
CME review article

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Health effects of indoor fungi

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Objective: To review the nontoxic harmful effects that poor indoor air quality caused by fungi can have on health.

Data Sources: We searched PubMed for publications related to the various topics discussed in this review, and we relied on our knowledge of the field.

Study Selection: Where more than one publication was relevant, we attempted to identify a consensus of the reports and cited the most relevant articles. Priority was given to randomized controlled trials and expert reports when available, although much of the information herein relates to laboratory research.

Results: Actively growing fungal colonies can release volatile substances that have an unpleasant smell, leading to psychological responses in the occupants such as fatigue and nausea. Symptoms that are likely caused by indoor fungi include respiratory complaints that involve the nose and lungs, eye symptoms, and mucous membrane irritation. These adverse effects can occur by a variety of mechanisms, including IgE-mediated hypersensitivity, fungal infection, irritant reaction to spores or fungal metabolites, and possibly toxic reaction to mycotoxins.

Conclusions: Reduced fungal exposure can reasonably be expected to improve health. Removal of moisture from the indoors and proper maintenance of air filters can aid in prevention and elimination of fungi from the home environment. Small areas of present contamination can be cleaned with a dilute bleach solution, which kills viable colonies and removes their mycelia. If fungal contamination is not addressed early, substantial damage can occur, requiring professional remediation. Above all, the individual should not panic at the first sight of fungi growing in the home. Regular inspection and cleaning can prevent many fungus-related problems.

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INTRODUCTION

Indoor air quality has become a significant public health concern. The Environmental Protection Agency has reported that indoor air can be 2 to 5 times more polluted than outdoor air.¹ Since people spend up to 90% of their time indoors, this issue merits serious consideration. With new construction practices that reduce ventilation and inclusion of greater amounts of synthetic materials in homes that may produce volatile organic compounds, our lifestyles may be contributing to the epidemic of asthma and other respiratory illnesses.²

In addition to volatile chemicals and materials, adverse health effects from indoor exposures are suspected to be caused by the presence of a number of substances, including allergens such as dust mite, cockroach, pet dander, tobacco smoke, volatile organic compounds, and lead.³ A more recent concern has been the realization that many homes have substantial amounts of fungi (mold). A controversy, driven in part by the media coverage of adverse effects of fungal exposure, leads symptomatic individuals to conclude (rightly or wrongly) that fungi cause their symptoms. Fear of toxin exposures has generated debate over the possible toxic health effects of airborne fungi; however, several recent reviews discount the health impact of mycotoxin through indoor exposures.⁴ Unfortunately, media coverage of the so-called black or toxic mold has so extensively focused attention on

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the unproven harmful effects caused by mycotoxins produced by *Stachybotrys* that bona fide harmful effects of common molds, which are known to occur, have been downplayed or overlooked.⁵ This article, therefore, reviews the nontoxic harmful effects that poor indoor air quality caused by fungi can have on health.

The presence of fungi in the indoor environment should concern health care professionals and others because of the potential health effects of exposure to fungi and their metabolic products,⁶ the effect fungal contamination has on the structural integrity of a building,¹ and the negative aesthetic effects fungi can produce on both the human visual and olfactory systems.⁷⁻⁹ Although there is little question that a seriously contaminated building can experience structural damage and that a foul-smelling, fungus-filled structure is aesthetically displeasing,¹⁰ the issue of whether exposure to indoor fungi causes adverse health effects remains controversial.¹¹

FUNGAL MECHANISMS OF ADVERSE HEALTH EFFECTS

An evaluation of possible health effects usually occurs in response to reported symptoms by occupants of a suspected building. Symptoms related to fungal exposure need to be made plausible by proposing specific mechanisms by which they develop. Such symptoms include respiratory complaints that involve the nose and lungs, eye symptoms, and mucous membrane irritation. Since these systems come into direct contact with the outside environment, allergens or irritants could account for such symptoms in an affected individual. Adverse effects that are more difficult to explain include central nervous system symptoms, such as dizziness, headaches, fatigue, and memory loss, and gastrointestinal symptoms, such as nausea, vomiting and diarrhea, rashes not due to cutaneous infections, and muscle cramps. Although psychological responses from exposure to microbially derived volatile organic compounds (MVOCs) could account for some of the central nervous system effects, little evidence exists for MVOC-related toxic effects. Differences in susceptibility may lead to discrepant symptom histories from equally exposed people. Adverse health symptoms associated with fungal contact can occur through 1 of 4 mechanisms: IgE-mediated hypersensitivity, fungal infection, irritant reaction to spores or fungal metabolites, and toxic reaction to mycotoxins.

