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Comments to NTP Board of Scientific Counselors Regarding Mold Neurotoxicity¹

Mold neurotoxicity is a highly un-recognized problem. I recently presented some of my research on this topic at the 2007 Annual Meetings of the National Academy of Neuropsychology. Two doctors independently reported to me that they had suffered mold neurotoxicity. One of the doctors was very familiar with the field of neurotoxicity, yet even he failed to make the connection between flooding at his house and the onset of neurological symptoms until two years after exposure, when his consciousness cleared to some degree.

I have attached some of my research regarding mold neurotoxicity.

It is likely that the prevalence of mold neurotoxicity is much larger than suspected because of the difficulties for patients with mold neurotoxicity in getting an accurate diagnosis. Note that most doctors have very little experience in neurotoxicology, and therefore find that they cannot make such a diagnosis. Neuropsychologists and psychologists tend to have minimal experience in toxicology, so they may not be able to accurately perceive and diagnose this condition. Toxicologists - who may have experience studying mold toxicity - are often not skilled in examining patients. So mold neurotoxicity patients tend to fall through the cracks of the medical system.

While there is plentiful scientific research in this field, including in vitro, animal, and human epidemiological and case reports, some doctors with an introduction to the field of mold neurotoxicity may miss the bigger picture, and seem to prefer reasons other than mold neurotoxicity to explain why a person may be ill.

Unfortunately, mold neurotoxins, like other neurotoxic substances, can damage any part of the nervous system, leading to decline in any nervous system function. Also, reliable environmental testing for patients of the exposure levels are notoriously difficult to achieve, as the actual exposures occurred in the past; the exposure levels vary with temperature and humidity cycles, whereas environmental testing is under a static condition; and some of the suspected neurotoxic products of repeated water intrusions, such as mycotoxins, glucans, endotoxins, and volatile organic compounds are not measured.

Thank you for your efforts in elucidating and publicizing insidious effects of mold neurotoxicity.

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CLINICAL EVALUATION OF SUSPECTED MOLD NEUROTOXICITY

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ABSTRACT

Doctors and forensic scientists are increasingly being challenged to evaluate individuals with mold exposure for health injuries, such as neurotoxicity. A significant body of research, described below, shows possible mold neurotoxic effects. Individuals presenting with neurotoxicity can be effectively evaluated with a standard neuropsychological evaluation, as follows. A 47-year-old married nurse, exposed to numerous molds over a 10-year period, with periods of peak exposures, became ill with multi-system symptoms, referable to respiratory, autonomic and central nervous system function. Carpeting dust analysis over various locations in the office showed elevated mold levels, including *Stachybotrys*.

Work and home history did not indicate mold or other neurotoxic substance exposure, other than mold from office. Immune function testing found elevated antibodies to *Stachybotrys* and other molds. Neuropsychological testing found deficits in working memory, processing speed, word fluency, manual dexterity, visual perception and executive function. Emotional function and personality were generally within normal limits. Although evaluated by many medical specialties, no competing diagnosis was found, resulting in a probable diagnosis of mold neurotoxicity.

INDEX TERMS: Adverse effects, mycotoxins, neurotoxicity, neuropsychology, toxic mold

INTRODUCTION

Objective: To show diagnostic procedures for analyzing an individual case with suspected mold neurotoxicity affecting central nervous system function.

Mycotoxins are formed by the hyphae and spores of common molds growing under a variety of conditions. Other prominent compounds include volatile organ-

ic compounds (VOC's), alcohols and aldehydes – these are not mycotoxins, although with sufficient concentration, they could have neurotoxic effects. Mycotoxins and possibly other by-products may be responsible for symptoms of headache, dizziness, and eye and mucous membrane irritation among individuals in fungus-contaminated buildings (Levetin 1995).

Mycotoxin exposure at doses capable of producing chronic disease are usually far below those responsible for acute effects (Samson 1992). Some are “neurotoxins, which in low doses may cause sustained trembling in animals, but at only slightly higher doses cause permanent brain damage or death” (Samson 1992).

Case reports and other medical evidence of mold neurotoxicity: Johanning and Landsbergis (2001) reported that a majority of patients with fungal exposure had at least three nervous system complaints (such as headaches, nervousness, concentration problems, dizziness, and excessive fatigue) with 77 percent reporting at least one CNS symptom. Chronic fatigue was found in 50% of the subjects. Craner (2001) reported neuropsychological symptoms following mold exposure, including a case where the subject developed “marked behavioral changes, difficulty concentrating and short-term memory impairment, and profound fatigue,” with neurocognitive impairment persisting after removal from the contaminated house. Auger (2001) reported four cases of chronic toxic encephalopathies apparently related to exposure to toxigenic fungi. Sigsgaard (2001) reported neurological and neuropsychological symptoms increasing with the number of hours spent in a damp building. The symptoms included headache, tiredness, and sleeping difficulties. Gordon (2001) studied twenty people who reported cognitive changes following exposure to fungi. All subjects were found to be neuropsychologically impaired on at least one measure, with 65 percent of the sample meeting three or more of the impairment criteria.

In summary, there is significant support in the scientific literature (including descriptions of mechanisms, group studies, and individual neuropsychological evaluations) for diagnosing individual cases of fungal/mold neurotoxicity. In the past, neuropsychological analysis has been helpful for the diagnosis of individual cases with numerous types of neurotoxic substance exposures (Singer 1990; Singer 2003a; Singer 2003b).

METHODS

A standard neurobehavioral toxicology protocol was utilized, including extended history-taking, record review, and neuropsychological testing.

