Neurobehavioral and pulmonary impairment in 105 adults with indoor exposure to molds compared to 100 exposed to chemicals

Kaye H Kilburn

Abstract
Patients exposed at home to molds and mycotoxins and those exposed to chemicals (CE) have many similar symptoms of eye, nose, and throat irritation and poor memory, concentration, and other neurobehavioral dysfunctions. To compare the neurobehavioral and pulmonary impairments associated with indoor exposures to mold and to chemicals. 105 consecutive adults exposed to molds (ME) indoors at home and 100 patients exposed to other chemicals were compared to 202 community referents without mold or chemical exposure. To assess brain functions, we measured 26 neurobehavioral functions. Medical and exposure histories, mood states score, and symptoms frequencies were obtained. Vital capacity and flows were measured by spirometry. Groups were compared by analysis of variance (ANOVA) after adjusting for age, educational attainment, and sex, by calculating predicted values (observed/predicted × 100 = % predicted). And p < .05 indicated statistical significance for total abnormalities, and test scores that were outside the confidence limits of the mean of the percentage predicted. People exposed to mold had a total of 6.1 abnormalities and those exposed to chemicals had 7.1 compared to 1.2 abnormalities in referents. Compared to referents, the exposed groups had balance decreased, longer reaction times, and blink reflex latencies lengthened. Also, color discrimination errors were increased and visual field performances and grip strengths were reduced. The cognitive and memory performance measures were abnormal in both exposed groups. Culture Fair scores, digit symbol substitution, immediate and delayed verbal recall, picture completion, and information were reduced. Times for peg-placement and trail making A and B were increased. One difference was that chemically exposed patients had excess fingertip number writing errors, but the mold-exposed did not. Mood State scores and symptom frequencies were greater in both exposed groups than in referents. Vital capacities were reduced in both groups. Neurobehavioral and pulmonary impairments associated with exposures to indoor molds and mycotoxins were not different from those with various chemical exposures.

Keywords
Balance, visual field performance, memory, trichothecene–mycotoxin, neuropsychological impairment, neurophysiological tests, cognitive function, memory deficits

Introduction
People’s adverse health effects were attributed to indoor air after the 1973 energy crisis increased air recycling and decreased air leaks from buildings (Dalley et al., 1981; Kress, 1990; Small and Borus, 1983). Mold disease emerged in the 1990s with infantile pulmonary hemosiderosis in Cleveland, Ohio (Centers for Disease Control and Prevention [CDCP], 1994; Etzel et al., 1998; Montana et al., 1997). News media, insurance companies, courts, physicians, and government agencies have doubts about indoor air disorders attributing to molds. Literally, people’s descriptions of sickness related to musty odors and...
in excessively humid homes were
Rhizopus californicus (species: Cladosporium, Toxicology and Industrial Health 25(9-10) species, (Shinn, 2000) and the doubling
682
the 202 referent subjects (Kilburn et al.,
expressed as percentage of predicted and compared
patient’s scores to their predicted values for each test
exposed (UE) control subjects. We compared each
exposed to chemicals (CE) without asymptomatic
were evaluated interspersed with 100 patients
an association.
1998) and in several Caribbean Islands suggesting
(Andersson, 1997; Kilburn 2002,
3 to chlordane, and 27 to 11 other chemicals.
versus floors. Surface samples lifted on transparent
tape helped identify molds microscopically. Cultures
of indoor air samples and scraping frequently grew Stachybotrys chartarum, Aspergillus, Penicillium, Chaetomium, Alternaria, Fusarium, and Rhizopus.
For most homes that were sampled, concentrations
of mold spores in indoor air samples exceeded those
in outdoor air by multiples of 4 or more.
The 100 consecutive CE patients (53 women and
47 men) tested concurrently had 19 exposed to hydrogen sulfide, 13 to diesel exhaust, 9 to formaldehyde
and indoor air, 8 to organophosphate insecticides, 7
to glutaraldehyde, 7 to cleaning chemicals, 4 to poly-
chlorinated biphenyls, 4 to carbon monoxide, 3 to
chlorine, 3 to chlorodane, and 27 to 11 other chemicals.
The 105 mold patients (69 women and 36 men), and
the 100 CE patients (53 women and 47 men), and 202
(107 women and 95 men) UE people were compared
by analysis of variance (ANOVA) after every observed
value was divided by its predicted value. Each subject-
observed values for each test was divided by the
predicted value, multiplied by 100, and expressed as
percentage predicted that adjusted each measurement
for gender, height, weight, and education (highest
school grade completed). Kindergarten through 12th
grade equals 12 years, a bachelor’s degree equals
16 years, and a doctoral degree equals 20 years.
The 202 UE subjects group’s data were pooled and
distributions plotted, and numbers transformed when
that improved symmetry and then regression
equations were developed to predict each persons score for each test. The 202 UE subjects were drawn at random from voter registration rolls. They were interviewed to exclude occupational chemical exposures and medical or neurological diseases and 105 women and 95 men measured to develop the prediction equations (Kilburn et al., 1998a,b). The UE subjects were reimbursed for their time.

