for all 3,000 zones used to model the trade center complex.

"CONTAMW's capabilities are continually being applied in new ways by creative engineers, so it is hard to say what the limits of its applications are," Dols tells ***IEQS*** enthusiastically. "We're hoping that after we set up our new Web site, engineers will submit case studies of what they've been able to accomplish with it." As more and more examples appear on the NIST Web site, they in turn should stimulate an even wider expression of CONTAMW capabilities among the user community. Dols says NIST hasn't yet determined an address for the new Web site, but once it is active, it will be linked to the current CONTAMW site.

For more information, contact W. Stuart Dols, mechanical engineer, Indoor Air Quality & Ventilation Group, Building and Fire Research Library, National Institute of Standards and Technology, 100 Bureau Drive, Stop 8633, Building 226, Room A313, Gaithersburg, MD 20899-8633. Tel: (301) 975-5860; Fax: (301) 975-4409; E-mail: wsdols@nist.gov.

PRACTICAL RESEARCH BRIEFS

A Review: Studies on the Association of Ventilation Rates and CO_2 Levels with Health and Other Human Outcomes

Ventilation rates under 10 liters per second (l/s) per person are consistently associated with statistically significant worsening of one or more adverse health or perceived air quality outcomes in nonresidential and nonindustrial buildings. That is what researchers from three highly regarded institutions concluded after they reviewed the findings of 20 studies of ventilation rates and 21 studies of carbon dioxide (CO_2) levels performed between 1986 and 1999. The ventilation studies estimated relative risks of 1.5-2 for respiratory illnesses and 1.1-6 for "sick building syndrome" (SBS) symptoms at low ventilation rates compared to high ventilation rates. A relative risk of 1.0 designates no increased risk while 2.0 would specify twice the risk. Overall, the 41 studies included some 60,000 occupants of more than 750 offices, schools, nursing homes, daycare centers, and other nonresidential buildings in Europe, Scandinavia, Japan, and the US. Since only 5 of these studies took place in hot, humid climates, the review results primarily apply to temperate and cool climates.

Some ventilation studies in the review found further significant decreases in SBS symptoms or significant improvements in perceived air quality as ventilation rates increased from 10 l/s to 20 l/s per person. About half of the CO_2 studies indicated that the risk of SBS symptoms continued to diminish as CO_2 levels declined below 800 parts per million (ppm).

Olli Seppänen (professor at Helsinki University of Technology, Laboratory for Heating, Ventilating and Air Conditioning in Espoo, Finland) teamed with William Fisk (staff scientist, Lawrence Berkeley National Laboratory, Indoor Environment Department, Environmental Energy Technologies Division, Berkeley, California) and Mark Mendell (epidemiologist at the Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, Cincinnati, Ohio) to perform the review. They reported their results in "Association of Ventilation Rates and CO_2 Concentrations with Health and Other Responses in Commercial and Institutional Buildings" in December 1999.

Objectives of Review

When they began their review, the researchers wished to answer several questions about the association of ventilation rates with human health and other human responses in commercial and institutional buildings, such as:

1. Does the magnitude of ventilation rate (or CO_2 concentration) within the normally encountered range affect human health and other human responses?
2. Can a no-effect threshold value for ventilation rate (or CO_2 concentration) be found above or below which the prevalence of negative outcomes does not change measurably?

3. Can an average dose-response relationship between ventilation rates (or CO_2 concentrations) and human responses be inferred from existing research data?

The reviewers note that ventilation supplies outdoor air and dilutes or removes pollutants generated indoors. Therefore, the rate of ventilation alters indoor environmental quality, including the level of air pollutants, which may affect occupants' health or their perception of indoor air quality (IAQ). In the real world, however, a number of other factors are at play, including the distribution of ventilation, operating schedule of the ventilation system, the quality of air filtration, location of indoor and outdoor pollution sources, and the amount of outdoor air that infiltrates through the building envelope.

Scientists believe that CO_2 doesn't directly impact health at the concentrations of 350-2,500 ppm normally encountered indoors. CO_2 levels are often considered a surrogate for the rate of ventilation per occupant. In reality, the CO_2 level varies even when ventilation and occupancy rates are constant, so CO_2 concentration often is a poor indicator of ventilation rates.

