Position paper

The medical effects of mold exposure

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Exposure to molds can cause human disease through several well-defined mechanisms. In addition, many new mold-related illnesses have been hypothesized in recent years that remain largely or completely unproved. Concerns about mold exposure and its effects are so common that all health care providers, particularly allergists and immunologists, are frequently faced with issues regarding these real and asserted mold-related illnesses. The purpose of this position paper is to provide a state-of-the-art review of the role that molds are known to play in human disease, including asthma, allergic rhinitis, allergic bronchopulmonary aspergillosis, sinusitis, and hypersensitivity pneumonitis. In addition, other purported mold-related illnesses and the data that currently exist to support them are carefully reviewed, as are the currently available approaches for the evaluation of both patients and the environment.
(J Allergy Clin Immunol 2006;117:326-33.)

Key words: *Mold, fungi, hypersensitivity, allergy, asthma*

Abbreviations used
ABPA: Allergic bronchopulmonary aspergillosis
CRS: Chronic rhinosinusitis
HP: Hypersensitivity pneumonitis
MVOC: Volatile organic compound made by mold
VOC: Volatile organic compound

Exposure to certain fungi (molds) can cause human illness. Molds cause adverse human health effects through 3 specific mechanisms: generation of a harmful immune response (eg, allergy or hypersensitivity pneumonitis [HP]), direct infection by the organism, and toxic-irritant effects from mold byproducts. For each of these defined pathophysiologic mechanisms, there are scientifically documented mold-related human diseases that present with objective clinical evidence of disease. Recently, in contrast to these well-accepted mold-related diseases, a number of new mold-related illnesses have been hypothesized. This has become a particular issue in litigation that has arisen out of unproved assertions that exposure to indoor molds causes a variety of ill-defined illnesses. Many of these illnesses are characterized by the absence of objective evidence of disease and the lack of a defined pathology and are typically without specificity for the involved fungus–fungal product purported to cause the illness.

In this position paper we will review the state of the science of mold-related diseases and provide interpretation as to what is and what is not supported by scientific evidence. This is important for members of the allergy–clinical immunology community, who are frequently asked by patients, parents, and other interested parties to render opinions about the relationship of mold exposure to a variety of patient complaints. Given the nature of this document, key rather than exhaustive citations are provided. The latter can be found in documents such as the Institute of Medicine reports ''Damp indoor spaces and health''[1] and ''Clearing the air: asthma and indoor air exposure.''[2]

THE RELATIONSHIP OF MOLDS TO ALLERGY AND ASTHMA

It is estimated that approximately 10% of the population have IgE antibodies to common inhalant molds.[3] About half of these individuals (5% of the population) are predicted to have, at some time, allergic symptoms as a consequence of exposure to fungal allergens.[4] Although indoor fungal allergen exposure occurs, outdoor exposure is generally more relevant in terms of sensitization and disease expression. The role of indoor fungi in the pathogenesis of allergic disease has been extensively reviewed in recent reports from the Institute of Medicine of the National Academy of Science.[1]

Sensitization to fungi, particularly *Alternaria alternata*, has been linked to the presence, persistence, and severity of asthma.[5] Exposure to atmospheric fungal spores

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Received for publication November 18, 2005; revised November 28, 2005; accepted for publication December 1, 2005.
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0091-6749/$32.00

doi:10.1016/j.jaci.2005.12.001

(principally in the outdoor environment) has been related to asthma symptoms and medication use in children with asthma.[6]

The association of asthma symptoms and exposure to indoor fungi is less clearly established. Literature reviews suggest that children living in damp houses, homes with visible mold growth, or both were more likely to experience lower respiratory tract symptoms of cough and wheeze than children who do not.[7,8] Recent prospective epidemiologic studies have shown that infants at risk for asthma, defined by a maternal history of asthma, who are exposed to high concentrations of indoor fungi (in addition to cockroach allergen and nitrogen dioxide sources) in the first year of life are at risk for persistent wheezing and cough.[9,10] These and similar epidemiologic reports fall short of prospective studies that control for confounding factors, such as humidity and other airborne allergens and irritants.

