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SICK BUILDING SYNDROME

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The term "sick building syndrome" has been used for 20 years without an operational definition.[33] Nevertheless, attempts to provide alternative names, i.e., problem buildings, building-related occupant complaint syndrome (BROCS), abused building syndrome, and many others, have not met with success, and the term remains in common use. Attempts at defining alternatives reveal two major confusions: (1) Which is the primary concern and problem—the buildings or the occupants? (2) Is the issue the worker's sick feelings and dysfunctional appearance, or are problems objectively measurable?

These confusions distract from the knowledge we do have about human complaints related to the indoor environment and prevent some interested parties from asking the more important questions about mechanisms and prevention. Although empiric data are available for both questions, the data frequently are discussed without an attempt at synthesis. The controversy over the syndrome of idiopathic environmental entolerance (IEI), or multiple chemical sensitivity (MCS), appears to wallow in a similar trap. In fact, the critical questions leading to explicit hypotheses appear quite similar for both syndromes, at least as far as the physiologic effects are concerned. Many practitioners experience patients with the label IEI/MCS as distinct from the vast majority of patients with building-related complaints. Recent data suggest that complaints labeled IEI/MCS are quite common.[45,47] Nevertheless, quantitative approaches based on questionnaire descriptions may fail to capture essential components of the doctor-patient or patient-healthcare provider relationship that defines IEI/MCS.

This chapter summarizes what we know about human symptoms and discomfort in the built environment and formulates several critical hypotheses that show striking parallels to the questions arising from discussions of the syndrome of IEI/MCS. Although the questions are similar, the tone of discussion about MCS often reflects strong beliefs of the discussants, who frequently fail to include major portions of information from the peer-reviewed literature. It is tempting to speculate that the parallels and divergence in opinions about sick building syndrome (SBS) and MCS/IEI reflect physicians' and other scientists' beliefs about and attitudes toward patients and clients, rather than merely the underlying science. In the clinical world this has been called countertransference,[83] and could be explored in a scientific fashion. In addition to published, quantitative data on symptoms considered to comprise SBS, this author has encountered individual patients with symptoms related to low levels of exposure that may fit some criteria for either of two syndromes. These observations (described below) may serve to sharpen the focus of questioning.

THE SPECTRUM OF PATIENTS

Case 1: A 53-year-old design engineer, with both a successful consulting practice and direct responsibility for a major hospital in the mid-West, described confusion and eye irritation whenever he was in laboratories with low levels of exposure to xylene and other solvents. These symptoms had been present for over 20 years. No over-exposures could be identified in his occupational history. He had no chronic diseases. As he was able to control his environment, and rarely entered laboratories, this did not pose a problem to him in his activities of daily living and working.

Case 2: A 55-year old administrative assistant in a courthouse in western Pennsylvania described mucosal irritation, associated with odors of solvents, occurring regularly at work. Air from an engine repair shop in her building circulated into her space through wall perforations. In addition, the ventilation system did not deliver 20 cubic feet of outside air per occupant per minute (cfm) to her space. Over time, her mucosal irritation was accompanied by headaches. Despite intervention by her supervising judge, the building owner was unwilling to bring the space up to professional design specifications. The patient left work. Her symptoms recurred when exposed to strong odors and low levels of solvents and interfered with her ability to work and in her private life.

Case 3: A 35-year-old mother of three children developed generalized mucosal irritation and headaches around the use of a furnace at home. Detailed assessment of the home revealed no cross-contamination or flu entrainment of furnace exhaust gases. She identified a relationship between being at home surrounded by odors and the home where she was sexually abused as a child in a fashion that outlined a therapeutic need. The new sense of danger and "exposedness" in her current home presented therapeutic opportunities. Although she was clearly affected by her illness, after some discussions of leaving the suburban area in which she worked and moving to Montana, she was able to continue in her life activities. Her symptoms did not resolve completely.

Case 4: An executive assistant in a major law firm experienced mucosal irritation and headaches after exposure to paints during painting of occupied space, cleaning with specific agents in her space, and exposure to furniture oils that were used regularly. The global ventilation rate to the building was adequate (approximately 20 cfm oa), and the area of her desk was sparsely occupied. The office management was unwilling to change its strategies of using cleaning agents and renovating because a well-known major indoor environment firm had told them they were "bringing in enough outside air."

