Overcoming the Barriers to Establishing Quantitative Health Guidance Values for Airborne Mold
The Association Between Mold and Asthma

Evidence-Based Conclusions from Current Research

- IOM (2004) and WHO (2009) conclude “sufficient evidence of association” between exposure to damp and moldy conditions and asthma, wheeze, rhinitis and HP, but find insufficient evidence for establishing quantitative health guidance values to inform risk.
- Mendell et al. 2011 concludes “based on available evidence, the presence of dampness, water damage, visible mold or mold odors or a history of water damage provides more reliable indicators of D/M related health risks than do current quantitative microbiologic assessments” and further concludes “current evidence does not support (even) measuring specific indoor microbiologic factors to guide health-protective actions.”

The Gap Between Research and Practice

- Industrial hygienists and environmental consultants in the U.S. and around the world routinely conduct indoor air sampling for mold in their IAQ investigations and use the lab results together with other findings to assess risk to occupants and to guide recommendations for health-protective actions and for assessing post-remediation clearance.
AIHA Air Sampling Guidance

• “Airborne culturable and countable fungal data can be used to determine the acceptability of indoor air quality to avoid an exposure that might result in allergy or allergic symptoms.” (AIHA Greenbook - 2008 p. 173)

• “Air sampling for viable fungal propagules is a useful tool to detect fungal contamination; however, it should be used in conjunction with…a careful visual inspection…the significant presence of fungi in indoor air not present or as a minor component of the outdoor air mycoflora is taken as unacceptable from a health and building performance point of view” (AIHA Fieldguide - 2005 p. 115)

• “TLV’s for culturable or total fungal structures are not scientifically supportable…” (AIHA Greenbook - 2008 p. 173)

• The interpretation of airborne fungal data is therefore left to the professional judgement of the industrial hygienist or other qualified environmental practitioner.
Using Air Sampling as a Tool in Guiding Health Protective Advice

Mold growth conditions in PTAC units in high-end residential high rise

<table>
<thead>
<tr>
<th>Airborne mold (spore trap) with PTAC unit off</th>
<th>Airborne mold (spore trap) with PTAC unit on</th>
</tr>
</thead>
<tbody>
<tr>
<td>MBR: <em>Pen/Asp</em> 93 structures/m³&lt;br&gt;Outdoor: <em>Pen/Asp</em> 0 structures/m³</td>
<td>MBR: <em>Pen/Asp</em> 2800 structures/m³&lt;br&gt;Outdoor: <em>Pen/Asp</em> 110 structures/m³</td>
</tr>
</tbody>
</table>

Outcome: 1) Resident discontinued occupancy 2) Client’s respiratory symptoms resolved
Using Air Sampling as a Tool in Guiding Health Protective Advice

Mold growth conditions in PTAC units in high-end residential high rise

<table>
<thead>
<tr>
<th>Fiberglass insulation (culture)</th>
<th>Airborne mold with PTAC unit on (spore trap)</th>
</tr>
</thead>
</table>
| *Cladosporium cladosporiodes*: 260,000 CFU  
  *Penicillium corylophilum*: 420,000 CFU  
  *Yeast*: 130,000 CFU | *Living room*: *Penicillium/Aspergillus* 8900 structures/m³  
  *Outdoor*: *Penicillium/Aspergillus* 110 structures/m³ |

Outcome: 1) Resident discontinued occupancy 2) Client’s respiratory symptoms resolved
Case #2

**Using Air Sampling as a Tool in Guiding Health Protective Advice**

Mold growth conditions in supply trunk of HVAC system in landmark church

<table>
<thead>
<tr>
<th>Airborne mold (spore trap)</th>
<th>HVAC system on</th>
<th>Indoor Pen/Asp 11,000 structures/m³</th>
<th>Outdoor Pen/Asp 0 structures/m³</th>
</tr>
</thead>
<tbody>
<tr>
<td>Airborne mold (spore trap)</td>
<td>HVAC system off</td>
<td>Indoor Pen/Asp 760 structures/m³</td>
<td>Outdoor Pen/Asp 0 structures/m³</td>
</tr>
</tbody>
</table>

Outcome: 1) Use of rooftop unit discontinued 2) Airborne mold levels declined substantially
Can Air Sampling Detect Hidden Mold Growth?

Yes. Sometimes air sampling can detect hidden mold growth and inform risk to occupants.

