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,
38. 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.**

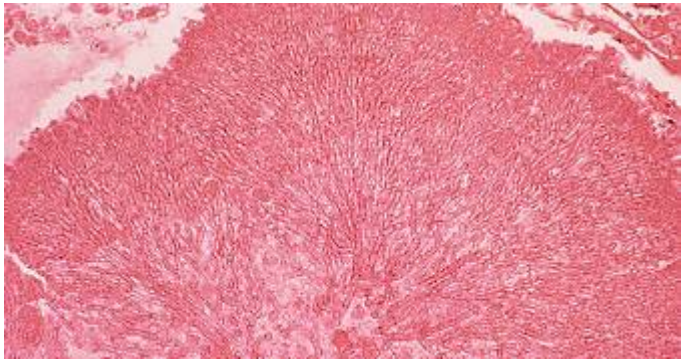
(DESTRUCTION OF CONTAMINATED DWELLING)

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

categories from

International Agency for Research on Cancer

World Health Organization

- ❖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.

Types of epidemiologic evidence

Experimental studies

Randomized, controlled intervention trial

Observational studies

Cohort – prospective or retrospective

Case-control

Cross-sectional

Strong evidence for causality

Large effect

Chance effect unlikely (p-values, CIs)

Bias unlikely

Dose-response

Biologic plausibility (toxicology, biology)

