EPIDEMIOLOGICAL INVESTIGATION OF A MOLD-CONTAMINATED "SICK" BUILDING

James Craner[1,a,2,3], Stuart Alderman[3] and Neil Willits[3,4]

[1]Private Practice, Occupational & Environmental Medicine, Reno, NV, U.S.A.
[2]Department of Medicine, University of Nevada School of Medicine, Las Vegas, NV, U.S.A.
[3]Verdi Technology Associates, Verdi, NV, U.S.A.
[4]Department of Statistics, University of California, Davis, CA, U.S.A.
[a]Contact author email: JC@EpIAQ.com

ABSTRACT

An innovative, software-based occupant health survey instrument and multivariate statistical analysis based on a retrospective cohort methodology was used to investigate occupant illness in a water-damaged, "sick" office building. Based on a case definition conservatively derived through principal components analysis, a highly statistically significant incidence and attributable risk of respiratory, neurocognitive, and constitutional symptoms was measured among occupants in comparison with those in a control building. Logistic regression analysis demonstrated that the collective symptoms were not explained by such building-related illnesses as asthma or hypersensitivity pneumonitis, nor by pre-existing medical conditions, smoking, or residential environmental factors. Cases were uniformly distributed among occupants throughout the building. The epidemiological findings were consistent with the known health effects of indoor mold exposure, and were not explained by either an allergic or infectious mechanism of disease.

INDEX TERMS: Sick building syndrome, Epidemiology, Building related symptoms, Indoor air quality, Mold

INTRODUCTION

In the past 10 years, exposure to certain types of mold in water-damaged buildings has been increasingly implicated as the cause of sick building syndrome (SBS). Epidemiological investigation of occupants within a given building or workplace population is a well-established scientific method used to identify and measure the nature, distribution, and cause of occupational or environmental illness. In its publication, *Bioaerosols: Assessment and Control*, the American Conference of

Governmental Industrial Hygienists underscored the importance of epidemiological investigation of occupant/indoor air quality (IAQ)-related health problems as a means to "clarify whether there is a building-related problem and, if so, its nature as well as possible means for resolution," and emphasized the need for improved study design and statistical analysis for conducting an inherently complex investigation (ACGIH, 1999). However, most published, paper-based occupant health questionnaires and analysis methods have suffered from significant methodological limitations in their ability to define and measure occupant symptomatology as a multi-organ syndrome, and control for confounding variables (AIHA, 1996). The study herein employed a new epidemiological instrument and approach to analysis of complex occupant symptoms in a water-damaged "sick building" that had predominantly hidden mold contamination.

METHODS

Study and control buildings: The study building, located in northern Nevada, was a leased, 1-story, *ca.* 10,000 square foot office facility with central heating and air conditioning that housed a government agency since the late 1970's. Ongoing, unexplained employee health complaints among the 110 full-time government employees and an associated increase in employee absences and medical treatment occurred over a period of years. Traditional IAQ measures (CO_2, CO, temperature, relative humidity) were normal, and the ventilation system was found to be operating within acceptable parameters. The building was ultimately deemed to be a "sick building." An IAQ investigation in 2001 revealed a longstanding history of un-repaired roof leaks resulting in stained suspended ceiling tiles and dripping water from the ceiling onto desks and floor space throughout the building. It was learned that in 1998, two interior walls in separate corners of the building had been discovered to be saturated with water. Occupants had observed musty odors in these areas since then. The landlord had responded by painting over these walls. In 2001, numerous bulk culture and tape samples of water-damaged gypsum board surfaces and on HVAC return filters demonstrated *Stachybotrys chartarum*, *Aspergillus versicolor*, *A. niger*, and/or *Penicillium* hyphae and spores. Non-viable (Air-O-Cell) air samples were dominated by *Aspergillus/Penicillium* spores.

The control building was a one-story, approximately 20,000 square foot, centrally heated and cooled, county government facility located in southern Nevada, constructed in 1995. There were 98 full-time occupants. The building had a history of a few minor plumbing leaks which had been promptly repaired, but otherwise did not have a history of occupant health complaints, investigations, or IAQ problems including visible mold contamination. A formal visual inspection and environmental sampling of the entire building identified some old water-stained ceiling tiles in various areas of the building, but no associated surface mold growth or odors.