Subject: A 47 year old white woman, with 16+ years of school and a B. S. in Nursing, married with 5 children, was referred by her doctor for further evaluation

following mold exposure and subsequent illness. She was unemployed and in a worker's compensation case. Her main symptoms were deteriorated memory, concentration and learning skills; difficulty with multi-tasking; fatigue; and need for excessive sleep (10 hours per night). She was examined 8 months after workplace exposure ceased.

Exposure and symptoms: The subject worked a 40-hour week from June 1991 through February 2001 as a visiting nurse, spending 3-5 hours per day in the same office. She brought materials and clothing from the office to her car to visit clients on a daily basis. In 1994, after office renovations, there were plumbing and roofing leaks, resulting in sagging ceiling tiles. Buckets were placed to catch further precipitation from the ceiling, with the area blocked off with chairs. Although the exterior roof underwent various repairs, the roof continued to leak, and there was no remediation of the water from the roof, affecting the interior ceiling, walls, or carpet. The roofing leaks began to spread in the office with repeated water intrusions.

In 1995, the subject began experiencing bladder incontinence, fatigue, numbness and tingling of her heels and face, leg twitching at night, and dizziness, which occasionally progressed to true vertigo. She then developed bowel incontinence. She was examined by numerous medical specialists, who found no medical cause for her condition. She began to have significant fatigue all the time, with frequent bouts of colds and influenza. The symptoms continued through 1999, at which time the room in her office that had been blocked off because of leaks was reopened and reconnected with the general offices. All of the office and patient supplies were placed in this room, and conferences, staff meetings, and in-service meetings were held there, so there was significant potential exposure to this patient when she was in this room. In 2000, her desk was placed next to the open doorway of this room. She quickly and progressively became more ill, with confusion, and was in three mild automobile accidents (with no head trauma) within three months. She developed a chronic sinus condition, with a bronchial cough. She felt better on the weekends. Other coworkers also were reportedly sick, at least one with blood indicators of mold exposure, such as those of *Stachybotrys* exposure.

In January 2001, elevated levels of molds were found in the office (see below). The staff moved their own office supplies to another office, which had been vacated and remodeled because of toxic mold problems. In February, her condition worsened, with significant difficulties in automobile driving and concentrating, so she asked for medical leave.

RESULTS

Environmental testing: On 1/5/2001, fungal air and surface testing of the facility was conducted. The employees in the problem building surveyed their symp-

toms, refused to work in the contaminated building, and presented the results, which were included in the environmental testing report. The most common complaints among co-workers, all nurses or other health care workers, were respiratory difficulties, headaches, sleepiness, decreased concentration, sluggishness, irritability, anxiety, and mental sluggishness. Other reported symptoms included muscle twitching and jerking, clumsiness and incoordination, extreme sensitivity to odors and light, nosebleeds, and burning itchy eyes and skin.

The left half of the floor in the women's rest room was 80-100 percent saturated with water; the other half of the floor was at 20-40 percent relative saturation. The ceiling tiles were stained in the locations where roof leaks were reported. The environmental survey revealed that substantial quantities of *Stachybotrys* and other mold spores and contaminated dust were released during the demolition/construction work.

Carpet dust composite analysis: This method is expected to reflect a relatively long-term "record" of particles that have been airborne in the offices, and is thought to be the best single record of the levels of exposure throughout the office over the time that the subject was present. The sample was collected as a composite on one occasion, with some of the dust drawn from the carpet in several locations around the office which would normally be difficult to reach with a vacuum cleaner and might therefore be long-term repositories of dust

Table 1. Carpet dust composite analysis

Fungus type	Non-viable counts per 100 mg of carpet dust
<i>Stachybotrys</i>	200
<i>Aspergillus/ Penicillium</i>	400
<i>Cladosporium</i>	600
Basidiospores - phaeo	700
Summary total	3200

Medical testing results: Brain MRI and NCV were reported as normal. Based on reports of numerous medical specialists, no medical cause of her illness has been confirmed, other than the fungal exposure. Significant fungal antibodies were found in the subject's blood, as follows (all units are reported as ELISA by Immunosciences Lab, Inc.):

Table 2. Fungal and myelin antibody testing

Date	Type	Result	Norms
11/28/00	IgG <i>Stachybotrys</i>	3100	0-1600
11/28/00	IgG <i>Cladosporium herbarum</i>	5500	0-1600
11/28/00	IgG <i>Pullularia pullulans</i>	4900	0-1600
4/10/01	IgM Myelin basic protein	55	0-50
7/17/01	IgG <i>Penicillium notatum</i>	4500	0-1600
7/17/01	IgG <i>Pullularia pullulans</i>	3300	0-1600
7/17/01	IgG <i>Stachybotrys</i>	2100	0-1600

Neuropsychological testing results

Symptom Testing: Positive on the Neurotoxicity Screening Survey (Singer 1990), which assesses the consistency of responses to that of subjects with diagnosed neurotoxicity.

Cognitive and Executive Function Testing: The subject was tested on two occasions by different neuropsychologists (using different tests), as she sought further consultation from a neurotoxicologist. The significant findings are as follows:

Pre-exposure IQ ¹	95 th percentile
WAIS-III Working Memory	25 th percentile
Processing Speed	32 nd percentile
WMS-III Auditory	47 th percentile
WMS-III Auditory Delayed	42 nd percentile
WMS-III Visual Delayed	58 th percentile
WMS-III General Memory	58 th percentile
Controlled Oral Word Association Test	10 th percentile
Grooved Pegboard Test	8 th and 9 th percentiles
Paced Auditory Serial Addition Test	<1 st percentile
Benton Visual Retention Test	Indicates Acquired Impairment
Stroop Color and Word Test	4 th percentile (Color/Word)
Army Trail Making Test, part B	21 st percentile
Visual Search and Attention Test	1 st percentile

Emotional Testing: Emotion was within normal limits, as measured on six scales of emotional function.

