PART I:

HEALTH EFFECTS – EPIDEMIOLOGICAL RESEARCH ABSTRACTS

NIOSH Field Studies on Dampness and Mold and Related Health Effects

Jean M. Cox-Ganser

Over the past decade studies by our indoor environmental quality research team at NIOSH (Morgantown) have indicated increase in asthma onset from working in damp buildings. In addition, we found consistent associations between markers of exposure to dampness and mold and upper and lower respiratory symptoms that improve when away from the building (building related), as well as with asthma onset after damp building occupancy. We have documented poorer quality of life and increased sick leave use in occupants with building related respiratory illness, and found evidence for a nonallergic mechanism of building related asthma associa ted with water damage. Our work in a large office building indicated that despite large remediation and repair efforts, there was no overall improvement in respirato ry health indices over a three year interval for employees for whom we had paired pulmonary function and questionnaire data. Employees classified as respiratory cases who were relocated within the building had decreases in medication use and sick leave.

A scoring system based on a standardized observational assessment of damp ness and mold, as well as measures of hydrophilic fungi and ergosterol (a compo nent of fungal cell walls) from floor dust have proven useful as indicators of adver se health effects. Endotoxin (a component of gram negative bacteria cell walls) exposure may change the effect of fungal exposure on respiratory health or vice versa.

We have found associations between the observational score and environmental measurements such as total culturable fungi, total culturable bacteria, β D glucan (a

component of fungal cell walls), ergosterol, and the moisture content of walls and flooring. We are presently developing software for a practical assessment tool for dampness and mold and are working with a number of school districts to imple ment this as a way to help prioritize expenditures and respond promptly to water incursions and damage.

Visual contrast sensitivity testing has been used in studies of exposure to neuro toxins in situations other than damp indoor environments. Currently, its usefulness in investigations of mold exposed populations in indoor environments is not well understood. A recent health hazard evaluation report by NIOSH investigators from Cincinnati described lower visual contrast sensitivity in staff at a severely water damaged school in comparison to staff from a school without significant water damage. The investigators described limitations relating to the suitability of the comparison school. We are currently undertaking a similar investigation where a suitable comparison school is available.

How to find, how to manage? Developing guidelines for mold problems through research.

Aino Nevalainen, Martin Täubel, Helena Rintala and Anne Hyvärinen

The indoor air quality and health problems associated with building dampness and mold were originally brought up by practical experiences of people and less by means of learning through science. This paper summarizes the process how damp ness, moisture and mold problems have been managed as a public health issue in Finland, and gives an overview of the present research in the field.

The phenomenon was originally documented with extensive epidemiological population studies e.g. in Canada and USA (Dales et al., 1991; Brunekreef et al., 1989) and the findings were also verified in Finland (Pirhonen et al., 1996). The results of those studies clearly showed an association between building moisture problems and adverse effects on human health, although the causal relationship between exposing agents and symptoms were far from clear. This hazard identifica tion can be considered the first step of a risk assessment process, which is still going on. After this association between observations of damp, moisture and mold in indoor premises and ill health of the occupants was repeatedly shown in a number of studies in different countries, climates and conditions around the world, more systematic documentation on different aspects of the problem and its causal links was gradually increasing in the scientific literature. Today, the documentation of the phenomenon has been thoroughly evaluated by several expert committees (e.g.,

IOM 2004; WHO 2009) but we are still underway to reveal the characteristics of microbial exposures that are harmful to health and that should be controlled in buildings.

Guideline development is problematic for building mold. For one thing, the control of the indoor air quality is practically in the hands of the owner of each individual building, and cannot be approached in a similar, region or society scale approach than, say, outdoor air quality. Furthermore, since the causal links between exposure and health effects are not known, no health based threshold limit values can be set to prevent the exposure of the occupants. With these limitations in mind, it is however necessary to develop meaningful guidance and instructions for the public how to manage the problem. A pragmatic approach can be used as the evidence based understanding concerning the roots of the problem is relatively clear. The microbial growth on building surfaces and structures, "mold", is the critical source of exposure, and this growth is only possible with the presence of excess moisture, i.e., water. As microbial exposures are complex to measure, the detection of signs of moisture can be used as a surrogate of the exposure. While the causal connection between an individual's illness and mold exposure may be hard to verify, it is beneficial for both the occupants' health and for the building itself to repair any dampness or moisture problems and remove any mold from the building surfaces.