All subjects in the three groups gave informed consent to the protocol approved by the Human Studies Research Committee of the University of Southern California, Keck School of Medicine.

Questionnaires were checked by computer-guided reading, so subjects rectified their omissions as they completed them. They rated the frequencies of 35 common health complaints (Kilburn et al., 1987) from 1 for never to 11 for daily. They answered the American Rheumatism Association lupus erythematosus questions (Levin et al., 1984); a standard respiratory questionnaire (Ferris, 1978); and gave histories of occupational and other exposures to chemicals, pesticides and herbicides, tobacco, alcohol, and drug use (prescription and illicit). Histories recorded unconsciousness, anesthesia, head trauma, and medical and neurological psychiatric illnesses (Kilburn, 1994). Questionnaires had been tested in groups of people exposed to formaldehyde (Kilburn et al., 1987), thermolysis products of PCBs (Kilburn et al., 1989), to toluene-rich chemical waste (Kilburn and Warshaw, 1995), and subjects without (known) chemical exposure (Kilburn and Warshaw, 1995; Kilburn et al., 1998a,b).

**Neuropsychological tests**

Immediate and 30-min delay verbal recall was measured with two stories from Wechsler’s Memory Scale, revised (Wechsler, 1945, and 1987). Culture Fair tested non-verbal non-arithmetical intelligence with four sets of designs (Cattell, 1951; Cattell et al., 1941). It resembles Raven’s progressive matrices (Raven et al., 1988). The 46-word multiple choice vocabulary test was from the multidimensional aptitude battery (Jackson, 1985). Digit symbol substitution from the Wechsler Adult Intelligence Scale-revised (WAIS-R; Wechsler, 1981, 1987) tested attention and integrative capacity. Information, picture completion and similarities, from the WAIS-R, tested long-term (embedded or hold) memory. Time needed to place 25 pegs in the Lafayette slotted pegboard and to make trails A and B assessed dexterity, coordination, and decision making. These tests and fingertip number writing errors that measured peripheral sensory discrimination were from the Halstead-Reitan battery (Reitan, 1958, 1966).

Responses to 65 terms describing feelings for the preceding week were assessed by the Profile of Mood States (POM) (1971/1981). The Limbic checklist assessed somatic and functional responses (Teicher et al., 1993). Recall of Rey’s 15 figures assessed visual memory and gave clues as to possible malingering (Rey, 1964).

Expiratory flows and vital capacities were measured by blowing rapidly (exhaling) a full inspiration into a volume displacement (Ohio) spirometer while standing (using a nose clip). Forced expirations were
repeated until two agreed within 5% (ATS Statement, 1987). Records were traced into a computer and compared to predicted values adjusted for height, age, gender, and years of cigarette smoking (Miller et al., 1986). Alcohol and carbon monoxide were measured in air expired after a 20-second breath hold using appropriate fuel cell analyzers.

Statistical analysis

Scores and computed data were entered into an IBM compatible microcomputer. Stepwise linear regression modeling of each measurement in 293 symmetrically distributed subjects had produced prediction equations for each test that adjusted for differences in age, education, gender, height, and weight, using Strata Statistical Software (Strata Corporation, College Station, TX). Then the observed measurements were compared to individual predicted values and expressed as percentage predicted (Kilburn et al., 1998a). The two exposed groups’ mean values, as percentage predicted were compared to the control group mean values by ANOVA. Family income, hours of general anesthesia, POMS score, and depression score were excluded because of insignificant coefficients. Statistical significance was defined as \( p < .05 \). Abnormalities for the patient’s and referent’s were counted (Table 1) valuing bilateral tests 0.5 per side, except that hearing and visual field performance counted 1 per side and balance 1 for eyes open and 1 for eyes closed.