IgE-MEDIATED HYPERSENSITIVITY

Fungi, as is true for any inhaled airborne biologically derived substance, have the potential to induce the production of specific IgE antibodies in predisposed individuals. Once the specific IgE has formed, the affected individual becomes hypersensitive to subsequent exposure to the fungus. The important consideration here is that unaffected individuals can experience the same amount of exposure to fungi without manifesting any symptoms.

To determine whether an individual has fungal allergy, one must demonstrate the presence of specific IgE antibodies to at least one of the fungi to which the person has been exposed by either allergy skin tests or in vitro tests. The results of environmental testing can guide the IgE measurements, because numerous fungi exist that can be tested. In the absence of specific environmental data, the most common fungi found in contaminated homes include *Cladosporium*, *Aspergillus*, *Penicillium*, *Alternaria*, basidiospores, *Chaetomium*, *Periconia*, and *Stachybotrys*.¹² Unfortunately, since extracts are not available for testing of all of these fungi, an autologous extract may need to be prepared with the fungus recovered from the patient's own environment. Absolute certainty that the individual is clinically sensitive to the fungus would require challenge tests. Although the presence of specific IgE by itself does not confirm the presence of fungal allergy, when combined with a history of symptoms following exposure to the fungi, the diagnosis is as certain as it would be for any other inhalant allergen. Depending on how rigorously the hypothesis needs to be tested, this generally should suffice to determine fungal allergy.

FUNGAL INFECTION

Viable fungi have the potential to enter the respiratory tract and, once located there, could begin to grow.¹³ Most common indoor fungi do not easily grow inside the human body, because they prefer to grow near room temperature. For this reason, thermophilic fungi, such as *Aspergillus* spp, are more likely to cause infections. Most other fungi tend to infect the skin, nails, and other areas of the body that function at lower temperatures.

To determine whether a person has a fungal infection, one must demonstrate the presence of viable growing fungi in the human tissues that are affected. Ideally, this should be done by culturing biopsy specimen or lavage material, but at times radiographic evidence may suffice. Affected individuals usually have a known immunodeficiency or an unusually high exposure to viable spores or reside in a geographic region with endemic mycosis.

IRRITANT REACTIONS TO FUNGI AND THEIR METABOLITES

Irritant reactions are nonspecific responses to substances that cause inflammation in anyone exposed to them. The individual does not need to have a specific hypersensitivity to the substance to experience a reaction. Even so, each person may have a different degree of sensitivity to the exposure. For example, an individual who has asthma is more sensitive to irritants than someone who does not have asthma. Substances produced by fungi that are suspected to cause irritant reactions include MVOCs, ergosterols, and glucans.

MICROBIALY DERIVED VOLATILE ORGANIC COMPOUNDS

MVOCs are produced by fungi as a byproduct of their metabolism. Although species-specific volatiles may serve as

marker compounds for the selective detection of fungal species in indoor domestic and working environments,¹⁴ their health effects remain to be determined. MVOCs may cause nontoxic adverse effects on an irritant basis, or they may trigger psychological effects when present above the odor threshold for an individual. Toxic reactions do not likely occur as a result of MVOC exposure due to the low (parts per trillion) concentrations present in even the most contaminated environments.