Multiple, diverse studies of strong design

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

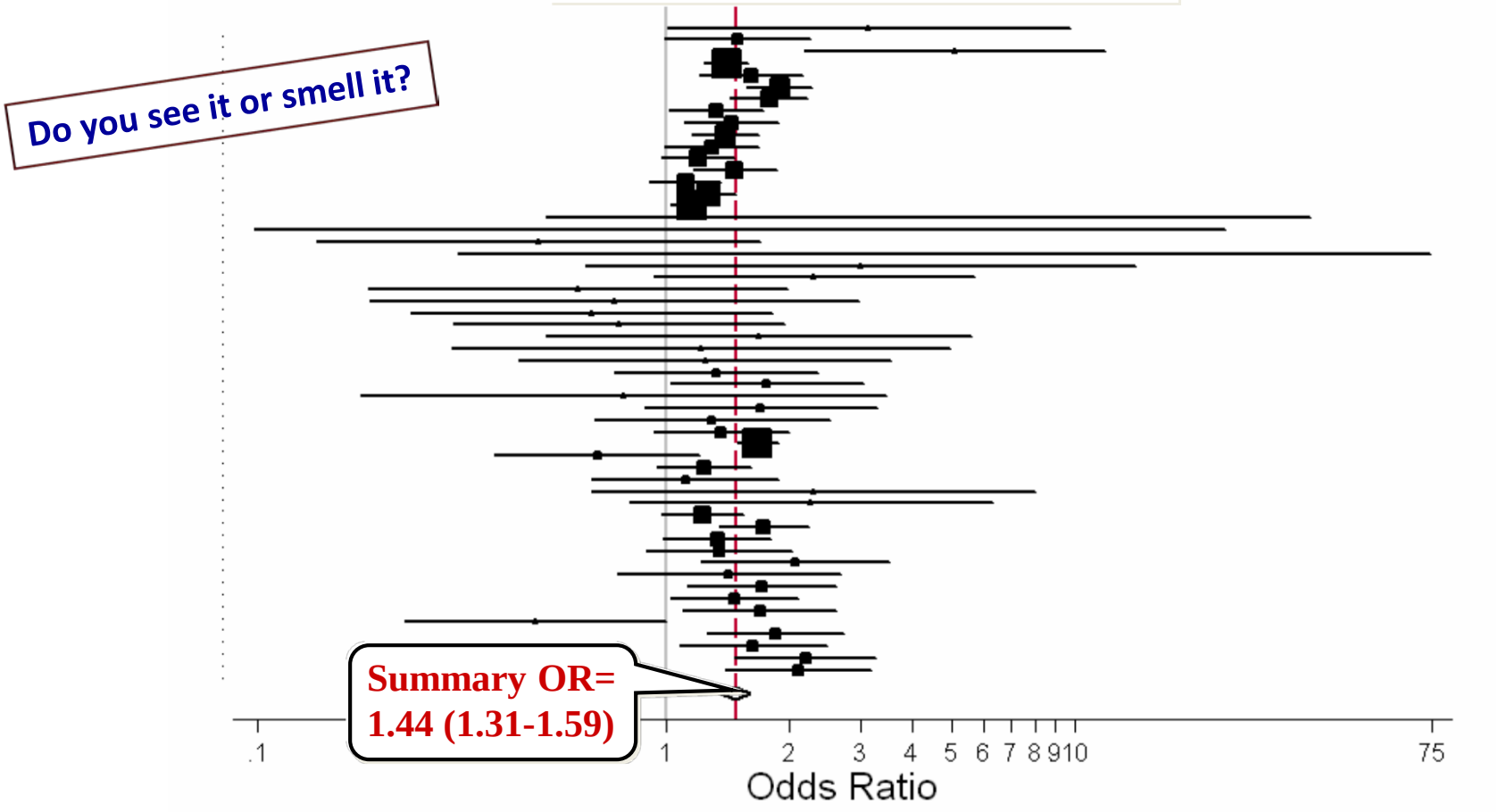
less than 1 → *decreased* risk

e.g., OR (95% CI: 2.3 (1.6-3.4)

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

Meta-analyses summarize, across studies, the strength of association between exposures and effects

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



* Fisk WJ et al. 2010

Epidemiologic studies have examined associations of health effects with dampness or mold, assessed in two ways

- Visible water damage
- Visible moisture
- Visible mold
- Mold odor
- Leaks (current or past)

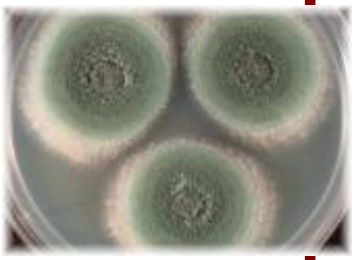
Do you see it or smell it?

"Evident" indoor dampness or mold

= qualitative

(in air / in dust)

- Total culturable fungi
- Specific culturable fungi
- Total culturable bacteria
- Mold spore counts
- Bacterial endotoxins
- 1-3-beta glucans, ... etc. (> 52 so far)



"Measured" microbiologic factors

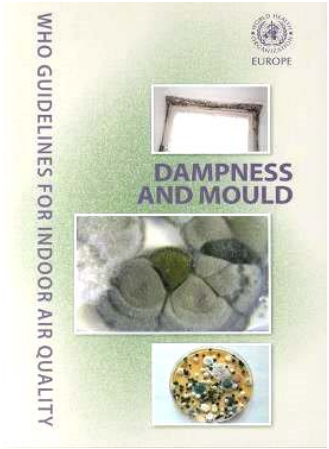
= quantitative

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

Environmental Health PERSPECTIVES

- 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) –

evidence strongly suggestive of causation *

Diseases

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

Symptoms

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

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

2015 - Qualitative dampness/mold exposures have a causal link or association with multiple respiratory health effects

Do you see it or smell it?

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

per IOM 2004 review+

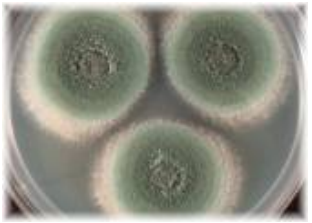
* new conclusions in 2011 review

** new conclusion 2015 review

Quantitative (measured) dampness/mold exposures indoors: no consistent associations with respiratory health effects

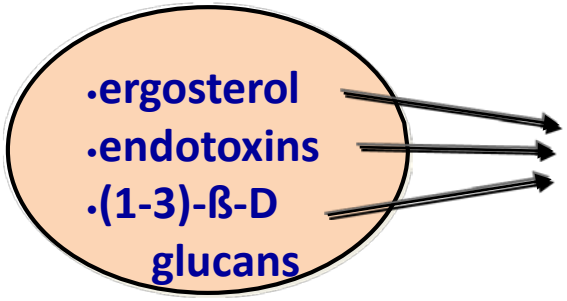
Documented "causal" relationships – none

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 . . .