The characterization of the moldy building issue as a public health problem in Finland was started with a cross sectional study on prevalence of moisture damage observations in the Finnish housing stock (Nevalainen et al., 1998). A random sample was drawn from the building registry to obtain a representative sample of single family houses built in each decade between 1960ies and 90ies. The houses were inspected by trained civil engineers to register all the signs of moisture, e.g., damp or moldy patches, discolored wood or peeling paint. As a result, it was observed that, when even the slightest signs were recorded, 80% of houses had some signs of present or previous dampness or moisture, and 50% of homes needed at least some minor repair or more thorough investigation. As it was already known that such dampness or mold is a risk factor for respiratory and other symptoms, the efforts to find tools to identify problematic buildings and understand the whole phenomenon were started. The guideline development has been strictly based on both national and international research.

Hypersensitivity Pneumonitis

E. Neil Schachter

Diseases of sifters and measurers of grain. Ramazzini

"I have often wondered how so noxious a dust can come from grain as whole some as wheat... All kinds of grain and in particular wheat... have mixed in with them a very fine dust... hence, whenever it is necessary to sift wheat or other kinds of grain to be ground in the mill, or to measure it when corn merchants convey it hither and thither, the men who sift and measure are so plagued by this kind of dust that when the work is finished they heap a thousand curses on their calling.

The throat, lungs and eyes are keenly aware of serious damage... almost all who make a living by sifting or measuring grain are short of breath and cachectic and rarely reach old age". (Ramazzini, 1940)

INTRODUCTION:

Hypersensitivity Pneumonitis (aka Extrinsic Allergic Alveolitis) is an immunolo gically mediated inflammation of the pulmonary parenchyma, involving alveolar walls and terminal airways secondary to the repeated inhalation of sensitizing agents including micro organisms, organic dusts and simple chemicals.

Histopathologically it is characterized by a granulomatous interstitial pneumoni tis with occasional bronchiolitis obliterans

Diagnosis is usually based on clinical presentation, exposure history and radio logic appearance. Bronchoscopic and histologic features are helpful in characterizing the disease.

Removal of the affected individual from the toxic environment, particularly early on in the course of the disease, can arrest and reverse the progression of hypersen sitivity pneumonitis to an irreversible stage. Anti inflammatory treatment may redu ce symptomatic manifestations of the disease.

Health Complaints, Lung Function, and Immunologic Effects in German Compost Workers from Long-term Exposures to Bioaerosols

Jürgen Bünger, Anja Deckert, Frank Hoffmeyer, Dirk Taeger, Thomas Brüning, Monika Raulf-Heimsoth, Vera van Kampen

Employees at workplaces in composting facilities are exposed to high bioaero sol concentrations containing airborne actinomycetes and molds (organic dust). We investigated work related symptoms and diseases of 190 currently exposed compost workers and 38 non exposed control subjects in a cross sectional study at 31 com posting plants situated in Northern Germany.

Participants of the study were asked for symptoms and diseases, exposures to bioaerosols, atopic diseases, and smoking habits using a standardized protocol. They underwent a physical examination by an occupational physician and a lung function measurement according to ATS criteria. Contents of specific IgE to environmental allergens and molds were measured as possible markers of allergic occupational asthma. Specific IgG to molds and actinomycetes was investigated since they may serve as biomarkers of exposure.

Compost workers suffered more often from chronic cough and mucous mem brane irritation syndrome (MMIS) than the controls. Work related influenza like symptoms were reported by 11 compost workers (5.8%) but none control subject. Lung function parameters of compost workers were within the reference ranges. Nevertheless, the values for the forced vital capacity (FVC% predicted) of compost workers were significantly lower than for control subjects (p 0.01). The significan ce was even higher when only non smoking study participants were compared (p 0.001). Specific IgE values to environmental allergens and molds were positive in 25.3% and 7.4% of currently exposed compost workers. There were no significant differences in specific IgE and IgG concentrations between the two groups.