These four cases outline critical questions:

- When is occupied space, or the ambient environment, "acceptable" for human occupancy?
- Are there formal criteria levels for specific pollutants below which we do not expect effects?
- Are "low" levels of pollutants defined well enough that we can state when the substances are below levels expected to cause health effects?
- Can common point sources generate exposures that are adequate to lead to adverse health effects?
- How do we define "adverse health effects?
- Is there objective evidence that individuals with symptoms have physiologic evidence for these symptoms?

Although the psychological contribution to symptoms, and disease in general, is of paramount importance in primary care, a critical examination of the determinants of feeling ill or well; the personality styles and characteristics associated with states of health; the influence of work stress and organizational function (or dysfunction); and the social and legal environment that defines disability in the United States goes beyond the page limitations of this chapter. Work organization, the perception and induction of stress in the work environment, and personality characteristics that lead to specific responses all may be important determinants of the boundary between the two syndromes, if they are different.

SYMPTOMS AND THE BUILT ENVIRONMENT

It is instructive to view the evolution of building complaints from the perspective of occupants empirically and contrast that with the engineering perspective of systems and their evolution.

People

Around the time of the first use of the term SBS, studies strove not merely to describe but also to identify causal relationships. Some clearly identified exposures related to symptoms;[41] others clearly recognized diseases.[8,19] In fact, problems associated with formaldehyde, cleaning agents, moisture, and **bioaerosols** were recognized and well defined. Associations with the complex mixtures that comprise typical indoor pollutant exposures and their potential control through ventilation also were well defined.[73] In fact, one of the early reviews[42] suggested that "traditional industrial hygiene approaches" were unsuccessful. However, thoughtful, innovative, critical investigators generally have been able to identify problems and solve them. Many investigators believe that once specific causes have been identified, the problem under investigation should no longer be called SBS.

Most investigators incorporated "work-relatedness," i.e., that symptoms be "building-related," or improve when away from work, into their case definitions. Nevertheless, it is meanwhile clear that some individuals develop similar problems in the home; 25–50% of complainers describe their symptoms as not being work-related. In addition, in comparisons of two of the commonly used questionnaires,[6] there was only poor agreement on temporal patterns between the two instruments. If some individuals are more susceptible to pollutant effects, then defining only "work-related" symptoms as being of interest and including individuals with persistent symptoms in the control or comparison groups may lead to the introduction of biases in statistical analyses.

Several fundamentally different strategies have been pursued in documenting symptoms. The most widely recognized literature describes symptom prevalence in units of frequency over a time denominator of months or years.[10,20,49,63] These studies generally have failed to identify relationships between symptoms and environmental measures. A separate strategy has been pursued in attempts to document relationships and the effectiveness of interventions,[27,28,82] and these studies have identified relationships between symptoms and a range of exposures, including particulates, low relative humidity, and **volatile organic compounds** (VOC). Finally, some investigators have pursued evidence of physiologic markers of ocular[21,22,37] and nasal physiology.[55,56,79] These document an objective basis for the mucosal irritation that is commonly considered an integral part of the syndrome.

One set of investigations has suggested inter-relationships among the symptom groupings, with mucosal symptoms far more strongly related to each other than to other symptoms.[27] Several basic mechanisms may then be involved in the generation of complaints among office workers, in part across organs. The common chemical sense, based on predictable dose-response relationships of the irritant receptor, may be involved in eye and nose irritation.[12] Some evidence supports traditional allergy as contributing to at least some portion of nasal symptoms.[45,50] In fact, even headaches appear to be more frequent in allergy sufferers in office environments.[45] It is clear that objective measures of personal susceptibility are related both to increased symptom rates[65] and to symptoms at lower exposure levels.[38]

Two separate research directions evolved, one generally supporting the bioaerosols hypothesis, the other the VOC hypothesis. These two hypotheses postulate specific triggers for discomfort and health symptoms that work stress and thermal discomfort may exaggerate.

