Moldy: Identification and Treatment of Mold and Fungal-Related Illness

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Disclosure

- I, Kelly McCann, have nothing to disclose. I have NO financial ties to any laboratory, medication, or supplement product to be discussed in this presentation.

Objectives

- Discuss the scope of the problem of mold and mycotoxins
- Health impacts of mold from allergies to digestive issues
- Review definition and diagnostic criteria for Environmentally Acquired Illness (formerly known as CIRS – Chronic Inflammatory Response Syndrome)
- Highlight interventions and treatment strategies both from the Shoemaker and Brewer protocols
- Introduce concepts of the mycobiome and fungal biofilms and the emerging literature on health impacts
- Brief exploration of Mast Cell Activation Disease; diagnosis, testing and treatment
- Review literature on phosphatidyl choline and membrane stabilizing therapies
- Discuss specific patient teaching points

Mold and Fungi

- Over 200,000 species of fungi, including mold, yeast, and mushrooms. More than 100,000 mold species have been identified.
- Molds are ubiquitous outside and live on many plants and food. They spread and reproduce by producing spores.
- Fungus and mold comprise 25% of the world's biomass.
- Exposure to molds can also occur by ingestion, inhalation of contaminated air and dermal contact
- Indoor molds proliferate in environments that contain excessive moisture, such as from leaks in plumbing, roofs, walls, and potted plants.
- The most common molds found indoors are Cladosporium, Penicillium, Aspergillus, and Alternaria,

  Stachybotrys and Trichoderma species.

Daschner A. An Evolutionary-Based Framework for Analyzing Mold and Dampness-Associated Symptoms in DMHS. Front. Immunol. 2017; 7:672

Beneficial uses of molds

- Koji mold, an aspergillus species is used in the making of **soy sauce**
- Koji molds also break down the starch in rice, barley, sweet potatoes in the production of **sake and other distilled spirits**.
- Some **sausages** incorporate starter cultures of molds to improve flavor and reduce bacterial spoilage during curing.
- Geotrichum candidum and Penicillium species are used in the production of various **cheeses** including Brie and Blue cheese.
- Derived from Penicillin notatum, Alexander Fleming's discovery of **Penicillin** in 1928 transformed medicine.
- Used for centuries in China as both food and medicine, **red yeast rice** is made by fermenting a type of yeast called Monascus purpureus over red rice> it is used today for lowering cholesterol as it contains a chemical called monacolin K, has the same makeup as the drug lovastatin.
- Discovered in 1971, **Cyclosporine** immunosuppresses T cells without excessive toxicity. Cyclosporine was isolated from the fungus Tolypocladium inflatum by J. F. Borel.
- Decomposition of living matter.

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Negative health effects of molds and fungus

- Mold and fungal allergy or hypersensitivity reactions – IgE, IgG
- Susceptibility to infections
- Mycotoxicoses
- Consequences of ingestion of molds and mycotoxins
  - Alimentary Toxic Aleukia
  - Environmental Enteropathy
- Environmentally Acquired Illness (CIRS – Chronic Inflammatory Response Syndrome)
- Mycobiome and Fungal biofilms
- Systemic mycoses - Fungal infections

Fungal Allergy and Asthma

- Many fungi, esp Alternaria, Penicillium, Aspergillus and Cladosporium spp., is strongly associated with type 1 allergic (IgE) responses
- Fungi are also well-known sources of type III (or IgG-inducing) antigens.
- At high concentrations, fungi may also be involved in combined type III and IV hypersensitivity reactions, including hypersensitivity pneumonitis.
- Numerous studies correlating asthma with fungal exposure and elevated ERMI scores
- Exposure to fungi, dust mites and endotoxins increase risk of eczema, allergy and asthma.

Baxi, SN. et al. Exposure and Health Effects of Fungi on Humans. J Allergy Clin Immunol Prac. 2016 4(3):396-404.
Vesper S, Wymer L. Relationship between ERMI and asthma. Int J Hyg Envirn Health 2016. 219(3): 233-8.
McSharry C, et al. Decreased FEV1% in asthmatic adults with high ERMI values. Clin Exp Allergy 2015. 45(5):902-7.
Sharpe, RA, et al. Risk of atopic disease due to indoor fungal exposure. Clin Exp Allergy 2015. 45(10): 1566-78.

Alimentary Toxic Aleukia (ATA)

- Associated with eating grains (corn and wheat) which have been under snow the previous winter.
- Grains are contaminated with Fusarium and Stachybotrys
- First appeared in 1913 in eastern Siberia
- >100,000 Russians died between 1942-1948. 60% mortality rate.
- Necrotic ulcers in mouth, throat, nose, stomach and intestines
- Bleeding from nose, mouth, GI tract and kidneys
- Anemia, Leukopenia, Agranulocytosis due to bone marrow suppression
- Microscopic observations of the alimentary tract showed erosion of the gastric epithelium, frequently with bacterial invasion and cryptitis
- Pulmonary hemosiderosis, congestion and edema

Drobotko. Stachybotryotoxicosis. Am Review of Soviet Med 1945, 2:238-42.
Lutsky and Mor. Alimentary Toxic Aleukia. Am J Path 1981. 104(2):189-191.
Mayer, CF. Endemic panmyelotoxicosis in the Russian Grain Belt. 1953, 113:173-89.

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Environmental Enteropathy

- Condition characterized by increased intestinal permeability, villous atrophy, impaired gut immune function, malabsorption, growth faltering, and oral vaccine failure without overt diarrhea.
- Pathology changes similar to celiac disease, but not tropical sprue.
- Unclear etiology. Possibly related to fecal-oral contamination or mycotoxin contamination.
- Maize and groundnuts common in developing world diet. Often contaminated with Aspergillus and Fusarium.
- Mycotoxins aflatoxin (AF), fumonisin (FUM) and deoxynivaenol (DON) mediate intestinal damage
- Aspergillus strains can produce AF and ochratoxin and Fusarium mold strains can produce FUM, DON, and zearalenone.

Korpe and Petri. Environmental Enteropathy. Trends Mol Med. 2012 June ; 18(6): 328–336.
Smith. Food chain mycotoxin exposure, gut health, and impaired growth. Adv Nu... 2012 J... 1;3(4):526-31.

Mycotoxins and Mycotoxicoses

- Mycotoxins are secondary metabolites produced by many molds.
- Between 350-400 known mycotoxins, about a dozen with health effects.
- Some Aspergillus, Penicillium, Fusarium, Alternaria and Stachybotrys genera are known to produce mycotoxins.
- **Mycotoxins are NOT ALIVE!**
- Aflatoxins
  Ochratoxins
- Tricothecenes Gliotoxin
- Ergot Alkaloids Fumonisins
- Patulin
  Zearalenone
- Deoxynivalenol (DON)

Numerous Health Effects

- Inhibition of protein synthesis
- Anemia Nephropathy
- Hepatotoxicity Carcinogenic
- Allergies Headaches
- Myalgias Fatigue
- Neurological damage
- Neural tube defects Visual disturbances
- Cognitive changes Respiratory illnesses
- Pulmonary hemorrhage
- Immunosuppression Depression
- Systemic inflammation
- Increased intestinal permeability

Bennett, JW and Klich, M. Mycotoxins. Clinical Microbiology Review, July 2003; 497-516.

Mycotoxins in food

Mycotoxin	Major Foods	Species	Health Effect	LD50 (mg/kg)
Penitrem	Walnuts	Penicillum aurantiogriseum	Tremors	1.05 (mouse)
T-2 toxin	Cereals	Fusarium sporotrichioides	Alimentary toxic aleukia	4 (rat)
Ergotamine	Rye	Claviceps purpurea	Neurotoxin	
Zearolenone	Maize, barley, wheat	Fusarium graminearum	Estrogenic	Not acutely toxic?

Peraica, M, et al. Toxic Effects of Mycotoxins in humans. Bulletin of the WHO. 1999; 77(9): 754-765.

Mycotoxin	Major Foods	Species	Health Effect	LD50 (mg/kg)
Aflatoxin	Maize, groundnuts, figs, tree nuts, milk, milk products	Aspergillus flavus Aspergillus parasiticus	Hepatotoxic, carcinogenic	0.5 (dog) 9.0 (mouse)
Cyclopiazonic acid	Cheese, maize, groundnuts, Rodo millet	Aspergillus flavus Penicillium aurantiogriseum	Convulsions	36 (rat)
Deoxynivalenol	Cereals	Fusarium graminearum	Vomiting, food Refusal, DNA damage	70 (mouse)
Fumonisin	Maize	Fusarium moniliforme	Esophageal Cancer	?
Ochratoxin	Maize, cereals, coffee beans	Penicillium verrucosum Aspergillus ochraceus	Nephrotoxic	20-30 (rat)
Patulin	Apple juice, damaged apples	Penicillium expansum	Edema, hemorrhage, cancer	35 (mouse)

Effects of Mycotoxins

T2 toxin, DON, AFB
gastroenteritis
intestinal hemorrhages
impaired rumen function
diarrhea
ketosis

Ergots
impaired
thermoregulation
convulsions

DON – Deoxynivalenol
ZEN – Zearalenone
AFB_1 – Aflatoxin B_1
T-2 Toxin
Ergots - Ergot Alkaloids
Endotoxins

Zen, Ergots
irregular heats
low conception rates
ovarian cysts
embryonic loss
abortions
low testicular development
low sperm production

T2 toxin, DON, Ergots
decreased feed intake
decreased feed efficiency

AFB, T2 toxin, DON
milk contamination
decreased milk production
mastitis

DON, Ergots, Endotoxins
Laminitis (lameness)

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Effects of Mycotoxins

Zen, T2, DON, Ergots
Irregular heats
abortion
pseudo pregnancy
low conception rates
embryonic loss
tail necrosis
nymphomania
uterine hypertrophy
shrunken udder
stillbirths

T2, DON, AFB, OTA, FUM
intestinal hemorrhage
kidney damage
fatty liver
pulmonary edema
increased water intake

DON – Deoxynivalenol
ZEN – Zearalenone
AFB_1 – Aflatoxin B_1
T-2 – T-2 Toxin
FUM – Fumonisins
OTA – Ochratoxin A
Ergots – Ergot Alkaloids
Endotoxins

T2, DON, Ergots
Decreased feed intake
Dermal/ oral lesions
Feed refusal
vomiting
vasoconstriction
necrosis
impaired growth

AFB, T2, OTA
diarrhea
blood in feces and urine
bladder and kidney inflammation

T2, DON, AFB, OTA, FUM
decreased performance
immunosuppression
pancreatic necrosis

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Not just a developing world problem

- Food and Agricultural Organization (FAO) estimates 25% of crops are contaminated with molds, though multi-analyte methods show almost 100% of grain crops are contaminated.
- Climate change will continue to impact food mold and mycotoxin contamination.
- Mycotoxins can be found in coffee. Spanish study 21 mycotoxins. Only 11% of coffee was mycotoxin free.
- Ochratoxin A in coffee samples was 71.5% and 93.3% at 1ng/mL and 10ng/mL concentrations.

- De Saeger, S. et al. Report from the 5th International Symposium on Mycotoxins and Toxigenic Moulds. Toxins 2016, 8, 146.
- García-Moraleja, et al. Analysis of mycotoxins in coffee and risk assessment in Spanish adolescents and adults. Food Chem Toxicol. 2015 Dec;86:225-33.
- Jo, EJ, et al. Detection of ochratoxin A (OTA) in coffee using chemiluminescence resonance energy transfer (CRET) aptasensor. Food Chem. 2016 Mar 1;194:1102-7.
- Peraica, M, et al. Toxic Effects of Mycotoxins in humans. Bulletin of the WHO. 1999; 77(9): 754-765

No Pizza for you!

- 60 samples of pizza dough
- 9 mycotoxins detected
- 100% samples contaminated with at least 3 mycotoxins
- 12% exceeded EU limits
- Cow feed of maize contaminated with Aflatoxin B1 shows up in milk as aflatoxin M1

Quiles, JM et al. Occurrence of mycotoxins in refrigerated pizza dough and risk assessment of exposure for the Spanish population. Food Chem Toxicol. 2016 May 21;94:19-24
Van de Fels-Klerx. Presented at 5th International Symposium on Mycotoxins and Toxigenic Moulds. May 2016.

Exposure to Fumonisins and the Occurrence of Neural Tube Defects along the Texas–Mexico Border

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Along the Texas–Mexico border, the prevalence of neural tube defects (NTDs) among Mexican-American women doubled during 1990–1991. The human outbreak began during the same crop year as epizootics attributed to exposure to fumonisin, a mycotoxin that often contaminates corn. Because Mexican Americans in Texas consume large quantities of corn, primarily in the form of tortillas, they may be exposed to high levels of fumonisins. We examined whether or not maternal exposure to fumonisins increases the risk of NTDs in offspring using a population-based case–control study. We estimated fumonisin exposure from a postpartum sphinganine:sphingosine (sa:so) ratio, a biomarker for fumonisin exposure measured in maternal serum, and from maternal recall of periconceptional corn tortilla intake. After adjusting for confounders, moderate (301–400) compared with low (≤ 100) consumption of tortillas during the first trimester was associated with increased odds ratios (ORs) of having an NTD-affected pregnancy (OR = 2.4; 95% confidence interval, 1.1–5.3). No increased risks were observed at intakes higher than 400 tortillas (OR = 0.8 for 401–800, OR = 1.0 for > 800). Based on the postpartum sa:so ratio, increasing levels of fumonisin exposure were associated with increasing ORs for NTD occurrences, except for the highest exposure category (sa:so > 0.35). Our findings suggest that fumonisin exposure increases the risk of NTD, proportionate to dose, up to a thres… results also call for popul… and assess effects on the… Mexican Americans, myc… doi:10.1289/ehp.8221 av…

In 1990–1991, an outb… defects (NTDs) occ… County, Texas (USA), … bordering Mexico wher… births occurred in 6 w… NTDs are embryonic de… spinal cord resulting from… tube to close. Spina bif… (failure of anterior tube closure) are the most common forms of NTD. Investigation of the cluster revealed a high prevalence of NTDs in this region (27 per 10,000 live births) (Texas Department of Health, unpublished report) that proved endemic to the entire Texas–Mexico border region. Just before the NTD

exposure measured in maternal serum, and from maternal recall of periconceptional corn tortilla intake.