Compost workers suffered significantly more often from MMIS which is likely to be associated with occupational exposures to organic dust. The elevated inci dence of chronic cough indicates cases of chronic bronchitis according to WHO criteria. Also the reduced FVC% predicted may be caused by this exposure. There is no higher frequency of mold sensitization in the group of compost workers pro bably due to a healthy worker effect. Reports of work related influenza like sym ptoms may indicate cases of hypersensitivity pneumonitis or organic dust toxic syn drome in the compost workers.

INTRODUCTION

Employees at workplaces in composting facilities are exposed to high bioaero sol concentrations containing airborne actinomycetes and molds (organic dust). In

general, these microorganisms can show infectious, allergenic, and toxic properties. Diseases like infections, chronic bronchitis, occupational asthma, and hypersensiti vity pneumonitis were reported in workers exposed to similar bioaerosols in other industries and agriculture. The review of twenty epidemiological studies resulted in an excess of upper airway and eye irritation so called mucous membrane irritation syndrome (MMIS) in bioaerosol exposed workers (Schlosser et al., 2009). The eva luation of case reports revealed cases of hypersensitivity pneumonitis, organic dust toxic syndrome (ODTS), and allergic bronchopulmonary aspergillosis (ABPA) (Schlosser et al., 2009). Especially allergens of molds can trigger type I allergies, such as bronchial asthma and allergic rhinitis (Bünger et al., 2007). Also skin and gastroin testinal problems have been reported in biowaste collectors (Bünger et al., 2000, Ivens et al., 1999). The aim of this study was monitoring of the health status of bioaerosol exposed workers in German composting plants.

Airborne workplace exposure to microbial metabolites in waste recycling plants

Stefan Mayer, Vinay Vishwanath, Michael Sulyok

In waste recycling plants employees are exposed to a complex mixture of airbor ne bioaerosols. To which degree the exposure to airborne mould in waste recycling plants is associated with a toxic health risk emanating from microbial metabolites is largely unknown.

Settled dust samples were taken at waste recycling plants for municipal waste and for waste paper. The settled dust samples were analyzed for 186 fungal and bacteri al metabolites using liquid chromatography / tandem mass spectrometry (LC MS/MS). Additionally the concentration of airborne dust was measured. Based on these data the concentrations of airborne microbial metabolites and further on the airborne exposure was calculated for regular and worst case conditions.

In total 38 microbial metabolites were detected in the settled dust samples con sisting of 33 fungal and 5 bacterial metabolites. Samples from municipal waste recy cling plants contained a higher number of microbial metabolites which occurred in higher concentrations compared to recycling plants for waste paper.

Apart from outliers the inhalable airborne dust concentration is usually below the German occupational threshold limit value of 10 mg/m³.

The calculated amount of inhaled microbial metabolites under regular working conditions during an 8 hours work shift averaged to 37 and 8 ng/70 kg bw for muni cipal waste and waste paper recycling respectively. Under worst case conditions the

corresponding amounts would be 5573 and 4841 ng/70 kg bw. Different approaches to assess these exposure rates are discussed.

