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Patients and the sick building syndrome

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Sections

- [Abstract](#)
- [Approach to Humans](#)
- [Approach to the Environment](#)
- [Alara](#)
- [Remediation and Occupancy](#)
- [Summary](#)
- [References](#)
- [Publishing and Reprint Information](#)

Abstract

TOP

Physicians encounter patients who have complaints related to indoor environments with increasing frequency. Physicians must distinguish between approaches to identify disease in individual patients, characterization of group effects, and analysis of environmental exposure characteristics. Simultaneously they must consider the influence of illness behavior, work stress, and organization function on the presentation of complaints. They must distinguish discomfort and irritation from disabling disease and communicate the implications of pathophysiology and the limits of knowledge to patients. Joint teams with engineers and industrial hygienists, and, at times, organizational analysis is an approach to problem solving for indoor environmental problems. (J ALLERGY CLIN IMMUNOL 1994;94:335-43.)

ALARA As low as reasonably achievable**SBS** Sick building syndrome**TLV** Threshold limit values**VOC** Volatile organic compound

(Click on a term to search this journal for other articles containing that term.)

Key words: [Sick building syndrome](#), [occupational disease](#)

Physicians who practice environmental and occupational medicine approach problems on three different levels at the same time: (1) that of the patient alone, (2) that of the group from which the patient is drawn ("sentinel events" concept), and (3) that of the environment that is producing disease. Each entails a traditional way of linking disease to exposure. Traditional clinical practice is based primarily on "scientific" approaches and hypothesis testing with an emphasis on avoiding type I errors, or minimizing the likelihood that two unrelated factors will be falsely related. Public health approaches to problem solving may involve actions to resolve hazards with full recognition of the likelihood of type II errors, that is, protecting persons where they may not need to be protected. The latter approach often involves poorly defined risk trade-offs. In addition, prudent actions in specific situations may be guided by economic or other consequences of failing to act expeditiously rather than relying on actual previously documented hazards. Indoor air and the sick building syndrome (SBS) serves as a paradigm of modern occupational and environmental medicine with its inherent scientific uncertainties, expectations, and knowledge on the part of affected persons, and economic conflicts between owners, managers, tenants, and occupants. This article will explore the three approaches to occupant complaints and provide a framework for problem solving.

Approach to Humans

[TOP](#)

Individual approaches

The first approach physicians generally take with patients who have a specific concern regarding potential environmentally caused disease is to obtain a careful medical and occupational history and perform a physical examination and, when applicable, laboratory tests. The first goal is to exclude other conditions that might be causing the problem. Physicians may identify an underlying condition (such as inadequate tear film production and stability or fatigue associated with hypothyroidism) associated with other diseases that may influence the pertinent symptoms. The next step is to identify the likely pathophysiologic mechanism underlying the complaint and quantify organ function. Complaints of chest tightness or wheezing require documentation of changes in airways related to work using peak expiratory flow tracings or spirometry before and after work. If no abnormality is found, no "measurable disease" is present. That is, physicians can convincingly state that even if discomfort is present, it does not represent measurable pathology.¹ As always, timing in disease is important; disease may progress, and tests may need to be repeated if a patient's condition worsens. Physicians must also recognize that the appropriate test has sometimes not

been applied or even identified. When discomfort is convincingly associated with particular work environments and no physiologic dysfunction is identified, the absence of “disease” makes it possible for physicians to explain both the ubiquitousness of discomfort and irritation and the idea that discomfort does not usually represent true disease that progresses or leads to disability. Such discussions are designed to prevent destructive illness behavior.

In the absence of physiologic dysfunction or anticipated impairment, the question is always raised as to whether some discomfort may have to be tolerated in the workplace in the same fashion as at home or on the street. One aspect of the discussion is to refocus the problem to discomfort and economic trade-offs for employers. It is often much easier to persuade employers that general irritation may lead to discomfort and decreased productivity than to deal with adversarial workers' compensation procedures. Such an approach will work only if there is general agreement on goals of solving problems.

