Health Effects of Indoor Dampness and Mold – What Do We Know? What Should We Do?

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This presentation will summarize what we know, from epidemiology, about health effects of dampness and mold.

How do we decide what we know?

What do we know now?

What should we do?
3,000+ years ago, the Bible prescribed investigation and repair (or destruction) of moldy houses (Leviticus 14:33-54)

(INVESTIGATION)

35. The owner of the house must . . . tell the priest, 'I have seen something that looks like mildew ["leprosy"] in my house.'

36. The priest is . . . to . . . inspect the house.

37. . . . if it has greenish or reddish depressions that appear to be deeper than the surface of the wall, the priest shall . . . close it up for seven days.

(REPAIR)

39. On the seventh day . . . . If the mildew has spread on the walls,

40. he is to order that the contaminated stones be torn out and thrown into an unclean place outside the town.

41. He must have all the inside walls of the house scraped and . . . dumped into an unclean place outside the town.

42. Then . . . take other stones to replace these and take new clay and plaster the house.

(DESTRUCTION OF CONTAMINATED DWELLING)

43. If the mildew reappears in the house . . .

44. . . . it is a destructive mildew; the house is unclean.

45. It must be torn down—its stones, timbers and all the plaster—and taken out of the town to an unclean place.”
In the modern era, some specific health effects of fungal exposures are clearly established.

IgE mold allergy, leading to allergic rhinitis or asthma

Respiratory hypersensitivity (hypersensitivity pneumonitis) and organic toxic dust syndrome, from high exposure levels

Fungal infections in immunocompromised individuals
Recent epidemiologic findings have expanded knowledge about health effects associated with dampness and mold.

How do we actually decide if a specific exposure causes a specific disease?
How do we decide what we know about indoor dampness/mold and health?
We evaluate the strength of the epidemiologic evidence about effects of dampness and mold on respiratory health.

- **Sufficient evidence of a causal relationship**
- **Sufficient evidence of an association**
- **Limited or suggestive evidence of an association**
- **Inadequate or insufficient evidence to determine if an association exists**
There are many potential flaws in the validity of an epidemiologic study

- **Chance (random error)**
  - Effect seen by chance only?
  - Or, is confidence interval (or p-value) inconsistent with a chance finding?

- **Bias (systematic error)**
  - Confounding bias (e.g., lung cancer / coffee / smoking)
  - Selection bias (e.g., COPD / miners / maintenance jobs)
  - Information bias (e.g., cancer / interview / increased recall)
We evaluate the epidemiologic evidence on each potential association between an exposure and a health effect.

**Experimental studies**
- Randomized, controlled intervention trial

**Observational studies**
- Cohort – prospective or retrospective
- Case-control
- Cross-sectional

- Large effect
- Chance effect unlikely (p-values, CIs)
- Bias unlikely
- Dose-response
- Biologic plausibility (toxicology, biology)
- Multiple, diverse studies of strong design

Types of epidemiologic evidence

Strong evidence for causality
In epidemiologic studies, odds ratios (ORs) or risk ratios (RRs) show how an exposure is associated with an effect.

- **OR or RR**
  - greater than 1 → *increased* risk
  - equals 1 → *no change in risk*
  - less than 1 → *decreased* risk

**95% Confidence Interval:**
If excludes 1.0, suggests that the effect seen in the study is not consistent with a chance finding.

e.g., OR (95% CI: 2.3 (1.6-3.4))
Meta-analyses summarize, across studies, the strength of association between exposures and effects.

Example Meta-Analysis:
Dampness/Mold and Respiratory Infections*

Do you see it or smell it?

Summary OR= 1.44 (1.31-1.59)

* Fisk WJ et al. 2010
Epidemiologic studies have examined associations of health effects with dampness or mold, assessed in two ways.

**“Evident” Indoor Dampness or Mold**
- Visible water damage
- Visible moisture
- Visible mold
- Mold odor
- Leaks (current or past)

**“Measured” Microbiologic Factors**
- Total culturable fungi
- Specific culturable fungi
- Total culturable bacteria
- Mold spore counts
- Bacterial endotoxins
- 1-3-beta glucans, . . . . etc. ( > 52 so far)
What do we know about dampness/mold and health?
Current knowledge on “dampness and mold” and health is based on recent comprehensive epidemiologic reviews

2004 – Institute of Medicine

2009 – World Health Organization

2015 – Kanchongkittiphon, Mendell, Gaffin, Wang, Phipatanakul

Environmental Health Perspectives
- Updates 2000 IOM report on asthma
- Evaluates evidence for indoor asthma triggers

2011 – Mendell, Mirer, Cheung, Tong, and Douwes

- Updates WHO review
- Summarizes 145 epidemiologic studies
- Evaluates “evident” dampness and mold and measured microbiologic factors
2009/2011 - Qualitative dampness/mold exposures are associated with multiple respiratory health effects

Do you see it or smell it?