Respiratory Health and Flood Restoration Work in the Post-Katrina Environment

Roy J. Rando, John J. Lefante, Laurie M. Freyder, Robert N. Jones

Post Katrina flood restoration workers have been exposed to bioaerosols from microbial overgrowth of flooded materials and debris. As part of a 5 year longitu dinal examination of flood restoration workers, the prevalence of post Katrina respiratory illness and symptoms was assessed. Spirometry and interview were per formed on 791 participants who worked for various public and private institutions, or were private residents of the New Orleans area, and most worked in the building construction and maintenance trades or custodial services. Administered question naire included information on respiratory health and symptoms, smoking history, and time spent performing post Katrina restoration work including demolition, trash removal, landscape restoration, sewer/drain repair, and mold remediation. Prevalence of symptoms and percent predicted lung function parameters were examined statistically for correlation with time spent in restoration work. 74% of study participants reported time spent in restoration work since Katrina with an ave rage of 1,646 hours. Since Katrina, 29% of study participants reported at least one episode of transient fever/cough, 48% reported sinus symptoms, and 4.5% develo ped new onset asthma. Prevalence rate ratios of fever/cough (PRR: 1.7) and sinus symptoms (PRR: 1.3) were statistically elevated for those who did any restoration work and increased with restoration work time; new onset asthma prevalence (PRR: 2.2) was elevated but not statistically significant. Lung function parameters were slightly depressed in the overall population, but were not significantly different bet ween those with and without restoration work exposure. Analysis of symptoms and lung function in this cohort of post Katrina New Orleans workers indicates mode rate adverse respiratory effects, including ODTS and sinusitis, associated with resto ration work.

Mold species identified in flooded dwellings

Denis Charpin

Nowadays, heavy rains and flooding occur more frequently in some regions, probably due to climate change, and they are responsible for mold proliferation in dwellings (Diaz, 2007). Around 80 mold species are considered to live indoors (Kuhn, Ghannoun, 2003). In vitro, these mold species demonstrate different meta bolic production, and have different allergenic properties (Nielsen, 2003). Thus, the health impact of mold exposure and the decontamination procedures which need to be implemented may depend on the mold species under consideration. The mold species developing in a given dwelling depend on environmental conditions (Nielsen, 2003). Thus, one may anticipate that mold species encountered in flooded dwellings may be different from those encountered in other unhealthy buildings. Surprisingly, very few data are available on this important issue. In this paper, we compared mold species identified in flooded dwellings compared to those found in unhealthy dwellings.

Attributable fractions of risk factors of respiratory diseases among children in Montreal, Canada

Louis Jacques, Céline Plante, Sophie Goudreau, Leylâ Deger, Michel Fournier, Audrey Smargiassi, Stéphane Perron, Robert L. Thivierge

The objective of this cross sectional study was to estimate the attributable frac tions among the child population living in Montréal, in Canada, of asthma, respira tory infections and winter allergic rhinitis associated with known important risk fac tors, including both the indoor and the outdoor environment.

Fungi and Chronic Rhinosinssitis (CRS): Cause and effect

E B Kern, J U Ponikau, D A Sherris and H Kita

Fungi are present in the airway mucus of chronic rhinosinusitis (CRS) patients and in normal healthy controls. Fungi (especially *Alternaria*) induce the production of cytokines (IL 13 and IL 5) crucial for the eosinophilic inflammation. This immu ne response occurred only in CRS patients but not in healthy controls. Fungi indu ce an eosinophilic tissue airway inflammation in mammals (mice), which is in con trast to a neutrophilic response to bacteria. Fungi can induce an eosinophilic airway

inflammation and congestion in patients. Eosinophils, in vivo, target fungi in the mucus with CRS and nasal polyps. Fungal antigens with a molecular weight of 61 kilo Daltons (kDa) cause activation and degranulation of human eosinophils via the beta 2 integrin on the CD11b receptor. Clinically, antifungal drugs can reduce nasal polyps, improve computed tomography (CT) scans, and decrease levels of interleu kin 5 (IL 5) and markers of eosinophilic inflammation. However, using different antifungal applications and different outcome measures can produce conflicting results. While fungi are present in the nasal and sinus airway mucus in both CRS patients and in normal controls, the evidence suggests that it is the fungi that initia tes the cytokine cascade that produces CRS. In other words, evidence points to CRS as an immunologic disease triggered by inert fungi in the airway mucus and media ted by the activated and degranulating eosinophil.

