A Family with ME/CFS Following Exposure to Molds, Mycotoxins and Bacteria in a Water-Damaged Home: A Case Report

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Abstract: The health of a family of five exposed to molds, bacteria and mycotoxins in a water-damaged home deteriorated within 2 months. Airborne nonviable spore counts ranged from 12 thousand to over 3 million per cubic meter. ERMI-36 tests of dust from the refrigerator compressor area identified several species of *Aspergillus* and *Penicillium, Chaetomium globosum* and *Stachybotrys chartarum*. Mycotoxins identified in urine samples from each of the family members matched results identified in dust samples collected within the home including both ochratoxin and trichothecenes. The family developed enlarged lymph nodes, skin rashes, unrefreshing sleep, neurocognitive decline, and orthostatic changes consistent with Myalgic Encephalomyelitis-Chronic Fatigue Syndrome (ME/CFS). We propose that the family developed Sarcoidosis as a result of the exposure to fungal micro particles and have been chronically ill for over 3 years following the initial exposure. They currently reside in a home with no known water-damages resulting in mold growth, but continue to experience symptoms of ME/CFS.

Keywords: Molds, mycotoxins, bacteria ME/CFS.

INTRODUCTION

Water intrusion into buildings and homes leads to the presence of microbial growth, including molds and bacteria, endotoxins, microbial volatile organic chemicals (mVOCs) and nano particulates containing secondary microbial metabolites (mycotoxins and 1, 3-beta-D-glucans), and other bio-contaminants. Exposure to any one of these biocontaminants can lead to adverse health effects in occupants [1, 2]. Occupants of these environs can develop a chronic illness, expressing multiple symptoms [3, 4]. A variety of health problems have been associated including cognitive impairment [10-13]; chronic fatigue [1, 2]; upper and lower respiratory infections (5, 6); fungal rhinosinusitis [7-9]; fungal pneumonia and pulmonary bleeding [14, 15]; liver and mitochondrial damage [16]; and stimulation of proinflammatory cytokines. While considered to be an autoimmune disease, Sarcoidosis has been successfully treated with antifungal therapy suggesting a fungal etiology [17-20].

MATERIALS AND METHODS

Family Homes and Schools

The family consists of the father, age 38 y, the mother, age 34 y and three daughters (ages 17, 15 and 7 yrs). They lived in a water-damaged home for five months (October 2011 to February 2012). Within 60 days after occupation of the home, they began experiencing a decline in their health. After discovering and testing for molds, bacteria and mycotoxins in their home they moved into a motel for one month and then into the home of the father's parents. They sought medical help on May 23, 2012. For the past 2.75 years they have been living in a home that was tested and cleared of water-damage and mold. The original moldy home did not have sewer or gas odors, or pesticide exposure. The family has reported that they continue to have chronic health problems.

Neurophysiological and Pulmonary Function Tests

Neurophysiological and pulmonary function testing were performed on the father and mother according to the methods of Kilburn [11, 12]. The three daughters were not tested because of financial constraints of the family budget.

FitBit Sleep Data

A sleep study was performed on each family member using a FitBit Surge monitor available through Best Buy retail outlets. The monitor was set on ultra normal, which automatically tracks and stores information regarding sleep as follows: duration of sleep, number of times awake, duration of restless sleep and un-refreshing sleep. Each family member

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was recorded for five consecutive nights. All time-recorded events were converted to the mean ± stand deviation in minutes.

AAA and Air & Water Sciences, Inspection and Mold Testing Services

Airborne mold spores were determined using non-viable air samples collected with Air-O-Cell spore trap cassettes. All samples were collected for 5 minutes at 15 liters per minutes for a total volume of 75 liters of air. Samples were collected at room temperature, with closed windows, doors, and without the HVAC operating. After sample collection, the cassette was sealed, labeled, and shipped to Microtest Laboratories, Fair Oaks, CA under chain of custody for the identification to the Genus the airborne mold spores per cubic meter.

Dust samples were obtained from the master bedspread, bathroom carpeting, and the refrigerator coil and insulation, and were sent to Natural Link Mold Laboratories under chain of custody to culture and identify mold and bacteria. Molds were cultured at 25^{o}C MEA – Malt Extract Agar: non-selective (which allows for recovery of wide variety of fungi); DG18 – Dichloro Glycerol 18 % Agar (which allows for recovery of xerophilic fungi); CEL – Cellulose Agar (which selects for cellulolytic fungi). The bacteria were cultured at 37^{o}C and identified to the Genus using the following three media: TSA, CN and MAC.

Refrigerator compressor and insulation dust samples were sent to RealTime Laboratories, Carrollton, TX, under chain of custody for ERMI-36 (PCR DNA) testing to determine mold species. The ERMI rating was ignored as irrelevant for consideration. The dust samples were also tested for the presence of aflatoxins, ochratoxin and trichothecenes as previously published [21, 22].

Visual Inspection

The home is a single-story, single-family dwelling with a raised foundation located in a rural area outside of Sacramento, California. The residence has T1-11 exterior siding and an asphalt shingle roof. The family moved into the home and observed a musty odor which the management company tried to resolve by cleaning the carpets multiple times, however, the odors did not abate.

Several months after moving in the family identified wet carpeting due to a leaking showerhead in the master bedroom. Initial remedial efforts were performed by an untrained general contractor who neglected standard remediation protocols including the use of containment and negative air pressure enclosures, and HEPA filtered mechanical devices. The contractor removed water damaged and moldy drywall exposing over 40 square feet of microbial growth and then placed a box fan on the growth that was within the master bedroom. The family was not provided alternative housing and continued to sleep in the room. The walls were kept open for drying purposes until the family called for a mold inspection and relocated shortly thereafter.

Roofing leaks were likely present prior to the family moving in and were immediately observed upon the first rains and all subsequent raining events during their occupancy. The rain affected the cellulose-type attic insulation that measured approximately 6-8 inches thick with a total affected area of approximately 400 square feet of attic space (neglecting insulation thickness). Microbial growth identified within the insulation and on the back-side of the ceiling drywall included *Aspergillus versicolor* and *Stachybotrys chartarum.* It is highly likely that these molds were present within the home prior to and throughout the occupancy by the family.

FINDINGS

Family Symptoms

The health history and symptoms of each family member prior to occupation of the water-damaged home, during occupation and in the current home are summarized in Table **1**. Prior to occupation the family experienced common health conditions such as colds and annual flu. Upon occupying the water-damaged home, they developed multiple health conditions that varied in each family member. The common symptoms that they all developed involved nasal congestion and sinusitis, neurocognitive decline, requirement for sleep (Hypersomnsolence) and fatigue. Despite subsequently occupying the cleaner home for 2.75 years, they still experience many of the symptoms. The most debilitating health problems are the persistence of chronic fatigue (ME/CFS) and cognitive decline.

