Dr. Ann Shippy
Certified Functional Medicine
Board Certified Internal Medicine

Its Personal!

Objectives

- Define Mold Terms
- Scope and Source of the epidemic
- What to look for to help consider Mold as a diagnosis
- Who is most susceptible?
- How to utilize the limited testing we have on humans
- How to utilize the limited testing we have for the environment
- Reducing mold exposure- Is remediation on option?
- Functional medicine approach to recovery
- Where do we go from here?

What is Toxic Mold?

- *A Mold that makes chemicals called mycotoxins and mVOC's*
  - *Very small molecules that enter the body through inhalation or absorption through the skin or gut*
  - *They are "poisons"*
- *Often from a hidden source*
- *Can also colonize or cause infections in the body*

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Water Damaged Building Statistics

- Human health costs estimated at $3.5B annually – just for Asthma associated with indoor mold - *Mold Remediation in Schools and Commercial Buildings. EPA 402-K-01-001*
- The report concluded that 47% of US homes have 'dampness or mold' - *Lawrence Berkeley National Laboratory reports 2009*
- For other buildings, the same report states that '85% percent of buildings had past water damage and 45% had current water leaks'.

Water Damaged Building Statistics

- For U.S. schools, a survey by the General Accounting Office reported that 30% of schools had plumbing problems and 27% had roof problems.
- The property remediation costs are not well known but in 2009, a non-profit reported that the cost of repairing mold related damage is $73 billion annually in the US.
- A study published in 2011 by the Lawrence Berkeley National Laboratory and EPA on the benefits of improving indoor air quality in US offices, estimated that improving indoor air quality and removing dampness and mold would result in increased work performances, reduced mold exposure symptoms, and reduced absenteeism with a net result of $20 billion dollars of economic benefit.

The Challenge!

- Mold can grow on virtually any organic material as long as moisture and oxygen are present
- There are molds that grow on almost everything -wood, paper, carpet, fabric, food, dirt/dust anywhere including AC ducts and insulation.
- Because mold eats and digests what it is growing on, it can damage a building and its furnishings.
- If left unchecked, mold eventually can cause structural damage to building materials.
- Since the 1970's, Building Techniques and Materials have increased the incidence of indoor mold

Mycotoxins and Health Effects

- As molds grow, some produce potentially toxic byproducts called mycotoxins under some conditions.
- > 200 mycotoxins from common molds have been identified, and many more remain to be identified
- Amount and types of mycotoxins produced by a particular mold depends on many environmental and genetic factors.
- No one can tell whether a mold is producing mycotoxins just by looking
- Some mycotoxins are known to affect people, but for many mycotoxins little health information is available.
- Research on mycotoxins is ongoing. Exposure to mycotoxins can occur from inhalation, ingestion, and skin contact.
- It is prudent to avoid unnecessary inhalation exposure to mold.

2004 Institute of Medicine Report, Damp Indoor Spaces and Health, published by The National Academies Press in Washington, DC,

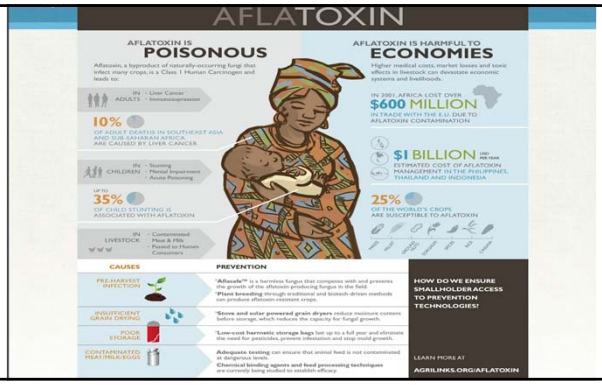
The Most Common Toxic Molds

SPECIES - MYCOTOXIN

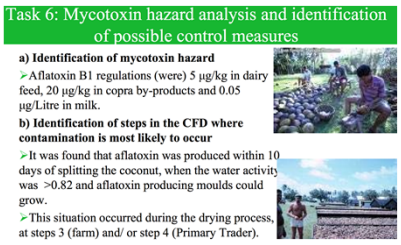
- Aspergillus avus - A aflotoxin
- A. ochraceus - Ochratoxin A
- A. niger -Ochratoxin A
- A. versicolor- Sterigmatocytosin
- A. fumigatus –Gliotoxin
- Penicillium verrucosum -Ochratoxin A
- *Stachybotrys* chartarum -Macrocyclic Trichothecenes
- Chaetomium globosum -Chaetoglobosin A, C
- Wellemia –Walleminol and walleminon

Aflatoxin

- Indoor environments with Mold
- Cereals, oilseeds, spices, tree nuts, maize, ground nuts, chilies, dried fruit
- Milk and cheese products
- Potent carcinogen
- Liver damage
- Lungs, kidney, brain, heart also affected
- May play a role in Reye's syndrome and kwashiorkor



Another reason dairy may be inflammatory - Lauren Castle Study in UK



Ochratoxin

- Nephrotoxin both acute and chronic
- Genotoxic
- Teratogenic
- Carcinogen
- Detected in breast milk
- Wheat and other grains / coffee / grapes / wine
- Water-damaged buildings

Tricothecenes

- Teratogen
- Cytotoxic
- Immunotoxic
- Genotoxic
- Carcinogen
- …..Biological Warfare agents

Gliotoxin

- Gliotoxin is a mycotoxin produced by *Aspergillus fumigatus*, a major cause of death in immunocompromised patients (e.g. transplant, HIV, Cancer).
- Gliotoxin has been demonstrated to have significant immunosuppressive effects and may play a role in the evasion of host defenses in Invasive Aspergillosis.
- Aspergillus fumigatus is also commonly detected in the ERMI (Environmental Relative Moldiness Index) PCR test on environmental samples taken from water damaged buildings and home

Other Toxins -Similar Effects To Mold

- Tick-borne microbes
  - Borrelia, babesia, bartonella, anaplasma, ehrlichia
- Cyanobacteria (blue green algea)
  - Cylindropsermopsis, microcystis
- Marine dinoflagellate Ciguatera toxin
  - Humans ingest in fish that have fed on it

Environ Sci Pollut Res Int. 2016 Apr 11. [Epub ahead of print]

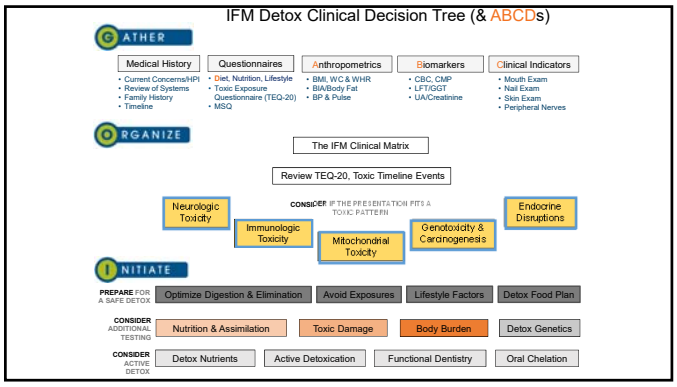
Multiple effects of a commercial Roundup® formulation on the soil filamentous fungus Aspergillus nidulans at low doses: evidence of an unexpected impact on energetic metabolism.

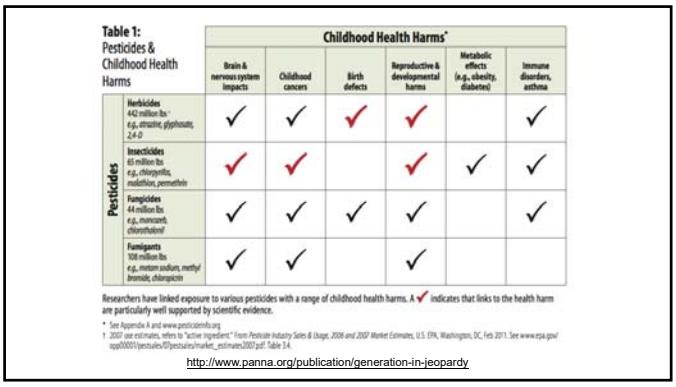
Nicolas V[1], Oestreicher N[2,3], Vélot C[4,5,6].

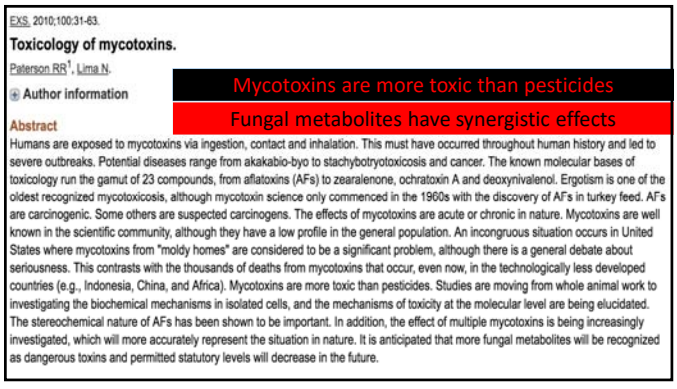
Author information

Abstract

Soil microorganisms are highly exposed to glyphosate-based herbicides (GBH), especially to Roundup® which is widely used worldwide. However, studies on the effects of GBH formulations on specific non-rhizosphere soil microbial species are scarce. We evaluated the toxicity of a commercial formulation of Roundup® (R450), containing 450 g/L of glyphosate (GLY), on the soil filamentous fungus Aspergillus nidulans, an experimental model microorganism. The median lethal dose (LD_{50}) on solid media was between 90 and 112 mg/L GLY (among adjuvants, which are also included in the Roundup® formulation), which corresponds to a dilution percentage about 100 times lower than that used in agriculture. The LOAEL and NOAEL (lowest- and no-observed-adverse-effect levels) associated to morphology and growth were 33.75 and 31.5 mg/L GLY among adjuvants, respectively. The formulation R450 proved to be much more active than technical GLY. At the LD_{50} and lower concentrations, R450 impaired growth, cellular polarity, endocytosis, and mitochondria (average number, total volume and metabolism). In contrast with the depletion of mitochondrial activities reported in animal studies, R450 caused a stimulation of mitochondrial enzyme activities, thus revealing a different mode of action of Roundup® on energetic metabolism. These mitochondrial disruptions were also evident at a low dose corresponding to the NOAEL for macroscopic parameters, indicating that these mitochondrial biomarkers are more sensitive than those for growth and morphological ones. Altogether, our data indicate that GBH toxic effects on soil filamentous fungi, and thus potential impairment of soil ecosystems, may occur at doses far below recommended agricultural application rate.