If patients do not have measurable or identifiable disease, they may have complaints consistent with the SBS. As the description here makes clear, the physiologic basis of the SBS is under active investigation. Even as the arguments are being made that the syndrome is primarily a matter of discomfort, efforts to explain that discomfort suggest that there are identifiable physiologic responses to the “sick building” environment. To date there is no evidence suggesting that these responses lead to long-term impairment or established disease. Nevertheless, several investigations cited under the appropriate organ system suggest that conditions in general may be associated with at least physiologic if not pathologic responses.

Components of the SBS

The SBS has been classified in a series of categories (■Table I) by several authors.^{2 3} This classification does not respect pathophysiologic boundaries. Each grouping has at least some postulated underlying mechanisms and will be discussed separately.

TABLE I. SBS categories

Mucous membrane irritation
Eye irritation
Nose irritation
Throat irritation
Neurotoxic symptoms
Headaches
Fatigue
Irritability
Difficulty concentrating
Asthma-like symptoms

Chest tightness

Wheezing

Skin complaints

Dry skin

Irritated skin

Gastrointestinal symptoms

Diarrhea

TABLE II. Investigation methods

Eye

Tear film break-up time

Fat layer determination

Conjunctival photography

Lissamine green staining (punctate conjunctivitis)

Nose

Acoustic rhinometry

Anterior and posterior rhinomanometry

Nasal lavage

Stereoscopic microscopic examination

Chest

Peak flow meters

Spirometry

Central nervous system

Neuropsychologic testing

Evoked potentials

Vestibular testing with solvent provocation

Mucous membrane irritation

The trigeminal nerve supplies the irritant receptors of the common chemical sense in the eye, nose, and mouth to the base of the tongue. Irritation farther down the oropharyngeal cavity relies on the glossopharyngeus and hypoglossic nerves.⁴ A standard test method was developed for animals and has been widely used to document the effects of office products on mucous membranes.^{5 6}

The epidemiology of the SBS⁷ suggests that mucous membrane irritation is widespread. Field studies of office workers in buildings not identified as “sick” throughout the world have documented prevalence rates above 20% in most buildings. In fact, there is little evidence that buildings perceived as “sick” have higher rates of discomfort as measured by questionnaires than do other buildings.⁸ The bioaerosol hypothesis suggests that even in “outbreaks” of building-associated disease, such as asthma and hypersensitivity pneumonitis, mucous membrane irritation is common. At least one postulated mechanism is volatile organic compounds (VOCs),⁶ which have been documented in controlled studies of animal and human exposures as a contributor to simple chemical irritation of the common chemical sense. Irritation may also occur as a result of exposure to specific allergens or nonspecific factors such as endotoxin or β -1,3-glucan.

Physiologic tests available to document irritation in the nose include anterior and posterior rhinomanometry, acoustic rhinometry, nasal lavage, nasal biopsy, and stereoscopic investigations. Several authors have used techniques to study nasal function and demonstrated nonallergic responses to environmental stimuli.^{9, 10} Only one study has led to a published report of more than one case in the setting of indoor environmental discomfort, and even this report was for research purposes and was not an investigation of a problem building. Anecdotal reports have identified adverse clinical effects from office products even without documented hypersensitivity.¹¹ At least one author has used sophisticated techniques to investigate health effects from agents in the indoor air in studies of persons reporting sensitivity to environmental tobacco smoke.¹² The clinical utility of these tests remains to be documented because no data on sensitivity, specificity, or positive predictive values are available. On the other hand, until such techniques have been studied systematically, physicians may remain uncertain about whether subjective discomfort represents a physiologic deviation from normal. The correct techniques may not yet have been used to demonstrate adverse health effects from indoor pollutants. Viewing patients' complaints as unjustified may then be premature.

Substantially more information exists for tests of eye irritation. In fact, a series of investigations from one group in Denmark suggests that office work is associated with a series of abnormalities in tear film. The techniques include the determination of irritant⁴ and odor thresholds or the determination of tear film characteristics.¹³⁻¹⁵ Franck and Skov¹⁶ have demonstrated that eye complaints in office workers, measured with two different questionnaires, are associated with more rapid tear film break-up time and some underlying pathophysiology. Office workers with complaints and less stable tear film had worked in offices longer than did others, which raises the question of causal relationships rather than simple individual susceptibility.