Neurological Test Results: Father and Mother

The results of the neurophysiological and pulmonary function tests are summarized in Figure **1**. The father had a total of 10.5 neurological

Table 1. Health History of each Family Member: Prior to Occupations, during Occupation and 3 Years after moving out of the Water-Damaged Home

Family Member	Prior Health	Symptoms in Water-Damaged Home	Cleaner Home Apr 2014 Follow-up
Father, 32 y	Common Colds Annual Flu	SOB, Chest tightness, H.A.s, Heavy fatigue, Sinus and nasal congestion, Raspy cough, Runny nose, Sore throat, Memory loss, Light headed, Dizzy spells, Vomiting blood with severe coughing, High blood pressure. Requires sleep, fatigue. Muscle and joint pain, flu-like feeling. Enlarged Cervical and Axilllary lymph nodes	SOB, Chest tightness and pain, Heavy fatigue, H.A.s, Sinusitis, Raspy cough, Sore throat, Abdominal pain, Memory loss, mental fog, difficulty with concentrating, Vertigo and dizzy spells. Symptoms have improved but still remain, Daily work activity exacerbates CFS, Requires sleep, ME/CFS
Mother, 31 y	Common Colds Annual Flu, Auto accident (back and knee pains)	SOB, Chest tightness and pain, H.A.s, Heavy fatigue, Sinus and nasal congestion, Raspy cough, Sore throat, Abdominal pain, Memory loss, Mental fog, Difficulty concentrating, Vertigo, Dizzy spells. Requires sleep, fatigue, Muscle and joint pain, flu-like feeling. Rashes on neck and back.	SOB, Chest tightness and pain, Heavy fatigue, Sinus and nasal congestion, Abdominal pain, Memory loss, mental fog, difficulty concentrating, Vertigo, Dizzy spells, swelling of lymph nodes, chronic rhinitis, Pain in knees, elbows and calves, decreased work performance, skin rashes, linear sclero-derma, Requires sleep. ME/CFS
Daughter, 13 y	Common colds Annual flu	Abdominal pain, Leg rashes, H.A.s, Difficulty concentrating, Sinus pain, Sore throat, Raspy cough, Fatigue, Vomiting, Difficulty in P.E, Wheezing and tiredness. Requires sleep, fatigue, Muscle and joint pain, flu-like feeling, Enlarged cervical lymph nodes	SOB with exertion, Wheezing Abdominal pain, Scars on legs from rash, H.A.s, Sinus pain, Chronic Rhinitis, Difficulty concentrating, difficulty in school and tests, Fatigue, Difficulty in P.E, - Wheezing and tiredness. Requires Sleep, ME/CFS
Daughter, 11 y	Common colds, Annual flu, Inattentive at school	Abdominal pain, Difficulty concentrating, Sinus pain, Dry cracking skin under nose, H.A.s, Vomiting. Requires sleep, fatigue, Muscle and joint pain, flu-like feeling	Abdominal pain, Difficulty concentrating, Sinus pain, on- going U.T.Is, enlarged submandibular nodes, Dry cracking skin under nose, H.A.s. Requires sleep, ME/CFS
Daughter, 4 y	Common Colds Annual flu	Ear Infections, Heart murmur, Exhaustion, Runny nose with red rash under nose, Vomiting, Fever, Lethargy, Fatigue, skin rashes, Raspy cough. Requires sleep, fatigue, Muscle and joint pain, flu-like feeling	Heart murmur, Raspy coughs though out the day, rhinitis, Alternating runny nose, dry and crusty. Post inflammatory pigmentation of skin, Requires extra sleep (napping), ME/CFS

Father – 10.5 Abnormalities

Test	Observed	Predicted	Limit	Abn
NEUROPHYSIOLOGICAL				
Simple Reaction Time (ms)	282	275.88	371.29	0
Choice Reaction Time (ms)	484	475.20	602.29	0
Sway-Balance (cm/sec) Eyes Open	.73	.67	.90	0
Sway-Balance (cm/sec) Eyes Close	.98	1.02	1.50	0
Blink Reflex R				
Blink Reflex L				
Grip Strength (kg) R	62.40	59.71	43.81	0
Grip Strength (kg) L	69.60	58.09	42.19	0
Color Vision R	14.10	11.24	12.66	.5
Color Vision L	17.80	11.24	12.66	.5
Visual Fields Performance R				
Visual Fields Performance L				
Hearing R				
Hearing L				
COGNITIVE FUNCTION				
Culture Fair Score	28	33.10	25.40	0
Vocabulary Score	12	25.59	15.95	1
Digit Symbol Score	38	58.45	43.99	1
RECALL				
Verbal Recall (Immediate)	8	24.19	13.99	1
Verbal Recall (Delayed)	2	19.84	8.65	1
Rey 15 Figures	15			
PERCEPTUAL MOTOR SPEED				
Pegboard, Dominant (sec)	79	66.00	82.30	0
Trails A (sec)	28	27.03	41.14	0
Trails B (sec)	151	59.39	97.44	1
Finger Writing Errors R	0	1.53	6.70	0
Finger Writing Errors L	5	.66	4.73	.5
LONG-TERM OR CRYSTALLIZED MEMORY				
Information	7	20.36	14.00	1
Picture Completion	13	16.43	12.45	0
Similarities	12	21.77	14.56	1
AFFECTIVE STATUS				
Profile Of Mood States	83		50	1
Tension	26			
Depression	20			
Anger	19			
Vigor	8			
Fatigue	11			
Confusion	15			
Symptom Frequency	4.68	2.63	4.35	1
Beck's Depression Scale	9			
Limbic System Checklist	34			
PULMONARY FUNCTION				
FVC				
FEV1				
F 25-75				
F 75-85				
FEV1/FVC				

ABNORMALITIES: Neurological 10.5 Visual Quadrant 0 Smell Recognition 1
Pulmonary Function 4