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Health Effects

- Kidney Toxicity
- Immune Suppression and Dysregulation
- Neurotoxicity
- Depression / Anxiety / Irritabilty / OCD
- Chronic Fatigue Syndrome
- Cancer
- Acute Pulmonary Hemorrhage
- Aplastic Anemia / low platelets
- Birth Defects
- Autoimmunity

Symptoms

- Fatigue
- Muscle pain
- Joint pain
- Fasciculations
- Neuropathy – weakness, pain
- Transient numbness, Tingling
- Dizziness / Vertigo
- "Brain Fog"
- Memory loss
- Computational skills
- Lower executive function
- Decision making
- ADHD, ADD
- Tremor
- Easily frustrated or angered
- Poor depth perception

Symptoms - continued

- Night Sweats
- Sugar Cravings
- Urticaria / Hives / Rash / Eczema
- Allergies/ Sinus congestion
- Asthma / Chronic cough
- Heart burn / Nausea
- Abdominal pain / Bloating
- Urinary urgency / Incontinence
- Weight gain without dietary changes
- Weight loss due to malabsorption
- Headaches
- Autonomic dysfunction
- Food sensitivities
- Excessive thirst, dehydration
- Tics
- Autoimmune disorders
- Raynaud's syndrome
- Inflammatory bowel disease
- Recurrent yeast infections
- Recurrent sinus infections
- Nose bleeds
- Metallic Taste

Common S/Sx Manifestations of Toxic Involvement:

1. Neurologic & Psychiatric Manifestations

- ✓ Concentration, Memory & Learning Issues
- ✓ ADHD, Autism Spectrum
- ✓ Chronic Headaches, Insomnia
- ✓ Peripheral Neuropathy, Tremor
- ✓ **Autonomic dysfunction**
- ✓ Neurodegenerative Diseases: Alzheimer's, Parkinson's, ALS
- ✓ Mood disorders: Depression, Anxiety, Irritability, etc.

Common S/Sx Manifestations of Toxic Involvement:

2. Immune Dysfunction

- ✓ Atopic Syndrome: Allergies, Asthma
- ✓ Autoimmune Diseases
- ✓ Chronic Inflammatory Diseases
- ✓ Recurrent or Chronic Infections
- ✓ Chronic Dermatitis
- ✓ Adverse Food Reactions (ARF)
- ✓ Multiple Chemical Sensitivities (MCS)

Common S/Sx Manifestations of Toxic Involvement:

3. Mitochondrial & Metabolic

- ✓ Fatigue; Chronic Fatigue Syndrome
- ✓ Fibromyalgia, Muscle Aches, Weakness
- ✓ Loss of appetite, Nausea/Vomiting, GERD
- ✓ Constipation/Diarrhea, IBS, Abdominal Pain
- ✓ Dysbiosis & Pathogenic Overgrowth
- ✓ Osteoporosis

Common S/Sx Manifestations of Toxic Involvement:

4. Endocrine Disruption

- ✓ Weight gain / Obesity
- ✓ Dysglycemia (Hypo- / Hyperglycemia)
- ✓ Insulin resistance/DMII
- ✓ Hormonal Abnormalities (HPA / Thyroid)
- ♀ Premature puberty, PMS, PCOS, Infertility, Endometriosis, Fibroids
- ♂ Oligospermia; Sperm Dysmotility, Hypoandrogenism

Common S/Sx Manifestations of Toxic Involvement:

5. Genotoxicity / Carcinogenesis

- ✓ Cancer
- ✓ Developmental Disorders / Birth Defects
- ✓ Lost Pregnancies

Other Possible Findings

- ✓ Anemia
- ✓ Leukopenia

Toxins (Basel). 2013 Apr 11;5(4):605-17. doi: 10.3390/toxins5040605.

Detection of mycotoxins in patients with chronic fatigue syndrome.

Brewer JH[1], Thrasher JD, Straus DC, Madison RA, Hooper D.

Author information

Abstract

Over the past 20 years, exposure to mycotoxin producing mold has been recognized as a significant health risk. Scientific literature has demonstrated mycotoxins as possible causes of human disease in co Pa of ma sp

93% of Chronic Fatigue Patients had at least one mycotoxin present

equivocal range). Almost 30% of the cases had more than one mycotoxin present. OTA was the most prevalent mycotoxin detected (83%) with MT as the next most common (44%). Exposure histories indicated current and/or past exposure to WDB in over 90% of cases. Environmental testing was performed in the WDB from a subset of these patients. This testing revealed the presence of potentially mycotoxin producing mold species and mycotoxins in the environment of the WDB. Prior testing in a healthy control population with no history of exposure to a WDB or moldy environment (n = 55) by the same laboratory, utilizing the same methods, revealed no positive cases at the limits of detection.

Toxins (Basel). 2013 Dec 24;6(1):66-80. doi: 10.3390/toxins6010066.

Chronic illness associated with mold and mycotoxins: is naso-sinus fungal biofilm the culprit?

Brewer JH[1], Thrasher JD, Hooper D.

Author information

Abstract

It has recently been demonstrated that patients who develop chronic illness after prior exposure to water damaged buildings (WDB) and mold have the presence of mycotoxins, which can be detected in the urine. We hypothesized that the mold may be harbored internally and continue to release and/or produce mycotoxins which contribute to ongoing chronic illness. The sinuses are the most likely candidate as a site for the internal mold and mycotoxin production. In this paper, we review the literature supporting this concept.

Toxicol Ind Health. 2009 Oct-Nov;25(9-10):583-615. doi: 10.1177/0748233709348386. Epub 2009 Sep 30.

The biocontaminants and complexity of damp indoor spaces: more than what meets the eyes.

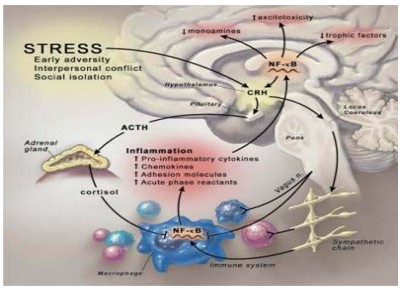
Thrasher JD[1], Crawley S.

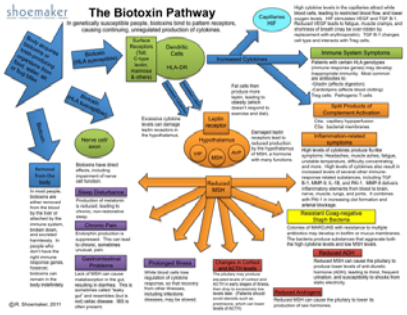
Author information

Abstract

Nine types of biocontaminants in damp in (1) indicator molds; (2) Gram negative ar mycotoxins; (5) volatile organic compoun proteins; (7) galactomannans; (8) 1-3-bet endotoxins). When mold species exceed bacterial endotoxins, LPS in indoor envir Bacillus species, Actinomycetes (Strepto The Actinomycetes are associated with h Mycobacterial mycobacterium infections immunocompetent individuals. In animal G and aflatoxin B1 to damage the olfacto liver (aflatoxin B1). Aflatoxin B1 and prob tract to the temporal lobe. Co-cultured St produce a cytotoxin similar to doxorubicin and actinomycin D (chemotherapeutic agents). Trichothecenes, aflatoxins, gliotoxin and other mycotoxins are found in dust, bulk samples, air and ventilation systems of infested buildings. Macrocyclic trichothecenes are present in airborne particles <2 microm. Trichothecenes and stachylysin are present in the sera of individuals exposed to S. chartarum in contaminated indoor environments. Haemolysins are produced by S. chartarum, Memnoniella echinata and several species of Aspergillus and Penicillium. Galactomannans, glucans and LPS are upper and lower respiratory tract irritants. Gliotoxin, an immunosuppressive mycotoxin, was identified in the lung secretions and sera of cancer patients with aspergillosis produced by A. fumigatus, A. terreus, A. niger and A. flavus.

Mycotoxins are transported along the olfactory tract into the temporal lobe and in to the body through the respiratory tract. They can also be produced in the body when mold is growing





mVOC's –Microbial Volatile Organic Compounds

- The health effects of inhaling mVOCs are largely unknown.
- Exposure to mVOCs has been linked to symptoms such as headaches, nasal irritation, dizziness, fatigue, and nausea.
- More research is needed to determine the human health effects from non-occupational indoor exposures to mVOCs.

Environ Toxicol. 2014 May;29(7):829-36. doi: 10.1002/tox.21825. Epub 2012 Nov 9.

Drosophila melanogaster as a model to characterize fungal volatile organic compounds.

Inamdar AA[1], Zaman T, Morath SU, Pu DC, Bennett JW.

Author information

Fungal VOC's had greater effect than formaldehyde, xylene, benzene and toluene

Abstract

Fungi are implicated in poor indoor air quality and may pose a potential risk factor for building/mold related illnesses. Fungi emit numerous volatile organic compounds (VOCs) as alcohols, esters, ethers, ketones, aldehydes, terpenoids, thiols, and their derivatives. The toxicity profile of these VOCs has never been explored in a model organism, which could enable the performance of high throughput toxicological assays and lead to a better understanding of the mechanism of toxicity. We have established a reductionist Drosophila melanogaster model to evaluate the toxicity of fungal VOCs. In this report, we assessed the toxicity of fungal VOCs emitted from living cultures of species in the genera, Trichoderma, Aspergillus, and Penicillium and observed a detrimental effect on larval survival. We then used chemical standards of selected fungal VOCs to assess their toxicity on larval and adult Drosophila. We compared the survival of adult flies exposed to these fungal VOCs with known industrial toxic chemicals (formaldehyde [37%], xylene, benzene, and toluene). Among the tested fungal VOC standards, the compounds with eight carbons (C8) caused greater truncation of fly lifespan than tested non-C8 fungal VOCs and industrial toxins. Our data validate the use of Drosophila melanogaster as a model with the potential to elucidate the mechanistic attributes of different toxic VOCs emitted by fungi and also to explore the potential link between reported human illnesses/symptoms and exposure to water damaged and mold contaminated buildings.

Water Damaged Buildings Study

- 100 patients with mold exposure
- Mold sensitivity and exposure confirmed via intradermal testing 44-98%
- 64% respiratory issues
- 80% immune system dysfunction
- 70% neurological issues
- 100% autonomic dysfunction
- 86% abnormal PET scans
- Short term memory impairment, concentration, executive function and hand/eye coordination
- Rea WJ, et al. Effects of toxic exposure to molds and mycotoxins in building-related illnesses. Arch Environ Health 2003 Jul;58(7): 399-405.