Materials and Methods

Study population. We identified study participants through the Texas Department of Health's Neural Tube Defect Project. Participant identification and data collection methods have been described previously in detail (Hendricks et al. 1999; Suarez et al 2000). In brief, the project included multi-source active surveillance, a case–control study to identify risk factors for NTD occurrence, and a follow-up folic acid intervention program to reduce NTD recurrence. Cases

had relatively high average fumonisin levels (Hendricks 1999). Other regions with high corn-based food consumption and documented fumonisin contamination (Dombrink-Kurtzman and Dvorak 1999; Yoshizawa et al. 1994) also have high prevalences of NTDs (Moore et al. 1997; Mutchinick et al. 1999).

during the same period. Control women were randomly selected annually, frequency

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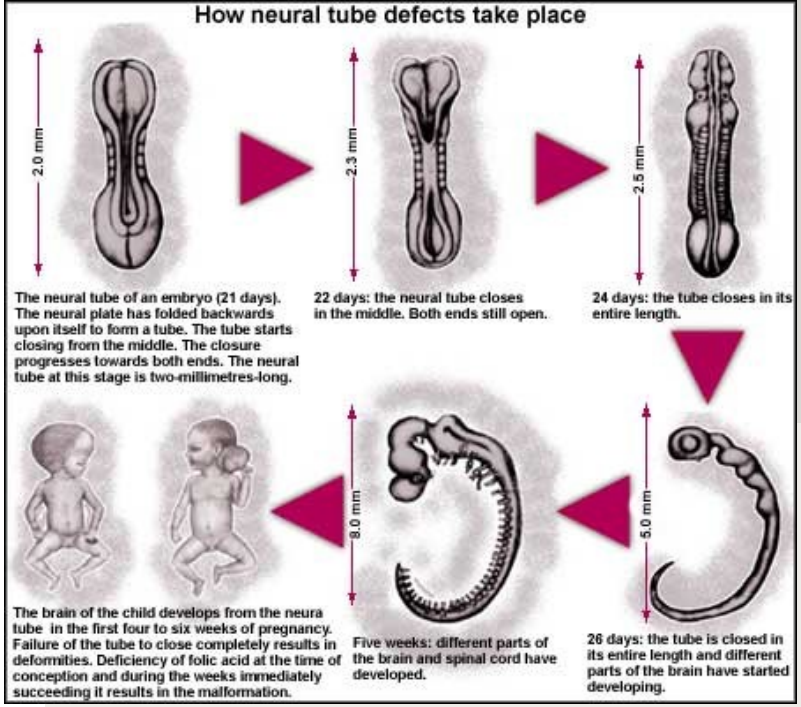
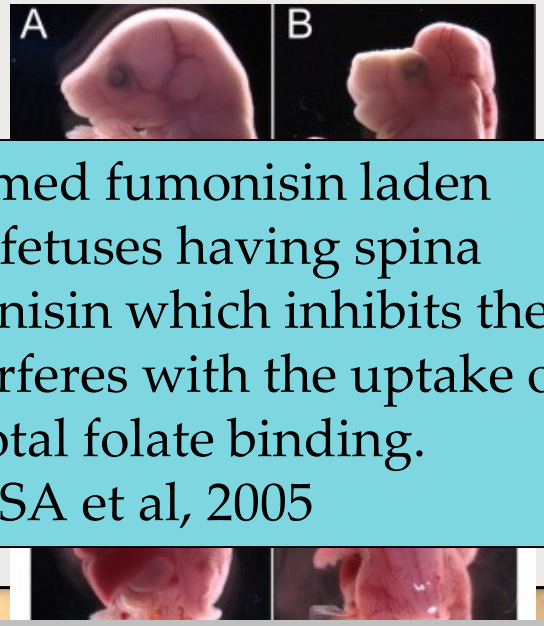




Women in their first trimester who consumed fumonisin laden tortillas had a significant increase in their fetuses having spina bifida/craniofacial anomalies due to fumonisin which inhibits the biosynthesis of phospholipids, which interferes with the uptake of 5-methyltetrahydrofolate and decreases total folate binding.

Missmer SA et al, 2005

NeuroLipid Research, Dr. Patricia Kane

"It's not wallpaper Maury. It's MOLD!"

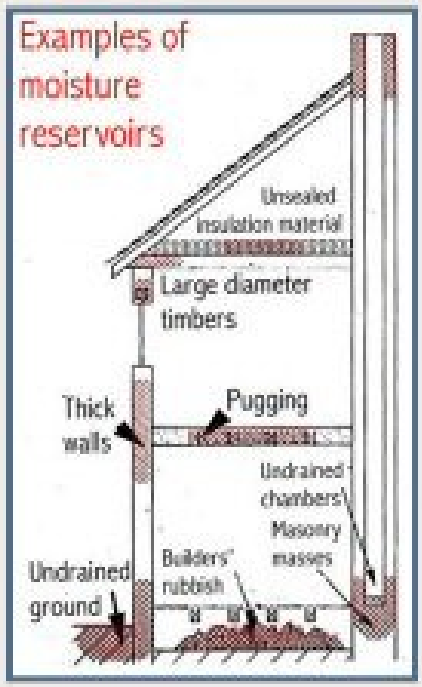
Water Damage and Dampness

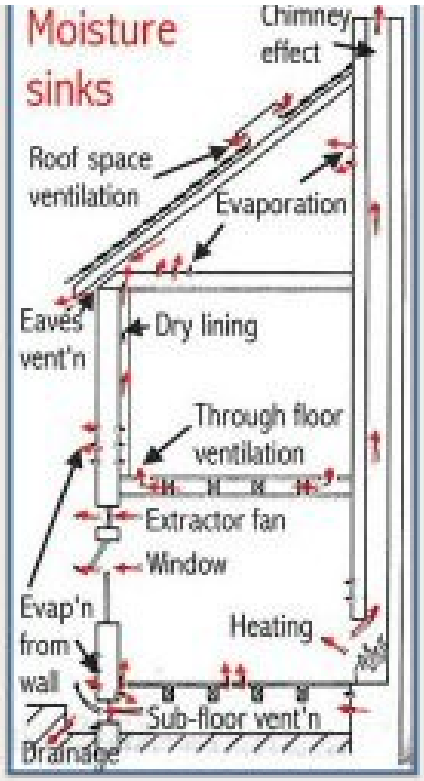
- Dampness in buildings ranges from 20% in studies in Europe and Canada to 50-60% in USA and parts of Asia.
- Case control studies of asthma in West bank and Gaza reveal 56-78% damp problems, leaks or indoor mold.
- Lower income and lower education associated with higher likelihood of dampness and mold.
- Lawrence Berkeley report from 2009. 47% of US homes with dampness or water damage. 85% percent of other buildings had past water damage and 45% had current water leaks.

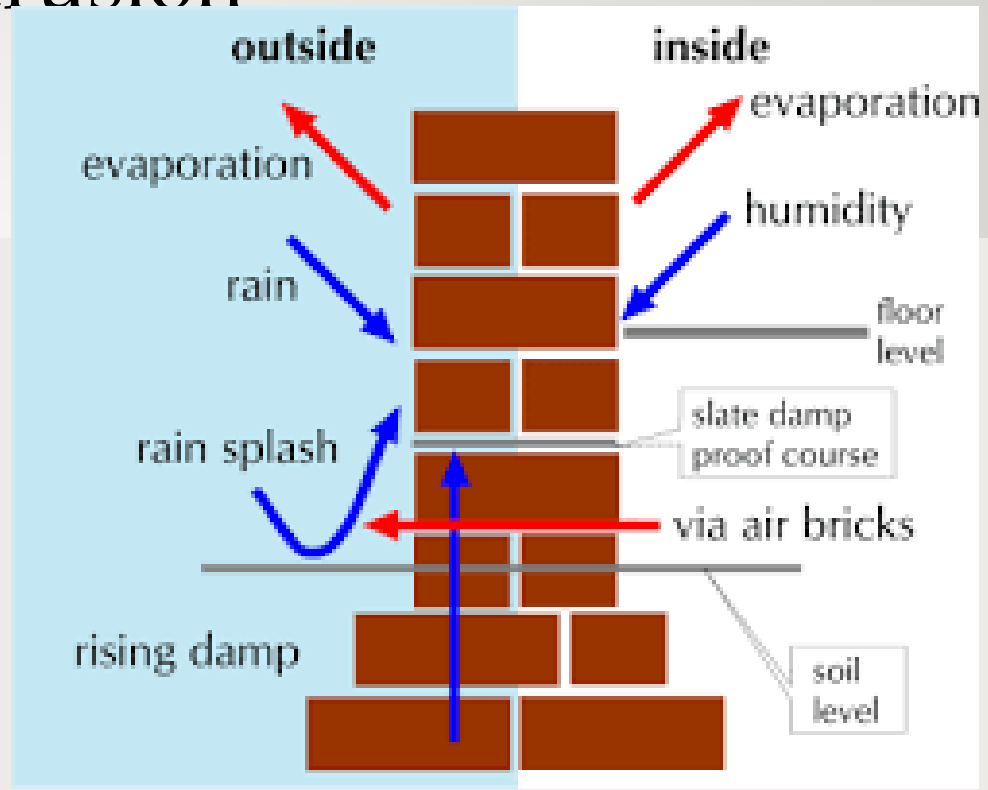
- WHO guidelines for indoor air quality: dampness and mould 2009, http://www.who.int/indoorair/publications/7989289041683/en/
- https://iaqscience.lbl.gov/dampness-prevalence

Let's talk about indoor molds and water intrusion

- **Many sources of moisture are hidden.**







- **Remember that what is in the wall spaces travels throughout the building.**

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Other ingredients in the Indoor mold toxic soup

- Gram negative bacteria
- Gram positive bacteria
- Cell fragments
- Beta Glucans
- Mannans
- Hemolysins
- Proteinases
- Chitinases
- Endotoxins
- Mycobacteria
- Lipopolysaccharides

- Hyphal fragments
- Actinomycetes
- Nocardia
- Microbial VOCs
- Building material VOCs
- Coarse particulates
- Fine and ultrafine particulates
- Nano-sized particulates
- Mycoplasma
- Protozoa
- Dust mites

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- Rasimus, ,et al. Amylosin of Bacillus from moisture-damaged buildings is immunotoxic. Appl. Environ Microbiol. 2015 Apr; 81(8): 2939-49
- Thrasher JD, Crawley S. The biocontaminants and complexity of damp indoor spaces: more than what meets the eyes. Toxicol Ind Health. 2009 Oct-Nov;25(9-10):583-615.

Microbial Volatile Organic Compounds (mVOCs)

- Fungi emit numerous VOCs as alcohols, esters, ketones, aldehydes, terpenoids, etc.
- Exposure to mVOCs has been linked to symptoms such as headaches, nasal irritation, dizziness, fatigue, and nausea.
- Human health effects will require more study.
- mVOCs may be used for early mold detection.

- In animal model Drosophila melanogaster, mVOCs had greater toxic effect than formaldehyde, xylene, benezene and toluene.
- Specific VOC 1-octen-3-ol caused neurotoxicity, shortened lifespan, developmental defects, and various other toxicities.

Inamdar, et al. Drosphila as a model to characterize fungal VOCs. Environ. Toxic 2014 May:29(7):829-36.
Bennett, JW. Silver linings. Front Microbiol. 2015 Mar 18;6:206.
Betancourt, et al. Microbial VOCs from Stacybotrys. BMC Microbiol. 2013 Dec5:13:283.

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Exposure history

- Do you live or work in a building that has any water damage such as roof leaks, floods, plumbing problems, slab leaks?
- Do you have a flat roof? Crawl space? Damp basement? Humidity problems? Window condensation?
- How old is the building? Has there been recent construction?
- Visible mold? Moldy or musty smells?
- Development of illness after change in buildings?
- Do you feel better being in fresh air locations?

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Other Mold Toxicity Manifestations

- Fatigue
- Weakness
- Headaches
- Chemical sensitivity
- EMR and Electrical sensitivity
- Adrenal dysfunction
- Endocrine dysfunction
- Dysautonomia
- Nutritional depletion
- Hypoxia
- Confusion/Memory Problems
- Chronic pain
- Insomnia
- Celiac disease or gluten sensitivity
- Weight gain
- Respiratory and sinus problems
- Chronic infections
- Poor wound healing
- Myalgias
- Reduced exercise tolerance

Etzel RA. Mycotoxins. JAMA 2002; 287;425-427.
Shoemaker.

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Review

Medical diagnostics for indoor n

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Indoor mol
between the occurrence of individual mold species and health effects. Apart from the allergic bron-
chopulmonary aspergillosis (ABPA) and the mycoses caused by mold, there is only sufficient evidence for
the following associations between moisture/mold damages and different health effects: Allergic respi-
ratory diseases, asthma (manifestation, progression, exacerbation), allergic rhinitis, exogenous allergic

Table 1
Evidence for an association between exposure to moisture/mold damage indoors and diseases without mold mycoses, modified according to (Fisk et al., 2007, 2010; Mendell et al., 2011; Palaty and Shum, 2012; WHO, 2009b).

Causal relationship
No evidence
Sufficient evidence for an association
Allergic respiratory diseases
Asthma (manifestation, progression, exacerbation)
Allergic rhinitis
Hypersensitivity pneumonitis (HP)/Exogenous allergic alveolitis (EAA)
Promoting respiratory infections, bronchitis
Restricted or suspected evidence for an association
Mucous membrane irritation (MMI)
Atopic eczema (atopic dermatitis; manifestation, progression, exacerbation)
Inadequate or insufficient evidence for an association
Chronic obstructive pulmonary disease (COPD)
Acute idiopathic pulmonary hemorrhage in children
Rheumatism
Arthritis
Sarcoidosis
Cancer
Neurotoxic effects

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Environmentally Acquired Illness due to Biotoxins (formering CIRS)

- Dr. Ritchie Shoemaker
- Environmentally Acquired Illness is caused by poor clearance of biotoxins produced by dinoflagellates, algae and mold.
- Genomic, multi-system, multi-symptom illness
- Chronic illness will perpetuate if no intervention

- Normal innate immune response allows for the production of antibodies by the adaptive system to remove the biotoxin.
- Defective antigen presentation in dysregulated innate immune system results in chronic inflammation

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EAI due to Biotoxins- Case definition

- 1. History, signs and symptoms consistent with biotoxin exposure. In the case of Mold-related illness, must have history of exposure to water damaged building with amplified microbial growth evidenced by:
  - A. Presence of visible mold
  - B. Musty odor
  - C. Commercial testing verifying mold growth
- 2. Genetic predisposition to biotoxin-related illness based on HLA haplotype.
- 3. Abnormalities documented by Visual Contrast Sensitivity (VCS) testing.
- 4. Biomarkers consistent with Biotoxin abnormalities and favorable response to treatment in 5 out of 8 biomarkers.