Results

Exposure

The 105 patients had observed black mold growing on indoor walls and smelled musty odors that were enhanced when electrical switch and socket plates were removed and air-conditioning ducts that accessed inner walls were opened. Microscopy showed mold on surface imprint tapes. Usually indoor air grew more colony units of mold genera than outdoor air and grew bacteria including ones producing endotoxins.

The 100 CE patients and the 202 UE subjects had not observed mold in their homes and denied mold exposure.

The 69 ME women and 36 ME men and the 53 CE women and 47 CE men were not significantly older than the 202 UE subjects (Table 1), but both groups had more years of education, mean 14.7 and 13.6 than 12.9 in the UE group. Comparisons of function were as percentage predicted (% pred.) to the UE group which adjusted for these differences with statistically significant ones described. More years of education would raise scores acting against decreases due to either exposure. Both exposed groups mean simple reaction times were significantly prolonged compared to UE subjects, % pred 103.6, 105.8 versus 99.9 and \( p < .0001 \). CRT was 102.2 and 104.1 versus 100.0 \( p < .0001 \). Balance, measured as sway speeds were faster, 141.3 and 195.0 versus 100.2 for eyes open \( p < .0001 \) and 174.2 and 216.3 versus 103.1 eyes closed \( p < .0001 \) and extremely abnormal. Blink reflex latencies, R-1, were delayed, 113.4 and 112.3 versus 99.4 on the right \( p < .0001 \) \( p < .054 \) and 111.9 and 109.9 versus 96.4 on the left \( p < .0001 \).

Color discrimination errors were increased (however observed values decreased compared to predicted ones because they were the reciprocals of quadratic power), right eye 70.3 and 74.6 versus 102.6 \( p < .0001 \) and left eye 73.9 and 62.1 versus 102.6 \( p < .0001 \). Visual field performances were significantly reduced in both eyes, right 91.7 and 86.9 versus 100.0 \( p < .0016 \) and left 92.0 and 88.8 versus 101.1 \( p < .0009 \).

Grip strengths were significantly weaker, right 91.3 and 87.9 versus 99.3 in referents and left 87.0 and 83.8 versus 99.1 in referents \( p < .0001 \). Hearing losses were not significantly different in either exposed group compared to the UE subjects.

Problem solving tests showed significantly lower scores for Culture Fair 92.9 and 89.9 versus 101.2 \( p < .0006 \), digit symbol substitution 91.3 and 90.8 versus 101.5 \( p < .0001 \). Vocabulary was 87.7 and 81.6 versus 99.2 \( p < .002 \) \( p < .0001 \). Immediate verbal recall (of stories) was significantly lower at 81.0 and 76.0 versus 99.8 \( p < .0001 \) and decreased after 30 min at 71.4 and 63.9 versus 99.9 \( p < .0001 \).

Times needed for peg placement were 92.9 and 88.8 versus 101.8 \( p < .001 \), trail making A 103.6 and 106.6 versus 100.3 \( p < .0006 \) and trail making B 103.1 and 104.5 versus 100.4 \( p < .004 \) were significantly prolonged, showing perceptual motor slowing. Fingertip number writing errors did not differ from UE subjects, but were significantly greater in CE people. Information 82.5 and 81.9 versus 101.5 \( p < .0001 \) and picture completion 81.2 and 79.8 versus 99.3 \( p < .0001 \), differed from UE subjects, but not similarities 93.1 and 89.4 versus 98.1 \( p < .246 \) and \( p < .092 \). These three tests are usually unaffected by chemical exposures or are last to show impairment (Ryan et al., 1987).
CE subjects' impairments matched those of the ME except that finger tip number writing errors were abnormal only in CE people Table 1. One test in 26 could be different by chance alone.

Twelve of 14 physiological functions and 10 of 13 psychological tests, a total of 22 of 26 tests were abnormal in ME compared to 23 abnormalities in CE people.

The ME group averaged 9.8 abnormal tests Figure 1A compared to 10.2 in CE people (p < .0001), Figure 1C and 2.3 in the referents (p < .0001), Figure 1B.