Bioaerosols

In the course of searching for moisture and humidifier fever[5] in buildings, Finnegan et al. Found that symptoms were associated with **humidification and ventilation**.[20] Subsequently other early, large-scale investigations identified a high prevalence of symptoms belonging to a range of organs and potential mechanisms.[10,63]

Cross-sectional studies subsequently have supported an association of higher rates of symptoms with endotoxin exposure[70] and with the presence of unwanted moisture in ventilation systems.[61] A small portion of individuals with building-related nasal complaints appear to have allergies to specific agents identified in their building.[50] In addition, individuals with IgE antibodies to agents commonly found in buildings appear to have more symptoms than do individuals without such antibodies.[45] On the other hand, Kjaergard[38] showed that individuals with atopy reacted to a defined concentration of a complex VOC mixture at substantially lower concentrations than controls without atopy. Similarly, Shusterman[58a] demonstrated that atopic individuals decrease their nasal airway resistance substantially more than nonatopic individuals after a challenge with chlorine.

Several recent case reports have identified building moisture as associated with symptoms that are poorly understood but may represent some immunological effect.[30,35] In fact, in one recent study, a building with a single confirmed case of hypersensitivity pneumonitis had a substantially elevated rate of "nonspecific" symptoms (which also were consistent with hypersensitivity pneumonitis), but failed to show any objective evidence of disease in patients.[77] These reports suggest that symptom excess in the presence of moisture represents some phenomenon related to bioaerosols exposure.

VOLATILE ORGANIC COMPOUNDS

Investigators in Denmark[22,23,39,52] pursued the hypothesis that complex mixtures of volatile organic compounds might be the primary cause of mucosal irritation, a prominent symptom, and that these agents might also contribute to headaches, fatigue, and dizziness. The associated, though generally unspoken, accompanying hypothesis was that these agents were recognized as a cause of solvent neurotoxicity at higher concentrations and that dose-response relationships with less severe forms of disease were simply not well understood.[52]

Evidence exists that volatile organic compounds are important in occupant complaints in large buildings. Chamber studies have demonstrated associations,[31,52] although more recent, smaller studies have not replicated the results. Several field studies demonstrated associations. Hodgson et al.[27] demonstrated a univariate relationship between VOCs measured with a flame ionization detector. Hodgson et al.,[28] using a VOC measurement method with substantially greater imprecision, showed relationships between VOCs and mucosal irritation after controlling for perceptions of work stress. Sundell demonstrated an association of symptoms with decreases in VOC concentrations from supply to exhaust air within rooms,[66,67] suggesting that the mechanism identified by Wechsler termed "indoor chemistry" leads to "lost VOCs" and is associated with mucosal irritation. The topic recently has been reviewed.[3] Brinke suggested an association between symptom groupings and VOCs clustered by likely source.[69]

Cain and Cometto-Muniz[12] have conducted a series of chamber studies documenting predictable dose-response relationships between homologous series of alcohols, acids, and aldehydes and stimulating the common chemical sense, i.e., the irritant receptor. Abraham et al.[1] used these to develop a quantitative structure activity relatiionship that allows the prediction of irritation based on the physical characteristics of the molecules. At least at concentrations in the vicinity of the irritant threshold, the dose-response relationships support simple dose-additivity.[15a] The nature of such relationships at concentrations well below irritant thresholds remains to be clarified fully. Alarie et al.[2] demonstrated that some "reactive" species trigger symptoms that do not follow this predictable pattern, and that, therefore, reactive species must act through a different mechanism. In addition to simple triggering of a receptor, irritation also may .arise from chemical reactions in the mucosa.

Wechsler[75,76] suggested one mechanism by which more potent irritation may be induced in indoor environments than would be expected from the usual agents encountered indoors. The presence of reactive species, of ozone for example, allows the formation of **Criegee radicals** and **the oxidation of less reactive species to aldehydes**. In the presence of air exchange rates of more than 1 air exchange per hour and ozone levels above 0.1 ppm, aldehyde levels are likely to be irritating to office occupants.

In one investigation of hospitals, moisture-associated deterioration of building materials was found to lead to elevated exposures of irritants,[78] although this is disputed by some because concentrations of relatively inert VOCs do not reach irritant concentrations.