Dining Room Pen/Asp 15,000 structures/m³
Family Room/Kitchen Pen/Asp 13,000 structures/m³
Master Bedroom Pen/Asp 10,000 structures/m³
Outdoors Pen/Asp 1,100 structures/m³

Outcome: 1) Occupants permanently relocated 2) Significant improvement in client’s respiratory condition (no O₂)
Common Denominators in IPF/HP Cases: High-End Housing, Hidden Mold

- Air sampling can be a valuable tool in assessing hidden mold growth conditions.
- But, air sampling should never be used as a standalone tool, and there are no authoritative quantitative guidelines for interpreting mold air sampling laboratory results.
- A properly conducted mold inspection should always include the four WHO markers for D/M conditions: 1) visible mold; 2) visible water damage; 3) excessive surface moisture – observed or measured, and; 4) moldy odor
- In addition, an inspection should always include learning the water damage history of the premises and inspecting all components of the HVAC system.
- Finding the hiding places often means conducting minimally invasive inspections.
### Air and Surface Sample Results from Initial Inspection

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct microscopic examination (air – spore trap)</td>
<td></td>
</tr>
<tr>
<td>Indoor</td>
<td><em>Pen/Asp</em> 27 spores/m³, <em>Stachybotrys</em>: 36 spores/m³</td>
</tr>
<tr>
<td>Outdoor</td>
<td><em>Pen/Asp</em> 0 spores/m³, <em>Stachybotrys</em>: 0 spores/m³</td>
</tr>
</tbody>
</table>

**Revealed during inspection**

- *Stachybotrys* - very high
- *Ulocladium* - very high
- *Cladosporium* - very high

**Outcomes**

1) Occupants temporarily relocated
2) Resumed occupancy post-remediation
3) Client’s conditions resolved.
The Problem Caused by the Absence of HGV/MRL’s for Airborne Mold

The interpretation of laboratory results are left to the professional judgement of individual practitioners resulting in a wide range of interpretation criteria, undermining the credibility of the laboratory results as a risk assessment tool in the eyes of clients, fellow practitioners, physicians and the courts.
Establishing HGV’s for Airborne Mold – The 30 Year Quest


These 15 agencies and organizations set MRL’s for indoor air at 150 - 1000 CFUs/m³. These risk levels were based on personal experiences (professional judgement), not on dose response-based studies, and in each case were withdrawn or allowed to expire.

Authors cite urgent need for dose response-based studies and for development and widespread use of standard protocols for air sampling.
Overcoming the Barriers to Establishing HGV’s for Airborne Mold

- Many barriers to the establishment of PEL’s and TLV’s cited by the AIHA (Green Book)
  - Variation in individual susceptibility
  - Variations in sampling and analytical methods
  - Temporal variability in airborne mold levels
  - Absence of dose-response based risk assessment data

- Overcoming the barriers
  - Make clear that HGV’s are for atopic individuals
  - Make clear that HGV’s are for most commonly used method (spore trap) - telephone survey of major labs - spore trap sampling 15-20x more common than culture sampling (>1,000,000/yr). AIHA Field Guide recognizes spore trap sampling as useful tool in assessing indoor air quality.
  - Make clear that HGV’s are subject to false negatives but not false positives
  - Assess current scientific evidence; encourage research community to design study methods such that results can be used to inform HGV’s; design and conduct dose-response based research studies.
Bridging the Gap between Environmental Research & Practice

Identifying the Research Questions

In 2015, Mendell issued *A Research Agenda on Assessing and Remediating Home Dampness and Mold to Reduce Dampness-Related Health Effects* (supported by HUD) recommending research be conducted that “would increase scientific support for evidence-based public health policies on residential D/M” and proposed priority research questions for short-term research to be completed over the next 2-3 years for assessing unhealthy levels of indoor D/M.
Bridging the Gap between Environmental Research & Practice

Research Question, Aim and Hypothesis

• Mendell Research Question #1: “What are the best currently reported quantified microbiological measurements for indicating increased health risks (in a dose-related manner if possible) that could be used in health-protective guidelines for indoor D/M?... The current evidence has not been systematically mined for this information.”

• Specific Aim Study #1: Conduct a systematic review to assess the homogeneity or heterogeneity of findings in studies that examined the associations between exposure to elevated levels of mold in indoor air and adverse respiratory health outcomes using evidence-based inclusion criteria, and examine the criteria used in these studies to define elevated levels.