Overview of Studies Used

Seppänen, Mendell, and Fisk used rigorous selection criteria to choose the studies in their review. Many potential confounding factors may bias study findings (see Table 1). After considering this, the reviewers agreed it was best to document gender and other personal confounders as critical. Therefore, cross-sectional studies needed at least three spaces, statistical analyses, and control for confounding by personal factors. Experimental studies generally needed statistical analyses and features to minimize suggestion effects.

The 20 studies of ventilation rates and human outcomes included nearly 30,000 people in more than 350 buildings in 15 cross-sectional and 5 experimental studies. Most involved office workers of both genders, while a few dealt with nursing home residents, school students, Army trainees, hospital workers, or jail inmates. Most of the American studies involved buildings with sealed windows, while most of the European studies took place at buildings with windows that opened. Those windows weren't necessarily opened, however, since most of the studies occurred during winter.

The 21 studies of CO_2 levels and human outcomes in the review involved more than 30,000 people in more than 400 buildings. As was true for the ventilation studies, most of the CO_2 studies were conducted during winter.

Overall Ventilation Study Findings

The reviewers found that, in many studies, lower ventilation rates significantly correlated with greater health effects and a worsening of perceived IAQ, more consistently at the lower range of ventilation. "Of the 19 studies meeting our selection criteria which [also] included ventilation rates less than 10 l/s per person, lower ventilation rates in 18 of these studies were significantly associated with a worsening of at least one [adverse] health outcome" or the perception of significantly poorer quality indoor air. We were not able to identify a no-effect threshold value of ventilation rate above which further increases had little or no effect on outcomes.

"Of 27 assessments with SBS symptoms as outcomes, 20 found a significantly higher prevalence of one or more symptoms with lower ventilation rates.... The findings of significantly increased outcome were particularly consistent when the lower ventilation rate was below 10 l/s per person. There was no clear ventilation-rate threshold above which no further reduction in SBS symptoms occurs," the reviewers continue. "Several studies ... suggested that the risk of sick building symptoms continues to decrease with increasing ventilation rates above 10 l/s per person possibly up to 25 l/s per person.... However, 4 assessments did not find increases in ventilation rates above 10 l/s per person to be associated with a significant change in symptoms. Three studies found a significant *increase* in the prevalence of symptoms with increases in ventilation rate." The reviewers explain that, because these studies were performed in Nordic countries in winter when very low indoor humidities occur with high ventilation rates, these findings, "may possibly be a consequence of low relative humidity caused by increased ventilation rates."

"All studies of respiratory illness found a significant increase in the risk of illness in the group with a lower ventilation rate. The relative risk for respiratory illness varied between 1.51 and 4.7." Regarding IAQ, the occupants and panels in 7 of 8

Table 1 — Examples of Potential Confounding Factors in Studies of Ventilation Rates and Sick Building Syndrome Symptoms

Personal Characteristics	Work-Related Factors	Building-Related Factors	Indoor Environmental Factors
Gender Atopy (allergic disposition) Asthma history Smoking history Type of job Medical treatment (especially for asthma and atopy)	Job stress or satisfaction Use of carbon-free copy paper Use of or proximity to photocopy machines Use of video display terminals	Type of ventilation system Type of humidification Quantity of carpet or textile surfaces Sealed windows Building age	Air temperature Air humidity Environmental tobacco smoke Dusty surfaces

studies perceived air quality as worse when ventilation rates were lower. In 6 studies that involved perceived inferior air quality, as many as half of the occupants considered the IAQ unacceptable.

Overall CO_2 Study Findings

In the studies of CO_2 concentration, 9 of 18 assessments having SBS symptoms as outcomes involved a significant increase in symptoms when CO_2 levels were higher. The levels of CO_2 varied considerably from study to study. As higher CO_2 levels were included in studies, the percentage of studies with a significant association between CO_2 levels and SBS symptoms also increased. The researchers also noted that, as with ventilation rates, there was no clear CO_2 threshold below which continuing drops in CO_2 levels were not associated with continuing declines in symptoms of SBS.