Extensive air (viable and non-viable) and settled dust carpet samples demonstrated no atypical mold contaminant taxa.

Survey participants (respondents) in the study building were full-time occupants who were recruited by the employer at the beginning of the environmental and occupant health investigation. Control building respondents were recruited as part of an unrelated epidemiological study in 2001. All respondents provided written informed consent to participate in the survey.

Survey instrument and methodology: The epidemiological study was of a retrospective cohort design, with a non-problem building serving as the control. Occupant health data was collected using the EpIAQ® software (Verdi Technology Associates, LLC, Verdi, NV, U.S.A.), a proprietary, entirely computer-based occupant health survey instrument that was developed based upon existing, widely-accepted and utilized methods of epidemiological investigation of building-related illness/symptoms (NIOSH, 1996; Quinlan, 1989). All questions beyond demographics were closed-ended, with either yes/no or multiple choice responses. The design, content, and interaction features of this PC-based survey instrument obviated many of the methodological limitations of currently available and/or previously published, paper-based SBS/BRI/IAQ surveys. Specifically, major sources of recall, response, interviewer, and misclassification bias were eliminated or minimized by ensuring data collection reliability and enforcing completion of all survey questions with unequivocal responses; providing multi-level question complexity using conditional logic to query about symptom frequency and effect when away from the building; individualizing each respondent's symptom questions by temporal and geographic parameters related to the building's construction, occupancy, and layout; addressing potentially confounding pre-existing medical conditions, habits, and non-occupational environmental factors; measuring internal validation of response consistency and reliability; and providing program security features to ensure medical confidentiality, privacy and data integrity. Internal validation measures for consistency and plausibility of responses were incorporated into the survey design.

The SAS statistical analysis software (v. 8.1, SAS Institute, Cary, NC, U.S.A.) was used for data analysis. All tests were conducted at a significance (α) level of 0.05 (two-tailed), and reported as either *p* values or odds ratios. Demographic parameters were compared using t-tests for continuous variables, and Mann-Whitney or chi-square (χ^2) tests for non-continuous variables. Principal components analysis (PCA, also known as factor analysis), a multivariate statistical methodology that analyzes the interrelationship of variables in complex data (Johnson, 1982), was employed to measure the inter-relationship between 61 primary symptom questions and, for each affirmative response, 5 follow-up sub-questions related to symptom frequency and building-relatedness among all responses from both buildings. Multivariate analysis of variance (MANOVA) on the first six principal components was then performed with respect to building, and reported as an F-statistic (Wilks Λ). If this overall building difference was statistically significant, a univariate ANOVA on each principal component was conducted. The first principal component (largest eigenvalue and a statistically significant ANOVA) was selected to conservatively define a case of "building-related illness" ("BRI") based on the 95th percentile of control building symptom factor scores. The incidence of "BRI" in the study building relative to the pre-defined, conservatively assumed incidence (5%) in the control building was calculated as an attributable risk and attributable risk percentage, i.e., the proportion of illness among study ("exposed") building respondents that is attributable to the building.

The symptoms most and least associated with the PCA-derived case definition of "BRI" were ranked according to their principal-component-derived eigenvector coefficients (i.e., factor loadings). The "BRI" case definition was compared to clinical case definitions of traditionally accepted building-related illnesses including asthma, hypersensitivity pneumonitis, and somatization disorder (as a surrogate for "mass hysteria") to determine whether the collective symptomatology was clinically consistent with one or more of these disorders. The effect(s) of potentially confounding variables, namely pre-existing medical conditions, current and past smoking, and residential environmental factors, was analyzed using logistic regression analysis. Temporal and geographic variables and their effect on risk for and distribution of "BRI" was analyzed by logistic regression according to office/work area location; relative time spent in the office, building, or outside the building; and duration of occupancy. Finally, several forms of internal validation for symptom number outliers and response consistency were compared between buildings using χ^2 tests.