Critical to this discussion is the fact that a dose-related increase in symptoms does appear at levels one to two orders of magnitude below permissible exposure levels and threshold limit values. These relationships support population-based studies suggesting that the presence of widespread symptoms is not implausible simply because "exposures are below all permissible levels." In recognition of this observation, concentration levels recommended for indoor environments generally are substantially lower than those relied upon in the occupational hygiene field (Table 1).

TABLE 1. Comparison of Guidelines and Standards Pertinent to Indoor Environments[a]

	Canadian	WHO/Europe	NAAQS/EPA	SMAC	NIOSH REL	OSHA	ACGIH	MAK
Formaldehyde	0.1 ppm [L] 0.05 ppm [L][b]	0.081 ppm [30 m]			0.016 ppm 0.1 ppm [15m]	0.75 ppm 2 ppm [15m]	0.3 ppm [C]	0.5 ppm 1 ppm [5m]
Carbon dioxide	3,500 ppm [L]				5,000 ppm 30,000 ppm [15m]	10,000 ppm 30,000 ppm [15m]	5,000 ppm 30,000 ppm [15m]	5,000 ppm 10,000 ppm [1h]
Carbon monoxide[c]	11 ppm [8h] 25 ppm [1h]	87 ppm [15m] 52 ppm [30m] 26 ppm [1h] 8.7 ppm [8h]	9 ppm[g] 35 ppm [1h][g]		35 ppm 200 ppm [C]	35 ppm 200 ppm [5m] 1500 [C]	25 ppm	30 ppm 60 ppm [30m]
Nitrogen dioxide	0.05 ppm 0.25 ppm [1h]	0.2 ppm [1h] 0.08 ppm [24h]	0.05 ppm [1y]		1 ppm [15m]	1 ppm [15m]	3 ppm 5 ppm [15m]	5 ppm 10 ppm [5m]
Ozone	0.12 ppm [1h]	0.08–0.1 ppm [1h] 0.05–0.06 ppm [8h]	0.12 ppm [1h] 0.08 ppm [8h]		0.1 ppm [C]	0.1 ppm 0.3 ppm [15m]	0.05 ppm 0.2 ppm [15m]	0.1 ppm 0.2 ppm [5m]
Particles[e] < 2.5 MMAD[d]	0.1 mg/m^3 [1h] 0.040 mg/m^3 [L]					5 mg/m^3	3 mg/m^3	
Particles[e] < 10 MMAD[d]			0.05 mg/m^3 [1y] 0.15 mg/m^3 [24h][g]				10 mg/m^3	
Total particles[e]						15 µg/m^3		
Sulfur dioxide	0.38 ppm [5m] 0.019 ppm	0.19 ppm [10m] 0.13 ppm [1h]	0.03 ppm [1y] 0.14 ppm [24h][g]		2 ppm 5 ppm [15m]	2 ppm 5 ppm [15m]	2 ppm 5 ppm [15m]	2 ppm 4 ppm [5m]
Lead	Minimize exposure	0.5–1.0 µg/m^3 [1y]	1.5 µg/m^3 3 months		< 0.1 mg/m^3 [10h]	0.05 mg/m^3	0.05 mg/m^3	0.1 mg/m^3 1 mg/m^3 [30m]
Radon		2.7 pCi/L [1y]	4 pCi/L [L][f]					2 ppm 4 ppm [5m]

This table was prepared with Hal Levin for an appendix of Standard 62 ("Ventilation for Acceptable Air Quality") and Guideline Project Committee 10 within the standards development process at the American Society for Heating, Refrigerating, and Airconditioning Engineers.

(Table notes continued on next page.)

[ ] Numbers in brackets refer to either a ceiling or to averaging times of less than or greater to 8 hours (m = minutes; h = hours; y = year; C = ceiling, L = long-term) Where no time is specified, the averaging time is 8 hours.

