

Improving the Health of Workers in Indoor Environments: Priority Research Needs for a National Occupational Research Agenda

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Indoor nonindustrial work environments were designated a priority research area through the nationwide stakeholder process that created the National Occupational Research Agenda. A multidisciplinary research team used member consensus and quantitative estimates, with extensive external review, to develop a specific research agenda. The team outlined the following priority research topics: building-influenced communicable respiratory infections, building-related asthma/allergic diseases, and nonspecific building-related symptoms; indoor environmental science; and methods for increasing implementation of healthful building practices. Available data suggest that improving building environments may result in health benefits for more than 15 million of the 89 million US indoor workers, with estimated economic benefits of \$5 to \$75 billion annually. Research on these topics, requiring new collaborations and resources, offers enormous potential health and economic returns. (*Am J Public Health*. 2002;92:1430–1440)

In 1996, the National Institute for Occupational Safety and Health (NIOSH) and diverse partners within the US occupational health community, with input and review by more than 500 organizations and individuals including employers, employees, safety and health professionals, public agencies, and industry and labor organizations, developed the National Occupational Research Agenda (NORA). NORA identified 21 priority areas in which new research could most effectively reduce work-related illnesses, injuries, and deaths in the coming decade.¹ For each priority area, NIOSH convened a multidisciplinary, multistakeholder team of individuals internal and external to NIOSH to further define and then facilitate this national research agenda. This article presents a defined research agenda for 1 NORA priority area—the indoor work environment.

INDOOR WORK ENVIRONMENTS AND HEALTH

Almost 70% of US workers—approximately 89 million persons—are employed in nonindustrial, nonagricultural indoor settings, referred to here as indoor work environments. Scientific studies have associated

some indoor environmental conditions with increased risks of nonspecific symptoms, respiratory disease, and impaired performance.^{2–5} These findings suggest that improved building practices could prevent many health and performance problems associated with indoor environmental conditions. The potential health and economic benefits of improving indoor work environments are largely unrecognized in the United States. Establishment of a national research effort with strategic priorities selected to aid both identification and implementation of health-protective features and practices in buildings could result in a broad reduction in illness and discomfort for the 89 million indoor workers in the United States. Fiscal constraints on occupational safety and health research, however, make a coordinated and focused research agenda necessary.

Epidemiological studies, mostly European,^{6–11} have provided hypotheses to focus future research. In the United States, the Environmental Protection Agency has surveyed representative institutional and commercial buildings (via the Building Assessment and Survey Evaluation [BASE] Study) to provide baseline data; however, no comprehensive national research effort has been undertaken to

provide a scientific basis for improving health in indoor work environments.

Despite the limitations in available scientific documentation, some guidance and standards are available on health-protective building practices. Many current building codes, standards, and guidelines, however, although intended to be health protective, are based primarily on practical experience within the building sector or on non-health-related criteria such as perceived acceptability of air (e.g., immediate perception of odor or irritation), and these codes are not always sufficiently health protective. Additional scientific research is needed to provide a health basis for standards and practices and to develop knowledge of indoor environmental and building science to implement these practices while considering cost and energy efficiency.

Furthermore, the availability of information on health-protective building practices and of adequate building science and technology does not in itself guarantee implementation in buildings for the benefit of occupants. A complex set of institutional and economic barriers and incentives affects decisions on design, operation, and maintenance of buildings throughout their lifetimes. Even with recognized potentially fatal building-related illnesses such as Legionnaires' disease, implementation of available prevention strategies is not universal. Current building codes generally regulate only the design and construction of buildings. Few US legal standards, excepting ordinances in several states, mandate that *occupied* buildings provide healthful indoor air quality, comfortable thermal conditions, or even some minimum amount of outside air. Thus, nonregulatory incentives now determine most postconstruction decisions on building environments.

Benefits from investing in good indoor environmental quality (IEQ) have been little documented and may not be currently evident to building decisionmakers. The consequences of poor IEQ, if considered at all, may be perceived as remote long-term risks primarily affecting others, e.g., occupants. Building owners often keep immediate costs lower through design, construction, equipment, maintenance, operation, and renovation that do not consider IEQ. This cost-saving strategy may, however, cause adverse consequences later for the employers and workers, including impaired health and quality of life and increased costs associated with health care, absenteeism, and impaired performance. In the event of widespread health problems related to a building, the employer and sometimes the owner bear the high costs of environmental investigation, mitigation, relocation, and loss of productivity. In this situation, the owner may also suffer from devaluation of the property, difficulty in finding new tenants, and possibly litigation.

THE PRESENT OBJECTIVES

The NORA Indoor Environment Team (i.e., the authors) included expertise from the fields of engineering, architecture, occupational medicine, epidemiology, industrial hygiene, physiology, and chemistry. The deliberations of the team, supplemented by external review from diverse interested individuals and organizations, form the basis of the priorities described here for research on health in indoor work environments. These priorities will require new collaborations and resources. Implementation of this research agenda will provide knowledge on which employers and unions, building owners and managers, financial institutions, professional associations, and government can base policies.

METHODS

Selection of Priority Research Needs

With the practical goal in mind of protecting the health and performance of indoor workers, the Indoor Environment Team considered “research” as including the following: development of new knowledge or technology, critical synthesis of existing knowledge,

or development or evaluation of methods, diagnostic procedures, and other tools needed to improve IEQ or evaluate human health and performance. The team accordingly considered research needs in 3 interrelated areas: (1) causation and prevention of adverse health effects among indoor workers; (2) science and technology of indoor environments and buildings, necessary to evaluate and improve the healthfulness of indoor work environments; and (3) barriers to and incentives for implementation of healthful building practices. The first 2 of these areas involve learning what needs to be implemented, and the third involves learning how to implement what is known.

On the basis of the members’ multidisciplinary expertise and judgment, the team limited its scope of assessment to health effects thought to result from exposure to indoor contaminants. (Not considered here, although constituting substantial public health problems, were adverse effects caused by ergonomic factors and by psychosocial or work organization–related job stressors; each of these effects is the focus of another NORA team.) For eligible types of health effects, we estimated both health and economic impacts related to indoor work environments, including the magnitudes of current adverse effects as well as the potential benefits from improving IEQ.

Selection of a specific health effect for priority research (based on the team’s judgment) from among the eligible adverse health effects required (1) important morbidity, mortality, or economic loss from the health effect; (2) substantial evidence that characteristics of the nonindustrial occupational indoor environment influence the prevalence or severity of the health effect; and (3) insufficient knowledge about causation of the health effect to direct prevention strategies. Research priorities in the areas of indoor environmental and building science and of barriers and incentives were based on the multidisciplinary experience and judgment of the team.

Estimates of Health and Economic Effects

Measures of health-related adverse effects included number of workers affected; severity (including mortality), frequency and duration

of the health effect; and proportion of morbidity or mortality potentially preventable through improved indoor work environments. We estimated the number of indoor workers with each type of health effect (generally from both work and nonwork exposures), either by using available prevalence estimates directly or by applying general prevalence estimates for the US population to the population of indoor workers. For each type of health effect, we multiplied the number of workers with the health effect by the proportion of the health effect estimated as preventable through improved indoor work environments. Most estimates were for 1996.