The MVOCs may circulate from distant locations in a building or they may be produced by actively growing fungi that are not producing spores.¹⁵ Their concentrations therefore do not necessarily correspond with spore counts or allergen concentrations to which an affected person is exposed. A major problem is the lack of threshold values for irritant and psychological reactions, both in the home or workplace and in outdoor air. MVOCs have been suspected of causing symptoms such as lethargy, headache, and irritation of the eyes and mucous membranes of the nose and throat, but these health effects have not been confirmed by controlled exposure studies.¹⁶ It is believed that exposure to MVOCs may provoke direct sensory irritation, such as a burning sensation in the eyes, upper airways, and skin.¹⁷

GLUCANS AND ERGOSTEROL

Two fungal-derived substances that correlate with fungal biomass include ergosterol and β (1–3) D-glucan. In addition to serving as a marker for fungal biomass, β (1–3) D-glucan from mold cell walls is suspected to produce inflammation due to attachment to lipopolysaccharide-binding protein, CD14 cell surface protein, and toll-like 4 receptors. This protein binding results in local production of inflammatory cytokines with subsequent migration of inflammatory cells into the lung and the penetration of cytokines into the blood. These events lead to airways inflammation and systemic symptoms. Inhalation challenges in animals and field studies in humans have confirmed the relation between these effects and exposure to glucans.¹⁸

In a study of 2 schools, for example, the amount of airborne β (1–3) D-glucan was significantly higher in the problem school than in the control school (15.3 vs 2.9 ng/m³).¹⁹ The number of respiratory, as well as general, symptoms was higher among the pupils in the problem school. The extent of respiratory symptoms among people who had a history of allergies was similar to those without allergies in the control school but significantly higher in the problem school. The difficulty with this type of study is that numerous confounding factors, including the fungi themselves, could account for the symptoms. Although glucans can trigger inflammation in culture and animal studies, clinical evidence remains circumstantial until controlled challenge studies are performed.

TOXIC REACTIONS

The health effects of mycotoxins have been intensely studied, particularly in the context of contaminated food and feed; however, the amount of respiratory intake of mycotoxins

from air necessary to cause health effects has not undergone sufficient scrutiny. Toxic secondary metabolites have been found in airborne spores and airborne dust and bioaerosols.^{20,21} The health risks associated with this exposure to an individual cannot be estimated reliably unless the person's exposure to mycotoxins is determined qualitatively and quantitatively. In addition, the amount, duration, and route of exposure, other than ingestion necessary to cause any particular health effect, have not been determined for mycotoxins.

HEALTH EFFECTS DUE TO FUNGAL EXPOSURE

Exposure to indoor fungi can occur either by inhalation of airborne spores or allergens from disturbed dust. The correlation between the two appears to be poor, with dust representing a reservoir of accumulated fungal allergens and air representing spore exposure during a single moment of time. Although elimination of fungal-contaminated materials can stop the production of new spores and reduce airborne spore exposure, fungal allergens in dust may persist for a long time, causing episodic allergy symptoms in sensitive individuals when the dust is disturbed.

More than 80 genera of the major fungal groups have been associated with respiratory tract disorders. The most commonly identified belong to 3 distinctive fungal groups: Ascomycota, Basidiomycota, and Deuteromycota.²² Exposure to fungi has been linked to a wide range of illnesses,²³ including asthma and rhinitis.^{24–28} Occupants of buildings prone to excessive moisture more frequently develop mold-related allergies.²⁵ Twenty-six percent to 36% of homes have mold or moisture problems, whereas other indoor air quality measurements put those estimates as high as 50%.^{9,29} A recent study of samples collected from 160 homes across the country and tested for the presence of 10 different fungal species found mold to be present in every home tested.³⁰ Mold appears in most rooms whether suspected of having a problem or not. Mold is most frequently found on windowsills, refrigerator seals, spaces underneath kitchen sinks, and air vents.