[a] **The values summarized in this table include:**

- Canadian: Recommended maximum exposures for residences developed in 1987 by a committee of Provincial members convened by the federal government to establish consensus, "guideline"-type levels. A revised version is being considered. These were not designed to be enforceable. They were designed explicitly for the residential environment.
- WHO/Europe: Environmental (non-industrial) guidelines developed in 1987 by the WHO Office for Europe (Denmark).
- NAAQS: Criteria for outdoor air developed under the Clean Air Act by the US EPA. The guidelines must, by law, be reviewed every five years, although this does not always occur. These levels are ostensibly selected to protect most sensitive individuals. Exposure level may vary by duration of exposure. Sensory irritation was not a consideration in establishing levels.
- NIOSH: Recommended maximum exposures for industrial environments developed by NIOSH (Centers for Disease Control). NIOSH criteria documents contain both a review of the literature and a recommended exposure guideline. Sensory irritation was not a consideration in establishing levels. These are not enforceable and not reviewed regularly. These levels are not selected to protect most sensitive individuals.
- OSHA: Enforceable maximum exposures for industrial environments developed by OSHA (US Department of Labor) through a standard setting process. Once a standard has been set, levels can be changed only through reopening the rule-making process. These levels are not selected to protect most sensitive individuals. Sensory irritation was not a consideration in establishing levels.
- ACGIH: Recommended maximum exposures for industrial environments developed by ACGIH's Threshold Limit Values Committee. The committee reviews the scientific literature and recommends exposure guidelines. The assumptions are for usual working conditions, 40 hour weeks, and single exposures. These levels are not selected to protect most sensitive individuals. Sensory irritation was not a primary consideration in establishing levels.
- MAK: Recommended maximum exposures for industrial environments developed by the Deutsche Forschungs Gemeinschaft, a German institutions akin to the National Academy of Sciences and Institutes of Health, without regulatory powers. Levels are set on a regular basis, with annual reviews and periodic republication of criteria levels. These levels are enforceable in Germany. These levels are not selected to protect most sensitive individuals. Sensory irritation was not a consideration in establishing levels.
- SMAC: Spacecraft Maximal Allowable Concentrations were developed by a Committee of Toxicology convened by the National Academy of Sciences. They were developed for prolonged exposure periods with consideration of continuous (24 hours per day) exposure. The Committee Report was funded by NASA.

[b] Target level of .05 ppm because of its carcinogenic effects. Total aldehydes limited to 1 ppm.

[c] As one example, readers should consider the applicability of carbon monoxide concentrations. The concentrations considered acceptable for non-industrial, as opposed to industrial occupational, exposure are substantially lower. This is due to the recognition that individuals with pre-existing heart disease may develop exacerbation of heart disease at levels below 15 ppm.

[d] MMAD = mass median aerodynamic diameter in microns (micrometers). Less than 2.5 mm are considered respirable; less than 10 mm are considered inhalable.

[e] Nuisance particles not otherwise classified, not known to contain significant amounts of asbestos, lead, crystalline silica, known carcinogens, or other particles known to cause significant adverse health effects.

[f] The U.S. EPA has promulgated a guideline value of 4 pCi/L indoor concentration. This is not a regulatory value but an action level where mitigation is recommended if the value is exceeded in long-term tests.

[g] Not to be exceeded more than once per year.

The four major questions to be considered in relying on the data from this table are:

- Does the standard aim to prevent the effect of concern in the setting in which it is being used?
- Does the standard recognize the presence of susceptible groups or address the "normal" population?
- Are interactions between various contaminants of concern considered?
- Are the assumptions and conditions set forth by the standard met (such as 8-hour day, 40-hour work week)?

At times, the selection of a specific target level is best made by a team with wide experience in toxicology, industrial hygiene, and exposure assessment.

Individual Susceptibility

Investigations on the physiology of mucosal irritation in buildings suggested that individuals with building-related complaints had, as a group, more rapid tear film break-up time and were more likely to suffer from punctate conjunctivitis.[22,23] It is unclear whether these effects represent a marker of susceptibility, a consequence of exposure, or a mechanism. Tsubota[71] has reviewed the physiology of tear film production and suggests two mechanisms by which underlying susceptibility might increase eye complaints. First, both decreased basal and reflex stimulation lead to dry eye complaints. In addition, decreased Meibomian gland lipid secretion will allow more rapid evaporation of tear fluid in the presence of enlarged exposed ocular surface during computer screen work.[72]

Although some work suggests that individuals with building-related nasal complaints have increased nasal reactivity,[55,56] as a group such subjects do not demonstrate decrements in nasal volume[6] (Roberts, personal communication).

