MOLD INVESTIGATION MEDICAL GUIDANCE

INTRODUCTION

Molds may affect human health by three mechanisms: infection (by exposure of a susceptible individual to mold spores, generally, but not always, a person who is immunocompromised), hypersensitivity (allergy to mold spores, components or toxins, including asthma and hypersensitivity pneumonitis), or direct irritation (by mycotoxins, the toxins produced by mold).

In general, results from a large indoor air study found that:

- Culturable airborne fungal concentrations in indoor air are lower than those in outdoor air.
- Fungal concentrations are highest in the fall and summer and lowest in the winter and spring.
- Geographically in the continental U.S., fungal concentrations are highest in the southwest, far west, and southeast.
- The most common culturable airborne fungi, both indoors and outdoors and in all seasons and regions, were Cladosporium, Penicillium, nonsporulating fungi, and Aspergillus.

Considerable interest and controversy have been generated recently about searching for and identifying specific molds in buildings. The Centers for Disease Control and Prevention (CDC) currently state that determining what type of mold exists is unnecessary, and that all molds should be treated the same with respect to potential health risks and removal.

Mold may proliferate almost anywhere that has too much moisture. Even if renovation is done properly, recurrence of moist conditions may lead to mold regrowth. In one study, uninstalled wallboard available from local distributors was found to contain a baseline bioburden, including Stachybotrys chartarum. The authors noted that sanitation and preservation treatment of the wallboard can markedly delay regrowth of certain fungi, particularly of S. chartarum.

Mold has been considered as a causative agent of building-related illness (BRI). BRIs are caused by known pathogens, have specific symptoms, and may be serious. Specific diseases include those caused by Legionella species (Pontiac Fever, Legionnaire’s Disease) and humidifier fever. Other airborne infectious diseases may have increased transmission when there is inadequate ventilation (e.g., Tuberculosis, Varicella, and Q fever). Other symptoms from indoor air contamination of offices where workers shared ventilation contaminated with algal toxins (Pfiesteria piscicida, a dinoflagellate) are suspected to have occurred.

Prudent health practice dictates limiting exposure of immunocompromised persons to excessive levels of mold spores and limiting exposure of sensitized (allergic) individuals to airborne or surface contamination of the specific mold to which the individual is sensitized.
THE PHYSICIAN’S ROLE IN THE INVESTIGATION AND RESOLUTION OF MOLD-RELATED PROBLEMS

The medical member of the indoor environmental quality (IEQ) investigative team can contribute valuable expertise in advising what organisms the industrial hygienist (IH) should sample for. If there is reason to suspect a particular species of mold - because of worker concern, fungal infection, or identification by a worker’s health care provider (HCP) of allergy to a specific mold - IH can be asked to direct sampling to recover and appropriately identify that organism. Requesting IH to “sample for molds” because of non-specific symptoms in workers will generally not be helpful, since simply the presence of molds may be insignificant with respect to human health.

Communication between medical and other team members is important when trying to determine if there is an exposure pathway. For example, discovery of mold on surfaces may be incidental in a situation where airborne contamination is the problem (e.g., Legionella).

RETURNING WORKERS TO A BUILDING UNDER INVESTIGATION

In general, it is preferable not to keep workers out of the work area, nor to advise workers to avoid returning to a building unless: (1) a diagnosis of a building-related illness has been established, or (2) a building-related diagnosis is suspected based on symptoms, disease patterns, and findings consistent with a BRI.

If a worker is confirmed to have building-related mold allergy, the worker should not be allowed back into the building until remediation has been completed and post-remediation sampling documents reduced levels of mold. After remediation, re-exposure should be done with caution. It may be appropriate to have medical care immediately available in the case of serious allergic reactions. If remediation has been adequate, there is reason to expect the worker may successfully return to a building with few or no mold-related symptoms.10