Establishing typical or normal levels for indoor fungi is difficult and controversial. Many argue that the complete absence of airborne spores in indoor air is desirable; however, like cat allergen, zero exposure levels are not practical. A prospective cohort study on fungal air samples collected from infant bedrooms and main living areas in 1,000 homes in the northeast United States found mean indoor levels of 1033.5 CFU/m³ using malt extract agar and 846.0 CFU/m³ using DG-18 agar.³¹ In an examination of 12,026 fungal air samples (9,619 indoor samples and 2,407 outdoor samples) from 1,717 buildings located across the United States collected with an Andersen N6 sampler (Thermo Electron Corporation, Waltham, MA),²⁴ investigators reported mean indoor levels of 300 CFU/m³ and mean outdoor levels of 930 CFU/m³ with the mean indoor-outdoor ratio of 1.1. They also reported the 95th percentile of indoor collections to be 1,300 CFU/m³ and the 95th percentile of indoor to outdoor ratio to be 2.8. Clearly, critical values for indoor spore levels must be interpreted with reference to ambient outdoor levels and the

percentage of the total indoor level attributable to specific problem species such as *Aspergillus* or *Penicillium*. From these studies, it seems reasonable to expect that total airborne spore counts attributable to indoor sources greater than 1,000 spores/m³ indicate a concern and those greater than 10,000 spores/m³ indicate a definite problem.

Fungi affect humans in complex ways. They can cause diseases in a variety of ways through infectious, allergic, irritant, and toxic mechanisms as previously discussed. Fungal exposure is associated with exacerbations of asthma, although it remains unclear that this exposure causes the disease. Home dampness, which is associated with increased fungal exposure, and respiratory health effects are strongly associated.⁴

A number of studies have suggested that exposure to indoor fungi can trigger allergic symptoms.³²⁻³⁴ Exposure to *Alternaria*, *Aspergillus*, *Penicillium*, and *Trichoderma* has been shown to exacerbate symptoms of asthma and allergic rhinitis in sensitive individuals.^{35,36} More recently, a direct relationship was found between the amount of exposure to indoor fungi and the incidence of lower respiratory tract illnesses in children younger than 1 year.³⁷ Researchers tested 499 homes for the presence of 13 different fungi. Species that were most significantly associated with illness were airborne *Penicillium*, dust-borne *Cladosporium*, and dust-borne *Zygomycetes*. The study adjusted for sex, birth season, whether children were breast-fed or had siblings, and whether homes had visible water damage or mold or mildew. Children in homes that tested in the 90th percentile for 1 or more fungal taxa had an 86% increased risk of developing both wheezing and nonwheezing lower respiratory tract illness, such as pneumonia, croup, bronchitis, or bronchiolitis.

Li and associates³⁸ established a descending order for spore counts by location in 15 homes in Ontario, Canada. Overall counts were highest in living rooms, followed by family rooms, kitchens, bathrooms, and bedrooms. The highest diversity of spore types was found in the kitchens. Although the presence of damp conditions and carpets increased spore counts, forced air-heating systems, dehumidifiers, air filters, and air conditioners reduced them. Allergic symptoms were higher in people living in damp residences.

The most extensive study of the association between allergen reactivity and respiratory disease to date is the National Health and Nutrition Examination Survey in which 4,295 individuals were tested to 8 allergens (house dust, cat, dog, *Alternaria*, mixed giant and short ragweed, oak, perennial ryegrass, and Bermuda grass).³⁹ The prevalence of asthma and allergic rhinitis was directly correlated with the number of positive allergen skin test results. Although 8 allergens were tested, patients with asthma were 5.1 times more likely to react to house dust and to *Alternaria* and not to the others. When both asthma and allergic rhinitis were present, only house dust and *Alternaria* remained associated, highlighting the importance of fungal exposure and development of respiratory allergies.⁴⁰

CONTROLLING INDOOR FUNGI

Given the evidence that fungal exposure can trigger allergic diseases, it is reasonable to expect reduced exposure could lead to improved health. This has been demonstrated for several types of exposure, including dust mite,^{41,42} although controlled trials have not been conducted for fungal exposure. Buildings that are heavily contaminated will require extensive remediation by professional services; however, damage that is localized may be repairable by the homeowner. Successful remediation strategies require identification and elimination of sources of contamination.

CONTROL OF MOISTURE

The best way to control indoor mold is to remove its source. Many studies have looked at conditions in the indoor environment that encourage certain types of fungal growth. For the most part, fungal growth is encouraged in homes that are damp, have high humidity levels due to daily activities such as showering and cooking, or have cold surfaces onto which moisture can condense.⁴³ This creates moist microclimates, such as is found in a damp basement or a humid bathroom, which within an otherwise mold-free house can encourage fungal growth that may spread to the rest of the house.