J Biol Chem. 2007 Mar 23;282(12):8969-77. Epub 2007 Jan 16.

Fungal peptide Destruxin A plays a specific role in suppressing the innate immune response in Drosophila melanogaster.

Pal S[1], St Leger RJ, Wu LP.

Author information

Abstract

Destruxins are a class of insecticidal, anti-viral, and phytotoxic cyclic depsipeptides that are also studied for their toxicity to cancer cells. They are produced by various fungi, and a direct relationship has been established between Destruxin production and the virulence of the entomopathogen Metarhizium anisopliae. Aside from opening calcium channels, their in vivo mode of action during pathogenesis remains largely uncharacterized. To better understand the effects of a Destruxin, we looked at changes in gene expression following injection of Destruxin A into the fruit fly Drosophila melanogaster. Microarray results revealed reduced expression of various antimicrobial peptides that play a major role in the humoral immune response of the fly. Flies co-injected with a non-lethal dose of Destruxin A and the normally innocuous Gram-negative bacteria Escherichia coli, showed increased mortality and an accompanying increase in bacterial titers. Mortality due to sepsis was rescued through ectopic activation of components in the IMD pathway, one of two signal transduction pathways that are responsible for antimicrobial peptide induction. These results demonstrate a novel role for Destruxin A in specific suppression of the humoral immune response in insects.

Toxicol Mech Methods. 2015 Mar;25(3):184-91. doi: 10.3109/15376516.2015.1006743. Epub 2015 Feb 11.

Deoxynivalenol induces cytotoxicity and genotoxicity in animal primary cell culture.

Singh S[1], Banerjee S, Chattopadhyay P, Borthakur SK, Veer V.

Author information

Abstract

Deoxynivalenol (DON), a mycotoxin produced by Fusarium graminearum, is widely found as a contaminant of food. DON is responsible for a wide range of toxic activities, including gastro-intestinal, lymphoid, bone-marrow and cardiotoxicity. But, the complete explorations of toxicity in terms of hepatotoxicity, nephrotoxicity, cytotoxicity and genotoxicity as well have not been documented well. Again, the mechanisms through which DON damages the DNA and promotes cellular toxicity are not well established. Considering the above fact, this research article is focused on the effects of DON-induced toxicities on experimental animal model as well as its effects on cellular level via various toxicological investigations. DON treatment showed cytotoxicity and DNA damage. Further, flow cytometric analysis of hepatocytes showed cellular apoptosis, suggesting that DON-induced hepatotoxicity is, may be partly, mediated by apoptosis. Moreover, significant differences were found in each haematology and clinical chemistry value, either ($p > 0.05$). No abnormality of any organ was found during histopathological examination. Hence, it can be concluded that DON induces oxidative DNA damage and increases the formation of centromere positive micronuclei due to aneugenic activity.

KEYWORDS: Acute oral toxicity; cytotoxicity; deoxynivalenol; genotoxicity; mycotoxin

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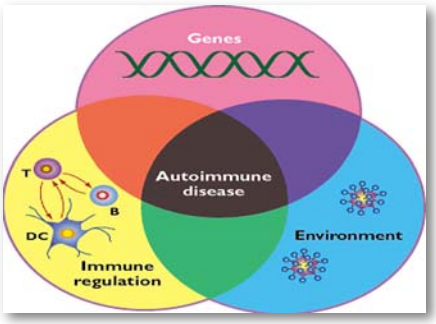
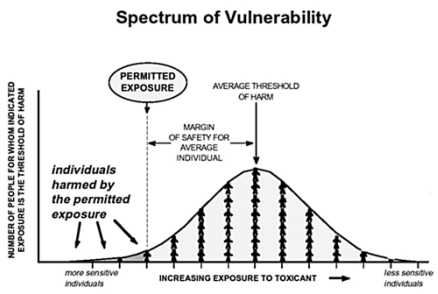
Who is Susceptible?

- Everyone, but some get symptoms earlier
- Everyone has different combinations of symptoms even in the same environment
  - Example of drug side effects
  - Example of tobacco, alcohol,
  - environmental toxins – mercury, lead, asbestos
- Depends on combinations of immune system genes, detoxification genes and previous environmental exposures



Who is Susceptible?

- Everyone with high enough exposure – chronic or high dose exposure
- Immunosuppressed
- Fetus, Children and Elderly
- Genetic (HLA, P450, methylation, comt, glutathione, NAT, vdr, hist)
- Other toxic load impacting detox pathways, immune system and repair
- Synergistic toxins



Who is Most affected by Mold?

- High Exposure or Chronic Exposure
- Children (increased respiratory rate, developing immune, detox and neurological systems)
- Nutrient deficiencies
- High sugar, low protein, low fat diet
- Toxin Load: heavy metals, pesticides, solvents and plastics
- Stress, emotional trauma
- Intestinal dysbiosis
- Detox Methylation and Immune Genomics SNP's

Exposure bioaccumulation is consistent with disease incidence

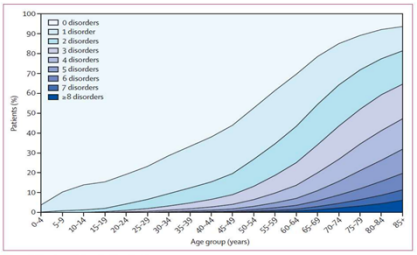


Figure 1: Number of chronic disorders by age-group

Barnett et al., Lancet 2012

I think most of us are affected in some way – similar to Lead in children the 60's

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Technology Advances

- Used to just be able to test for Allergy to Mold
- Now we can test for some of the mycotoxins in humans and the environment
- Now we can test for some of the Mold's DNAs to see if it is present in human tissue and in the environment
- Still a long way to go
  - Many more mycotoxins
  - Many more DNA's

Mycotoxins With Commercial Testing

- Aflotoxin
- Tricothecene
- Ochratoxin
- Gliotoxin

Human Mycotoxin Testing

- RealTime Labs has been most reliable for me
- There are several other labs – may not be testing the correct trichothecenes

Mycotoxins Tested By RealTime Labs

- Ochratoxins -Ochratoxin A
- Aflatoxins –
  - Aflatoxin B1
  - Aflatoxin B2
  - Aflatoxin G 1
  - Aflatoxin G2
- GliotoxinT
- Trichothecenes
  - Satratoxin G
  - Satratoxin H
  - Isosatratoxin F
  - RoridinA
  - Roridin E
  - Roridin H
  - Roridin L-2
  - Verrucarin A
  - Verrucarin J

Glutathione Challenge

- Started noticing my sickest patients that I suspected had mycotoxin exposure were testing negative for mycotoxins
- Then found that they often had glutathione snp's
- Or were depleted in glutathione

14 year old Boy with Severe Facial Tic

Cytochrome P-450

Result	Gene
✔	CYP1A1 *
🔴	CYP1B1 *
🔴	CYP2A6
✔	CYP2C9 *
🔴	CYP2C19 *
✔	CYP2D6
✔	CYP3A4 *

Methylation

Result	Gene	SNP Location	Affects
++	COMT	V158M	Liver/Gut

Acetylation (N-acetyltransferase)

SLOW METABOLIZER POLYMORPHISM

Result	Gene	SNP Location	Affects
--	NAT1	R64W	All Cells
--	NAT1	R187Q	Liver/Gut
++	NAT2	I114T	Liver/Gut
--	NAT2	R197Q	Liver/Gut
--	NAT2	G286E	Liver/Gut
--	NAT2	R64Q	Liver/Gut

FAST METABOLIZER POLYMORPHISM

Result	Gene	Location	Affects
+-	NAT2	K268R	Liver/Gut

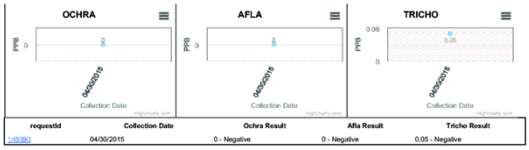
Glutathione Conjugation (Glutathione s-transferase)

Result	Gene	Location	Affects
ABSENT	GSTM1	1p13.3	Liver/Kidney
++	GSTP1	I105V	Brain/Skin
++	GSTP1	A114V	Brain/Skin

Ochratoxin A - Procedure by ELISA
Aflatoxin Group - Procedure by ELISA
Trichothecene Group - Procedure by ELISA

Results:

Code	Test	Specimen	Value	Result	Negative if less than	Equivocal if between	Positive if greater or equal
E8501	Ochratoxin A	Urine	0 ppb	Negative	1.8 ppb	1.8-2.0 ppb	2.0 ppb
E8502	Aflatoxin Group	Urine	0 ppb	Negative	0.8 ppb	0.8-1.0 ppb	1.0 ppb
E8503	Trichothecene Group	Urine	0.05 ppb	Negative	0.18 ppb	0.18-0.2 ppb	0.2 ppb



requestId	Collection Date	Ochra Result	Afla Result	Tricho Result
149390	04/30/2015	0 - Negative	0 - Negative	0.05 - Negative

Ochratoxin A - Procedure by ELISA
Aflatoxin Group - Procedure by ELISA
Trichothecene Group - Procedure by ELISA

Results:

Code	Test	Specimen	Value	Result	Negative if less than	Equivocal if between	Positive if greater or equal
E8501	Ochratoxin A	Urine	13.55 ppb	Positive	1.8 ppb	1.8-2.0 ppb	2.0 ppb
E8502	Aflatoxin Group	Urine	0 ppb	Negative	0.8 ppb	0.8-1.0 ppb	1.0 ppb
E8503	Trichothecene Group	Urine	0.22 ppb	Positive	0.18 ppb	0.18-0.2 ppb	0.2 ppb

Director Signature _____

Tests such as this should be used only in conjunction with other medically established diagnostic elements (e.g.,symptoms, history, clinical impressions, results from other tests, etc). Physicians should use all the information available to them to diagnose and determine appropriate treatment for their patients.
Disclaimer: This test was developed and its performance characteristics determined by RealTime Lab. It has not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. This laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88) as qualified to perform high complexity clinical laboratory testing.

requestId	Collection Date	Ochra Result	Afla Result	Tricho Result
149818	05/27/2015	13.55 - Positive	0 - Negative	0.22 - Positive
149390	04/30/2015	0 - Negative	0 - Negative	0.05 - Negative

LAB #: B
PATIENT ID: SHRI
SEX: Ma
AGE: 14

On 4tsp/day of Redisorb Glutathione and time at grandparents' Symptoms resolved in 2 months

Glutathione; Erythrocytes

	Within	Outside	Reference Range
Glutathione*	1414		1000 - 2000 µmoles/L

Glutathione (GSH) is a tripeptide (λ-glutamyl-cysteinylglycine) synthesized in most cells. The level of GSH in erythrocytes is a sensitive indicator of intracellular GSH status, the overall health of cells, and of the ability to endure toxic challenges. GSH is the most abundant non-protein thiol in mammalian cells. It is involved in many biological processes including detoxification of xenobiotics, removal of oxygen-reactive species, regulation of the redox state of cells and the oxidative state of important protein sulfhydryl groups, and regulation of immune function. GSH levels are thousands of times higher in cells than in plasma. Plasma GSH represents primarily that synthesized and exported from the liver. Reduced GSH (rGSH) is the active form of the tripeptide and the ratio of rGSH: oxidized GSH (GSSH) is normally about 9:1. Once a blood sample is obtained, Erythrocyte rGSH is very susceptible to oxidation and the rGSH:GSSH ratio drops rapidly. Specimen handling to prevent the *ex vivo* oxidation of rGSH is impractical and direct measurement of rGSH *in vivo* is not feasible outside of a research setting. However, research clearly indicates that undesirable ratios of rGSH:GSSH are equally associated with abnormally low levels of total cellular GSH. Therefore, it is clinically meaningful to assess the level of total erythrocyte GSH as an indicator of GSH status and metabolism.