Mother – 14 abnormalities

Test	Observed	Predicted	Limit	Abn
NEUROPHYSIOLOGICAL				
Simple Reaction Time (ms)	367	275.88	371.29	0
Choice Reaction Time (ms)	489	473.66	600.34	0
Sway-Balance (cm/sec) Eyes Open	.68	.67	.90	0
Sway-Balance (cm/sec) Eyes Close	1.22	.99	1.44	0
Blink Reflex R				
Blink Reflex L				
Grip Strength (kg) R	46.20	35.05	23.50	0
Grip Strength (kg) L	20.40	32.79	22.44	.5
Color Vision R	12.80	11.04	12.14	.5
Color Vision L	11.80	11.04	12.14	0
Visual Fields Performance R				
Visual Fields Performance L				
Hearing R				
Hearing L				
COGNITIVE FUNCTION				
Culture Fair Score	25	35.03	27.34	1
Vocabulary Score	20	29.40	19.75	0
Digit Symbol Score	28	71.12	55.07	1
RECALL				
Verbal Recall (Immediate)	10	25.83	15.63	1
Verbal Recall (Delayed)	3	20.79	9.60	1
Rey 15 Figures	14			
PERCEPTUAL MOTOR SPEED				
Pegboard, Dominant (sec)	96	60.76	74.31	1
Trails A (sec)	98	25.59	38.95	1
Trails B (sec)	173	49.06	80.49	1
Finger Writing Errors R	12	1.81	7.28	.5
Finger Writing Errors L	10	.96	5.49	.5
LONG-TERM OR CRYSTALLIZED MEMORY				
Information	10	20.35	13.99	1
Picture Completion	8	15.89	11.73	1
Similarities	14	23.06	16.42	1
AFFECTIVE STATUS				
Profile Of Mood States	65		50	1
Tension	15			
Depression	16			
Anger	7			
Vigor	4			
Fatigue	18			
Confusion	13			
Symptom Frequency	5.91	2.63	4.35	1
Beck's Depression Scale	16			
Limbic System Checklist	31			
PULMONARY FUNCTION				
FVC				
FEV1				
F 25-75				
F 75-85				
FEV1/FVC				

ABNORMALITIES: Neurological 14 Visual Quadrant 0 Smell Recognition 1
Pulmonary Function 4

Figure 1: This figure summarizes the results of neurological testing on done of the father and mother.

abnormalities that included the following: color vision, vocabulary, digit symbol, verbal recall (immediate and delayed), trails B, finger writing (left), long-term crystallized memory, profile mood states, symptom frequency and smell recognition. The results of the mother's testing showed higher score of 14 abnormalities with a pattern similar to the father. Both had abnormal PFT tests results suggesting decreased pulmonary flow and increased resistance (data not shown).

Sleep Studies

The father made the following general comments regarding sleep patterns: (1) father stated "I generally do have trouble falling to sleep because of exhaustion during the middle to the end of the day. Exercise does exacerbate the fatigue and I feel drained after physical exercise. (2) The same occurs with my wife. (3) The youngest daughter immediately falls asleep in the backseat when I pick her up from school. She takes short naps during the day when at home. (4) The two oldest daughters stay up late and sleep late."

FitBit Sleep Data

The results of the FitBit sleep data are summarized in Table **2**. The data are listed as total minutes for each measurement, except for number of times awake for the five days of monitoring. The average duration of sleep ranged from 9.1 (youngest daughter) to 8.1 (mother) hours. The number of times awake ranged from a mean of 0.8 times per night (daughter, 15 y) to 3.4 times (mother). The mean duration of restless sleep measured the least for two daughters (ages 17 and 15) at a mean of 13 and 9.8 minutes, respectively. The mean duration of restless sleep for the youngest daughter was 14.8 minutes, while the findings for the father and mother were 19.3 and 19.5 minutes, respectfully. The duration of un-refreshing sleep for each family member was as follows: Father (42.8 minutes), mother (38 minutes), daughter, 17 y (25.2

Table 2. Results of Sleep Monitoring Events in each Family Member using FitBit Surge Monitor

Event	Father, 36 y	Mother, 34 y	Daughter, 17 y	Daughter, 15 y	Daughter, 7 y
Sleep Minutes	477±62.5	508.2±68.1	407±67.7	431.6±45.9	551.4±62.2
Times Awake	3±1.6	3.4±1.3	2.2±1.3	0.8±1.3	1.5±1.5
Restless	19.3±3.2	19.6±9.5	13±6.5	9.8±5.3	14.8±6.2
Un-refreshing Sleep	42.8±6.7	38±20.8	25.2±18.4	32.6±12.2	26.6±12.4

Table 3. Total Airborne counts/m^3 and the Percentage of each Genus Nonviable Fungal Spores in Three Rooms of the Home and Outdoors (Front and Back Yards)

Fungal I.D.	Back Yard		Front Yard		Mstr Bath		Family Rm		Child's Bdrm	
	Count	%	Count	%	Count	%	Count	%	Count	%
Alternaria	0	0	0	0	0	0	27	0.1	13	0.1
Arthinium	0	0	0	0	489	0.02	27	0.1	27	0.2
Ascospores	440	34	1600	38	0	0	0	0	1880	16
Basidiospores	60	6	160	4	120	0.004	240	1	360	3
Chaetomium	**0**	**0**	**0**	**0**	**14,530**	**0.5**	**373**	**2**	**147**	**1**
Curvularia	0	0	0	0	0	0	13	0.1	0	0
Cladosporium	160	12	760	18	240	0.01	1320	7	1400	12
Epicoccum	67	5	40	1	13	0.0004	27	0.1	0	0
Fragments	0	0	40	1	680	0.02	120	1	80	1
Pen/Asp	**40**	**31**	**1240**	**29**	**3090427**	**99**	**16156**	**81**	**8078**	**67**
Pollen	0	0	0	0	120	0.004	160	1	0	0
Scopulariopsis	0	0	360	8	1360	0.04	120	1	0	0
Smuts/Peric/Myxomycetes	160	12	0	0	240	0.01	0	0	0	0
Stachybotrys	**0**	**0**	**0**	**0**	**387**	**0.01**	**0**	**0**	0	0
Ulocladium	0	0	0	0	80	0.003	93	0.5	40	0.3
Total Spore Counts/m^3	**1,306**		**4,239**		**3,114,515**		**19,928**		**12,024**	

minutes), daughter 15 y (32.6 minutes), and youngest daughter (26.6 minutes). The youngest daughter takes 3 to 4 naps during the day, with a difficulty in staying awake.

Nonviable Airborne Spore Counts

The airborne nonviable spore counts in the back and front yards and three rooms in the home are listed in Table **3**. The predominating molds were *Aspergillus*/ *Penicillium*. Airborne *Chaetomium* was identified in the master bath, family room and the child's room ranging from 240 to 1,400 spores per cubic meter of air. Airborne *Stachybotrys* spores were present in the master bath. The highest overall spore count was in the master bath at 3.11 million followed by the family room (19,928) and the child's bedroom (12,024) per cubic meter of air. Outside air samples were dissimilar for both quantity (with all 3 samples showing amplified or elevated levels of *Chaetomium* and *Aspergillus/ Penicillium* type spores) and the rank and file of the fungal ecology.