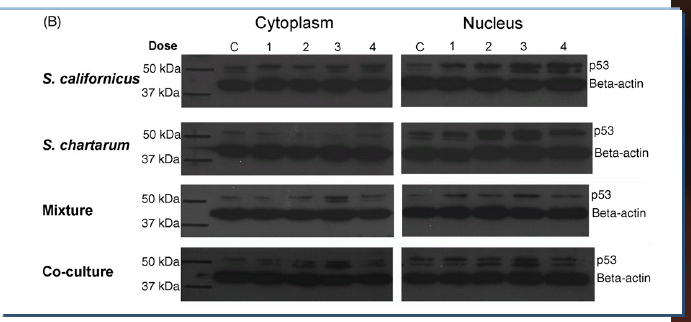


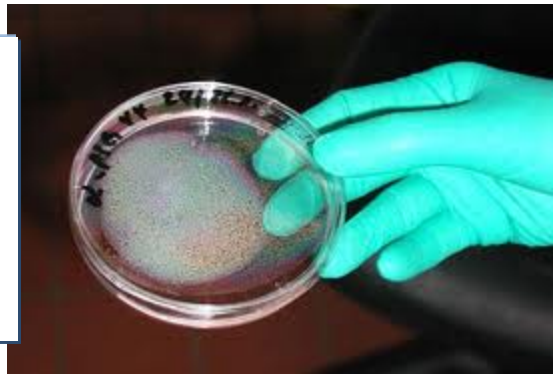
BUT:

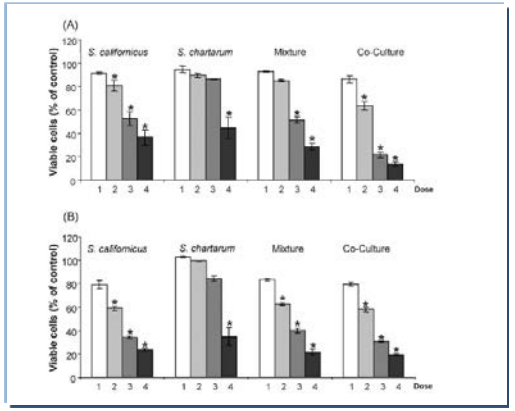
- few studies available
- for endotoxins and beta glucans – both increased and decreased risks!

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





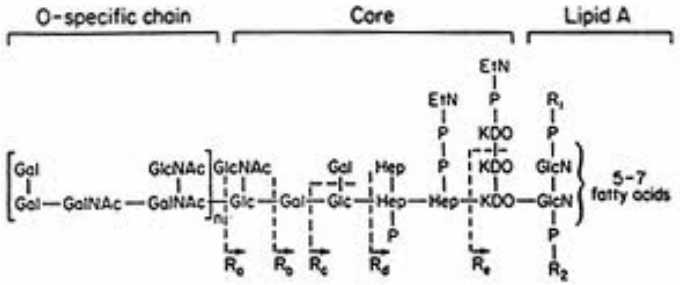


"Toxicological evidence obtained in vivo and in vitro supports these [epidemiologic] findings, showing the occurrence of diverse inflammatory and toxic responses after exposure to microorganisms isolated from damp buildings, including their spores, metabolites and components."

