Indoor Toxicity and Fungal Inhalation Risk of Patients and Clinical Findings

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Int Arch Occup Environ Health (1996) 68:207–218

ORIGINAL ARTICLE

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Philip Morey · Bruce Jarvis · Paul Landsbergis

Health and immunology study following exposure to toxigenic fungi (*Stachybotrys chartarum*) in a water-damaged office environment

Received: 3 May 1995/Accepted: 17 October 1995

Fungal Research Group
Foundation 2008

Fungal Exposure:
Various agents and disease outcomes

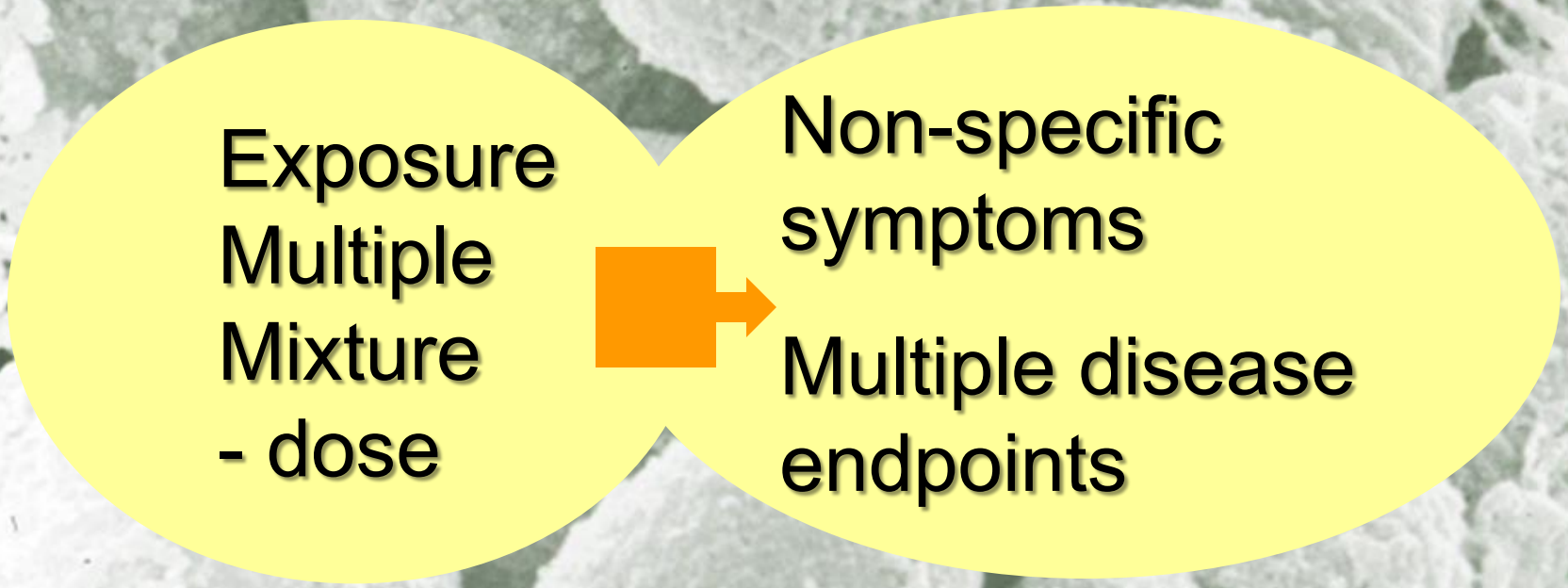
Agents:

- Allergens
- Ergosterol
- (1-3)-ß-D-glucan
- Mycotoxins
- microbial volatile organic compounds (MVOCs)
- ???

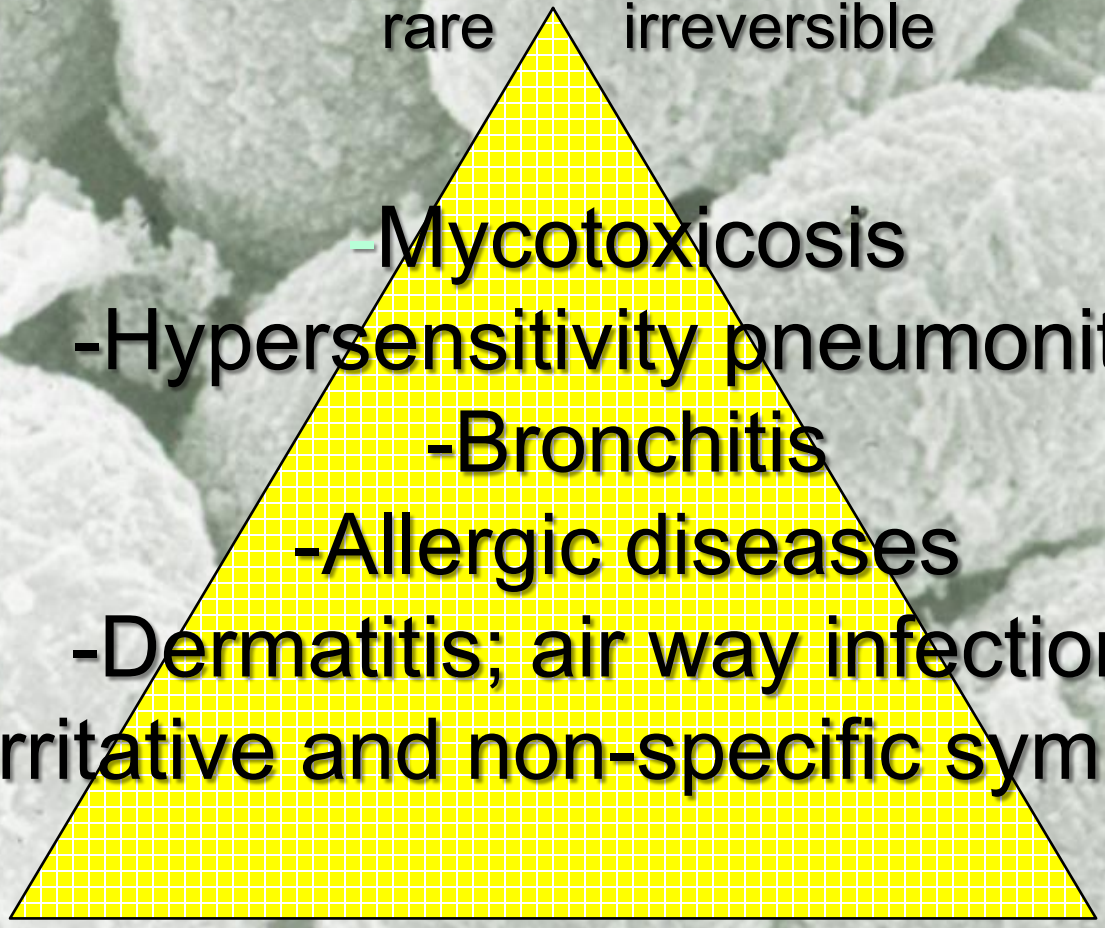
Allergy + Non-allergic

- Dermatitis,
- Urticaria
- Rhinitis, Sinusitis
- Asthma
- Extrinsic allergic alveolitis “humidifier fever”
- Organic dust toxic syndrome
- Toxic – irritant effects

Diagnostic problems



Health effects of fungi



Database

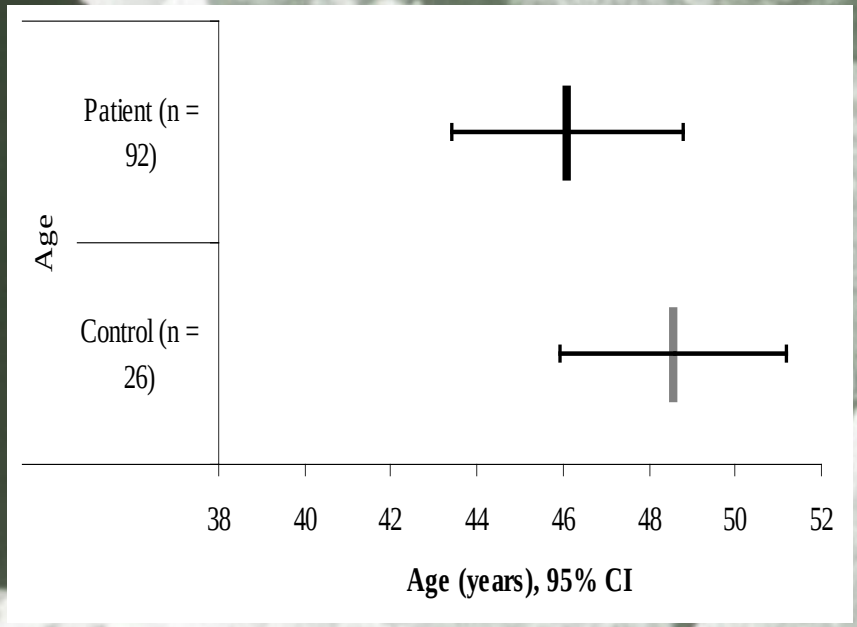
Patients evaluated in occupational and environmental health clinic from **December 1999 to February, 2005**

* Adult patients (Patients ≥ 18 years at time of visit, exposure duration ~ 2y)
* Advanced environmental testing (including airborne cytotoxicity study MTT)
* Completed self-administered health questionnaire.

