,^{22,23} volatile organic compounds,²⁴ bioaerosols (eg, bacterial endotoxins, molds, dust mites),^{25,26} low ambient humidity,²⁷ environmental tobacco smoke,²⁸ odors,²⁹ and psychosocial factors.³⁰

From 1971 through 1988, the National Institute for Occupational Safety and Health (NIOSH) conducted health hazard evaluations in 529 problem buildings (TABLE 3).³¹ Its findings suggested that a single problem (eg, inadequate ventilation from HVAC malfunction) causes most cases of sick building syndrome. However, after additional years of experience with these investigations, NIOSH now recognizes that most problem buildings have multiple environmental deficiencies, and that it is difficult to determine specific causes for occupant health complaints.³² This admission is consistent with the observation of some investigators that many cases of sick building syndrome are multifactorial.³³

Psychosocial factors such as dull, repetitive work, demand overload, an authoritarian organizational structure, unusual workplace stress, and female gender have all been observed in sick building syndrome. Industrial outbreaks of mass psychogenic illness have also been described in such circumstances.³⁴ However, the diagnosis of mass psychogenic illness must be made cautiously, in accordance with accepted diagnostic criteria, and not until all other potential causative factors have been excluded by a thorough environmental evaluation.

Nonetheless, clinicians should not ignore

Asbestos risk has probably been overstated



the typical anxiety-related complaints that are frequently present in sick building syndrome. Indeed, one investigator suggested that non-toxic levels of pollutants may affect a worker's level of general arousal, perceived threat, and overall anxiety.¹⁹

In my experience, it is not unusual for initial symptoms of sick building syndrome to evolve into a multiple chemical sensitivity pattern in which multiple subjective complaints are precipitated by small concentrations of chemically diverse substances encountered in other environments.

■ EVALUATING AND MANAGING BUILDING-ASSOCIATED ILLNESS

The role of the primary care physician in evaluating and managing building-associated illness is limited, but important. It is essential to promptly recognize:

- Potentially serious conditions such as hypersensitivity pneumonitis, asthma, and carbon monoxide poisoning.
- Previously undiagnosed medical conditions such as endocrine disease or autoimmune disorders that may be contributing to an individual patient's symptoms.
- Any complicating psychological factors such as anxiety and depression.

A thorough medical and environmental history, physical examination, and appropriate laboratory studies usually suffice for these purposes. If a specific medical or toxic illness cannot be identified after a thorough evaluation, the primary care physician can reassure the patient that he or she will probably recover without disability. More difficult cases should be referred to an occupational medicine specialist.

Evaluation of the problem building requires an interdisciplinary approach involving various professionals, including industrial hygienists and ventilation engineers. The active involvement and concern of the employer or building manager is essential to a successful outcome.

Both NIOSH and the EPA have developed guides to help building owners and facility managers investigate complaints about indoor air quality.^{35,36} The usual approach is to conduct an initial walk-through inspection of the building and to interview the occupants to determine the nature and prevalence of symptoms. If no obvious contaminant or ventilation defect is found, the inspectors measure the levels of several index air pollutants (eg, carbon dioxide, volatile organic compounds) and evaluate the HVAC system thoroughly.

A private consultant or government agency can provide these services. NIOSH evaluates problem buildings as part of its Health Hazard Evaluation Program. This service is available only to industry and must be requested by three workers, a union representative, or management. Some state departments of health conduct indoor air quality evaluations in private homes on request.

Results of the evaluation should be communicated to the building occupants, even if a specific cause cannot be identified. Remediation measures depend on the findings. If specific causal factors cannot be identified with confidence, certain measures, such as increasing the ventilation rate, increasing the ambient humidity, and servicing the HVAC system, may dramatically improve the occupants' perception of indoor air quality. Moving an especially "sensitive" worker to an area he or she can tolerate may occasionally be necessary. ■

Do not ignore anxiety-related complaints in sick building syndrome

■ REFERENCES

1. Bureau of National Affairs. Indoor air—OSHA request for information spurs debate over form of future regulation. (0095–3237) Washington DC. *Occup Saf Health Rpt* 1992; 92:1097–1098.
2. Burr G, Alderfur R. Case Studies—Sick building syndrome: factors associated with employee-reported symptoms. *Appl Occup Environ Hyg* 1992; 7:352–354.
3. Menzies R, Tambllyn JP, Farant J, et al. The effect of varying levels of outdoor-air supply on the symptoms of sick building syndrome. *N Engl J Med* 1993; 328:821–827.
4. Mendell MJ, Smith AH. Consistent pattern of elevated symptoms in air conditioned office buildings: a reanalysis of epidemiological studies. *Am J Pub Health* 1990; 80(10):1193–1199.
5. World Health Organization (WHO). Indoor air quality research. (Euro-Reports and Studies No. 103) Copenhagen, Denmark: WHO Regional Office for Europe, 1984.
6. Kreiss K, Hodgson MJ. Building associated epidemics. In: Walsh PJ, Dudley CS, Copenhagen E, eds. *Indoor air quality*. Boca Raton FL: CRC Press 1984:87–106.

