The Role of Stachybotrys Mycotoxins in Building-Related Illness

Recently there has been increased attention among both the public and health professionals regarding the potential role of mycotoxins, primarily from fungi of the genus Stachybotrys, as etiologic agents related to illness among persons exposed to the indoor (nonindustrial) environment. Recommendations for the remediation of buildings are being made based in part on reported health effects believed to be due to mycotoxins. A search of NICEDITS literature database maintained by the National Institute for Occupational Safety and Health and MEDLINE (from 1966 to present) for literature related to fungi, mycotoxins, and the indoor environment was conducted. References from relevant articles were also reviewed.

This strategy yielded 13 articles for complete review and 18 additional articles for partial review. These studies were deemed adequate in addressing the issues raised in the literature review. The following articles were generally consistent in their findings and conclusions.

Building-related illnesses include a variety of recognized disease entities that are characterized by objective clinical findings related to specific exposures in the indoor environment. A number of microorganisms, including many species of bacteria and fungi, are well established as potential etiologic agents of building-related illnesses. The fact that there has been increased attention among both the public and health professionals regarding the potential role of mycotoxins as etiologic agents related to illness among persons exposed to the indoor environment. That type of concern has led to recommendations for the remediation of buildings based in part on the expected association of various health effects with exposure to mycotoxins. The goal of this article is to clarify the available information concerning mycotoxins and their potential health effects in the indoor environment.

Keywords: building-related illness, fungi, indoor, mycotoxins, Stachybotrys

BACKGROUND

Fungi are a term used to encompass different plants of the Kingdom Fungi, which has five main phyla: Chytridiomycota, Zygomycota, Ascomycota, Basidiomycota, and Deuteromycota. They are characterized by the absence of chlorenchymatous examples include mushrooms, woody plants, grasses, mosses, algae, and fungi. Fungi comprise 25% of the biomass on earth. Human exposure to fungi is ubiquitous. Superspore fungi (i.e., those utilizing moldy organic matter as a food source) inhabit soil, vegetation, water, or are reservoirs that can provide an ample supply of nutrient. Fungi are thought to produce adverse health effects by several different mechanisms, some better understood than others, including (1) immune-mediated hypersensitivity to the fungus, (2) fungal infection (i.e., mycosis), and (3) toxic reactions.
Toxic reactions such as organic dust toxic syndrome have been reported among workers in a variety of agricultural and industrial settings and are thought to involve inhalation exposure to a variety of dusts or other particles. Mucocutaneous reactions specifically refer to a reaction to toxins produced in the fungal environment. In addition, fungal toxins can cause various occupational respiratory allergies (OVARs). More than 300 VOCs have been identified from a variety of fungi, the most common being ethyl alcohol.

Many mold species produce mycotoxins, which are non-steroidal, fungus metabolites with the potential to cause toxic reactions in humans and animals. Mycotoxin production is poorly understood, but thought to be at least partially due to a variety of conditions such as fungal strain, temperature, humidity, moisture content, and various chemical factors. The mycotoxins are a commonly occurring category of mycotoxins. There are more than 150 mycotoxins identified to be produced by a variety of fungi, including Zearalenone, Trichothecene, Ochratoxin, and Tuberatoxin. All have double bond at C8 and C9 and an epoxy ring at C12,13, and are thus called 12,13-epoxy-trichothecenes. The trichothecenes are grouped into two classes (A, B, C, D) based on chemical properties and the fungi that produce them. Their primary mechanism of action is inhibition of protein synthesis.

Fungi of the genus Stachybotrys are found worldwide and have been isolated from soil and a wide variety of substances rich in cellulose, such as hay, wood pulp, cotton, grains, various dead plant components, paper, and inbook bindings. Buildings where Stachybotrys growth problems have been reported typically have experienced chronic water damage (e.g., due to leaking roofs or plumbing, water, air conditioner condensation, etc.) and were kept at a temperature conducive to the growth of Stachybotrys (temperature range for optimal growth is 22-27°C). Stachybotrys chartarum (synonym Stachybotrys): is one of many fungi capable of producing trichothecene mycotoxins (examples of different trichothecenes include nortricin, verrucarin, and thexantrons) and under certain environmental conditions. Trichothecenes have been found in the aerosolized spores of this fungus, indicating the potential for inhalation exposure to these compounds.