One implication of the studies on eye and nose irritation is that not everyone may have the same level of protection against environmental insults. Therefore physicians may expect subjects to demonstrate a different level of subjective irritation at one single exposure level of environmental toxin. Such responses may result from either secretion products of bioaerosols or VOCs from man-made products in the indoor environment.

Neurotoxic symptoms

Headaches, too, may result from a variety of mechanisms, including parasympathetic reflexes,

direct effects on mucous membranes, and neurogenic inflammation. At levels of exposure in general one to two orders of magnitude higher, solvent mixtures are well known to lead to adverse central nervous system health effects, called solvent neurotoxicity.¹⁷ Little evidence supports the idea that headaches among office workers represent solvent neurotoxicity, although a case report¹ and an outbreak¹⁸ have described the use of neuropsychological testing that demonstrated abnormalities in office workers who were symptomatic. The work of Molhave¹⁹ and Kjaergard,²⁰ on the other hand, described changes in tests of cognitive efficiency and fine motor skill in groups of susceptible persons, studied in blinded fashion, at the low levels of exposure seen in offices. Otto, who studied volunteers without self-reported VOC-induced symptoms, demonstrated minor symptom changes but no physiologic decrements. Physiologic tests²¹ of neuropsychological function that may be used in field studies include individual tests such as the Continuous Performance Test or batteries such as the Pittsburgh Occupational Exposures Test battery or self-administered, computer-based instruments such as the Neurobehavioral Evaluation System.

Skin complaints

Dry and itching skin are well described among office workers. In the past these complaints have been attributed to low relative humidity alone or to VOCs in combination with low relative humidity.²² Some authors have suggested that these complaints are in fact more frequent in buildings with humidification,²³ possibly because of microbial contamination. Dermatologic problems have also been attributed to office products in animal and human studies.²⁴ ²⁵ Again, a physiologic mechanism may exist but appropriate clinical tests remain to be developed and validated.

Asthma-like symptoms

Chest tightness and asthma-like symptoms are common. Some persons have documentable variability in their airways caliber related to work; asthma caused by or exacerbated by a particular environment is traditionally not considered part of the SBS. One report describes the new development of asthma and exacerbations in the workplace in a group of office workers.²⁶ Other workers in the building described excess coughing, wheezing, and mucous membrane irritation. Outbreaks of hypersensitivity pneumonitis have demonstrated a similar association. This suggests that at least some office workers may have unrecognized asthma or pneumonitis. There may be another group of persons who have subjective chest tightness, wheeze, or cough in whom there is no physiologic abnormality. This occurrence may be associated with β -1,3-glucan exposure.²⁷ Use of peak flow meters and spirometry before and after exposure is essential in efforts to differentiate building-related asthma from SBS and to clarify whether this symptom complex is distinct from reactive airways disease.

In summary, individual complaints may be characterized and attempts at confirmation or quantification undertaken. The absence of physiologic abnormalities may allow physicians to move the level of patient discourse to discomfort rather than disease. On the other hand, if individual patients have convincing symptoms alternative approaches to documentation must be undertaken.²⁸ These include traditional challenge tests or n-of-one clinical trials.

Approach to group effects

Patients are usually a member of some group defined through common exposures. They may perceive themselves as the most sensitive persons or simply be the only ones willing to voice complaints. It is rare for an office to generate complaints in only a single patient. If diagnostic tests in individual patients alone are inconclusive but strong suspicion continues to exist, physicians may then choose to examine the group members informally, during a walk-through, or formally.

Group measurements should be undertaken thoughtfully, with a clearly defined goal. This goal may be to obtain more information on the spectrum or prevalence of complaints, to compare symptom frequencies with some external control groups (other buildings), or to address disease.

Many surveys in indoor air first involve the administration of a questionnaire. Such instruments may be validated or unvalidated. Even if they are thought to have both internal and external validity, that is, measure disease consistently and accurately, stress and psychological factors may influence complaint rates.²⁹ Because “normal” values have not been published for questionnaires, all surveys should incorporate control groups. In fact, in our experience, all buildings have occupants with complaints. Numerous questionnaires exist, but only one has undergone formal validation attempts.^{30 31} Comparisons between instruments³² or between questionnaires and physiologic abnormalities¹⁷ are few. The result is that misclassification of symptom frequency, intensity, and even work-relatedness remain to be well defined.