(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

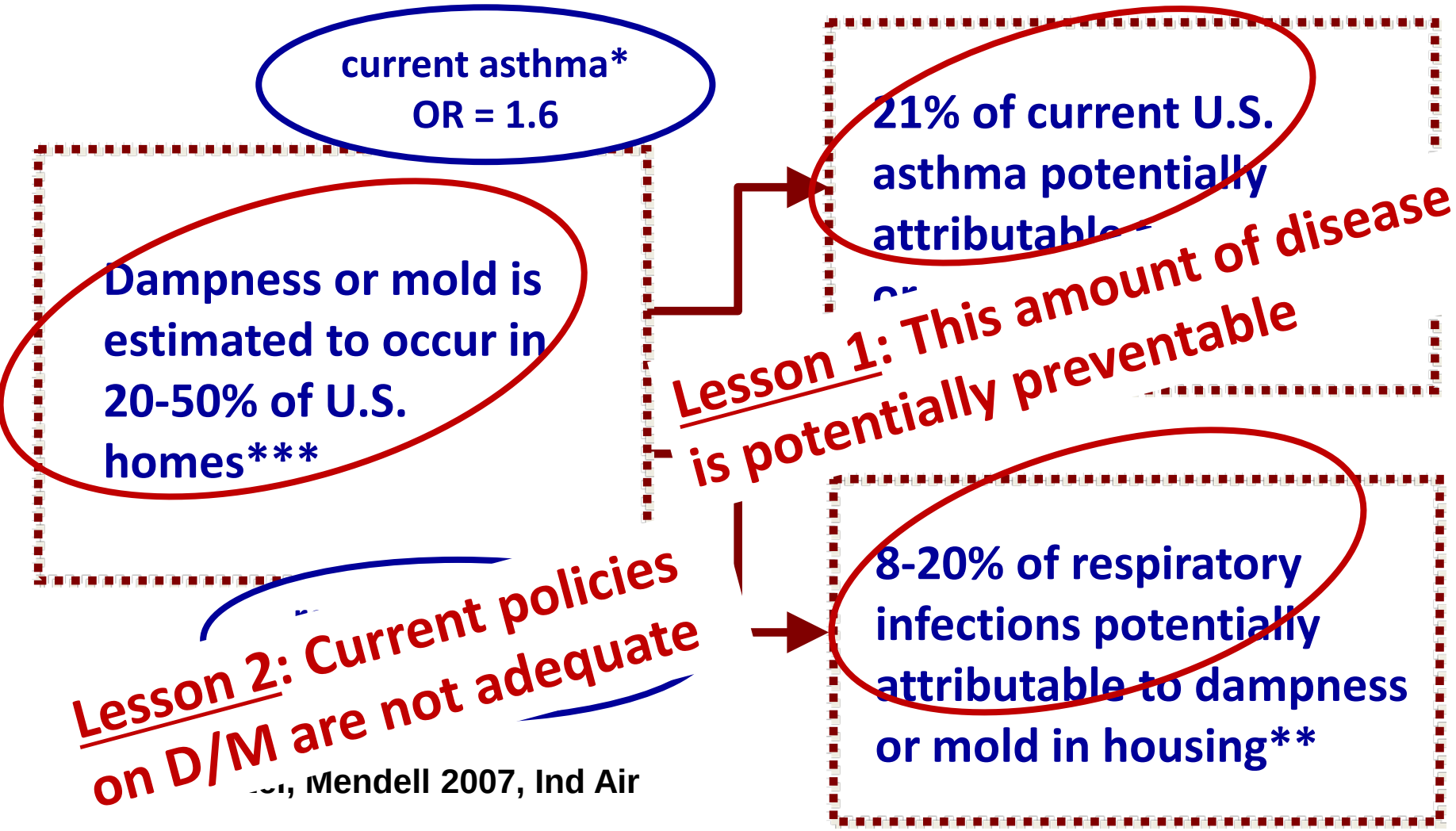
Paradox!

- **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)



, 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
respiratory infections
allergic rhinitis
eczema

Do you see it or smell it?

evident dampness or mold

measured microbial factors

- Lack of consistent associations with microbial measurements not understood
- Specific causal agent(s) not identified
- Allergic and non-allergic mechanisms involved

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

Do you see it or smell it?

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

A recent expert review on housing remediation* concluded:

- **eliminating moisture intrusion and leaks**

AND

- **removing moldy items**

✓ **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.

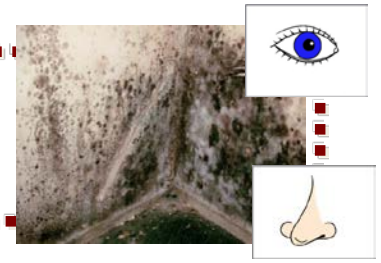
Current advice*

- ✓ 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.



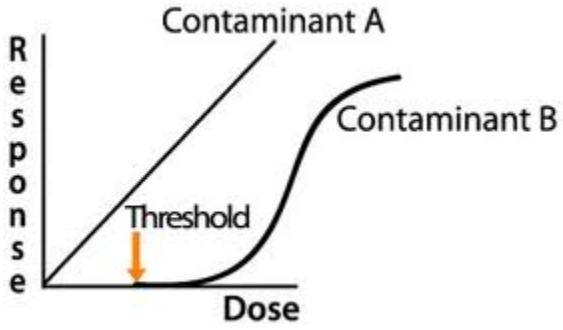
Useful, but not quantitative – no clear threshold for action