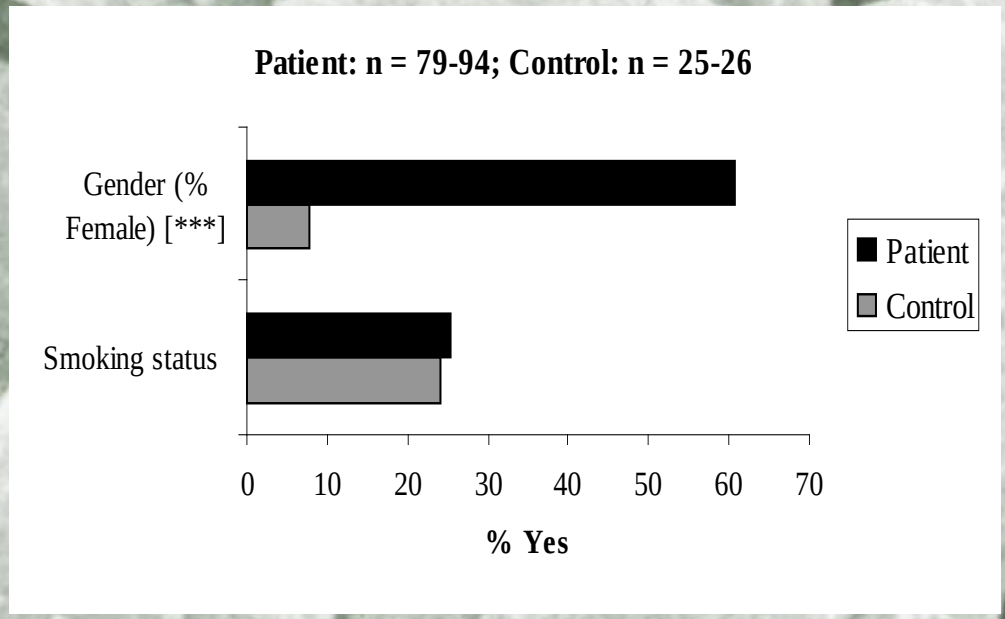
Compared to adult clinic patients (controls) without self-reported exposure to dampness/mold at home or at work.