"Several studies — 7 of 16 — suggested that the risk of sick building symptoms continued to decrease with decreasing CO_2 concentrations below 800 ppm, corresponding to steady state ventilation rates of 11.6 l/s per person," the reviewers observe. "None of the assessments found an increase of symptoms with decreasing CO_2 concentration." Of the 12 studies with perceived IAQ as an outcome, 6 reported an association with CO_2 level. These suggested that as CO_2 levels diminished to 500-600 ppm, which corresponds to 34.7-20.8 l/s per person, perceptions of air quality improved.

The reviewers report that the studies associating CO_2 levels with health and perceived IAQ outcomes generally support the findings of a link between ventilation rates and these outcomes. A "larger proportion of the CO_2 studies [than of] ventilation studies, however, failed to find a significant relationship between CO_2 and … outcomes." Seppänen, Fisk, and Mendell suspect, however, that variation among the studies in the CO_2 metrics and timing of CO_2 measurements may explain this. "More consistent results would be expected," they conclude, "if all studies used either the peak or time-average indoor CO_2 concentration. The spatial variability in indoor CO_2 concentrations and the variability in the outdoor concentration have also not been addressed in many of the studies." Finally, CO_2 values measured in the studies were subject to measurement errors, failure to account for variability in outdoor CO_2 levels, and other oversights.

Discussion of Findings

The reviewers assessed the possibility of chance, rather than genuine, associations between ventilation rates and SBS symptoms. "For several reasons," they say, "these findings appear not to be mere chance associations. First, when no actual relationship exists, chance negative associations are as probable as chance positive associations. However, there are only 4 reported significant negative associations (i.e., worse outcomes at higher ventilation rates) compared to 20 positive associations. Second, in every study with a reported significant association, the number of significant associations for different outcomes relative to the number of statistical tests performed exceeds the 1-in-20 expected by chance.... Third ... there are several reported dose-response relationships, which are less likely to be caused by chance."

The reviewers point out that various other potential biases are improbable. Bias from the selection of buildings is unlikely since the investigators would not know the ventilation rates until they measured them. Building occupants rarely know ventilation rates, which would prevent that factor from biasing their responses. Finally, airflow tools do not measure building infiltration, and "actual ventilation rates are in most cases higher than reported...." This suggests that "ventilation rates even higher than those found in this review are associated with improved occupant outcomes."

The reviewers also address the increase in energy cost of the increased ventilation associated with improved health among building occupants. "The study data in this review indicates substantial variation in ventilation rates both within and among buildings," they note. "The large range of ventilation rates within buildings suggests an opportunity to improve health and perceived air quality through better balancing and control of airflows within buildings.... Due to the dose-response relationships evident from this review, the average level of SBS symptoms and perceived air quality should be improved without increasing the total ventilation rate of the building or the associated energy use. There is an analogous opportunity to alleviate symptoms and improve perceived air quality in the overall building stock without increasing energy consumption by increasing ventilation rates in buildings with low ventilation rates and decreasing [them] in buildings with high ventilation rates. It seems quite possible that better ventilation control and balancing could simultaneously improve health and perceived air quality while saving energy."

Conclusions

The complex relationship between ventilation rates and IAQ, entangled with multiple other variables, requires caution in reaching conclusions about associations between ventilation rates, health outcomes, and perceived air quality. Many studies in this review did not control for confounding factors that could alter research results. Others did not fully describe the buildings studied or the study methods used. Despite these shortcomings, the reviewers observe that nearly all of the aforementioned studies show that buildings with ventilation rates of less than 10 l/s per person had at least one health outcome with a significantly worsened prevalence. These studies also found a significantly increased perception of significantly poorer quality of indoor air. The available studies also show that increasing ventilation rates beyond 10 l/s per person up to about 20 l/s per person are sometimes linked with a significant decline in occurrence of SBS symptoms or with improvements in perceived IAQ. The data from several studies also indicates a dose-response relationship between ventilation rates up to some 25 l/s per person and health outcomes and IAQ perceptions, though the data provided is insufficient to determine an average dose-response relationship, the reviewers report. The reviewers sum up by saying:

> Based on these results, we conclude that in office buildings or similar spaces constructed using current building practices, increases in ventilation rate in the range between 0 and 10 l/s per person will, on average, significantly reduce occupants symptoms and improve perceived air quality. Increases in ventilation rate above 10 l/s per person up to 20 l/s per person may further reduce symptoms and improve air quality, although these benefits are currently less certain based on available data.... As ventilation rates increase, benefits gained for occupants ... are likely to decrease in magnitude and require larger studies for convincing demonstration. Benefits which have yet to be consistently demonstrated in this way ... may still be of substantial public health importance.