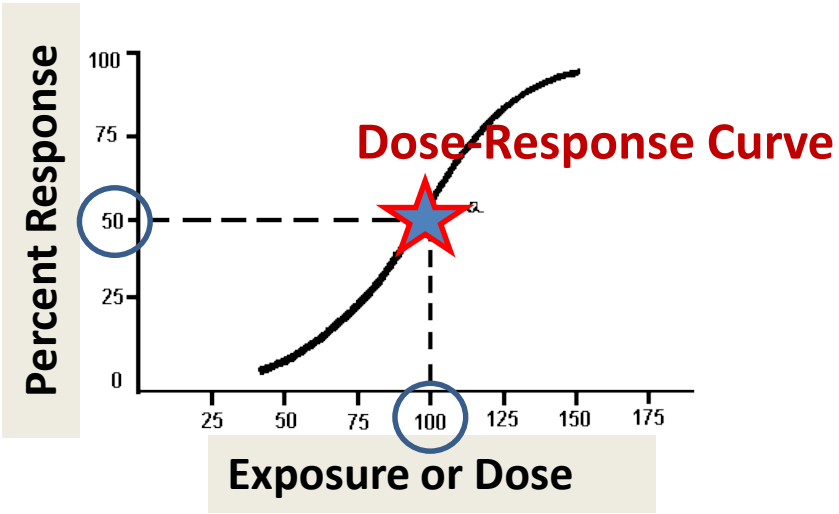
Want *quantitative D/M* assessment metrics

- 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





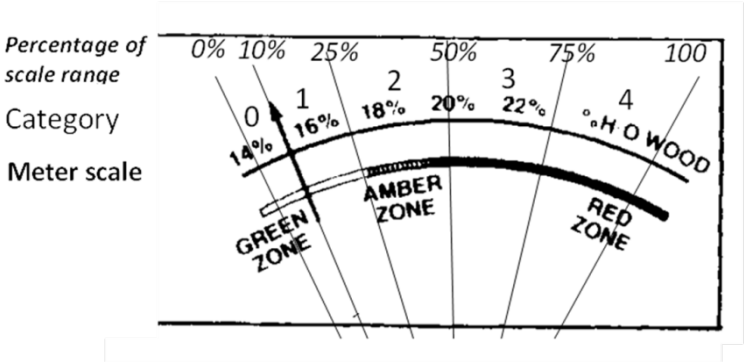
But, we don't have this evidence for D/M . . .

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?

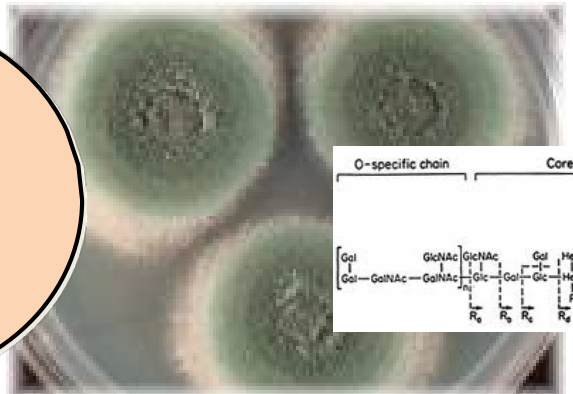
Quantify relationships



2) Objective measurement of building moisture

Quantify relationships

Identify microbial agents - Quantify relationships



3) Objective measurement of microorganisms or their components or products

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

Reference	Exposure Metric
(Dales et. al., 1991)	• number of visible mold sites reported by parent: 0, 1, or 2
(Haverinen et. al., 2001)	• 3-level index of D/M, based on most severe damage and number of damaged locations
(Pekkanen et. al., 2007)	• 3-level index of the maximum severity of researcher-assessed moisture damage
(Karvonen et. al., 2009)	• 3-level index of moisture damage
(Iossifova et. al., 2007)	• Visible mold: none, low visible mold (area <0.2 m^2), high visible mold (area ≥0.2 m^2)
(Iossifova et. al., 2009)	• Visible mold: none, low (moldy odor or moisture damage or visible mold area <0.2 m^2), high (moisture damage and visible mold area ≥0.2 m^2)
(Piacini et. al., 2010)	• 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)
(Northcott et. al., 2013)	• multi-level dampness score (history of, or recent, water damage, or leaks) • mold score (history of, or recent, mold) • number of rooms with mold
(Park et. al., 2004)	• 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