ME subjects' mood states (POMS scores, the sum of 5 adverse moods minus vigor) were slightly lower than the CE, but nearly twice the UE group. Limbic system complaints like memory flashbacks, unusual

Table 1. Neurobehavioral function for mold exposed (ME) subjects (105) and chemically exposed (CE) subjects (100) compared to 202 referent subjects as percent of predicted, means and standard deviations (SD), p values by analysis of variance

<table>
<thead>
<tr>
<th></th>
<th>A 105 Mold Mean ± SD</th>
<th>B 100 Chemical Mean ± SD</th>
<th>C 202 Referent Mean ± SD</th>
<th>p Values A vs C</th>
<th>p Values B vs C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>46.5 ± 13.3</td>
<td>46.5 ± 10.3</td>
<td>47.2 ± 20.2</td>
<td>.621</td>
<td>.98</td>
</tr>
<tr>
<td>Educational level (years)</td>
<td>14.7 ± 2.6</td>
<td>13.6 ± 2.8</td>
<td>12.9 ± 2.3</td>
<td>.0001</td>
<td>.014</td>
</tr>
<tr>
<td>Physiological tests</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simple reaction time (ms)</td>
<td>103.6 ± 6.0</td>
<td>105.8 ± 6.5</td>
<td>99.9 ± 3.7</td>
<td>.0001</td>
<td>.0001</td>
</tr>
<tr>
<td>Choice reaction time (ms)</td>
<td>102.2 ± 4.0</td>
<td>104.1 ± 4.1</td>
<td>100.0 ± 2.5</td>
<td>.0001</td>
<td>.0001</td>
</tr>
<tr>
<td>Balance sway speed (cm/sec)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eyes open</td>
<td>141.3 ± 60.9</td>
<td>195.0 ± 193.5</td>
<td>100.2 ± 20.0</td>
<td>.0001</td>
<td>.0001</td>
</tr>
<tr>
<td>Eyes closed</td>
<td>174.2 ± 93.5</td>
<td>216.3 ± 184.1</td>
<td>103.1 ± 26.8</td>
<td>.0001</td>
<td>.0001</td>
</tr>
<tr>
<td>Blink reflex latency R-1 (ms)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>113.4 ± 13.0</td>
<td>112.3 ± 12.2</td>
<td>99.4 ± 14.6</td>
<td>.0001</td>
<td>.054</td>
</tr>
<tr>
<td>Left</td>
<td>111.9 ± 15.2</td>
<td>109.9 ± 10.2</td>
<td>96.4 ± 13.2</td>
<td>.0001</td>
<td>.0001</td>
</tr>
<tr>
<td>Hearing losses</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>98.1 ± 36.5</td>
<td>98.3 ± 30.3</td>
<td>101.5 ± 24.5</td>
<td>.673</td>
<td>.454</td>
</tr>
<tr>
<td>Left</td>
<td>99.4 ± 35.2</td>
<td>97.4 ± 25.0</td>
<td>99.3 ± 21.7</td>
<td>.533</td>
<td>.606</td>
</tr>
<tr>
<td>Color discrimination errors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>70.3 ± 43.3</td>
<td>74.6 ± 49.2</td>
<td>102.6 ± 51.1</td>
<td>.0001</td>
<td>.0001</td>
</tr>
<tr>
<td>Left</td>
<td>73.9 ± 46.1</td>
<td>62.1 ± 46.1</td>
<td>102.6 ± 51.1</td>
<td>.0001</td>
<td>.0001</td>
</tr>
<tr>
<td>Visual field performance</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>91.7 ± 23.2</td>
<td>86.9 ± 21.7</td>
<td>100.0 ± 22.7</td>
<td>.0016</td>
<td>.0002</td>
</tr>
<tr>