Documented “causal” relationships – none

Documented “associations” (sufficient evidence) –

**Diseases**
- asthma exacerbation
- asthma development*
- current and ever asthma*
- allergic rhinitis
- eczema
- bronchitis
- respiratory infections*

**Symptoms**
- dyspnea*
- wheeze
- cough
- upper respiratory tract symptoms

*new conclusions 2009, 2011 reviews per IOM 2004 review +

Evidence strongly suggestive of causation *
2015 - Qualitative dampness/mold exposures have a causal link or association with multiple respiratory health effects

Documented “causal” relationships –

- asthma exacerbation** (in children)

Documented “associations” (sufficient evidence) –

**Diseases**
- asthma development*
- current and ever asthma*
- allergic rhinitis
- eczema
- bronchitis
- respiratory infections*

**Symptoms**
- dyspnea*
- wheeze
- cough
- upper respiratory tract symptoms

* new conclusions in 2011 review
** new conclusion 2015 review

per IOM 2004 review+
Quantitative (measured) dampness/mold exposures indoors: no consistent associations with respiratory health effects

Documented “causal” relationships – none
Documented associations – none

Limited/suggestive associations –
- cultured airborne fungi (indoors) and asthma exacerbation (in specifically sensitized children – so not really news)
- fungi (single or multiple or index) in dust by QPCR
- several microbial compounds in dust . . .

BUT:
- few studies available
- for endotoxins and beta glucans – both increased and decreased risks!

So, quantified microbial exposures (indoors) not yet consistently associated with adverse health effects
Evidence from toxicology (in vitro, or in animals) supports the epidemiologic findings on observed dampness/mold.

“Toxicological evidence obtained in vivo and in vitro supports these [epidemiologic] findings, showing the occurrence of diverse inflammatory and toxic responses after exposure to microorganisms isolated from damp buildings, including their spores, metabolites and components.”

(WHO Guidelines for Dampness and Mold, 2009)
No single biologic mechanism proposed can explain all the epidemiologic observations

- **Dampness and mold** → **both allergic and non-allergic disease**
  - e.g., increased respiratory infections

- **Dampness/mold** → **both allergic and non-allergic individuals**
  - continued finding in multiple studies

- **Some early microbial exposures reduce later atopy**
  - e.g., endotoxin; living with farm animals
  - bacterial and fungal diversity

- **But dampness or mold consistently increases respiratory risks in infants, children, and adults (so early exposures not all good)**
We can propose some explanations for the paradoxical epidemiologic findings

- True causal agents not yet identified / measured well
  - non-culturable fungal spores or fragments?
  - moisture-loving bacteria?
  - dampness-related chemical emissions?

- Synergy of fungi, e.g., with bacteria; endotoxin; amoebas; dampness-related chemicals . . . ?

- Effects of age at exposure? intensity / length of exposure?

- Multiple biologic responses involved?
  - Non-allergic mechanisms (pro-inflammatory, cytotoxic?)
  - Some allergens may have effects in nonsensitized also – mold, dust mites, cockroaches!! (Kanchongkittiphon et al. 2015)
We can estimate from available data how much respiratory disease is associated with dampness and mold (D/M)

Dampness or mold is estimated to occur in 20-50% of U.S. homes***

**21% of current U.S. asthma potentially attributable to dampness or mold in housing**

8-20% of respiratory infections potentially attributable to dampness or mold in housing**

**21% of current U.S. asthma potentially attributable to dampness or mold in housing**

**8-20% of respiratory infections potentially attributable to dampness or mold in housing**

Lesson 1: This amount of disease is potentially preventable

Lesson 2: Current policies on D/M are not adequate

* Fisk, Lei, Mendell 2007, Ind Air

** Fisk, Eliseeva, & Mendell 2010

*** Mudarri and Fisk, 2007 Indoor Air
In summary, evident dampness and mold indicate increased risks for multiple respiratory and allergic effects.