Causes of Environmentally Acquired Illness due to Biotoxins

Dysfunctional Adaptive Immunity → overactive Innate Immunity → Dysregulation Multiple systems in the body

Loss of antibody production against biotoxins

Chronic Inflammation

Autoimmunity, hormonal imbalances, neurological disturbances, fatigue, chronic pain

Environmental Acquired Illness Diagnosis – Symptoms

Age <19 – 19/37 Symptoms
Age > 19 – 25/37 symptoms

- Fatigue
- Myalgias
- Joint pains
- Red eyes
- Blurred vision
- Decreased assimilation of new knowledge
- Word finding problems
- Shortness of breath
- Tingling
- Unusual pain
- Sinus congestion
- Excessive thirst
- Appetite swings
- Abdominal pain
- Disorientation
- Sweats (esp night sweats)
- Skin sensitivity/rashes

Environmental Acquired Illness Diagnosis – Symptoms

Age <19 – 19/37 Symptoms
Age > 19 – 25/37 symptoms

- Weakness
- Headaches
- Morning stiffness
- Tearing eyes
- Vertigo
- Gluten sensitivity
- Muscle Aches
- Light sensitivity
- Memory impairment
- Decreased concentration
- Tremors
- Metallic taste
- Cough
- Confusion
- Nocturia
- Numbness
- Static shocks
- Temperature regulation issues
- Increased urinary frequency

Cluster analyses

Cluster analyses: Give 1 point for any or all symptoms in a category. 6 or more points for children. 8 or more teens and adults. Circle any that apply

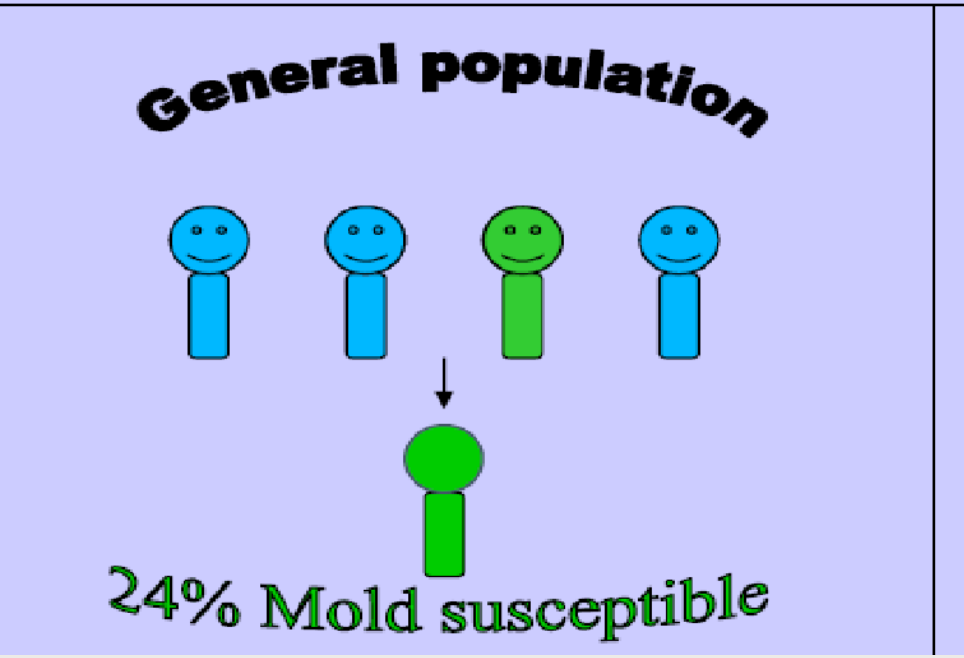
- **Fatigue**
- **Weakness, difficulty assimilating new information, muscle aches, headaches, light sensitivity**
- **Memory problems, word finding difficulties**
- **Problems with Concentration**
- **Joint pains, morning stiffness, muscle cramps**
- **Unusual skin sensations, tingling**
- **Shortness of breath, sinus congestion or nasal drainage**

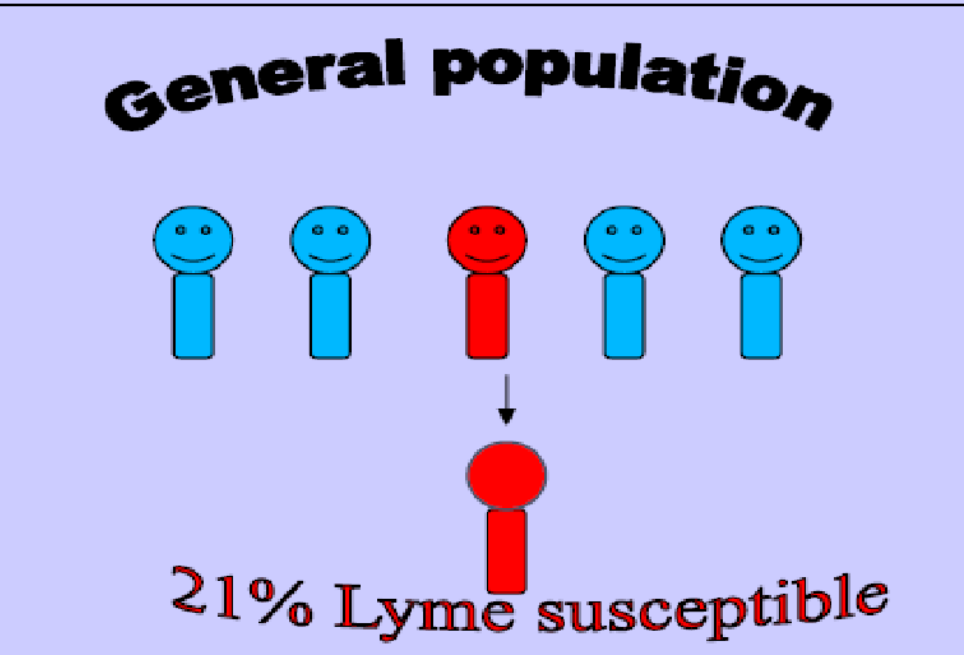
Cluster analyses

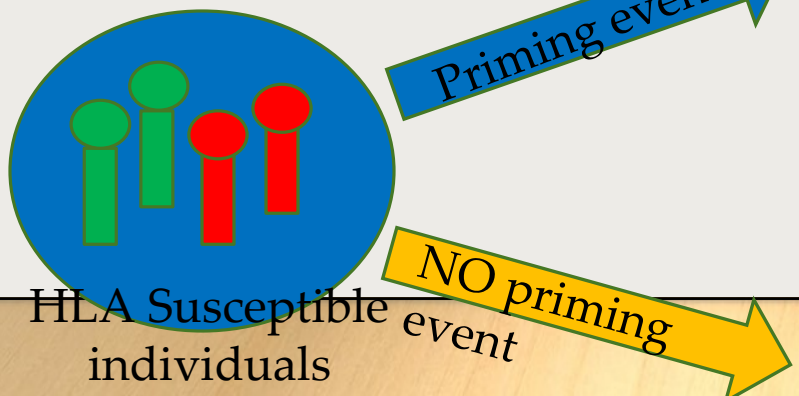
Cluster analyses: Give 1 point for any or all symptoms in a category. 6 or more points for children. 8 or more teens and adults. Circle any that apply

- **Cough, increased thirst, confusion**
- **Appetite swings, body temperature regulation, urinary frequency/urgency**
- **Red eyes, blurred vision, excessive or nighttime sweating, mood swings, unusual pains esp. "ice pick pains"**
- **Abdominal tenderness or pain, diarrhea or loose stools, numbness**
- **Eye tearing, disorientation, metallic taste**
- **Static shocks, vertigo**
    - **Total number:**

Statistics Based on International Gene Registries







Biotoxin illness will occur with exposure to biotoxins

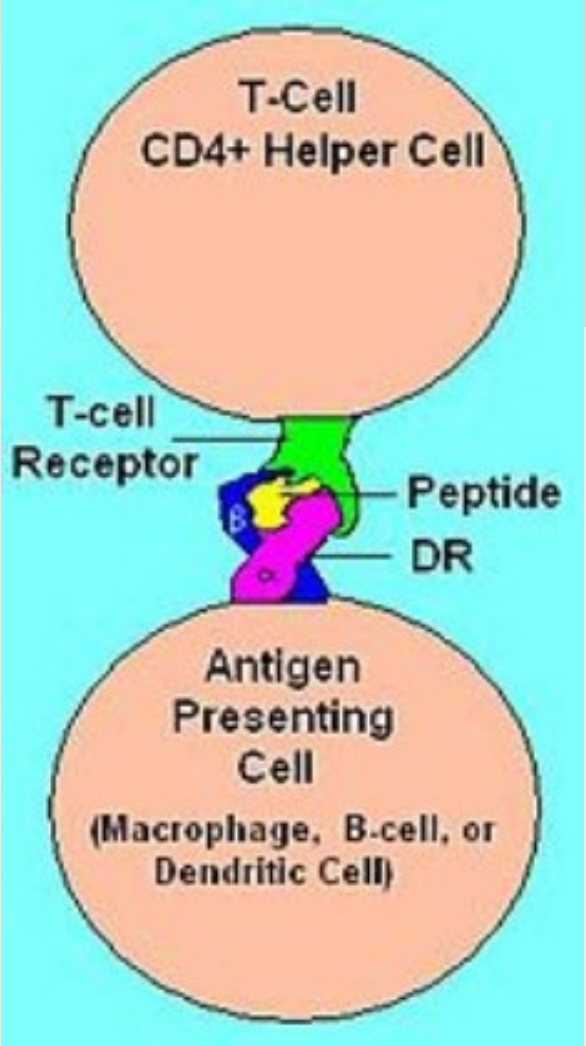
Some possible priming events include: influenza, Lyme disease, pneumonia, coxsackie viruses, ECHO viruses, surgery, trauma, stress, etc.

No Biotoxin -illness

~5 % of Biotoxin patients are not genetically susceptible. Tend to heal faster but require priming event.

HLA-DR

- HLA-DR is a major histocompatibility (MHC) class II cell surface receptor.
- Graft vs host compatibility
- Involved in immune responses, autoimmune conditions
- Extensive genetic polymorphisms
- Found on macrophages, B-cells and dendritic cells
- Presents antigens to T cells
- Stimulation of T cells through HLA-DR, leads to antibody production by B cells



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HLA Susceptibility

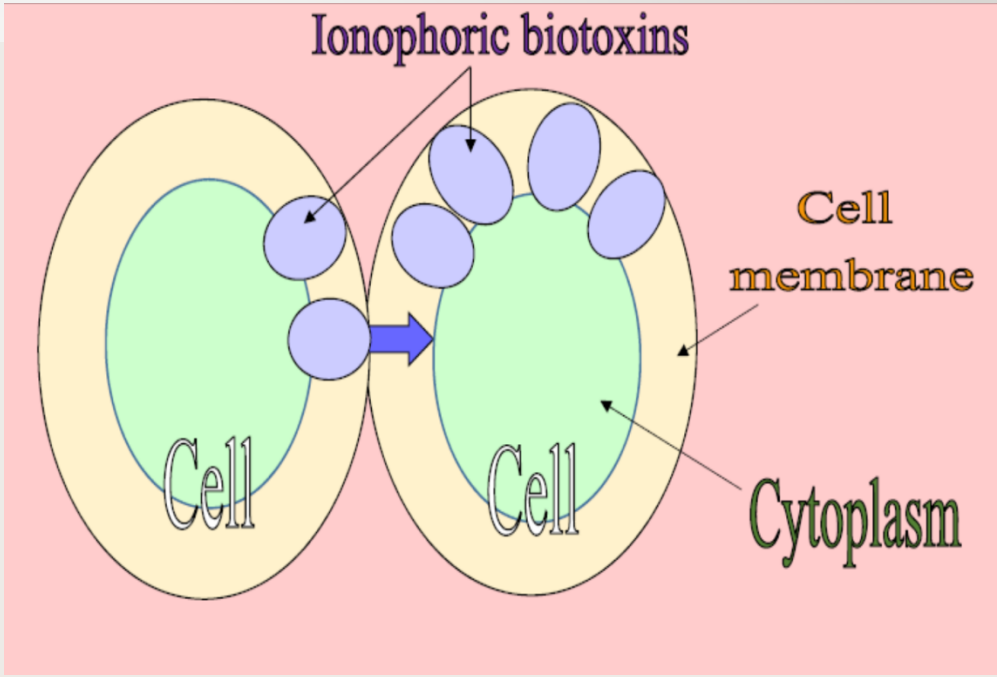
Dr. Shoemaker's HLA Rosetta Stone

Susceptibility	DRB1	DQ	DRB3	DRB4	DRB5
Multisusceptible	4	3		53	
	11/12	3	52B		
	14	5	52B		
Mold Susceptible	7	2/3		53	
	13	6	52A, B, C		
	17	2	52A		
	18*	4	52A		
Borrelia, post Lyme Syndrome	15	6			51
	16	5			51
Dinoflagellates (Pfiesteria, ciguatera)	4	7/8		53	
Multiple Antibiotic Resistant Staph Epidermis (MARCoNS)	11	7	52B		
Low MSH	1	5			
No recognized significance	8	3, 4, 6			
Low-risk Mold	7	9		53	
	12	7	52B		
	9	9		53	

Shoemaker R. Linkage disequilibrium in alleles of HLA DR: differential association with susceptibility to chronic illness following exposure to biologically produced neurotoxins. American Society of Microbiology 2003. (conference peer review).