Kjaergard and coauthors have presented evidence from chamber studies that atopic individuals may be more susceptible to the irritant effects of VOCs at low concentrations. They documented that atopic individuals describe more severe irritation at lower thresholds than do nonatopics.[38,39]

Stenberg suggested that subjects with dermal complaints were more likely to describe eczema and to describe more severe irritation on a standardized test of dermal response to a dilute acid ("stinger test") than individuals without complaints.[65]

Headaches, Stress, and Thermal Discomfort

Headaches are recognized as a common symptom among office workers,[59,60] though these generally have not been classified into standard categories.[32] In addition, many employers have moved beyond the passive counting of complaints into interventions and have demonstrated several successful intervention programs directed at individuals.[58] It remains unclear how headache proneness, work-relatedness, and the social and organizational aspects of work contribute to the development of complaints.

Since the early part of this century, engineers have recognized that thermal discomfort is a major contributor to indoor environmental complaints. Flugge demonstrated that odor perception and heat sensation were the main reasons for ventilating occupied space.[34] Subsequent empiric work has confirmed that the thermal comfort envelope does not provide an adequate margin of "comfort" when other modalities of exposure approach their own acceptability boundaries.

Finally, it is hard to consider occupant discomfort and symptoms in the built environment without acknowledging that all discomfort and disease have a psy-

chologic component. It is clear that symptoms are strongly associated with psychological factors.[18,49] As importantly, work stress appears to explain a greater proportion of the variance of symptoms than do the measured exposures.[28] This may simply reflect our much more robust ability to characterize work stress and our lack of knowledge about specific exposure assessment techniques, than a true stronger relationship.

Engineering Aspects of Buildings

Engineers have been concerned about the requirements for ventilation in occupied space since the last 19th century. Although some considerations occurred earlier, as von Pettenkofer used carbon dioxide as a marker of ventilation requirements, the first formal, scientifically derived standard was suggested in 1892 by Billings.

Jansen[34] recently reviewed the history of ventilation. The first issue of the Transaction of the American Society for Ventilating Engineers in the 1890s suggested the need for 30 cubic feet of outside air per occupant per minute, primarily to prevent disease transmission . Odors and heat were recognized as distinct discomfort-inducing environmental parameters by Flugge in the early part of this century. Subsequently, chamber experiments in Yaglou's laboratory in Boston in the 1920s and 1930s documented the need for ventilation for odor control and the increased ventilation requirements for environmental tobacco smoke comfort.

The American Society for Heating, Refrigerating, and Air-Conditioning Engineers (ASHRAE) promulgated its ventilation standard in 1972. Subsequently the "energy crisis" led to a reduction in recommended ventilation rates. Recognizing that these 5 cfm oa were simply inadequate where tobacco smoking was permitted, ventilation requirements were raised in the presence of smoking. The ensuing controversy, and pressure from various parties, led to a delay in the next revision until 1989, when version 62-89 maintained that all buildings should be ventilated at 20 cfm oa per occupant, and, hidden in a footnote, that "this addresses a small amount of smoking." When continuing controversy prevented the issuance of an updated version, the standard went into "continuous maintenance." As new knowledge emerges, it is incorporated without rewriting the whole standard. The smoking footnote has been removed. There is agreement that buildings need at 20 cfm oa to remove usual human odors and emissions and that strong sources require more ventilation.

Thermal comfort standards have been developed in a series of chamber studies beginning with the Pierce Foundation studies in the 1920s. There is clear overlap between the expression of thermal discomfort and mucosal irritation, as with other domains of symptoms. Temperatures in buildings with complaints often exceed the recommended thermal envelope. In addition, the thermal comfort envelopes for women and men do not completely coincide, so that individuals of one gender may express, on average, discomfort when individuals of the other gender feel satisfied.

Although engineering models are developed and refined on the basis of empirical evidence, the theoretical derivations generally are incorporated into voluntary professional design standards, which are then used on a daily basis. Although the science of engineering represents a complex interplay between empirically derived standards and sophisticated theoretical thinking, the daily practice of engineering is far more mundane. Even though buildings may have, on balance, adequate ventilation, air often is distributed in nonuniform fashion to the spaces within buildings, leading to local outdoor air deficits. Similarly, retrofits, additional thermal loads from machines (computers), and office redesign may lead to local thermal loads in

excess of design. Similarly, although most trades have standardized approaches to doing things (captured in apprenticeship courses, codes, and manuals), a recent conference (Bugs, Mold, and Rot III 1999) recognized that the daily practice of construction may lag far behind the state of knowledge inherent in standards.