Demographics

Age

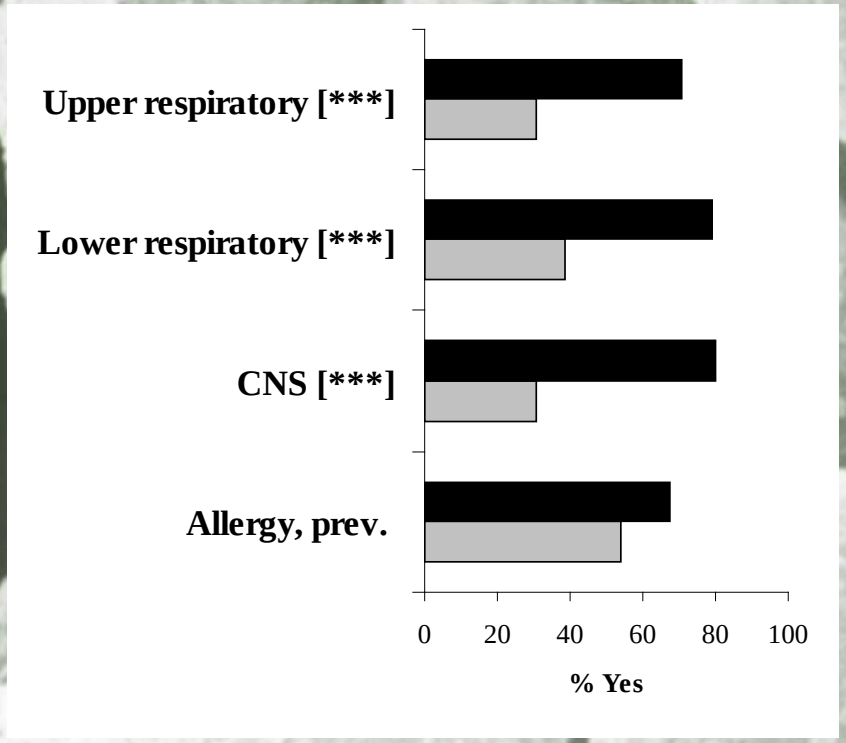


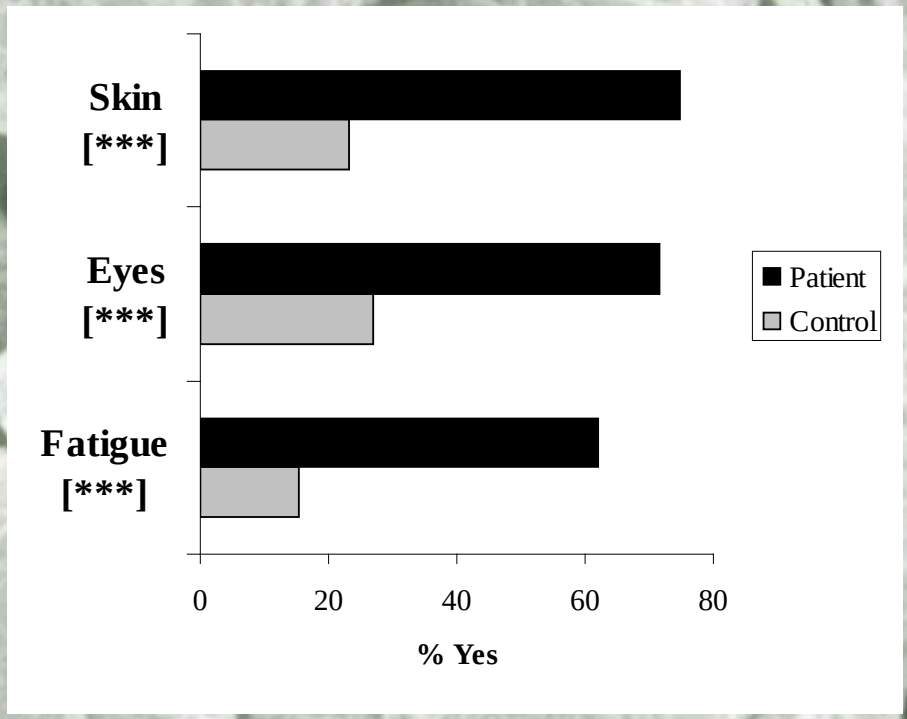
Gender - Smoker



*** = p < 0.001

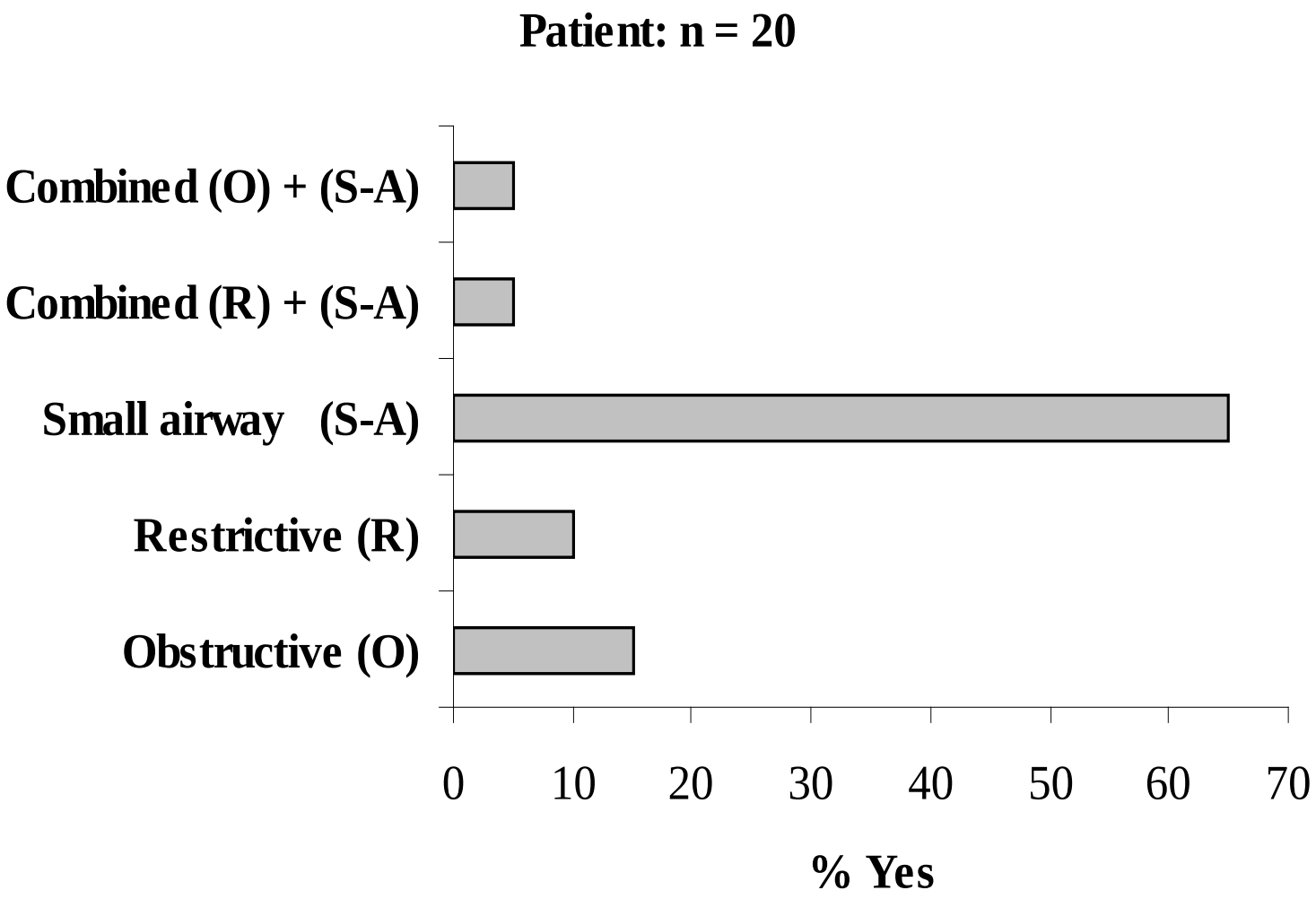
Symptom complex



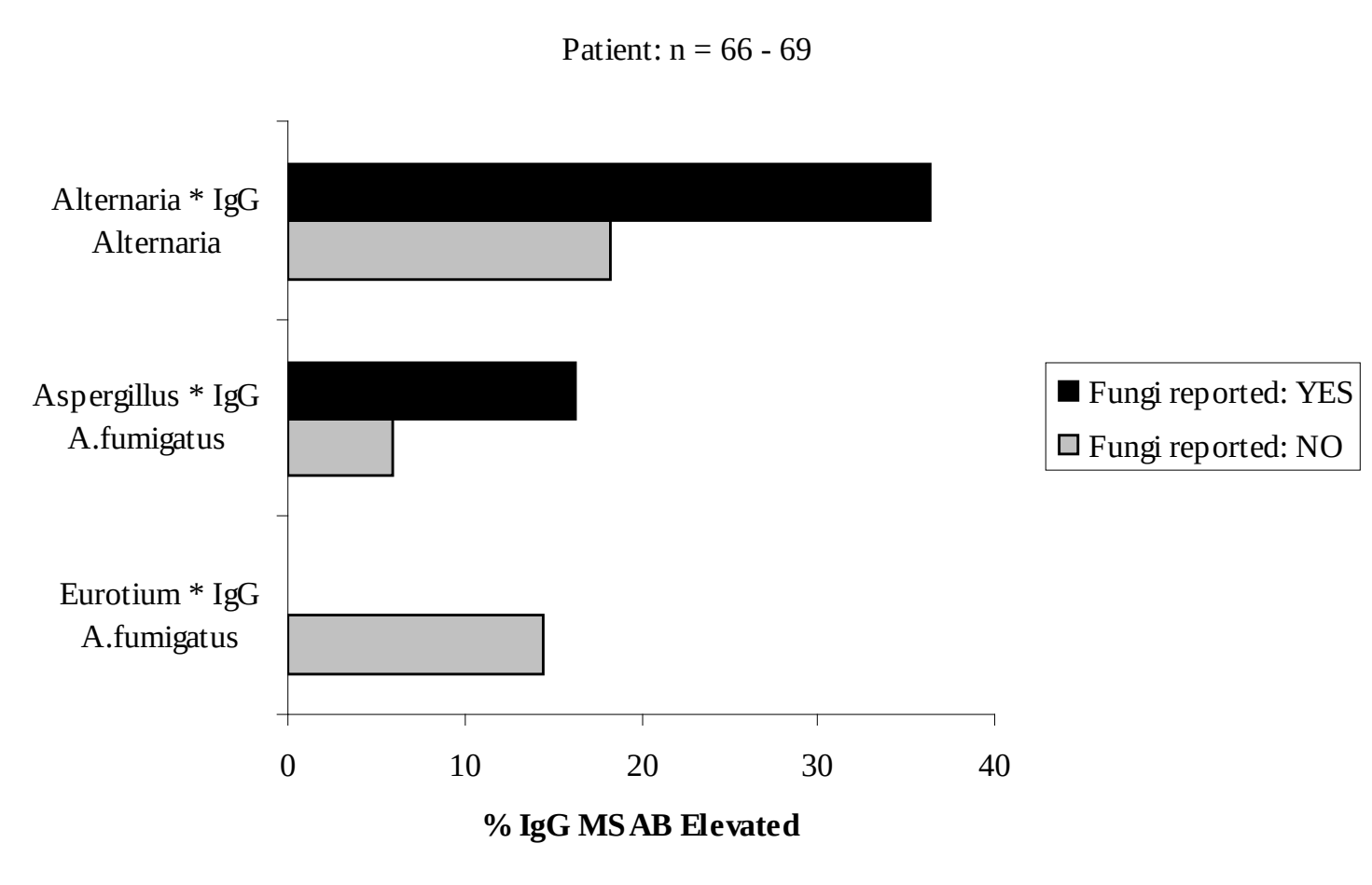


Patient: n = 95; Control: n = 26

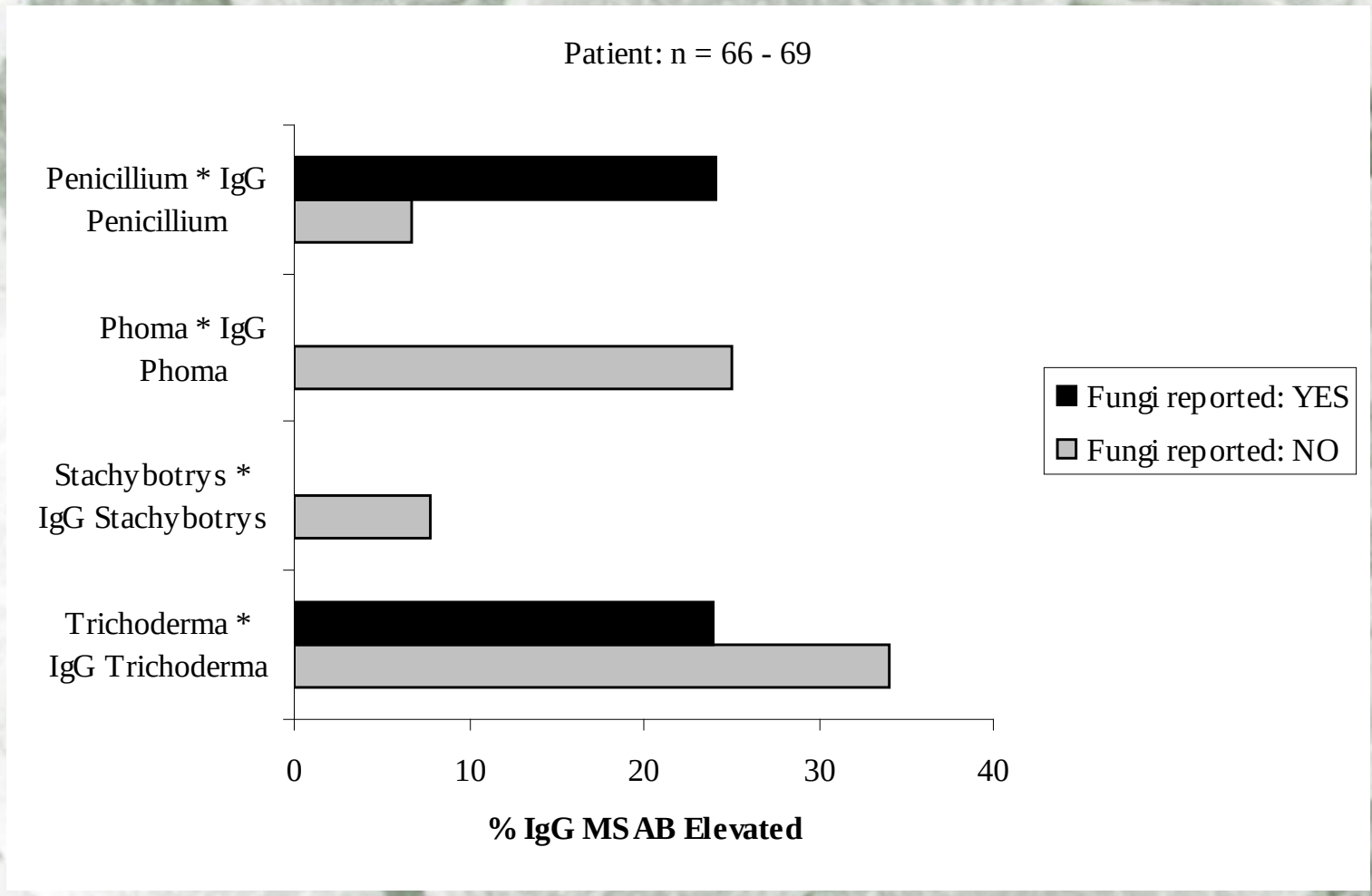
Pulmonary function test abnormalities



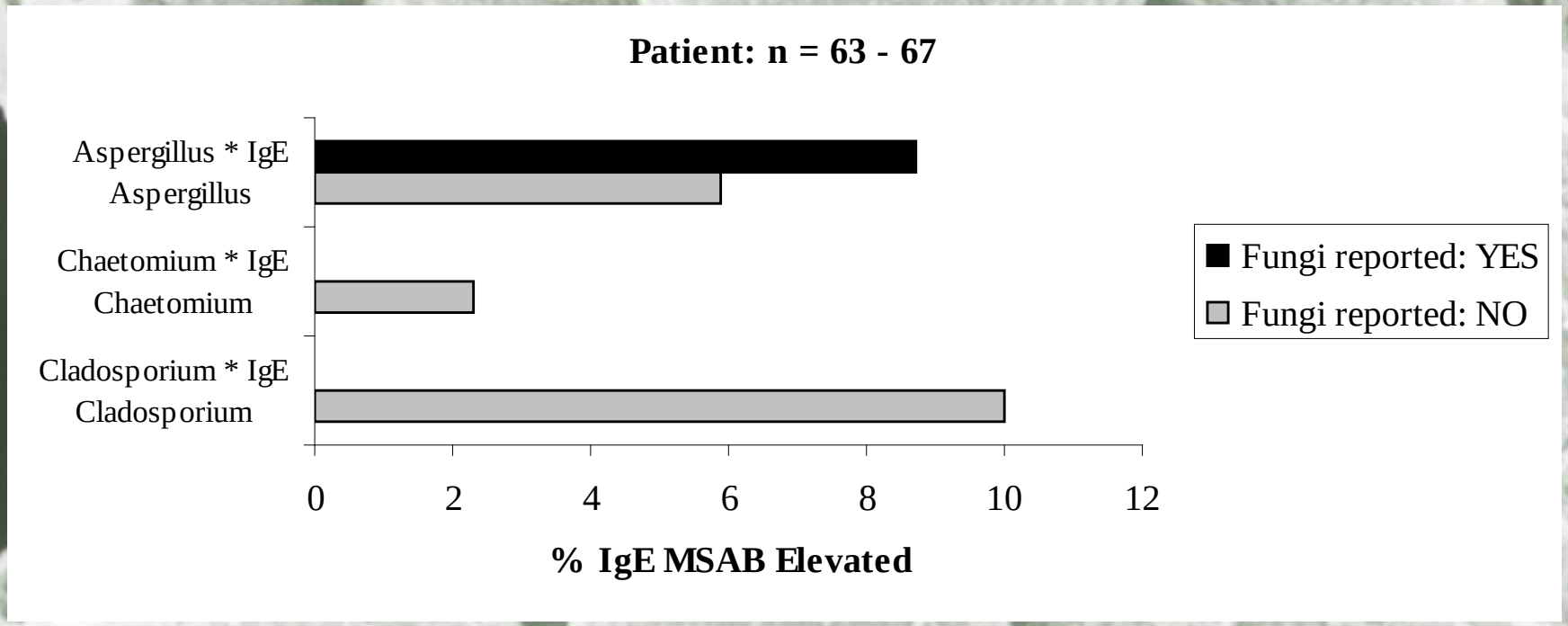