Ionophoric Biotoxins

- Ionophoric biotoxins are very small and easily move in and out of cells
- They are not easily detected in the blood
- Secreted by liver into the bile and reabsorbed into the body unless tagged by the immune system.
- In genetically susceptible individuals since unable to tag the biotoxins, they are not removed which leads to chronic inflammation.



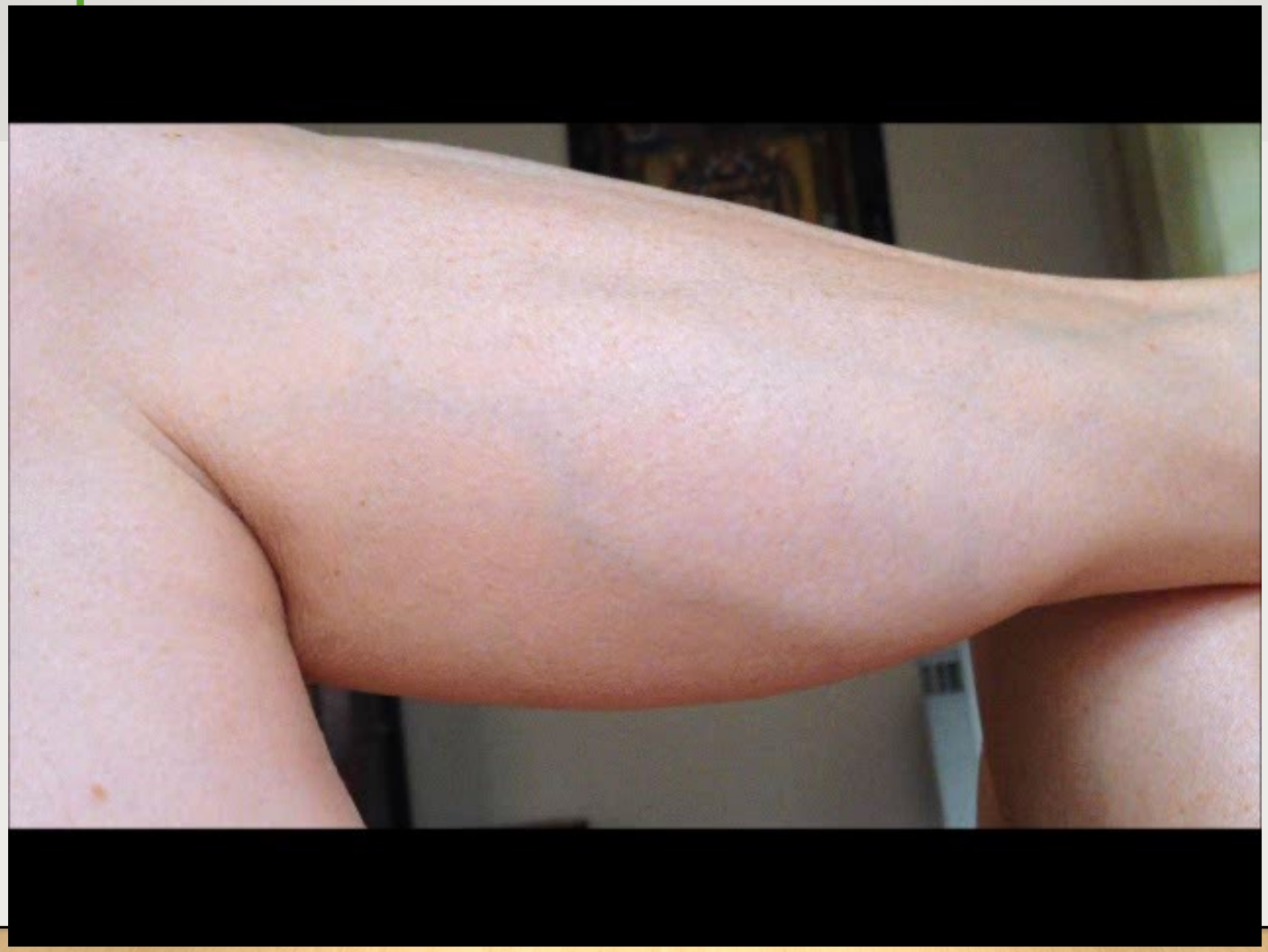
Biotoxin	Microorganism Souce	Route of transmission
Ciguatera	*Gambierdiscus toxicus* (dinoflagellate algae)	Ingestion of contaminated fish
Possible estuarine-associated syndrome (PEAS)	*Pfiesteria piscicida*	Direct contact with contaminated water or inhalation of aerosolized toxins, esp in the area of fish kills.
Lyme Biotoxin	*Borrelia burdorferi* spirochete	Tick bite
Brown Recluse Spider toxin		Spider bite
Babesiosis	*Babesia microti* or *duncani* or BLO	Tick bite

(Information for table taken from (Shoemaker, 2011, June 27, DVD))(

Case 1: December 2013

- 45 year old woman with history of seasonal allergies and mild PMS presents with depression, new onset insomnia, worsening food sensitivities, lower leg muscle fasciculations, and urinary frequency.
- PSHx: tonsillectomy age 18
- Medications: none
- Family history: Mom 70 –celiac, glaucoma, peripheral neuropathy; Dad 72 – htn, hyperlipidemia, carpal tunnel; sister 38 – htn
- Social Hx: no tobacco, social Etoh
- Location: Recently moved into an older home with moldy smell in the master bathroom

Case 1: Physical Exam



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Case 1: PE and Labs

PE – Wt 114Lb, Ht 5’4”
BP 108/68, HR 74

- Rest of physical exam unremarkable except for allergic shiners and intermittent muscle fasciculations on left calf

LABS: hs crp 0.3 mg/L =2.86nmol/L
thyroid wnl
Chol 208 mg/dL = 5.38 mmol/l
LDL 107 mg/dL= 2.77 mmol/l
HDL 85 mg/dL= 2.19 mmol/l
trig 80 mg/dL = 0.9032 mmol/l
pattern A
wbc 4.9, hgb 13.3
Cmp wnl, GGT 14
HgA1c 5.6 %
ANA neg
Vit D25oh 65 ng/mL= 162.5nmol/L

- **MTHFR** – C677t++

Case 1: Labs

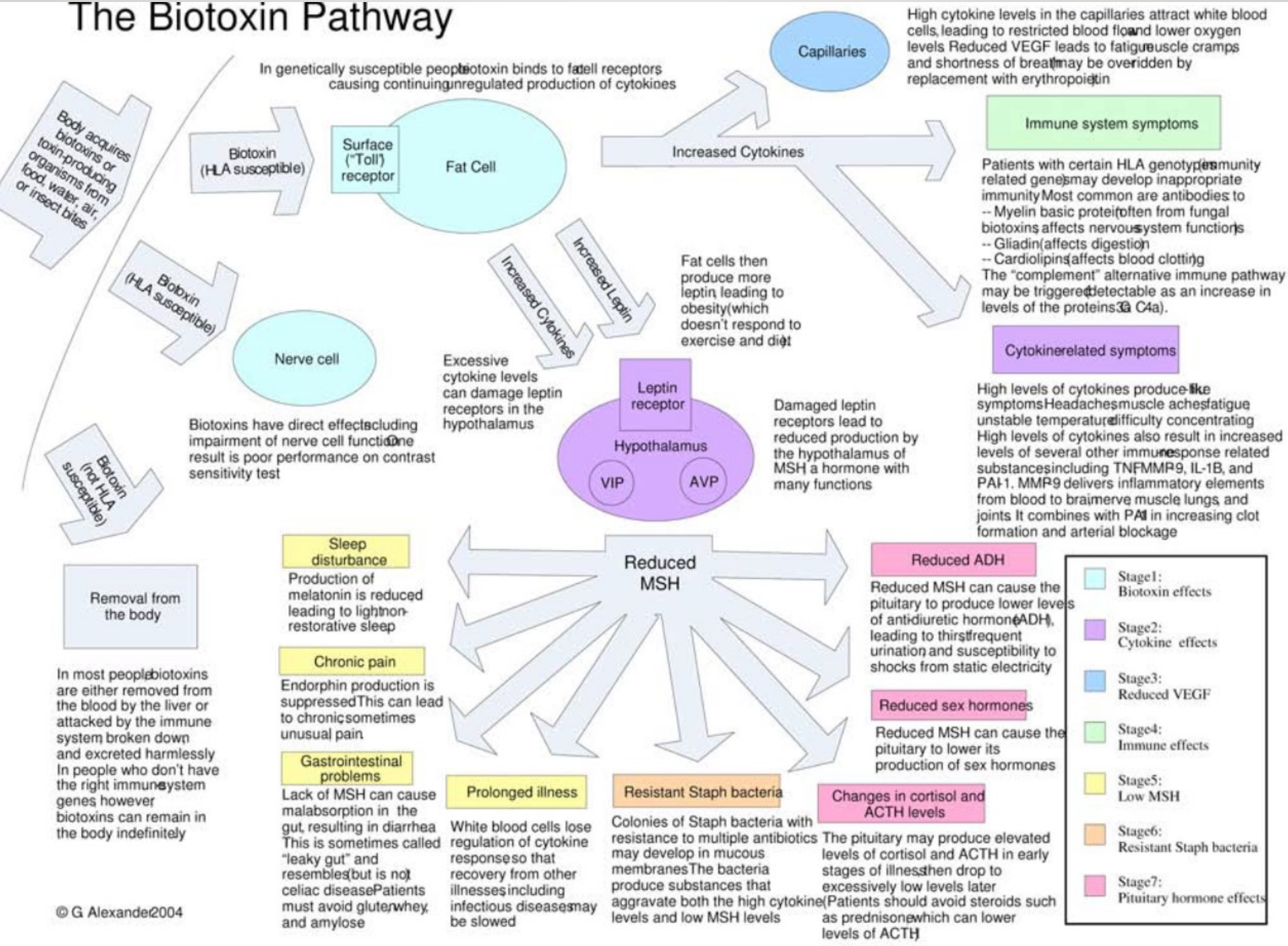
- **HLA DR** 4-3-53 multi-susceptible, 17-2-52A mold susceptible
- **Transforming Growth Factor Beta 1** - 9520 pg/mL (344-2382)
- **VasoIntestinal Active Peptide (VIP)** <16.8 (23-63 pg/mL)
- **Melanocyte Stimulating Hormone (MSH)** <8 (35-81pg/mL)
- **VEGF** <31 (31-86 pg/mL)
- **C4a –** 1672 (0-2830 ng/mL)
- **ADH –** <1.0 (1.0-13.3 pg/mL)
- **Osm –** 293 (278-305 mOsm/kg)
- **MMP-9 –** 928 (<332)

- Cyrex array 5 – numerous predictive autoantibodies.
- IgG Food sensitivity testing – highly reactive to all dairy, gluten, almonds, rice, peas, eggs, mushrooms, yeast.
- CDSA Stool test – low pancreatic elastase, low diversity, no fungal growth.

Other Labs to be Considered

- Routine labs – CBC, CMP, ferritin, iron/TIBC
- Hormones - thyroid, adrenal, aldosterone, sex hormones
- Autoimmunity, ANA, RF, Antibody sub-fractions
- Predictive autoantibodies
- Gluten sensitivity/celiac panel
- Food sensitivity testing
- Chronic infection work- up – Lyme and co-infections, viral infections
- Toxicant testing
- Heavy metal testing
- Inflammatory markers – CRP, ESR will be normal in CIRS
- Immune system dysfunction – Immunoglobulin panel, T&B cells, NK cell panel, complement levels, IgE
- Von Willebrands
- Hypercoagulability through Esoterix labs
- Cultures for nasal bacteria/fungus and stool studies
- Mold allergy and sensitivity testing
- Nutritional analysis
- Genomic analysis

The Biotoxin Pathway



Physician Order Sheet

Please Draw	Test	Lab to Use		Code #	DX Codes	CPT codes
	HLA DR by PCR	LabCorp	Spec	167120	D84.1 D83.1 D89.89	81375
	VIP	Quest	Lavender, room temp	920	D84.1 D89.89	84586
	MSH	Lab Corp only	Lav - freeze-trasylol	010421	E23.0 R65.10	83519
	Leptin	LabCorp	Lav - freeze-trasylol	146712	E23.0 R65.10	82397
		Quest	Lav - freeze-trasylol	90367	E23.0 R65.10 995.93	83520
	ADH	LabCorp	SST - freeze	10447	E23.0 R65.10 995.93	84588
		Quest	SST - freeze	252	995.93 R65.10	83930 84588
	Osmo	Labcorp	LAV freeze	2071	E23.2	83930
		Quest	LAV freeze	677	R65.10 995.93	83930
	ACTH	Labcorp	SST - freeze	004440	E27.4	82024
		Quest	SST - freeze	211	E27.40 255.41	82024
	Cortisol	LabCorp	Lav - freeze	004051	E27.40 255.41	82533
		Quest	Lav - freeze	42 2	E27.40 255.41	82533
	DHEAS	LabCorp	SST freeze	004020	E27.40 255.41	82627
		Quest	SST freeze	402	E27.40 255.41	82627
	Testosterone	LabCorp	SST - freeze	140103	E29.1	84402 84403
		Quest	SST - freeze	873	E29.1	84402 84403
	Androstenedione	LabCorp	red top - room temp	500171	E27.40 255.41	82157
		Quest	red top - room temp	17182x	E27.40 255.41	82157
	CRP	LabCorp	SST - freeze	120766	R79.82	86141
		Quest	SST - freeze	17182x	R79.82	86141
	ESR	LabCorp	SST - room temp	5215	D89.89 279.49	85652
		Quest	SST - room temp	809	D89.89 279.49	85652
	TGF-B1	LabCorp	Lav	905036	D84.1 D83.1	83520
		Quest	Lav	91238	D84.1 D83.1	83520
	MMP-9	LabCorp	Lav freeze (platelet poor plasma)	500124	D89.89 R53.81	83520
	PAI-1	LabCorp	SST- freeze	146787	I67.8	85415
		Quest	SST - freeze	36555	D68.9 286.9 I67.8	85415
	CBC	Quest	Lav - room temp	17182x	E27.40 255.41	85025
		LabCorp	Lav room temp	5009	E27.40 255.41	85025
	CMP	LabCorp	SST - room temp	322000	E27.40 255.41	80053
		Quest	SST - room temp	10231x	E27.40 255.41	80053
	CCT	LabCorp	SST - room temp	001958	E27.40 255.41	82977
		Quest	SST room temp	10231x	E27.40 255.41	82977
	VEGF (not serum)	LabCorp	Rm temp	117006	E23.0 R65.10	83520
		Quest	Rm temp	14512	995.93 R65.10	83520
	Erythropoietin	LabCorp	Red- freeze	140277		82668
		Quest	Red - freeze	427x		82668
	Anticardiolipins	LabCorp	Red - freeze	161950	M32.1	86147
		Quest	Red - freeze	7352	285.9 D68.9	86147
	Anticiliedin, IgA, IgG	LabCorp	SST - freeze	161646/161687	K90.0	83516
		Quest	SST - freeze	8889x	279.8/D89.89	83516
	C3a RIA (not Futhan)	Quest only	SST - freeze	17689	279.8/D89.89	86160
	C4a RIA (not Futhan)	Quest only	Lav - freeze	19956	279.8 / D89.89	86160
	IgE	Quest	Lav - freeze	542x	279.03 D80.3	82785
		LabCorp	Lav - freeze	002295	279.03 D80.3	82784
	Lyme WB	Quest	SST - freeze	8593	088.81/A69.20	86617
	TSH	LabCorp	SST - freeze	004259	244.8	84443
		Quest	SST - freeze	899x	244.8	84443
	von Willebrand's profile	Quest	SST - freeze	15540x	286.9 D68.9	85240
	Fe / TIBC	Quest	Blue freeze - 3 aliquots	7573x	R53.81	83540
		LabCorp	Blue freeze - 3 aliquots	001321	R53.81	83540