Seppänen, Mendell, and Fisk observe that 10 of the 15 cross-sectional ventilation surveys include buildings with ventilation rates of less than 2.5 l/s per person. These low rates usually do not violate building codes and standards, which tend to specify the minimum ventilation rates a system should be designed for but not the minimum rates the system actually delivers. "New or revised building codes and standards may need to specify minimum ventilation rates *during building occupancy* to maintain acceptable levels of occupant health and satisfaction," they suggest.

The reviewers also find it essential that future researchers conduct well-designed cross-sectional studies or well-designed, blinded, and controlled experiments to better assess the impacts that ventilation rates between 10 l/s and 25 l/s per person have on occupants' health and air quality perceptions. "In addition ... we also need studies to specify the causative agents of adverse health outcomes. The most effective strategies to improve indoor air quality (e.g., source removal) cannot be specified before the agents and their sources are known."

Finally, since increasing ventilation may also use more energy, the reviewers suggest that it is important to identify practical ways to decrease ventilation requirements by reducing pollution emissions from building materials and systems. Alternatively, research teams could determine how ventilation could more effectively control pollutant exposures without boosting energy use.

For more information, contact William J. Fisk, Lawrence Berkeley National Laboratory, 1 Cyclotron Road, MS 90-3058, Berkeley, CA 94720. Tel: (510) 486-6591; Fax: (510) 486-6658; E-mail: WJFisk@lbl.gov.

CASE STUDY

*[In each issue, **IEQS** presents a case study on an indoor air investigation in a particular building. The information in the cases comes from various sources, including published material, reports in the public record, and, in some cases, reports supplied by the consultants involved in the case. **IEQS** presents a variety of approaches to investigation and mitigation implemented by consultants with a broad range of experience, philosophies, and expertise. Inclusion of a particular case study in the newsletter does not imply **IEQS**'s endorsement of the investigative procedures, analysis, or mitigation techniques employed in the case. **IEQS** invites readers to submit comments, suggestions, and questions concerning the case. At the discretion of the editors, correspondence may be presented in a future issue.]*

Diagnosing the Cause of a "Sick Building": An Epidemiological and Microbiological Investigation

Occupants of a large, modern office building had suffered prolonged illnesses, with no apparent explanation, since shortly after moving into the building. Their symptoms included irritated eyes; runny nose and sinus congestion; sore throat, cough, and shortness of breath; rashes; extreme fatigue; and difficulty with concentration and impaired short-term memory. Investigations by industrial hygienists and building maintenance staff detected no chemical contamination or functional ventilation problems. Typical air quality tests eliminated carbon monoxide (CO) and volatile organic compounds as possible causes. Baffled managers and industrial hygienists declared it a "sick building."

Sick building syndrome (SBS) occurs when a significant percentage of a building's occupants develop unexplained symptoms that involve several organ systems including the skin and respiratory and nervous systems. Traditionally, environmental investigators have sought causative factors, which include inadequate ventilation, organic vapors, asphyxiant gases (e.g., CO), and psychogenic dynamics — almost always without success. Published investigations of buildings have increasingly revealed mold contamination as the source of illnesses that produce the same clinical picture as SBS.

Building Description

This case involves a five-story state-government office building constructed in Nevada from 1992-1994. The sealed structure gets ventilation from eight roof-mounted air-handling units (AHUs). These AHUs contain the heating, ventilating, and air conditioning (HVAC) units and evaporative cooling components. They provide ventilation through some 250 variable air volume (VAV) boxes distributed throughout the building. Each VAV box contains a secondary heating coil unit with hot water supplied by a separate, treated water system. Return air passes through ceiling-mounted grills into a common plenum in each zone. Exhaust units expel the return air through rooftop vents that are more than 50 feet from the air intake units. Indoor humidity typically ranged from 40%-50% and temperatures ranged from 70°F-74°F. Outdoor humidity tended to be between 10% and 25%. Building managers used the evaporative cooling system with return air mixed with outdoor air in a 20:80 ratio during the summer when outdoor temperatures commonly exceeded 85°F. After occupant complaints