Molds are often presumed to be an important cause of the other atopic manifestations, including allergic rhinitis and, to a far lesser degree, atopic dermatitis. Abundant published data have established that sensitization (by skin testing, circulating IgE antibodies, or both) to one or more airborne molds occurs in these diseases, although sensitization is less frequent to molds than to pollens, animal danders, and house dust mite.

Current studies do not conclusively demonstrate a causal relationship of airborne mold exposure and clinical manifestations of allergic rhinitis. The data on outdoor molds (eg, *Alternaria* species and basidiomycetes) purportedly causing allergic rhinitis are indirect and conflicting.[11-13] Studies attempting to correlate indoor molds with symptomatic allergic rhinitis are even more problematic because of such methodological uncertainties as lack of quantitative mold sampling[14-16] and inclusion of upper respiratory tract infections.[17]

Published reports document mold sensitivity in some children and adults with atopic dermatitis.[18-20] However, there are no publications that establish a causal role for airborne molds in this disease rather than the IgE antibodies simply reflecting an expected concomitant of their atopic state. There are no credible reports in the medical literature documenting indoor exposure to molds as a cause of the nonatopic IgE-mediated diseases (eg, urticaria-angioedema and anaphylaxis).

Conclusions:

- Atopic patients (those with allergic asthma, allergic rhinitis, and atopic dermatitis) commonly have IgE antibodies to molds as part of polysensitization.
- Allergic responses to inhaled mold antigens are a recognized factor in lower airway disease (ie, asthma).
- Currently available studies do not conclusively prove that exposure to outdoor airborne molds plays a role in allergic rhinitis, and studies on the contribution of indoor molds to upper airway allergy are even less compelling.
- Exposure to airborne molds is not recognized as a contributing factor in atopic dermatitis.
- Exposure to airborne molds is not recognized as a cause of urticaria, angioedema, or anaphylaxis.
- Patients with suspected mold allergy should be evaluated by means of an accepted method of skin or blood testing for IgE antibodies to appropriate mold antigens as part of the clinical evaluation of potential allergies.

ALLERGIC BRONCHOPULMONARY ASPERGILLOSIS AND SINUSITIS

Allergic bronchopulmonary aspergillosis (ABPA) is a well-recognized clinical entity affecting individuals with asthma or cystic fibrosis.[21] A variety of fungi in addition to *Aspergillus fumigatus* can produce a similar clinical picture. The critical element in ABPA is an underlying anatomic change in the lung and not a specific mold exposure because at-risk individuals will have ongoing exposures caused by the ubiquitous nature of the fungi involved. Exposure to *A fumigatus* can occur both from indoor and outdoor sources.

Allergic fungal sinusitis is similar to ABPA in that it is a localized hypersensitivity condition resulting from fungal growth in an area of abnormal tissue drainage.[22] Although originally attributed primarily to *A fumigatus*, other fungi, particularly mitosporic (formerly known as Deuteromycetes or imperfect fungi) fungi are more commonly implicated (eg, *Curvularia* and *Bipolaris* species). Almost uniformly there is allergic sensitization to multiple allergens, including the fungus implicated in the affected sinus. Criteria for this condition have been well delineated, and it is generally readily distinguishable from typical chronic sinusitis. Specific criteria for diagnosis include eosinophilic mucus demonstrating noninvasive fungi, type 1 hypersensitivity (history, positive skin test result, or positive *in vitro* test result to allergens), nasal polyposis, and characteristic radiographic findings.

It has recently been proposed that most cases of chronic rhinosinusitis (CRS) are attributable to sensitivity to fungi. In particular, *Alternaria* species were suspected because most patients had these organisms recovered by means of culture from sinus surgery specimens. However, these organisms are frequently recovered from the nasal cavities of healthy individuals. Although some evidence for an immune response to these fungi in patients with CRS has been presented, clear-cut evidence for this as the cause of CRS is still lacking, and treatment with intranasal antifungal agents (eg, amphotericin) has not been conclusively demonstrated to be an effective treatment.[23]

Conclusions:

- ABPA and allergic fungal sinusitis are manifestations of significant hypersensitivity to fungi, particularly A*spergillus* species.
- Data supporting the role of fungi in CRS are lacking at this time.

