



JOHNS HOPKINS
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SCHOOL of PUBLIC HEALTH

**Association of Occupational and Environmental Clinics
Society for Occupational and Environmental Health**

**AOEC/SOEH Clinicians' Panel on Management of
Mold-Exposed Individuals**

**Report of a Workshop at the
Johns Hopkins Bloomberg School of Public Health
December 11-12, 2003**

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Sponsors

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Executive Summary

On December 11-12, 2003, a workshop on the management of mold-exposed individuals was held at the Johns Hopkins Bloomberg School of Public Health. The workshop had three goals: (1) to assist clinicians seeing patients with concerns about mold-related health problems; (2) to assist others -- building owners and managers, employers, workers, insurers, and regulatory bodies -- to understand clinical issues involved, so that they can better prevent or manage mold-related problems; and (3) to identify potential areas of research related to clinical management of mold-exposed individuals.

INTRODUCTION

Concerns about the health effects of mold, and the clinical management of mold-exposed individuals, have been increasing in the United States. On December 11-12, 2003 the Association of Occupational and Environmental Clinics (AOEC) and Society for Occupational and Environmental Health (SOEH) held the first in a series of workshops on mold and its health effects. The purpose of the workshops was to help AOEC and SOEH members – clinicians and occupational safety and health professionals – to assess, manage, and prevent health effects related to mold exposures. The purpose of the December workshop, held at the Johns Hopkins Bloomberg School of Public Health, was to begin to develop a set of recommendations and an agenda for future research related to the prevention, evaluation, diagnosis, treatment and management of mold-related health problems.

One measure of interest in the subject is the amount of legal, regulatory, and economic activity around mold issues. Several different groups are exploring issues related to mold, including experts in heating, ventilation, and air conditioning, experts in building science, and experts in safety. However, many of these groups have expressed similar frustration regarding guidance from the medical community on exactly what kinds of health effects, dose response, and mitigation measures can reasonably be predicted to occur when people are exposed to mold indoors.

REVIEW OF RECENT PROGRESS IN THE HEALTH EFFECTS OF MOLD

There have been several recent meetings and proceedings on the subject of the health effects of mold. In general, the panelists noted that even with the recent attention, there was still considerable discussion and difference of opinion when it came to some of the most important questions related to mold's health effects, for example whether and to what extent exposure to molds causes non-immunologic toxic effects that have been widely circulated in the media.

There was extensive discussion related to the management of health effects. Dr. Storey discussed some of the work at the University of Connecticut related to developing recommendations for the clinical management of mold health effects. Much of the discussion centered on questions that were addressed in subsequent sections of the meeting, particularly with respect to issues such as return to specific environments, abatement, and the utility of specific diagnostic or treatment modalities.

A similar theme, though with different specific answers, was noted in a recent meeting in Saratoga Springs. Dr. Johanning reported that while specific papers and the proceedings had yet to be published, there was considerable interest in issues related to the clinical management of mold-exposed individuals.

IMMUNOLOGIC HEALTH EFFECTS OF MOLD

The first session addressed questions related to the effects of mold on allergic/immunologic disorders. There was a consensus among participants on many of the allergic disorders, which have been extensively reviewed elsewhere (1-5). The panel agreed that there are as yet important questions related to allergic disorders and mold, including:

- ♦ Mechanisms: what do we know about the relationship between specific molds and the onset of allergic disorders?
- ♦ While there is evidence that exposure to molds is associated with an increase in atopy among children (6;7), and good evidence that it can exacerbate pre-existing asthma in adults, what is the risk that exposures of adults to mold-contaminated environments cause new-onset allergic disorders, including asthma (8-12)? What do we understand of dose-response?
- ♦ What is the utility of imaging, culture, skin testing, RAST, and other technologies in the diagnosis and management of mold-exposed individuals?
- ♦ Is there any benefit to specific environmental assessment (e.g., identification and quantification of specific molds) in the diagnosis and management of patients?
- ♦ How do we think about “clearance”, that is, return of allergic individuals to environments where they have had problems? Is there a role for testing/environmental assessment in this situation?
- ♦ In addition to immediate hypersensitivity, how do inflammation and irritation contribute to allergic disorders associated with mold (13-15)?
- ♦ How do we distinguish between symptoms associated with mold, bacteria, components such as endotoxin, the irritant properties of microbial volatile organic compounds (MVOCs), and particulates (16)?