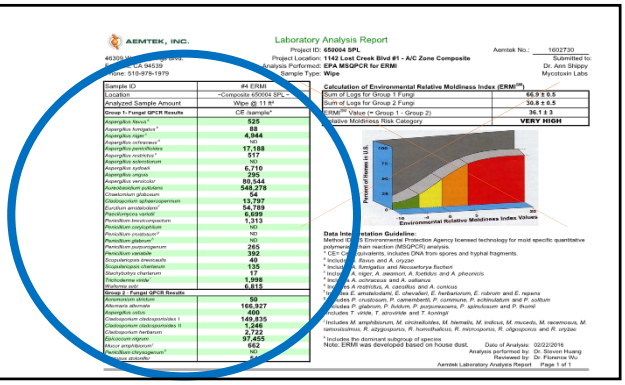
Low levels of GSH have been reported in cardiovascular disease, cancer, AIDS, autism, alcoholism, debilitating neurodegenerative diseases such as Alzheimer's and Parkinson's, and chronic retention of potential toxic elements (mercury, lead, arsenic, cadmium manganese, iron), chemicals, and some drugs. Intracellular GSH biosynthesis and intracellular levels can be upregulated as a protective mechanism. Some factors that result in increased biosynthesis and "high normal" erythrocyte GSH levels include, but are not limited to, moderate alcohol consumption, smoking, regular physical exercise, and acute exposure to toxic metals. Under such conditions it is essential to provide the body with the key nutrients involved in GSH synthesis in order to sustain functionally appropriate levels of GSH. Magnesium and potassium are required for both energy dependent enzymatic steps in GSH synthesis; cysteine is the rate limiting amino acid. Nutritional products that have been documented to increase erythrocyte GSH/GSH biosynthesis include high quality whey protein preparations, α-lipoic acid, curcumin, oral liposomal GSH, nebulized GSH, and to a lesser extent, N-acetyl-L-cysteine.

Objectives

- Define Mold Terms
- Scope and Source of the epidemic
- What to look for in patients to help consider Mold as a diagnosis
- Who is most susceptible?
- How to utilize the limited testing we have on humans
- How to utilize the limited testing we have for the environment
- Reducing mold exposure - Is remediation on option?
- Functional medicine approach to recovery
- Where do we go from here?

Could I have toxic mold in my environment?

- *Testing*
  - *PCR (part of the ERMI test)*
  - *Mycotoxin*
- *Traditional testing-with air samples misses 50-75%*



AEMTEK, INC.

Laboratory Analysis Report

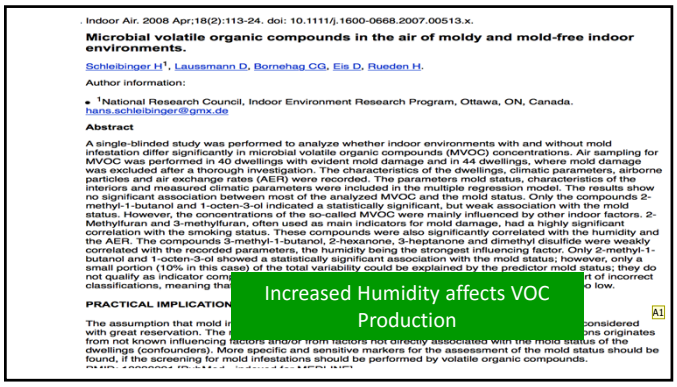
Project ID: 650004 SPL
Project Location: 1142 Lost Creek Blvd #1 - A/C Zone Composite
Analysis Performed: EPA MSQPCR for ERMI
Sample Type: Wipe

Aemtek No.: 1602730
Submitted to: Dr. Ann Shippy
Mycotoxin Labs

Sample ID	#4 ERMI
Location	~Composite #50004 SPL~
Analyzed Sample Amount	Wipe @ 11 ft²
Group 1- Fungal QPCR Results	CR Sample*
Aspergillus flavus	525
Aspergillus fumigatus	88
Aspergillus niger	4,944
Aspergillus ochraceus	ND
Aspergillus penicillioides	17,188
Aspergillus restrictus	517
Aspergillus sclerotiorum	ND
Aspergillus sydowii	6,710
Aspergillus unguis	295
Aspergillus versicolor	89,544
Aureobasidium pullulans	548,278
Chaetomium globosum	54
Cladosporium sphaerospermum	13,797
Eurotium amstelodami	54,789
Penicillium brevicompactum	6,699
Penicillium corylophilum	1,313
Penicillium crustosum	ND
Penicillium glabrum	ND
Penicillium purpurogenum	265
Penicillium variabile	392
Scopulariopsis brevicaulis	40
Scopulariopsis chartarum	135
Stachybotrys chartarum	ND
Wallemia sebi	1,998
Wallemia sebi/ sebula	6,815
Group 2 - Fungal QPCR Results	
Acremonium strictum	50
Alternaria alternata	166,927
Aspergillus ustus	400
Cladosporium cladosporioides 1	149,835
Cladosporium cladosporioides II	1,246
Cladosporium herbarum	2,722
Epicoccum nigrum	97,455
Mucor amphibiorum	662
Penicillium chrysogenum	ND
Phoma glomerata	ND

Calculation of Environmental Relative Moldiness Index (ERMI™)

Sum of Logs for Group 1 Fungi	46.9 ± 8.5
Sum of Logs for Group 2 Fungi	36.8 ± 6.5
ERMI™ Value (= Group 1 - Group 2)	36.1 ± 3
Relative Moldiness Risk Category	VERY HIGH



Indoor Air. 2008 Apr;18(2):113-24. doi: 10.1111/j.1600-0668.2007.00513.x.

Microbial volatile organic compounds in the air of moldy and mold-free indoor environments.

Schleibinger H[1], Laussmann D, Bornehag CG, Eis D, Rueden H.

Author information:

• [1]National Research Council, Indoor Environment Research Program, Ottawa, ON, Canada. hans.schleibinger@gmx.de

Abstract

A single-blinded study was performed to analyze whether indoor environments with and without mold infestation differ significantly in microbial volatile organic compounds (MVOC) concentrations. Air sampling for MVOC was performed in 40 dwellings with evident mold damage and in 44 dwellings, where mold damage was excluded after a thorough investigation. The characteristics of the dwellings, climatic parameters, airborne particles and air exchange rates (AER) were recorded. The parameters mold status, characteristics of the interiors and measured climatic parameters were included in the multiple regression model. The results show no significant association between most of the analyzed MVOC and the mold status. Only the compounds 2-methyl-1-butanol and 1-octen-3-ol indicated a statistically significant, but weak association with the mold status. However, the concentrations of the so-called MVOC were mainly influenced by other indoor factors. 2-Methylfuran and 3-methylfuran, often used as main indicators for mold damage, had a highly significant correlation with the smoking status. These compounds were also significantly correlated with the humidity and the AER. The compounds 3-methyl-1-butanol, 2-hexanone, 3-heptanone and dimethyl disulfide were weakly correlated with the recorded parameters, the humidity being the strongest influencing factor. Only 2-methyl-1-butanol and 1-octen-3-ol showed a statistically significant association with the mold status; however, only a small portion (10% in this case) of the total variability could be explained by the predictor mold status; they do not qualify as indicator com… …rt of incorrect classifications, meaning tha… …o low.

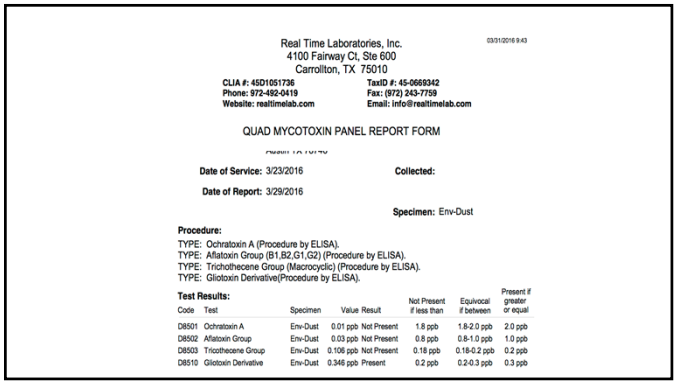
PRACTICAL IMPLICATION

The assumption that mold ir… …considered with great reservation. The … …ons originates from not known influencing factors and/or from factors not directly associated with the mold status of the dwellings (confounders). More specific and sensitive markers for the assessment of the mold status should be found, if the screening for mold infestations should be performed by volatile organic compounds.

Increased Humidity affects VOC Production

Environmental Mycotoxin testing

- RealTime Labs currently best option
- They will ship kits directly to patients
- Used with the PCR of the ERMI test decreases false negatives



Real Time Laboratories, Inc.
4100 Fairway Ct, Ste 600
Carrollton, TX 75010

03/31/2016 9:43

CLIA #: 45D1051736 TaxID #: 45-0669342
Phone: 972-492-0419 Fax: (972) 243-7759
Website: realtimelab.com Email: info@realtimelab.com

QUAD MYCOTOXIN PANEL REPORT FORM

Date of Service: 3/23/2016 **Collected:**

Date of Report: 3/29/2016

Specimen: Env-Dust

Procedure:
TYPE: Ochratoxin A (Procedure by ELISA).
TYPE: Aflatoxin Group (B1,B2,G1,G2) (Procedure by ELISA).
TYPE: Trichothecene Group (Macrocyclic) (Procedure by ELISA).
TYPE: Gliotoxin Derivative(Procedure by ELISA).