HYPERSENSITIVITY PNEUMONITIS

HP, also referred to as extrinsic allergic alveolitis, is a disease that exists in acute, subacute, and chronic forms but with considerable overlap. It is an allergic disease in which the allergen is inhaled in the form of an organic dust of bacterial, fungal, vegetable, or avian origin. Both sensitization and the elicitation of the disease state generally require high-dose exposure, prolonged exposure, or both to the causative allergen. Many cases are, in fact, occupational because of this. There are reports of a similar, if not identical, disease from workers exposed to inhaled chemicals, especially isocyanates. A few instances of the disease have been attributed to systemically administered drugs.

HP is rare, and most cases have been reported in certain occupations, such as farming, and in hobbyists, such as persons who raise pigeons. It is not a reportable disease, and therefore prevalence and incidence are difficult to estimate. The immunopathogenesis of the disease is believed to be cell-mediated (delayed) hypersensitivity. Allergen-specific precipitins are often present in serum and are important is establishing exposure. Precipitins might also play a role in the mechanism of the acute phase of the disease. HP results in acute episodes of noninfectious, immunologically mediated interstitial pneumonitis (ie, alveolitis), which might eventually produce restrictive irreversible lung disease.

The diagnosis requires a clinical and environmental history, relevant physical examination findings, chest radiography or computed tomographic scanning, high-resolution computed tomographic scanning, pulmonary function testing, bronchoalveolar lavage, and transbronchial or open lung biopsy. Specific diagnosis of the responsible allergen is performed by testing for IgG antibody to the allergen extract, typically by testing for the presence of precipitins in the Ouchterlony double-diffusion assay. In some instances provocation inhalation challenge to the suspected allergen extract might be necessary to replicate pertinent clinical and laboratory responses. Finally, a favorable response to the elimination of the inhaled antigen, administration of prednisone, or both is confirmatory. Because a differential diagnosis covers a number of respiratory diseases, an accurate diagnosis of HP demands that the clinical diagnosis be ensured.

Exposure to domestic specific indoor fungal spores is an extremely unlikely cause of HP, except in highly unusual circumstances, such as workplace exposure.

Conclusions:

- HP is an uncommon but important disease that can occur as a result of mold exposure, particularly in occupational settings with high levels of exposure.

INFECTION

Superficial mold infections (eg, tinea cruris, onychomycosis, and thrush) are common in healthy individuals and result primarily from local changes in the cutaneous or mucosal barrier, resident microflora, or both.[24,25] These infections are not the result of environmental exposure, except occasionally as related to certain animal vectors. Indeed, molds of the *Malassezia* genus are resident on the vast majority of human subjects and only become evident as ''tinea versicolor'' during periods of more exuberant growth. A limited number of molds (eg, coccidiomycosis, histoplasmosis, and blastomycosis) are aggressive pathogens in otherwise healthy persons. Acquisition of these infections is generally related to specific outdoor activities-exposures. Individuals with recognized primary and secondary immunodeficiency disorders are at increased risk for infection with a wide range of opportunistic fungi, with the risk varying with the degree and nature of the specific immunodeficiency. Opportunistic fungal infections are typically associated with cellular rather than (isolated) humoral immunodeficiencies. Generally, host factors, rather than environmental exposure, are the critical factor in the development of opportunistic mold infection in immunocompromised individuals because exposure to potential fungal opportunistic pathogens (eg, *Aspergillus* species) is ubiquitous in normal outdoor and indoor environments. Accepted histologic and microbiologic methods should be used to make the diagnosis of fungal infection.

Conclusions:

- Common superficial fungal infections are determined by local changes in the skin barrier, resident microflora, or both.
- A very limited number of aggressive fungal pathogens can be acquired through specific outdoor exposures.
- Host factors, rather then environmental exposure, are the main determinant of opportunistic fungal infection.