RESULTS

52% of the study building occupants completed the EpIAQ® survey. Four (4) incomplete surveys were eliminated from the analysis, and no duplicate surveys were identified. Participation in the control building was 69%, with no incomplete or duplicate surveys identified. Demographic comparison of the two building populations showed no statistically significant differences with regard to distribution of gender, age, smoking (current and past), residential factors, and workplace indoor exposure measures. The frequency of various pre-existing conditions, including asthma, allergic rhinitis/hay fever, depression, and chronic sinusitis was also similar, except for a slightly greater prevalence of obesity in the control building (p = 0.05). The prevalence of common (and uncommon) pre-existing medical conditions in both populations was comparable and consistent with national prevalence figures.

MANOVA on all six of the principal components with respect to building demonstrated a highly significant difference (Wilks $\Lambda = 11.00$, $p < 0.0001$) in occupant symptomatology between the two buildings. The first principal component explained a substantial part of the variability in symptoms among subjects, with a highly significant building difference ($F = 34.35$, $p < 0.0001$), and was selected as the basis for the case definition of "BRI." The difference in the mean number of symptoms among respondents in the study (22) vs. control (8) buildings was also highly significant ($t = 7.26$, $p < 0.0001$). 49% of the respondents of the study building met the case definition of "BRI" versus the pre-defined 6% (rounded off) in the control building, the difference of which was highly statistically significant ($\chi^2 = 24.82$, $p < 0.0001$). The attributable risk between study and control buildings was 43%, and the attributable risk percentage was 88%. Neurocognitive (forgetfulness, short-term memory loss) and respiratory symptoms (shortness of breath, shortness of breath with exertion) contributed most significantly to the case definition of "BRI," i.e., symptoms with the highest eigenvector coefficients. Other symptoms also highly associated with "BRI" included difficulty concentrating, mood irritability, unexplained sadness, loss of interest in sex, and unusual fatigue. "Dummy" symptoms unrelated to IAQ comprised most of the least associated symptoms. None (0%) of the "BRI" cases in the study building was comprised of a combination of symptoms consistent with or explained by asthma, hypersensitivity pneumonitis, upper respiratory tract infections, or somatization.

Logistic regression analyses on numerous pre-existing immunocompromising diseases demonstrated no predictive relationship to or increased the risk for "BRI," except for "intravenous antibiotic treatment" ($p = 0.02$) and treatment with oral corticosteroids (Prednisone, Medrol, $p = 0.09$). Among the plausibly building-aggravated upper or lower respiratory tract allergic or infectious diseases (asthma, hay fever/seasonal allergies, or chronic sinusitis), none (0%) had a statistically significant association with "BRI." For pre-existing psychiatric conditions, depression ($p = 0.03$) and panic attacks ($p = 0.02$) were significantly associated with risk for "BRI." Current ($p = 0.36$) and past ($p = 0.64$) cigarette smoking also had no statistical association with risk of "BRI." Residential exposure factors including second-hand smoke, pets, and water damage in the home, did not explain or increase risk for "BRI." Respondents in the study building were significantly more likely to seek medical attention for building-related symptoms than those in the control building ($p = 0.0009$), and within the study building itself, respondents with "BRI" had an increased likelihood ($p = 0.0003$) of seeking medical attention versus those who did not have "BRI." The frequency of self-reported or misdiagnosed conditions of "continuous or unusually severe allergies" ($p = 0.0003$) and "frequent head colds and/or respiratory infections" ($p < 0.0001$) was significantly greater among occupants with "BRI," though the prevalence of these specific disorders as pre-existing conditions was similar between buildings. The geographic distribution of "BRI" within the study building was uniform ($p = 0.99$). Logistic regression analysis on relative time spent in the office/work area ($p = 0.86$), total time spent inside the study building ($p = 0.96$), and duration of occupancy ($p = 0.92$) demonstrated no statistical association with risk for "BRI."

