

### Mold Science and Conflict of Interest

*To the editor*—I am writing in response to your recent article on ACOEM's 2002 position statement on adverse human health effects associated with molds in the indoor environment.<sup>1</sup>

It is regrettable that this issue continues to take up editorial time and space. Those who read the article will quickly discern that the focus of this "critique" is not the ACOEM statement on mold, but ACOEM itself. The article is almost entirely devoted to Dr. Craner's concerns about a process that occurred more than six years ago. By contrast, essentially no evidence is presented that calls ACOEM's conclusions into question.

His strongest criticism of the ACOEM statement is that it did not contain an explicit statement describing an association between damp indoor environments (with or without mold) and development of upper respiratory tract symptoms. In making this point, Dr. Craner referred to the NAS report, *Damp Indoor Spaces and Health*, which was published two years after the ACOEM statement. He noted that NAS had found sufficient evidence of such an association, but he failed to note that NAS specifically found insufficient evidence of a causal relationship.

On this particular point, the ACOEM statement observed that indoor mold was believed to cause building-related symptoms, but that a causal relationship remained unproven. The statement also said that the growth of indoor mold indicated unacceptably damp environments "that must be corrected" and "should not be tolerated." In other words, there may be differences of nuance, but not content,

between the 2002 ACOEM statement and the 2004 NAS report.

More generally, Dr. Craner has selectively quoted from e-mails and other documents in a way that paints a misleading picture. In some cases, his statements are unsupported and incorrect.

However, this is an old issue; by the time this letter is published, nearly seven years will have passed since the events in question. More importantly, during the more than six years since the adoption of the ACOEM statement, no major medical organization or agency has reached conclusions that contradict the statement. Accordingly, we see few benefits to *IJOEH* readers or the broader OEM community for us to indulge in point by point refutation.

ACOEM and the *Journal of Occupational and Environmental Medicine* have explicit conflict-of-interest and disclosure policies, and both the College and the *Journal* continually seek to maintain and improve the scientific quality and accuracy of our publications. It is lamentable that Dr. Craner has unjustifiably maligned ACOEM, its officers, and the selfless volunteers who contribute substantial time and effort to improve the health of workers and the public through their professional activities.

ROBERT R. ORFORD, MD, MS, MPH,  
FACOEM

*President*

*American College of Occupational and Environmental Medicine*

#### *References*

1. Craner J. A Critique of the ACOEM Statement on Mold: Undisclosed Conflicts of Interest in the Creation of an 'Evidence-Based' Statement. *Int J Occup Environ Health*. 2008;14:283-98.

#### *ACOEM Response Fails to Address Central Issues*

*To the Editor*—The response of Dr. Orford, President of ACOEM, to my article is disappointing but not altogether unexpected. Dr. Orford's response regrettably corroborates my criticisms of the organization's lack of accountability toward its members and its stakeholders—the workers and others whose very interests ACOEM is dedicated to serve—and the resulting impact it has on the organization's reputation and credibility. In particular, the response further substantiates concerns that ACOEM's policies and actions are biased in favor of industry, as discussed in a number of recent publications.<sup>1-4</sup>

Dr. Orford claims that my article "paints a misleading picture," but does not refute the validity of any of the points made in it. Specifically, his response does not offer any evidence that contradicts the numerous internal ACOEM documents and deposition transcripts cited in my article that unambiguously show how the entire process by which the ACOEM Mold Statement was created was biased, unaccountable, and ultimately perverse. In his blanket defense of ACOEM, Dr. Orford fails to provide evidence to refute my conclusion that the Mold Statement has had significant, negative influence on ACOEM members' and other health and safety professionals' attitudes and actions toward patients with mold exposure and related health complaints and concerns, and that through legal decisions the Mold Statement has adversely impacted the health, safety, and financial security of

workers and individuals that ACOEM purports to represent.<sup>5</sup>

More specifically, the ACOEM response fails to address the critical point made in my article that the selection of Statement authors who had obvious biases and vested financial interests was never forthrightly disclosed to the ACOEM membership, peer reviewers, or the *Journal of Occupational and Environmental Medicine (JOEM)* which published the Statement. Dr. Orford does not explain or justify why some ACOEM members who had expressed an interest and/or who had known expertise in the subject matter were intentionally excluded from participating in the Mold Statement's development. Moreover, he does not comment on the haphazard peer review process which enabled the handful of meaningful peer review criticisms and recommendations received after the first draft of the Mold Statement to be quietly dismissed or merely given lip service in subsequent drafts and the final version. Dr. Orford totally ignores the disingenuous, sleight-of-hand transformation of an organizational position paper into an "evidence-based statement." Finally, he offers no justification for the hurried, unabridged publication of the Statement in *JOEM* without any independent editorial oversight. Instead, Dr. Orford rationalizes that ACOEM had "explicit conflict-of-interest and disclosure policies" in place to obviate the possibility of such preposterous events. If that were so, these policies should have prevented the issuance and publication of the ACOEM Mold Statement, which by the Council of Scientific Affairs' own admission remained "a defense argument" despite several revisions.