TOXIC EFFECTS OF MOLD EXPOSURE

Ingestion

Ingestion of mycotoxins in large doses (generally on the order of a milligram or more per kilogram of body weight) from spoiled or contaminated foods can cause severe human illness.[26] Toxicity from ingested mycotoxins is primarily a concern in animal husbandry, although human outbreaks do occur occasionally when starvation forces subjects to eat severely contaminated food. Specific adverse effects from a given toxin generally occur in a narrower and better-defined dose range than for immunologic or allergic effects that might vary across much broader dose ranges. Some mycotoxins, such as ocratoxins and aflatoxins, are commonly found in food stuffs, including grain products and wines, and peanut products, respectively, such that there are governmental regulations as to the amounts of allowable aflatoxin in foods.[27,28] Acute high-intensity occupational exposures to mixed bioaerosols have given rise to a clinical picture called ''toxic dust syndrome.'' The nature of the responsible agent or

agents in that condition remains undefined, and the observed adverse effects reported have been transient. Such exposures are highly unlikely in nonoccupational settings.

Toxicity caused by inhalation

The term *mold toxicity* as used here refers to the direct injurious effects of mold-produced molecules, so-called mycotoxins, on cellular function. Toxicity should not be used to refer to changes related to innate immune responses (eg, nonspecific inflammation caused by mold particulates) or to adaptive immune responses (eg, induction of IgE or IgG antibodies). Mycotoxins are low-molecular-weight chemicals produced by molds that are secondary metabolites unnecessary for the primary growth and reproduction of the organisms. In-depth review of the toxicology of mycotoxins and their potential for adverse health effects can be found elsewhere.[1,2] It is important to emphasize key principles of toxicology relevant to patient concerns about possible toxic effects from mold exposure.

Only certain mold species produce specific mycotoxins under specific circumstances. Importantly, the mere presence of such a mold should not be taken as evidence that the mold was producing any mycotoxin. For a toxic effect to occur in a subject, (1) the toxin must be present, (2) there must be a route of exposure, and (3) the subject must receive a sufficient dose to have a toxic effect. In the nonoccupational setting the potential route of exposure is through inhalation. Mycotoxins are not volatile and, if found in the respirable air, are associated with mold spores or particulates. They are not cumulative toxins, having half-lives ranging from hours to days depending on the specific mycotoxin. Calculations for both acute and subacute exposures on the basis of the maximum amount of mycotoxins found per mold spore for various mycotoxins and the levels at which adverse health effects are observed make it highly improbable that home or office mycotoxin exposures would lead to a toxic adverse health effects.[1,29]

Thus we agree with the American College of Occupational and Environmental Medicine evidence-based statement and the Institute of Medicine draft, which conclude that the evidence does not support the contention that mycotoxin-mediated disease (mycotoxicosis) occurs through inhalation in nonoccupational settings. Furthermore, the contention that the presence of mycotoxins would give rise to a whole panoply of nonspecific complaints is not consistent with what is known to occur; when a toxic dose is achieved (eg, through ingestion of spoiled foods), there is a specific pattern of illness seen for specific mycotoxins.

Conclusions:

- The occurrence of mold-related toxicity (mycotoxicosis) from exposure to inhaled mycotoxins in nonoccupational settings is not supported by the current data, and its occurrence is improbable.

IRRITANT EFFECTS OF MOLD EXPOSURE

The Occupational Health and Safety Administration defines an irritant as a material causing ''a reversible inflammatory effect on living tissue by chemical action at the site of contact.'' Irritant effects are dose related, and the effects are transient, disappearing when the exposure has decreased or ceased.

Molds produce a number of potentially irritating substances that can be divided into volatile organic compounds (VOCs) and particulates (eg, spores, hyphae fragments, and their components). The threshold level of irritant response depends on the intrinsic properties of the specific material involved, the level plus length of exposure, and the innate sensitivity of the exposed tissues (eg, the skin versus nasal mucosa).

VOCs made by molds (MVOCs) are responsible for their musty odor. MVOCs include a wide range of alcohols, ketones, aldehydes, esters, carboxylic acids, lactones, terpenes, sulfur and nitrogen compounds, and aliphatic and aromatic hydrocarbons.[30] Although levels causing irritant effects have been established for many VOCs, MVOC levels measured in damp buildings are usually at a level so low (on the order of nanograms to micrograms per cubic meter) that exposure would not be expected to cause complaints of irritation in human subjects.[31] Because there are other sources of VOCs indoors, measurement of indoor airborne concentrations of MVOCs is rarely done.