We calculated economic costs by applying available estimates of the costs of health care, of absence due to illness, and of other performance losses to the numbers of workers with each kind of health effect. Estimates of economic costs and potential benefits did not include a monetary equivalent for deaths. We estimated potential economic benefits from improving indoor work environments by multiplying economic costs by the proportion of the health effect estimated to be preventable through improvements to work environments. Estimates of benefits do not reflect costs of research or of necessary indoor environmental improvements and thus may overestimate net benefits; however, example cost–benefit analyses have shown economic benefits to exceed costs by approximately a factor of 10.¹²

RESULTS

Causes and Prevention of Building-Related Adverse Health Effects

For each type of health outcome known or suspected to be caused by contaminants in indoor work environments, Table 1 provides estimates (when available) of the total adverse health effects produced by US indoor work environments and of the proportions of adverse effects preventable by improving these environments. The estimated potential annual reductions in adverse health effects include 5 to 7 million communicable respiratory infections, a 6% to 15% reduction in exacerbations of asthma among the 4.7 million indoor workers with asthma, and a 20% to 50% reduction in nonspecific building-related symptoms. (Sources for and details on the esti-

TABLE 1—Estimated Health Impacts of Contaminants in Indoor Work Environments in the United States, and Potential Benefits of Improved Environments

Contaminant-Related Health Effect	Health Impacts			
	No. of Workers With Health Effect Due to Work or Nonwork Exposures ^a (of 89 Million Total Indoor Workers in US)	Severity	Frequency (Duration)	Estimated Potential Annual Reduction (% and No.) in Health Effect From Improved Work Environments Among Indoor Workers
Communicable respiratory infections: building-influenced, occupant sources (e.g., influenza, common cold, tuberculosis)	Influenza and common cold: 52 million cases; tuberculosis not in health care or prison settings: unknown	Usually moderate, fewer than 70 000 hospitalizations and unquantified fatalities	~0.58 cases of common cold and influenza per year among working-age population (duration varies, days to months)	Estimated 10% to 14%; 5–7 million cases (estimate has substantial uncertainty)
Asthma, hypersensitivity pneumonitis, and allergic disease	Asthma: 4.7 million; allergies: 18 million	Allergies: mild to severe; asthma: mild to fatal	Asthma and allergies: many to all days per year (duration of both usually chronic)	Estimated 6% to 15%; asthma episodes among 0.3–0.7 million cases; allergy episodes among 1–3 million cases (estimates have substantial uncertainty)
Nonspecific building-related symptoms (acute effects of indoor exposures or conditions, including so-called sick building syndrome)	35–60 million workers with one or more weekly building-related symptoms (effects from work exposures only)	Usually mild to moderate	Often while at work (chronic with chronic exposure)	Estimated 20% to 50%; 8–30 million cases (estimate has substantial uncertainty)
Respiratory infections: building sources (Legionnaires' disease, Pontiac fever, fungal infections)	2700–6000 estimated cases per year of Legionnaires' disease; unknown number of Pontiac fever and fungal infection cases	Legionnaires' disease: often severe, 5% to 15% of documented cases are fatal; Pontiac fever: moderate; fungal infections: can be severe or life threatening	Legionnaires' disease and Pontiac fever: usually once per lifetime (duration varies); fungal infections: varies	Unknown, probably fairly high (e.g., >50%); Legionnaires' disease: 1400–3000 cases, including >70 deaths; Pontiac fever, fungal infections: unknown
Health effects of environmental tobacco smoke	Among 10–30 million exposed, acute irritation, respiratory effects, reproductive effects: unknown; cardiovascular effects: 2000–11000 deaths; lung cancer: 100–600 cases (effects from work exposures only)	Acute irritation: mild to moderate; respiratory and reproductive effects: moderate to severe; cardiovascular effects: severe to fatal; lung cancer: fatal	Acute irritation with exposure; respiratory effects: chronic; cardiovascular effects and cancer: chronic, often fatal	100%; 2000–11 000 cardiovascular disease deaths; 100–600 lung cancer cases including 90–530 deaths

Note. Sources for and details on effect estimates are available from the authors and as a supplement to the on-line version of this article.
^aEstimates in this column that reflect the effects of work-related exposures only are identified.

mates of effects described in Tables 1 and 2 are available from the authors and as a supplement to the on-line version of this article.)

Table 2 provides estimates of the adverse economic consequences of contaminant-related health effects in indoor work environments and of the potential economic benefits from improved indoor work environments. The most uncertain estimate—and, at \$20 to \$70 billion, the largest—is that for productivity losses from building-related symptoms. The estimates shown in Table 2 indicate that the combined annual costs of these adverse health effects range from \$50 to \$100 billion, with about \$5 to \$75 billion potentially preventable.

On the basis of the criteria described earlier and the estimates of cost shown in Tables 1 and 2, the team identified 3 types of health effects as priorities for increased research: (1) building-influenced communicable respiratory infections, (2) building-related asthma and allergic disease, and (3) nonspecific building-related symptoms. In the case of each of these priorities, implementation of the findings from research on causation and prevention could prevent adverse health effects among estimated millions of indoor workers and could provide annual economic benefits of several hundred million to many billions of dollars. Despite substantial limitations from multiple assumptions, missing data, and un-

certain precision, these quantitative estimates of impact and potential benefit yield valuable information for prioritizing research. Estimates here on the costs of indoor work-related illness exceed previous estimates.¹³

The team has not proposed research on all adverse health effects potentially related to indoor work environments. Rather, on the basis of current evidence, the team has targeted health conditions that affect large numbers of indoor workers and for which research on indoor environments holds promise to fill key information gaps, allowing development of effective preventive strategies. For some exposures, such as those that might influence cancer, neurotoxic effects, reproduc-

TABLE 2—Estimated Annual Economic Impacts of Contaminant-Related Health Effects in Indoor Work Environments in the United States, and Potential Benefits of Improved Environments

Contaminant-Related Health Effect	Annual Economic Impacts			
	Health Care Costs of Effects due to Work or Nonwork Exposures ^a	Costs From Absence Due to Illness and From Other Performance Losses due to Work or Nonwork Exposures ^a	Estimated Economic Consequence for Indoor Workforce due to Work or Nonwork Exposures ^{a,b}	Estimated Economic Benefits Possible From Improved Indoor Work Environments ^{b,c}
Communicable respiratory infections: building-influenced, occupant sources (e.g., influenza, common cold, tuberculosis)	\$10 billion in health care costs	\$19 billion in absence from work; \$3 billion from reduced performance at work	\$32 billion	\$3 to \$4 billion (estimate has substantial uncertainty)
Asthma, hypersensitivity pneumonitis, and allergic disease, building related	Asthma, \$2.6–\$2.8 billion; allergic rhinitis, \$580 million; other, not estimated	Asthma, \$340 million; allergic rhinitis, \$377 million; other, not estimated	\$3.9–\$4.1 billion	\$200 to \$600 million (estimate has substantial uncertainty)
Nonspecific building-related symptoms (acute effects of indoor exposures or conditions, including so-called sick building syndrome)	Unknown (effects from work exposures only)	\$20–\$70 billion (effects from work exposures only)	\$20–\$70 billion (effects from work exposures only)	\$4–\$70 billion (estimate has substantial uncertainty)
Respiratory infections: building sources (Legionnaires' disease, Pontiac fever, fungal infections)	Legionnaires' disease: \$26–\$40 million in health care costs; Pontiac fever: minimal health care costs; fungal infections: unknown costs	Legionnaires' disease: \$5–\$8 million in absence from work; Pontiac fever: unknown absence costs (1 week/case); fungal infections: unknown costs	Greater than \$30–\$50 million	Tens of millions of dollars
Health effects of environmental tobacco smoke	\$30–\$140 million in health care costs for cardiovascular disease and lung cancer (effects from work exposures only)	Costs of absence from work and other performance losses not estimated	\$30–\$140 million (costs of absence from work and other performance losses not estimated; effects from work exposures only)	\$30–\$140 million (costs of absence from work and other performance losses not estimated)

Note. Sources for and details on effect estimates are available from the authors and as a supplement to the on-line version of this article.