Distortion and Malingering Testing: Based on nine negative indicators, as well as her social history, malingering is unlikely to be a significant factor.

Personality Testing: Using the Neo Personality Inventory Revised, and comparing the results with her social history, the subject was found to probably have a deterioration of personality, although definite abnormality was not reached.

DISCUSSION AND CONCLUSION

With regard to time- or concentration-dependent exposure indicators of mold exposure, scientists cannot intentionally expose people to mold, mycotoxins and other products of damp buildings, while constantly monitoring levels of exposure, in order to have an exact determination of exposure, because that would be unethical. Therefore, the carpet samples and biomarkers provide some of the best possible indicators of exposure.


The excessive antibody production to multiple toxic molds found in the patient's blood probably means excessive exposure, especially in light of the patient's severe symptoms. In addition, the composite carpet sample provided a good indicator of long-term exposure. The carpet sample would reflect the chronic exposure; however, there were periods of acute exposure resulting from building renovations releasing mold spores and mold parts, of which we have no specific environmental measurements, as is probably always the case; measurements are almost never considered until after people have become seriously ill.

The immune function testing found elevated antibodies to many of the same excessive levels of molds identified in the carpet sample. These molds were capable of producing the symptoms found, based upon the literature cited in this report.

The findings are most consistent with mold neurotoxicity. The subject reported no occupational or household exposure to pesticides, neurotoxic substances, no head injuries or other serious injuries, or diagnoses of psychiatric disorders. It is unlikely that the results reflect senile dementia, as her vocabulary and reasoning skills (which deteriorate with dementia) were at the 95th percentile, and the onset of symptoms was at age 39. Depression was ruled out by the Beck Depression Inventory. No competing diagnoses were found in the extended medical record. Brain MRI was normal, ruling out stroke, tumor, etc. Other workers were reported to be ill with symptoms resembling mold toxicity, by self report. The proposed method has provided substantial evidence, within reasonable scientific certainty, that the subject's central nervous system has deteriorated following extended exposure to various molds.

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Forensic Evaluation of a Mold (Repeated Water Intrusions) Neurotoxicity Case

Civil Forensic Grand Rounds, National
Academy of Neuropsychology, 25th
Annual Meeting, Tampa, Florida,
October 22, 2005.

Author

- Raymond Singer, Ph.D., evaluating neurotoxicity cases since 1979.
- 4 year post-doctoral training in Environmental Epidemiology under Dr. Irving J. Selikoff, of asbestos fame, at the Environmental Sciences Laboratory, Mt. Sinai School of Medicine, New York City.

Can Mold Cause Neurotoxicity?

► Yes



Definitions

- ▶ **Mold**, a filamentous fungus, is from the **Fungi Biological Kingdom**, organisms that absorb food in solution directly through their cell walls and reproduce through spores. Includes slime molds, mushrooms, smuts, rusts, mildews, molds, stinkhorns, puffballs, truffles and yeasts.
 - Kingdoms: Animals, plants, fungi, Protista [microorganisms]
- ▶ Near the end of the growth phase or during stationary phase, fungi can excrete **secondary metabolites, some of which are mycotoxins**, poisonous substances of fungi.

Biologists say:

Recent molecular evidence strongly suggests that fungi are probably more closely related to animals than to either plants or protists!

What are the toxic qualities of mold?-1

- ▶ Spores
- ▶ Mycotoxins: Very numerous types and amounts, like biological warfare agents, to control territory by killing competing species
- ▶ Digestive aids: Fungi produce extra-cellular enzymes that digest complex organic compounds into smaller molecules, which can then be absorbed.
- ▶ Antibiotics, alkaloids

Toxic qualities of mold - 2

- ▶ Allergens: Any one fungal species may produce dozens of allergens.
- ▶ Toxic structural agents: Fungi contain glucan in the cell wall; experimental administration causes illness of the liver, lung and spleen.
- ▶ Volatile organic compounds: VOC's
- ▶ Indoor water intrusions also causes the development of toxic bacteria

Who knows the causative agent ?

- ▶ Which molds are present? Approximately 69,000 species of fungi have been described, and estimates for the total number of species exceed 1.5 million.
- ▶ What environmental and/or blood studies are needed? For which molds, which mycotoxins?

Additive or synergistic effects?

- ▶ Neurotoxicity of each individually.
- ▶ Potential combinations.
- ▶ Probably synergy of neurotoxicity as different toxins attack slightly different nervous system and other organ structures and functions

Why Repeated Water Intrusions in Title?

- ▶ What happens when you add water to indoor, organic materials, under stagnant indoor conditions? And it repeatedly dries out then re-moisturizes?
- ▶ Produces a panoply of molds, mycotoxins, bacteria, mold parts, spores, etc., all occurring at different segments of time, unlikely to be adequately sampled.
- ▶ Likely that repeated water intrusions and chronic exposures are necessary to produce

Scientific evidence for mold neurotoxicity - 1

- ▶ Rationale for mold neurotoxicity: In vivo, in vitro, animal, human, epidemiological and case studies are available.
- ▶ In addition to direct action on nervous system tissue, complex interactions between the immune, endocrine, and nervous system increase vulnerability.