Since fungal growth depends on moisture and a carbon source, the most important strategy for reducing or eliminating its growth is controlling the amount of moisture present.⁴⁴ A few simple measures significantly reduce available moisture: maintain indoor relative humidity at no greater than 50%; seal all leaks to prevent water accumulation; increase the use of bathroom and kitchen ventilation by using exhaust fans; ventilate clothes dryers to the outside; reduce the number of live indoor plants that must be watered; use air conditioning during the summer months at times of high humidity; heat all rooms in the winter and add heating to outside wall closets; use a dehumidifier in the basement or other areas of dampness; and use a sump pump in basements that are prone to flooding.⁴⁵

CLEANING AND REMOVAL OF CONTAMINATED MATERIALS

Building materials that encourage fungal growth include water damaged, aged organic materials with cellulose, such as wood, jute, wallpaper, and cardboard.⁴⁶ *Cladosporium* and *Penicillium* can reside in the air filters of air-handling units in a multistory office building. One can significantly decrease visible indoor mold growth by maintaining a low level of humidity in the home, keeping windows closed, repairing water leaks, and cleaning regularly with bleach-based products that have been shown to kill mold.¹⁵

Carpets, wallpaper, paneling, and heating or air conditioning systems are known to harbor fungal spores.⁴⁷ A recent study conducted at the University of Arizona showed that windowsills have the highest presence of mold, whereas bathroom shower grouts ranked the lowest, although still significant, with mold present in the shower grouts nearly

50% of the time. Frequent vacuuming can reduce fungal spore levels; however, replacement of carpeting with hardwood, tile, or other types of flooring materials is more effective. Since allergens may persist in house dust for long periods after their source has been eliminated, it may help to spray a dilute bleach and detergent solution to denature them.

Treatment of nonporous surfaces, such as wallpaper and paneling, with a dilute bleach and detergent solution can effectively kill growing fungi and prevent its recurrence. Treatment can also be performed on washable surfaces with a commercial fungicidal compound or an antibacterial product specific for molds or mildew, although not all products are equally effective.⁴⁸ Wallpaper or paneling may have to be removed to reduce a severe fungal contamination. Contaminated air ducts and filters may be cleaned to reduce fungal exposure as well.⁴⁹

It can take time for allergenic proteins to dissipate. For example, removal of fur-bearing pets and exterminating cockroaches decrease allergen count, but it often takes several months. After removing a cat from a home, it can take 6 months or longer for cat allergen levels to return to levels found in homes without cats. After cockroach extermination, it takes 6 months for allergen levels to decrease by 70% to 90%.⁵⁰ It is well known that at high concentrations sodium hypochlorite (the active ingredient in bleach) dissolves proteins and is capable of killing bacteria, viruses, and inactivating viral antigens. In a recent study, professional cleaning of kitchens and bedrooms with a commercial bleach solution led to reductions in cockroach allergen (Bla g 1); however, concentrations in more than half of the homes continued to be elevated.⁵¹

Recent studies also have shown that weak solutions of sodium hypochlorite can break up allergenic proteins. Chen and Eggleston⁵² also showed that chlorine bleach in concentrations commonly used in household products can significantly reduce the allergenicity of proteins. When purified mouse urinary allergen was incubated with a 2.4% sodium hypochlorite solution (molar ratio of 100:1) for 1 to 2 minutes, IgE binding on Western blot was greatly reduced. At higher sodium hypochlorite concentrations, the protein fragmented and eventually became undetectable. Matsui and co-workers⁵³ also investigated the ability of sodium hypochlorite to inactivate recombinant feline allergen and found that chlorine bleach renders it biologically inactive. In a dose response manner, the weakened allergen stimulated less and less histamine release from donor blood as measured by a basophile histamine release assay. The same effects were seen when cat hair extract was treated with chlorine bleach, although higher concentrations were required.