<td>Left</td>
<td>92.0 ± 24.5</td>
<td>88.8 ± 23.7</td>
<td>101.1 ± 21.6</td>
<td>.0009</td>
<td>.0007</td>
</tr>
<tr>
<td>Grip strength</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>91.3 ± 18.7</td>
<td>87.9 ± 23.2</td>
<td>99.3 ± 17.5</td>
<td>.0003</td>
<td>.0001</td>
</tr>
<tr>
<td>Left</td>
<td>87.0 ± 20.8</td>
<td>83.8 ± 24.7</td>
<td>99.1 ± 17.5</td>
<td>.0001</td>
<td>.0001</td>
</tr>
<tr>
<td>Psychological tests</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Culture fair</td>
<td>92.9 ± 22.6</td>
<td>89.9 ± 23.6</td>
<td>101.2 ± 20.0</td>
<td>.0006</td>
<td>.0001</td>
</tr>
<tr>
<td>Digit symbol</td>
<td>91.3 ± 11.4</td>
<td>90.8 ± 14.3</td>
<td>101.5 ± 9.2</td>
<td>.0001</td>
<td>.0001</td>
</tr>
<tr>
<td>Vocabulary</td>
<td>87.7 ± 31.9</td>
<td>81.6 ± 31.2</td>
<td>99.2 ± 30.8</td>
<td>.002</td>
<td>.0001</td>
</tr>
<tr>
<td>Verbal recall</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immediate</td>
<td>81.0 ± 24.2</td>
<td>76.0 ± 28.1</td>
<td>99.8 ± 31.1</td>
<td>.0001</td>
<td>.0001</td>
</tr>
<tr>
<td>Delayed</td>
<td>71.4 ± 36.4</td>
<td>63.9 ± 34.5</td>
<td>99.9 ± 41.3</td>
<td>.0001</td>
<td>.0001</td>
</tr>
<tr>
<td>Pegboard</td>
<td>92.9 ± 15.2</td>
<td>88.8 ± 16.0</td>
<td>101.8 ± 25.7</td>
<td>.001</td>
<td>.0001</td>
</tr>
<tr>
<td>Trails A</td>
<td>103.6 ± 8.1</td>
<td>106.6 ± 9.5</td>
<td>100.3 ± 8.3</td>
<td>.0006</td>
<td>.0001</td>
</tr>
<tr>
<td>Trails B</td>
<td>103.1 ± 9.0</td>
<td>104.5 ± 8.7</td>
<td>100.4 ± 7.5</td>
<td>.004</td>
<td>.0001</td>
</tr>
<tr>
<td>Finger writing errors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>98.9 ± 7.6</td>
<td>102.7 ± 8.5</td>
<td>100.0 ± 7.4</td>
<td>.233</td>
<td>.020</td>
</tr>
<tr>
<td>Left</td>
<td>99.7 ± 9.6</td>
<td>103.5 ± 9.0</td>
<td>100.0 ± 7.8</td>
<td>.825</td>
<td>.004</td>
</tr>
<tr>
<td>Information</td>
<td>82.5 ± 34.9</td>
<td>81.9 ± 35.6</td>
<td>101.5 ± 39.4</td>
<td>.0001</td>
<td>.0001</td>
</tr>
<tr>
<td>Picture completion</td>
<td>81.2 ± 39.0</td>
<td>79.8 ± 35.6</td>
<td>99.3 ± 32.2</td>
<td>.0001</td>
<td>.0001</td>
</tr>
<tr>
<td>Similarities</td>
<td>93.1 ± 32.0</td>
<td>89.4 ± 41.5</td>
<td>98.1 ± 41.2</td>
<td>.246</td>
<td>.092</td>
</tr>
<tr>
<td>Total abnormalities</td>
<td>9.8 ± 4.9</td>
<td>10.2 ± 5.6</td>
<td>2.3 ± 2.4</td>
<td>.0001</td>
<td>.0001</td>
</tr>
</tbody>
</table>
behavior, staring, twitching, and sensory hallucinations were frequent, did not differ between ME to CE, but were much higher than unexposed. Frequencies of 35 symptoms averaged $4.8 \pm 1.2$ (standard deviation) in ME and $5.2 \pm 2.0$ in CE. Both were significantly different from referents $2.6 \pm 1.1$ ($p < .0001$; Table 2).