Mold Research Studies

- ▶ Multiple case reports: at least 5 reports in the scientific literature, with multiple cases, involving perhaps 100 subjects
- ▶ Epidemiologic reports: at least 4 reports in the scientific literature, with multiple cases, involving perhaps 100 subjects

An epi study

- ▶ Arch Environ Health. 2003 Jul;58(7):390-8. **Indoor mold exposure associated with neurobehavioral and pulmonary impairment: a preliminary report. Kilburn, K.**
- ▶ 65 consecutive outpatients exposed to mold in their respective homes in Arizona, California, and Texas were compared with 202 community subjects who had no known mold or chemical exposures.
- ▶ The mold-exposed group compared with referents showed significantly decreased function for balance, reaction time, blink-reflex latency, color discrimination, visual fields, and grip;
- ▶ digit-symbol substitution, peg placement, trail making, verbal recall, and picture completion. 21/26 functions tested were abnormal.
- ▶ 52% of mold-exposed patients had current symptoms of peripheral neuropathy, and 62% compared with 14% of unexposed subjects had a history of peripheral neuropathy.

Detailed Neuropsychological Studies

- **Cognitive Impairment Associated with Exposure to Toxigenic Fungi:** Wayne Gordon, Ph.D., Eckardt Johanning, M.D., M.Sc., Lisa Haddad, BA. Wayne Gordon is a Professor, Department of Rehabilitation Medicine, Mount Sinai School of Medicine; Eckardt Johanning is an Adjunct Instructor, Department of Community Medicine, Mount Sinai School of Medicine. Chapter in Bioaerosols, Fungi and Mycotoxins: Health Effects, Assessment, Prevention and Control. Update and Revised Reprint, Edited by: Eckardt Johanning, M.D., M.Sc. 2001.

Cont: Detailed Neuropsychological Studies

- ▶ All 20 subjects were found to be impaired on at least one neuropsychological measure, with 65 percent of the sample meeting three or more of the impairment criteria.
- ▶ Subjects had difficulty integrating visual spatial information, difficulty learning new verbal information, difficulty paying attention and difficulty shifting set.
- ▶ These findings strongly suggest that long-term exposure to toxigenic molds results in cognitive impairment in some people.
- ▶ The pattern of cognitive impairment observed was quite similar to that reported in individuals who have sustained a minor traumatic brain injury.

4 : Detailed Neuropsychological Studies

The chronicity of cognitive impairment associated with exposure to toxic mold.

Wayne A. Gordon, Joshua Cantor, Heather Charatz, Janis Breeze, and at the Eckardt Johanning. Proceedings, Fifth Annual International Conference on Bioaerosols, Fungi, Bacteria, Mycotoxins and Human Health, Saratoga Springs, New York, September 10-12, 2003.

- ▶ Eight people with histories of exposure to toxic mold were retested 12-36 months later.
- ▶ Cognitive impairment was found to be chronic.

5 : Detailed Neuropsychological Studies

- ▶ **Neuropsychological performance of patients following mold exposure.**

Baldo JV, Ahmad L, Ruff R.

Applied Neuropsychology, 2002, Vol. 9, No. 4, 193–202

- ▶ This study investigated the effects of mold exposure (ME) on human cognition by analyzing neuropsychological data from patients who were exposed to mold in their homes or workplaces. Compared to normative data, ME patients were impaired (<10th percentile) on a number of cognitive measures.

6a: Detailed Neuropsychological Studies

- ▶ Singer, R. (2005). Clinical evaluation of suspected mold neurotoxicity. Proceedings of the Fifth International Conference on Bioaerosols, Fungi, Bacteria, Mycotoxins and Human Health, Albany, New York: Boyd Printing.
- ▶ A 47-year-old married nurse, exposed to numerous molds over a 10-year period, with periods of peak exposures, became ill with multi-system symptoms, referable to respiratory, autonomic and central nervous system function. Carpeting dust analysis over various locations in the office showed elevated mold levels, including stachybotrys. Immune function testing found elevated antibodies to stachybotrys and other molds.

6b: Detailed Neuropsychological Studies

- ▶ Neuropsychological testing found deficits in working memory, processing speed, word fluency, manual dexterity, visual perception and executive function. Emotional function and personality were generally within normal limits. Although evaluated by many medical specialties, no competing diagnosis was found, resulting in a probable diagnosis of mold neurotoxicity.

Toxic Mold, World Health Organization Publication

- ▶ Toxic effects of mycotoxins in humans.
Bull World Health Organ. 1999;77(9):754-66

Mycotoxicoses often remain unrecognized by medical professionals, except when large numbers of people are involved.

Mycotoxins Used as Bioweapons

- ▶ Medical Aspects of Chemical and Biological Warfare , Chapter 34, Trichothecene Mycotoxins: Robert W. Wanamaker, Jr., Ph.D. and Stanley L. Wiener, M.D.: Dr. Wanamaker was Assistant Chief, Toxicology Division, U.S. Army Medical Research Institute of Infectious Diseases
- ▶ Some mycotoxins are known to cause illness, including disorders of digestion, **nervous system**, immunosuppression etc..
- ▶ During the 1970-1980s, a highly toxic mycotoxin, **trichothecene**, was the putative biological warfare agents, "yellow rain". In attacks with weapons supplied by the Soviet Union, over 10,000 deaths resulted from yellow rain.
- ▶ In 1942-1947, Fusarium killed more than 10 percent of the population of the town in Siberia from eating moldy grain.

Photographs of indoor mold



Photographs of Indoor Mold



What is lurking behind that wall?



A Moldy Attic



The Forensic Question

- ▶ State legal standard: Is it more likely than not that the plaintiff was hurt by exposure to repeated water intrusions?