^aEstimates in this column that reflect only the effects of work-related exposures are identified.

^bEstimated economic consequence includes estimated health care costs, value of absence from work, and value of productivity decreases at work when health effect is experienced. All estimates exclude any monetary equivalent for deaths.⁸³(^{other comments})

^cEstimated benefits do not reflect costs of research or of necessary indoor environmental improvements.

tive effects, or “multiple chemical sensitivity,” insufficient evidence was available to estimate health or economic effects in indoor work environments. For other exposures, such as radon, asbestos, and carbon monoxide, effects and strategies for prevention in indoor environments are well understood.

Building-influenced communicable respiratory infections. Indoor workers in the United States experience approximately 52 million cases of common cold or influenza per year, with estimated annual costs of \$32 billion relating to health care, absence from work, and reduced performance at work (Table 2). If practical changes in indoor work environments could reduce transmission of these respiratory illnesses among occupants even

slightly, public health and economic benefits would be substantial.

Theoretical relationships between characteristics of indoor environments and incidence rates of communicable respiratory diseases depend on disease-specific routes of transmission. Routes may include direct contact (person to person), indirect contact (person to object to person), or inhalation of infectious bioaerosols (e.g., small virus-containing aerosols expelled by coughing or sneezing). Infection by short-range transport of bioaerosols can occur through coughing or sneezing toward an uninfected person, but infection by long-range transport of bioaerosols requires infectious particles to remain both airborne and viable for several meters or

more. Infectious aerosols are known or thought to contribute substantially to transmission of the common cold (e.g., rhinovirus infections), influenza, adenovirus, measles, tuberculosis, and other common respiratory illnesses.^{14–22} Still, the relative importance of possible transmission mechanisms for many common respiratory illnesses, as well as the period of infectivity,²³ remains unresolved.

In theory, disease transmission by inhalation of airborne infectious aerosols may be influenced by factors affecting indoor concentrations of infectious agents, transport pathways between individuals, viability of infectious agents, or susceptibility of individuals. Related building or indoor environment factors include the following:

- rate and effectiveness of outdoor air ventilation, which dilutes concentrations of indoor aerosols

- rate and efficiency of air filtration
- disinfection, as by ultraviolet light, which may deactivate infectious organisms
- rate of air recirculation, which influences transport between regions of the building
- density of occupancy, use of private work spaces, or use of barriers between occupants, which influence the effective distance between individuals

- temperature and humidity of air, which affect the period of viability of infectious aerosols and human susceptibility²¹

- indoor toxic or fungal exposures, which may alter human susceptibility to infection^{24,25}

All of these factors may theoretically influence long-range airborne transmission of disease. The first 4 factors may have little or no effect on disease transmission that occurs only through short-range airborne transport or contact.

Although the distances involved in airborne transmission of common diseases in the indoor work environment have not been clearly documented, readily available strategies such as increased ventilation rate or enhanced treatment of recirculated air have the *theoretical* potential to reduce disease transmission indoors, particularly any long-range transmission. In addition to theoretical considerations, several kinds of real-world evidence suggest that building factors do influence disease transmission, even if that influence is not apparent to building occupants or operators. First, long-range indoor airborne transmission has been well documented in nonviral diseases such as Q fever, legionellosis (Legionnaires' disease), tuberculosis, histoplasmosis, brucellosis, and inhalation anthrax,^{26,27} as well as for viral diseases such as chickenpox, smallpox, measles, coxsackievirus, (probably) influenza and adenovirus, and many animal viruses.^{20,21,26,28,29}

Second, an influence of the physical characteristics of indoor environments on the risk of communicable respiratory infections is suggested by findings from several observational and experimental studies. A large US Army study revealed 50% higher rates of clinically confirmed acute respiratory illness with fever

among recruits housed in newer barracks with closed windows, low rates of outside air supply, and extensive air recirculation than among recruits in older barracks with frequently open windows, more outside air, and less recirculation.⁴ Low ventilation rates and recirculation of air are suspected risk factors because of their theoretical impact on exposures to infectious aerosols.²² An experimental field study conducted in US Navy barracks revealed a 23% lower rate of respiratory illness with fever among recruits housed in barracks with ultraviolet irradiation of air near the ceiling than among recruits in comparison structures without irradiation.³⁰ A study in a crowded jail showed that, during an epidemic of pneumococcal disease, the disease attack rate was 95% higher in jail cells with the lowest volume of outside air supply per person.³¹

Thus, building factors influencing primarily long-range transport of infectious bioaerosols had strong effects on the incidence of communicable disease even in densely populated settings where short-range airborne transmission or contact would seem primary. As a result, these findings are relevant to less crowded settings such as offices, where long-range transport of bioaerosols would be relatively more important.

Two findings from less crowded indoor work settings offer some direct evidence in regard to this issue. In 1 study, increased risk of tuberculin conversion among health care workers in hospitals was strongly associated with inadequate ventilation rates in hospital rooms.³² A 34% lower rate of short-term absence resulting from illness, considered likely to be related to respiratory disease, was found in office buildings with twice the recommended levels of ventilation relative to other buildings occupied by the same company with lower levels of ventilation.³³ Other studies of work or residential environments have also revealed building or ventilation characteristics to be significantly associated with occurrence of communicable respiratory diseases among occupants.^{24,34–39} Overall, 6 of the 11 studies cited here showed that some particular characteristic of the building or indoor environment was associated with a 50% or greater difference in the metric of illness.

These reported associations do not confirm a causal relationship between aspects of in-

door work environments and communicable respiratory infections. However, theoretical principles, documentation of long-range airborne transmission for viral and nonviral diseases, and suggestive epidemiological findings, together with the large potential public health benefits, make research on this relationship a priority. It is critical that future studies isolate the effects of specific building risk factors on infection by specific agents. Measurement tools for confirming infections and identifying causal organisms are now available to facilitate this research.⁴⁰

The reduction in communicable respiratory illness estimated here as a potential benefit of improving indoor environments—prevention of 5 to 7 million cases of disease annually (Table 1)—would also produce an estimated \$3 to \$4 billion annual benefit from reduced health care costs and reduced absenteeism (Table 2). While there is substantial uncertainty regarding the estimated preventable proportions of these infections, even a small proportional reduction in respiratory infections among indoor workers would have an important impact on the national burden of disease and on related costs.

Building-related asthma and allergic disease. About 18 million (20%) indoor workers have allergies, and about 5 million (5.3%, most with allergies) have asthma.^{41,42} Asthma incidence is increasing globally in much of the developed world, and part of this increase may be related to IEQ. Studies conducted in residences and in schools have indicated that moisture and mold problems, also common in nonindustrial workplaces, are related to lower-respiratory-tract symptoms, associated with asthma.^{43,44} Serious allergic diseases such as hypersensitivity pneumonitis and asthma have been documented among office workers.^{45,46} Causes have included microbiological exposures resulting from water leaks, contaminated ventilation system components, or other building inadequacies.^{27,47,48} Exposures to allergens from dust mites, pets, cockroaches, rodents, and pollen, as well as exposure to tobacco smoke, have been associated with allergy and asthma in residential studies. These same exposures occur in the nonindustrial work environment; however, their magnitude and effects are poorly understood. Research is also needed to assess building-

related influences on allergic rhinitis and chronic sinusitis, widely reported anecdotally but virtually unstudied.