- **Lab Corp**

HLA DR, MMP-9, MSH, VIP, cd 57 – if desired

- **QUEST**

VEGF, ADH, OSM, and C4a – if able

- **TGfbeta1 needs to go to Cambridge Biomedical**
- **C4a needs to go to National Jewish on dry ice**

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Case Definition Specific Labs

- HLA haplotype
- MARCONS
- ADH/osmolality 4 abnl tests <11 yrs +diagnostic for CIRS
- ACTH/Cortisol 5 abnl tests >11 yrs +diagnostic for CIRS
- MMP-9
- MSH
- VIP
- TGF beta 1
- C4a
- Anticardiolipin antibodies
- Anti-gliadin antibodies
- Also check VCS. Use handheld device rather than online.

Environmentally Acquired Illness Labs

TGF-beta 1 (Transforming Growth Factor Beta 1)

- A marker of an overactive immune system. Directs immunity towards TH17, often results in autoimmunity.
- Potent immune suppressor, leading to chronic infections.
- Also role in tumor suppression and promoting tolerance to allergens and self- antigens.

C4a level (complement cascade)

- Split product of complement activation. Increased vascular permeability, capillary hypoperfusion.
- Represent an excessive innate immune response to biotoxins.
- High C4a levels may also be seen in Lupus and Lyme disease.

Environmentally Acquired Illness Labs

MMP-9 (Matrix metalloproteinase-9) level

- Zinc-dependent enzyme involved in remodeling extracellular matrix
- Correlates with high toxin load. Marker for disease progression.
- Associated with increased permeability in the blood brain barrier
- Implicated in pathogenesis COPD by destruction of lung elastin, in rheumatoid arthritis, atherosclerosis, cardiomyopathy, demyelinating diseases and abdominal aortic aneurysm.

VEGF (vascular endothelial growth factor) level

- A marker of capillary hypo-perfusion.
- A low level of skeletal muscle VEGF is associated with decreased muscle endurance. Other symptoms include persistent fatigue, cognitive difficulties, difficulty recovering from even mild activity
- Early in biotoxin illness, VEGF can run high, a sign that it is trying to help compensate for low oxygen delivery to issues.

Environmentally Acquired Illness Labs

VIP (vasointestinal active peptide) level

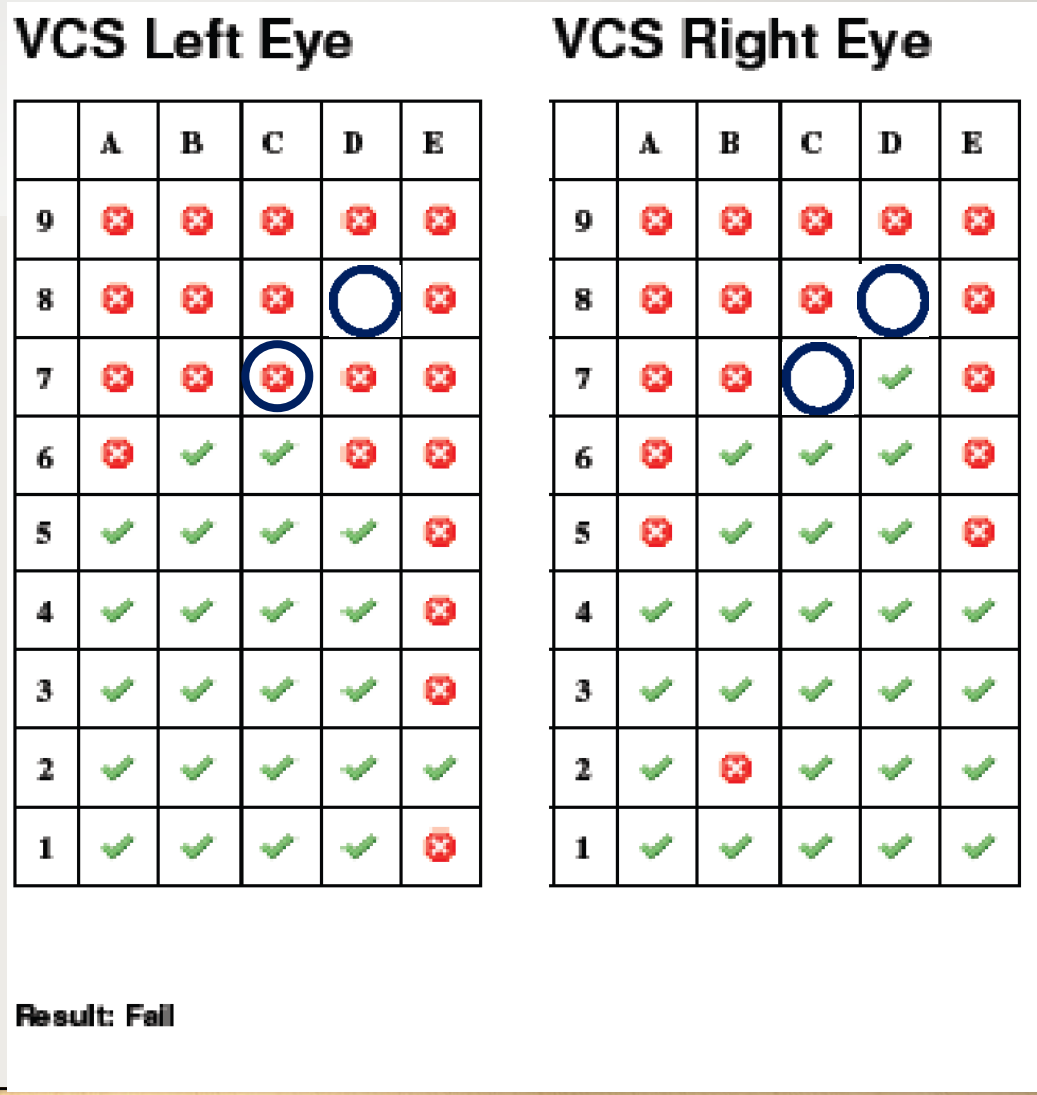
- Neuroregulatory hormone, regulates cytokines and inflammatory responses.
- Marker of blood flow regulation and distribution.
- Low levels are associated with capillary hypo perfusion and abnormal pulmonary artery pressure at rest or in response to exercise.

MSH (melanocyte stimulating hormone) level

- Marker of neuropeptide control of multiple functions.
- Alpha MSH binding to receptors in the brain and on white blood cells reduces inflammatory responses, including decreased production of pro-inflammatory cytokines.
- Symptoms often include fatigue and unusual pain syndromes.

Visual Contrast Sensitivity (VCS) test

- The nerve fibers in the upper/outer portions of the optic nerve carry "edge detection" information, ability to discern visual contrast.
- Test is designed to distinguish differences in shading, thickness and separation of grey on grey lines.
- To pass the VCS screen, must be correct for row 7, column C and row 8, column D (see blue circles)
- Patients with CIRS, 92% will fail and 8% will pass.
- Must have 20/50 acuity to test.



Online screening or purchase of handheld device: www.survivingmold.com or www.vcstest.com

Kelly K. McCann, MD

MaRCoNS – Multidrug Antibiotic Resistant Coagulase Negative Staph

Microbiology Dx

LABORATORY REPORT

14 CROSBY DRIVE
BEDFORD, MA 01730
TEL: (781)275-0855 * FAX: (781)275-9703
DR. J. D. MUSTO, DABB, BCIC
PRESIDENT & LAB DIRECTOR

PATIENT:

CLIENT: GENERAL DOCTOR ACCOUNT
14 CROSBY DR.
BEDFORD, MA 01730

D.O.B./SEX:
DATE COLLECTED:
TIME COLLECTED:
LAB NUMBER:

DOCTOR:
DATE RPTD:
DATE PRNT:
PATIENT ID:

PAGE: 1

** FINAL REPORT **

** FINAL REPORT **

RESULTS

TEST NAME	NORMAL	ABNORMAL	REFERENCE RANGE	UNITS

NARES CULTURE

MARCoNS present

SOURCE: NARES

ORGANISM: STAPH COAG NEGATIVE - LARGE AMOUNT
METHICILLIN RESISTANT

SUSCEPTIBILITY

PENICILLIN-G	)=0.5	R	OXACILLIN MIC	)=4	R
GENTAMICIN	(=0.5	S	CIPROFLOXACIN	)=8	R
LEVOFLOXACIN	)=8	R	ERYTHROMYCIN	)=8	R
CLINDAMYCIN	)=8	R	VANCOMYCIN	1	S
TETRACYCLINE	2	S	TIGECYCLINE	(=0.12	S
NITROFURANTOIN	32	S	RIFAMPICIN	(=0.5	S
CEFAZOLIN		R			

- Bacterial colonizer in the nasal passages and possibly dental reservoirs.
- Creates biofilms
- Releases exotoxins that suppress alpha MSH.
- Differentially activates gene expressions
- Fungal nasal cultures available
- Company now tests strength of biofilms

Shoemaker R, Hudnell K, et al. Association of nasal carriage of methicillin resistant and multiple antibiotic resistant coagulase negative staphylococci species with deficiency of alpha melanocyte stimulating hormone in Chronic Fatigue Syndrome. American Society of Microbiology 2003. (conference peer review)

MaRCoNS – Multidrug Antibiotic Resistant Coagulase Negative Staph

- Rarely found in nature
- Reservoirs in dogs, but not cats
- In family members with low MSH.
- Found in Chronic Fatigue Syndrome and chronic facial pain patients
- Kids rarely have MARCoNS
- No eradication of MARCoNS, there was no improvement

- 80% patients with low MSH have MARCoNS.
- 60% had methicillin resistances.
- If a patient has low MSH, do a nasal swab.

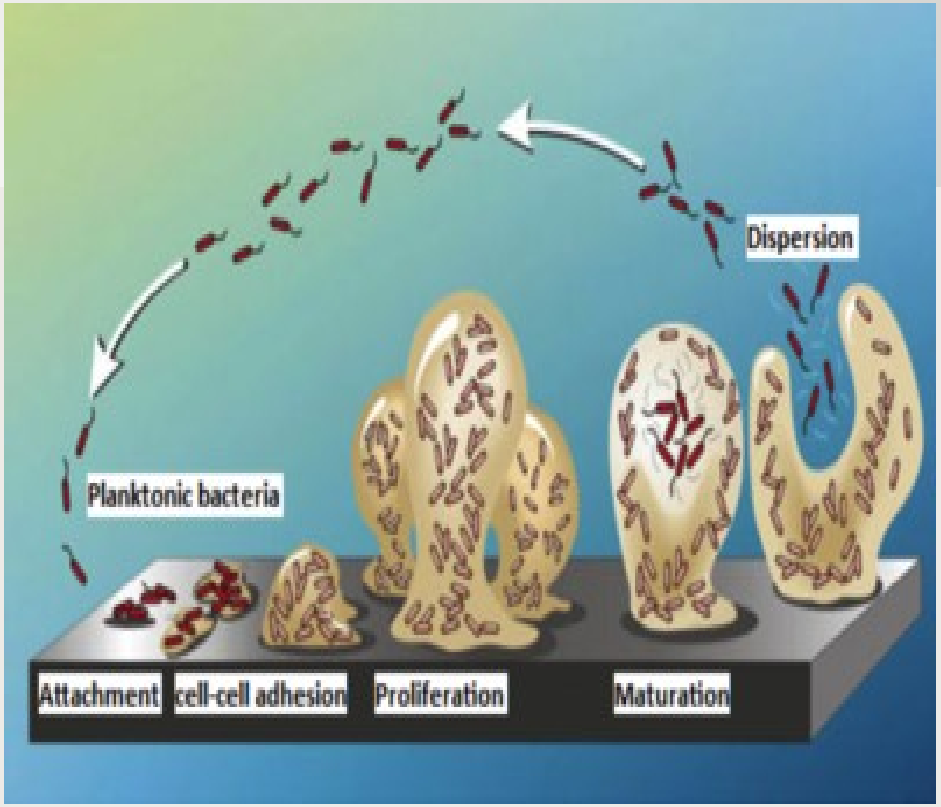
- If one round of treatment doesn't eradicate, MARCoNS, consider sending to biological dentist to evaluate for cavitations.