Two traditions in epidemiology use survey instruments differently. One tradition requires the use of previously validated instruments, such as the chest questionnaires of the American Thoracic Society or the International Union Against Tuberculosis. An alternative is the United Kingdom instrument. A second tradition in field epidemiology is to use a questionnaire that captures a working case definition developed from current index cases. Subsequently, validation efforts must be incorporated into the survey. Both strategies use questionnaires as measurement instruments that compare rates in populations. Questionnaires may also be used as screening instruments to narrow a group of potentially exposed persons so as to increase the yield of face-to-face interviews.

In the evaluation of the SBS, the goal of questionnaire surveys alone is to identify primary discomfort and concerns among occupants and to compare rates rather than to quantify “disease” rates. The choice of the questionnaire, whether it focuses on comfort, acceptability, or disease, influences the range of potential responses. Questionnaires that focus on SBS complaints may document a broad range of discomfort. This alone may be reason enough to intervene for productivity.

The test characteristics of most tests used in building-associated diseases are poorly defined. Therefore measurements of group rates and the demonstration of group differences after selection of appropriate control groups may be the only useful approach. Given the overlap in symptoms between recognized diseases such as asthma and hypersensitivity pneumonitis and the SBS, physicians should exercise due caution before concluding that a building is harmless. Similarly, physicians should remember that questionnaire responses often differ from those obtained in face-to-face interviews and not make diagnoses of hypersensitivity pneumonitis or asthma simply on the basis of questionnaire responses.

If a building-related disease such as asthma or hypersensitivity pneumonitis was documented in one or more cases, screening for further disease among occupants is appropriate. Questionnaires are appropriately used in such settings. If no further cases are identified but complaints are widespread, investigators may remain in a quandary. They should then establish a surveillance system to identify new clinical cases as they occur.

Psychological aspects

Studies have generally supported a relationship between work stress and the SBS.^{30 33 35} This holds equally true for problem building investigations.³⁶ At the same time, because physicians are generally familiar with the scientific literature supporting associations between “real disease” and work stress,³⁷ such relationships are not surprising. Current models of work stress, such as the person-environment-fit model, suggest an interplay between personality styles and characteristics, coping skills, and external pressures. Most “stress” questionnaires address only personality styles and characteristics and coping skills and fail to identify the very real external predictors of stress, such as role conflict, job task ambiguity, workload, and job-related tension. Each of the three provides a different route of intervention; the latter is accessible through organizational analysis rather than through individual approaches.

More importantly, Bauer et al.³⁸ suggested that in at least one outbreak of disease, stress became more severe because of the duration of time required to repair the problem. Literature on recovery from traumatic injuries suggests that “culpability” is a major predictor of delayed return to work. Persons whose injuries were caused by factors beyond their control returned to work later than those with self-inflicted injuries. Persons who had warned of preventable factors that were not repaired returned even later. A similar construct of persisting complaints without adequate intervention may explain the persistence of complaints long after remediation.

Approach to the Environment

TOP

Elsewhere in this supplement authors emphasize the importance of team approaches to building investigations. Joint walk-throughs with health scientists, industrial hygienists, and engineers are quite helpful.

A first step is usually to define the building characteristics, use patterns, and system characteristics.³⁹ This involves lengthy conversations with building engineers, maintenance crews, and occupants. Often, no single person knows all the pertinent aspects of the building in question. Review of the building plans alone sometimes documents the cause of the problem. Walking through the building in question floor by floor and room by room becomes important to identify all potential sources. Opening and closing conferences to agree on specific goals and establish a formal communication pathway are essential.

Engineering analysis

Engineering approaches to buildings are described elsewhere in this supplement. The physician

should inquire whether the building systems met standard professional design criteria or whether it was designed merely to code specifications. The latter are minimal requirements according to most professionals. They generally require less ventilation and thermal control than professional standards suggest. Codes often do not address pressure characteristics between areas. Pollutant migration patterns are almost never predictable simply on the basis of engineering design review.