The panel felt that it was important to develop a better understanding of the precise mechanisms and contribution of different constituents in indoor air (including molds) because of the significance for prevention, abatement and remediation. In addition, the disparity between clinical experience and epidemiology was noted as an opportunity for further research. For example, while panelists were comfortable ascribing individual cases of asthma to mold exposure in heavily contaminated buildings, the absence of population-based data in this area was seen as a need. Finally, the panel noted that there were particular symptoms or symptom complexes – for example, metallic taste and laryngitis – that were frequently observed but whose mechanisms, and relationship to mold exposure, had not been adequately explained. The panelists also discussed the management of mold-exposed individuals with allergic disorders and agreed that given current knowledge, there were no objective (numerical) criteria for returning patients with symptoms to specific environments where symptoms had previously been provoked.

Non-allergic immunologic pulmonary disorders were also briefly discussed. These include disorders such as hypersensitivity pneumonitis (HP), also known as extrinsic allergic alveolitis, diffuse interstitial pneumonitis (sometimes termed organic toxic dust syndrome), and usual interstitial pneumonitis (UIP). HP is known to be caused by molds, and is typically seen in occupationally exposed populations such as farmers or bird breeders. Although it is relatively uncommon in typical office and residential settings, it has been reported in cases of heavy contamination (17-19).

There was considerable interest in symptoms related to the upper airway. There is interest in the extent to which molds may contribute to the development of rhinitis, sinusitis, and laryngitis, and whether some of these effects could be a combination of both allergic and irritant properties of the molds (20-25). There was also some consideration of the role that odors might play a role in these conditions, although there was not a great of data related to this question.

Finally, there was some discussion of the potential mechanisms by which toxic metabolic products (mycotoxins) might affect immune function (26-28). Although *in vitro* and *in vivo* studies have shown that some mycotoxins affect immune function, there is insufficient dose-response or exposure data in humans to know whether these potential effects are clinically important with common inhalation exposures.

NON-IMMUNOLOGIC HEALTH EFFECTS

There was extensive discussion of the non-allergic health effects of mold, which have been recently reviewed elsewhere (29-31). The panel discussed some of the current research into possible mechanisms of injury for mold, including toxic, inflammatory, and immunologic reactions.

Dr. Dearborn provided a review and an update on studies conducted in Cleveland involving infants with pulmonary hemorrhage (32;33). Studies at the time and subsequently have raised the possibility that toxic products of various fungi including *Stachybotrys* may produce an inflammatory response (26;34-36). However, there is considerable controversy over the clinical significance of these studies, and whether such effects have relevance to populations exposed to mold (31;37-42). The panel agreed that a number of scientific problems limited the conclusions that could be reached regarding non-allergic, non-infectious diseases related to mold exposures:

- ◆ The chemistry of fungi and their toxic products are incompletely understood.
- ◆ There are no reliable, validated biological markers of exposure to either whole fungi or toxic products of fungi.
- ◆ The biological behavior of potentially toxic compounds in humans is poorly understood. This extends to the pharmacodynamics of virtually all of the toxic compounds produced by fungi.

The panel did not discuss the infectious diseases related to mold exposure, though it is recognized that these may be significant in some circumstances (31).

RECOMMENDATIONS FOR FUTURE RESEARCH

The panel outlined some of its recommendations for future research in a number of areas. The broad categories of research included: (1) exposure models; (2) epidemiology of exposure and health outcomes; (3) biological markers of exposure and health outcomes; (4) intervention effectiveness studies related to exposure; and (5) treatment effectiveness studies.

Table 1. Workshop recommendations for future research areas related to health effects of mold and management of mold-exposed individuals

Exposure

Integrated exposure-dose studies

Better understanding of different source contributions (e.g., furniture, clothing)

Cumulative exposure

Role of different exposure routes (e.g., inhalation, dermal, ingestion, etc.)

Exposures associated with specific environments (e.g., portable classrooms)

Assessment of para-occupational (take home) secondary exposures in remediation workers

Epidemiology

Need exposed populations (both those using PPE and those without PPE) for case-control and cohort studies

- ◆ Maintenance workers
- ◆ Remediation workers
- ◆ Construction workers
- ◆ Teachers, office workers

Use of existing data bases for epidemiologic research

- ◆ NIOSH SENSOR data
- ◆ AOEC data base

Prospective studies of exposure and sensitization in exposed populations

Development of clinical populations for both exposure and outcome studies

- ◆ Patients with specific disease outcomes (e.g., chronic bronchitis and housing conditions)

Development of questionnaires and indices on specific exposures and outcomes of interest

Need to assess new exposure and outcome biomarkers in population-based studies

Studies of potential risk factors (e.g., atopy)