Instead of offering evidence to support his defense of ACOEM and *JOEM*, Dr. Orford inveighs obliquely and unpersuasively about the issue of causation of mold-related health effects. This allows him to disregard the salient point

made in my article that ACOEM Position Papers are intended not to serve as legal evidence documents to assist attorneys in proving or refuting causation in court, but rather to provide guidance for physicians and other health and safety professionals in caring for patients with occupational and environmental exposures.<sup>6</sup>

Dr. Orford suggests that my article is irrelevant because it recounts events that took place over six years ago. According to this specious argument, any communication concerning the history of medicine and its lessons for the future<sup>7</sup> would be irrelevant to occupational medicine—*particularly* if it is critical of ACOEM as an organization.<sup>8</sup> Here again, Dr. Orford's misdirected response implies that ACOEM leadership either does not understand or does not care about how its heavy-handed process of forging its version of an "evidence-based" guideline has resulted in substantive harm over time to the health and safety of workers, workplaces, and environments that ACOEM is dedicated to championing.<sup>9</sup>

Finally, this official ACOEM response ignores the Mold Statement's authors' own testimony admissions that they and their consulting firm or institution have reaped large monetary profits as consultants and expert witnesses testifying on behalf of defendants as a result of their "voluntary" authorship of the Mold Statement. Nor does Dr. Orford deny that certain ACOEM members have similarly benefited from basing their expert witness opinions and testimony for defendants in mold litigation by relying upon the organization's "evidence-based statement" as if an accountable, systematic, and unbiased process had led to its creation.

The many positive comments I have received in response to my article from ACOEM members—including two OEM residency directors—as well as physicians in other medical specialties, and professionals in the fields of industrial

hygiene, public health, indoor air quality, building science, mold remediation, and occupational and environmental health policy and regulation, substantively contradict the defensive tenor and content of Dr. Orford's letter. ACOEM's official response should lead these professions to question how much ACOEM really speaks for its membership or, for that matter, occupational and environmental medicine.

Sincerely,

JAMES CRANER, MD, MPH,  
FACOEM, FACP

#### References

1. LaDou J, Teitelbaum DT, Egilman DS, et al. American College of Occupational and Environmental Medicine (ACOEM): A professional association in service to industry. *Int J Occup Environ Health*. 2007;13:404-426.
2. LaDou J. Occupational medicine: the case for reform. *Am J Prev Med*. 2005; 28: 396-402.
3. Greenberg M. Commentary on effects of exposure to industry influence on ACOEM. *Int J Occup Env Health*. 2007; 13:427.
4. Teitelbaum DT, Egilman DS, Frank AL, et al. Industry partisanship of ACOEM. *Int J Occup Env Health*. 2008;14:81. Letters.
5. Grilli R, Magrini N, Penna A, et al. Practice guidelines developed by specialty societies: the need for a critical appraisal. *Lancet*. 2000;355:103-106.
6. ACOEM. Procedures for Creating ACOEM Position Papers and Guidance Statements.[Internet] Available from: <http://www.acoem.org/guidelines.aspx?id=560>
7. Gochfeld M. Occupational medicine practice in the United States since the industrial revolution. *J Occup Environ Med*. 2005;47:115-131.
8. McLellan RK. ACOEM denies industry partisanship. *Int J Occup Environ Health*. 2008;14:79. Letters.
9. ACOEM. Vision/Mission Statement. [Internet] Available from: <http://www.acoem.org/vision.aspx>.