7. Ganier M, Lieberman P, Fink JN, et al. Humidifier lung. An outbreak in office workers. *Chest* 1980; 77:183-187.
8. Burge PS, Finnigan M, Horsfield N, et al. Occupational asthma in a factory with a contaminated humidifier. *Thorax* 1985; 40:248-254.
9. Fraser DW, Tasi TF, Orenstein W, et al. Legionnaires disease: description of an epidemic of pneumonia. *N Engl J Med* 1977; 297:1189-1197.
10. Lubart J. The common cold and humidity imbalance. *NY State J Med* 1962; 62:817.
11. Sterling TD, Sterling E, Dimich-Ward H. Building illness in the white-collar workplace. *Int J Health Serv* 1983; 13:277-287.
12. Kreiss K, Gonzalez MG, Conright KL, Scheere AR. Respiratory irritation due to carpet shampoo; two outbreaks. *Environ Int* 1982; 8:337-342.
13. Kreiss K. The epidemiology of building-related complaints and illness. *Occupational Medicine: State of the Art Reviews* 1989; 4:575-592.
14. Morgan MS, Camp JE. Upper respiratory irritation from controlled exposure to vapor from carbonless copy forms. *J Occup Med* 1986; 28:415-419.
15. LaMarte FP, Merchant JA, Casale TB. Acute systemic reactions to carbonless copy paper associated with histamine release. *JAMA* 1988; 260:242-243.
16. Marks JG, Trautlein JJ, Zwillich CW, Demers LM. Contact urticaria and airway obstruction from carbonless copy paper. *JAMA* 1984; 252:1038-1040.
17. Marks JG. Allergic contact dermatitis from carbonless copy paper. *JAMA* 1981; 245:2331-2332.
18. Horvath EP, Anderson H, Pierce WE, Hanrahan L, Wendlick JD. Effects of formaldehyde on the mucous membranes and lungs. *JAMA* 1988; 259:701-707.
19. Bardana EJ. Building-related illness. In: Bardana EJ, Montanaro A, O'Hallaren MT, eds. *Occupational Asthma*. Philadelphia: Hanley and Belfus Inc, 1992:237-254.
20. Employee illness from underground gas and oil contamination. *MMWR* 1982; 31:451-452.
21. Molhave L. The sick buildings—a subpopulation among the problem buildings. In: Seifert B, Esdorn H, Fischer M, et al, eds. *Indoor Air 87. Proceedings of the IV International Conference on Indoor Air Quality and Climate, vol 2*. Berlin: Institute for Water, Soil, and Air Hygiene, 1987:469-473.
22. Mendell MJ. Non-specific symptoms in office workers: A review and summary of the literature. *Indoor Air* 1993; 4:227-236.
23. Sundell J, Lindvall T, Stenberg B. Influence of type of ventilation and outdoor air supply rates on the prevalence of SBS symptoms. In *IAQ91: Healthy Buildings*. Atlanta, ASHRAE, 1991:85-89.
24. Molhave L, Bach R, Pederson OF. Human reactions to low concentrations of volatile organic compounds. *Environ Int* 1986; 12:167-175.
25. Teeuw KB, Vandenbroucke-Grauls, VerHoeft J. Airborne gram-negative bacteria and endotoxin in sick building syndrome: a study in Dutch governmental office buildings. *Arch Intern Med* 1994; 154:2339-2345.
26. Harrison J, Pickering CAC, Faragher EB, et al. An investigation of the relationship between microbial and particulate indoor air pollution and the sick building syndrome. *Respir Med* 1992; 86:225-235.
27. Nordstrom K, Norback D, Akseleson R. Effect of air humidification on the sick building syndrome and perceived indoor air quality in hospitals: A four-month longitudinal study. *Occup Environ Med* 1994; 51:683-688.
28. National Academy of Science. *Indoor pollutants*. Washington DC: National Academy Press, 1981.
29. Boswell RT, DiBerardinis L, Ducatman A. Descriptive epidemiology of indoor odor complaints at a large teaching institution. *Appl Occup Environ Hyg* 1994; 9:281-286.
30. Heumann M, Campbell DT, Wright L. Report on an illness outbreak at the Commerce Building in Salem, Oregon, July 30, 31 and August 1, 1984. Oregon State Health Department (unpublished).
31. Seitz TA. NIOSH Indoor Air Quality Investigations 1971 through 1988. In: Weekes DM, Gammage RB, eds. *Proceedings of the Indoor Air Quality International Symposium*. American Industrial Hygiene Association: Akron OH, 1990:163-171.
32. Crandall MS, Sieber WK. The National Institute for Occupational Safety and Health indoor environmental evaluation experience. Part one: building environmental evaluations. *Appl Occup Environ Hyg* 1996; 11:533-539.
33. Fernandez-Caldas E, Fox RW, Richards IS, Varney TC, Brooks SM. Indoor air pollution. In: Brooks SM, Gochfeld M, Herzstein J, Jackson RJ, Schenker MB, eds. *Environmental Medicine*. St. Louis: Mosby-Year Book Inc, 1995:419-437.
34. Colligan MJ, Murphy LR. Mass psychogenic illness in organizations: An overview. *J Occup Psychol* 1979; 52:77.
35. National Institute for Occupational Safety and Health, Hazard Evaluations and Technical Assistance Branch, Division of Surveillance, Hazard Evaluations and Field Studies. *Guidance for indoor air quality investigations*. Cincinnati, Ohio, 1997.
36. US Environmental Protection Agency, US Department of Health and Human Services. *Building Air Quality—A guide for building owners and facility managers*. Washington DC: US Government Printing Office, 1991.

ADDRESS: Edward P. Horvath, MD, MPH, Section of Preventive Medicine, A11, The Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195.