The etiology of a worker’s condition may be unknown, but the worker’s condition is serious enough that further exposure to any potential offending agent represents an unacceptable health risk. In such cases, the prudent HCP may recommend against further exposure to a building until the medical workup is complete. However, the HCP should complete the workup thoroughly and accurately, being careful to avoid labeling the building a “health hazard” or stating that mold in the building is the etiology until after the facts have established such a link. Incorrectly identifying building mold as a source of health hazards can cause undue anxiety and loss of income among workers, decreased productivity, increased operating costs, and decreased readiness. Once a causal relationship has been established, however, relocation of affected workers to a different building may be appropriate.
A case report of office-related *Alternaria* allergy supports the following as “considerations” for concluding an association exists between IEQ-related mold exposure and illness in an occupational setting: symptoms and signs consistent with a medical diagnosis, either in vitro or in vivo evidence of exposure, environmental evidence of plausible biological exposure, and substantial improvement or resolution of the illness after appropriate building remediation.11

**REMEDICATION**

Successful remediation can result in a building that can be reoccupied without recurrent related illness, even in a subtropical climate.12

If sampling reveals pathogens suspected because of the symptoms or signs exhibited by building occupants, remediation effectiveness should be confirmed by clearance sampling before building reoccupation. Building processes (for example, heating, ventilation, air-conditioning and humidification systems or decorative fountains) that may be similar in other buildings may warrant preventive attention as a public health measure. Building engineers, inspectors, or public health officials may be appropriate points of contact in such situations.

**INFECTIONS DUE TO MOLD**

Molds are usually opportunistic pathogens, causing clinically significant infections in cases of overwhelming exposure or in individuals who are immune-compromised (i.e., debilitated by extremes of age, underlying infection, poor sanitation, inadequate nutrition, wounds), immune suppressed (chemotherapy, severe stress, pregnancy); or immune deficient (human immunodeficiency virus). A notable exception is the recent outbreak of *Cryptococcus gattii* originating in Vancouver Island, British Columbia, Canada, which infected apparently healthy adults, most likely from outdoor sources.13 Mold infection diagnoses will be made by appropriate microbial identification studies or clinical courses (which are beyond the scope of this document).

**ALLERGIES/ALLERGENS**

Respiratory or skin (allergic contact dermatitis) allergy symptoms are the most likely symptoms encountered from building-related mold allergy. Sensitivity to mold allergens is an important risk factor for adenoid hypertrophy in children with allergic rhinitis.14 Adult-onset asthma is associated with self-reported mold exposures in the home.15 Other organ system involvement, such as gastrointestinal hypersensitivity-related complaints, may be a clue that the offending exposure may not be indoor environment related, but rather related to an ingested allergen.

Allergens are common in most environments. Certain classes of allergens are especially pertinent to an indoor environmental quality investigation. The history given by those affected can be the most helpful information in determining the source of the problem. Buildings that have been water damaged for several days or more - whether from flood, leaking roofs or walls, broken plumbing, improperly installed or adjusted humidifiers or condensation on cold surfaces - may become culture media for any of a number of molds and fungi.
Specific IEQ-associated illnesses with an allergic (sensitization) basis include asthma, hypersensitivity pneumonitis, rhinitis or sinusitis, bronchitis or tracheitis (usually associated with sinusitis), and humidifier fever (HF). HF is thought to be allergic, as patients have shown sensitivity and symptoms with exposure to specific antigens in humidifiers. HF has been associated with contamination of humidifiers by biologicals including amoeba, fungi, Bacillus subtilis, endotoxins, flavobacterium, and Pseudomonas species. It is also possible that not all etiologies of IEQ-related allergic complaints are biologicals, as one report noted heating, ventilation, and air conditioning system “dust and mud.”

Spirometry may help document involvement of the lower respiratory tract. A peak flow meter may be the simplest way to document expiratory impairment or exacerbation of asthma with building exposure. A significant association was found between basophil histamine release showing serum IgE specific to one or more indoor molds, and building-related symptoms in individuals working in damp and moldy buildings. Skin testing (skin prick test) may be more sensitive than blood testing (radioallergosorbent test, commonly called RAST) in detecting sensitization to molds. However, determining a specific mold to which someone is allergic in a given situation may be difficult, as sensitized individuals often react to more than one species.

IRRITATION

Stachybotrys mycotoxins are biologically active, and it is thought that they act as irritants. Respiratory irritation has been documented to occur in rodents exposed to Stachybotrys. Special conditions may be necessary for mycotoxins produced by surface Stachybotrys in a building to reach sufficient concentrations to cause such effects, according to the results of one experimental study. The controversy is noted previously as to whether documentation is sufficient that direct irritation from mycotoxins, rather than a hypersensitivity-related response to molds or mycotoxins, has occurred in humans exposed to mold in indoor air.