Patient's IgG Antibody response and comparison with environmental sampling identification



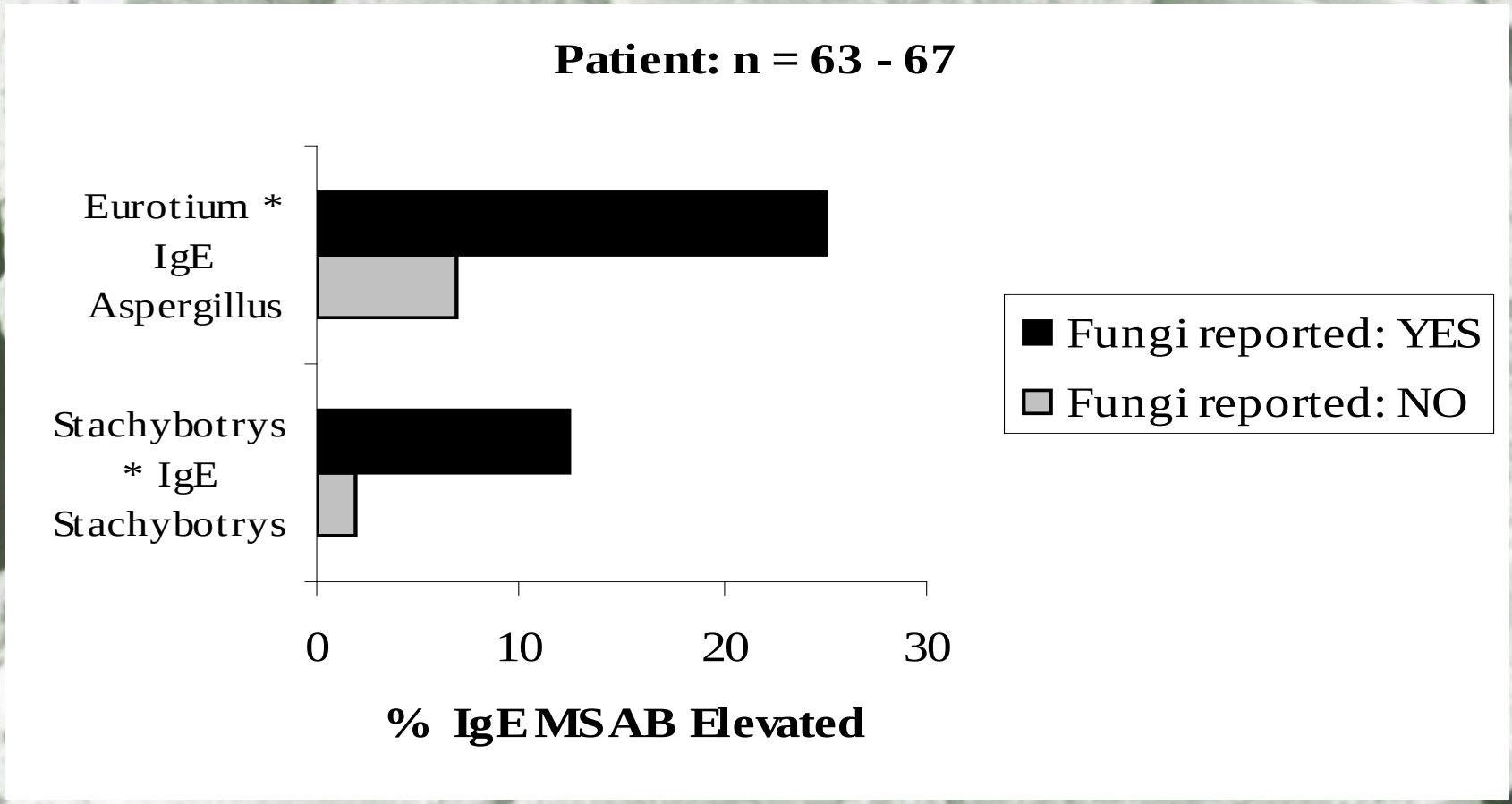
Patient's IgG Antibody response and comparison with environmental sampling identification



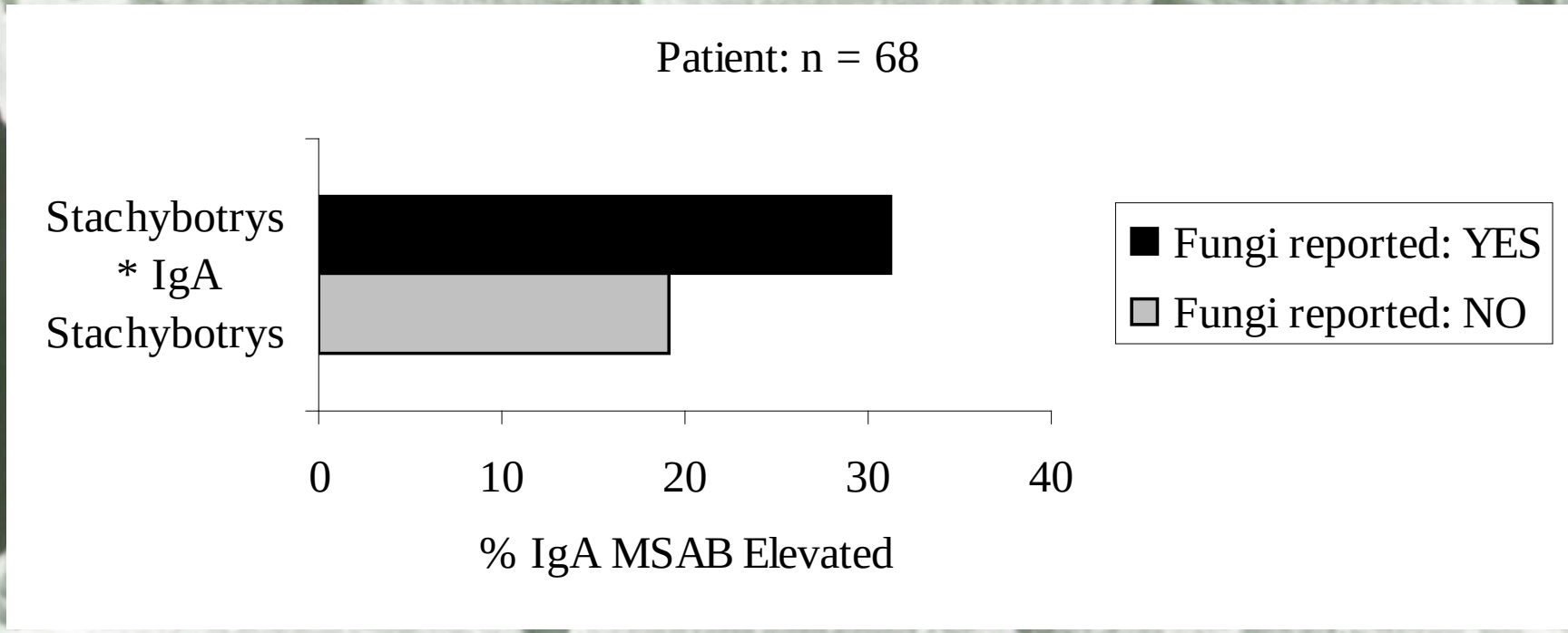
Patient's IgE Antibody response and comparison with environmental sampling identification