Data on the problems in buildings have been recognized over the years, beginning with early NIOSH attempts to classify the single most important factor causing problems.[48] The first International Conference on Indoor Air Quality and Climate, now a triennial conference series, was held in 1978. In recognition, ASHRAE instituted an Environmental Health Committee and an annual indoor air quality meeting. Several investigators documented that most buildings suffered from more than one deficiency, with the single most common problem being ventilation systems.[80] This included inadequate provision of outside air, inadequate distribution to occupied space, and inadequate filtration. Almost more importantly, the majority of building maintenance personnel in buildings with problems did not understand how the systems under their control had been designed and were to be operated. Ten years later at least outside air delivery may have improved,[15] though the techniques in such studies differ so dramatically that this may represent a wishful interpretation.

ARE THE SYNDROMES DIFFERENT?

Jaakola[33] has argued that the lack of an operational definition reflects the widespread recognition that the "syndrome" represents a theoretical construct for discussion purposes only. As outlined above, a broad range of symptoms has been attributed to the indoor environment, and a series of physiologic measures suggest several different mechanisms involved in the etiology of those symptoms. Exposures to bioaerosols and VOCs have been associated with symptoms. It is not likely that all symptom categories are caused by a single mechanism, or that a single pollutant class causes all problems. A major issue remains in discussions of SBS: that no operational definition exists and that there is not even agreement on whether individuals can suffer from "the" problem or whether it represents a simple quantitative problem definable only in groups.

Lack of Operational Definitions

Does the presence of regular eye irritation, with or without punctate conjunctivitis, in a single occupant represent SBS if there are a total of five regular building occupants? Four? Six? Some professionals have argued for a 20% cut-off threshold. If we acknowledge that there is a quantitative frequency threshold, for example of 20% prevalence, how often must such symptoms occur for them to count toward the syndrome? Every day? Most days of the week? Three or more days per week? Most weeks? On average one day per week? In any case, most scientists agree that buildings must be occupied and some proportion of individuals must complain for the label to have relevance.

SBS may be dealt with on three levels: **office workers who are sick, the building systems, and the work process itself**. This approach reflects a fundamental belief in occupational health, in which work, the worker, and the workplace are considered as three distinct, but key, ingredients.[65] The latter represents not just the work process in the physical sense—with engineering generation and control strategies—but also the social and organizational structure in the workplace. Unless problems are addressed at all three levels, it is hard to come to understand the processes or to intervene effectively. In a topic such as this, the true etiology is of interest be-

cause it may lead to intervention strategies in specific buildings as well as on an individual level, and, in the long run, it may guide engineering strategies.

This model also implies that organizational intervention is necessary and appropriate. The formation of air quality teams or committees in many buildings, the structure of the proposed indoor air standard from the Occupational Safety and Health Administration, and experience suggest the importance.

These strategies contrast dramatically with those of IEI/MCS: individuals develop a problem; the individual is labeled as being ill. Some might argue the distinction reflects professionals' beliefs and knowledge, rather than any specific scientific understanding, and guides intervention strategies.

What Do We Mean by Low Levels?

Many practitioners acknowledge that indoor environments generate pollutant concentrations "well below OSHA standards" and that these concentrations are nevertheless associated with effects. Less well known is how well documented "low-level" effects are or how widely held such views are even in the scientific community. The most complex issue remains that of VOCs. Much of the scientific and epidemiologic work on VOCs has been based on mass concentration approaches.[52,74,80] Although the experimental work has suggested dose-response relationships, the work has not led to the development of standards for two reasons. First, the degree of agonism between various agents at levels below their own irritant threshold remains unclear. If low levels of pollutants interact more strongly as there are more agents present, and as they are more lipophilic, many more agents must be studied before a reasonably predictive model of irritation can be established for simple irritation. Second, the presence of reactive species such as ozone can generate agents that cause irritation not just through the common chemical sense but also through other forms of irritation, i.e., direct toxic reactions. This reaction is dependent not just on the mixture of VOCs and the concentrations of the various reactive species, but also on the air exchange rate, which affects the duration that concentrations of reactive species are available for the formation of Criegee radicals and the oxidation to aldehydes. The differences between atopic and nonatopic individuals has been inadequately studied.

