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Rigor, transparency, and disclosure needed in mold position paper

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To the Editor:

Position papers of the American Academy of Allergy, Asthma and Immunology (AAAAI) should meet high standards in 3 areas: rigorous evaluation of the scientific literature, transparency in the process for attaining "AAAAI position paper" status, and full disclosure of authors' potential conflicts of interest. Credibility cannot be attained without high standards in each area. Only credible evaluations of the state of the science and identification of gaps in knowledge can improve clinical care and research. We believe that the AAAAI position paper "The medical effects of mold exposure"¹ promotes continued and unproductive contention among stakeholders rather than credible advancement of the field.

The claim by the AAAAI position paper to "review the state of the science of mold-related disease" is questioned because many important studies are not considered, and those considered are often accepted or rejected without evidence-based discussion. Apparent statements of fact are not supported by any references, or are supported only by reference to an author's 1-page editorial,² an outdated article,³ or an article with negative results,⁴ while ignoring positive results from the same⁵ and other authors. The claim that "studies do not conclusively prove" an association between outdoor or indoor mold exposure and allergic rhinitis is true only in the sense that the scientific method enables rejection, not proof, of hypotheses. The inability of many studies to reject the hypothesis that mold causes allergic rhinitis provided the weight of evidence for the Institute of Medicine's conclusions placed into the Congressional Record by the Centers for Disease Control and Prevention: "airborne fungal allergens were most often associated with ... allergic rhinitis/conjunctivitis, allergic asthma, and hypersensitivity pneumonitis" (HP).⁶ This testimony and many studies also oppose the authors' unreferenced contention that "exposure to domestic specific indoor fungal spores is an extremely unlikely cause of HP." In addition to "specific indoor fungal spores," the AAAAI position paper should consider the complex

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mixtures of airborne fungi, mycotoxins, bacteria, endotoxins, antigens, LPSs, and volatile organic compounds observed in water-damaged buildings (WDBs) that show evidence of microbial amplification.⁷ The conclusion that “data supporting the role of fungi in CRS [chronic rhinosinusitis] are lacking” cites only an author’s editorial² while ignoring many supporting studies and a National Institutes of Health press release announcing discovery of a non-IgE–mediated immunologic mechanism for mold-induced CRS.⁸ Two articles are cited without critical discussion in concluding that the literature on mold-induced immune system dysregulation “is of particularly poor quality.” Only one 12-year-old article is cited to support the conclusion that “measurement of serum cytokines” and other immunologic parameters “is not appropriate.”³ Hundreds of studies indicate that many individual components of the complex mixtures in WDBs induce inflammation by stimulating proinflammatory cytokine production. The simultaneous convergence of components such as *Stachybotrys chartarum*, other fungi, their metabolites, and actinomycetes like *Streptomyces californicus* on this common mode of action causes synergistic cytokine production.⁹ This evidence indicates that complex-mixture components interact in illness production. It is inappropriate, therefore, to conclude that “mycotoxin-mediated disease” is “highly unlikely at best” because the concentration of any single component is unlikely to reach a threshold level. Yet the position paper reiterates this conclusion originally reached by the American College of Occupational and Environmental Medicine (ACOEM) on the basis of a spore instillation study in rodents and indoor spore concentrations.¹⁰ Neither the AAAAI nor the ACOEM papers discusses evidence indicating that concentrations of airborne mycotoxin-containing fungal fragments are orders of magnitude higher than spore concentrations,^{11, 12} and neither paper applies standard risk assessment procedures to the calculations. Both cytokine-mediated and mycotoxin-induced illnesses are consistent with multiple-system symptoms,^{5, 13} although the position paper states without reference that “the presence of mycotoxins ... is not consistent with ... a whole panoply of nonspecific complaints.” Multiple-system symptoms and objective indications of neurologic dysfunction and hormonal imbalances were carefully described in a prospective study of human exposure to WDBs, another study not considered in the position paper.⁷ Rigorous, not cursory, reviews of the literature are needed to improve clinical care and design studies that can further describe the mechanistic pathways through which exposure to WDBs affects human health.

The AAAAI Web site states that position papers “contain an extensive bibliography” based on literature review, but the position paper contains only 44 references. The Web site further states that “because of their weight, Position Statements are created only after careful discussion and review” and a “consensus of experts.” The signatories and endorsers (see this article’s Online Repository at www.jacionline.org), some of whom are AAAAI members, are unaware of any discussion or peer review. An original author of the paper withdrew his name because his contributions were rewritten to reach unsupported conclusions. The position paper apparently states the opinions of a few, rather than the “consensus of experts.”

Several medical journals recently retracted articles and implemented procedures to disclose authors’ conflicts of interest because of postpublication revelations that impugned credibility. The conflicts of interest of position paper authors should be fully revealed, particularly consultant-related and litigation-related activities that invoke position papers, so that informed conclusions can be reached. The signatories of this letter have submitted conflict of interest statements to the AAAAI and thank the Academy for this opportunity to present an opposing viewpoint.


Appendix. Supplementary data

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Disclosure of potential conflict of interest: R. C. Shoemaker owns stock in ChronicNeuroToxins.com, and is an expert witness for plaintiff and defense litigation. H. Ammann has served as an expert witness in mold exposure cases for the state of Washington and has served as an expert witness in mold litigation for which she was compensated. R. Lipsey is employed by Lipsey and Assoc, Inc, and has served as an expert witness for plaintiff and defense litigation. E. Montz is employed by and owns stock in Indoor Air Solutions, and has served as an expert witness in plaintiff and defense litigation. K. Carstens is owner/moderator of a nonprofit support group that assists mold victims, and his wife is pursuing a workmen's compensation claim as a result of illnesses caused by mold exposure in the office environment. J. L. Wright is the director of the Fungal Disease Resource Center, Inc. The rest of the authors have declared that they have no conflict of interest.

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