Few data exist that directly link causation or exacerbation of allergic disease to indoor work environments. Up to 20% of all cases of adult-onset asthma are estimated to be work related.⁴⁹ Although agricultural or industrial materials implicated in sensitizing exposures are well known (e.g., compost, toluene diisocyanate), many work-related cases occur in indoor work settings.⁴⁹ The increase of allergic disease as a public health problem and the clear documentation that specific conditions in residential buildings can cause or exacerbate allergic disease⁴⁵ dictate priority research attention. A recent review noted that the effectiveness of specific exposure-limiting prevention strategies has been inadequately studied and offered suggestions for further research.⁴⁵ As with communicable respiratory illness, even small decreases in incidence or exacerbation of allergic disease achieved through improved indoor environments would result in large savings from reduced medical costs and increased productivity (Table 2).

Nonspecific building-related symptoms. Because symptoms such as eye, nose, and throat irritations, headaches, and fatigue may be related to many different disease processes, they are sometimes called nonspecific symptoms. Recent studies examining a total of more than 115 US office buildings, almost all without a history of publicized indoor environmental complaints, indicated that more than 40% of workers experienced frequent work-related symptoms^{50–52} (H. Brightman, US EPA BASE Study, written communication, October 1998). Thus, the relatively few publicized “problem” buildings are apparently only the visible part of a larger phenomenon.

Problem-solving investigations have often shown symptoms in buildings to be accompanied by new construction or renovation, moisture incursions, or deficiencies in ventilation, but practical investigations have rarely reported systematic testing of these relationships. Scientific studies provide evidence for the influence of building factors on nonspecific building-related symptoms. Increased occurrence of symptoms or of objectively measured adverse health effects has been

associated with building features such as air conditioning or mechanical ventilation systems, with inadequacies in ventilation systems, and with lower outdoor air ventilation rates.^{2,3,53–55} Improvements in symptoms or in objective health measurements have been associated with experimentally improved indoor environments.^{56–61} Building-related symptoms have also been associated with absenteeism,⁶² objectively measured adverse health effects,^{58,63} and impaired performance on work-related tests.^{60,64–68}

Scientific findings of associations suggest a number of causes biologically plausible for building-related symptoms. These causes include exposures to allergenic or irritating aerosols (particularly bioaerosols) and to volatile or semivolatile organic compounds (VOCs or SVOCs). Sources include ventilation systems, building structures, building materials, furnishings, office equipment, or products such as cleaning compounds or pesticides. Physical factors (particularly temperature), psychosocial stressors, and individual susceptibility are considered important cofactors. Widespread reduction of building-related symptoms will require either identification of causal agents and protective indoor exposure limits or more rigorous documentation of effective health-protective building practices.

Few scientifically based indoor exposure guidelines are available for preventing building-related symptoms, and it may not be possible to establish such guidelines with conventional indoor exposure measurements (e.g., total concentration of VOCs, total counts of fungi and bacteria), because these conventional metrics of indoor exposure have seldom been associated with occupant health problems. Furthermore, recent research has revealed increases in symptom prevalence associated with exposure metrics not traditionally used indoors: microbiological toxins such as endotoxins or β -1,3-glucans,^{69,70} correlated clusters of VOC concentrations indicating recognizable sources such as paint or vehicle exhaust,^{71,72} and combinations of low-level VOCs with additive irritation effects.⁷³ Other research has shown production of aldehydes and other highly irritant VOCs, not usually or easily measured, from reactions among common chemicals in indoor air, as well as increased pro-

duction of these irritant compounds at lower ventilation rates.^{74,75} We need to assess exposure in ways more relevant to place (e.g., personal rather than area samples), time (e.g., integrated rather than “grab” samples), and human response (targeting specific agents with documented adverse effects) than is currently customary or feasible.

Table 3 identifies recommended research priorities associated with the cause and prevention of these 3 types of building-related adverse health effects. Research is needed to better define the relationship of health effects to exposure and building factors, to test the effectiveness of proposed intervention measures, and to improve exposure assessment methods. (Closely related research on building science, essential to this health-related research, is described in the following section and in Table 4.)

Science and Technology of Indoor Environments and Buildings

We have an inadequate understanding of the interrelationships among indoor pollutant exposures, features and practices in buildings, and activities of occupants. Building *features* potentially affecting IEQ and occupant health include the design and materials of the building (e.g., the outside envelope, air handler, ventilation distribution system, indoor surfaces) and the contents (e.g., furnishings, office equipment). Building *practices* potentially affecting IEQ and occupant health include those related to (1) construction, commissioning, operation, maintenance, renovation, and repair of the building and ventilation system; (2) selection of materials in buildings and ventilation systems; and (3) protection of occupants from contaminants produced during construction and renovation.

The occurrence of incompletely understood chemical reactions indoors, producing irritant compounds not emitted directly by the materials present, provides an additional layer of complexity. Even to the extent that we can identify certain pollutants of concern, we have limited knowledge of the most effective means of reducing exposures.

We know that outdoor air ventilation can effectively reduce exposures to widely generated indoor pollutants, such as those from occupants, indoor surfaces, or indoor chemical

TABLE 3—Priority Research Needs for Improving Health of US Workers: Causes and Prevention of Building-Related Health Effects**Building-influenced communicable respiratory infections**

- Document and quantify the association of communicable respiratory infections among indoor workers with specific characteristics of indoor work environments (e.g., ventilation rate, filtration, pattern of outside airflow, density of occupancy, and physical separation of occupants)
- Estimate the proportion of these infections preventable by specific building practices
- Improve and apply tools (e.g., in molecular biology) to identify specific viral infections, their routes of transmission, and periods of infectivity and to assess exposure to infectious agents and agents that may alter susceptibility

Building-related asthma and other allergic disease

- Quantify, for hypersensitivity pneumonitis, asthma, and allergic rhinitis, the associations between onset or exacerbation of disease and specific characteristics of indoor work environments (e.g., ventilation rate, ventilation design and maintenance, sources of moisture or allergens indoors or in ventilation system, surface materials, housecleaning, air and surface dust)
- Estimate the proportion of causation or exacerbation of these diseases attributable to specific indoor environmental characteristics and the proportions preventable by specific exposure-reduction practices
- Improve and apply quantitative exposure assessment measures for bioaerosols, particularly their bioactive components (e.g., toxins, allergens, immunogens, and adjuvants)
- Develop appropriate uses in this area for human biomarkers of exposure or disease
- Evaluate the impact of exposure-reduction strategies on reducing relevant bioaerosol exposures
- Characterize exposure-response relationships for these diseases and measured indoor contaminants

Nonspecific building-related symptoms

- Quantify the relationships between building-related symptoms or sensory reactions and factors of building design, operation, maintenance, furnishings, equipment, and occupancy (with selection of research targets based on existing scientific evidence, further analyses of relevant existing data sets, and current empirically based knowledge, e.g., standards of best building practice among indoor environmental professionals)
- Quantitatively evaluate effectiveness of preventive measures
- Identify physiological processes and biochemical parameters that are associated with building-related symptoms or sensory reactions and identify or develop assessment tools
- Improve and apply strategies to identify chemical, microbiological, and physical exposures that are toxic, irritant, allergenic, or highly odorous and that cause occupant symptoms or sensory reactions in buildings; consider improving methods to predict adverse effects of indoor exposures, singly or in combination (e.g., prediction from known “structure-activity relationships” for related chemicals) (see also Table 4)
- Quantify exposure-response relationships for measured indoor contaminants and specific health effects represented by building-related symptoms
- Establish the mechanisms by which causal agents alter the occurrence of nonspecific symptoms or sensory reactions

reactions, but may increase indoor exposures to outdoor pollutants, such as ozone and particles. However, the complexities, costs, limitations, and inaccuracies of currently available methods for measuring ventilation rates in buildings have impeded research on ventilation and health and have also made it difficult for building professionals to maintain desired ventilation rates.