**METHODS FOR LITERATURE SEARCH**

This review focuses on human illness reported to be related to exposure to fungal toxins (mycotoxins) in the indoor environment. The search focused on identifying relevant literature using the broadest terms available to generate the largest number of articles. The medical subject heading terms "mycotoxin" and "fungi" were cross-searched with the terms "indoor environment" and "indoor air pollution" both in the medical subject heading ("indoor air pollution"). A separate search was done on Stachybotrys chartarum. The search terms used in the search were performed in MIPFILINE from 1986 to present and NIOSHTIC (a literature database maintained by the National Institute for Occupational Safety and Health). This strategy yielded more than 350 articles from which relevant articles were selected. Review articles and articles with the review title were not included. In addition to the strategy, the authors also reviewed relevant references cited in literature and discussing this topic. Of note, the search strategy was not designed to provide coverage of the extensive literature concerning laboratory studies of mycotoxins. A discussion provides a brief overview of related literature that adds perspective to the issue of potential health effects related to mycotoxin exposure.

**RESULTS OF LITERATURE REVIEW**

The search strategy yielded a total of 13 relevant articles. All but one article involve Stachybotrys, of the articles describe the same investigation of pulmonary hemorrhage in infants.

One widely referenced investigation reports an outbreak of potential trichothecene mycotoxin secondary to mold contamination in a home (120). In that case report, five occupants of a house reported a variety of symptoms, including cold and flu symptoms; nervousness; diarrhea; headaches; and patches of hair loss and fatigue. Medical investigations, not well described and apparent not conducted by the reporting authors, reportedly did not reveal any identifiable cause. In the home, a cold air return duct and a return air duct fiber board were contaminated with Stachybotrys. When the mold was cleaned up, the family members' symptoms reportedly were resolved. Extracts from the molds were injected into experimental animals. The animals died within 24 hours, and autopsy revealed hemorrhagic necrosis of the internal organs, similar to that reported in veterinary cases of trichothecene mycotoxins. The authors inferred that mycotoxins were responsible for the symptoms of the occupants.

In 1990, Johannesson et al. reported findings from a study of workers exposed to Stachybotrys in a wats-damaged office environment. The affected persons were 39 females and 14 males who worked in the building. The comparison group consisted of 13 females and 10 males who had no exposure to the building. Health complaints were assessed by means of a questionnaire. Affected persons had significantly more lower respiratory, dermatological, eye, constitutional (e.g., low-grade fever, tenderness of swollen lymph nodes, and myalgia), and chronic fatigue syndrome. Of 24 white blood cells, lymphocytes, and immune globulin tests, 3 showed statistically significant differences between exposed and comparison groups, or between exposure locations within the building. However, these differences are not likely to be clinically significant. Air and blood samples from the problem building were positive for Stachybotrys, Penicillium, Cladosporium, and Aspergillus, but no environmental assessment was performed for the comparison group.

In 1998, Hodgson et al. reported a study of employees of two buildings with histories of water intrusion. The authors stated that these symptoms were reported among occupants of the buildings compared to occupants of comparison buildings. In summary concerning respiratory, dermatological, systemic, and neurological symptoms or functional decline during the occupied and comparison buildings were not reported; other studies have shown that they do exist. A description of symptoms among building occupants was not conducted among "unexposed" workers. Exposure monitoring in the problem buildings revealed low concentrations of fungal endotoxins compared with contaminants, with differences in the types of fungi detected (Aspergillus fumigatus and Stachybotrys chartarum were detected indoors but not outdoors). Other than a seasonal respiratory response, symptoms in the comparison building were not described. Sputum samples from Stachybotrys chartarum contaminated ceilings, but not from air samples.