BEG/BEC spray

- BEG spray – Bactroban, EDTA, Gentamicin
- BEC – Substitute Clindamycin
- Available through compounding pharmacis
- Choice depends of resistance and tolerability
- 2 sprays each nostril 3 times daily for 1 month
- Reculture. Must confirm eradication.
- Do not use rifampin.
- Pretreatment with xylitol nasal spray may improve tolerability.
- Can also use Silver and EDTA

Nasal Fungal Culture and Intranasal Treatments

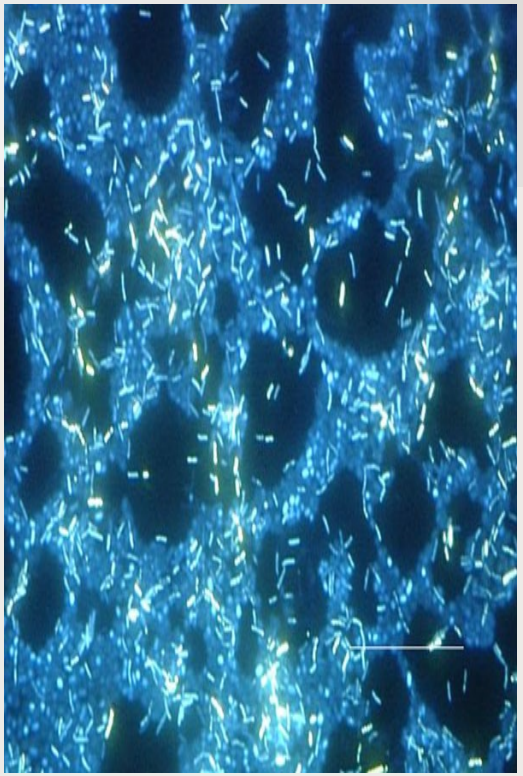
- Mold exposed patients may have both MARCoNs and fungal colonizers.
- Treatment with intranasal antifungals may help
- Amphotericin B, nystatin, ketoconazole, or itraconazole



Brewer JH, Thrasher JD, et al. Chronic illness associated with mold and mycotoxins: is naso-sinus fungal biofilms the culprit? Toxins 2013; 6(1) :66-80. PMID: 24368325
Brewer JH, Hooper D, et al. Intranasal antifungal therapy inpatients with chronic illness associated with mold and mycotoxins. GJMR 2015 Vol 15 2:29-33.
Brewer, JH, Hooper, D, et al. Intranasal nystatin Therapy in patients with Chronic Illness. GJMR 2015. 15(5).

Antifungal Nasal Sprays

- Nystatin 50,000 units/spray BID
- Itraconazole 40mg/spray BID
- Ketoconazole – not recommended
- Amphotericin B 5mg/spray BID



Addressing Biofilms

- Polysorbate 80 - nonionic surfactant
- Xylitol - variable effectiveness
- Mupirocin – ENT gold standard
- EDTA

- Sloup RE, et al. Polysorbates prevent biofilm formation and pathogenesis of Escherichia coli O104:H4. Biofouling. 2016 Oct;32(9):1131-1140.
- Jain R, etal. The in vitro effect of xylitol on chronic rhinosinusitis biofilms. Rhinology. 2016 Jul 10.
- Smith A, Buchinsky FJ, Post JC. Eradicating chronic ear, nose, and throat infections: a systematically conducted literature review of advances in biofilm treatment. Otolaryngol Head Neck Surg. 2011 Mar;144(3):338-47
- Drilling A, et al. Safety and efficacy of topical bacteriophage and ethylenediaminetetraacetic acid treatment of Staphylococcus aureus infection in a sheep model of sinusitis. Int Forum Allergy Rhinol. 2014 Mar;4(3):176-86

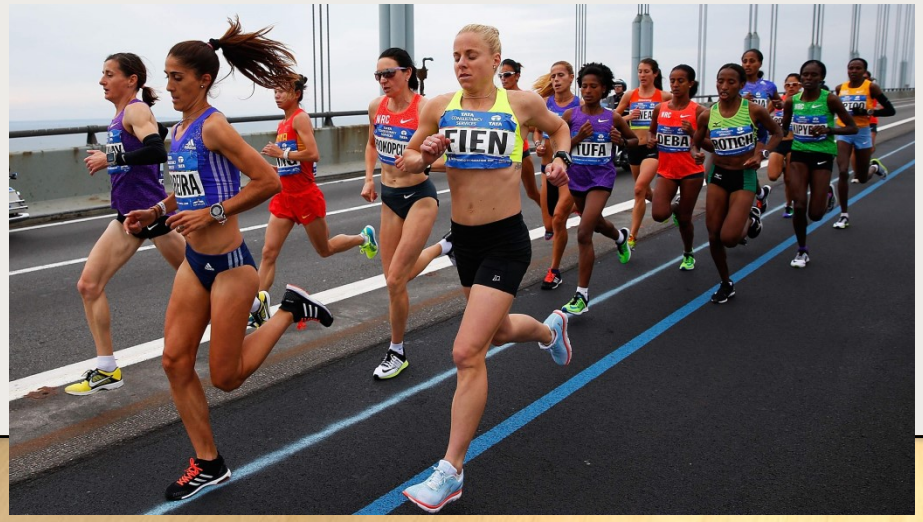
Atomizer versus Nasal Rinse

- Nasal Touch Atomizer
- Anecdotal evidence
- Less dilution of medication
- Costs $85

- Evidence based
- Readily available
- Inexpensive
- Contraindicated in ear issues
- Rinse can get into sinuses
- http://www.neilmed.com/usa/articles_nasalirrigation.php
- Brown and Graham. Current Opinion in Otolaryngology & Head and Neck Surgery 2004, 12:9–13

This is a marathon…..

- Treating for intranasal fungus is a marathon.
- Anticipate at least 6, if not 12 months of treatment.



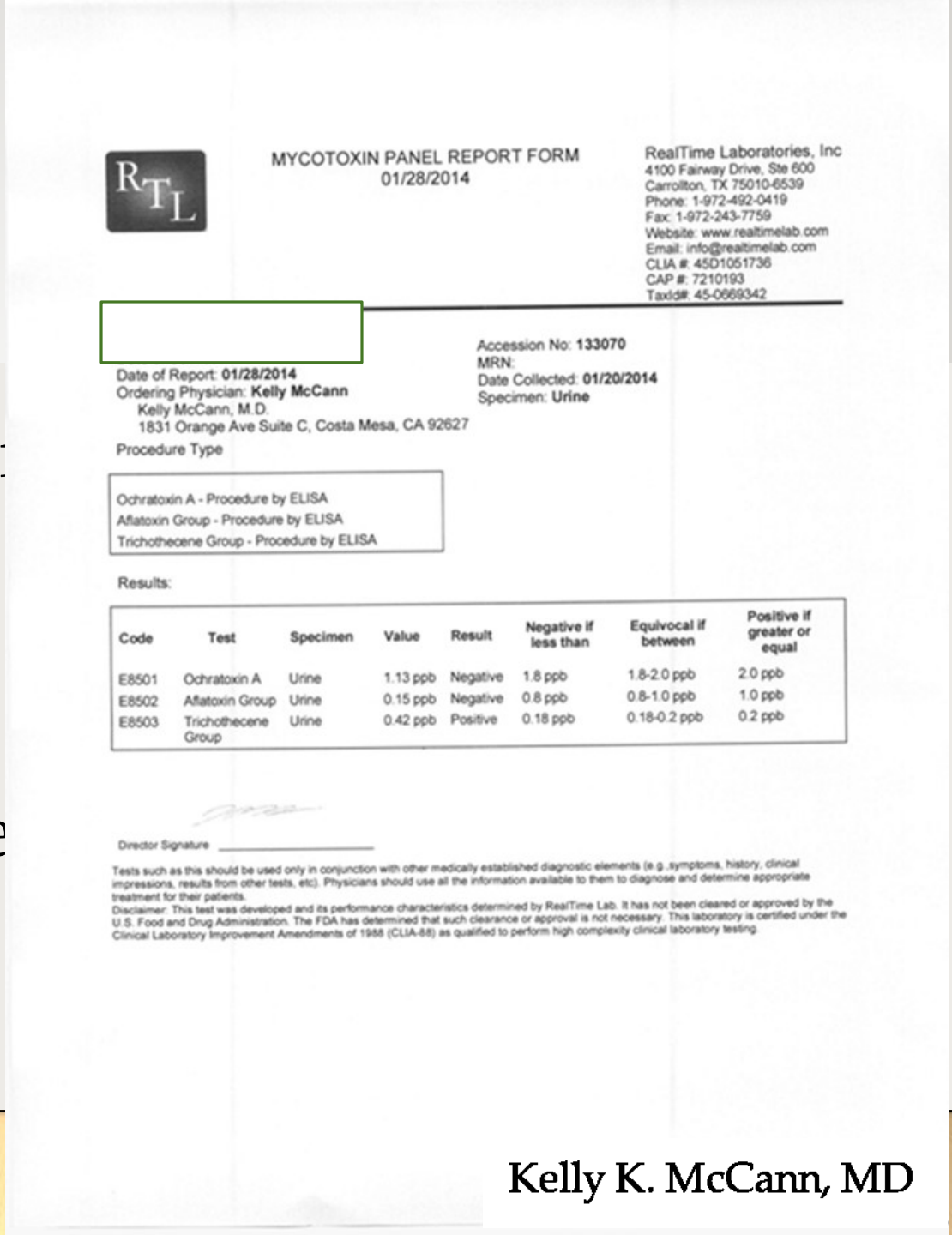
- Must rinse out the nasal passages with saline after the medications
- If live in humid or highly polluted areas may need to treat longer.
- Can continue every other day indefinitely

"Honey, do we have a problem with mold in our house?"

Case 1:

Urine test fo
mycotoxins

Aflatoxin
Ochratoxin
Tricothecene
Gliotoxin



MYCOTOXIN PANEL REPORT FORM
01/28/2014

RealTime Laboratories, Inc
4100 Fairway Drive, Ste 600
Carrollton, TX 75010-6539
Phone: 1-972-492-0419
Fax: 1-972-243-7759
Website: www.realtimelab.com
Email: info@realtimelab.com
CLIA #: 45D1051736
CAP #: 7210193
TaxId#: 45-0669342

Accession No: **133070**
MRN:
Date Collected: **01/20/2014**
Specimen: **Urine**

Date of Report: **01/28/2014**
Ordering Physician: **Kelly McCann**
Kelly McCann, M.D.
1831 Orange Ave Suite C, Costa Mesa, CA 92627

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	1.13 ppb	Negative	1.8 ppb	1.8-2.0 ppb	2.0 ppb
E8502	Aflatoxin Group	Urine	0.15 ppb	Negative	0.8 ppb	0.8-1.0 ppb	1.0 ppb
E8503	Trichothecene Group	Urine	0.42 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.

Research on urine mycotoxin testing

- Validated exposure biomarkers for aflatoxin were established 20 years ago.
- Urinary deoxynivalenol (DON) zearalenone, ochratoxin A (OTA), fumonisin B1 (FB1) found in farmers in South Africa.
- Belgian study in 2015 determined 100% of 394 study participants had DON urine mycotoxins.

- 93% of 112 CFS patients had one urine mycotoxin. 30% had numerous.
- OTA most common 83%, tricothecenes 44%
- 90% case histories indicate current or past exposure to WDB.
- 55 healthy controls = 0 mycotoxins

Brewer, et al. Detection of mycotoxins in CFS patients. Toxins (basel) 2013 April 11;5(4):605-17.
De Saeger, S. et al. Report from the 5th International Symposium on Mycotoxins and Toxigenic Moulds. Toxins 2016, 8, 146.
Shephard, etal. Multiple Mycotoxins exposure determined by urinary biomarkers in susbsistence farmers in South Africa. Food Chem Toxicol 2013 Dec:62:217-25.
Turner, PC, et al. Role of Biomarkers in human health concerns from fungal contaminants in food. Nutr Res Rev 2012 Jun:25(1): 162-179

Cases 2 and 3

- Wife – 41 year old presented in 5/2012
- Fatigue, Depression, Dysmenorrhea
- Gallbladder resected
- Chronic Headaches
- Chronic diarrhea
- Intermittent SOB, sweats, shaking, dizziness
- Developed joint pains, difficulty walking
- Foot drop (mom has Charcot-Marie-Tooth)
- +numerous symptoms also c/w Lyme disease. +positive IgM Lab corp test

- Husband – 44 year old presented in November 2015
- Mild depression – life long
- Increased fatigue
- Increased anxiety and fear of children
- Developed high blood pressure
- Headaches
- Glass sensations in his eyes
- Problems with focus
- Increased urination

LA Testing
520 Mission Street South Pasadena, CA 91030
Phone/Fax: (323) 254-9960 / (323) 254-9982
http://www.LATesting.com / pasadenalab@latesting.com

Order ID: 321515997
Customer ID: RRMT42
Customer PO:
Project ID:

Attn: Sean Dare
Rapid Response Mold Testing
123 S Figueroa St
#359
Los Angeles, CA 90012

Phone: (323) 247-9415
Fax:
Collected: 07/28/2015
Received: 07/28/2015
Analyzed: 07/29/2015

Proj:

Test Report: Air-O-Cell(™) Analysis of Fungal Spores & Particulates by Optical Microscopy (Methods EMSL 05-TP-003, ASTM D7391)

Lab Sample Number:	321515997-0001			321515997-0002			321515997-0003		
Client Sample ID:	21540272			21543032			21542989		
Volume (L):	75			75			75		
Sample Location:	Outside			Living Room			Bedroom Wall		
Spore Types	Raw Count	Count/m³	% of Total	Raw Count	Count/m³	% of Total	Raw Count	Count/m³	% of Total
Alternaria	2	80	1.8	1	40	4	-	-	-
Ascospores	2	80	1.8	2	80	8	-	-	-
Aspergillus/Penicillium	59	2500	54.7	4	200	20	30	1300	2.1
Basidiospores	3	100	2.2	-	-	-	-	-	-
Bipolaris++	-	-	-	-	-	-	-	-	-
Chaetomium	-	-	-	-	-	-	-	-	-
Cladosporium	38	1600	35	16	680	68	-	-	-
Curvularia	-	-	-	-	-	-	-	-	-
Epicoccum	1	40	0.9	-	-	-	-	-	-
Fusarium	-	-	-	-	-	-	-	59,900	-
Ganoderma	-	-	-	-	-	-	-	-	-
Myxomycetes++	2	80	1.8	-	-	-	-	-	-
Pithomyces	-	-	-	-	-	-	-	-	-
Rust	-	-	-	-	-	-	-	-	-
Scopulariopsis	-	-	-	-	-	-	-	-	-
Stachybotrys	-	-	-	-	-	-	1420	59900	96.8
Torula	-	-	-	-	-	-	-	-	-
Ulocladium	1*	10*	0.2	-	-	-	16	680	1.1
Unidentifiable Spores	-	-	-	-	-	-	-	-	-
Zygomycetes	-	-	-	-	-	-	-	-	-
Oidium	1	40	0.9	-	-	-	-	-	-
Trichocladium	1	40	0.9	-	-	-	-	-	-
Total Fungi	**110**	**4570**	**100**	**23**	**1000**	**100**	**1466**	**61880**	**100**
Hyphal Fragment	6	300	-	2	80	-	149	6290	-
Insect Fragment	-	-	-	-	-	-	2	80	-
Pollen	-	-	-	-	-	-	-	-	-
Analyt. Sensitivity 600x	-	42	-	-	42	-	-	42	-
Analyt. Sensitivity 300x	-	13*	-	-	13*	-	-	13*	-
Skin Fragments (1-4)	-	1	-	-	2	-	-	2	-
Fibrous Particulate (1-4)	-	1	-	-	1	-	-	2	-
Background (1-5)	-	2	-	-	2	-	-	3	-

Outside test is an air trap sample. The other samples are spore counts taken from a wall sample.