Mold particles (spores, hyphal fragments, and their structural components) are not volatile. These structural mold compounds (particulates) have been suggested to cause inflammation through deposition on mucus membranes of their attached glucans and mannans. However, whether such effects occur clinically remains unproved. In fact, subjects exposed to airborne concentrations of between 215,000 and 1,460,000 mold spores/m^3 at work showed no differences in respiratory symptoms at work versus while on vacation nor was there evidence of increased inflammatory markers in their nasal lavage fluids related to their mold exposure at work.[32] Thus mold particulates generally found indoors, even in damp buildings, are not likely to be irritating.

It should be emphasized that irritant effects involve the mucus membranes of the eyes and upper and lower respiratory tracts and are transient, so that symptoms or signs persisting weeks after exposure and those accompanied by neurologic, cognitive, or systemic complaints (eg, chronic fatigue) should not be ascribed to irritant exposure.

Conclusions:

- The occurrence of mold-related irritant reactions from exposure to fungal irritants in nonoccupational settings are theoretically possible, although unlikely to occur in the general population given exposure and dose considerations.
- Such irritant effects would produce transient symptoms-signs related to the mucus membranes of the eyes and upper and lower respiratory tracts but would

not be expected to manifest in other organs or in a systemic fashion.
- Further information about thresholds for irritant reactions in at-risk populations is needed to better define the role of molds, mold products, and other potential irritants in such individuals.

IMMUNE DYSFUNCTION

The question has been raised as to whether mold or mycotoxin exposure can induce disorders of immune regulation. At this time, there is no credible evidence to suggest that environmental exposure to molds or their products leads to a state of clinically significant altered immunity expressed as either immunodeficiency or autoimmunity. The published literature in this regard is of particularly poor quality and should not be relied on as scientifically valid.[33,34] Individuals who have had intense occupational mold exposures do not manifest opportunistic infections or other findings of immunodeficiency, and thus even the most intense form of airborne mold exposure is not a recognized cause of secondary immunodeficiency in human subjects. Some mycotoxins are immunosuppressive and used for this purpose clinically (eg, cyclosporine). However, the doses involved are not relevant to what might have been found in the environment. Doses that might be seen in environmental exposures are discussed in other sections of this article (toxicity and environmental sections). Testing of a wide range of nonspecific immunologic parameters, such as immunophenotyping of lymphocytes beyond those parameters having known clinical utility (eg, total B and CD3, CD4, and CD8 cells) or measurement of serum cytokines is not appropriate for assessing subjects for immunodeficiency in general and for mold-induced immune dysregulation specifically.[35]

There is also no reliable evidence for mold exposure in any setting being a linked to the induction of autoimmune diseases in human subjects. Although certain viral and bacterial infections appear to have a relationship to the induction-precipitation of autoimmune diseases, such an association has not been established for any known mold exposure. The measurement of clinically useful tests of autoimmunity (eg, antinuclear antibody), much less testing of a broad array of nonvalidated autoantibodies (eg, putative antibodies to central or peripheral myelin), is not indicated, and such testing should not be used to indicate mold exposure or mold-related disease.

This practice of testing many nonvalidated immune-based tests, as has been done previously to suggest an immunologic basis for idiopathic environmental intolerance (multiple chemical sensitivity), is expensive and does not provide useful information that will be of benefit in diagnosis, management, or both of disease and is to be discouraged.

Conclusions:

- Exposure to molds and their products does not induce a state of immune dysregulation (eg, immunodeficiency or autoimmunity).
- The practice of performing large numbers of nonspecific immune-based tests as an indication of mold exposure or mold-related illness is not evidence based and is to be discouraged.

LABORATORY ASSESSMENT

Patient assessment

Measurement of IgE antibodies to mold proteins. Assessment for IgE antibodies to mold antigens has clearly been validated as a measure of potential allergic reactivity to mold. This assessment can be done through either *in vivo* or *in vitro* testing. The relative strengths of these different forms of testing have been reviewed recently.[36,37] In general, there is a weaker correlation between *in vivo* and *in vitro* testing for IgE antibodies to mold antigens than for other antigens, partly as a result of the heterogeneity of extractable mold proteins. A positive IgE antibody level to mold proteins without appropriate clinical evaluation should not necessarily be taken as an indicator of clinical disease. In addition, the presence of IgE antibodies to a mold cannot be used to determine the dose or timing of prior exposures. Although IgE antibodies to *Stachybotrys* species can be detected through *in vitro* or *in vivo* testing, such testing should be discouraged. *Stachybotrys* species is unlikely to be a relevant clinical allergen in human subjects because it is poorly aerosolized and far less common than other well-established mold allergens.