Do Low Levels of Exposure Cause Real Health Effects?

Scientists have argued for years about the definition of "health effects" in the indoor environment.[13] Some have argued that "sensations" such as irritation represent purely subjective effects and therefore should not be considered evidence of pathophysiology. On the other hand, irritation is clearly recognized as an effect supported by animal models, large-scale epidemiology, and mechanistic thinking. The 1988 PELs decision, which remanded the Permissible Exposure Levels Project to the Occupational Safety and Health Administration, clearly acknowledged that irritation by itself was a reasonable basis for OSHA standards. Irritation is associated with impaired visual acuity,[57] which is likely a harbinger of decreased productivity and certainly an adverse economic, if not health, effect.

Patients whose symptoms are initially induced by acute irritant exposures may progress to longer term symptoms. The physiologic basis remains unclear. Nevertheless, the various syndromes of "unexplained symptoms" associated with perceived exposure affect larger groups of populations than expected.[43,47,53] At least war-related trauma is associated with earlier death from all causes, not just suicide and motor vehicle accidents,[7,26] and suggests that psychological determinants of well being and long-term mortality health may need to be considered.

Do Markers Exist?

Clinical studies have identified markers of group differences in eye and nasal function after VOC exposure and in association with symptoms. Still, none of these techniques have receiver-operating test characteristic curves that are well developed enough to permit clinical use in diagnosis, with the exception of tear film break-up time and conjunctival staining for punctate conjunctivitis, which is in use in clinical settings and widely available.

It remains unclear how useful tear film break-up time, fluorescent dye staining for punctate conjunctivitis, and other tests will be in distinguishing healthy from affected building occupants and individuals with building-related symptoms from patients with SBS/IEI, or in identifying individuals with an objective basis for IEI/MCS.

SUMMARY

There is reasonable evidence that an objective basis exists for SBS, based on both laboratory and field studies. Intervention strategies for environmental control in the office appear to solve many of the problems, although engineering design strategies sometimes are inadequate. Is there evidence that these data pertain to MCS?

A major problem arises from the missing agreed-upon case definitions for the two conditions. They are similar in that both appear to be due to low levels of agents, well below PELs, TLVs, and other levels established by scientific groups. This similarity may be due to one of two separate mechanisms. First, criteria levels do not appear to protect everyone against effects such as irritation, based on empiric field and laboratory data. Second, data do indicate that some individuals respond to concentrations of agents at levels below such "criteria" levels, because of definable and measurable problems such as atopy or more rapid tear film break-up time. Both syndromes appear to affect different organ systems, or at least be associated with symptoms attributed to different organ systems (mucosal irritation, chest symptoms, nausea, headaches). The problem of resolution after leaving work, or the inciting building, is somewhat more difficult, as questionnaire-based responses do not appear to show strong concordance between the two main questionnaires, administered simultaneously, that are used to define SBS symptoms. Psychological aspects clearly influence interpretations of symptoms in SBS. Although this is documented for some proportion of MCS/IEI, it remains controversial. Psychological aspects of discomfort, and stress, are clearly acknowledged to be important in office worker symptoms, at least as pertains to their magnitude.

Some years ago, the AMA Council of Scientific Affairs used one publication by this author[27] to distinguish the two conditions.[14] In the absence of more formal study, and better case definitions, the scientific evidence summarized here simply provides evidence supporting a physiologic basis for symptoms at very low levels, the influence of psychological states on symptoms, and the presence of reversible dose-related symptoms at levels below defined criteria levels. Still, this author feels uncomfortable equating the two syndromes, experiences patients who have been labeled MCS/IEI differently, and remains unconvinced that the syndromes are indistinguishable.

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MULTIPLE CHEMICAL SENSITIVITY/IDIOPATHIC ENVIRONMENTAL INTOLERANCE
Patricia J. Sparks, MD, Editor

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