Kelly K. McCann, MD

Cases 2 and 3: Potential flaws in urine mycotoxin testing

REALTIME LABORATORIES, INC
Cutting edge. Breaking barriers.

MYCOTOXIN PANEL REPORT FORM
08/27/2015

Carrollton, TX 75010
Phone: 1-972-492-0419
Fax: 1-972-243-7759
Website: www.realtimelab.com
Email: info@realtimelab.com
CLIA #: 45D1051736
CAP #: 7210193
TaxId#: 45-0669342

Accession No: **148639**
MRN:
Date of Service: **08/22/2015**
Specimen: **Urine**

Ordering Physician: **Kelly McCann**
Kelly McCann, M.D.
1831 Orange Ave Suite C, Costa Mesa, CA 92627

Procedure Type

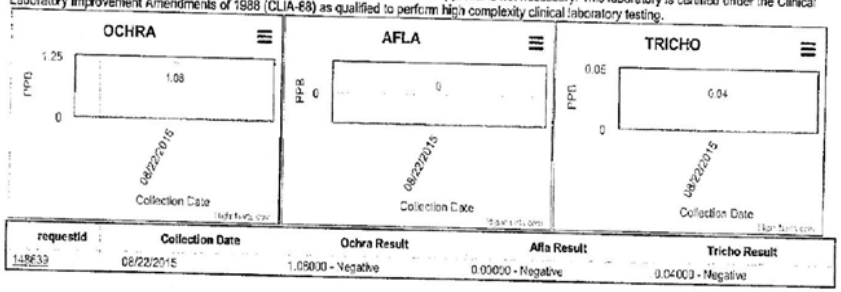
Ochratoxin A - Procedure by ELISA
Aflatoxin Group - Procedure by ELISA
Trichothecene Group - Procedure by ELISA

Results:

Code	Test	Specimen	Value	Result	Negative if less than	Equivocal if between	Positive if greater or equal
E8501	Ochratoxin A	Urine	1.08000 ppb	Negative	1.8 ppb	1.8-2.0 ppb	2.0 ppb
E8502	Aflatoxin Group	Urine	0.00000 ppb	Negative	0.8 ppb	0.8-1.0 ppb	1.0 ppb
E8503	Trichothecene Group	Urine	0.04000 ppb	Negative	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
148639	08/22/2015	1.08000 - Negative	0.00000 - Negative	0.04000 - Negative

REALTIME LABORATORIES INC
Cutting edge. Breaking barriers.

MYCOTOXIN PANEL REPORT FORM
09/15/2015

RealTime Laboratories, Inc
4100 Fairway Drive, Ste 600
Carrollton, TX 75010
Phone: 1-972-492-0419
Fax: 1-972-243-7759
Website: www.realtimelab.com
Email: info@realtimelab.com
CLIA #: 45D1051736
CAP #: 7210193
TaxId#: 45-0669342

Patient Date of Birth: **02/06/1971**
Date of Receipt: **09/11/2015**
Date of Report: **09/15/2015**
Ordering Physician: **Kelly McCann**
Kelly McCann, M.D.
1831 Orange Ave Suite C, Costa Mesa, CA 92627

Accession No: **148204**
MRN:
Date of Service: **09/7/2015**
Specimen: **Urine**

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	5.36000 ppb	Positive	1.8 ppb	1.8-2.0 ppb	2.0 ppb
E8502	Aflatoxin Group	Urine	1.68000 ppb	Positive	0.8 ppb	0.8-1.0 ppb	1.0 ppb
E8503	Trichothecene Group	Urine	1.03000 ppb	Positive	0.18 ppb	0.18-0.2 ppb	0.2 ppb

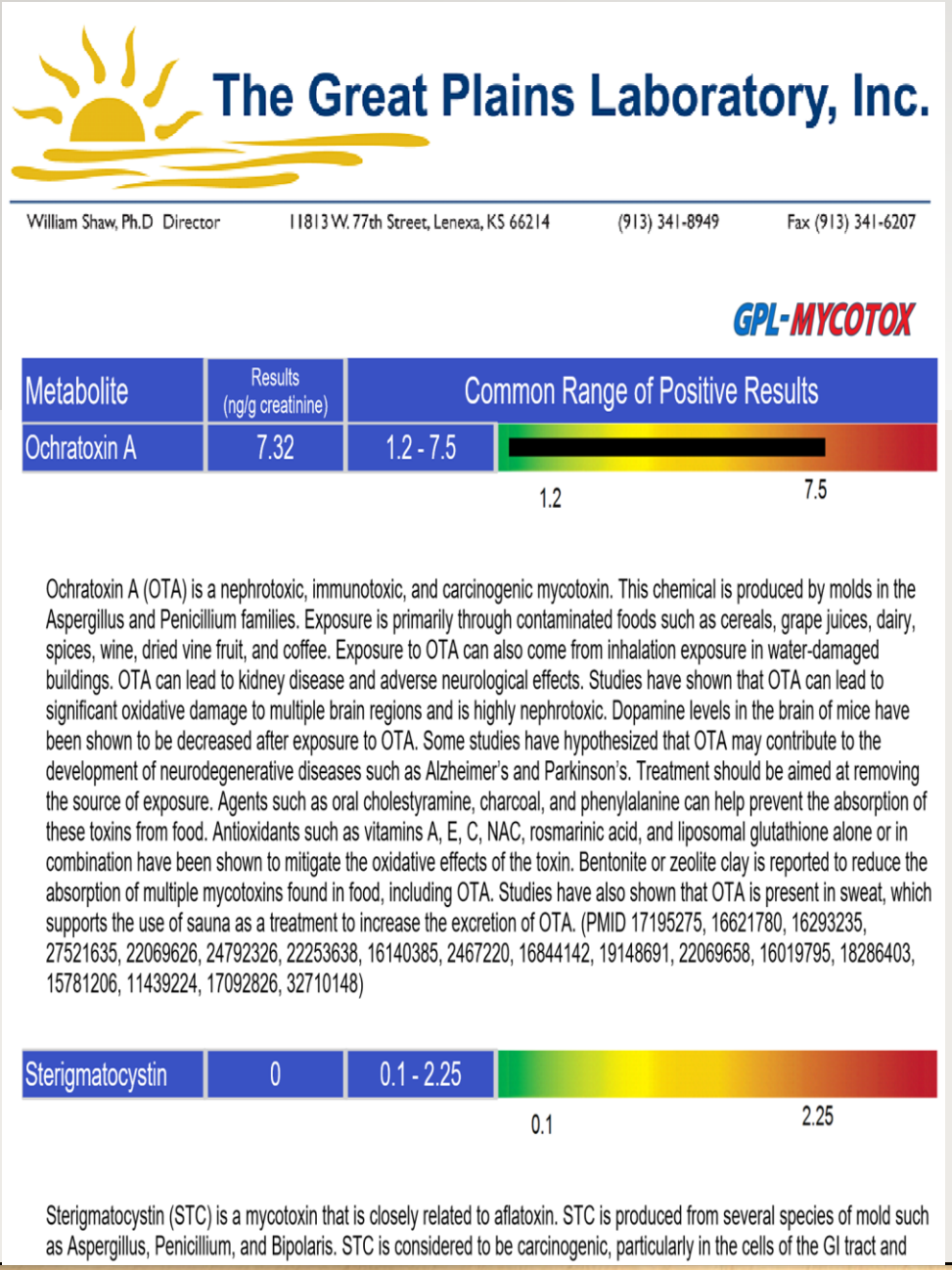
New Urine Mycotoxin test option

Mycotoxins

- Aflatoxin M1 (AFM1)
- Ochratoxin A (OTA)
- Sterigmatocystin (STG)
- Roridin E
- Verrucarin A
- Enniatin B1
- Zearalenone (ZEA)

Molds

- Aspergillus
- Penicillum
- Stachybotrys
- Fusarium



The Great Plains Laboratory, Inc.

William Shaw, Ph.D Director | 11813 W. 77th Street, Lenexa, KS 66214 | (913) 341-8949 | Fax (913) 341-6207

GPL-MYCOTOX

Metabolite	Results (ng/g creatinine)	Common Range of Positive Results
Ochratoxin A	7.32	1.2 - 7.5

1.2 7.5

Ochratoxin A (OTA) is a nephrotoxic, immunotoxic, and carcinogenic mycotoxin. This chemical is produced by molds in the Aspergillus and Penicillium families. Exposure is primarily through contaminated foods such as cereals, grape juices, dairy, spices, wine, dried vine fruit, and coffee. Exposure to OTA can also come from inhalation exposure in water-damaged buildings. OTA can lead to kidney disease and adverse neurological effects. Studies have shown that OTA can lead to significant oxidative damage to multiple brain regions and is highly nephrotoxic. Dopamine levels in the brain of mice have been shown to be decreased after exposure to OTA. Some studies have hypothesized that OTA may contribute to the development of neurodegenerative diseases such as Alzheimer's and Parkinson's. Treatment should be aimed at removing the source of exposure. Agents such as oral cholestyramine, charcoal, and phenylalanine can help prevent the absorption of these toxins from food. Antioxidants such as vitamins A, E, C, NAC, rosmarinic acid, and liposomal glutathione alone or in combination have been shown to mitigate the oxidative effects of the toxin. Bentonite or zeolite clay is reported to reduce the absorption of multiple mycotoxins found in food, including OTA. Studies have also shown that OTA is present in sweat, which supports the use of sauna as a treatment to increase the excretion of OTA. (PMID 17195275, 16621780, 16293235, 27521635, 22069626, 24792326, 22253638, 16140385, 2467220, 16844142, 19148691, 22069658, 16019795, 18286403, 15781206, 11439224, 17092826, 32710148)

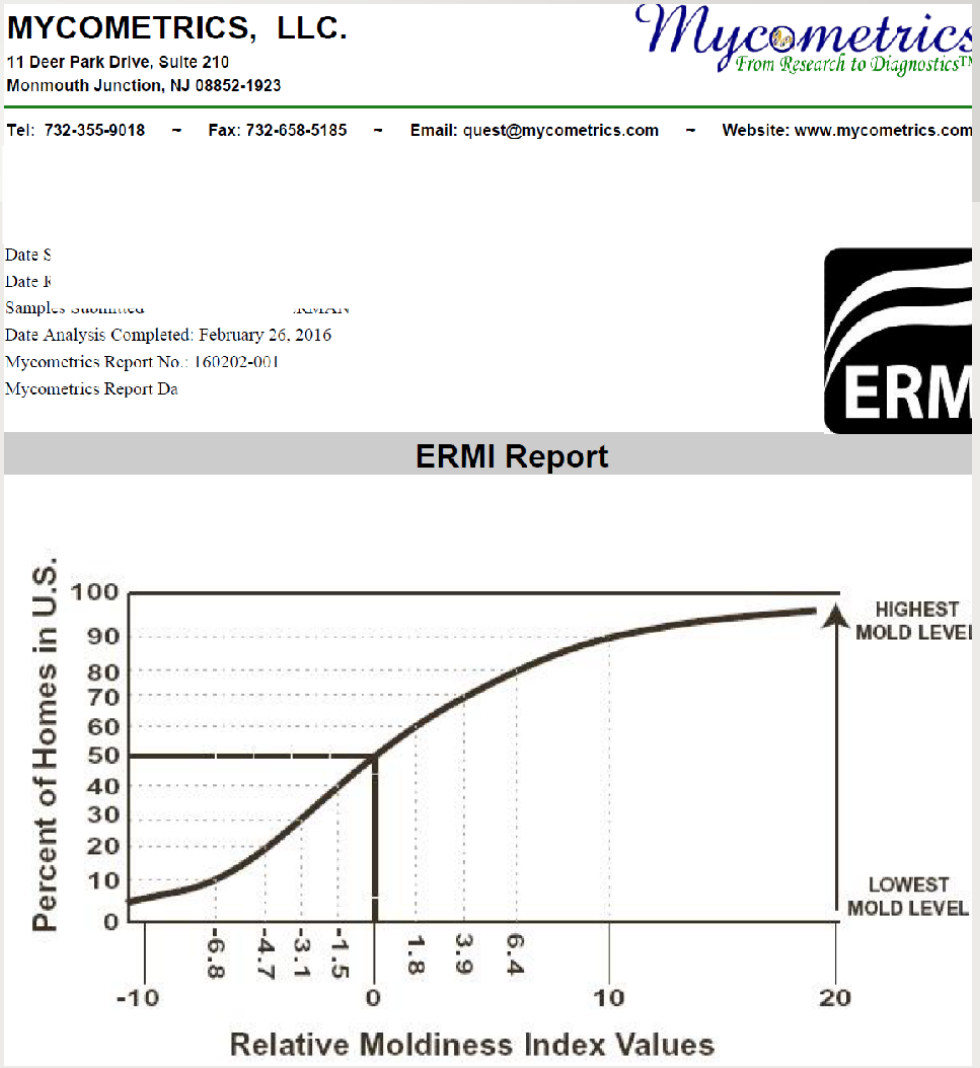
Sterigmatocystin	0	0.1 - 2.25

0.1 2.25

Sterigmatocystin (STC) is a mycotoxin that is closely related to aflatoxin. STC is produced from several species of mold such as Aspergillus, Penicillium, and Bipolaris. STC is considered to be carcinogenic, particularly in the cells of the GI tract and

Building Testing - ERMI

- ERMI – Environmental Relative Mold Index (Use Mycometrics)
- Looks for mold DNA 26 from toxin producing species and compares that to DNA from non-toxic molds.
- EPA holds patent on ERMI testing which uses vacuum canister attachment to collect dust. Swiffer cloth is used for surfaces.