IgE Mold Specific Antibodies & Environmental Exposure



IgA Mold Specific Antibodies & *Stachybotrys chartarum* exposure

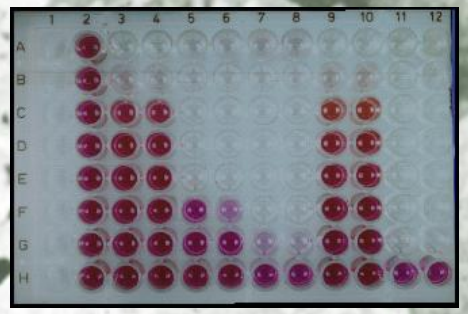


Serological Marker Sensitivity, Specificity, positive and negative predictive value

Agent – Serol-ogy	Sensitivity	Specificity	+ predictive value	- predictive value
A. fumigatus IgE	0.04	0.91	0.93	0.85
S. chartarum IgE	0.05	0.94	0.6	0.33
Alternaria a. IgG	0.22	0.74	0.53	0.42
Penicillium n. IgG	0.25	0.77	0.95	0.08
A. fumigatus IgG	0.24	0.83	0.17	0.88
S. chartarum IgG (adults only)	0.09	0.85	0.48	0.37
S. chartarum IgG (children only)	0.07	1	1	0.26
Trichoderma v. IgG	0.28	0.65	0.22	0.71

Airborne fungal toxicity assessment

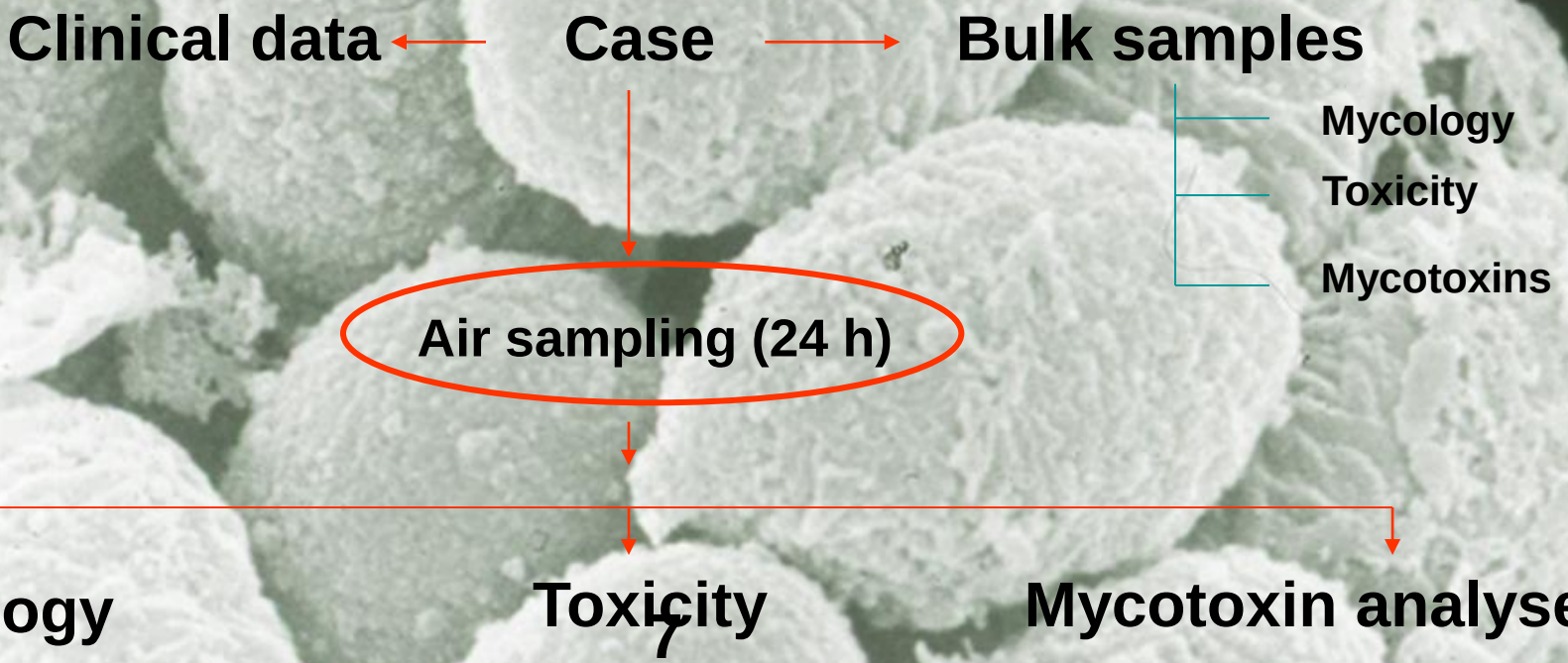
METHODS



Indoor environments of 55 patients (1999 and 2005) with verified moisture related building damage and indoor fungal growth were studied.

In total, 161 high-volume air samples were analyzed for trichothecene (Roridin A) content by the *ELISA* method and fungi in this comparison.

Inhalation Exposure - Logistics and Methodology



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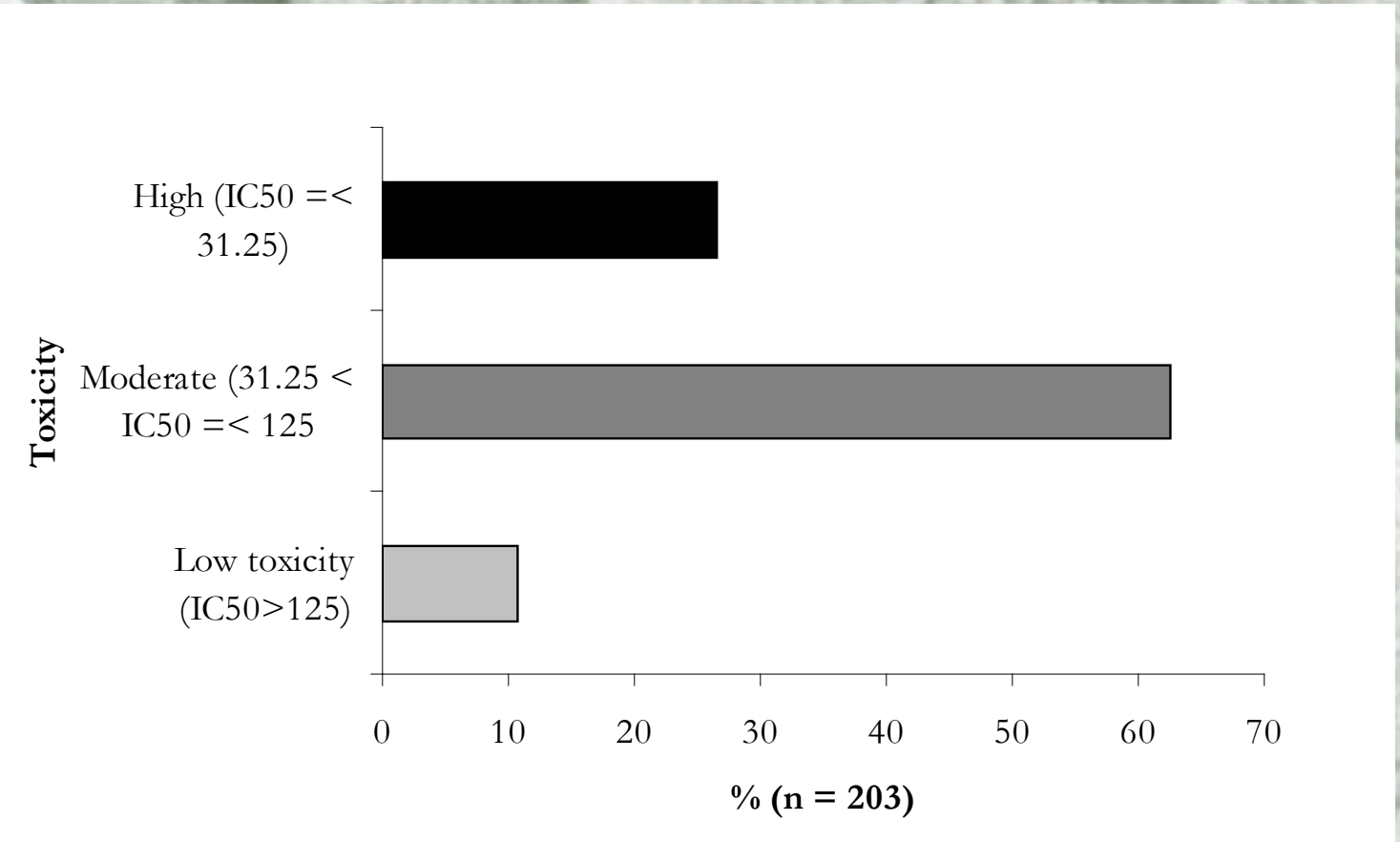
paper in preparation