A vigorous research program on the science and technology of indoor environments and buildings that closely complements the research focused on specific health effects is needed. This program would include research

on selected indoor pollutants of concern that are toxic, highly irritating, allergenic, or strongly odorous, such as VOCs, SVOCs (e.g., pesticides, fire retardants, plasticizers), bioaerosols, and other particles, as well as the precursors of these pollutants (Table 4). The relationship of these pollutants to source, building, and ventilation system factors should be studied as well. Research is also needed on measurement and control of ventilation rates and improvement of ventilation systems. Findings from such research would facilitate the design, implementation, and interpretation of health studies. They would also enable build-

ing professionals to design and operate indoor environments in ways consistent with building standards and guidelines.

Implementation of Health-Protective Features and Practices in Buildings: Barriers and Incentives

Research is essential to document the key features and practices in buildings that can make indoor workers healthier (as described earlier) and to achieve parallel advances in indoor environmental and building science (Tables 3 and 4). Success in these research areas, however, will not be sufficient to protect the health of indoor workers. Exposure to environmental tobacco smoke, for instance, still occurs in some workplaces despite its known hazards. Many social and economic forces, acting as barriers or incentives, influence whether available health-related knowledge is translated into action.⁷⁶ Decisions affecting IEQ are made primarily by building professionals (e.g., architects, engineers, operators) and owners, although decisions made by employers and workers also may have consequences for IEQ. These decisions occur at many stages of the life cycle of each building: during design, construction, operation, maintenance, and renovation and in the course of other activities related to sales, rental, and use.

Barriers that may obstruct consideration of IEQ in decisions include the following:

- lack of meaningful metrics for assessing IEQ or IEQ-related health effects
- limited information, guidelines, and standards on the relation of IEQ to health
- lack of necessary products and services for measuring or controlling IEQ
- lack of documentation of the costs vs benefits of specific health-protective building practices
- decisionmaking habits based on lowest first costs
- a legal and economic system in which the cost burden of poor IEQ generally falls on occupants rather than on building decisionmakers who did not consider IEQ

Incentives that may increase the implementation of healthful features and practices in buildings include the following:

TABLE 4—Priority Research Needs for Improving Health of US Workers: Science and Technology of Indoor Environments and Buildings**Improving exposure assessment for indoor contaminants of concern**

- Develop improved and more practical methods of assessing indoor exposures of concern, preferably personal exposures, including temporal and spatial variation
- Using standardized methods, establish reference distributions of indoor concentrations and, if possible, of personal exposures
- Characterize size distribution and composition of indoor particles

Relationships of indoor pollutants to building and ventilation factors

- Identify pollutant sources and rates of emissions for contaminants of concern
- Identify strategies that reduce or prevent indoor chemical and particulate pollutants of concern over the life cycle of buildings, including consideration of design, material choice, construction, and renovation; commissioning, operation, ventilation, thermal control, and filtration; and maintenance, cleaning, and pest management
- Characterize the influence on indoor microbiological colonization and bioaerosol exposures of features and practices in buildings, including building envelopes, indoor materials, indoor thermal conditions, ambient climate, filtration, ventilation operation and design, biocidal radiation, maintenance and cleaning activities, and occupant activities
- Characterize and quantify the sources (indoor and outdoor), concentrations, size distributions, composition, and fate of indoor particles (including consideration of transport and transformation), in relation to features and practices in buildings
- Develop models predicting indoor air contaminant levels resulting from sources in conjunction with specific building and ventilation system design, operation, and maintenance features

Research to improve ventilation designs

- Reduce risk of producing contaminants (e.g., through control of moisture or contamination within systems, or by making components highly accessible)
- Incorporate natural ventilation
- Increase effectiveness in removing contaminants
- Improve efficiency of outdoor air delivery to the breathing zone
- Improve the control of indoor temperature, with consideration of individual control
- Improve the control of indoor humidity, especially in humid climates

Ventilation rate measurement and control

- Develop accurate yet practical measurement technologies for determining ventilation rate
- Develop and evaluate improved strategies and systems to control ventilation rates, including demand-controlled systems using pollutant sensors and more accurate measurement of airflow within the system

sector incentives that would lead building decisionmakers to consider or experience the economic costs to others of poor IEQ (e.g., proactive loss prevention strategies by financial-sector organizations such as insurance companies or lenders to reduce IEQ-related risks); (2) evidence-based guidelines for healthful buildings and indoor environments produced jointly by engineering, health science, and other groups; (3) dissemination of critical new scientific information to mobilize market forces among building professionals and occupants; and (4) strategies used successfully in related fields or in other countries to foster action among building professionals (e.g., the strategies used to stimulate increased energy efficiency in buildings).

We outline in Table 5 a broad framework for research in this area, without specific priority research needs. Methods may include social research techniques (e.g., surveys, focus groups, interviews) focused on behavior, motivation, attitudes, and knowledge related to IEQ and health among key stakeholders (e.g., financial participants, designers, building owners and managers, employers, and employees).

DISCUSSION**Summary**

The research priorities identified here broaden the scope of research on the health of indoor workers to include communicable respiratory infections and suggest expanded research on the relationships between IEQ and asthma, allergies, and building-related symptoms. Research priorities also include indoor environmental and building science and technology related to IEQ, along with barriers and incentives to the implementation of health-protective features and practices in buildings. We aim to stimulate the commitment of new resources to support expanded research through partnerships among governmental agencies, professional societies, foundations, industry, academia, and other affected groups that share an interest in IEQ, public health, and worker performance. Healthy indoor work environments will benefit many groups in society that now pay for poor IEQ, some unknowingly.

- codes, regulations, and laws (local, state, or federal) based on science, professional consensus, or both
- nonregulatory government actions (e.g., tax incentives, subsidies, demonstration projects, guidelines, education)
- guidelines from professional consensus groups or other sources establishing a “standard of care”^{77,78}
- financial-sector incentives⁷⁹
- client-based incentives (e.g., IEQ-protective construction guidelines or lease terms for use by architectural clients or tenant groups)
- avoidance of liability
- scientific data documenting that improving IEQ can diminish adverse effects among building occupants

- educational or informational activities^{80,81} for building professionals and occupants

Such strategies can facilitate action at current levels of scientific knowledge, even as societal investment in research further strengthens the scientific basis for recommendations.