Test Results:

Code	Test	Specimen	Value	Result	Not Present if less than	Equivocal if between	Present if greater or equal
D8501	Ochratoxin A	Env-Dust	0.01 ppb	Not Present	1.8 ppb	1.8-2.0 ppb	2.0 ppb
D8502	Aflatoxin Group	Env-Dust	0.03 ppb	Not Present	0.8 ppb	0.8-1.0 ppb	1.0 ppb
D8503	Tricothecene Group	Env-Dust	0.106 ppb	Not Present	0.18 ppb	0.18-0.2 ppb	0.2 ppb
D8510	Gliotoxin Derivative	Env-Dust	0.346 ppb	Present	0.2 ppb	0.2-0.3 ppb	0.3 ppb

Shoemaker Recommendations for ERMI

- ERMI
  - < 2 (if MSH normal)
  - <7 1 (if MSH < 35 and C4a is > 20,000)
- HERTSMI 2
  - Based on shoemaker'stop 5 toxic molds
- SCORE
  - If < 11 likely safe for CIRS patients
  - 11 to 15 borderline
  - If > 15, 99% of CIRS patient relaps

Slide 65

A1 Author, 5/6/2016

ERMI and HERTSMI 2

- Has not been a good predictor for me – too lax
- Depends on the lab doing the test
- The scores can under predict the toxicity of the environment for some patients
- If any Chaetomium or Stachybotrys chartarum is present it is usually not clean enough for the sickest patients

Optimal Approach

- Combine surface ERMI (PCR) testing, surface mycotoxin testing and a knowledgeable thorough inspector to look for the subtle clues applying a detailed history of the building

Where things go Awry - Humidity

- Sometimes, humidity or dampness (water vapor) in the air can supply enough moisture for mold growth. Indoor relative humidity (RH) should be kept below 60 percent — ideally between 30 percent and 50 percent, if possible.
- Crawl spaces where relative humidity (RH) is high are common sites of hidden mold growth, particularly if the crawl space has a bare earth floor

Where Things Go Awry

- Buildings and building furnishings will often get wet.
- They must be dried or "allowed to dry" quickly (within 24-48 hours) in order to avoid mold growth.
- In general, increasing air circulation and using a dehumidifier will increase the speed of drying.

Where Thing Go Awry

- Some moisture problems have been linked to changes in building construction practices since the 1970s. These practices led to buildings that are tightly sealed but, in some cases, lack adequate ventilation. Without adequate ventilation, moisture may build up indoors and mold may grow
- Humidity levels can rise in a building as a result of the use of humidifiers, steam radiators, moisture-generating appliances such as dryers, and combustion appliances such as stoves. Cooking and showering also can add to indoor humidity

Where Things go Awry

- Condensation can be a sign of high humidity. When warm, humid air contacts a cold surface, condensation may form.
- You can measure your humidity with a simple monitor

Where things go awry – Vapor barriers

- Many buildings incorporate vapor barriers in the design of their walls and floors.
- A vapor barrier is a layer of material that slows or prevents the absorption or release of moisture from or into a wall or floor.
- Vapor barriers must be located and installed properly or the building may have moisture problems.
- Vapor barriers can prevent damp or wet building materials from drying quickly enough to prevent mold growth.

Sources of Moisture

- Leaking roofs.
- Leaking or condensing water pipes, especially pipes inside wall cavities or pipe chases.
- Leaking fire-protection sprinkler systems.
- Landscaping, gutters, and down spouts that direct water into or under a building.
- High humidity (> 60% relative humidity).
- Unvented combustion appliances such as clothes dryers vented into a garage. (Clothes dryers and other combustion appliances should be vented to the outside.)

Hidden Sources of Moisture

- Some moisture problems are not easy to see.
- Inside of walls where pipes and wires are run (pipe chases and utility tunnels) are common sites of mold growth.
- On walls in cold corners behind furniture where condensation forms.
- Poorly draining condensate drain pains inside air handling units.
- Porous thermal or acoustic liners inside duct work.
- Roof materials above ceiling tiles.
- The back side of drywall (also known as gypsum board, wallboard, or SHEETROCK®), paneling, and wallpaper.
- Underside of carpets and pads.
- You may suspect mold, even if you can't see it, if a building smells moldy.
- You may also suspect hidden mold if you know there has been a water problem in the building and its occupants are reporting health problems.

Hidden Mold – per the EPA

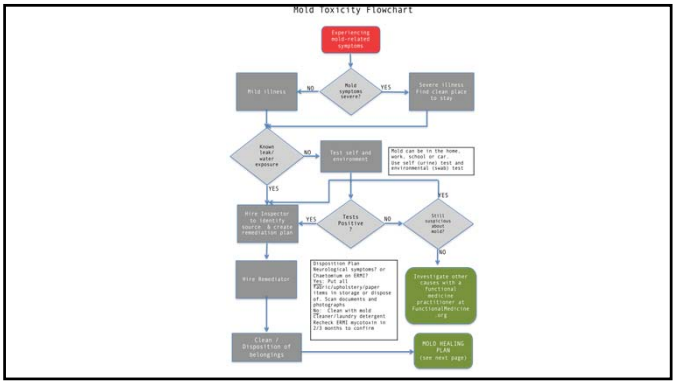
In some cases, indoor mold growth may not be obvious. Mold does not need light to grow: it can grow in dark areas and on hidden surfaces, such as the backside of drywall, wallpaper, and paneling; the top side of ceiling tiles; and the underside of carpets and pads. Possible locations of hidden mold also include damp areas behind walls and in crawlspaces, inside pipe chases and utility tunnels (areas in walls where water and other pipes are run), on acoustic liners in ventilation ducts, and on roof materials above ceiling tiles.

Investigating hidden mold can be difficult and may require a professional with experience investigating water and mold-damaged buildings. Specialized equipment such as borescopes and moisture meters, and in some cases special sampling techniques, may be helpful in locating and identifying hidden mold areas. Investigating hidden mold requires caution since disturbing moldy areas may spread mold throughout the building. Opening and closing air handlers, for example, can send high levels of dust and mold into the air. Personal protective equipment (PPE) is not always needed when looking for mold, but it should always be available. If mold might be released into the air, investigators should use PPE to reduce exposure.

Personal Protective Gear should always be available

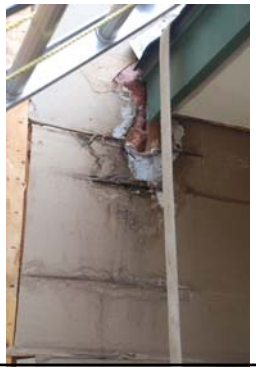
Per The EPA Website

- One of the biggest problems related to mold testing happens when people misinterpret equivocal or negative findings.
- It is a common, yet serious error to conclude that a mold problem does not exist simply because tests failed to find evidence of it.
- Most mold testing simply **cannot** prove the absence of a problem, and it should never be used as the basis for dismissing complaints or to defend inadequate efforts to investigate or solve potential problems.



Objectives

- Define Mold Terms
- Scope and Source of the epidemic
- What to look for in patients to help consider Mold as a diagnosis
- Who is most susceptible?
- How to utilize the limited testing we have on humans
- How to utilize the limited testing we have for the environment
- Reducing mold exposure- Is remediation on option?
- Functional medicine approach to recovery
- Where do we go from here?



Remediation Guidelines

- Total Surface Area Affected determines
  - Protective gear – is it enough?
    - May include powered air purifying respirators with HEPA filters
    - Full head to foot covering sealed with duct tape
    - Goggles/ eye protection
    - Disposable clothing
    - Gloves
  - Containment Guidelines
  - Contaminated waste disposal

Testing The Environment for Mold Post Remediation

- Bioaerosol sampling (air sampling for mold or other biological contaminants) usually is not necessary to determine remediation effectiveness. In fact, bioaerosol sampling may be less effective at determining the success of remediation than visual and sensory surveys of the area.
- Although sampling may be of some help in judging remediation effectiveness, remember that a negative sampling report must not be used in place of a visual survey.
- Factors such as barometric pressure, inside and outside temperatures, activity levels, and humidity may dramatically reduce or increase the spore levels within a building.
- Air sampling for mold provides information on what was in the air only for the moment when the sampling occurred. It is important, therefore, that sampling not replace visual inspection.

The testing Dilemma Post Remediation

How Do You Know When You Have Finished Remediation/Cleanup?

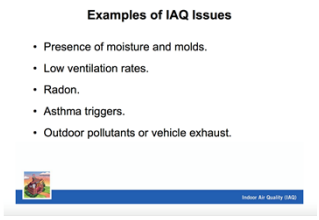
1. You must have completely fixed the water or moisture problem.
2. You should have completed mold removal. Use professional judgment to determine if the cleanup is sufficient. Visible mold, mold-damaged materials, and moldy odors should not be present.
3. If you have sampled, the kinds and concentrations of mold and mold spores in the building should be similar to those found outside, once cleanup activities have been completed.
4. You should revisit the site(s) shortly after remediation, and it should show no signs of water damage or mold growth.
5. People should be able to occupy or re-occupy the space without health complaints or physical symptoms.
6. Ultimately, this is a judgment call; there is no easy answer.

I recommend retesting 2 months, 6 months, and 1 year later

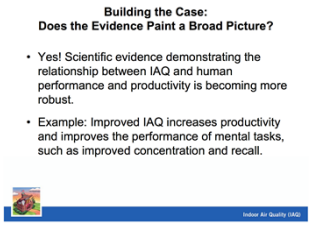
Finding a Mold-Free Place to Learn

- One of my biggest challenges for kids and teachers in Austin…
- Is this a nation-wide issue?

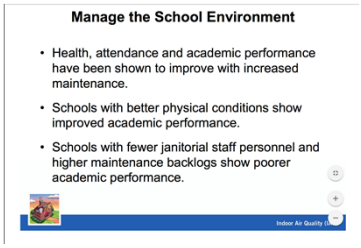
EPA Presentation



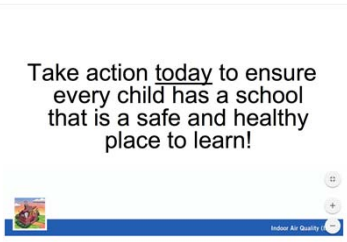
EPA Presentation



EPA Presentation



EPA presentation



Prevention

- Promptly and properly repairing any leaks or water damage.
- Removing standing water under the cooling coils of air handlers by making sure the drain pans slope toward the drain and the drain is flowing freely.
- Making sure ducts are properly sealed and insulated in all non-air-conditioned spaces so moisture due to condensation does not enter the system and the system works as intended. To prevent condensation, the heating and cooling system must be properly insulated. Operating and maintaining any in-duct humidification equipment strictly according to the manufacturer's recommendations.
- Making sure that carpets, drapes, furniture, and other furnishings are dried promptly after they have been cleaned.