Internal validation measures demonstrated that all of the "high symptom number" (95^{th} percentile) respondents were from the study building ($\chi^2 = 5.49$, $p = 0.0192$), whereas 91% of the asymptomatic, or "low symptom number" (5^{th} percentile) respondents were from the control building ($\chi^2 = 9.75$, $p = 0.0018$). The frequency of inconsistent responses to validation questions and redundant questions was comparable between buildings ($\chi^2 = 0.051$, $p = 0.82$).

DISCUSSION

Occupants of the study building experienced a significant incidence (attributable risk and attributable risk percentage) of building-related, upper and/or lower respiratory tract and neurocognitive symptoms. A consistent, single disease entity among symptomatic occupants was demonstrated by the collective findings of a relatively high incidence of symptoms attributable to the study building, the prominent neurocognitive/non-respiratory symptoms statistically associated with the case definition through multivariate analysis, a uniform distribution of symptomatic respondents throughout the building, a lack of cumulative or temporally-related effects of building occupancy, and a strong association of symptoms with self/mis-diagnoses of "allergies," "frequent upper respiratory tract infections," and treatments with antibiotics and corticosteroids. The approach of analyzing symptoms collectively and using PCA to develop a case definition of a symptom complex (syndrome) in comparison with a control building enabled this epidemiological method to distinguish that the building-related health effects were not plausibly explained by, or simply a variant of an allergic or otherwise immunologically-mediated, building-related illnesses such as asthma, hypersensitivity pneumonitis, or allergic rhinitis–diseases which a number of researchers and reviewers have concluded or attempted to show by relying upon methods that have analyzed symptoms in isolated manner using crude summary statistics and arbitrarily created, symptom category-based definitions solely among study building occupants (Kolstad, 2002, ACOEM, 2002; Hodgson, 1998). Occupants with a variety of pre-existing immunological and respiratory disorders, as well as past and present cigarette smokers, were also not at increased risk of symptomatology consistent with respiratory tract or other infectious disease, though symptoms were self/misdiagnosed as such–a finding which also contradicts a commonly espoused but scientifically unsupported risk dictum for mold-contaminated buildings (NYCDOH, 1999). Occupant illness was not explained by other carefully sought, potentially confounding medical or environmental variables, "mass hysteria," disease misclassification, collection bias, or chance. The major limitation of the study was the study building participation rate which, while consistent with other published SBS studies (Kolstad, 2002), was not sufficient to generalize the findings to the entire building population with statistical confidence.

CONCLUSIONS AND IMPLICATIONS

The epidemiological findings in this mold-contaminated, "sick" building are consistent with the health effects that have been described for certain taxa of toxigenic fungi that grow on certain water-damaged building materials and disseminate as spores into the occupied spaces of buildings (IICRC, 2003). In contrast to the commonly propounded theory that "non-specific" building-related symptoms do not represent a single medical disorder (Menzies, 1997), the principal symptoms measured in this "sick" building, as well as their distribution and building-relatedness, were collectively consistent with "building-related symptoms" (ACGIH, 1999), "building-related illness arising from microbial contamination of building materials caused by condensation and leaks" (AIHA, 1996), "non-infectious fungal indoor exposure syndrome" (NIFIES; Craner, 1999), and "fungal syndrome" (Johanning, 1999), each of which is clinically indistinguishable from SBS. The uniform distribution of cases throughout the building also contradicts the presumption that exposure to mold spores (and spore by-products) is confined only to localized areas where visible mold is found (NYCDOH, 1999), and underscores the importance of identifying "hidden" mold contamination (AIHA, 1996). Although the specific biochemical mechanism(s) and dose-response relationship by which these molds cause their effects remains speculative, these epidemiological findings point strongly toward a unifying toxicological mechanism (IICRC 2003). While occupant symptomatology has been the principal health endpoint which all epidemiological methodologies in the SBS/BRI/IAQ research field have focused upon, this new, more robust epidemiological instrument and approach described herein represents an advancement in scientific understanding of a complex occupational and environmental disease syndrome and its relationship to particular indoor environmental conditions and contaminants. Further epidemiological research using this approach will provide direction and support for clinical research into pathophysiological responses, toxicological mechanisms, and routes of exposure in occupants of "sick" buildings.

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