• Hypothesis Study #1: The current body of scientific evidence does support the conclusion that there is a significant association between exposure to elevated levels of specific genera of mold in the indoor air and adverse respiratory health outcomes.
A Systematic Review of Studies Examining the Associations between Exposure to Elevated Levels of Indoor Airborne Mold and Asthma and Other Respiratory Health Outcomes

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¹City University of New York School of Public Health, NY, USA
²Microecologies, Inc, NY, USA
Summary of Main Findings (PRISMA – Discussion #24)

• 20 of the 21 studies that met primary and secondary inclusion criteria found significant risk between exposure to elevated levels of indoor mold and asthma or other respiratory outcomes irrespective of criteria used to define elevated levels.

• Only 2 of these 21 compared indoor to outdoor levels, and only 1 study provided data that could contribute to the development of HGV’s for indoor airborne mold.

• *Penicillium* was the genus most frequently associated with adverse outcomes (10 of 21), followed by *Cladosporium* (5 of 21), *Alternaria* (3 of 21) and *Aspergillus* (2 of 21).
Conclusion and Relevance of Findings in Key Groups (PRISMA – Discussion #24 and #26)

• Results suggest that current scientific evidence does support measuring the indoor airborne mold subset of specific indoor microbiologic measurements in assessing respiratory health risks to occupants of D/M homes.

This finding validates the practices of environmental consultants who routinely use air sampling results as a tool together with other findings to assess respiratory health risk to occupants.

• These findings do not contribute to establishing dose-response based HGV’s for indoor airborne mold.

For research to inform the establishment of dose-response based HGV’s, researchers will need to align their study methods with the methods required by the AIHA be followed by environmental practitioners for the collection of airborne mold samples and interpretation of laboratory results.
A Nested Case-Control Study Examining the Associations between Exposure to Elevated Levels of Mold in Indoor Air and Wheeze Among Atopic Children in Cuba

William M. Sothern\textsuperscript{1,2}, Silvia-Josefina Venero-Fernández\textsuperscript{3}, Ramón Suárez-Medina\textsuperscript{3}, Teresa-Irene Rojas\textsuperscript{4}, Kenia Sánchez-Espinosa\textsuperscript{4}, Michel Almager-Chavez\textsuperscript{4}, Chris Mikrut\textsuperscript{2}, Ariunaa Jalsrai\textsuperscript{5}, Marilyn Aguirre-Molina\textsuperscript{1}

\textsuperscript{1}City University of New York School of Public Health, NY, USA, \textsuperscript{2}Microecologies, Inc., NY, USA, \textsuperscript{3}National Institute of Hygiene, Epidemiology, and Microbiology, Havana, Cuba, \textsuperscript{4}University of Havana, Department of Microbiology and Virology, Havana, Cuba, \textsuperscript{5}EMLab P&K environmental laboratories, NJ, USA
Bridging the Gap between Environmental Research & Practice

Research Question, Aim and Hypothesis

• Mendell Research Question #2: “What standard for combined multi-level D/M (indices) can be constructed, from combinations or expansions of the most strongly health-related D/M (or microbiologic) assessments in current studies, using information easily collected in a building, that have potential for dose-related associations with key health effects that are even stronger than current metrics, and that could be compared in future studies?”

• Specific Aim Study #2: Establish a quantitative dose-response based benchmark for genera-specific airborne mold above which there is a significant respiratory health risk (wheeze) to atopic residents of D/M homes by conducting a nested case-control study in Havana, Cuba.

• Hypothesis Study #2: There is a determinable dose-response based quantitative level that can be expressed in fungal structures per cubic meter for specific genera of indoor airborne mold above which there is a significant respiratory health risk to atopic occupants.
Research in Preparation for Havana Trip

- Literature search conducted to find studies that examine associations between environmental risk factors and asthma in preparation for Cuba preparation for January 2016 trip
- Prevalence of current wheeze in Havana, Cuba – school children 17.5%
  
  Primary risk factors identify presence of:
  - eczema (OR 2.09, 95% CI 1.48-2.94)
  - family history of asthma (OR 2.05, 95% CI 1.60-2.62)
  - poor ventilation (OR 1.99, 95% CI 1.48-2.67)
  - male sex (OR 1.52, 95% CI 1.19-1.96)
  - no. smokers in house (p <0.03 for trend)

- Potential research gap identified - water damage, excessive moisture and mold not considered major risk factor in infant wheeze study
Objective  Conduct a nested case-control pilot study with participants selected from the 1956-participant 2010-2011 INHEM Infant Wheeze Cohort to assess the association between exposure to elevated levels of mold in indoor air and wheeze.

Proposal  In November/December 2015, we reached out to and established a dialogue with Dr. Venero-Fernandez and Dr. Suarez-Medina who responded favorably to and shared our interest in conducting the pilot study.