What if I have a leak? Per EPA

- Building materials and building furnishings will often get wet.
- They must be dried or "allowed to dry" quickly (within 24-48 hours) in order to avoid mold growth.
- In general, increasing air circulation and temperature will increase the speed of drying.
- Commercial firms that do mold remediation work or work on water- and fire-damaged buildings often use large fans, dehumidifiers, and other equipment to dry wet buildings and items quickly before mold has a chance to grow. This action can save money in the long run, because if the building or furnishings are dried completely and quickly, mold will not grow, and a mold remediation will not be needed.

You have 24-48 hours to do things correctly or it is likely mold will grow

"Dead Mold"

- Dead mold is allergenic and may cause allergic reactions and other health effects in some individuals, so it is not enough to simply kill the mold. It must also be removed.
- Mold does not have to be alive to cause an allergic reaction. Dead or alive, mold can cause allergic reactions in some people.
- Because mVOCs often have strong or unpleasant odors, they can be the source of the "moldy odor" or musty smell frequently associated with mold growth. A moldy odor suggests that mold is growing in the building and should be investigated
- Desiccated mycotoxins are not addressed anywhere in EPA or other literature- but it is implied

Desiccated Mold –Mycotoxin and mVoc Production and Release

- Much more research is needed
- Clinically, there does not need to be an active water leak to make people (and their pets) sick

What about Crawl Spaces and Basements

- Construction guidelines need to be improved
- Avoid if possible!
- if you have a Basement or Crawl space, hire an Expert that understands the potential consequences
- Remember – what is in the wall spaces travels throughout the building

Interesting Food Facts- We need better controls in the US – learning from EU again

- The EU has set limits for OTA in cereals, dried vine fruits, roasted coffee beans and ground coffee, soluble coffee, wine and grape juice. Limits vary according to the commodity, but range from 2-10 µg/kg. The limit for unprocessed cereals is 5.0 µg/kg, but for processed cereal products intended for direct human consumption it is 3.0 µg/kg. The limit for dried vine fruits is 10 µg/kg. There is also a limit of 0.50 µg/kg for OTA in processed cereal-based foods for infants and young children.
- In 2010, additional limits were set for OTA in spices and licorice products. The maximum permitted level for spices, including chili powder, paprika, pepper, nutmeg, and turmeric, is set at 30 µg/kg until mid 2012, when it will be reduced to 15 µg/kg. The limit for licorice root is 20 µg/kg and for licorice extract it is 80 µg/kg.
- *Others*
- Switzerland applies a limit of 5.0 µg/kg for all foods except cereal based infant foods, where the limit is 0.5 µg/kg, and Turkey has set limits of between 3.0 and 10 µg/kg for various food commodities.
- Few other countries outside Europe have imposed limits for OTA, but a number have proposals to do so. Uruguay sets a limit of 50 µg/kg for rice, cereals and dried fruits and Canada sets a limit of 2,000 µg/kg for OTA in pig and poultry feed

If you drink coffee, consider Bullet Proof Brand

Objectives

- Define Mold Terms
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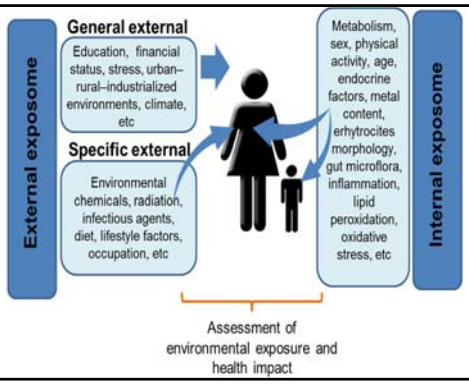
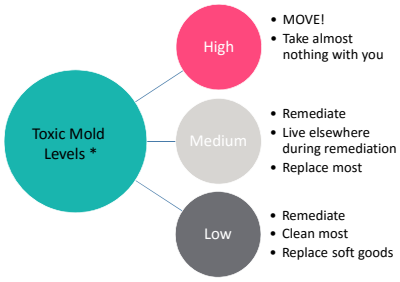


I've got Mold – Now What?

- Depends on:
  - Type of mold
  - Amount of mold
  - Severity of Illness

Foundation for Healing

- A clean living environment – low Mold DNA from ERMI results (and no chaetomium) and mycotoxin test
  - Move
  - Or Remediate (may not be possible with neurological symptoms)
- Avoid Moldy environments (work, school, shopping) until well
- Avoid other environmental toxins (most become sensitive to them)
  - Pesticides
  - Formaldehyde
  - Fragrances
  - Plastics
  - Chemicals (skin care, mattresses, new car, carpet, paint)
  - Metals
  - EMF's



- Based on levels and types of mold and mycotoxins/ illness severity

Dietary Goals for Healing

- Eat foods that promote low inflammation
- Eat foods that are high in phytonutrients
- Eat foods that support detoxification and the immune system

Anti-Fungal Diet

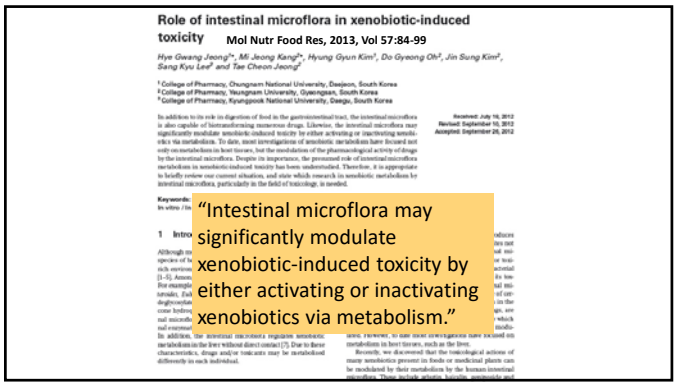
- No sugar, fruit, grains, alcohol
  - Feeds yeast
- No gluten, dairy or grains
  - Inflammatory foods
- Increase vegetables
  - Promotes healthy detox
- Include good fats
  - Nuts, seeds, olives, avocado
- Avoid moldy and fermented foods
  - Kombucha, kim-chi, nutritional yeast, vinegar, wine, coffee, chocolate, melons, mushrooms

Steps to Healing – Functional Medicine

- Get in a clean environment
- Repair the gut
- Reduce colonization/ infection
- Reduce inflammation
- Detoxify - Remove the toxins
- Rebuild mitochondria
- Restore the nervous system
- Balance hormones and adrenals
- Replete base nutrients
- Optimize Methylation
- Reset limbic system

Repair the Gut

- Critical step with mold patients
- Always disrupted
- Shippymd.com



Reduce Colonization/ Infection

- Anti yeast diet
- Herbs – caprylic acid, oregano, ginger, turmeric, olive leaf
- Grape seed extract
- Enzymes (Candex)
- Citrus nasal spray
- Prescription antifungals

Reduce Inflammation

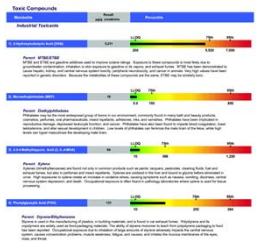
- Camu or liposomal Vit C
- Fish oil
- Curcumen
- Quercitin
- Proteolytic enzymes

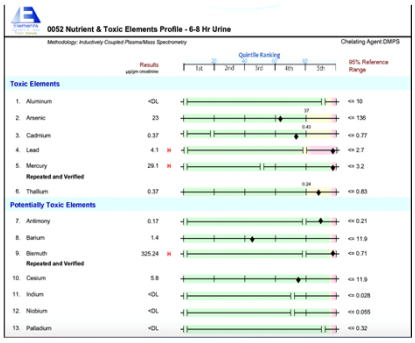
Optimal Biotransformation

- Nutritional support
  - Phase I: Macronutrients and broad-spectrum micronutrient support
  - Phase II: Cofactors for conjugation
- Antioxidants to quench free radicals produced by Phase I reactions
- Phytonutrient inducers of Phase II enzymatic reactions

IFM

Great Plains Tox Screen





0052 Nutrient & Toxic Elements Profile - 6-8 Hr Urine

Methodology: Inductively Coupled Plasma/Mass Spectrometry — Chelating Agent DMPS

		Results µg/gm creatinine	Quintile Ranking 1st 2nd 3rd 4th 5th	95% Reference Range
Toxic Elements				
1.	Aluminum	<DL		<= 10
2.	Arsenic	23	37	<= 136
3.	Cadmium	0.37	0.43	<= 0.77
4.	Lead	4.1 H		<= 2.7
5.	Mercury	29.1 H		<= 3.2
	Repeated and Verified			
6.	Thallium	0.37	0.24	<= 0.83
Potentially Toxic Elements				
7.	Antimony	0.17		<= 0.21
8.	Barium	1.4		<= 11.9
9.	Bismuth	325.24 H		<= 0.71
	Repeated and Verified			
10.	Cesium	5.8		<= 11.9
11.	Indium	<DL		<= 0.028
12.	Niobium	<DL		<= 0.055
13.	Palladium	<DL		<= 0.32

Detoxify – Remove the toxins

- Glycine
- Liposomal glutathione
- GI-detox charcoal
- Modified citrus pectin
- Chlorella
- Liver support – Milk thistle, alpha lipoic acid, NAC
- Dietary Fiber
- Clay and Magnesium salt baths
- Infrared sauna

Toxicol Appl Pharmacol. 2015 Dec 1;289(2):341-8. doi: 10.1016/j.taap.2015.09.010. Epub 2015 Sep 18.

The influence of N-acetyl-l-cysteine on damage of porcine oocyte exposed to zearalenone in vitro.

Lai FN[1], Ma JY[2], Liu JC[1], Wang JJ[2], Cheng SF[2], Sun XF[1], Li L[2], Li B[3], Nyachoti CM[4], Shen W[5].