Physicians should be aware of the basis of professional standards. For example, the ventilation standard developed by the American Society of Heating, Refrigerating, and Air-conditioning Engineers, 621-89 "Ventilation for Acceptable Air Quality," suggests ventilation rates developed for human source (body odor) control. Yet Fanger et al.⁴⁰ have suggested that more than 80% of perceived odors and pollution in buildings come from other sources such as ventilation systems, office machines, and tobacco smoke. Newer strategies focus on pollutant reduction through source control, which are discussed elsewhere in this supplement.⁶

The physician should approach the problem with engineers and identify potential causes that the engineer might consider less important but may be the source of the problem, for example, new machines, odor characteristics, negative pressurization, and the like.

Several authors⁴¹ have suggested that all problem buildings have major flaws in design, installation, operations, and maintenance strategies. These flaws may be addressed even in the absence of a documented causal relationship with human health. Persistence of such inadequate approaches is likely to lead to further difficulties in the future even if they cannot be blamed for the current difficulties.

Industrial hygiene approaches

A traditional industrial hygiene approach to building investigations has been to sample for specific agents of interest and concern, compare the results with established criteria, and decide on the presence of a problem on the basis of overexposure. This approach is no longer considered adequate as defined in recent position papers from the American Conference of Governmental Industrial Hygienists⁴² and the American Industrial Hygiene Association.⁴³ Threshold limit values (TLVs) were developed in an attempt to protect the health of most exposed persons, that is, to prevent toxicity. They were not to replace attempts at reducing exposures to "levels as low as reasonably achievable" and were not established to prevent irritation.

The following paragraphs summarize the conceptual problems with the traditional industrial hygiene approach in indoor air.

Dose-response relationships

For some agents adequate data exist to demonstrate what levels of a specific compound, primarily formaldehyde and carbon monoxide, are associated with some specific adverse effect, whether it be irritation or odor discomfort. Still, in the absence of a well-characterized dose-response relationship, it is difficult to determine the actual trade-offs may be engineers in design. No data have been collected that characterize both individual intensity or severity and group percentages of discomfort at the dose ranges applicable to indoor air. Without such knowledge, engineers and

consumers will remain uncertain of the actual percent dissatisfied that are expected from the building, furnishings, and ventilation systems under the design assumptions.

Dose-response models have been developed for only a very few agents. Where they exist, irritation does not disappear at a specific threshold. An increasingly smaller group of persons is expected to have complaints or suffer ill health as the concentration decreases. Formaldehyde may serve as an example. Even at levels below all of the criteria established by various standard-setting bodies (World Health Organization, Occupational Safety and Health Administration, and American Conference of Governmental Industrial Hygienists), many persons will describe eye and nose irritation. An economic decision must then be made concerning the desired level of occupant comfort.

Multiple contaminants problem

A broad range of pollutants is present in indoor spaces. Even something as easily recognized as environmental tobacco smoke consists of multiple pollutants that cause irritation and annoyance. The specific culprits are still unknown. Nevertheless, the broad range of pollutants trigger responses in several receptors. How effects on similar receptors can be summed remains uncertain. When agents affect the same receptor, such as the “irritant” receptor of the Trigeminal nerve (common chemical sense), it is reasonable and possible to model their joint effects.

On the other hand, different chemical classes may trigger that receptor differently. Where irritants have differing mechanisms of action, their interactions (antagonism and synergism) remain unpredictable.⁴⁴ Given the broad range of agents and their influences that are present in indoor spaces, ranging from particulates to volatile organic compounds and air currents, joint modeling and effect estimation is certainly difficult now and may remain impossible.

At the present we do not know enough to identify all important compounds in the indoor air that cause annoyance and odor or how to sum their effects.

Appropriate outcomes and previously developed standards

Outcomes of interest in research depend on the funding agency and the interests of the investigator. Therefore not all studies on the same agent examine the same outcome, even when they occur at similar dose ranges. For example, particulate matter is associated with subjective discomfort (eye and chest irritation) and with lung function abnormalities. Data that define dose-response relationships between lung function abnormalities and dust levels may not be pertinent for the prediction of annoyance and irritation. Most standards (TLVs and permissible exposure levels) were not established with the goal of preventing mucous membrane irritation.