Master Bedspread Viable Mold and Bacteria

The viable mold and bacteria cultured from the dust sample are shown in Tables **4** and **5**. The species of molds present in the bedspread were identified using four different culture media. The identified molds included *Aspergillus versicolor* and *niger*, four species of *Penicillium* (*chrysogenum*, *brevicompactum*, *crustosum*, and *glabrum*), *Acremonium, Aureobasidium, yeasts, Phoma, Epicoccum, Chaetomium, Cladosporium, Mucor* and *Scopulariopsis*. The viable spore counts ranged from 10,000 to 340,000 spores per gram of dust, with *Aspergillus versicolor* at 340,000 CFU/gram of dust. The total spore count was 1,140,000 viable spore per gram of dust. The total bacterial count on TSA medium was 8,400,000 CFU/gram of dust. The isolated bacteria were predominately Gram-positive organisms and included *Bacillus*, *Micrococcus, Alloiococcus/Staphylococcus, Krytococcus* and *Actinobacteria* (e.g. *Streptomyces*). Gram-negative bacteria were <1 % of the total viable count.

Table 4. Viable Species of Mold Cultured in the Dust from the Master Bed Spread in Hree different Culture Media

Identified Fungus	CFU/ Plate	Optimal Medium	CFU/g of Dust
A. versicolor	34	CEL	340,000
A. Niger	2	MEA	20,00
P. chrysogenum	13	MEA	130,000
P. brevicompactum	5	DG18	50,000
P. crustosum	3	MEA	30,000
P. glabrum	1	DG18	10,000
Acremonium	20	MEA	200,000
Aureobasidium	10	DG18	100,000
Yeasts	10	MEA	100,000
Phoma	8	CEL	80,000
Epicoccum	3	MEA	30,000
Chaetomium	1	CEL	10,000
Cladosporium	1	MEA	10,000
Mucor	1	MEA	10,000
Non-sporulating	1	MEA	10,000
Scopulariopsis	1	CEL	10,000
Total Count/g of Dust			1,140,000

MEA – Malt Extract: Non selective, allows for recovery of wide variety of fungi
DG18 – Dichloro Glycerol 18 % Agar: Allows for recovery of xerophilic fungi
CEL – Cellulose Agar: Selective for cellulolytic fungi

Table 5. Bacteria Identified in a Dust Sample taken from the Bed Spread in the Master Bedroom

Isolation Media -TSA - Total Counts – 8,400,000 CFU/g - CNA - Total Counts – 5,100,000 - MAC - Total Counts – 50,000
Bacterial Break by genera/and or species – Estimated Percentages o Gram Positive Bacteria = 99 % Gram Positive Cocci = 90 % -A variety were isolated on TSA and CAN. These included *Micrococcus* (25 %); *Alloiococcus/Staphylococcus* (6 %) *Krytococcus* (4 %) and many others at lower percentage. o 2 colonies of Actinomycetes were isolated on TSA with morphology suggestive of *Streptomyces*. o Gram negative bacteria = Total of 4 colonies on MC.MCA =<1 % o Coliform bacteria – Two colonies on MCA = <1 %

ERMI-36 Results on Refrigerator Compressor and Insulation Dust

The results of the ERMI-36 (PCR-DNA) test on the dust sample from the refrigerator compressor-insulation are summarized in Table **6**. The identified species were as follows: *Aspergillus flavus, A. fumigatus, A. versicolor, A. ochraceus, A. niger* and *A. sydowii*; *Eurotium amstelodami*, *Penicillium purpurogenum, P. pullulans, P. corylophilum,* and *P. crustosum*, *Scopulariopsis chartarum*, *Trichoderma viride*, *Wallemia sebi*, *Chaetomium globosum* and *Stachybotrys chartarum*.

Table 6. The Results of the ERMI-36 Test Performed on the Dust Sample taken from the Area of the Refrigerator Compressor and Insulation (Species of each Mold is given as the Number of Spores Per Milligram of Dust)

Fungal Species	Number of Spores/mg of Dust
Aspergillus flavus	8
Aspergillus fumigatus	33
Aspergillus versicolor	78
Aspergillus ochraceus	151
Aspergillus niger	33
Aspergillus sydowii	10
Eurotium amstelodami	785
Penicillium purpurogenum	7
Aureobasidium pullulans	114
Penicillium corylophilum	27
Penicillium crustosum	1,946
Scopulariopsis chartarum	44
Trichoderma viride	12
Wallemia sebi	25
Chaetomium globosum	3
Stachybotrys chartarum	1

Mycotoxin Tests Results – Refrigerator Dust and Urine Samples

The results of the tests for mycotoxins in the refrigerator dust and family urine samples are summarized in Table **7**. Ochratoxin A (0.7 ppb) and trichothecenes (3.86 ppb) were detected in the refrigerator dust. Ochratoxin (range 1.4 to 2.8 ppb) and trichothecenes (0.22 to 0.97 ppb) were detected in urine samples from all family members.

Table 7. Mycotoxins Identified in the Dust Sample from the Refrigerator Compressor Area and in the Urine of the Five Occupants of the House (The concentrations are in ppb)

Sample I.D.	Aflatoxin	Ochratoxin	Trichothecene
Refrigerator Dust	0	0.7	3.86
Urine (Father) 32 y	0	1.4	0.81
Urine (Mother) 31 y	0	2.1	1.26
Daughter 15 y	0	2.8	0.91
Daughter 12 y	0	1.4	0.97
Daughter 5 y	0	1.4	0.22

Urine Ochratoxin References: <1.8 ppb (negative), 1.8-2.0 (equivocal, 2.0 ppb (positive)). Trichothecene References: ≥ 0.2 ppb (positive).

DISCUSSION

Exposure

The home occupied by the family in this study was heavily contaminated with fungi and bacteria. The sources of water damage were likely present prior to their moving in. The showerhead leak was somewhat hidden by furniture and wallpaper, thereby delaying detection. The roofing leaks affected cellulose-type attic insulation that measured approximately 6-8 inches thick, with a total affected area of approximately 400 square feet of attic space (neglecting insulation thickness). Upon first discovery the family notified the management company. A roofing company provided recommendations that the entire roof needed replacement and stated that temporary repairs would be ineffective. The roofing leaks were not resolved during their occupancy.

The nonviable airborne spore counts ranged from 12,204 to over 3 million spores per cubic meter (Table **3**). The viable fungal count detected in the master bedspread was above 1 million CFU/gram of dust Table **4**. The bacteria isolated from the bedspread was over 90% gram positive bacteria, while Gram negative bacteria were < 1%. In addition Actinomycetes were also cultured (Table **5**). Finally, the ERMI-36 (PCR-DNA) testing of refrigerator compressor and insulation identified several species of *Aspergillus*, *Eurotium amstelodam*i, two species of *Penicillium*, *Trichoderma viride*, *Stachybotrys chartarum*, and *Chaetomium globosum* (Table **6**). All of these molds produce mycotoxins. Thus, the fungal, bacterial, and mycotoxin contaminants identified in this home adds and agrees with the previously published observations on the role of these biocontaminants in adverse health effects that occur in water-damaged indoor environments [1, 2, 14-16, 21-31].