The primary indicator that symptoms among workers may be caused by building-related mold is that there is a temporal relationship of the symptoms to building exposure. Mold allergy may involve both IgG and IgE immunoglobulins. Thus, an allergic reaction may occur immediately on entering a building, after several hours of exposure, or even 2 to 8 hours after leaving the building. A clear worker history of a temporal association of allergy symptoms with building exposure should alert the health care provider to the possibility of building-related allergy.

It is unknown how much exposure time is required before sensitivity to mold develops. As many molds are commonly found outside of the workplace, it is expected that some individuals have been sensitized prior to any occupational exposure. Further, since development of allergy to some substances may take over 30 years of exposure, it is probable that in certain individuals, sensitization develops only after many years.
HEALTH CONSIDERATIONS OF SPECIFIC MOLDS

**ASPERGILLUS**

*Aspergillus* species molds are commonly found. Three types of *Aspergillus*-related lung disease are recognized: colonization of airways; allergic disease including extrinsic allergic alveolitis, asthma, allergic bronchopulmonary aspergillosis, bronchocentric granulomatosis and chronic eosinophilic pneumonia (possibly progressing to allergic granulomatosis and angiitis, also called Churg-Strauss syndrome); and invasive infections such as pseudomembranous tracheobronchitis, acute bronchopneumonia, angioinvasive aspergillosis, chronic necrotizing aspergillosis and invasive pleural disease.\(^{32,33}\) It should be noted that both hypersensitivity and infection may be present simultaneously (i.e., a person with an allergic reaction to *Aspergillus* may also have an *Aspergillus* infection).\(^{34}\) Inhalation of *Aspergillus* conidia or mycelium fragments may result in airway colonization, which may subsequently cause infections in susceptible hosts, and may simultaneously induce hypersensitivity (allergy).\(^{35}\) A significant relationship was found between the incidence of invasive nosocomial aspergillosis and the degree of fungal contamination of air and surfaces in patient rooms in a bone marrow transplantation unit and two hematology wards.\(^{36}\) As an antigen, hypersensitivity to *A. fumigatus* may cause *Aspergillus* asthma and allergic bronchopulmonary aspergillosis (ABPA).\(^{37}\) Specific IgE and IgG may be detected in ABPA. Radiographic studies (x-rays) are characterized by fleeting pulmonary infiltrates that are often confused with pulmonary tuberculosis on chest x-ray, and by central bronchiectasis on chest computerized tomography (CT). Early diagnosis and therapy may alter the course of the disease and prevent the development of end-stage lung fibrosis.\(^{38}\)

*Aspergillus candidus*, common in grain dust, has been suggested to be an etiologic factor in organic dust toxic syndrome\(^{39}\) and to pose an important occupational hazard for grain handling workers through its immunomodulating properties.\(^{40}\)

*Aspergillus versicolor* has been found in an investigation of building-related complaints, but no association was seen between IgE or IgG antibodies and the presence of disease.\(^{41}\)

**STACHYBOTrys**

*Stachybotrys chartarum* (also called *Stachybotrys atra*) has been known as an animal pathogen, and has recently attracted attention as possibly having a role in human IEQ-related disease.\(^{42}\) It is a toxigenic fungus frequently found in water-damaged buildings.\(^{43}\) In one study, *S. chartarum* was identified in the indoor air in 6% of the buildings studied and in the outdoor air of 1% of the buildings studied.\(^{44}\) *S. chartarum* has been found to produce volatile organic compounds that are quite different from those produced by *Aspergillus*.\(^{45}\)
\textit{S. chartarum} produces trichothecene mycotoxins, which are biologically active and can produce a variety of physiological and pathologic changes in humans and animals, including modulation of inflammation and altered alveolar surfactant phospholipid concentrations. Sensitivity to \textit{Stachybotrys} has been found to involve both immunoglobulins IgE and IgG against antigenic proteins of \textit{S. chartarum}. Effects of \textit{S. chartarum} may be related to direct irritant as well as immunologic properties. Inhalation of \textit{S. chartarum} extract aerosols was observed to provoke sensory irritation in the airways of both naive and immunized mice. Alveolar type II cells are sensitive to exposure to \textit{S. chartarum} spores and mycotoxin (isosatratoxin-F, a trichothecene).