#### *Literature on Mycotoxins and Human Health at the Time of the ACOEM Report*

*To the Editor*—We read with interest the review by Dr. Craner<sup>1</sup> outlining a long-standing controversy on fungal mycotoxins, exposures, and the possibility of disease. The obvious question is whether scientific lit-

erature supported an association of mycotoxins and human health effects at the time of the ACOEM position paper<sup>2</sup> and whether that evidence appeared correctly. In support of the association between mycotoxins and adverse human health effects, we would like to present a logic offered to the Institute of Medicine in 2003 during the committee meetings for the reviews of the IOM's report, "Damp Indoor Spaces and Health."<sup>3</sup> While the logic was disregarded at that time, it was also discussed at a public meeting sponsored by the Association of Occupational and Environmental Clinics in December 2003<sup>4</sup> and widely known within the community of scientists active on the topic, but simply not acknowledged by the many clinical reviews, state of the art papers, and position documents.

A substantial body of work, even as of May 2003, documented associations between fungi, moisture, and human pulmonary disease other than hypersensitivity pneumonitis and asthma, even attributable to mycotoxins. The first cluster of human pulmonary cases linked to fungal exposures, labeled "pulmonary mycotoxicosis," was described in 1975.<sup>5</sup> Later clusters and outbreaks of disease had been attributed to fungal TOXIC exposures but some or all cases failed to meet usual criteria for asthma or hypersensitivity pneumonitis.<sup>6-10</sup> Still, outbreaks of even hypersensitivity pneumonitis alone, investigated by the Centers for Disease Control,<sup>11-13</sup> had led to warnings about moisture and buildings as early as 1984 in CDC's *Morbidity and Mortality Weekly Report*, the standard public health tool in the U.S.<sup>14</sup> The presence of disease in infants has been widely discussed, and that controversy distracts from the point of this letter. Associations between moisture, bioaerosols, and disease were also documented for Usual Interstitial Pneumonitis<sup>15,16</sup> and for sarcoidosis.<sup>17,18</sup>

As controlled human exposures to study etiology are usually consid-

ered unethical in occupational and environmental health, scientists rely on congruence with animal and mechanistic studies.<sup>19</sup> Is there supporting evidence besides human epidemiology? Animal models are widely used to document specific organ effects, although routes of exposure and dose-extrapolation provide challenges. Does such evidence exist even though not cited as supporting of evidence in the recent mold-related clinical reviews? Exposure studies of mature whole animals<sup>20-22</sup> and infant animals<sup>23</sup> show diffuse pulmonary damage after nasal or tracheal instillation. Although these can be crude, represent massive exposure, and may overwhelm the pulmonary natural defenses, these studies do document that exposure can cause non-specific pulmonary inflammation, such as documented in the past. They are the standard for such testing and at least four different laboratories have produced the same results. Rand's studies have found the NOAE in adult mice to be <30 *Stachybotrys* spores/gm body weight.<sup>21</sup> What mechanism is likely and can that be expected to occur in humans at levels encountered in the home or office? In the words of a recent energetic interchange on the limits of animal models, misquoting Clint Eastwood, "a mouse should know its limitations."<sup>24</sup>

Are there studies of isolated human cell lines and exposures that allow direct extrapolation to human physiology and support the development of quantitative risk assessment for this hazard? Experimental evidence for the association of mycotoxins and human cell lines involved in pulmonary disease was first shown by investigators in 1987.<sup>25</sup> This work was in fact done at the Institute of which one of the ACOEM review authors in question was deputy director and a practicing toxicologist over many years. Dr. Sorenson and coworkers assessed cellular and immunological effects in isolated pulmonary cell lines at toxin con-

centrations likely to occur indoors using alveolar macrophage survival, thymocyte proliferation, and protein-synthesis inhibition. These are all outcomes affected by mycotoxins released by *Stachybotrys c* (recently reviewed by Pestka et al.<sup>26</sup>). The NIOSH investigators generated airborne dust, collected samples gravimetrically, extracted toxins, and created concentrations of toxins in a fluid bath corresponding to appropriate doses. They showed damage to pulmonary macrophages, implying the possibility of alveolar disease, from exposure to dusts. The ED<sub>50</sub> for protein synthesis for satratoxin H is 0.007 micromolar.<sup>27</sup> Subsequent work shows that each *Stachybotrys* spore can contain as much as ~1 millimolar macrocyclic trichothecenes,<sup>27</sup> released quickly (in minutes) to the local aqueous environment.<sup>28</sup> This implies effects at exposures over five orders of magnitude lower than that expected in the immediate environment around spores or spore fragments, and suggests that such exposures are likely to have very deleterious, local effects on the surrounding lung cells. These local effects do not require systemic absorption (the core of the ACOEM critique), are the major source of the lung damage seen in the animal studies, and are the likely initiating factors in the pathophysiology seen in humans.