Medical Evaluations

The entire family began to develop a variety of symptoms [within 2 months after occupation of the mold/bacterial contaminated home (Table **1**). Their health history prior to this was limited to common colds and annual flu. The mother had residual back and knee pains resulting from an auto accident. While symptoms related to the exposure to mold and bacteria varied among the family members, they all developed common symptoms. These included enlarged lymph nodes, shortness of breath (SOB), cough, wheezing, skin rashes and a flu-like feeling. Their most disturbing symptoms were fatigue, memory loss, difficulty

concentrating, light-headiness, dizziness, and Hypersomnsolence. In addition, the two older daughters began to have difficulty in school studies and functions, while the youngest required constant motherly care, taking unscheduled naps and immediately falling asleep in the car. The mother was relieved of her employment with the city government because of her own decreased work performance, and extra time she needed to take care of the ill children. As a result, the family sought medical attention of Janette Hope, M.D, Santa Barbara, CA. Ochratoxin and trichothecene mycotoxins were detected in urine of all family members, confirming exposure to the same mycotoxins, which were detected in the dust sample taken from the refrigerator compressor/insulation area (Table **7**).

Inspection of Table **1** of the symptom complex still present in the 2014 medical follow-up reveals that the health of each family member agrees with the findings of IOM. In addition, the neurophysiological tests results in Figure **1** demonstrate persistent neurocognitive deficits are present in the mother and father. Finally, the FitBit data presented in Table **2** demonstrate that each family member has a significant amount of restless and unrefreshing sleep, thus, adding to the medical history and neurophysiological abnormalities that have led to the diagnosis of ME/CFS in this family.

Neurophysiological testing confirmed the neuro-degenerative (neurocognitive) dysfunction in the parents. The father had 10.5 neurological abnormalities, and the mother had 11 abnormalities. The daughters were not tested as a result of financial constraints (Figure **1**). The results of the PFT tests performed on the parents were not available for review. However, symptoms of SOB suggest the possibility of asthma or pulmonary conditions (e.g. hypersensitivity pneumonitis, fungal pneumonitis) resulting from the exposure to the conditions of the water damaged home. Neurocognitive deficits, neurological abnormalities and lung disease have been reported in mold exposed adults and children [2-13, 17-20, 37-40].

Mold and Mycotoxin Related Illnesses in Literature

Mycotoxins have been reported in body fluids, biopsies and autopsy specimens in individuals exposed to molds in water damaged indoor environments. Various specimens include biopsies, autopsies [21]; autopsy from fungal pneumonia and pancytopenia [15]; another autopsy from an 18 month old boy who died from pulmonary bleeding [14]; breast milk and liver (in a Reye's-like infant death [15]; urine, sinuses, uterus and umbilical cord in a family who had an infant born with NF Type 1 [22]; serum of individuals exposed *to Stachybotrys chartarum* [32]; CSF following indoor mold exposures [33, 34]; a case of sphenoid sinus aspergilloma [9]; several cases of fungal sinusitis [7, 8]; and sera of cancer patients with aspergillosis [35].

The Institute of Medicine reviewed the peer-reviewed literature regarding Myalgic Encephalo-myelitis-Chronic Fatigue Syndrome (ME/CFS). The symptoms of the ME/CFS include: 1) reduction and impairment to carry out normal daily activities, accompanied by profound fatigue; 2) Post-exertional malaise; 3) unrefreshing sleep; 4) cognitive impairment; 5) orthostatic intolerance; 6) and failure to recover from prior infections and abnormal immune function [36].

Although the IOM Committee did an extensive review of the literature regarding ME/CFS, they did not find a causal link of the illness with respect to environmental exposure to toxins. All of the references cited in the IOM have been reviewed via the National Library Medicine. None of the papers looked for a causal link to exposure to environmental toxins, including those present in water-damaged buildings. Two papers have summarized the ongoing health of individuals with CFS exposed to water-damaged and mold infested indoor environments. Both papers list CFS as an illness in their patients [1, 2]. Recent publications have demonstrated that exposure to mold micro-particulates that contain 1, 3-beta-D-glucan, various mold generated proteins, and mycotoxins are causally related to Sarcoidosis of occupants of mold infested homes and occupants of water-damaged office buildings [17-20, 37, 40]. Thus, the professionals of toxicology and medicine must become aware of this pervading health problem.

Sarcoidosis is a systemic inflammatory disease of unknown cause that is characterized by the *in vitro* and *in vivo* release of pro-inflammatory mediators. There is evidence that such inflammation can result from of exposure to fungal cell wall nano-particulates [38, 40]. These cell wall fragments are a least 1000-fold greater in concentration than are airborne mold spores [41-43]. The aerodynamics of these fragments readily allows deposition in the nasal cavity and lungs of occupants of water-damaged buildings [44].

Since Sarcoidosis is a debilitating systemic inflammatory disease that can affect multiple organ systems and result in chronic fatigue and other

symptoms of ME/CFS, we recommend that the role of hazardous indoor fungal and bacterial biocontaminants be further investigated as triggers or causes of Sarcoidosis. Also, considering recent disaster-producing weather conditions, we recommend that further epidemiological studies of occupants in water-damaged indoor environments be urgently conducted to investigate the frequency of this potentially wide-spread environmental public health problem [45-55].

CONCLUSIONS

In conclusion, animal and human studies have demonstrated that toxin-laden nano-particulates are present in the water-damaged indoor environment and polluted outdoor air. The sources of these ultrafine particulates are fungi and bacteria in the indoor environment as well as air pollution, e.g. smog. They enter humans and animals via two major routes: (1) via the olfactory nerve spreading directly into the brain damaging the hypothalamic-pituitary axis, and (2) via nano-particulates undergoing translocation into the systemic circulation from the surfactants in the alveoli. Both routes lead to pathology of the nose, lung, heart and brain, upper and lower respiratory tract via the production of pro-inflammatory cytokines and oxidative stress in humans and animal models [56-66]. Recently published research has shown that fungi are present in the CNS of patients with Alzheimer's disease and Amyotrophic lateral sclerosis [67, 68]. Mycotoxins are involved in various aspects of microbial infection and related pathogenesis [69]. Thus, the professionals of toxicology and medicine should be aware of health problems caused by toxin laden nano-particulates.

CONFLICTS OF INTEREST

Jack Dwayne Thrasher and Chip Prokop have testified as expert witnesses for both plaintiffs and for defense. Curtis Roberts does not have known conflicts of interest related to this subject. Dennis Hooper is a principal owner of RealTime Laboratories which offers diagnostic tests, e.g. PCR-DNA; urine and tissue mycotoxins.