Vital capacity and forced expiration volume in 1 second ($\text{FEV}_1$) were significantly reduced in ME (Table 3). CE subjects had reduced vital capacities with reductions of $\text{FEV}_1$ that were almost significant ($p < .125$). Vital capacity as percentage predicted was decreased more than $\text{FEV}_1$ in both exposed groups.

Fifty-two percent of ME people had symptoms of peripheral neuropathy compared to 14% of CE and 2% of referents. Frequent neurological signs in ME-exposed subjects exceeded those for CE-exposed subjects were past pointing in 75%, ataxia in 49%, slow alternating movements in 32%, dysmetria in 25%, and tremors in 18%. And 30% had abnormal cerebellar tests.

**Discussion**

The 105 people exposed to molds and mycotoxins at home were impaired to a similar extent as the 100 CE people. Exposures were associated with slowed reaction times and impairment in balance, color discrimination, visual field performance, and grip strength, but not decreased hearing. Verbal recall was decreased. Perceptual motor functions were impaired for peg placement and trail making. Problem solving was reduced in digit symbol substitution and Culture Fair. Even functions considered refractory to chemical damage like vocabulary, information, and picture completion were impaired, but classification, finding similarities was not impaired. Abnormal balance was associated with abnormal neurological tests of cerebellar function. This finding confirmed and extended our previous studies (Northup and Kilburn, 1977; Kilburn, 2002, 2003) and those of others (Baldo et al., 2002; Gordon et al., 2004). Small airways obstruction had reduced vital capacity, but $\text{FEV}_1/\text{FEV}$ ratio increased, which is characteristic of small airways disease rather than asthma (Northup and Kilburn, 1977; Miller et al., 1986).

**Strengths and limitations**

Finding that 105 consecutive symptomatic ME patients had neurobehavioral abnormalities that matched 100 CE patients, confirms previous findings that mold exposure adversely affects the human brain. Opportunities for bias are reduced by large numbers and individuals appearing randomly, so groups were

**Figure 1.** (a) The frequency of total abnormalities of 105 mold exposed (ME) patients showed a symmetrical distribution around the mean of 9.8. (b) The frequency of total abnormalities for 202 referent subjects was skewed sharply left from the mean of 2.3. (c) The frequency of total abnormalities for 100 chemically exposed (CE) patients was symmetrically distributed around the mean of 10.2 and resembles that of the mold-exposed (ME) group.
aggregated after being tested. Asymptomatic-exposed individuals were not included as they were not motivated to seek testing.

Standardized testing and data handling ensured comparability. There was no way to quantify neither mold/mycotoxin exposures nor chemical exposures. Methods were not available to assay dozens of patients’ homes for toxins from molds or other chemicals (Brasel et al., 2005; Straus, 2009). Many homes had had interventions to reduce exposure, especially to mold before the residents’ impairment was verified by testing. When assays become available it would be more practical to measure people exposed in schools or office buildings where many people shared exposures rather than in homes (Brasel et al., 2005).

People’s ages, wellness, and hours per day of exposure vary more in a home-based group than in a workforce. Self-selection (bias) may increase reporting of symptoms but has not affected neurobehavioral measurements (Kilburn 1997a,b, 1999; Kilburn and Warshaw, 1993) nor have such patients manipulated tests or malingered in previous studies (Kilburn, 2000a,b). Clinical judgment favored molds and mycotoxins as primary causes although homes, schools and offices contain other toxic chemicals (Dally et al., 1981; Storey et al., 2004).

People’s mold exposure impairments resembled those associated with formaldehyde and the indoor air syndrome, including lengthened blink reflex latency (Kilburn, 2000a). Prolonged blink reflex latency has been associated with exposure to chlorinated solvents (Kilburn, 2000b; Kilburn and Warshaw, 1993) including polychlorinated biphenyls (Kilburn et al., 1989) chloride (Kilburn, 2000c), and to arsenic (Kilburn, 1997a) and occurs from other chemicals (Kilburn, 1997b).

Bioassays for toxic activity on cells or enzymes as models to assay trichothecene activity have been explored to characterize air samples and particles (Brasal et al., 2005; Gorny et al., 2002; Johanning et al., 2002; McLaughlin et al., 1977; Savilathi et al., 2000; Smoragiewicz et al., 1993) from a Montreal office building assayed by thin layer

---

Table 2. Profile of mood states for 108 mold exposed (ME) and 100 chemically exposed (CE) compared to 202 unexposed (UE) subjects (POMS score is the sum of tension, depression, anger, fatigue, and confusion minus vigor)