Rhinosinusitis and mold as risk factors for asthma symptoms in occupants of a water-damaged building

Ju-Hyeong Park

Mold exposure has been associated with nasal symptoms and asthma develop ment in damp building occupants. However, progression of building related (BR) rhinosinusitis to asthma due to mold exposure is poorly understood. We examined risk of asthma development in relation to prior BR rhinosinusitis symptoms and microbial exposure in occupants of a damp building. We conducted four cross sec tional health and environmental surveys on occupants of a water damaged office building. We defined BR rhinosinusitis symptom and comparison groups from par ticipants' first questionnaire responses. We compared the odds for asthma develop ment and BR asthma symptoms between the two groups over the last three surveys. We used logistic regression models adjusted for demographics, smoking status, year of building occupancy, and initial exposures to culturable fungi, endotoxin, and ergosterol in floor dust. The BR rhinosinusitis symptom group had higher odds for developing BR asthma symptoms [odds ratio (OR) 2.2; 95% confidence interval (CI) 1.3 3.6] and self reported physician diagnosed current asthma (OR 2.0; 95% CI 0.7 5.4) in any of the follow up surveys. The highest tertile mold exposure group had an OR of 3.5 (95% CI 1.6 7.5) for developing BR asthma symptoms as compared to the lowest tertile exposure group. The BR rhinosinusitis symptom group with higher mold exposure within the building had an OR of 7.3 (95% CI 2.7 19.7) for developing BR asthma symptoms, compared to the lower exposu re group without symptoms. Our findings suggest that rhinosinusitis associated with occupancy of water damaged buildings may be a sentinel for increased risk for asthma onset in such buildings.

Conclusions on health implications of airborne molds: Analysis of airborne molds in 11 contaminated houses using a new method of evaluation

Urban Palmgren, Judith Müller

Airborne molds in 11 contaminated houses were investigated using a new method of evaluation.

There was a fluctuation of colony forming units/m from < 1% to > 90% when compared to the levels of total cell count method (tcc). The results of the outdoor samples are always higher as the indoor samples.

The investigation with a cfu/tcc evaluation showed the influence of time on the results in 5 ways:

In an older microflora, many molds have not survived the elapsed period of time and can because of this not be confirmed by the determination of colony forming units/m (cfu/m). Older mold sources emit more spores and mycelia parts to the air as younger sources. Through an air flow close to the contaminated surface of the building material the mold spores and fragments will get airborne and these microorganisms will show the same age as those on the building material. The com parison of cfu/tcc can be used as an indication of the age of the source of the air borne contamination with molds (cfu/tcc evaluation). Outdoor and indoor samples are seldom of the same age and this indicates that the indoor and outdoor sources of airborne molds have come from different places and should consequently not be used as reference measurements.

Out of 29 measurements of just cfu/m there were no information indicating an indoor mold source. When additional methods of confirmation were used (cfu/tcc evaluation) there were 18 samples indicating indoor mold sources.

The toxic and allergenic potential of airborne molds is dependent on the amount of biomass/m or on the total number of microorganisms/m and inde pendent of the number of colony forming units/m (cfu/m). In conclusion with all results of this investigation an attempt to correlate the number of airborne colony forming units to any types of health problems is irrelevant.

Observational Epidemiology and Water Damaged Buildings

Joseph Q. Jarvis, and Philip R. Morey

A NIOSH team reported their questionnaire based public health investigation of respiratory symptoms and asthma in employees in relation to damp indoor environ

ments of two hospitals which was induced by the discovery of six sentinel cases of work related asthma (Indoor Air, 2009). They achieved a participation rate of 64%, which they characterized as 'fairly good', but noted that employees who worked in departments with dampness problems were somewhat more likely to take part in the survey, raising some concern about a possible volunteer bias. They did not use medi cal records or medical testing to validate participant reports of physician diagnosed asthma, except for the six sentinel cases. The NIOSH team concluded that follow up of sentinel reports of building related illness is warranted, noting that new onset building related asthma in relation to water damage can occur.