Next steps
   - Design the study
   - Identify the research team members – consider qualifications & training requirements
   - Acquire the necessary field instrumentation & air sampling cassettes
   - Schedule the meetings to finalize project design, training, data and sample collection, logistics
Pilot Study Design - Methods

Selection of Cases and Controls

- 2010-2011 Infant Wheeze Cohort comprised of 1,956 infants aged 12-15 mo from 17 randomly selected polyclinic catchments in 4 of the 15 municipalities in Havana. Questionnaires (ISAAC) administered annually by family pediatrician to participants’ parents. At time of selection for pilot study (2012/2013 questionnaire) cohort comprised of 1,543 children aged 3 - 4. For pilot study, participant pool selected from 2 municipalities - eligible pool 799 children.

- Inclusion criteria for pilot study limited to children whose parents answered “yes” to questions “family history of asthma” (2010/2011 questionnaire) and “visible mold/dampness” (2012/2013 questionnaire), leaving pool of 95 eligible children. Parents of 69 eligible children answered “yes” to “any wheeze in the past 12 months” question and 26 answered “no” (2016 questionnaire).

- From remaining pool, 36 participants randomly selected for pilot study, 18 cases (wheeze) and 18 controls (no wheeze).
Pilot Study Design - Methods

- Air Sample Collection and Laboratory Analysis
  - Samples collected Feb-Jun 2016 indoors (children’s bedroom) and outdoors (directly outside home) onto Air-O-Cell spore trap cassettes using Zefon Bio-Pumps calibrated to 15 LPM for 5 minutes.
  - Samples retrieved from Cuba and returned to U.S. for analysis at EMLab P&K.

- Laboratory Results Interpretation
  - Results interpreted by comparing indoor levels to outdoor levels by genera (in accordance with AIHA guidelines) for each home.

- Statistical Analysis
  - Based on a review of laboratory results and previous research, the exposed group defined as children who lived in homes where the levels of *Pen/Asp* and *Cladosporium* in the indoor air were elevated contrasted to the levels in the outdoor air by >200 str/m³.
Pilot Study - Results

- Air sampling results show that *Pen/Asp* airborne mold levels in the child’s bedroom > 200 str/m³ higher than outdoor levels in 13 of the 34 homes (11 cases, 2 controls), indicating a significantly increased risk of current wheeze among children exposed to *Pen/Asp* at these levels (OR 11.0; 95% CI, 1.90-63.83).

- Air sampling results show that *Cladosporium* airborne mold levels in the child’s bedroom > 200 str/m³ higher than outdoor levels in 10 of the 34 homes (6 cases, 4 controls) indicating there is not a significantly increased risk of current wheeze among children exposed to *Clad* at these levels (OR 1.5; 95% CI, 0.34-6.70).

- The air sampling results show that there were only four genera representing >1% of the total fungal organisms in both the indoor and outdoor air of the 34 homes, and that the only genera where the mean indoor levels exceeded mean outdoor levels was *Pen/Asp*.

- The outdoor air sampling results comparing mean outdoor levels in New York in June to mean levels outside the 34 homes in the subtropical climate of Cuba (samples taken February through June 2016) show that only four genera represented > 1% of total outdoor fungal organisms in both geographies and climates. This data also shows that levels of *Pen/Asp*, the water damage related fungi most frequently associated with adverse respiratory health outcomes, were within the same range in both geographies and climates.
Pilot Study - Conclusions

• Conclusion #1
  ∙ Children with family history of asthma exposed to Pen/Asp in indoor air > **200 str/m³** higher than outdoor air are at significant risk for wheeze.
  ∙ The strength of association between exposure to elevated levels of Pen/Asp and wheeze in this pilot study supports our hypothesis that air sampling results can be a useful tool in providing health protective advice to occupants and their physicians.
  ∙ Pilot study results suggest defining elevated levels of mold as indoor levels of Pen/Asp > **200 str/m³** higher than outdoor levels may be useful starting point/benchmark for examination in larger similarly designed studies that can test the reliability of this quantitative value.

• Conclusion #2
  ∙ Pilot study results support our conducting larger (229 cases and controls) nested case-control study.
    • Data collection commenced in September 2018.
    • Quantitatively assessed D/M exposure parameters expanded to include 4 WHO markers of D/M conditions (visible mold, visible water damage, moisture measurements and mold odor) associated with adverse respiratory health effects.
    • Statistical analysis will measure the strengths of association between and among each of these parameters and asthma among the now 8 and 9 year old children in the cohort.
Examples of changes in best practice, policy and law:
AIM 1999; NIEHS 2013; NYC Building Code 2014; NYCHA 2018
Questions?

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