Specific human outcomes must be defined in a valid way for scientific work to be understandable. Most funded research on “health effects” relies on the documentation of adverse health effects, that is, lung function abnormalities, rather than on assessment of discomfort. On the other hand, discomfort is likely to be a more important component of office occupant dissatisfaction than adverse chronic health effects. Discomfort can be measured through questionnaires or panel ratings.

The populations in which the health effect is measured also affects the ability to generalize that effect estimate. Studies in human volunteers may not be applicable to office workers because volunteer populations may have inherent biases. That is, they may be selected or volunteer because of perceived nonsusceptibility. Susceptible persons or populations may respond differently and may not have been studied. The discrepancy between studies of low levels of VOCs and health effects⁶ represents such a distinction.

Any environmental criteria that are listed or used must therefore be classified by the specific outcome that the standard was developed to protect.

Representative compound problem

Agents that are actually complex mixtures, such as environmental tobacco smoke or mixtures of VOCs, may require very sophisticated measurement technology. This may be unavailable and imprecise. Calibration and analytic technique require continuous certification. The stability or instability of representative compounds may lead to different substances being measured over time. Furthermore, representative compounds may be substantially more difficult or simple to measure than the complex mixture. Therefore the agent assumed to be representative may be identified or may be missed. Recent data suggest that even environmental tobacco smoke may be very difficult to implicate even when it is the cause of a problem in buildings.

Alara

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An alternative to approaches based on thresholds is that of ALARA, “as low as reasonably achievable,” a concept well known in industrial hygiene. It has been widely used, equated in importance with TLVs, and is the foundation of all exposure control in radiation health. It more clearly provides an incentive to reduce levels through a combination of low emissions selection, source control, and, only finally, dilution ventilation, a very inefficient way of approaching contaminants.

Remediation and Occupancy

[TOP](#)

Buildings can always be improved. Most renovation efforts do not involve a major hazard to health. On the other hand, some interventions clearly have the potential for adverse human health effects. Criteria for total or partial evacuation of buildings have been discussed among professionals but no formal publications address this topic.

There is widespread recognition that renovation of occupied space leads to substantial occupant discomfort. Several studies have documented higher complaint rates among occupants whose work area has been renovated within the last 3 months before a survey. In addition, modeling of building occupant exposures has suggested that VOC exposures from paints, coatings, glues, and other products such as new carpets are present in concentrations that are irritating to mucous membranes.

The American Society of Heating, Refrigerating, and Air-conditioning Engineers conducted a forum

on the topic of renovation while office workers remain in the area. There was widespread recognition that such renovations were a major cause of occupant discomfort and, more importantly, were not infrequent predictors of persisting problems. Alternatives such as isolation of ventilation systems and the moving of occupants are available but are associated with some cost. Failure to control solvent exposures during renovation may lead to exposure of office workers to industrial environments. Employers who fail to treat the office workplace with respect may have short-term cost savings at the expense of substantially greater long-term costs. An additional concern around the issue of continued occupancy has arisen in the presence of materials that are severely contaminated with biologic agents. Remediation is often associated with substantial exposures, potentially leading to sensitization. Many experts currently recommend preventing occupant exposures during such remediation by using asbestos containment procedures.

Finally, continued occupant presence involves the reasonable assurance of no adverse health effect. That is, if persons are likely to develop asthma or hypersensitivity pneumonitis, buildings may not be "safe" for continuous occupancy. Investigators must consider the likelihood of future adverse health effects resulting from the failure to remove people. Remediation should therefore occur promptly. It must be undertaken in a fashion that prevents human exposures. The threat of building evacuation may prompt owners and managers to intervene more energetically.

Summary

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Physicians should approach each patient cautiously and ensure that no identifiable disease is present by obtaining a careful history and performing a physical examination. Laboratory tests may be ordered to exclude specific diseases. Evidence suggests that tests are not available to adequately characterize most health outcomes in office workers. Group effects investigations may be useful but should be undertaken with a clear goal. Identified source and engineering design problems can be remedied without further human investigation. Physicians should always remain mindful of personal and organizational psychological aspects of such investigations.

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[TOP](#)

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