\textit{S. chartarum} has been associated with nasal bleeding in adults. Stachylysin, a mycotoxin, may be one chemical responsible for the hemorrhagic effects. Stachyrase A, a chymotrypsin-like proteinase from \textit{S. chartarum}, has been isolated from a child with pulmonary hemorrhage. A possible association between \textit{S. chartarum} and pulmonary hemorrhage/hemosiderosis in infants has been reported, but further review of evidence by the CDC and other experts concluded that the association was unproven.

Articles are not consistent as to the significance of \textit{Stachybotrys} in relation to human health. Two reviews have found inadequate evidence to clearly establish the place of \textit{Stachybotrys} in human disease.

\textbf{OTHER MOLDS AND MOLD-RELATED ORGANISMS}

Thermophilic \textit{Actinomyces} and \textit{Aspergillus fumigatus} have been suggested as possibly having a causative antigenic role in stipatosis, a hypersensitivity pneumonitis found in Mediterranean-area stucco workers exposed to those organisms in esparto grass (\textit{Stipa tenacissima}). Note that although the name \textit{Actinomyces} suggests a fungus, actinomycosis is a bacterial infection.

\textit{Cladosporium cladosporioides} was found to be the etiologic agent of hypersensitivity pneumonitis associated with a hot tub. Skin sensitization to \textit{C. cladosporioides} was the most commonly found mold skin sensitization in a small population in Toronto, Canada.

\textit{Fusarium} species infections in a hospital led to an investigation that identified the water distribution system of the hospital as the reservoir of \textit{Fusarium}. Aerosolization of \textit{Fusarium} species was documented after running the showers.

IgG to \textit{Sporobolomyces salmonicolor} was the most commonly detected anti-mold immunoglobulin associated with exposure in a Finnish military hospital building with severe, repeated, and enduring water and mold damage. Rhinitis, asthma, and alveolitis were noted among personnel reacting positively to \textit{S. salmonicolor} provocation tests.

\textit{Streptomyces albus} was found to be responsible for a biopsy-proven case of hypersensitivity pneumonitis.

An increased risk of developing asthma in adulthood has been found to be significantly related to IgG antibodies to \textit{Trichoderma citrinoviride} (but not to other molds).
Allergic bronchopulmonary mycosis caused by *Schizophyllum commune* in an otherwise healthy woman has been reported.62

Acute eosinophilic pneumonia with precipitating antibodies to *Trichosporon cutaneum*, *Trichoderma viride*, as well as *Aspergillus* species has been reported.63 Other fungal species isolated from individuals with similar pulmonary disease include *Candida albicans*, *Penicillium*, *Geotrichum candidum*, *Stemphylium lanuginosum*, *Culvularia lunata*, and *Drechsleria hawaiensis*.64

For more information on IEQ medical guidance, contact Occupational Medicine at (757) 953-0769 or occmed@nehc.med.navy.mil.

**REFERENCES CITED**


13.4-7


15 Thorn J, Brisman J, Toren K. Adult-onset asthma is associated with self-reported mold or environmental tobacco smoke exposures in the home. Allergy. 2001 Apr;56(4):287-92. PMID 11284794


23 Lebedev SV, Aleksandrovskii VG, Chekhonin VP. Humidifier fever [Russian]. Ter Arkh. 1988;60(11):90-3. PMID 3238588


25 Lander F, Meyer HW, Norn S. Serum IgE specific to indoor moulds, measured by basophil histamine release, is associated with building-related symptoms in damp buildings. Inflamm Res. 2001 Apr;50(4):227-31. PMID 11392611


13.4-10
49 Rand TG, Mahoney M, White K, Oulton M. Microanatomical changes in alveolar type II cells in juvenile mice intratracheally exposed to Stachybotrys chartarum spores and toxin. Toxicol Sci. 2002 Feb;65(2):239-45. PMID 11812928