Measurement of IgG antibodies to mold proteins. Assessment of IgG antibodies to mold proteins can be performed through immunoprecipitation–double diffusion or solid-phase immunoassays.[37] Such testing has demonstrated value in assessment of individuals with suspected HP or allergic bronchopulmonary mycosis. Immunoprecipitation assays have been classically used for the assessment of HP, and although they measure all classes of antibodies present, they are primarily detecting IgG antibodies. Such testing (immunoprecipitation or solid-phase IgG testing) is appropriate to perform only in the setting of a clinical picture, including history, physical examination, imaging studies, and other laboratory assessments, suggesting HP or allergic bronchopulmonary mycosis as part of the differential diagnosis. Use of these tests as screening procedures for these diseases in the absence of an appropriate clinical picture is discouraged.

Immunoprecipitation testing remains the standard approach because the presence of precipitating antibodies is strong supportive evidence in the appropriate clinical setting. However, as many as half of highly exposed individuals might have precipitating antibodies in the absence of any clinical disease. Solid-phase immunoassays have not been widely used for the specific diagnosis of these diseases. Although newer assays are quantitative, the actual level of IgG antibody that would be associated with either HP or ABPA has not been defined. Therefore a level of mold antigen–specific IgG antibody above a statistically defined reference range cannot be taken as evidence for HP or ABMA with the same strength as immunoprecipitation testing. Limited studies suggest that

the level of a specific IgG antibody that would be associated with HP could be 5-fold or greater than the upper limit of the nondiseased group reference range. Use of older-generation, semiquantitative, solid-phase immunoassays is not recommended.

Testing for IgG antibodies to mold proteins cannot be used as a surrogate to assess either the level or timing of specific mold exposures.[38] This is not surprising given the widespread occurrence of molds in the environment.

Measurement of antibodies of isotypes other than IgG (eg, IgA and IgM) to mold is not useful to assess mold exposure. However, the differential response of IgM and IgG antibodies is useful in diagnosis with specific organisms (eg, coccidioidomycosis). IgM levels have not been shown to relate to specific airborne exposures to molds in the absence of infection because mold exposure is common and generally ongoing. Measurement of IgA antibodies to airborne molds has not been shown to be related to a specific timing of exposure, and the claim that increased IgA antibodies to mold represents a more recent exposure than IgG antibodies is not supported by scientific evidence. Measurement of salivary IgA to mold as a marker of mold exposure has not been shown to have scientific validity.

Measurement of antibodies to mycotoxins. Mycotoxins are not proteins but low-molecular-weight chemicals. There is no scientific basis to support measurement of alleged naturally occurring antibodies to various mycotoxins as a marker of exposure to mycotoxins. Evidence of natural exposures from ingestion in human subjects and animals and use of these compounds in clinical medicine does not support the concept of naturally occurring antibodies. Such testing has not been validated and cannot be relied on as an indication of exposure to any mycotoxin.[39]

Conclusions:

- Measurement of antibodies to specific molds has scientific merit in the assessment of IgE-mediated allergic disease, HP, and allergic bronchopulmonary mycosis.
- Measurement of antibodies to molds cannot be used as an immunologic marker to define dose, timing, and/or location of exposure to mold antigen inhalation in a noninfectious setting.
- Testing for antibodies to mycotoxins is not scientifically validated and should not be relied on.