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REFERENCES

[1] Thrasher JD, Crawley S. The biocontaminants and complexity of damp indoor spaces: More than meets the eyes. Toxicol Indust Health 2009; 25(9-10): 583-615. http://dx.doi.org/10.1177/0748233709348386

[2] World Health Organization. Dampness and Mould. 327 pages. http://www.euro.who.int/__data/assets/pdf_file/0017/43325/E92645.pdf

[3] Curtis, L, Lieberman A, Stark M. Rea W. Vetter M. Adverse health effects of indoor molds. J Austral College Nutrition Environ Med 2004; 23(1): 3-8. http://dx.doi.org/10.1080/13590840400010318

[4] Gray MR, Thrasher JD, Crago R, Madison RA, Arnold L, Campbell W, Vojdani A. Mixed mold mycotoxicosis: Immunological changes in humans following exposure in water-damaged buildings. Arch Environ Health 2003; 58 (7): 410-20.

[5] Fisk WJ, Eliseeva E, Mendell M. Association of residential dampness and mold with respiratory tract infections and bronchitis: A meta analysis. Environ Health 2010; 9: 72. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3000394/pdf/1476-069X-9-72.pdf

[6] Fisk WJ, Lei-Gomez Q, Mendell MJ. Meta-analyses of the associations of respiratory health effects with dampness in homes. Indoor Air 2007; 17(4): 284-96. http://dx.doi.org/10.1111/j.1600-0668.2007.00475.x

[7] Dennis D. Chronic sinusitis: Defective T-cells responding to super antigens treated by reduction of fungi in the nose and air. Arch Environ Health 2003; 58(7): 433-41.

[8] Dennis D, Robertson D, Curtis L, Black J. Fungal exposure endocrinopathy in sinusitis with growth hormone deficiency: Dennis-Robertson syndrome. Toxicol Indust Health 2009; 25(9-10): 369-680.

[9] Gray MR, Thrasher JD, Hooper D, Dumanov MJ, Cravens R, Jones T. Sphenoid aspergilloma: diagnosed as a malignancy: A case report. Otolaryngology 2015; 5: 3. http://www.omicsonline.org/open-access/sphenoid-aspergilloma-diagnosed-as-a-malignancy-a-case-report-2161-119X-1000190.pdf

[10] Empting LS. Neurological and neuropsychiatric syndrome features of mold and mycotoxin exposure. Toxicol Indust Health 2009; 25(9-10): 577-91. http://dx.doi.org/10.1177/0748233709348393

[11] Kilburn, KH. Behavioral and pulmonary impairment in 105 adults with indoor exposure to molds compared to 100 exposed to chemicals. Toxicol Indust Health 2009; 55(9-10): 681-91. http://dx.doi.org/10.1177/0748233709348390

[12] Kilburn KH, Thrasher JD, Immers N. Do terbutaline and mold-associated impairments of the brain and lung relate to autism? Toxicol Indust Health 2009; 55(9-10): 703-10. http://dx.doi.org/10.1177/0748233709348391

[13] Jedrychowski WJ, Maugeri U, Stigter L, Jankowski J, Butscher M, Mroz E, *et al.* Cognitive function of 6-year old children exposed to mold-contaminated homes in early postnatal period. Prospective birth control cohort study in Poland. Physiol Behavior 2011; 104(5): 989-95. http://dx.doi.org/10.1016/j.physbeh.2011.06.019

[14] Thrasher JD, Hooper DH, Taber J. Family of six, their health and the death of a 18 month old male from pulmonary hemorrhage: Identification of mycotoxins and mold in the home, lungs, liver and brain of deceased infant. Internat J Clin Toxicol 2014; 2: 1-10. http://dx.doi.org/10.14205/2310-4007.2014.02.01.1

[15] Gray MR, Hooper D, Thrasher, JD. Molds and mycotoxins in autopsy specimens in a death related to fungal pneumonia and pancytopenia marijuana usage and a water-damaged home: A case report. Internat J Clin Toxicol 2014; 2: 11-20. http://dx.doi.org/10.14205/2310-4007.2014.02.01.2

[16] Gray MR, Thrasher JD, Hooper D, Crago R. A case of Reyes-like syndrome in a 68 day old infant: Water-damaged home, mold bacteria and aflatoxins. Internat J Clin Toxicol 2014; 2: 42-54. http://dx.doi.org/10.14205/2310-4007.2014.02.02.1

[17] Tercelj A, Salobar B, Harlander M, Rylander R. Fungal exposure in homes of patients with sarcoidosis – an environmental exposure study. Environ Health 2011; 10: 8. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3036600/pdf/1476-069X-10-8.pdf http://dx.doi.org/10.1186/1476-069X-10-8

[18] Tercelj M, Stopinsek A, Ihan B, Salobar V, Simcic S, Wraber B, Rylander R. *In vitro* and *In vivo* reactivity to fungal cell wall agents in sarcoidosis. Clin Exper Immunol 2011; 166: 87-93. http://dx.doi.org/10.1111/j.1365-2249.2011.04456.x

[19] Tercelj M, Salobar B, Zupancic M, Wraber B, Rylander R. Inflammatory and pulmonary granuloma infiltration in sarcoidosis. Respirology 2014; 19(2): 225-30. http://dx.doi.org/10.1111/resp.12199

[20] Tercelj M, Salobar B, Zupancic M, Rylander R. Sarcoidosis treatment with antifungal medications: A follow-up. Pulmonary Med 2014; http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4274827/pdf/PM2014-739673.pdf

[21] Hooper DG, Bolton VE, Guilford FT, Straus DC. Mycotoxin detection in human samples from patients exposed to environmental molds. Int J Mol Sci 2009; 10(4): 1465-75. http://dx.doi.org/10.3390/ijms10041465

[22] Thrasher JD, Gray MR, Kilburn KH, Dennis DP, Yu A. Water-damaged home and health of the occupants. J Environ Public Health 2012. http://dx.doi.org/10.1155/2012/ 312836.