Mold odor, among the subjective D/M assessments, was the most strongly associated with the health effect, for both new asthma and rhinitis (Jaakkola group)

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

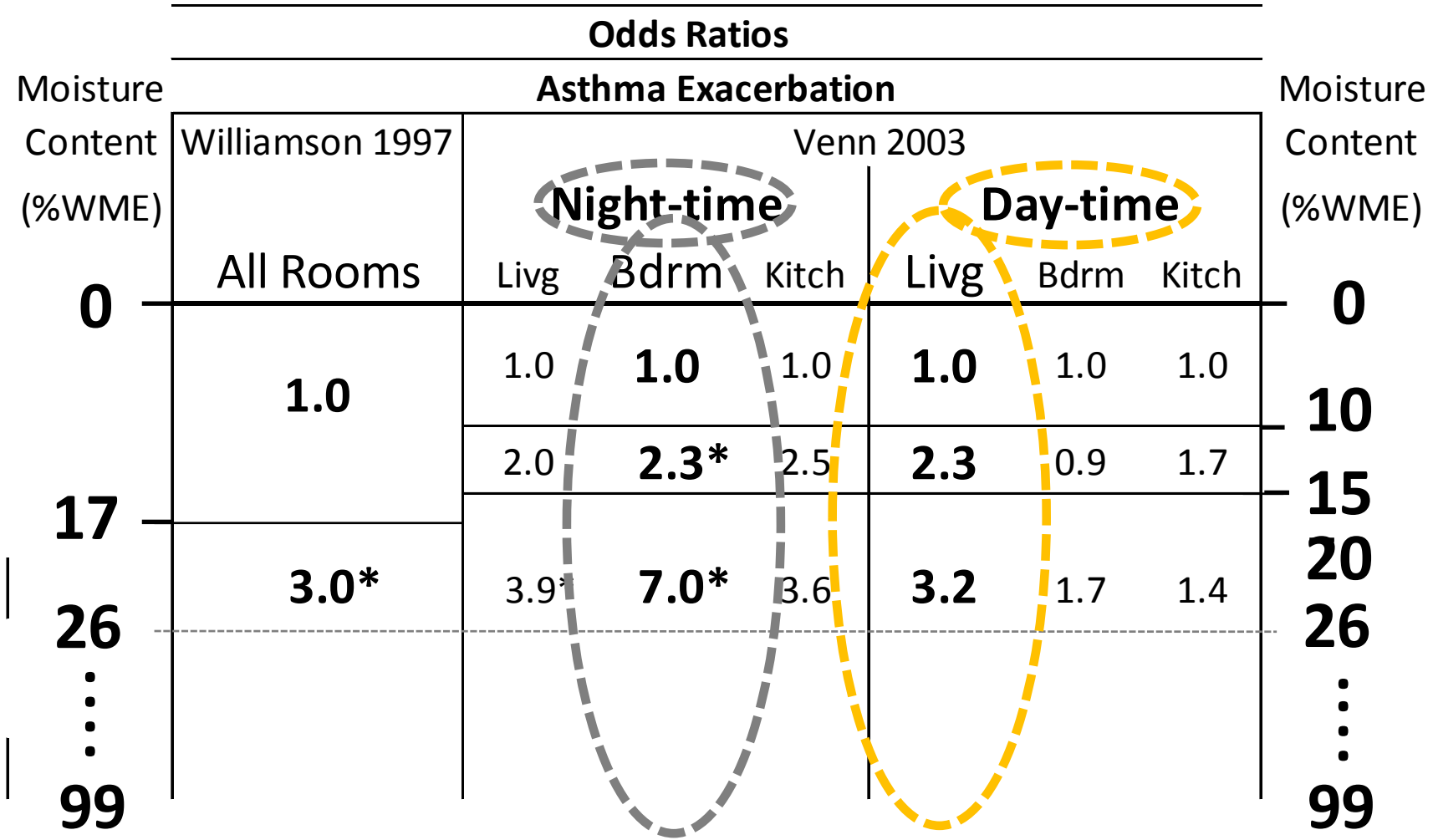
How feasible to develop health-based limits for measured moisture in buildings?