The Sorenson 1987 paper suggested that mycotoxins have such local effects, identified a mechanism by which these occur, and allowed the development of dose-response data fifteen years before the publication of the ACOEM position paper. Of course it is only a single paper, but no one else had looked at the time. A search now on *Stachybotrys* in PubMed identifies hundreds of studies, many focused on mechanisms and other pertinent arguments. The issue is, though, what was known then, and the science cited here stands for itself.

Sincerely

MICHAEL J HODGSON, MD, MPH

DORR G DEARBORN, PH.D, MD  
Swetland Professor and Chair of  
Environmental Health Sciences  
Case Western Reserve University

The views expressed here represent those of the authors and not those of any Federal agency.

### References

1. Craner J. A critique of the ACOEM statement on mold: undisclosed conflicts of interest in the creation of an "evidence-based" statement. *Int J Occup Environ Health*. 2008, Oct-Dec;14(4): 283-98.
2. Adverse Human Health Effects Associated with Molds in the Indoor Environment. *J Occup Environ Med*. 2003; 45(5):470-478.
3. Institute of Medicine (IOM). Damp indoor spaces and health. Washington DC, National Academy of Science, 2004. [Internet] Available from: [www.nap.edu/books/030909934/html](http://www.nap.edu/books/030909934/html).
4. Mitchell C. AOEC/SOEH Clinicians' Panel on Management of Mold-Exposed Individuals. [Internet] Available from: <http://www.soeh.org/July04pdfs/ClinicianReport.pdf>
5. Emanuel DA, Wenzel FJ, Lawton BR. Pulmonary mycotoxicosis. *Chest*. 1975;67:293-7.
6. Auger PL, Gourdeau P, Miller JD. Clinical experience with patients suffering from a chronic fatigue-like syndrome and repeated upper respiratory infections in relation to airborne molds. *Am J Ind Med*. 1994; 25:41-2.
7. Johanning E, Landsbergis P, Gareis M, et al. Clinical experience and results of a Sentinel Health Investigation related to indoor fungal exposure. *Environ Health Perspect*. 1999;107 Suppl 3:489-94.
8. Johanning E, Biagini R, Hull D, et al. Health and immunology study following exposure to toxigenic fungi (*Stachybotrys chartarum*) in a water-damaged office environment. *Int Arch Occup Environ Health*. 1996;68:207-18
9. Hodgson MJ, Morey P, Leung W, et al. Pulmonary disease and mycotoxin exposure in Florida associated with *Aspergillus versicolor* and *Stachybotrys atra* exposure. *J Occup Environ Med*. 1998; 40:241-9
10. Croft WA, Jarvis BB, Yatawara CS. Airborne outbreak of trichothecene toxicosis. *Atmosph Environ*. 1986;20:549-552
11. Arnow P, Fink JN, Schlueter DP, et al. Early detection of hypersensitivity pneumonitis in office workers. *Am J Med*. 1978;64:236-42
12. Hodgson MJ, Morey P, Attfield M, et al. Pulmonary disease in an office building: single-breath carbon-monoxide diffusing capacity as a cross-sectional field tool. *Arch Environ Health*. 1985;40:96-101.
13. Hodgson MJ, Morey PR, Simon J, et al. Acute and chronic hypersensitivity pneumonitis from the same source. *Am J Epidemiol*. 1987; 1 25:631-8.
14. Anonymous. Outbreaks of respiratory illness among employees in large office buildings. *MMWR*. 1984;33:506-513.
15. Mullen J, Hodgson M, DeGraff CA, Godar T. A case-control study of diffuse interstitial pneumonitis. *Journal of Occupational and Environmental Medicine*. 1998;40(4):1-5.
16. Baumgartner KB, Samet JM, Coultas DB. Occupational and environmental risk factors for idiopathic pulmonary fibrosis: a multicenter case-control study. *Collaborating Centers. Am J Epidemiol*. 152:307-15 (2000).
17. Ortiz C, Hodgson MJ, McNally D, Storey E. A case-control study of sarcoidosis. In: Johanning E, editor. *Bioaerosols, Fungi, and Mycotoxins: Health Effects, Assessment, Prevention, and Control*. Proceedings of the Third International Conference on Bio-aerosols. Mount Sinai School of Medicine, Federal Occupational Health, New York, NY. 1999: 476-481
18. Kucera GP, Rybicki BA, Kirkey KL. Occupational risk factors for sarcoidosis in African-American siblings. *Chest* 123: 1527-35 (2003)
19. Brennan TA. Untangling causation issues in law and medicine: hazardous substance litigation. *Ann Intern Med*. 1987;107:741-7.
20. Nikulin M, Reijula K, Jarvis BB, Hintsikka EL. Experimental lung mycotoxicosis in mice induced by *Stachybotrys atra*. *Int J Exp Pathol*. 1996;77:213-8.
21. Flemming J, Hudson B, Rand TG. Comparison of inflammatory and cytotoxic lung responses in mice after intratracheal exposure to spores of two different *Stachybotrys chartarum* strains. *Toxicol Sci*. 2004;78:267-75.
22. Rao CY, Brain JD, Burge HA. Reduction of pulmonary toxicity of *Stachybotrys chartarum* spores by methanol extraction of mycotoxins. *Appl Environ Microbiol*. 2000;66:2817-21.
23. Yike I, Dearborn D. Pulmonary effects of *Stachybotrys chartarum* in animal studies. *Adv Appl Microbiol*. 2004;55: 241-73.
24. Wenzel S, Holgate TS. Pro/Con Editorial: Rebuttal from Drs. Wenzel and Holgate. *Amer J of Resp and Critical Care Med*. 2006;174:1177-1178.
25. Sorenson WG, Frazer DG, Jarvis BB, et al. Trichothecene mycotoxins in aerosolized conidia of *Stachybotrys atra* *Appl Environ Microbiol*. 1987 Jun; 53(6):1370-5.
26. Pestka JJ, Yike I, Dearborn DG, et al. *Stachybotrys chartarum*, trichothecene mycotoxins, and damp building-related illness: new insights into a public health enigma. *Toxicol Sci*. 2008;104:4-26
27. Yike I, Dearborn D. Pulmonary effects of *Stachybotrys chartarum* in animal studies. *Adv Appl Microbiol*. 2004;55: 241-73
28. Yike I, Rand TG, Dearborn DG. Acute inflammatory responses to *Stachybotrys chartarum* in the lungs of infant rats: time course and possible mechanisms. *Toxicol Sci*. 2005 Apr;84(2):408-17. Epub 2005 Jan 12.