The search strategy was not designed to provide coverage of the extensive literature concerning laboratory studies of mycotoxins. A discussion provides a brief overview of related literature that adds perspective to the issue of potential health effects related to mycotoxin exposure.
Employers with two or more symptoms in the problem building did not have higher levels of antibodies to fungi identified in the building than did controls.

Moldben report on an investigation that was performed in 1996 in an office building in the Pacific Northwest where there had been health complaints. The office building described had a history of maintenance problems and moisture in the building. The environmental evaluation found various bacteria and fungi present in air, bulk, and surface samples. The epidemiologic study, consisting of interviews and questionnaire administration, revealed that the most commonly reported symptoms were fatigue, head ache, difficulty concentrating, and sinus congestion; no evidence of objective illness among building occupants was reported.

Auger et al. reported several cases of chronic fatigue and respiratory infections in persons living in homes where there were toxic fungi such as Trichoderma, Penicillium, and Paecilomyces. The authors propose that research concerning mold exposure is important in the attempt to explain indoor environmental quality problems, but no data on occupational exposure is provided in this brief communication.

In November 1994, the Centers for Disease Control and Prevention (CDC), private physicians, and public health officials in Cleveland, Ohio, reported a cluster of eight cases of water-purified hemolysis in hemodialysis that had occurred during January 1993-November 1994 among infants in one area of the clinic. Two additional cases were identified in December 1994. A case-control study was performed in which past water damage to these homes was assessed by questionnaire. The study revealed an association between symptomatic hemolysis/hemodialysis and parental reports of water damage at home in the 8 months prior to the hemolysis in the affected infant (odds ratio 6.0, 95% confidence interval CI = 2.5 to 10). In a follow-up investigation, air sampling was done to assess potential exposure in the homes of cases and controls by using an "aggressive" sampling strategy (performed by purposefully stirring up potential contaminants in the dwelling, for example, by vacuuming and hanging the air ducts). The CDC has recently released the detailed findings of its internal and external reviews, which concluded that a possible association between pulmonary hemolysis/hemodialysis and exposure to mold, specifically Stachybotrys chartarum, was present.

Two recent case reports have been published concerning pulmonary hemosiderosis in children. In the first, 74 an intensive effort to uncover pulmonary disease exposed workers. Exposure mons revealed lower concentrations of outdoors, with differences in the epidermis, including then and Stachybotrys chartarum but not outdoors. Other than cliquel of fungi in the comparison build- ing were isolated from Stachybotrys chartarum, but not from air samples.

The authors stated that while some clinical evidence suggests that exposure to certain mycotoxins may cause pulmonary hemosiderosis, such as in the case of Talaromyces flavus and Stachybotryswhere spores, as well as spores of other fungi, were found in air and surface samples from the infant's bedroom. In addition, a portion of the contaminated glass in the water-damaged areas of the bedroom was evaluated for the presence of mycotoxin, several trichothecenes, including specific types of nodular and trichothecene, were found.

In the second recent case report, Stachybotrys was isolated from the Badin, Wisconsin, strain of the BAL fluid of a 7-year-old boy. This boy had blood, rash, fatigue, and recurring pneumonia at age 5. At the time of the reported medical evaluation, findings included a left lower lobe consolidation, anaemia, and a moderate amount of hemosiderin-laden macrophages in the BAL. Culture of BAL fluid on Sabouraud dextrose agar grew Stachybotrys. Much relevant clinical information that would be expected to be present in this type of medical evaluation (such as evaluation of the endoscopy of the left lower lobe pneumonia) was omitted from the report. Surface cultures from the bronchi showed mycological and mycology lab was negative for Stachybotrys but were positive for Stachybotrys in samples taken from the home, which had suffered extensive water damage. The patient was relocated to a relative's home (which was not evaluated for the presence of Stachybotrys) while his home was remodeled. His symptoms reportedly resolved within 1 month after removal from the home.