Case Demographics

▶	Age:	54
▶	Gender:	Female
▶	Race:	White
▶	Height:	5' 2"
▶	Weight:	140 lbs
▶	Education:	14 years
▶	Marital status:	Divorced once, post-exposure
▶	Children:	Two grown children
▶	Occupation:	Owner/Broker, Real Estate Business, Owner of Xerox business

Patient reported

- ▶ Three years repeated water intrusions to her home, from below and above.
- ▶ Home was lowest unit of the townhouses. In back of the house was a pond sited higher than the basement elevation of the house. The sump pump ran all the time.
- ▶ Shortly after moving in, water ran down walls into the rooms in the unfinished areas. The house began to get black mold appearing on the dry wall. The dry wall was fixed, but then the black mold showed up in other places.

Patient reported air testing

- ▶ Air testing at the town house found *Stachybotrys*, *Aspergillus*, and *Penicillium* - three toxic molds - inside walls and under carpet, and possibly in **cold air intake** cabinet of the forced air **central a/c and heating** unit.

Air Testing Detail

- ▶ **First floor entry** area had a total mold count of 706 CFU/m³, **more than 3 times their recommended limit of 200** CFU/m³, including Cladosporium, a toxic mold, at 565 CFU/m³, Acremonium, a toxigenic fungi, Alternaria alternata, a toxigenic fungi that is known to produce mycotoxins, and pithomyces, an allergen.
- ▶ The **basement workshop** had a total of 600 CFU/m³, **3 times** the recommended guideline of 200 CFU/m³. Included in this was Aspergillus glaucus at 71 CFU/m³, Aspergillus versicolor at 283 CFU/m³, Cladosporium at 141 CFU/m³, and Penicillium at 71 CFU/m³. All of these are toxic, as detailed below.
- ▶ The **unfinished basement** area had a total mold concentration of 565 CFU/m³ where 200 is the recommended guideline. This included Aspergillus glaucus at 71, Aspergillus versicolor at 106, Cladosporium at 106, Penicillium at 212, and pithomyces chartarum at 71 CFU/m³. All of these are toxic, as explained below.

Mold Sampling

- ▶ Air samples of the dining room found mold at 633 CFU/m³, **3 times higher** than the recommended guideline of 200 CFU/m³. This was comprised of 4 genera known to be toxic: *Alternaria*, *Aspergillus*, *Cladosporium*, and *Penicillium*.
- ▶ The entry way closet contained a total of 300 CFU/m³, made up of *Aspergillus* and *Penicillium*, both toxic.
- ▶ **The basement workshop (bulk sample) showed an astounding total mold concentration of 1,424,211 CFU/m³, made up of *Aspergillus versicolor* and 1,035,790 *Stachybotrys chartarum*, "notorious" for mycotoxin production.**
- ▶ The wipe sample from the basement workshop showed 4,100 CFU/m³ of *Penicillium* and 73,800 CFU/m³ of *Stachybotrys chartarum*.

Testing Summary

- ▶ Midwest USA Environmental Services found obvious mold growth in the basement of the unit directly below the dining room window area. The mold growth was sampled and identified as a mix of *Stachybotrys chartarum* and *Aspergillus versicolor*.
- ▶ Wall cavity air samples of *Aspergillus versicolor* were taken from a stud cavity in the dining room and from an adjacent closet.
- ▶ *Stachybotrys* sp. and *Aspergillus* sp. in the interior of the unit and in the breathing air could have serious health consequences.

Exposure Summary

- ▶ Stachybotrys sp. growing in the open air, and several wall cavities with substantial amounts of at least two species of Aspergillus and other potentially harmful mold species, which will eventually find their way into the interior air and will be inhaled by anyone living in the unit. In view of the potential serious health effects, **we recommend you vacate the unit** until such time as the remediation project has been completed.

Quick Immunology - 1

An antibody is a protein (immunoglobulin) molecule, produced by the immune system, that recognizes a particular foreign antigen and binds to it; if the antigen is on the surface of a cell, this binding leads to cell aggregation and subsequent destruction.

Quick Immunology -2

- ▶ **IgG** (gamma globulin) is the most abundant immunoglobulin (80%), can bind to many kinds of pathogens, for example viruses, bacteria, and fungi and protects the body against them by complement activation (classic pathway), opsonization for phagocytosis and neutralisation (immunology) of their toxins.
- ▶ **IgM** (5-10%) forms large, insoluble complexes.
- ▶ **IgA** represent remainder of immunoglobulins

Blood Work

- ▶ IGG Trichothecene at 2101 where reference range is 0-1600
- ▶ IGM Trichothecene at 1880 where reference range is 0-1600.
- ▶ IGA Satratoxins at 2776 where reference range is 0-1600
- ▶ IGM Satratoxins at 5623 where reference range is 0-1600
- ▶ Thermoactinomyces spp. at 9 mcg/ml where the reference range is less than nine.

Symptoms During the Exposure

- ▶ Pain throughout her body (later diagnosed as fibromyalgia)
- ▶ Concentration problems,
- ▶ Memory problems,
- ▶ Headaches,
- ▶ Sleep disorder: couldn't get to sleep or stay asleep, complicated by pain;
- ▶ Light sensitivity,
- ▶ Diarrhea - severe,
- ▶ Severe depression
- ▶ Weight gain (70 pounds) and increased appetite, she believes due to depression, depression medication, inability to exercise, stress, and her health problems at the time. This weight gain led to high blood pressure and borderline diabetes, followed by stomach reduction surgery.

Main Symptoms at Exam

After moving from house, "I am now working 12 hours a day." However, she reported that she still suffers from:

- ▶ Chronic pain in muscles and joints, diagnosed as fibromyalgia. Condition improved (with Mayo prescribed medications).
- ▶ Sleep disorder: insomnia and lack of REM sleep;
- ▶ Restless leg syndrome (a neurological disorder that causes leg tremors at night);
- ▶ Fatigue;
- ▶ Concentration problems;
- ▶ Memory problems;
- ▶ Diarrhea that comes and goes;
- ▶ Bladder infections
- ▶ Numbness in feet and hands, intermittent but daily.