[23] Brasel TL, Douglas DR, Wilson SC, Straus DC. Detection of airborne Stachybotrys chartarum macrocyclic trichothecene mycotoxins on particulates smaller than conidia. Appl Environ Microbiol 2005; 71(1): 114-22. http://dx.doi.org/10.1128/AEM.71.1.114-122.2005

[24] Bloom E, Bal K, Nyman E, Must A, Larsson L. Mass spectrometry-based strategy for direct detection and quantification of some mycotoxins produced by Stachybotrys chartarum and Aspergillus spp. in indoor environments. Appl Environ Microbiol 2007; 73(13): 211-16. http://dx.doi.org/10.1128/AEM.00343-07

[25] Hintikka E, Holopainen R, Asola A, Jestoi, Peitzsch M, Kalso S, *et al.* Mycotoxins in the ventilation systems of four schools in Finland. World Mycotoxin J. 2009; 2:369-79. http://dx.doi.org/10.3920/WMJ2009.1155

[26] Bloom E, Nyman E, Must A, Pehrson C, Larsson L. Molds and mycotoxins in indoor environments—A survey in water-damaged buildings. J Occup Environ Hygiene 2009; 6(11): 671-78. http://dx.doi.org/10.1080/15459620903252053

[27] Polizzi V, Delmulle B, Adams A, Moretti A, Susca A, Picco M, *et al.* JEM spotlight: Fungi, mycotoxins and microbial volatile organic compounds in mouldy interiors from water-damaged buildings. J Environ Monitor 2009; 11: 1849-58. http://dx.doi.org/10.1039/b906856b

[28] Smoragiewicz W, Cossette R, Boutard A, Krzystyniak K. Trichothecene mycotoxins in the dust of ventilation systems in office buildings. Int Arch Environ Health 1993; 65(2): 113-17. http://dx.doi.org/10.1007/BF00405729

[29] Taubel M. Sulyok M, Vishwanath V, Bloom E, Turunen M, Jarvi K, et al. Co-occurrence of toxic bacterial and fungal secondary metabolites in moisture-damaged indoor environments. Indoor Air 2011; 21(5): 368-75. http://dx.doi.org/10.1111/j.1600-0668.2011.00721.x

[30] Tuomi T, Reijula K, Johnsson T, Hemminki K, Hintikka E-L, Lindroos O, *et al.* Mycotoxins in crude building materials from water-damaged buildings. Appl Environ Microbiol 2000; 66(5): 1899-904. http://dx.doi.org/10.1128/AEM.66.5.1899-1904.2000

[31] Gottschalk C, Bauer J, Meyer K. Detection of Satratoxin B and H in indoor air from a water-damaged building. Mycopathologia 2008; 166: 103-07. http://dx.doi.org/10.1007/s11046-008-9126-z

[32] Brasel TL, Campbell, Demers RE, Fink J, Vojdani A, Straus DC. Detection of trichothecene mycotoxins in sera from individuals exposed to Stachybotrys chartarum in indoor environments. Arch Environ Health 2004; 59(6): 317-23.

[33] Brewer JH, Thrasher JD, Straus DC, Madison RA, Hooper D. Detection of mycotoxins in patients with chronic fatigue syndrome. Toxins 2013; 5: 605-17. http://dx.doi.org/10.3390/toxins5040605

[34] Brewer JH, Hooper D, Muralidhar S. Intranasal antifungal therapy in patients with chronic illness associated with mold and mycotoxins: An observational analysis. Toxins 2013; 5: 605-617.

[35] Lewis RE, Wiederhold NP, Chi J, Han XY, Komanduri K, Kontoyiannis DP, Prince RA. Detection of gliotoxin in experimental and human aspergillosis. Infection Immunity 2005; 73(1): 635-37. http://dx.doi.org/10.1128/IAI.73.1.635-637.2005

[36] Institute of Medicine. Beyond Myalgic encephalomyelitis/ Chronic Fatigue Syndrome: Redefining an Illness. National Academies Press 2005; http:www.nap.edu

[37] Tercelj M, Salobir B, Harlander M, Rylander R. Fungal exposure in home of patients with sarcoidosis – an environmental exposure study. Environ Health 2011; 10: 8. http://www.ehjournal.net/content/10/1/8 http://dx.doi.org/10.1186/1476-069X-10-8

[38] Tercelj M, Stopinsek, Ihan A, Salobir B, Simcic S, Wraber B, Rylander R. In vitro and in vivo reactivity to fungal cell wall agents in sarcoidosis. Clin Exper Immunol 2011; 166: 87-93. http://dx.doi.org/10.1111/j.1365-2249.2011.04456.x

[39] Laney AS, Cragin LA, Blevins LZ, Sumner AD, Cox-Ganser JM, Kreiss K, *et al.* Sarcoidosis, asthma, and asthma-like symptoms among occupants of a historically waster-damaged office building. Indoor Air 2009; 19: 83-90. http://dx.doi.org/10.1111/j.1600-0668.2008.00564.x

[40] Tercelj M, Salobir B, Zupancic M, Wraber B, Rylander Inflammatory markers and pulmonary granuloma infiltration in sarcoidosis. Respirology 2014; 19: 225-30. http://dx.doi.org/10.1111/resp.12199

[41] Reponen T, Seo-S-Cm Grimsley F, Lee T, Crawford C, Grinshpun SA. Fungal fragments in moldy houses: A field study in homes in New Orleans and Southern Ohio. Atmos Environ 2007; 41(37): 8240-49. http://dx.doi.org/10.1016/j.atmosenv.2007.06.027

[42] Adhikari A, Reponen T, Rylander. Airborne fungal fragments in homes in relation to total fungal biomass. Indoor Air 2013; 23: 142-47. http://dx.doi.org/10.1111/j.1600-0668.2012.00799.x

[43] Seo SC, Choung JT, Chen BT, Lindsley WG, Kim KY. The level of submicron fragments in homes with asthmatic children. Environ Res 2014; 131: 71-76. http://dx.doi.org/10.1016/j.envres.2014.02.015

[44] Cho S-H, Seo S-C, Schmechel D, Grinshpun SA, Reponen T Aerodynamic characteristics and respiratory deposition of fungal fragments. Atmos Environ 2005; 39: 5454-65. http://dx.doi.org/10.1016/j.atmosenv.2005.05.042

[45] Gerke AK. Morbidity and mortality in sarcoidosis. Curr Opin Pulm Med 2014; 20(5): 472-78. http://dx.doi.org/10.1097/MCP.0000000000000080

[46] Rao DA, Dellaripa PF. Extrapulmonary manifestations of sarcoidosis. Rheum Dis Clin North Am 2013; 39(2): 277-97. http://dx.doi.org/10.1016/j.rdc.2013.02.007

[47] Spruit MA, Thomeer MJ, Gosselink R, Troosters T, Kasran A, Debrock AJT, *et al.* Skeletal muscle weakness in patients with sarcoidosis and its relationship with exercise intolerance and reduced health status. Thorax 2005; 60: 32-38. http://dx.doi.org/10.1136/thx.2004.022244

[48] Kallianos A, Zarogoulidis OM Ampatzogkou F, Trakada G, Gialafos E, Pitsou G, *et al.* Reduction of exercise capacity in sarcoidosis in relation to disease severity. Patient Preference Adherence 2015; 5: 1179-88.