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 . . .

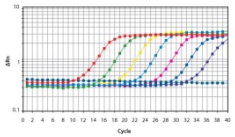
Measured moisture in home walls had a positive dose-related association with risk of asthma exacerbation (Venn et al. 2003; Williamson et al., 1997)

Measured wall moisture had dose-related association with asthma symptoms (Venn et al. 2003; Williamson et al. 1997)



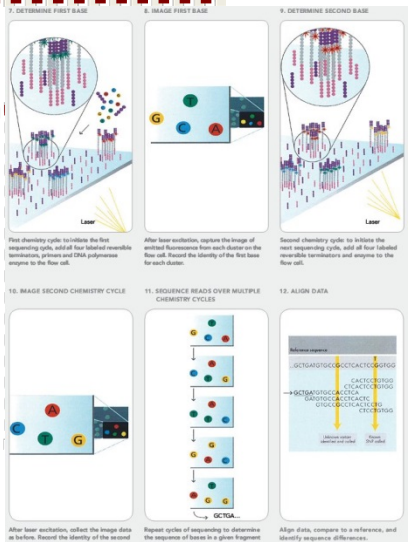
3-Improvements in microbial measurements will help us set action thresholds + identify causal damp-related agents

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



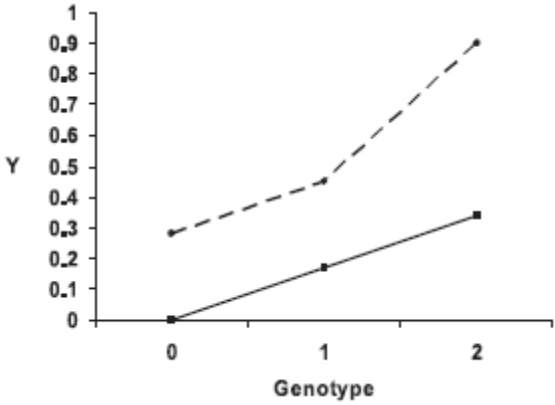
A set of 36 fungi in house dust, ID'ed by quantitative polymerase chain reaction (QPCR), predicted later asthma development in children (Reponen et al. 2011; 2012)

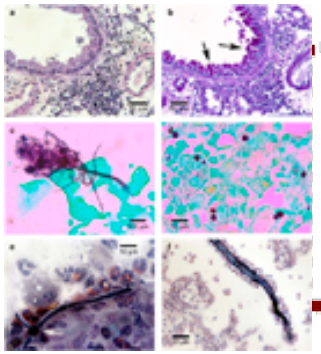
New sequence-based methods can comprehensively identify microbial species and entire microbial communities; while promising, they are not yet fully quantitative (or "deep").



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

- WHO (World Health Organization) Europe. 2009. WHO Guidelines for Indoor Air Quality: Dampness and Mould. Copenhagen: World Health Organization.
- IOM (Institute of Medicine). 2004. Damp Indoor Spaces and Health. Washington, DC: National Academies Press.
- Mendell MJ et al. Health Effects of Dampness, Mold, and Dampness-Related Agents: A Review of the Epidemiologic Evidence. Environmental Health Perspectives 2011; 119:748-756
- Fisk WJ et al. Meta-analyses of the associations of respiratory health effects with dampness and mold in homes. Indoor Air 2007;17:284-96.
- Fisk WJ et al. Meta-Analyses of the Associations of Bronchitis and Respiratory Infections with Dampness and Mold in Homes. Environmental Research 2010
- Antova T et al. Exposure to indoor mould and children's respiratory health in the PATY study. J Epidemiol Community Health 2008; 62:708–14.
- 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.
- Jaakkola MS et al. Association of indoor dampness and molds with rhinitis risk: a systematic review and meta-analysis. *J Allergy Clin Immunol. 2013; 132:1099-1110.*
- Kanchongkittiphon W et al. Indoor environmental exposures and asthma exacerbation: an update to the 2000 review by the Institute of Medicine. Environmental Health Perspectives 2014.

California Dept of Public Health – 2011 Statement on Building Dampness, Mold, and Health: http://www.cdph.ca.gov/programs/IAQ/Documents/statement_on_building_dampness_mold_and%20health2011.pdf

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?