- **asthma exacerbation**
- **asthma development**
- **allergic rhinitis**
- **eczema**
- **respiratory infections**

Lack of consistent associations with microbial measurements not understood

- Specific causal agent(s) not identified
- Allergic and non-allergic mechanisms involved

**Do you see it or smell it?**

**evident**

**dampness**

**or mold**

**measured**

**microbial factors**
What should we do?

• now, when D/M occurs

• to learn more, so can better protect from D/M
The World Health Organization has made recommendations based on a comprehensive scientific review.

Avoid or minimize dampness and microbial growth:
- persistent
- on interior surfaces
- or in building structures

As indicated by any of:
- condensation on surfaces or in structures
- visible mould
- mouldy odour
- history of water damage, leakage, or penetration

But we cannot now quantify relations between microbial exposure and health.

Therefore, no quantitative health-based guideline values or thresholds are recommended for acceptable levels of contamination with microorganisms.”

-- WHO IAQ Guidelines, Dampness and Mold 2009
Available scientific evidence supports the effectiveness of remediating evident dampness and mold

- eliminating moisture intrusion and leaks
- removing moldy items

A recent expert review on housing remediation* concluded:

- effective in reducing respiratory symptoms from asthma and allergies
- ready for widespread implementation

* Krieger et al. 2010
We still don’t know exactly what remediation is necessary.

This is not very well studied yet.

Current advice*

- Eliminate source of moisture
- Eliminate damp materials (dry or remove)
- Eliminate moldy materials (clean or replace)

*Calif Dept of Public Health Statement on Building Dampness, Mold, and Health, 2011
We want field-friendly tools to evaluate health risks in buildings related to dampness and mold

Current evidence-based advice on indoor D/M – If you see it or smell it, it’s a health risk, so fix it.

Useful, but not quantitative – no clear threshold for action

Want quantitative D/M assessment metrics
• dose-response relationship with health risks; e.g.,
  • multi-level index based on structured observations
  • or direct reading instrument
• to specify acceptable risk level to trigger remediation

Identifying causal microbial agents with quantified health-based exposure limits – not likely to happen soon, but a long-term goal
We want guidelines for indoor dampness and mold that are evidence-based, quantitative, and health-protective. But, we don’t have this evidence for D/M... How can we get the evidence?
Several types of indoor D/M assessment could improve the link to health effects

1) Subjective assessment of dampness or mold – do you see it or smell it?

2) Objective measurement of building moisture

3) Objective measurement of microorganisms or their components or products

Identify microbial agents - Quantify relationships

Quantify relationships
1- Multi-level indices of observed D/M show promise already

At least 9 epidemiologic studies have created multi-level indices of observed D/M that have a dose-response relationship with a studied health effect
9+ studies have reported dose-response associations with health effects for multi-level metrics of indoor D/M

<table>
<thead>
<tr>
<th>Reference</th>
<th>Exposure Metric</th>
</tr>
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<tbody>
<tr>
<td>(Dales et. al., 1991)</td>
<td>• number of visible mold sites reported by parent: 0, 1, or 2</td>
</tr>
<tr>
<td>(Haverinen et. al., 2001)</td>
<td>• 3-level index of D/M, based on most severe damage and number of damaged locations</td>
</tr>
<tr>
<td>(Pekkanen et. al., 2007)</td>
<td>• 3-level index of the maximum severity of researcher-assessed moisture damage</td>
</tr>
<tr>
<td>(Karvonen et. al., 2009)</td>
<td>• 3-level index of moisture damage</td>
</tr>
<tr>
<td>(Iossifova et. al., 2007)</td>
<td>• Visible mold: none, low visible mold (area &lt;0.2 m$^2$), high visible mold (area ≥0.2 m$^2$)</td>
</tr>
<tr>
<td>(Iossifova et. al., 2009)</td>
<td>• Visible mold: none, low (moldy odor or moisture damage or visible mold &lt;0.2 m$^2$), high (moisture damage and visible mold area ≥0.2 m$^2$)</td>
</tr>
<tr>
<td>(Biagini et. al., 2006)</td>
<td>• 3-level index of visible mold (no mold=no water damage, visible mold, moldy odor, or mold/water damage history; high mold= ≥0.2 m$^2$ area of mold in one room or of combined visible mold/water damage area on same surface; low mold=all others)</td>
</tr>
<tr>
<td>(Norbäck et. al., 2013)</td>
<td>• multi-level dampness score (history of, or recent, water damage, or leaks)</td>
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<td>(Park et. al., 2004)</td>
<td>• Individualized, semi-quantitative exposure index for D/M, based on room-specific observations of the amount of water stains, moisture, visible mold, or mold odor, and weighted by time subject spent in each room</td>
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</tbody>
</table>
2- Can we quantify the health risks of indoor dampness?