[49] Judson MA, Shapiro L, Freitas S, Polychronopoulos VS, Highland KB. Concomitant sarcoidosis and a connective tissue disease: Review of clinical findings and postulations concerning their association. Respir Med 2013; 107: 1453-59. http://dx.doi.org/10.1016/j.rmed.2013.01.004

[50] Imran TF, Nizami S, Eyzner I, Mirani N, Hossain T, Fede R, Capitle E. Vertigo as a predominant manifestation of Neurosarcoidosis. Case Report Med Vol. 2015; Article ID 397046, 4 pages. http://dx.doi.org/10.1155/2014/897956

[51] Kobayashi S, Nakata W, Sugimoto H. Spinal magnetic resonance imaging manifestations at onset in Japanese patients with spinal cord sarcoidosis. Intern Med 2013; 52: 2041-50. http://dx.doi.org/10.2169/internalmedicine.52.0186

[52] Kobak S, Sever F, Sivrikoz ON, Orman M. Sarcoidosis: Is it only a mimicker of primary rheumatic disease? A single center experience. Ther Adv Musculoskel Dis 2014; 6: 3-7. http://dx.doi.org/10.1177/1759720X13511197

[53] Mijajlovic M, Mirkovic M, Mihailovic-Vucinic M, Aleksic V, Covikovic-Sternic N. Neurosarcoidosis: Two case reports with multiple cranial nerve involvement and review of the literature. Biomed Rap Med Fac Univ Palacky Olomouc Czech Repub 2014: 158: 662-67.

[54] Orii M, Imanishi T, Akasaka T. Assessment of cardiac sarcoidosis with advanced imaging modalities. Biomed Research International Vol. 2014; Article ID 897956, 15 pages. http://dx.doi.org/10.1155/2014/897956

[55] Engelhard SG, Patel V, Reddy AR. Intermediate uveitis, posterior uveitis, and panuveitis in the Mid-Atlantic USA. Clin Ophthalmology 2015; 9: 1549-55. http://dx.doi.org/10.2147/OPTH.S89428

[56] Groen H, Dirkje S, Postma DS, Kallenberg CGM. Interstitial lung disease and myositis in a patient with simultaneously occurring sarcoidosis and scleroderma. Chest 1993; 164: 1298-1300. http://dx.doi.org/10.1378/chest.104.4.1298

[57] Calderon-Garciduenas L, Franco-Lira MA, Torres-Jardon R, Henriquez-Roldan C, Henriquez-Roldan C, Barragan-Mejia G, Valencia-Salazar D, *et al.* Pediatric respiratory and systemic effects of chronic air pollution exposure: Nose, lung, Heart and brain pathology. Toxicol Pathol 2007; 35: 154-62. http://dx.doi.org/10.1080/01926230601059985

[58] Genic S, Zadeoglulari Z, Fuss SH, Genic K .The adverse effect of air pollution on the nervous system. J Toxicol 2012; 2012: 782462. http://dx.doi.org/10.1155/2012/782462

[59] Calderon-Garciduenas L, Reed W, Maronpot RR, Henriquez-Roldan C, Delgado-Chavez R, Calderon-Garciduenas A, *et al.* Brain inflammation and Alzheimer's-like pathology in individuals exposed to severe air pollution. Toxicol Pathol 2004; 32: 650-58. http://dx.doi.org/10.1080/01926230490520232

[60] Block M, Calderon-Garciduenas L. Air pollution: Mechanisms of neuroinflammation & CNS disease. Trends Neurosci 2009; 32(9): 506-16. http://dx.doi.org/10.1016/j.tins.2009.05.009

[61] Garciduenas L, D'Angiulli A, Kulesza RJ, Torres-Jardon, Osnaya N, Romero L, *et al.* Air pollution is associated with brainstem auditory nuclei pathology and delayed brainstem auditory evoked potentials. Int J Dev Neurosci 2011; 29(4): 365-75. http://dx.doi.org/10.1016/j.ijdevneu.2011.03.007

[62] Block ML, Elder A, Austen RL, Bilbo SD, Chen H, Chen J-C, *et al.* The outdoor air pollution and brain health workshop. Neurotoxicol 2012; 33(5): 972-85 (on line). http://dx.doi.org/10.1016/j.neuro.2012.08.014

[63] Peters A, Veronesi B, Calderon-Garciduenas L, Gehr P, Chen LC, Geiser M, *et al.* Translocation and potential neurological effects of fine and ultrafine particles a critical update. Particle Fibre Toxicology 2006; 3: 13. HTTP//www.particleandfibretoxicology.com/content/3/1/13 http://dx.doi.org/10.1186/1743-8977-3-13

[64] Pestka JJ, Yike IY, Dearborn DG, Ward MDW, Harkema R. Stachybotrys chartarum, trichothecenes mycotoxins, and damp building-syndrome: New insights into a public health enigma. Toxicol Sci 2008; 104(1): 4-26. http://dx.doi.org/10.1093/toxsci/kfm284

[65] Carey SA, Plopper CG, Hyde DM, Islam Z, Pestka JJ, Harkema JR. Satratoxin-G from the black mold Stachybotrys chartarum induces rhinitis and apoptosis of olfactory neurons in the nasal airways of Rhesus monkeys. Toxicol Pathol 2012; 40: 887-98. http://dx.doi.org/10.1177/0192623312444028

[66] Islam Z, Harkema JR, Pestka JJ. Satratoxin G from the black mold Stachybotrys chartarum evokes olfactory sensory neuron loss in the murine nose and brain. Environ Res Perspec. 2006; 114(7): 1099-1107. http://dx.doi.org/10.1289/ehp.8854

[67] Doi K, Uetsuka K. Mechanisms of mycotoxin-induced neurotoxicity through oxidative stress-associated pathways. Int J Mol Sci 2011; 12: 5213-37. http://dx.doi.org/10.3390/ijms12085213

[68] Pisa D, Alonso R, Rabano A, Rodal I, Carrasco L. Different brain regions are infected with fungi in Alzheimer's disease. Sci Rep 2015; 5: 15015. http://dx.doi.org/10.1038/srep15015

[69] Alonso R, Pisa D, Marina AI, Morato E, Rabano A, Rodal I, Carrasco L. Evidence for fungal infection in cerebrospinal fluid and brain tissue from patients with Amyotrophic lateral sclerosis. Inter J Biol Sci 2015; 11(5): 546-58. http://dx.doi.org/10.7150/ijbs.11084

[70] Park S-H, Kim D, Kim J, Moon Y. Effects of mycotoxins on mucosal microbial infection and related pathogenesis. Toxins 2015; 7: 4484-4502. http://dx.doi.org/10.3390/toxins7114484

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