**DISCUSSION**

Discussion of Reviewed Literature

In the literature summarized here, important issues need to be addressed involving either the clinical implications reported on the documentation of exposure to a potential causative agent(s), or both. As a group, the articles reviewed present a wide spectrum of health effects attributed to mold exposure. Case definitions are either absent or poorly defined. For example, among frequently cited evaluations, Croft et al. described five individuals with a variety of nonspecific symptoms, with an unclear description of medical evaluations performed. Hodgson et al. used undefined clinical diagnoses and epidemiological case definitions, making it difficult to interpret the reported symptoms. The study results were difficult to interpret. Hodgson et al. did not detect cases, but rather compared employee and a problem building with those of a nonproblem building. Finding an excess of nonspecific symptoms in the studied populations.

The issue of exposure characterization in the reviewed literature is also problematic. Due to a variety of reasons, including incomplete understanding of bioaerosols, technical inability to document bioaerosol exposures that may be occurring, and also likely lack of clinically relevant exposures among the study subjects, the reviewed literature presents inadequate evidence of actual exposure to fungi or mycotoxins in the environments studied. For example, the case-control study of pulmonary hemosiderosis/Hemolyticuremic syndrome did not include a systematic evaluation of water damage in the evaluated homes, and the air sampling performed several months after onset of illness using aggressive sampling techniques is unlikely to be representative of actual exposure to fungi in the home. The articles by Hodgson et al. and Hodgson et al. noted that antibody testing, which potentially could be used as a measure of fungal exposure, was often not performed. The studies tested revealed no evidence of exposure to any specific fungi among problem buildings. The study compared the intervention group. Several of the studies have detected mycotoxins in samples from walls, ceiling tiles, and air ducts. Mycotoxins in the water-damaged areas of the bedroom were evaluated for the presence of mycotoxin; several trichothecenes, including specific types of nodular and trichothecenes, were found.

**Limitations of Related Literature**

Fatigue and non-specific symptoms thought to be caused by the inhaled mycotoxin nor was there evidence of intervention. Exact symptoms associated with the indoor environment, such as non-specific symptoms, were often not reported.
CONCLUSIONS

This review of the literature indicates that there is inadequate evidence to support the conclusion that exposure to mycotoxins in the indoor (nonindustrial) environment is causally related to symptoms or illness among building occupants. Support building-related illnesses in the nonindustrial environment should continue to be evaluated using the appropriate environmental, medical, and epidemiologic tools. Research involving the identification and isolation of specific fungal toxins in the environment and in humans is needed before a more definitive link between health outcomes and mycotoxins can be made. To support hypothesis regarding potential adverse health consequences of mycotoxin exposure in the nonindustrial environment, objective measures of adverse health effects must be associated with some measure of mycotoxin exposure, and comparisons must be made with appropriate control populations; to date, such evidence has not been forthcoming. Recognition of fungus-contaminated environments is warranted to reduce the likelihood of known health effects related to fungal exposures, regardless of the potential for exposure to mycotoxins. Currently, there is inadequate evidence to support recommendations for greater suspicion in cases where mycotoxins producing fungi have been isolated.

REFERENCES


AlTHAJ 621 September/October 2001 647
INCLUSIONS

The current evidence indicates that there is an inadequate conclusion that exposure to mycotoxins in the environment is causally related among building occupants. Suspect building and industrial environment should contain the appropriate environmental, medics. Research involving the identification of toxic factors in the environment and in a more definitive link between health can be made. To support hypotheses regarding health consequences of mycotoxicosis environment, objective measurements must be associated with some measure of comparisons must be made with appropriate controls to detect any evidence has not been of mycotoxins-contaminated environments. The likelihood of known health effects regardless of the potential for effects due to inadequate evidence to support further research in cases where mycotoxins are isolated.

REFERENCES