Airborne Cyto-Toxicity Results:

Samples



Airborne Cytotoxicity & Viable Fungi

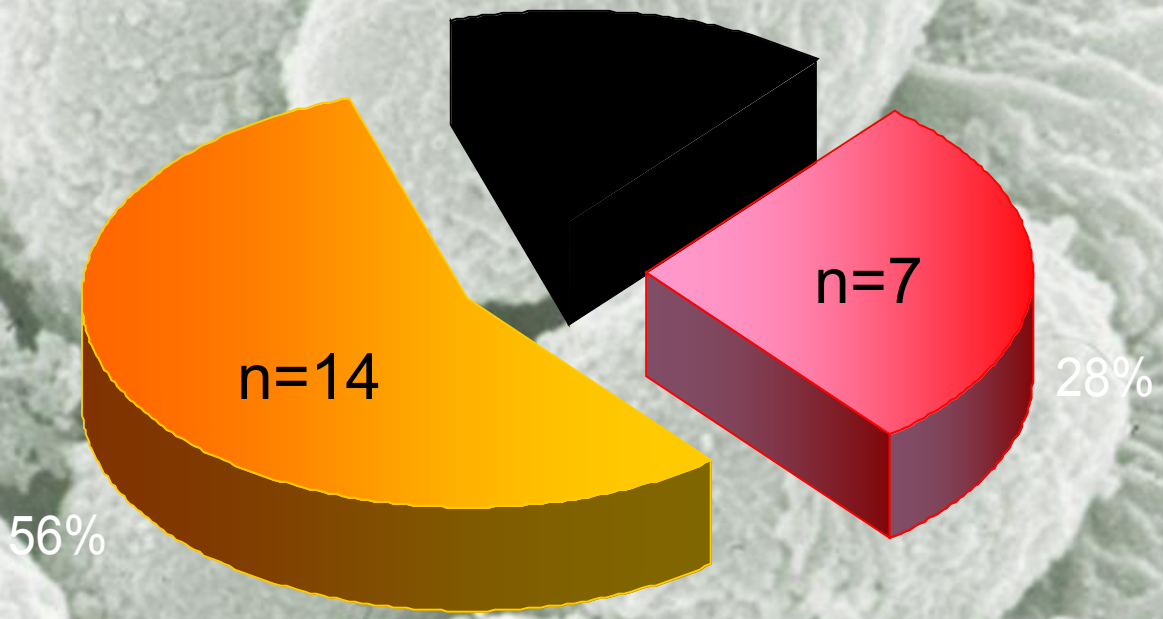
		RoA *Elisa* (ng/g)					Spearman's	
Viable fungi (% yes, (n))	level	< 2	2 < 5	5 < 10	10 < 50	=> 50	Approx. T	Approx. p
Acremonium sp.	(+)	4.0 (1)	4.0 (1)	4.0 (1)	0.0 (0)	0.0 (0)	-0.210	0.835
	+	8.0 (2)	8.0 (2)	8.0 (2)	16.0 (4)	16.0 (4)		
	++	8.0 (2)	4.0 (1)	8.0 (2)	4.0 (1)	4.0 (1)		
	+++	0.0 (0)	4.0 (1)	4.0 (1)	0.0 (0)	0.0 (0)		
Alternaria sp.	(+)	7.7 (1)	no data	7.7 (1)	0.0 (0)	0.0 (0)	0.504	0.624
	+	15.4 (2)	no data	15.4 (2)	7.7 (1)	15.4 (2)		
	++	15.4 (2)	no data	0.0 (0)	0.0 (0)	15.4 (2)		
Aspergillus sp.	(+)	2.0 (2)	2.0 (2)	2.0 (2)	0.0 (0)	0.0 (0)	0.386	0.700
	+	12.9 (13)	15.8 (16)	16.8 (17)	4.0 (4)	4.0 (4)		
	++	8.9 (9)	5.9 (6)	2.0 (2)	4.0 (4)	4.0 (4)		
	+++	5.9 (6)	1.0 (1)	5.0 (5)	2.0 (2)	2.0 (2)		
Chaetomium sp.	(+)	5.9 (1)	0.0 (0)	0.0 (0)`	0.0 (0)	0.0 (0)	-2.403	**0.030**
	+	0.0 (0)	5.9 (1)	17.6 (3)	5.9 (1)	23.5 (4)		
	++	11.8 (2)	0.0 (0)	5.9 (1)	0.0 (0)	0.0 (0)		
	+++	11.8 (2)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)		
Cladosporium sp.	(+)	1.4 (1)	1.4 (1)	4.1 (3)	1.4 (1)	0.0 (0)	1.599	0.114
	+	23.0 (17)	18.9 (14)	17.6 (13)	6.8 (5)	2.7 (2)		
	++	6.8 (5)	2.7 (2)	0.0 (0)	5.4 (4)	5.4 (4)		
	+++	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	2.7 (2)		
Paecilomyces sp.	(+)	0.0 (0)	3.6 (1)	10.7 (3)	3.6 (1)	0.0 (0)	-1.111	0.277
	+	32.1 (0)	10.7 (3)	10.7 (3)	7.1 (2)	14.3 (4)		
	++	3.6 (1)	0.0 (0)	3.6 (1)	0.0 (0)	0.0 (0)		
Penicillium sp.	+	10.8 (12)	14.4 (16)	10.8 (12)	9.0 (10)	4.5 (5)	-1.601	0.112
	++	14.4 (16)	4.5 (5)	5.4 (6)	4.5 (5)	2.7 (3)		
	+++	9.0 (10)	2.7 (3)	2.7 (3)	2.7 (3)	3.6 (4)		

Inhalation Exposition - Results

Cytotoxicity Testing of Filter Papers from 24 h Air Sampling

III

toxic samples



n cases	*Stachybotrys chartarum*	Macrocyclic Trichothecenes
5	+	+
5	-	+
3	+	-
8	-	-

Fungal toxicity and neurocognitive dysfunction

(W. Gordon, PhD et al)

Applied Neuropsychology
2004, Vol. 11, No. 2, 65–74

ARTICLES

Cognitive Impairment Associated With Toxigenic Fungal Exposure: A Replication and Extension of Previous Findings

Wayne A. Gordon and Joshua B. Cantor
Department of Rehabilitation Medicine, Mount Sinai School of Medicine, New York, New York, USA

Eckardt Johanning
Department of Community and Preventative Medicine, Mount Sinai School of Medicine, New York, New York, USA

Heather J. Charatz, Teresa A. Ashman, Janis L. Breeze, Lisa Haddad, and Steven Abramowitz
Department of Rehabilitation Medicine, Mount Sinai School of Medicine, New York, New York, USA

- **22 neurocognitive cases selected that included indoor air toxicity assessments**

Brain Injury Screening Questionnaire (BISQ) Results:

Gorden et.al., Applied Neuropsychology 2004, Vol. 11, No.2, 65-74

Table 2. *BISQ Symptom Report: Means and Standard Deviations and Results of ANOVAs Comparing Mean Numbers of BISQ Symptoms Between Groups*