<table>
<thead>
<tr>
<th>POMS</th>
<th>A 108 mold Mean + SD</th>
<th>B 100 chemical Mean + SD</th>
<th>C 202 referent Mean + SD</th>
<th>p values A vs C</th>
<th>p values B vs C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score</td>
<td>69.2 ± 37.9</td>
<td>83.1 ± 43.4</td>
<td>22.1 ± 25.0</td>
<td>.0001</td>
<td>.0001</td>
</tr>
<tr>
<td>Tension</td>
<td>17.3 ± 8.3</td>
<td>19.8 ± 8.0</td>
<td>8.9 ± 4.6</td>
<td>.0001</td>
<td>.0001</td>
</tr>
<tr>
<td>Depression</td>
<td>16.1 ± 12.9</td>
<td>21.9 ± 15.2</td>
<td>7.9 ± 7.1</td>
<td>.0001</td>
<td>.0001</td>
</tr>
<tr>
<td>Anger</td>
<td>13.3 ± 10.1</td>
<td>15.5 ± 9.8</td>
<td>7.7 ± 6.5</td>
<td>.0003</td>
<td>.0003</td>
</tr>
<tr>
<td>Fatigue</td>
<td>16.8 ± 7.9</td>
<td>18.3 ± 7.0</td>
<td>8.3 ± 5.6</td>
<td>.0001</td>
<td>.0001</td>
</tr>
<tr>
<td>Vigor</td>
<td>10.8 ± 6.9</td>
<td>10.0 ± 6.5</td>
<td>17.0 ± 6.2</td>
<td>.0001</td>
<td>.0001</td>
</tr>
<tr>
<td>Confusion</td>
<td>13.9 ± 6.8</td>
<td>16.3 ± 6.3</td>
<td>6.4 ± 3.7</td>
<td>.0001</td>
<td>.0001</td>
</tr>
<tr>
<td>Symptom frequency</td>
<td>4.8 ± 1.2</td>
<td>5.2 ± 2.0</td>
<td>2.6 ± 1.1</td>
<td>.0001</td>
<td>.0001</td>
</tr>
</tbody>
</table>

SD, standard deviation.

Table 3. Pulmonary function for 108 mold exposed (ME) subjects and 100 chemically exposed (CE) compared to 202 referent subjects as percentage of predicted, means and standard deviations (SD), p values by analysis of variance

<table>
<thead>
<tr>
<th>A 105 mold Mean + SD</th>
<th>B 100 chemical Mean + SD</th>
<th>C 202 referent Mean + SD</th>
<th>p values A vs C</th>
<th>p values B vs C</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC</td>
<td>91.2 ± 12.6</td>
<td>94.8 ± 16.1</td>
<td>101.6 ± 15.1</td>
<td>.0001</td>
</tr>
<tr>
<td>FEV&lt;sub&gt;1&lt;/sub&gt;</td>
<td>87.8 ± 14.0</td>
<td>90.4 ± 18.7</td>
<td>93.6 ± 15.8</td>
<td>.0008</td>
</tr>
<tr>
<td>FEF25-75</td>
<td>94.1 ± 29.1</td>
<td>102.6 ± 37.4</td>
<td>88.1 ± 35.0</td>
<td>.191</td>
</tr>
<tr>
<td>FEF75-85</td>
<td>90.2 ± 47.4</td>
<td>100.1 ± 53.8</td>
<td>78.1 ± 52.7</td>
<td>.099</td>
</tr>
<tr>
<td>FEV&lt;sub&gt;1&lt;/sub&gt;/FVC</td>
<td>77.4 ± 7.5</td>
<td>76.5 ± 8.9</td>
<td>72.8 ± 9.5</td>
<td>.0001</td>
</tr>
</tbody>
</table>

FEV<sub>1</sub>, forced expiration volume in 1 second, FVC = forced vital capacity, FEF 25-75 = forced expiratory flow 25% to 75%, FEF 75-85 = forced expiratory flow 75% to 85%
chromatography (TLC) using 4- (p-nitrobenzyl) pyridine to identify the 12,12-epoxy group of trichothecenes (Smoragiewicz et al., 1993). Methanol extracts of water-damaged building materials and gypsum board were 200 times as toxic as board extracts that were not water damaged for feline skin and lung cells. Another problem is that spores and fragments of three molds (Aspergillus versicolor, Penicillium melinii and Cladosporium cladosporioides) share antigens and immunological reactivity (Gorny et al., 2002). Inhibition of protein synthesis using firefly luciferase translation in rabbit reticulocytes has been correlated with fungal counts in indoor air (Yike et al., 1999) and attributed to trichothecenes. Also trichothecenes were identified in ultra-small mold particles (Brasel et al., 2005).