Author information

Abstract

Zearalenone (ZEA), one of the mycotoxins produced by Fusarium fungi, impacts porcine reproduction by interfering with the estrogen signaling pathway. Previous studies have shown that ZEA inhibits porcine oocyte maturation through the formation of aberrant spindle. To explore the effect of ZEA on porcine oocyte meiotic maturation, the extent of both nuclear and cytoplasmic maturation was examined in this study. Compared with control group, presence of ZEA (3 μM) during oocyte maturation, significantly inhibited the polar body extrusions from 71% to 51%, and significantly increased intracellular reactive oxygen species (ROS) level (12.01 vs. 5.89). Intracellular glutathione (GSH) content in ZEA treatment group was lower than in the control group (1.08 pmol/oocyte vs. 0.18 pmol/oocyte), and cortical granules of cortical area distributed oocytes were reduced (88% vs. 62%). ZEA decreases cumulus expansion in both morphology and mRNA level (HAS2, PTX3, TNFAIP6 and CX43). Addition of N-acetyl-l-cysteine (NAC) to the oocyte maturation media reversed the ZEA-induced inhibition of polar body extrusion (from 69% to 81%), up-regulated ROS (from 7.9 to 6.5), down-regulated GSH content (from 0.16 to 0.82 pmol/oocyte) and recovered cumulus cells expansion in morphology and mRNA level. It is concluded that ZEA affects both oocyte nucleus and cytoplasmic maturation during in vitro maturation, and NAC can reverse these damages to some extent.

Dietary Fiber

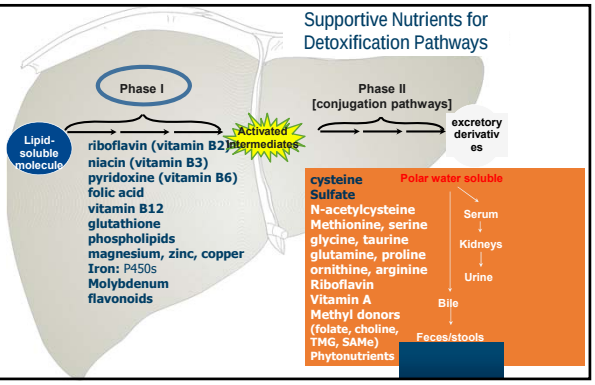
- Certain types of dietary fibers markedly **enhance both phase I and II detoxification** systems in the liver. Roland N *J Nutr* 1994 124:1581-7 (rats)
- **Higher fecal toxin excretion: via sequestering conjugated xenobiotic and endobiotics in the bile and this reduces level of bacterial deconjugating enzymes in stool.**
- **Net effect: reduced enterohepatic circulation**
- **Microbiota** – major detoxification facilitation
  - **Fermentation of short chain fatty acids** (butyrate, propionate, acetate) provide colonocyte energy needs and **genomic expression**

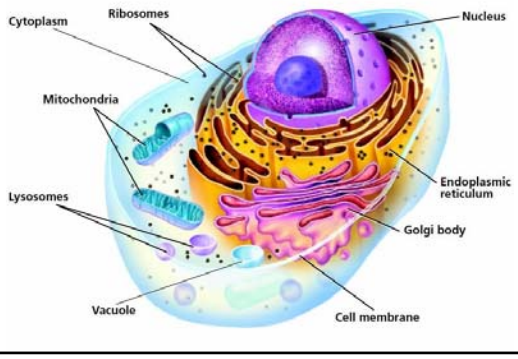
Sauna Can be Effective Treatment

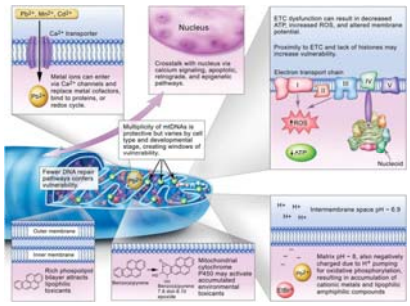
Compounds released in sweat:

- Bromide, Chloride, Chromium, Copper, Iron
- Potassium, Sodium, Magnesium Manganese, Zinc, Copper, Cobalt
- Antimony, Cadmium, Lead, Mercury, Nickel
- Medications
- PCBs
- Myoctoxins

Genuis SJ, et al. Blood, urine, and sweat (BUS) study: monitoring and elimina9on of bioaccumulated toxic elements. Arch Environ Contam Toxicol. 2011 Aug;61(2):344-57.







Rebuild Mitochondria

- Carnitine
- Coq10
- D-ribose
- Nicotinamide riboside
- Phosphatidyl choline
- NAC and Alpha lipoic acid
- PQQ (pyrroloquinoline quinone)
- Rhodiola rosea

Antioxidants Protect Mitochondria

Nutritional cofactor treatment in mitochondrial disorders

A2

Accumulation of toxic metabolites and reduction of electron transfer activity have prompted the use of antioxidants, electron transfer mediators (which bypass the defective site), and enzyme cofactors.

Metabolic therapies that have been reported to produce a positive effect include **Coenzyme Q(10); other antioxidants such as ascorbic acid, vitamin E, and lipoic acid; riboflavin; thiamine; niacin; vitamin K; creatine; and carnitine**.

Marriage B, et. al. Nutritional cofactor treatment in mitochondrial disorders. *J Am Diet Assoc.* 2003 Aug;103(8):1029-38.

Restore the Nervous System

- Mitochondrial support Plus:
- Phosphatidyl choline – high doses
- B vitamins
- Huperzia serrata
- Mct oil and fish oil
- Ne0 40 – replete Nitric oxide

Slide 123

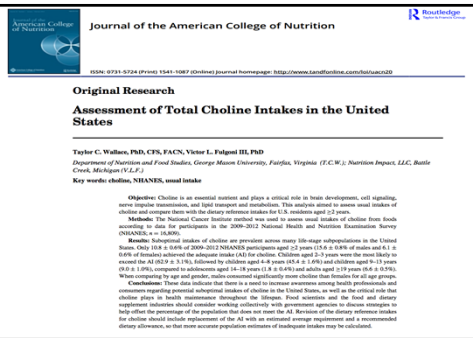
A2 Fix reference, textbox
Author, 6/9/2015

Roles of Choline

- **Cell signaling**
- Transport of lipids
- **Nerve impulse transmission**
- **Major source of methyl groups**

Choline

- Although choline is not by strict definition a vitamin, it is an essential nutrient. Despite the fact that humans can synthesize it in small amounts, choline must be consumed in the diet to maintain health. The majority of the body's choline is found in specialized fat molecules known as phospholipids, the most common of which is called phosphatidylcholine (1).
- Choline deficiency causes muscle damage and abnormal deposition of fat in the liver, which results in a condition called nonalcoholic fatty liver disease. Genetic predispositions and gender can influence individual variation in choline requirements and thus the susceptibility to choline deficiency-induced fatty liver disease



Journal of the American College of Nutrition

ISSN: 0731-5724 (Print) 1541-1087 (Online) Journal homepage: http://www.tandfonline.com/loi/uacn20

Original Research

Assessment of Total Choline Intakes in the United States

Taylor C. Wallace, PhD, CFS, FACN, Victor L. Fulgoni III, PhD

Department of Nutrition and Food Studies, George Mason University, Fairfax, Virginia (T.C.W.); Nutrition Impact, LLC, Battle Creek, Michigan (V.L.F.)

Key words: choline, NHANES, usual intake

Objective: Choline is an essential nutrient and plays a critical role in brain development, cell signaling, nerve impulse transmission, and lipid transport and metabolism. This analysis aimed to assess usual intakes of choline and compare them with the dietary reference intakes for U.S. residents aged ≥2 years.

Methods: The National Cancer Institute method was used to assess usual intakes of choline from foods according to data for participants in the 2009–2012 National Health and Nutrition Examination Survey (NHANES; *n* = 18,809).

Results: Suboptimal intakes of choline are prevalent across many life-stage subpopulations in the United States. Only 10.8 ± 0.6% of 2009–2012 NHANES participants aged ≥2 years (15.6 ± 0.8% of males and 6.1 ± 0.6% of females) achieved the adequate intake (AI) for choline. Children aged 2–3 years were the most likely to exceed the AI (82.9 ± 3.1%), followed by children aged 4–8 years (45.4 ± 1.6%) and children aged 9–13 years (9.0 ± 1.0%), compared to adolescents aged 14–18 years (1.8 ± 0.4%) and adults aged ≥19 years (6.6 ± 0.5%). When comparing by age and gender, males consumed significantly more choline than females for all age groups.

Conclusions: These data indicate that there is a need to increase awareness among health professionals and consumers regarding potential suboptimal intakes of choline in the United States, as well as the critical role that choline plays in health maintenance throughout the lifespan. Food scientists and the food and dietary supplement industries should consider working collectively with government agencies to discuss strategies to help offset the percentage of the population that does not meet the AI. Revision of the dietary reference intakes for choline should include replacement of the AI with an estimated average requirement and a recommended dietary allowance, so that more accurate population estimates of inadequate intakes may be calculated.

89% of Us Population has suboptimal intake of choline

Best Food Sources of Choline

- Beef liver, egg, beef, salmon, scallop, chicken, Brussels sprouts, cauliflower, broccoli, spinach

- Symptoms of low choline
  - Muscle aches
  - Nerve damage
  - Mood disorders
  - Fatigue
  - Cognitive decline

Balance Hormones and Adrenals

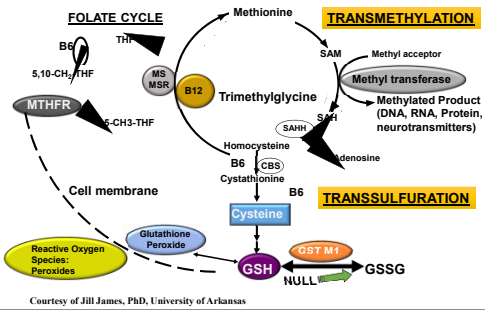
- Adaptogens
- B vitamins
- Magnesium
- Low inflammation high nutrient diet
- Fiber

Replete Base Nutrients – Assess with Ion Profile from Genova if Possible

- Multi
- B12, B complex
- Magnesium and other minerals****
- Vit D
- Calcium
- Protein powder/ green smoothie/ greens mix
- Ionic minerals

Optimize Methylation

METHYLATION/SULFATION



Doctor's Data Methlyation Profile

Methylation Profile; plasma

PRIMARY & INTERMEDIATE METABOLITES	RESULT	UNIT	REFERENCE INTERVAL
Methionine	2.8	µmol/dL	1.6– 3.6
Cysteine	33	µmol/dL	20– 38
S-adenosylmethionine (SAM)	83	nmol/L	86– 145
S-adenosylhomocysteine (SAH)	15.4	nmol/L	10– 22
Homocysteine	7.1	µmol/L	< 11
Cystathionine	0.02	µmol/dL	< 0.05