Similarly, chlorine bleach also appears to weaken or kill mold. Reynolds and colleagues³⁰ showed that sodium hypochlorite concentrations typically found in household cleaners reduced mold isolates from 160 volunteer homes to undetectable levels. Cultures of *Penicillium* and *Rhizopus*, 2 of the most commonly found species, grown from samples collected by adhesive tape were exposed to 2.4% sodium hypochlorite

for 5 minutes. Mold concentrations were reduced by 5- to 6-fold. Levels became undetectable after a 7-day incubation period at room temperature. Treatment of *Aspergillus fumigatus* with the same concentration of chlorine bleach reduced more than 90% of fungal allergen at all exposure times.³⁰

AIR FILTERS

Air filters can be used to remove particles from air. The most efficient type of filter is the high efficiency particle air (HEPA) filter.^{54,55} Electrostatic filters are less effective in removing spores from air environments.⁵⁶ Electronic air cleaners and negative ionizers have also been shown to have a moderate effect on spore counts.⁵⁷ Air filtration may be as good if not superior to mattress covers for dust mite and animal dander removal.⁵⁸

A healthy indoor environment requires the proper maintenance of the heating, ventilation, and air conditioning (HVAC) system. A contaminated HVAC can circulate spores through a building. Such contamination can be reduced by proper maintenance.⁴⁹ In one study, installation of a germicidal UV irradiation in the air conditioning system in a workplace produced a significant improvement in well-being among the office workers.⁵⁹

CONCLUSION

Fungi are commonly found in homes. In small concentrations, they are innocuous and most likely not associated with health effects. In the presence of moisture, either from condensation or intrusion, fungi can proliferate and cause problems. These problems may include structural damage to the building when extensive, aesthetic problems, such as an unpleasant appearance or foul smell, and direct health effects. These health effects generally occur due to allergy or irritation to fungal substances. Toxic reactions, although receiving much attention in the media, have not been shown to be a significant health problem.

Although much research needs to be done, the best known management of indoor fungal contamination at this time is prevention. Regular inspection for sources of moisture and their elimination is the most important strategy to prevent indoor fungal growth. When mold grows in our homes, dilute bleach solutions are effective in killing the viable mycelia and removing them from surfaces. HEPA filters can remove airborne spores, although it is better to eliminate their sources. If left unattended, fungi can cause extensive damage that requires professional remediation. Mold management is a case where an ounce of prevention truly is better than a pound of cure.

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Objectives: After reading this article, participants should be able to demonstrate an increased understanding of their knowledge of allergy/asthma/immunology clinical treatment and how this new information can be applied to their own practices.

Participants: This program is designed for physicians who are involved in providing patient care and who wish to advance their current knowledge in the field of allergy/asthma/immunology.

Credits: ACAAI designates each Annals CME Review Article for a maximum of 2 category 1 credits toward the AMA Physician's Recognition Award. Each physician should claim only those credits that he/she actually spent in the activity. The American College of Allergy, Asthma and Immunology is accredited by the Accreditation Council for Continuing Medical Education to sponsor continuing medical education for physicians.

CME Examination

1–5, Portnoy JM. 2005;94:313–320.

Self-Assessment Exam Questions

1. Which fungus is not commonly found in a mold-contaminated home?
 - a. *Cladosporium*
 - b. *Aspergillus*
 - c. basidiospores
 - d. *Stachybotrys*
 - e. *Ustilago*
2. The most effective way to kill fungi on nonporous surfaces is with:
 - a. air filtration
 - b. dilute bleach solution with detergent
 - c. soap and water
 - d. drying the surface
 - e. UV light
3. Sources of moisture in homes include all except:
 - a. intrusion
 - b. house plants
 - c. ventilation
 - d. leakage

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- e. cooking
4. Microbially derived volatile organic compounds cause respiratory inflammation via which mechanism?
- a. allergy
 - b. irritation
 - c. infection
 - d. mycotoxicosis
 - e. hypersensitivity pneumonitis

5. What concentration of spores is considered to be harmful to health?
- a. no level is safe
 - b. 100 spores/cm³
 - c. 1,000 spores/cm³
 - d. 10,000 spores/cm³
 - e. a harmful level has not been definitively defined