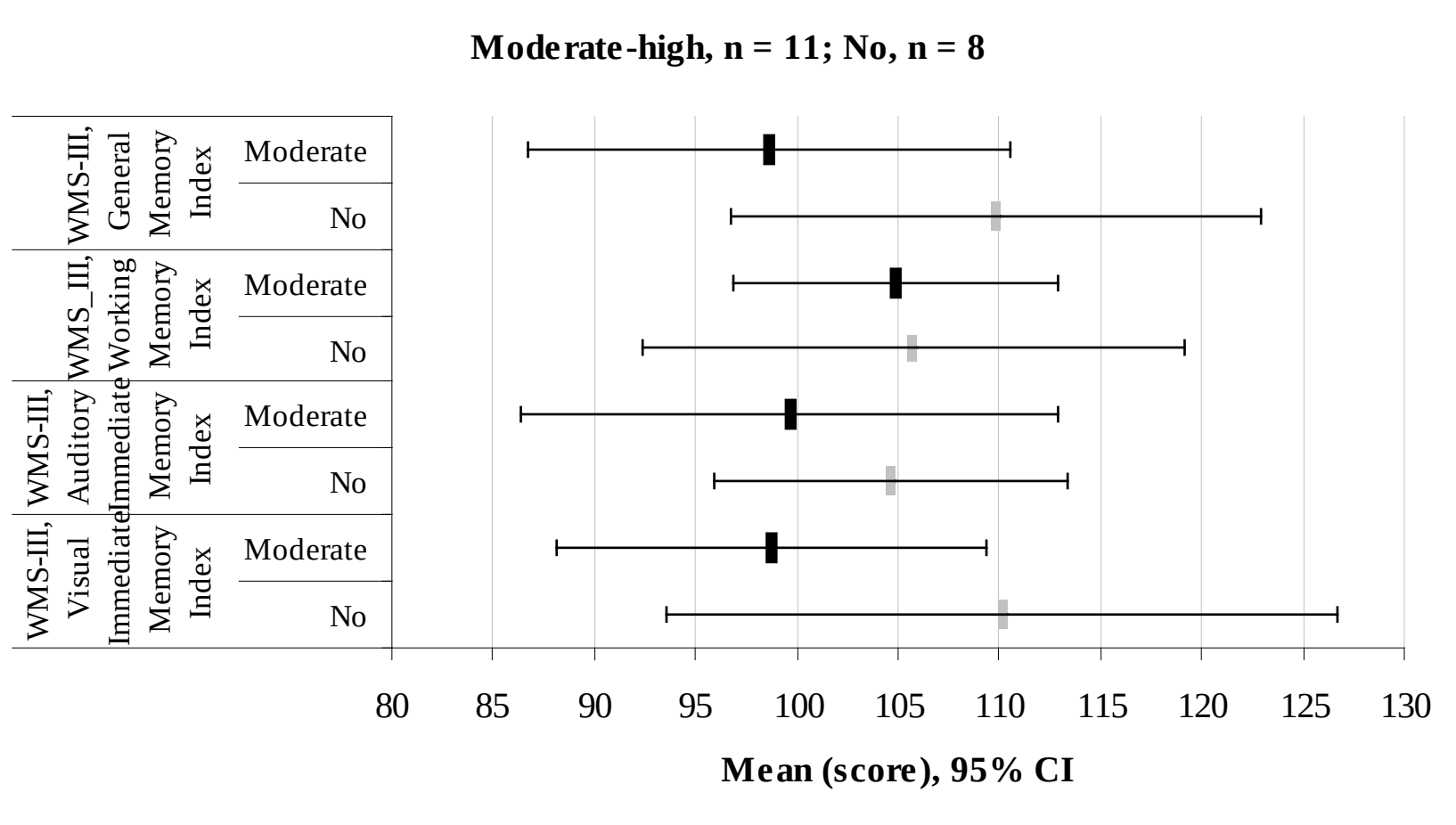
	Groups										
	Mold[a]		Mild TBI[b]		Moderate TBI[c]		No Disability[d]				
Type of Symptoms	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*df*	*F*	*p*
Physical	6.07	3.73	7.11	4.88	9.12	4.78	1.87	2.67	3	21.74	<.001
Cognitive	18.67	11.06	21.25	14.59	25.65	14.34	2.66	5.47	3	29.48	<.001
Behavioral	8.13	6.82	11.89	8.20	13.00	7.98	4.19	5.76	3	12.84	<.001
All	32.87	19.37	40.25	26.17	47.77	24.65	8.72	12.37	3	25.78	<.001
25 S&S[b]	10.10	6.23	8.72	6.38	11.27	6.85	1.02	2.53	3	25.43	<.001

Note. BISQ = Brain Injury Screening Questionaire; ANOVA = Analyses of Variance; TBI = traumatic brain injury.
[a]$n = 30$. [b]$n = 65$. [c]$n = 26$. [d]$n = 47$. [e]S&S = symptoms sensitive and specific to TBI (Gordon et al., 2000).

68

Patients with (toxigenic) indoor mold exposure history and traumatic brain injury report similar symptoms and problems

Neurocognitive Testing Results, WMS III, Airborne Toxicity Findings



Of 22 neurocognitive cases selected that included indoor air toxicity assessments

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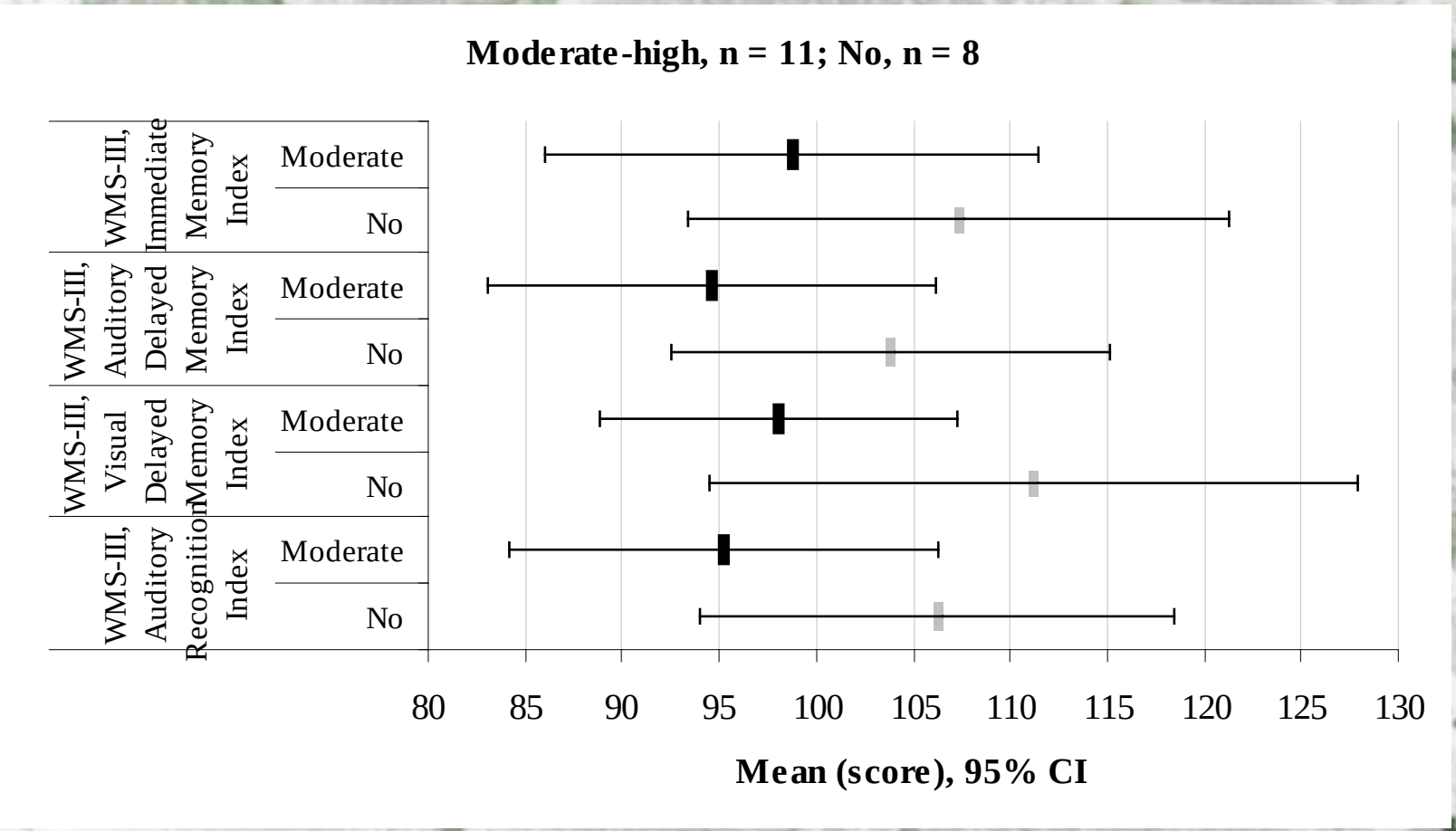
Neurocognitive Testing Results, WMS III, Airborne Toxicity Findings



Of 22 neurocognitive cases selected that included indoor air toxicity assessments

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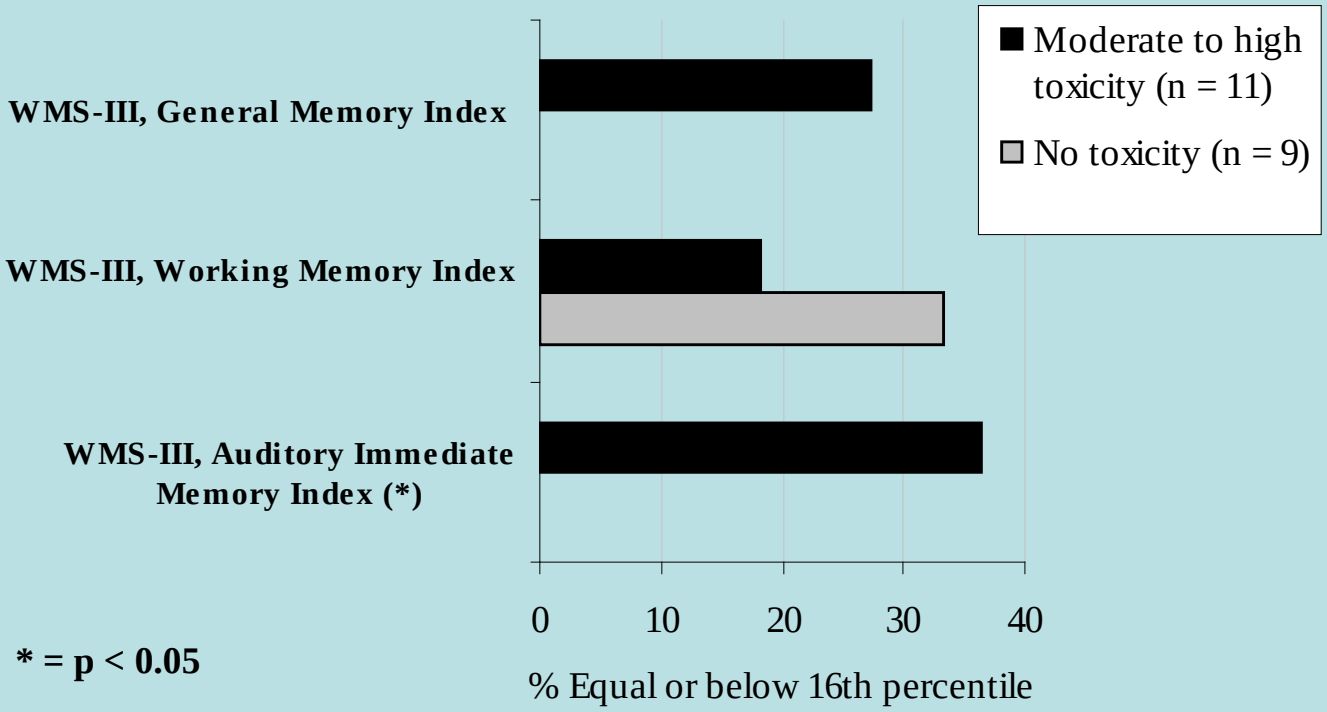
Neurocognitive Testing Results, WMS III, Toxicity, % Reduced functioning (≤ 16thpercentile)