Markers of Exposure and Health Outcomes

Need to develop biological markers of exposure and effects

Effectiveness and relevance of sampling as a predictor of health outcomes

Use of biomarkers in exhaled breath

Pharmacokinetic studies – kinetic markers and studies of toxic products and mycotoxins

Controlled exposure studies using microbial volatile organic compounds (MVOCs)

Mechanisms of Injury and Effect

Pathologic studies of affected organs (e.g., lung)
Role of the skin as a route of exposure, as a target organ for local reactions, and its role in systemic absorption and sensitization
Clinical studies in affected patients
Role of mold in rhino-sinusitis, eosinophilic rhino-sinusitis
In vivo and *in vitro* mechanistic studies of mycotoxin injury
Role of confounders (ETS, VOCs, mites, endotoxins, glucans) in sensitization and effort trigger and progression
Relationship of mold toxicity to multiple chemical sensitivity
Mechanisms of acute versus chronic effects
Psychological impact of home/workplace being contaminated
Studies of cognitive and developmental effects

Intervention Effectiveness to Reduce Exposures

Use of “N-of-1” clinical trials to assess the effectiveness of different treatments
Use of “clearance” levels
Effectiveness of personal protective equipment in reducing exposures and health effects
Effect of remediation on exposures in field-based, real-world studies
Effectiveness of legal/regulatory standards (e.g., New York and Canada) in exposure reduction

Management and Treatment Effectiveness

Effectiveness of different modalities, including those in the cognitive and affective/behavioral domains
Effectiveness of diagnostic techniques in mold-related rhino-sinusitis
Validity studies of alternative diagnostic tools such as immunologic tests, visual contrast studies
Randomized controlled trials of alternative therapies such as cholestyramine
Risk communication strategies

NEXT STEPS

The panel discussed the ways in which this process could contribute to an improved understanding of the health effects of mold and its management. The panel members elected to produce two documents as the logical next step in this process. The first document would be a series of recommendations for clinicians related to the evaluation and management of health concerns related to mold and indoor environments. The second would be a more detailed discussion of etiologic theories of disorders related to mold, moisture, and indoor environments, with research recommendations. The report outlines are described below:

Deliverable 1. Evaluation and Management of Health Concerns Related to Mold and Indoor Environments

1. Introduction and Review
2. Diagnostic/management protocol (for AOEC clinicians)

This document would address practical clinical issues of importance to providers working with mold-exposed individuals. It would review current recommendations for diagnoses that have been attributed to mold, including evidence-based recommendations for diagnosis and treatment.

Deliverable 2: Theories of Etiology of Disorders Related to Mold, Moisture, and Indoor Environments

1. Introduction/Moisture
2. Irritation
3. Upper Airway Effects
4. Lower Airway Effects
5. Pulmonary
6. Dermal
7. Central Nervous System
8. Biomarkers
9. Specific Toxins and End-Organ Findings

This document would address etiologic theories and potentially fruitful avenues of scientific investigation related to the health effects of mold. The emphasis would be on research related to clinical outcomes, particularly those areas that might be most important to improving the prevention, diagnosis, and management of patients concerned about mold exposures.

These manuscripts would be prepared for submission for publication some time in the mid- to late 2004, following the culminating conference in June in Washington, DC.

ATTENDEES

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AGENDA

December 11, 2003

- 8:00 AM Welcome and Introductions
8:30 AM Review of the Committee's Mission/Charge
9:00 AM Review of recent meetings/consensus statements on mold
Draft Monograph on Mold
Saratoga meeting
Detroit Meeting
10:00 AM Discussion 1: Is there a consensus concerning the assessment, diagnosis and management of mold-exposed individuals with allergic disorders? Specific controversies to be considered in the discussion, in addition to general questions of diagnosis and treatment: return to work, "clearance levels", causation of *de novo* cases of allergic disorders...

1:00 PM Lunch
2:00 PM Review: Update on Pulmonary Hemosiderosis
2:30 PM Review: Biological markers of exposure to fungi and their toxic products
3:00 PM Discussion 2: What are the potential explanations for the non-allergic health effects of mold exposure? What is the current evidence for/against these potential explanations?

6:00 PM Adjourn

December 12, 2003

- 9:00 AM Discussion 3: Is there a consensus regarding research needed to confirm/refute various theories of the pathogenesis of mold/fungi exposure?
11:00 AM Discussion 4: Is there a consensus regarding the assessment and management of mold-exposed individuals with non-allergic health effects?
1:00 PM Writing assignments and follow-up
2:00 PM Adjourn

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