



Editorial

Relationship between exposure to fungi and asthma—an ongoing conundrum



The relationship between exposure to fungi and either the development of asthma, risk of sensitization, or worsening of symptoms has been difficult to define despite herculean efforts by some of the best researchers in the field. Yet without this understanding, it is difficult to determine how to take a medically (and environmentally) useful history, what type of tests to perform, which fungi to test for, how to use the resulting information to recommend medical treatment, which environmental interventions to recommend, and which patients would likely benefit from them. At best, the relationship between exposure to fungi and asthma has been framed in terms of correlations between exposure and selected asthma outcomes. Demonstration of causality requires prospective interventional studies that are more difficult to do and that must control for so many factors that they rarely are able to demonstrate the desired outcome.

Many studies have looked for an association between fungal exposure and development of asthma later in life.¹ While correlations have been demonstrated, it is not clear whether the exposure was the cause or whether it was a marker for another factor that increased the risk of developing asthma. This is the problem with association studies. It isn't clear whether moving to a less moldy house would have helped exposed children avoid that increased risk or whether reducing mold in the houses they lived in would have worked just as well. Another problem with this type of study is that total exposure is hard to measure since people move around, occupy a variety of environments and because the studies were done retrospectively, the data rely on intrinsically faulty recall. Bias could clearly have been introduced as individuals who subsequently developed asthma might have had clearer memories of their mold-exposed youth. Association studies are limited for they cannot define the effects of a solitary species versus multiple species over time and do not clarify if there is a "window" of sensitization where exposure increases or decreases risk of developing asthma. Additionally, there is no known well-defined safe level of fungi exposure that may alter sensitization.

Studies of the correlation between symptoms and recent exposure to fungi have demonstrated an association between moldy smell, visible mold, and dampness and increased asthma.² A study by Kercksmar et al³ was able to demonstrate a decrease in asthma symptom-days and lower rates of exacerbations in an environmental mold reduction group when compared with a control group. Remarkably, the investigators were able to demonstrate a decrease in fungal allergen exposure in the absence of a reduction in other allergen exposures (cockroach, rodent, dust mite) in the intervention

group suggesting that the fungal exposure itself caused symptoms. A subsequent Cochrane systematic review by Sauni et al⁴ found moderate to very low-quality evidence that repairing fungus-contaminated houses and offices reduced asthma-related symptoms and respiratory infections in adults. In addition, reducing fungal exposure in schools was found to reduce student visits due to respiratory infections. This points out the limitations of home-based interventions: the home is not the only location where asthmatic children are exposed to fungi. Exposure also occurs outdoors and in the workplace which, for children, usually is their school.

In the current issue of *the Annals*, Baxi et al⁵ report the results of an ongoing study that measured fungal exposure in schools and sensitization rates of students who attended those schools. In this prospective longitudinal cohort study, the population was composed of urban children with known asthma who had symptoms that were evaluated several times throughout the year. The investigators compared their classroom fungal exposure with asthma outcomes including symptom days, days of missed school and pulmonary function tests. To do this, 75 students from 8-10 schools answered a questionnaire and had allergy testing, spirometry and measurement of exhaled nitric oxide. Exposure was determined by sampling airborne spores in each classroom in which a student attended.

The investigators were able to demonstrate a small increase in symptom days for children who were sensitized to total fungi and/or to *Alternaria*, but not for students who were not sensitized to fungi. In addition, exposure to high amounts of *Cladosporium* and *Penicillium/Aspergillus* was not associated with increased symptoms. This suggests that an allergic mechanism may be responsible, at least in part, for the observed asthma morbidity in some these patients. Since the overall fungal sensitization rate was 18.9% and the rate for *Alternaria* was 9.9%, this increase in symptoms affected a minority of students.

While most classrooms had had detectable *Cladosporium*, *Penicillium/Aspergillus*, basidiospores, ascospores, and smuts, geometric mean spore counts were relatively low. A few classrooms had very high spore counts; yet, except for *Alternaria* the individual species was not a marker for increased symptoms. This suggests that some factor(s) other than exposure to fungal allergens may have been involved in the asthma morbidity. The World Health Organization identified damp environments, regardless of mold exposure, as a risk for asthma morbidity.⁶ What seems likely is that fungi contribute to morbidity either through allergic or nonallergic mechanisms and that a combination of sensitization and exposure contributes to part of this morbidity.

Identification and management of environmental exposures is the cornerstone of allergy practice; however, it is difficult to fully enumerate a patient's cumulative exposure to allergens and irritants

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that could be responsible for their symptoms. To fully understand which interventions to recommend for an individual patient, this type of information is necessary since many interventions are specific to the type of exposure to be reduced.⁷ Whereas exposure to fungi requires interventions that address overall moisture,⁸ dust mite reduction focuses on creating a mattress and pillow barrier and on reducing humidity and reservoirs.⁹ Once a method for measuring a patient's complete environmental exposure is developed, the results can be combined with information about their sensitization to the exposures to which they are subjected. Only then is it possible to recommend personalized interventions for each patient beyond general environmental hygiene.¹⁰

Many important questions remain regarding the clinical effect of fungi in the various environments to which a patient exposed including their school and home. The current study moves us closer to that type of understanding by demonstrating the clinical importance of fungus sensitization and exposure in schools. In addition, it provides support for the recommendation that schools should have healthy air so that students can do their best.

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References

1. Quansah R, Jaakkola MS, Hugg TT, et al. Residential dampness and molds and the risk of developing asthma: a systematic review and meta-analysis. *PLoS One*. 2012;7:e47526.
2. Dales RE, Burnett R, Zwanenburg H. Adverse health effects among adults exposed to home dampness and molds. *Am Rev Respir Dis*. 1991;143:505–509.
3. Kerckmar CM, Dearborn DG, Schluchter M, et al. Reduction in asthma morbidity in children as a result of home remediation aimed at moisture sources. *Environ Health Perspect*. 2006;114:1574–1580.
4. Sauni R, Verbeek JH, Uitti J, et al. Remediating buildings damaged by dampness and mould for preventing or reducing respiratory tract symptoms, infections and asthma. *Cochrane Database Syst Rev*. 2015;(2):CD007897.
5. Baxi S, Sheehan W, Sordillo J, et al. Association between fungal spore exposure in inner-city schools and asthma morbidity. *Ann Allergy Asthma Immunol*. 2019;122:610–615.
6. World Health Organization. *WHO guidelines for indoor air quality: dampness and mould*. Copenhagen, Denmark: World Health Organization; 2009. <http://www.euro.who.int/pubrequest>. Accessed December 13, 2016.
7. Le Cann P, Paulus H, Glorennec P, et al. Home environmental interventions for the prevention or control of allergic and respiratory diseases: what really works. *J Allergy Clin Immunol Pract*. 2017;5:66–79.
8. Larenas-Linnemann D, Baxi S, Phipatanakul W, et al. Clinical evaluation and management of patients with suspected fungus sensitivity. *J Allergy Clin Immunol Pract*. 2016;4:405–414.
9. Portnoy J, Miller JD, Williams PB, et al. Environmental assessment and exposure control of dust mites: a practice parameter. *Ann Allergy Asthma Immunol*. 2013;111:465–507.
10. Kader R, Kennedy K, Portnoy JM. Indoor environmental interventions and their effect on asthma outcomes. *Curr Allergy Asthma Rep*. 2018;18:17.