We suggest that increasing the implementation of health-protective features and practices in buildings may require multiple social strategies, including both voluntary and regulatory approaches, to reduce barriers and increase incentives for health-protective building practices. Research is necessary to develop effective approaches, including some promising new strategies: (1) private-

TABLE 5—Framework for Research on Barriers and Incentives for the Implementation of Health-Protective Features and Practices in Buildings

<p>Identify and characterize, using social research techniques, the key decisionmakers in the life cycle of the building process and the decision processes that influence the implementation of key health-protective features and practices in buildings. Consider:</p> <ul style="list-style-type: none"> · Key trigger points (e.g., transactions) in the building process · Parties with leverage at trigger points (e.g., lenders, realtors, municipalities)
<p>Evaluate the effectiveness, costs, and benefits of alternate social strategies, including market-based strategies and public policies, either existing or available, that target key barriers and incentives related to health-protective decisions in the building process</p>
<p>Develop estimates, methods, or syntheses necessary to allow more effective decisionmaking related to buildings</p> <ul style="list-style-type: none"> · Quantitatively estimate the implementation costs and the health and economic benefits of key features and practices in buildings · Identify gaps in the health, building, and economic data needed for the above estimates to guide research priorities related to health in indoor work environments; fill these data gaps · Develop methods allowing decision makers to consider both economic and non-economic (e.g., health, quality of life) effects of choices in building practices · Assess the prevalence of specific higher risk building features and practices, to help estimate potential costs and benefits of new strategies · Synthesize the current findings of indoor environmental quality research to enable evidence-based public health recommendations

Suggested Research Strategies

Implicit in our agenda is recognition that multidisciplinary research efforts are critical to understanding the complex relationships between indoor environments and human health. Epidemiologists, physicians, molecular biologists, chemists, microbiologists, architects, engineers, economists, industrial hygienists and other exposure assessment experts, behavioral scientists, and aerosol scientists need to work together to understand the risk factors and mechanisms underlying health effects associated with building environments and to document means of prevention. Research projects lacking key disciplines have often fallen short in generating data convincing to the entire scientific community or to building professionals. To be efficient and persuasive, this research should use robust research methods, including experimental, cohort, or case-control studies; specific, relevant exposure metrics; and objective or other specific measures of health outcomes. Also critical is the parallel development of technologies designed to minimize the energy consumption and the economic and environmental costs of more healthful building practices.

Potential Benefits of Suggested Research

Implementation of findings from this proposed research agenda, according to the best available information, will potentially improve health and productivity among millions of indoor workers in this country, with benefits for business, government, and other organizations and also for nonworking building occupants such as customers, patients, and students. Potential public health benefits include a reduction of 6 to 11 million cases of mild to severe illness annually, the prevention of a number of deaths associated with communicable disease and asthma, avoidance of frequently experienced acute symptoms among 8 to 30 million workers, and an improved quality of life in the work environments where most adults spend one fourth of their lives.

The accompanying net economic benefits from reducing these adverse health outcomes (Table 2) are estimated at \$7 to \$75 billion annually, including more than \$1 billion from estimated reductions in costs of health care and more than \$6 billion from estimated reductions in illness-related absence and impaired performance at work, less the costs of

research and of building-related improvements. The productivity and competitiveness of the US workforce would benefit as well. Most of these estimated economic benefits would derive from potential reductions in communicable respiratory infections and building-related nonspecific symptoms.

Total federal research expenditures on indoor air in nonindustrial work settings and the associated health effects discussed here (excluding research on asthma and allergy in children, residential IEQ, and environmental tobacco smoke) are less than \$28 million annually.⁸² If the estimates here of potential benefits from improving indoor work environments are reasonably accurate, then a substantially expanded program of research is justified on the priority topics described in this report. With proper planning and prioritization, expanded research would enable important improvements in the health and performance of indoor workers. Despite uncertainty about precise benefits, the health and economic return on this research investment applied to the nation's indoor workplaces is potentially very large. ■

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The authors, as members of the NORA Indoor Environment Team, created the article through an extended process of discussion, revision, and consensus. M.J. Mendell performed much of the writing and most of the assembly and revision based on team contributions and discussions. W.J. Fisk provided most of the original data for the first 2 tables. K. Kreiss created a substantial amount of the original draft text. These 3, and all other authors (H. Levin, D. Alexander, W.S. Cain, J.R. Girman, C.J. Hines, P.A. Jensen, D.K. Milton, L.P. Rexroat, and K.M. Wallingford), contributed text, data, or ideas and reviewed the article.