Results of the Neurotoxicity Screening Survey

- ▶ Shows symptoms consistent with neurotoxicity in the following categories:
- ▶ Memory and Concentration
- ▶ Autonomic Nervous System
- ▶ Peripheral Numbness
- ▶ Sensory-Motor
- ▶ Emotionality

Employment at time of exam

- ▶ Owns real estate company, earning more than \$100,000 per year, and has no financial problems, but with a decline in income, post-illness.
- ▶ Note: Little motivation for possible “secondary gain”.

Medical Record Review

- ▶ Mayo Clinic diagnosed fibromyalgia
- ▶ Treated successfully for depression
- ▶ Medical record generally consistent with diagnosis of neurotoxicity

Vet record

- ▶ Increased GI illness of golden retriever, consistent with mold toxicity

Pre-Morbid Cognitive Function

- ▶ Excellent, based upon history and occupational success
- ▶ Based on a demographic formula (Vanderploeg, R. & Schinka, J. (1995). Predicting WAIS-R Premorbid Ability: Combining Subtest Performance and Demographic Variable Predictors. *Archives of Clinical Neuropsychology*, **10**(3), 230 & 232) which considers education, occupation, and vocabulary, expected pre-morbid IQ would be approximately:

▶	<u>Score</u>	<u>Percentile</u>	<u>SEe</u>
▶	Full Scale 115	84%	8.64

Current functioning: IQ

- ▶ Note the declines from pre-morbid IQ at the 84th percentile

▶ <u>Measure</u>	<u>Score</u>	<u>Percentile</u>	<u>Confidence Interval - 90%</u>
▶ Verbal IQ:	97	42%	93 - 101
▶ Performance IQ:	99	47%	93 - 105
▶ Full Scale IQ:	98	45%	95 - 101
▶ Index Scores:			
▪ Verbal Comprehension	100	50%	95 - 105
▪ Perceptual Organization	93	32%	87 - 100
▪ Working Memory	102	55%	96 - 108
▪ Processing Speed	96	39%	89 - 104

Current functioning: Memory

▶ <u>Measure</u>	<u>Score</u>	<u>Percentile</u>	<u>Confid. Interval</u> - 90%
▶ Auditory Delayed	102	55%	94 - 110
▶ Learning Slope	16	17%	
▶ Ruff Selective Reminding Test: 2nd0%			
▶ Benton Visual Retention Test: Suggestive of cognitive impairment			

Current functioning: Other

- ▶ Verbal fluency: 38th %, borderline deficit.
- ▶ Visual-perceptual function:
 - Visual Search and Attention Test, 11th %.
 - Symptomatic of organic brain dysfunction on the Psychiatric Diagnostic Interview - Revised.

Executive Function

- ▶ Elevated symptoms were found with the Frontal Systems Behavior Scale (FRSBE)
- ▶ Deficit on the Stroop Color-Word Test (18th%; the Army Trailmaking Test (24th%); and the PASAT (3rd %), results consistent with a decline in executive function.

Current function – other -2

- ▶ Wide Range Achievement Test: Note the declines from prior high level of function

SS	<u>Percentile</u>	<u>Grade Equiv.</u>	<u>Classification</u>
▶ Reading	90	25%	HS
▶ Spelling	104	61%	>HS
▶ Arithmetic	82	12%	6 <u>Deficit</u>

- ▶ Sensory-Motor Function (Grooved Pegboard): 7th percentile in the left hand, 50th in right

Some Health Status Measures

- ▶ Alcohol use problems were unlikely.
- ▶ A state of positive well-being was found.
 - No indication of malingering
- ▶ Activity levels of activity were deficit.
- ▶ Symptoms of multiple chemical intolerance were found, although these symptoms were not noticed in her initial presentation of symptoms.

Current emotional function

- ▶ Minimal anxiety, depression not found (Beck).
- ▶ Low levels of tension, depression, and anger (POMS).
- ▶ Schizophrenic thinking was not found (WIST).
- ▶ Personality Assessment (NEO-PIR): She appears to be an honest reporter of symptoms.

Personality disorders, including obsessive compulsion, were not found.

She is rated as an upbeat optimist, **hypo-sensitive, relaxed**, a mainstream consumer, a fun-lover, and a reluctant scholar.

Malingering measures - 1

- ▶ Amnesia Questionnaire. 13/14 correct, WNL
- ▶ Endorsement of Rare Symptoms. The Neurotoxicity Screening Survey presents 14 symptoms that are rare. If a number of these symptoms are endorsed, the question of distortion is highlighted. Only 1 endorsed, WNL
- ▶ Even-Odd Forced Choice Test requires the subject to add two single digit numbers, and determine whether the product is even or odd. All correct, WNL.
- ▶ Memorization of "16" Items (Iverson & Franzen, 1991).
Number correct: 16/16; WNL

Malingering measures - 2

- ▶ Miller Forensic Assessment of Symptoms Test (M-FAST) provides information regarding the probability that an individual is malingering psychiatric illness based on a structured interview. Total score cutoff = 6

	<u>Raw Score</u>	<u>% Negative Positive</u> <u>Prediction Prediction</u>	
▶			
▶			
▶ Reported vs. Observed	1		
▶ Extreme Symptomatology	0		
▶ Rare Combinations	0		
▶ Unusual Hallucinations	0		
▶ Unusual Symptom Course	0		
▶ Negative Image	0		
▶ Suggestibility	0		
▶ Total	1	100%	48%

- ▶ Interpretation: Non-malingering

Malingering - 3

- ▶ Portland Digit Recognition Test,
- ▶ Percent correct responses (5 sec delay): 5/5
- ▶ Percent correct responses (15 sec delay): 5/6
- ▶ Percent correct responses (30 sec delay): 5/5

- ▶ Interpretation: WNL

- ▶ Three Word Memory Test evaluates the presence of a memory disorder. A malingering subject may remember less than 40% of the words.