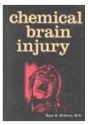
METHYLATION INDEX	RESULT	REFERENCE INTERVAL
SAM : SAH	5.4	> 4

PERCENTILE: 2.5th, 16th, 50th, 84th, 97.5th; 68th, 95th

Methionine

Chemical Brain Injury

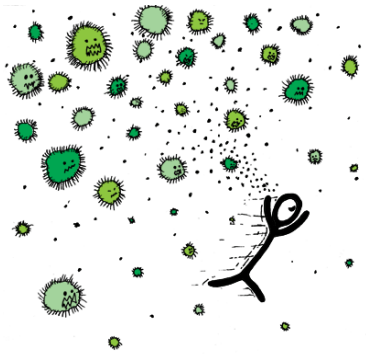
Kaye Kilburn,1998



- Hypothesis: "A Hidden Pandemic"
- Toxic exposures (arsenic, chlordane, PCBs, TCE, toluene, etc.) frequently lead to misdiagnoses of psychiatric illnesses, including somatization disorder and PTSD.
- Since the limbic system is most intertwined with the olfactory (the portal of entry), it displays the greatest effects, i.e. emotions

Limbic System

- The primary structures within the **limbic system** -include the amygdala, hippocampus, thalamus, hypothalamus, basal ganglia, and cingulate gyrus. The amygdala is the emotion center of the brain, while the hippocampus plays an essential role in the formation of new memories about past experiences
- It monitors both our internal and external environment. The Limbic System is known as the seat of social and emotional intelligence and is the brain's anxiety "switch".
- The Limbic System is also responsible for the formation of memories and regulating hormones.
- It regulates the functioning of the parasympathetic and sympathetic nervous systems, which means it controls things like pulse, blood pressure, breathing, and arousal in response to emotional circumstances.



Reset Limbic System

- Awareness of Inner Dialog
- Meditation
  - Muse
  - Yoga
  - CD's – Chopra, Naparstek
  - Apps –headspace, buddhify, calm, breathe2relax
  - Mindfulness training

Labs/ Tests

- Mycotoxin levels
- Marcons for nasal swab
- Shoemaker labs
- VCS – on-line or order from Shoemaker
- Genetics – methylation and detox pathways
- Neuroquant MRI
- Proteomics – Shoemaker / Pathway Studio
- Synergistic toxins – GPL, Genova
- Look for Fungal infections - OATS, Stool tests (Doctor's Data, Lab Corp)

A Case with Neuroquant

- 48 year old with recurrent concussions – 3 in 1.5 years
- Suspected there was an underlying Toxin making her more susceptible

Methylation

Result	Gene	SNP Location	Internet Information	Affects
+/−	COMT	V158M	www.genovations.com/gdv158m	Liver/Gut

Acetylation (N-acetyltransferase)

SLOW METABOLIZER POLYMORPHISM

Result	Gene	SNP Location	Internet Information	Affects
−/−	NAT1	R64W	www.genovations.com/gdr64w	All Cells
−/−	NAT1	R187Q	www.genovations.com/gdr187q	Liver/Gut
−/−	NAT2	I114T	www.genovations.com/gdi114t	Liver/Gut
−/−	NAT2	R197Q	www.genovations.com/gdr197q	Liver/Gut
+/−	NAT2	G286E	www.genovations.com/gdg286e	Liver/Gut
−/−	NAT2	R64Q	www.genovations.com/gdr64q	Liver/Gut

FAST METABOLIZER POLYMORPHISM

Result	Gene	SNP Location	Internet Information	Affects
−/−	NAT2	K268R	www.genovations.com/gdk268r	Liver/Gut

Glutathione Conjugation (Glutathione s-transferase)

Result	Gene	Location	Internet Information	Affects
ABSENT	GSTM1	1p13.3	www.genovations.com/gdrgstm1	Liver/Kidney
+/+	GSTP1	I105V	www.genovations.com/gdrgstp1	Brain/Skin
+/−	GSTP1	A114V	www.genovations.com/gda114v	Brain/Skin

Procedure Type

Ochratoxin A - Procedure by ELISA
Aflatoxin Group - Procedure by ELISA
Trichothecene Group - Procedure by ELISA

Results:

Code	Test	Specimen	Value	Result	Negative if less than	Equivocal if between	Positive if greater or equal
E8501	Ochratoxin A	Urine	0.00000 ppb	Negative	1.8 ppb	1.8-2.0 ppb	2.0 ppb
E8502	Aflatoxin Group	Urine	0.41000 ppb	Negative	0.8 ppb	0.8-1.0 ppb	1.0 ppb
E8503	Trichothecene Group	Urine	0.85000 ppb	Positive	0.18 ppb	0.18-0.2 ppb	0.2 ppb

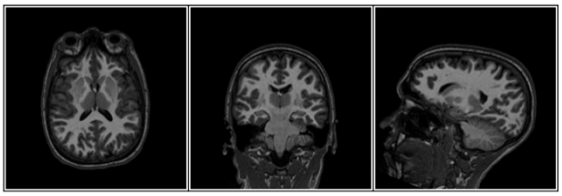
Gliotoxin Derivative - Procedure by ELISA

Results:

Code	Test	Specimen	Value	Result	Negative if less than	Equivocal if between	Positive if greater or equal
E8510	Gliotoxin	Urine	4.18000	Positive	0.2 ppb	0.2-0.3 ppb	0.3 ppb

NeuroQuant®
Triage Brain Atrophy Report

MORPHOMETRY RESULTS



Intracranial Volume (ICV) (cm^3)	ICV Z-score	ICV Percentile
1682.35	1.15	87

Brain Structure	LH Z-score	LH %	RH Z-score	RH %
Total Cerebral White Matter	-0.12	45	-0.27	39
Total Cerebral Grey Matter	> 1.65	> 99	> 1.65	> 99
Total Ventricle	0.46	68	-0.56	29
Cerebellar White Matter	0.86	80	0.89	81
Cerebellar Gray Matter	0.49	69	0.31	62
Brainstem	0.23	59	0.75	77
Thalamus	> 1.65	96	> 1.65	97
Ventral Diencephalon	-0.28	39	0.29	61
Hippocampus	1.31	90	> 1.65	97
Amygdala	0.85	80	0.27	61
Basal Ganglia				
Putamen	-0.53	30	-0.51	30
Caudate	< -1.65	2	< -1.65	1
Nucleus Accumbens	-1.64	5	0.73	77
Pallidum	-0.60	28	-0.72	23

Cortical Brain Regions	LH Z-score	LH %	RH Z-score	RH %
Frontal Lobe				
Precentral	> 1.65	> 99	> 1.65	97
Premotor	1.49	93	> 1.65	97
Superior Frontal	0.29	62	0.98	84
Anterior Middle Frontal	0.98	84	> 1.65	99
Pars Triangularis	0.32	63	0.99	84
Lateral Orbito Frontal	1.29	90	0.98	84
Pars Orbitalis	-0.10	46	> 1.65	> 99
Parietal Lobe				
Inferior Parietal	1.56	94	> 1.65	> 99
Superior Parietal	-0.18	43	1.37	92
Medial Parietal	> 1.65	98	1.30	90
Supra Marginal	> 1.65	> 99	1.02	85
Primary Sensory	0.74	77	-0.07	47
Primary Motor	> 1.65	> 99	> 1.65	> 99
Occipital Lobe				
Medial Occipital	> 1.65	> 99	> 1.65	> 99
Lateral Occipital	0.91	82	0.63	74
Temporal Lobe				
Fusiform	1.00	84	0.30	62
Anterior Medial Temporal	-0.89	19	0.53	70
Posterior Medial Temporal	-0.55	29	0.11	54
Temporal Pole	-0.53	30	1.03	85
Transverse + Superior Temporal	> 1.65	97	> 1.65	98
Posterior Superior Temporal Sulcus	0.72	76	-0.66	25
Middle Temporal	> 1.65	97	1.68	95
Inferior Temporal	0.24	60	1.67	95
Limbic Lobe				
Caudal + Rostral Ant Cingulate	> 1.65	98	> 1.65	> 99
Isthmus + Post Cingulate	> 1.65	> 99	> 1.65	> 99

Glutathione; Erythrocytes

	Within	Outside	Reference Range	
Glutathione*	1035		1000 - 2000	µmoles/L

Severe Mold Exposure – Intake for AC System was coming from a very MOLDY crawl space

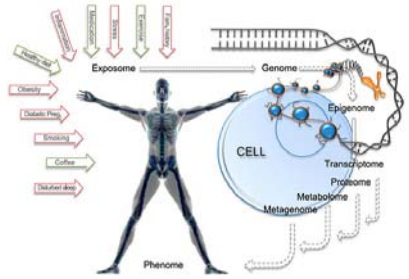


Figure 1—*The future of research on stratified diabetes medicine: a systems epidemiology approach to the discovery of interactions between the exposome (all nongenetic elements to which we are exposed) and the quantifiable elements of the human physiome.*

Franks et al. Diabetes Care 2013

Objectives

- Define Mold Terms
- Scope and Source of the epidemic
- What to look for in patients to help consider Mold as a diagnosis
- Who is most susceptible?
- How to utilize the limited testing we have on humans
- How to utilize the limited testing we have for the environment
- Reducing mold exposure- Is remediation on option?
- Functional medicine approach to recovery
- Where do we go from here?

Mold Myths- Let's Correct Them

- Mold is just an allergy issue
- Mold is everywhere so it can't be a problem
- If mold was making me sick my doctor would know
- You have to have an active leak to have a mold problem
- It's not mold because everyone in the building isn't sick
- It's not mold because I didn't get better by going to another place for a few days or moving to a new place

Prevention is the Best Medicine

- Proactively Detoxify and Nourish to stay ahead of the curve
- Maintain your living space and work space/ schools
  - Know what to do if there is a leak
  - Preventive maintenance
    - Caulking / flashing – windows / vents / seams/ wet areas
    - Water heater checks
    - Heating and air conditioning systems
  - Avoid wallpaper in wet areas
  - Outside grading to make sure water drains appropriately
- Improved Building Standards – for materials, ventilation, workmanship, humidity control

Vision for the future

- New building guidelines
- Annual building maintenance
- Building owners aware of how to handle water intrusion
- Healthy schools
- Better testing for buildings and humans
- Research linking genes, toxins, nutritional status to human health conditions and functional medicine solutions

Take - Away

- This is a major health issue of epidemic proportions
- It is possible to get well even with severe symptoms
- Much more research is needed
  - Role of genetics and nutrition
  - Optimal treatment
  - Testing – more toxins and molds in humans and environment
  - Building requirements and remediation – acceptable levels
  - Synergy of environmental toxins

Take the Mold Assessment

- Shippymd.com/moldquiz – coming soon