The controlling factor for mold/microbial growth in buildings is moisture.

So, moisture is the original cause of dampness- or mold-related health effects.

How feasible to develop health-based limits for measured moisture in buildings?

Could we do epidemiologic studies to look for relationships between measured moisture and health effects?

Two existing studies, from 1997 and 2003! Findings ignored and unrecognized . . .

Measured moisture in home walls had a positive dose-related association with risk of asthma exacerbation (Venn et al. 2003; Williamson et al., 1997)
Measured wall moisture had dose-related association with asthma symptoms (Venn et al. 2003; Williamson et al. 1997)

<table>
<thead>
<tr>
<th>Moisture Content (WME)</th>
<th>Odds Ratios</th>
<th>Asthma Exacerbation</th>
<th>Moisture Content (WME)</th>
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<tbody>
<tr>
<td></td>
<td>Williamson 1997</td>
<td>Venn 2003</td>
<td></td>
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<tr>
<td>All Rooms</td>
<td>Night-time</td>
<td>Day-time</td>
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<tr>
<td>0</td>
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<td>3.6</td>
<td>1.7</td>
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<td>1.4</td>
<td>1.4</td>
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</tbody>
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* p<0.05
3-Improvements in microbial measurements will help us set action thresholds + identify causal damp-related agents

Culture-based assays in air samples are flawed in many ways for indicating actual microbial exposures.

A set of 36 fungi in house dust, ID’ed by quantitative polymerase chain reaction (QPCR), predicted later asthma development in children (Reponen et al. 2011; 2012)

New sequence-based methods can comprehensively identify microbial species and entire microbial communities; while promising, they are not yet fully quantitative (or “deep”).
Recent studies give new hints about the biologic response to dampness-related agents

Specific genetic variation in chitinase (human enzyme targeting a fungal protein) greatly increased the adverse respiratory effects from airborne fungi (Wu et al. 2010)

Fungal proteases, emitted by fungi growing in the lungs unrecognized, may cause some asthma and allergies (Porter et al. 2011)

Unidentified fungi or bacteria on air-conditioning cooling coils, in a desiccation-resistant biofilm, may be linked to “sick building” symptoms (Menzies et al. 2003)
To support evidence-based policies related to dampness and mold in buildings, multidisciplinary research is needed

Microbiologic methods
- Develop microbial ID methods,
- Communities, organisms, components, products . . .

Measured moisture ↔ Microbiology

Microbiology and health
- improved microbial ID in health studies
- Identify causal species/compounds, quantify relationships
- Biologic response to microbial agents

Measured moisture and health

Microbiology, moisture, health, and buildings
- building factors associated with protective/adverse microbiology
- prevention and remediation
Questions?
Dampness, Mold, and Health: Selected Literature Reviews and Meta-Analyses

- Fisk WJ et al. Meta-Analyses of the Associations of Bronchitis and Respiratory Infections with Dampness and Mold in Homes. Environmental Research 2010
- Quansah R et al. Residential dampness and molds and the risk of developing asthma: a systematic review and meta-analysis. PLOS One 2012;7:e47526.

To support evidence-based policies related to dampness and mold in buildings, multidisciplinary research is needed.

**Microbiologic methods**
- Develop microbial ID methods, comprehensive and quantitative at species level, for fungi and bacteria and communities, organisms, components, products?

**Dampness and Microbiology**

**Microbiology and health**
- Use improved microbial ID in health studies
- Identify causal species/compounds for adverse and for positive health effects, and quantify relationships, so can set guidelines and standards
- (mechanisms, genetic interactions)

**Dampness and Health**

**Microbiology, dampness, health, and buildings**
- building factors associated with protective/adverse microbiomes
- prevention and remediation – what codes/guidelines to make buildings resist moisture through their lifetimes?