Measurement of molds and mold product exposure in the patient's environment

An in-depth analysis of methods to measure fungal organisms, mold products, and mycotoxins in the environment is outside the bounds of this article. Such information is reviewed in depth elsewhere.[40,41]

Measurement of fungi in the subject's environment. Measurement of airborne fungal spores in the subject's environment by using culture methods, nonculture methods, or both is commonly used. Air testing provides the most relevant measure of exposure and is usually reported as colony-forming units or spores per cubic meter of air. However, this testing suffers from the drawback that it is a snapshot that does not integrate exposure over time and provides data only about the location of sampling. Indoor testing must be compared with outdoor testing and preferably with more than one outdoor sample. Currently there are no standards as to what constitutes acceptable levels of outdoor or indoor airborne fungal spores.

Given these caveats, the levels of airborne fungal spores found in an indoor setting can be considered in relative and absolute terms. Indoor fungal spores arise from outdoor sources present within soil and vegetation. Therefore an increase in indoor-outdoor concentrations of specific fungi indicates the presence of an indoor source. Depending on clinical or other indications, it might be necessary to locate the source and, if necessary, take appropriate action. Total fungi spores that are greater in concentration in indoor than outdoor air might be potential evidence of increased fungal presence indoors. However, in normal indoor environments xerophillic fungi, such as *Aspergillus* and *Penicillium* species, might be found indoors at levels above those measured outdoors on a given day. Even when the fungal levels are greater indoors than those outdoors, health risks would be limited in most cases, except to the subject specifically allergic to the mold in question. Absolute fungal spore levels indoors can be put into context when one realizes that outdoor levels can reach tens of thousands of fungal spores per cubic meter and hundreds of thousands per cubic meter or higher around rotting vegetation compost or in agricultural settings, such as in grain elevators.

Bulk, surface, and within-wall cavity measurements of fungi, although sometimes indicating the presence of fungi, do not provide a measure of exposure. Fungi found in these places require a route of exposure through air (aerosolization and entry into the patient's respirable air) that involves many factors not included in these measurements. Such testing should not be used to assess exposure.

Measurement of fungal products in the patient's environment

Another approach to measure of potential fungal exposure is to test for fungal products in the environment.

Structural fungal materials. Testing for the levels of general mold structural material (eg, β-glucans in settled dust) has been used to try to integrate levels of potential exposure to molds in general over time. Although an interesting research avenue, such testing does not provide any information as to the nature of the specific fungi involved or their source (indoor or outdoor), is not useful for predicting health effects, and has not found general acceptance, as discussed elsewhere.

Mycotoxins. Specific molds can produce, under some conditions, a variety of mycotoxins or none at all. Thus measurements of spores cannot be used as surrogates of mycotoxin exposure. Mycotoxins can be measured directly. A variety of methodologies based on mass

spectroscopy have been applied to bulk samples with heavy fungal growth to identify the presence of mycotoxins; however, potential levels of mycotoxins in nonagricultural air samples are too low to be measured practically with this technology. The occurrence of mycotoxins in bulk sampling does not provide evidence of exposure because mycotoxins themselves are nonvolatile. Thus exposure requires inhalation of mycotoxin-containing spores or fungal fragments in the respirable air. For example, satratoxin H can be found in a sample of material with heavy *Stachybotrys chartarum* growth, but *Stachybotrys* species are not easily aerosolized. Testing with crude cytotoxicity of extracted bulk materials suffers from a lack of sensitivity and specificity. Such testing cannot be relied on to predict or evaluate health effects.

VOCs. See section on irritant effects above.

Conclusions:

- Sampling of both indoor and outdoor air for mold spores provides a measure of potential exposures and can be useful in certain clinical conditions, but it has many shortcomings.
- Bulk, surface, and within-wall cavity measurement or molds or mycotoxins, although having potential relevance for other purposes, cannot be used to assess exposure.
- Testing for airborne mycotoxins in nonagricultural environments cannot be used to diagnose mold exposure.

REMEDIATION

Issues regarding remediation of mold are beyond the scope of this article. Indoor mold growth should be addressed. These matters are reviewed at length in the Institute of Medicine 2004 report ''Damp indoor spaces and health.'' For an overview, the reader can refer to the Occupational Health and Safety Administration document ''A brief guide to mold in the workplace.''[42] The true challenges of mold remediation are currently being addressed in the flood-ravaged areas struck by hurricane Katrina, which will unfortunately provide a rich environment for the study of both mold-induced disease and mold remediation.[43,44]

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