Of 22 neurocognitive cases selected that included indoor air toxicity assessments

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Neurocognitive Testing Results, WMS III, Toxicity,

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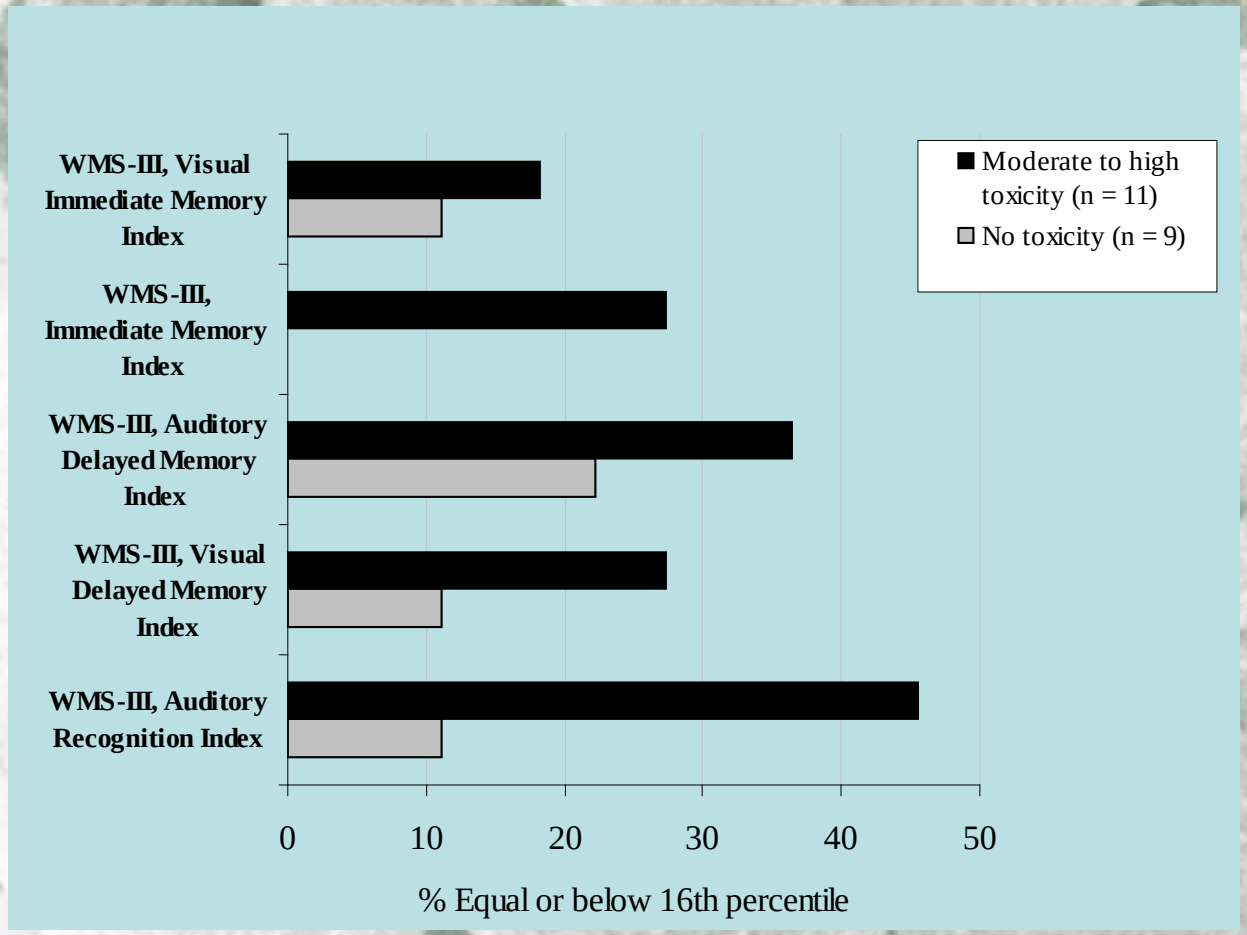

•22 neurocognitive cases selected that included indoor air toxicity assessments

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Reviews and committee papers –
who are the reviewer and what are their motives?

- ACOEM – "Mold - Evidence Paper"
  - American College of Occupational and Environmental Medicine (10/2002)
    - Authors: Hardin, Kelman, Saxon
    - See also: Manhattan Institute (same content) (7/03)
- IOM - Damp Indoor Spaces and Health
  - Institute of Medicine (2004)
- Kuopio Finland Toxic Mold Meeting (7/2004)
  - ISIAQ
- Norddamp (Bornehag et al, 2004)

Critique of “evidence Papers”

- The motives and intentions of the authors have been examined and questioned:
  - “A Critique of the ACOEM Statement on Mold: Undisclosed Conflicts of Interest in the Creation of an “Evidence-based” Statement”
    - *By JAMES CRANER in INT J OCCUP ENVIRON HEALTH 2008;14:283–298*
  - “Court of Opinion: Amid Suits Over Mold. Experts Wear Two Hats; Authors of Science Paper Often Cited by Defense Also Help in Litigation”
    - *By David Armstrong*. Wall Street Journal. (Eastern edition). New York, N.Y.: Jan 9, 2007.
  - “Position paper on molds by AAAAI is seriously flawed”.
    - A Critique of the AAAAI Statement on Mold: The medical effects of mold exposure. by Bush RK, Portnoy JM, Saxon A, Terr AI, Wood RA. J Allergy Clin Immunol 2006;117:326-33.
    - Letters to editor of journal by different authors see: J ALLERGY CLIN IMMUNOL VOLUME 118, NUMBER 3

Detection of Airborne *Stachybotrys chartarum* Macrocyclic Trichothecene Mycotoxins in the Indoor Environment

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Received 9 March 2005/Accepted 12 July 2005

allergens Can f 1, Der p 1, and Fel d 1. For test buildings, the results showed that detectable toxin concentrations increased with the sampling time and short periods of air disturbance. Trichothecene values ranged from <10 to >1,300 pg/m^3 of sampled air. The control environments demonstrated statistically significantly ($P < 0.001$) lower levels of airborne trichothecenes. ELISA specificity experiments demonstrated a high specificity for the trichothecene-producing strain of *S. chartarum*. Our data indicate that airborne macrocyclic trichothecenes can exist in *Stachybotrys*-contaminated buildings, and this should be taken into consideration in future indoor air quality investigations.

APPLIED AND ENVIRONMENTAL MICROBIOLOGY, Nov. 2005, p. 7376–7388 Vol. 71, No. 11

Conclusions

- Patient IgE and IgG show limited correlation with specific environmental findings (low sensitivity, good specificity)
- Patient show (also) non IgE- or IGG-mediated or associated exposure effects
- New onset of symptoms and abnormalities in non-sensitized patients (new onset Dx)

Conclusions

- Cognitive impairment symptoms similar to patients with traumatic brain injury (TBI)
- Airborne (fungal) toxicity appear to be correlated with some neurocognitive dysfunction
- Improved, specific exposure data necessary to improve environmental/occupational diagnosis
- Mycotoxin body burden indicator needed to validate study findings

Conclusions

- Airborne Satratoxins (macrocyclic trichothecenes)
- Detection of mycotoxins in air samples not or weakly correlated with fungal spores
- *S. chartarum* not necessarily correlated with the presence of satratoxins
- Other cytotoxic compounds could be detected by use of the bioassay
- Methods appears to be reliable to differentiate between cytotoxic and non-cytotoxic filter papers, i.e. toxic and non-toxic environments

“Wissen ist nicht genug – wir müssen handeln”

“Knowing is not enough; we must apply.”

- J. W. Goethe

Child with asthma in Spanish Harlem, N.Y. …

Johanning et al; EHP 1999;107 (3)