Outside of public health agency investigations of problem buildings, however, observational epidemiologic methods are not commonly employed in the United States in the setting of indoor air quality complaints. Our first experience with observational epidemiology in the setting of a water damaged building occurred 20 years ago. The subject building was a county owned structure with nearly 600 occu pants, located in a part of the US with a sub tropical climate. The building had been opened for four years at the time of the questionnaire survey. Widespread moistu re and fungal growth problems had been documented in the building practically since initial occupation after its construction. Our investigation was initiated after the local public health department had conducted its own evaluation of occupant complaints and concluded that building related symptoms were common and buil ding related allergic respiratory disease could not be excluded. We began the investi gation in standard public health fashion by conducting confidential interviews of approximately 50 volunteer subject building occupants. These interviews confirmed the findings of the local health department that building associated symptoms and building related allergic respiratory disease may have occurred. We sought to esta blish whether rates of symptoms were higher than would be expected in the pro blem building by conducting a cross sectional survey of occupants of both the sub ject building and a neighboring county owned building without known indoor air problems. 95% of subject building occupants and 93% of the occupants of a com parison county owned building participated in the questionnaire survey. Using con servative epidemiologic definitions, subject building occupants had a fourfold increase in building related symptoms and a threefold increase in respiratory illness over rates found in the comparison building. A nested case/control study design confirmed that exposure to water damage and visible mold at the individual work area conferred higher risk for both building associated symptoms and building rela ted respiratory disease. We conducted detailed clinical evaluations of 37 subject buil ding occupants which confirmed 15 cases of building related asthma. Based upon these data, the building owner chose to close the building for extensive remediation. Repeat questionnaire surveys were conducted four months after building evacuati on, just before the building was re occupied after remediation, and one month after the building was re opened and significantly contributed to the protection of the

comfort, safety, and peace of mind of the building occupants as well as the success ful prosecution of construction defects litigation in their behalf. Details of both the environmental and epidemiologic aspects of this building investigation have been published (Applied Occ Env Hyg 16, 2001).

Since that experience we have been invited to participate in the evaluation of many other water damaged buildings large enough to consider the use of epidemio logic methods, including commercial and public office buildings, hotels, residential high rise buildings, and schools. More often than not, the search for a possible sen tinel case found no health problem requiring follow up investigation, and in accor dance with standard public health practice, no observational epidemiologic study was attempted. When, however, building associated symptoms or building related ill ness may have occurred, as the NIOSH team stated, follow up is indicated.

Molds and Mycotoxins: Factors That Affect Exposure and Contribute to Adverse Health Effects

Karin K. Foarde, Timothy Dean, Doris Betancourt, Jean Kim, Anthony Devine, Grace Byfield, and Marc Menetrez

Fungal growth and the resulting contamination of building materials is a well documented problem, especially after the reports from New Orleans and the US Gulf Coast following Hurricane Katrina. Inhalation is thought to be a major route of exposure; however, relating surface contamination to airborne levels of spores and subsequent mycotoxin exposure is challenging. Exposure to fungi may result in respiratory symptoms of both the upper and lower respiratory tract such as allergy and asthma. Everyone is potentially susceptible. However, of particular concern are children with their immature immune systems and individuals of all ages that are immunocompromised. While exposure too many of the fungi can be considered problematic and many fungi produce toxins, *Stachybotrys chartarum* is used as our representative mycotoxin producing organism. There are numerous reports demon strating an association between exposure to *S. chartarum* and adverse respiratory health effects.

Our objectives were to:

1) quantify emissions of fungal spores from contaminated building materials
2) determine the mycotoxin content of the emissions
3) relate the level of emissions from contaminated building materials to expo sure
4) use cell free and cell based assays to begin relating the exposure results to potential adverse health effects.

Does Reversibility of Neurobehavioral Dysfunction by Monosodium Luminol have Diagnostic and Possible Therapeutic Use in Mold/Mycotoxin Exposed Patients?

Kaye H. Kilburn

Five points led me to suggest to patients to try anti inflammatory redox agents to intervene, to treat neurological inflammation from chemicals including those from molds and mycotoxins. First, functions of the human brain can be measured. Second, the number of total abnormalities can yield one number to quantify losses and recoveries. Third, neurologic inflammation oxidation coincided with irritation of skin, nose, upper airway and lung. Fourth, the olfactory nerve delivers chemicals to the temporal lobes such as monosodium luminol and glutathione, just as it does pitressin and insulin. Fifth, the human brain responds in the same time frame as do animal and cell models.