### Courtroom Impact of the ACOEM Statement on Mold

To the Editor—As an attorney who practices primarily in the construction defect arena, I read Dr. Craner's commentary<sup>1</sup> with particular interest. My practice includes both prosecution as well as defense of owners and developers in residential and commercial property cases, many of which have a "mold" component. Indeed, my deposition of Dr. Bruce Kelman in the *Kerruish v. Kimball Hill Homes* case is cited in Craner's article.

In my many years of experience on both the plaintiff and defense sides of the "mold" debate, i.e., whether and to what extent indoor mold arising in water-damaged buildings is a valid, diagnosable, treatable, and preventable environmental health disorder, I have, since its publication, consistently observed defense experts relying upon the ACOEM's statement on "Adverse Human Health Effects Associated with Molds in the Indoor Environment"<sup>2</sup> as the "final" scientific word on the issue. Plaintiff experts, on the other hand, are routinely challenged to defend and prove the scientific basis of their affirmative opinions as a rebuttal to the ACOEM Statement.

Those of us who practice in this area have long suspected that the heretofore concealed process by which the ACOEM Mold Statement was created was flawed and biased, not only in its content and balance as an "evidence-based" guideline, but especially in its tone, which blatantly comes across as a "defense argument" to any attorney willing to read it. How can any advocate come away with any other impression when the same experts who were profiting from defense medical/legal consultations and testifying in mold-related litigation were incredibly selected by ACOEM to be the primary authors of its organizational position statement on this subject?

Dr. Craner's critique has finally brought some light and balance to

the issue. Construction defects and resultant litigation related to indoor mold will go on, but I strongly suspect the ACOEM Mold Statement will no longer receive the same level of reliance or respect that it has been unduly given up to this point by attorneys and experts. ACOEM, as an organization, has major credibility problems as a

result of this document and would do well to follow Dr. Craner's recommendations to restore organizational integrity and respect.

DAVID A. FRENZNICK, JD  
*Wilke, Fleury, Hoffelt, Gould &  
Birney, LLP*  
Sacramento, CA

### *References*

1. Craner J. A critique of the ACOEM statement on mold: undisclosed conflicts of interest in the creation of an "evidence-based" statement. *Int J Occup Environ Health*. 2008 Oct-Dec;14(4): 283-98.
2. Adverse Human Health Effects Associated with Molds in the Indoor Environment. *Journal of Occupational and Environmental Medicine*:Volume 45(5): 470-478 (2003).