- ▶ Number correct: 13/13 trials
- ▶ Interpretation: Non-malingering

Malingering- 4

- ▶ Twenty-one Item Memory Test (Iverson and Franzen, 1989).
- ▶ Number of words correctly recalled:
 - ▶ Free recall: 5
 - ▶ Forced choice: 14
- ▶ Interpretation: Non-malingering

- ▶ Ungrouped Dot Counting From Lezak, 1983. Adapted from Rey, 1941. More than one pronounced deviation raises the likelihood that the patient is not acting in good faith.)
- ▶ Interpretation: Non-malingering

Diagnosis and Conclusion

- ▶ Brain dysfunction (neurotoxicity, toxic encephalopathy, disorders of cognition function) from a three-year exposure to mold and related substances, affecting cognition, memory, executive function, sensori-motor function, and earning ability.

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Forensic Evaluation of a Mold (Repeated Water Intrusions) Neurotoxicity Case¹

Objective: The scientific literature supports the possibility of neurotoxicity with extended exposure to repeated water intrusions and moldy household interior surfaces. This case will expand upon the existing literature and demonstrate a method for presenting neuropsychological data to a judicial body.

Method: A 54 year old woman, with two children and 14 years of marriage, divorced after the onset of her illness, had successfully owned and managed two businesses, and was actively self-employed at the time of examination, albeit at a reduced level of function. After relocation to a domicile subject to repeated water intrusions from a poorly designed roof and periodic ground flooding, she developed pain, difficulty with concentration and memory, headaches, light sensitivity, sleep disorder, depression, and weight gain.

Visible mold, and mold counts elevated more than three times the recommended limit at more than one site in the domicile were found, including 1,035,790 CFU/m³ *Stachybotrys chartarum*. Mayo Clinic diagnosed her with fibromyalgia. Elevated mycotoxin antibodies were found.

Results: Premorbid cognitive function was estimated to be at the 84th percentile. The Neurotoxicity Screening Survey showed a constellation of symptoms consistent with neurotoxicity. Deficit findings included WAIS-III Perceptual Organization, 32nd%ile and Processing Speed, 39%ile; Ruff Selective Reminding, 2nd%tile; Stroop Color-Word Test, 18th%tile; and Army Trailmaking Test, 24th%tile. Mood, emotions, and personality were well within normal limits.

Conclusions: This case illustrates classic findings of neuropsychological dysfunction following exposure to a known neurotoxic situation (repeated water intrusions), albeit with few case reports in the neuropsychological literature.

¹Forensic Grand Rounds, National Academy of Neuropsychology, 25th Annual Meeting, Tampa, Florida, presented October 22, 2005: *Forensic Evaluation of a Mold (Repeated Water Intrusions) Neurotoxicity Case*. Archives of Clinical Neuropsychology, 2005, Volume 20, Issue 7, pp. 808.

Neuropsychological Evaluation of a Practicing Physician with Mold Exposure

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Singer, R. and Gray, M. (2007). Neuropsychological evaluation of a practicing physician with mold exposure. Archives of Clinical Neuropsychology, Volume 22, Issue 7, September, p 892.

Objective: Differential diagnosis of mold-exposed patient demonstrates an application of neuropsychology to salient issues of medicine and toxicology.

Introduction: Scientific support for the identification of mold neurotoxicity can be found in numerous reports, including in vitro studies, animal studies and human studies (see references at end).

Case: The subject was a formerly financially successful chiropractic physician and former chemical engineer, still practicing medicine at the time of the exam. Symptoms included rapid weight loss, chronic fatigue, respiratory problems, erectile dysfunction, night sweats, hot flashes, and irritability, which began three years after working at the high school, in the spring of 2002, initially diagnosed as mild hyperthyroidism, but the diagnosis was not supported by tests of thyroid hormone levels - although his eyes remain mildly protruding. Sex hormone testing for erectile dysfunction was also negative.

Exposure duration: After treating patients at his private chiropractic practice in the early parts of the day, since the fall of 1999, he worked from 3 pm, five days a week, for a minimum of 3 and up to 10 hours a day, as the sports physician for 15 different sports at a local high school. He served the football team needs at all of the home and away games. On days when there were games at the high school, he worked up to 10 hours at the school. Roughly speaking, he worked roughly 30 hours a week, 30 weeks a year, in a potentially contaminated environment, for 7 years, from 1999 until the time of the examination in until Fall, 2006.

While at the high school, he spent most of his time in his office next to the laundry room. The laundry room was found to have mold in the fall of 2002; the washing machine in the laundry room was leaking water; the clothing dryer exhaust was not vented to outside the building, but vented into the laundry room.

The door between the laundry room and the subject's office door, which connected the laundry room and the subject's office, was often propped open by various coaches, because the laundry room was frequently overheated.

Although renovations took place to ameliorate the mold problems, completed in January, 2003, it was since discovered during a subsequent remodeling of the entire gym in the summer of 2007 that mold was still growing on the ceiling tile and in the cabinets.

Medical question: Was there any neuropsychological decline; what was the nature of the decline; if so, what is/was the cause; and could the exposure be impacting other medical conditions that have neuropsychological components? Knowing the cause helps to determine the treatment.