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References

- Rosenstock L, Olenec C, Wagner GR. The National Occupational Research Agenda: a model of broad stakeholder input into priority setting. *Am J Public Health*. 1998;88:353–356.
- Mendell MJ. Non-specific symptoms in office workers: a review and summary of the epidemiologic literature. *Indoor Air*. 1993;3:227–236.
- Sieber WK, Petersen MR, Stayner L, et al. The NIOSH indoor environmental evaluation experience: part three—associations between environmental factors and self-reported health outcomes. *Appl Occup Environ Hyg*. 1996;11:1387–1392.
- Brundage JF, Scott RM, Lednar WM, Smith DW, Miller RN. Building-associated risk of febrile acute respiratory diseases in army trainees. *JAMA*. 1988;259:2108–2112.
- Fisk WJ, Rosenfeld AH. Estimates of improved productivity and health from better indoor environments. *Indoor Air*. 1997;7:158–172.
- Burge S, Hedge A, Wilson S, Harris-Bass J, Robertson AS. Sick building syndrome: a study of 4373 office workers. *Ann Occup Hyg*. 1987;31:493–504.
- Skov P, Valbjorn O. Danish Indoor Climate Study Group. The “sick” building syndrome in the office environment: the Danish Town Hall Study. *Environment Int*. 1987;13:339–349.
- Stenberg B, Eriksson N, Höög J, Sundell J, Wall S. The sick building syndrome (SBS) in office workers: a case-referent study of personal, psychosocial and building-related risk indicators. *Int J Epidemiol*. 1994;23:1190–1197.
- Blyussen PM, de Oliveira Fernandes E, Groes L, et al. European Indoor Air Quality Audit Project in 56 office buildings. *Indoor Air*. 1996;6:221–238.
- Gyntelberg F, Suadicani P, Nielsen JW, et al. Dust and the sick building syndrome. *Indoor Air*. 1994;4:223–238.
- Mendell MJ, Fisk JF, Deddens JA, et al. Elevated symptom prevalence associated with ventilation type in office buildings: findings from the California Healthy Building Study. *Epidemiology*. 1996;7:583–589.
- Fisk WJ. Estimates of potential nationwide productivity and health benefits from better indoor environments: an update. In: Spengler J, Samet JM, McCarthy JF, eds. *Indoor Air Quality Handbook*. New York, NY: McGraw-Hill International Book Co; 2000: 4.1–4.36.
- Report to Congress on Indoor Air Quality; Volume II: Assessment and Control of Indoor Air Pollution. Washington, DC: US Environmental Protection Agency, Office of Air and Radiation; 1989. EPA publication 400/1-89/001C.
- Gwaltney JM, Moskalski PB, Hendley JO. Hand-to-hand transmission of rhinovirus colds. *Ann Intern Med*. 1978;88:463–467.
- Gwaltney JM, Hendley JO. Transmission of experimental rhinovirus infection by contaminated surfaces. *Am J Epidemiol*. 1982;116:828–833.
- Dick EC, Jennings LC, Mink KA, Wartgow CD, Inhorn SL. Aerosol transmission of rhinovirus colds. *J Infect Dis*. 1987;156:442–448.
- Jennings LC, Dick EC. Transmission and control of rhinovirus colds. *Eur J Epidemiol*. 1987;3:327–335.
- Couch RB, Cate TR, Douglas RG, Gerone PJ, Knight V. Effect of route of inoculation on experimental respiratory viral disease in volunteers and evidence for airborne transmission. *Bacteriol Rev*. 1966;30:517–529.
- Couch RB. Viruses and indoor air pollution. *Bull N Y Acad Med*. 1981;57:907–921.
- Knight V. Viruses as agents of airborne contamination. *Ann N Y Acad Sci*. 1980;353:147–156.
- Sattar SA, Ijaz MK. *Spread of Viral Infections by Aerosols*. Cleveland, Ohio: CRC Press; 1987:89–131. CRC critical reviews in environmental control, No. 17.
- Nardell EA, Keegan J, Cheney SA, Etkind SC. Theoretical limits of protection achievable by building ventilation. *Am Rev Respir Dis*. 1991;144:302–306.
- Sawyer MH, Chamberlin CJ, Wu YN, Aintablian N, Wallace MR. Detection of varicella-zoster virus DNA in air samples from hospital rooms. *J Infect Dis*. 1994; 169:91–94.
- Husman T. Health effects of indoor-air microorganisms. *Scand J Work Environ Health*. 1996;22:5–13.
- Dales R, Miller D, White J, Dulberg C, Lazarovits AI. Influence of residential fungal contamination on peripheral blood lymphocyte populations in children. *Arch Environ Health*. 1998;53:190–195.
- LaForce FM. Airborne infections and modern building technology. *Environment Int*. 1986;12: 137–146.
- Kreiss K. The epidemiology of building-related complaints and illness. *Occup Med*. 1989;4:1–18.
- Brosseau LM, Vesley D, Kuehn TH, Goyal SM, Chen S, Gabel CL. Identification and control of viral aerosols in indoor environments. *ASHRAE Trans*. 1994;100:368–379.
- Riley RL. Airborne infection. *Am J Med*. 1974;57: 466–475.
- Langmuir AD, Jarrett ET, Hollaender A. Studies of the control of acute respiratory diseases among naval recruits, III. The epidemiological pattern and the effect of ultra-violet radiation during the winter of 1946–1947. *Am J Hyg*. 1948;48:240–251.
- Hoge CW, Reichler MR, Dominguez EA, et al. An epidemic of pneumococcal disease in an overcrowded, inadequately ventilated jail. *N Engl J Med*. 1994;331: 643–648.
- Menzies D, Fanning A, Yuan L, FitzGerald JM, Canadian Collaborative Group in Nosocomial Transmission of TB. Hospital ventilation and risk for tuberculous infection in Canadian health care workers. *Ann Intern Med*. 2000;133:779–789.
- Milton DK, Glencross PM, Walters MD. Risk of sick leave associated with outdoor air supply rate, humidification, and occupant complaints. *Indoor Air*. 2000;10:212–221.
- Jaakkola JJK, Heinonen OP. Shared office space and the risk of the common cold. *Eur J Epidemiol*. 1993;11:213–216.
- New York State Commission on Ventilation. The prevalence of respiratory diseases among children in schoolrooms ventilated by various methods. In: *Ventilation: Report of the New York State Commission on Ventilation*. New York, NY: EP Dutton & Co; 1923: 417–451.
- Drinka PJ, Krause P, Schilling M, Miller BA, Shut P, Gravenstein S. Report of an influenza-A outbreak: nursing home architecture and influenza-A attack rates. *J Am Geriatr Soc*. 1996;44:910–913.
- Husman T, Koskinen O, Hyvarinen A, Reponen T, Ruuskanen J, Nevalainen A. Respiratory symptoms and infections among residents in dwellings with moisture problems or mold growth. In: Jaakkola JJK, Ilmarinen R, Seppänen O, eds. *Proceedings of Indoor Air '93: The 6th International Conference on Indoor Air Quality and Climate; 1993 Jul 4–8; Helsinki, Finland*. Helsinki, Finland: Indoor Air '93; 1993:171–174.
- Warshauer DM, Dick EC, Mandel AD, Flynn TC, Jerde RS. Rhinovirus infections in an isolated Antarctic station. Transmission of the viruses and susceptibility of the population. *Am J Epidemiol*. 1989;129:319–340.
- Richards AL, Hyams KC, Watts DM, Rozmajz PJ, Woody JN, Merrell BR. Respiratory disease among military personnel in Saudi Arabia during Operation Desert Shield. *Am J Public Health*. 1993;83:1326–1329.
- Johnston SL, Pattermore PK, Sanderson G, et al. The relationship between upper respiratory infections and hospital admissions for asthma: a time-trend analysis. *Am J Respir Crit Care Med*. 1996;154:654–660.
- Weiss KB, Gergen PJ, Wagener DK. Breathing better or wheezing worse? The changing epidemiology of asthma morbidity and mortality. *Annu Rev Public Health*. 1993;14:491–513.
- US Centers for Disease Control and Prevention. Forecasted state-specific estimates of self-reported asthma prevalence—United States. *MMWR Morb Mortal Wkly Rep*. 1998;44:1022–1025.