Trichothecenes were identified as toxic agents for swine kidney cell cultures by MTT cleavage using 3- (4,5-diMethylthiazol-2-yl) -2,5 diphenyltetrazolium bromide and characterized chemically by high pressure liquid chromatography with a diode array detector (HPLC-DAD) and gas chromatography-mass spectrometry (GC-MS; Yike et al., 1999). A chymotrypsin-like serin proteinase from Stachybotrys chartarum has been isolated and purified from the lung of an infant with pulmonary hemosiderosis. It cleaved lung proteinase inhibitors, bioactive peptides, and collagen, suggesting it could destroy lung tissue (Kordula et al., 2002). Most recently, an Elisa assay, was specific for trichothecenes on tiny mold fragments caught in ultra-fine filters (Brasel et al., 2005; Straus, 2009).

The 105 patient study confirmed the abnormalities in balance, reaction time, recall, memory, and trail-making in 20 previously evaluated patients exposed to Stachybotrys atra in one building (Kilburn, 2002) and people exposed to various molds and mycotoxins in homes and schools (Kilburn, 2003).

We postulate that inhaled mycotoxins adsorbed on spores and hyphae from mold growing indoors cause brain impairment. Trichothecenes and satratoxin are epoxides that covalently adduct DNA, RNA, protein, and microtubules of nerve axons (Hayes and Campbell, 1986; McLaughlin et al., 1977) and impair protein synthesis to damage lung, brain, and the immune system. Molds: Penicillium and Streptomyces make penicillin, aminoglycosides, and other therapeutic antibiotics (Waksman, 1967), ergot alkaloids, coumadins, adriamycin C, used to treat cancer and Aflatoxin B1 and others that cause liver cell cancer in people exposed to hepatitis B (Ross et al., 1992; Squire, 1981). And Ochratoxin A may cause cancer of the human kidney (Creppy, 1999).

Since ancient times, asthma, cancer, wasting, hemorrhage, inanition, and death have been linked to mold exposures (Rall and Schleifer, 1985). The current wave of sickness from molds has developed since World War II, and paralleled in time the construction of the interior walls of homes shifted to plasterboard (gypsum sandwiched between paper-cellulose layers) from wood or metal lath, plaster with a lime coat. When inner walls became damp from inadequate venting of moisture of from (Hintekka, 1977) leaky walls, roofs, or plumbing mold grew on paper cellulose and gypsum (Nielsen et al., 1998). Drying after being wet appears to stress molds to produce spores and toxins such as trichothecenes and satratoxins that escape into living and working spaces. Recently, these toxins have been measured in serum from people exposed in moldy homes. Plaster is strongly alkaline and discourages the growth of toxigenic molds. The PCR has been used to amplify fungal DNA and show mold exposure in human tissue and in urine (Hooper et al., 2009).

There are no antidotes for mold toxins (Rall and Schleifer, 1985). Methoxymethane (dimethylether) removes aflatoxins from peanuts (Aibara and Yano, 1977), but no evidence has been found that it applies to the removal of satratoxins or trichothecenes or to other agents. Agents developed to lessen mold exposure must not be toxic. Cholestyamine, an oral cholesterol lowering agent has been administered to lower trichothecene burdens in the gut (Shoemaker and House, 2005).

**Prevention**

Avoiding brain damage from molds and mycotoxins requires primary prevention. Molds cause neurological and respiratory damage and illnesses that appear to progress and become irreversible and so avoidance of exposure is imperative. First, the building must be designed to prevent moisture within walls. This means preventing intrusion from roofs (rain and snow) condensation (including within air-conditioning ducts, and plumbing leaks (supply, icemakers and sewers). Facilitate ventilation of walls and roofs so they breathe. Second, construction materials that do not aid the growth of Stachybotrys and other toxic molds should be used. Strongly alkaline building materials for repair and new construction such as lime, plaster, and concrete deter mold growth.

**Acknowledgments**

The assistance of Gerrie G Kilburn is appreciated. Examination and testing were paid for by patients, their medical
insurance and by several law firms ascertaining whether to undertake litigation. All subjects gave informed consent after explanation of the protocol that was approved by the Human Studies Research Committee of the University of Southern California, Keck School of Medicine, USA.

**Declaration of Conflicting Interests**
Dr Kilburn provides expert testimony for plaintiffs and defendants.

**References**