Method: Interview, neuropsychological testing, medical and exposure records review.

Exposure assessment:

Visual inspection showed mold on the drywall, metal studs in the wall, ceiling tile, and in cabinets. The studs in the laundry were deteriorated from rust and corrosion.

Air testing in the subject's high school office on Dec 4, 2002 for spores showed the following counts/M3, "background corrected" (minus the amounts of the spores found in the outdoor environment):

Aspergillus/Penicillium, 457; Stachybotrys, 549.

In the American Industrial Hygiene Association periodical "Synergist" (Geoffrey A. Clark, November 2001), spore counts above 2,5000 indicates possible contamination. However, molds vary extremely widely in their potential toxicity, so this number is not meaningful.

Stachybotrys represents a special mold problem because it produces mixed trichothecenes mycotoxins which interfere with protein synthesis at a cellular level, and have been weaponized because of it's damage potential.

Mycotoxins, by-products of fungal metabolism: The trichothecenes are a very large family of chemically related toxins produced by various species including *Stachybotrys*. They are markedly stable under different environmental conditions. All trichothecenes are mycotoxins, but not all mycotoxins are trichothecenes. This family of mycotoxins causes multiorgan effects including emesis and diarrhea, weight loss, nervous disorders, cardiovascular alterations, immunodepression, hemostatic derangements, skin toxicity, decreased reproductive capacity, and bone marrow damage (Chapter 34, TRICHOTHECENE MYCOTOXINS. ROBERT W. WANNEMACHER, JR., PH.D. AND STANLEY L. WIENER, M.D., Medical Aspects of Chemical and Biological Warfare, 1997)

Medical record review:

12/15/03 Spirometry shows mild obstructive airways disease; flow volume loop demonstrates large airway obstruction; static lung volumes show hyperinflation is present; diffusion capacity shows normal diffusion capacity. DIAGNOSIS: Hypoxia Occupational exposure.

1. Dr. Michael Gray, second author of this paper found:
 - a. 06/01/06: Positive fungus culture for Cladosporium species and Beauveria species
 - b. 06/05/06: Mycotoxin report taken from urine: positive for Tricothecenes.
 - c. 06/12/06: Decreased Natural Killer cells, slightly elevated Activator Suppressor cells and elevated Activated T cells.
 - d. 06/22/06: Patient's Immunosciences Laboratory fungal, mold and mycotoxin panels had multiple positives with multiple IgMs positive and several IgEs positive.
 - e. Weight loss, suspect trichothecene mycotoxicosis.
 - f. Gray's panel at AAL was positive for 6/8 mold congruity factors in the autoimmune series...no herpes, no candida. ANA was negative...his hypersensitivity pneumonitis panel was positive for 5/8 of the fungal specific antigens for which IgG was evaluated.
 - g. The Immunosciences fungal, mold and mycotoxin panels revealed multiple positives for the various fungi associated with damp indoor environments. Several of the neural antigen antibody screens were positive, consistent with injury to CNS neurons, and the mycotoxin assays were also positive for multiple mycotoxins at a significant abnormal level.
 - h. In his original set of neurologic tests, he was showing abnormalities on six of the areas tested including abnormal sway balance with eyes closed, visual performance on the visual field testing was abnormal bilaterally, and his long-term crystallized memory for information and recognition of similarities was abnormal.

- i. 08/31/06: Abnormalities on physical exam and neuropsychological testing:
Neurological: 6 abnormal items. Visual Quadrant: 1 abnormal item. Smell Recognition: 1 item. Pulmonary function: 2 items.
 - j. 09/07/06: DNA tissue/fluid panel report - sputum samples: positive for mold *Aspergillus niger*.
2. 08/29/06 Quantitative EEG with neurometric analysis produces results that are statistically significant and of clinical significance, reported as consistent with results found in over 250 individuals who had toxic mold exposure.

Results:

Dates of exam: 11/15/06
 Gender: Male
 Age at exam: 43
 Educational level: 16+
 Height: 6'0"
 Weight: 188 lb
 Ethnicity: White
 Marital Status: Single
 Number of Children: 0

Function	Percentile rank	Score
Neurotoxicity Screening Survey		Elevated: Consistent with neurotoxicity
Pre-morbid IQ	97	128
WAIS-III Processing Speed	58	
WMS III: Auditory Process Learning Slope	25	
WMS III: Verbal Paired Associates 1 st Recall Total	37	
WMS-III Immediate Memory	70	
WMS-III Auditory Retrieval	21	
Ruff Figural Fluency	40	
Stroop Color-Word	10	

Visual Search and Attention Test	40	
WRAT-II Reading	50	
Beck		Mild anxiety and depression
Quick Environmental Exposure and Sensitivity Inventory		Elevated
TOMM		47, 50, 50
Boone et al. Dot Counting		E-Score: 7 E-Score Cutoff: 22
Portland Digit Recognition Test		15/15 correct
FRSBE		Symptomatic of executive dysfunction
Ruff Neurobehavioral Inventory	No distortion	Elevated on the scales E (emotional), At (attention and concentration), An (anger and aggression), So (Psychosocial integration and recreation) and Nr (neurological status).
Neo Personality Inventory	Emergence of possible personality disorder	Paranoid, obsessive-compulsive, but not anti-social.

Conclusions: Symptoms were found consistent with mold toxicity, affecting multi-systems, including respiratory, immune and nervous. Neuropsychological testing showed mild declines in function, consistent with self-report, affecting memory, concentration and personality. Clinical diagnosis was mold neurotoxicity. Differential diagnosis found no competing diagnoses.

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