43. Peat JK, Dickerson J, Li J. Effects of damp and mould in the home on respiratory health: a review of the literature. *Allergy*. 1998;53:120–128.
44. Brunekreef B, Dockery DW, Speizer FE, Ware JH, Spengler JD, Ferris BG. Home dampness and respiratory morbidity in children. *Am Rev Respir Dis*. 1989; 140:1363–1367.
45. Committee on the Assessment of Asthma and Indoor Air, Institute of Medicine. *Clearing the Air: Asthma and Indoor Exposures*. Washington, DC: National Academy Press; 2000.
46. Seuri M, Husman K, Kinnunen H, et al. An outbreak of respiratory diseases among workers at a water-damaged building—a case report. *Indoor Air*. 2000;10:138–145.
47. Hoffman RE, Wood RC, Kreiss K. Building-related asthma in Denver office workers. *Am J Public Health*. 1993;83:89–93.
48. Hodgson MJ, Morey PR, Simon JS, Waters TD, Fink JN. An outbreak of recurrent acute and chronic hypersensitivity pneumonitis in office workers. *Am J Epidemiol*. 1987;125:631–638.
49. Milton DK, Solomon G, Morse E, Herrick R. Risk and incidence of asthma attributable to occupation among members of an HMO. *Am J Ind Med*. 1998;33: 1–10.
50. Nelson NA, Kaufman JD, Burt J, Karr C. Health symptoms and the work environment in four nonproblem United States office buildings. *Scand J Work Environ Health*. 1995;21:51–59.
51. Fisk WJ, Mendell MJ, Daisey JM, Faulkner D, Hodgson AT, Macher JM. Phase 1 of the California Healthy Building Study: a summary. *Indoor Air*. 1993; 3:246–254.
52. Brightman HS, Wallace LA, Sieber WK, McCarthy JF, Spengler JD. Comparing symptoms in United States office buildings. In: Raw G, Aizlewood C, Warren P, eds. *Proceedings of Indoor Air '99: The 8th International Conference on Indoor Air Quality and Climate; 1999 Aug 8–13; Edinburgh, Scotland*. London, England: Construction Research Communications Ltd; 1999: 847–852.
53. Wälinder R, Norbäck D, Wieslander G, Smedje G, Erwall C, Venge P. Nasal patency and biomarkers in nasal lavage—the significance of air exchange rate and type of ventilation in schools. *Int Arch Occup Environ Health*. 1998;71:479–486.
54. Wälinder R, Norbäck D, Wieslander G, Smedje G, Erwall C. Nasal mucosal swelling in relation to low air exchange rate in schools. *Indoor Air*. 1997;7:198–205.
55. Seppänen O, Fisk WJ, Mendell MJ. Association of ventilation rates and CO₂ concentrations with health and other human responses in commercial and institutional buildings. *Indoor Air*. 1999;9:226–252.
56. Kemp PC, Dingle P, Neumeister HG. Particulate matter intervention study: a causal factor of building-related symptoms in an older building. *Indoor Air*. 1998;8:153–171.
57. Leinster P, Raw G, Thomson N, Leaman A, Whitehead C. A modular longitudinal approach to the investigation of sick building syndrome. In: Walkinshaw D, ed. *Proceedings of Indoor Air '90: The 5th International Conference on Indoor Air Quality and Climate; 1990 Jul 29–Aug 3; Toronto, Canada*. Ottawa, Ontario, Canada: International Conference on Indoor Air Quality and Climate; 1990:287–292.
58. Wyon D. Sick buildings and the experimental approach. *Environ Technol*. 1992;13:313–322.
59. Skyberg K, Skulberg KR, Kruse K, Huser PO, Levy F, Djupesland P. Dust reduction relieves nasal congestion—a controlled intervention study on the effect of office cleaning using acoustic rhinometry. In: Raw G, Aizlewood C, Warren P, eds. *Proceedings of Indoor Air '99: The 8th International Conference on Indoor Air Quality and Climate; 1999 Aug 8–13; Edinburgh, Scotland*. London, England: Construction Research Communications Ltd; 1999:153–154.
60. Wargocki P, Wyon DP, Baik YK, Clausen G, Fanger PO. Perceived air quality, sick building syndrome (SBS) symptoms, and productivity in an office with two different pollution loads. *Indoor Air*. 1999;9: 165–179.
61. Wyon D, Tham KW, Croxford B, Young A, Oreszczyn T. The effects on health and self-estimated productivity of two experimental interventions which reduced airborne dust levels in office premises. In: Seppänen O, Säteri J, eds. *Healthy Buildings 2000; August 6–10; Espoo, Finland*. Helsinki, Finland: SIY Indoor Air Information; 2000:641–646.
62. Preller L, Zweers T, Brunekreef B, Boleij JSM. Sick leave due to work-related complaints among workers in the Netherlands. In: Walkinshaw D, ed. *Proceedings of Indoor Air '90: The 5th International Conference on Indoor Air Quality and Climate; 1990 Jul 29–Aug 3; Toronto, Canada*. Ottawa, Ontario, Canada: International Conference on Indoor Air Quality and Climate; 1990:227–230.
63. Franck C, Skov P. Evaluation of two different questionnaires used for diagnosing ocular manifestations in the sick building syndrome on the basis of an objective index. *Indoor Air*. 1991;1:5–11.
64. Nunes F, Menzies R, Tamblin RM, Boehm E, Letz R. The effect of varying level of outside air supply on neurobehavioral performance function during a study of sick building syndrome. In: Jaakkola JJK, Ilmarinen R, Seppänen O, eds. *Proceedings of Indoor Air '93: The 6th International Conference on Indoor Air Quality and Climate; 1993 Jul 4–8; Helsinki, Finland*. Helsinki, Finland: Indoor Air '93; 1993:53–58.
65. Wargocki P, Wyon DP, Sundell J, Clausen G, Fanger PO. The effects of outdoor supply rate in an office on perceived air quality, sick building syndrome (SBS) symptoms, and productivity. *Indoor Air*. 2000; 10:222–236.
66. Wargocki P, Wyon DP, Fanger PO. Productivity is affected by the air quality in offices. In: Seppänen O, Säteri J, eds. *Healthy Buildings 2000; August 6–10; Espoo, Finland*. Helsinki, Finland: SIY Indoor Air Information; 2000:635–640.
67. Myhrvold AN, Olsen E, Lauridsen O. Indoor environment in school pupils' health and performance in regard to CO₂ concentrations. In: Yoshizawa S, Kimura K, Ikeda K, Tanabe S, Iwata T, eds. *Proceedings of Indoor Air '96: The 7th International Conference on Indoor Air Quality and Climate; 1996 Jul 26–29; Nagoya, Japan*. Nagoya, Japan: SEEC Ishibashi Inc; 1996: 369–374.
68. Myhrvold AN, Olsen E. Pupils' health and performance due to renovation of schools. In: Woods JE, Grimsrud DT, Boschi N, eds. *Proceedings of Healthy Buildings/IAQ (Indoor Air Quality) '97: Global Issues and Regional Solutions; 1997 Sept 27–Oct 2; Washington DC*. Washington, DC: Healthy Buildings/IAQ (Indoor Air Quality) '97; 1997:81–86.
69. Teeuw KB, Vandenbroucke-Grauls CMJE, Verhoef J. Airborne gram-negative bacteria and endotoxin in sick building syndrome. *Arch Intern Med*. 1994;154: 2339–2345.
70. Rylander R, Persson K, Goto H, Yuasa K, Tanaka S. Airborne β -1,3-glucan may be related to symptoms in sick buildings. *Indoor Environment*. 1992;1: 263–267.
71. Ten Brinke J, Selvin S, Hodgson AT, et al. Development of new volatile organic compound (VOC) exposure metrics and their relationship to “sick building syndrome” symptoms. *Indoor Air*. 1998;8:140–152.
72. Apte MG, Daisey JM. VOCs and sick building syndrome: application of a new statistical approach for SBS research to the US EPA BASE study data. In: Raw G, Aizlewood C, Warren P, eds. *Proceedings of Indoor Air '99: The 8th International Conference on Indoor Air Quality and Climate; 1999 Aug 8–13; Edinburgh, Scotland*. London, England: Construction Research Communications Ltd; 1999:117–122.
73. Cometto-Muñiz JE, Cain WS. Perception of odor and nasal pungency from homologous series of volatile organic compounds. *Indoor Air*. 1994;4:140–145.
74. Weschler CJ, Shields HC. The influence of ventilation on reactions among indoor pollutants: modeling and experimental observations. *Indoor Air*. 2000;10: 92–100.
75. Wolkoff P, Clausen PA, Wilkins CK, Nielsen GD. Formation of strong airway irritants in terpene/ozone mixtures. *Indoor Air*. 2000;10:82–91.
76. Regulatory Alternatives Development Corp. *Promising Approaches for Improving IAQ*. Washington, DC: US Environmental Protection Agency; 1993.
77. *Proposed American National Standard: Ventilation for Acceptable Indoor Air Quality*. Atlanta, Ga: American Society of Heating, Refrigeration and Air-Conditioning Engineers; 1996.
78. Cutter Information Corp. Science center proposes hosting “reborn” IAQ alliance. *Indoor Air Quality Update*. 1996;9(1):2–3.
79. Chen A, Vine EL. A scoping study on the costs of indoor air quality illnesses: an insurance loss reduction perspective. *Environ Sci Policy*. 2000;2:457–464.
80. *Building Air Quality—A Guide for Building Owners and Facility Managers*. Washington, DC: US Environmental Protection Agency; 1991. EPA publication 400/1-91/033.
81. *Building Air Quality Action Plan*. Washington, DC: US Environmental Protection Agency; 1998. EPA publication 402-K-98-001.
82. *Indoor Pollution: Status of Federal Research Activities*. Washington, DC: US General Accounting Office; 1999:70–80. GAO publication RCED-99-254.
83. *The Costs and Benefits of Smoking Restrictions—An Assessment of the Smoke-Free Environment Act of 1993 (H.R. 3434)*. Washington, DC: US Environmental Protection Agency, Office of Radiation and Indoor Air; 1994.