Location	Spore E./mg
Fungal ID \ Sample ID	**EC4275 Kit, LR, MBR**
Aspergillus flavus/oryzae	<1
Aspergillus fumigatus	1
Aspergillus niger	14
Aspergillus ochraceus	ND
Aspergillus penicillioides	7
*Aspergillus restrictus**	ND
Aspergillus sclerotiorum	ND
Aspergillus sydowii	ND
Aspergillus unguis	<1
Aspergillus versicolor	ND
Aureobasidium pullulans	15
Chaetomium globosum	<1
Cladosporium sphaerospermum	37
*Eurotium (Asp.) amstelodami**	3
Paecilomyces variotii	<1
Penicillium brevicompactum	5
Penicillium corylophilum	ND
*Penicillium crustosum**	ND
Penicillium purpurogenum	1
*Penicillium spinulosum**	ND
Penicillium variabile	ND
Scopulariopsis brevicaulis/fusca	1
Scopulariopsis chartarum	<1
Stachybotrys chartarum	<1
*Trichoderma viride**	<1
Wallemia sebi	5
Sum of the Logs (Group I):	**6.63**
Acremonium strictum	ND
Alternaria alternata	8
Aspergillus ustus	<1
Cladosporium cladosporioides 1	96
Cladosporium cladosporioides 2	80
Cladosporium herbarum	130
Epicoccum nigrum	150
*Mucor amphibiorum**	1
Penicillium chrysogenum	23
Rhizopus stolonifer	<1
Sum of the Logs (Group II):	**10.43**
ERMI (Group I - Group II):	**-3.80**

ERMI

ERMI score = Group I- Group II

In environmentally acquired illness cases;

- A score < 2 is considered mold-safe if MSH is normal.
- If MSH is <35 and C4a >20,000, ERMI must be <-1 to be considered safe.
- A score of > 2 is consider mold-unsafe.

Building Testing - HERTSMI 2

- HERTSMI 2 – DNA analysis of the 5 toxin producing molds

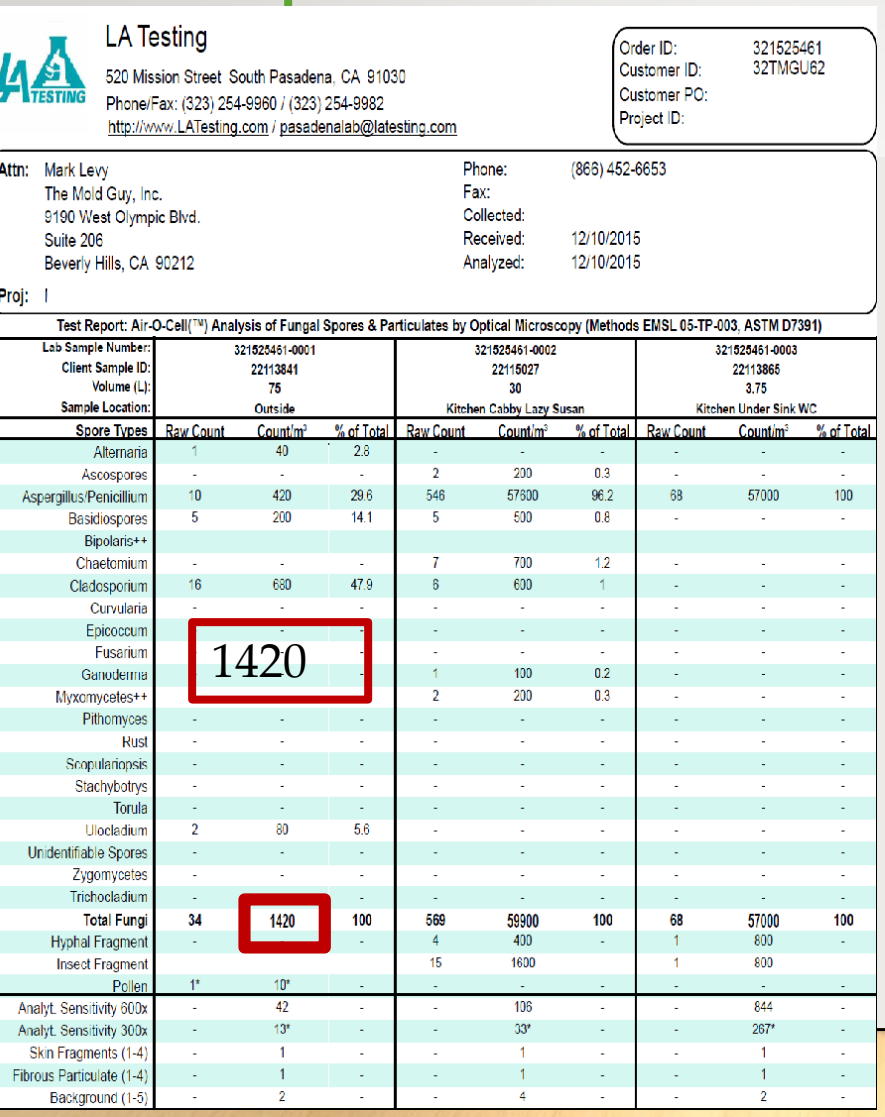
Points	4	6	10
Aspergillus penicilloides	10-99	100-499	500+
Aspergillus versicolor	10-99	100-499	500+
Chaetomium globosum	5-24	25-124	125+
Stachybotrys	5-24	25-124	125+
Wallemia	100-499	500-2499	2500+

- Interpretation:
- <11 statistically safe to enter for those with CIRS
- 11-15 Borderline, clean first and then recheck
- >15 Dangerous for those with CIRS
- Disclaimer: HERTSMI-2 is a building index and doesn't replace careful observation and lab markers.

Other environmental testing options

- The RealTime Laboratories Environmental Mycotoxin Test will determine the presence or absence of 15 of the most common and most toxic mycotoxins, including 9 Macrocyclic Trichothecenes produced by the “Black Mold”, Stachybotrys. Testing is simple, only requiring small amounts of dust or material from AC or heater filters. $299. can be order directly by patient.

Case 1: House Mold Testing



LA Testing
520 Mission Street South Pasadena, CA 91030
Phone/Fax: (323) 254-9960 / (323) 254-9982
http://www.LATesting.com / pasadenalab@latesting.com

Order ID: 321525461
Customer ID: 32TMGU62
Customer PO:
Project ID:

Attn: Mark Levy
The Mold Guy, Inc.
9190 West Olympic Blvd.
Suite 206
Beverly Hills, CA 90212

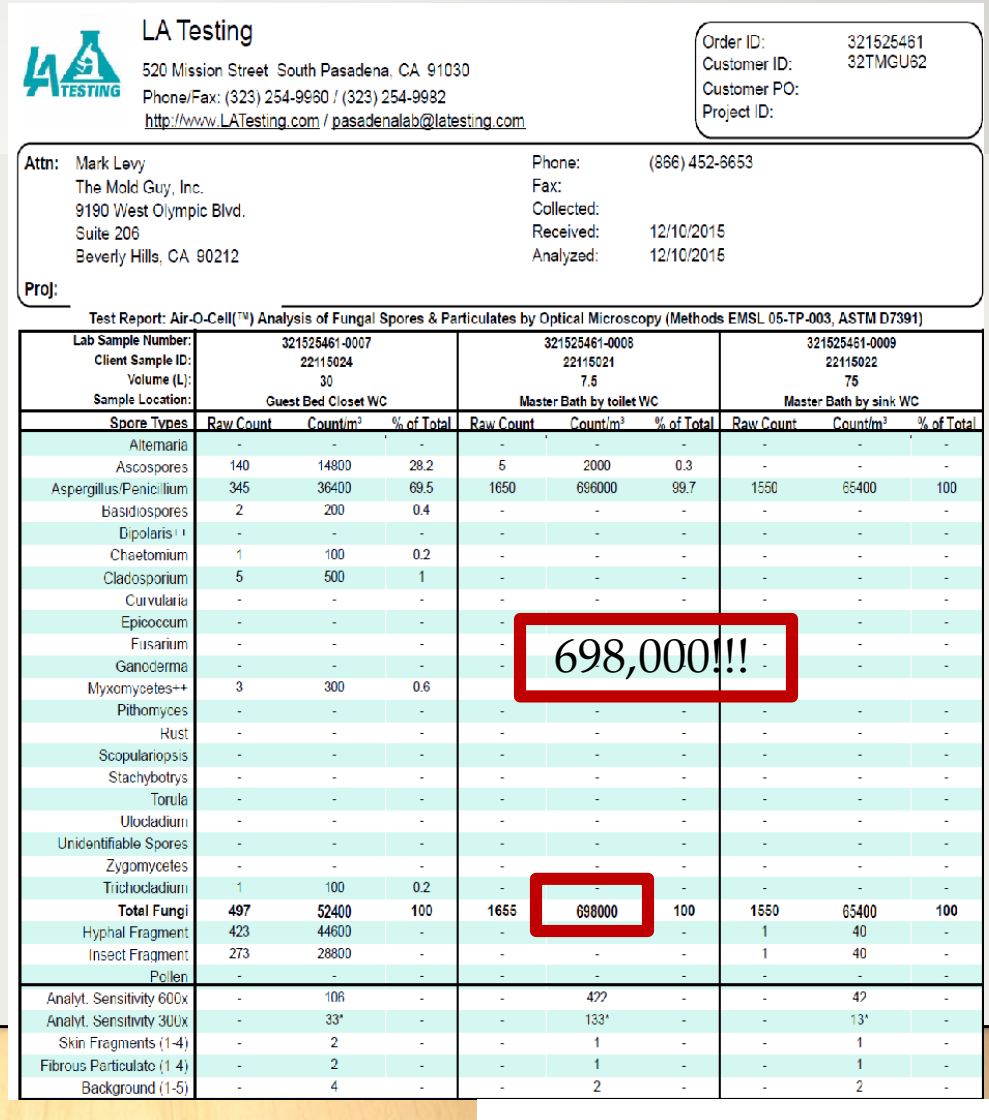
Phone: (866) 452-6653
Fax:
Collected:
Received: 12/10/2015
Analyzed: 12/10/2015

Proj: I

Test Report: Air-O-Cell(™) Analysis of Fungal Spores & Particulates by Optical Microscopy (Methods EMSL 05-TP-003, ASTM D7391)

Lab Sample Number:	321525461-0001			321525461-0002			321525461-0003		
Client Sample ID:	22113841			22115027			22113865		
Volume (L):	75			30			3.75		
Sample Location:	Outside			Kitchen Cabby Lazy Susan			Kitchen Under Sink WC		
Spore Types	Raw Count	Count/m³	% of Total	Raw Count	Count/m³	% of Total	Raw Count	Count/m³	% of Total
Alternaria	1	40	2.8	-	-	-	-	-	-
Ascospores	-	-	-	2	200	0.3	-	-	-
Aspergillus/Penicillium	10	420	29.6	546	57600	96.2	68	57000	100
Basidiospores	5	200	14.1	5	500	0.8	-	-	-
Bipolaris++									
Chaetomium	-	-	-	7	700	1.2	-	-	-
Cladosporium	16	680	47.9	6	600	1	-	-	-
Curvularia	-	-	-	-	-	-	-	-	-
Epicoccum	-	-	-	-	-	-	-	-	-
Fusarium	-	-	-	-	-	-	-	-	-
Ganoderma	-	-	-	1	100	0.2	-	-	-
Myxomycetes++	-	-	-	2	200	0.3	-	-	-
Pithomyces	-	-	-	-	-	-	-	-	-
Rust	-	-	-	-	-	-	-	-	-
Scopulariopsis	-	-	-	-	-	-	-	-	-
Stachybotrys	-	-	-	-	-	-	-	-	-
Torula	-	-	-	-	-	-	-	-	-
Ulocladium	2	80	5.6	-	-	-	-	-	-
Unidentifiable Spores	-	-	-	-	-	-	-	-	-
Zygomycetes	-	-	-	-	-	-	-	-	-
Trichocladium	-	-	-	-	-	-	-	-	-
Total Fungi	**34**	**1420**	**100**	**569**	**59900**	**100**	**68**	**57000**	**100**
Hyphal Fragment	-		-	4	400	-	1	800	-
Insect Fragment				15	1600		1	800	
Pollen	1*	10*	-	-	-	-	-	-	-
Analyt. Sensitivity 600x	-	42	-	-	106	-	-	844	-
Analyt. Sensitivity 300x	-	13*	-	-	33*	-	-	267*	-
Skin Fragments (1-4)	-	1	-	-	1	-	-	1	-
Fibrous Particulate (1-4)	-	1	-	-	1	-	-	1	-
Background (1-5)	-	2	-	-	4	-	-	2	-

1420



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Phone/Fax: (323) 254-9960 / (323) 254-9982
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Order ID: 321525461
Customer ID: 32TMGU62
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Attn: Mark Levy
The Mold Guy, Inc.
9190 West Olympic Blvd.
Suite 206
Beverly Hills, CA 90212

Phone: (866) 452-6653
Fax:
Collected:
Received: 12/10/2015
Analyzed: 12/10/2015

Proj:

Test Report: Air-O-Cell(™) Analysis of Fungal Spores & Particulates by Optical Microscopy (Methods EMSL 05-TP-003, ASTM D7391)

Lab Sample Number:	321525461-0007			321525461-0008			321525461-0009		
Client Sample ID:	22115024			22115021			22115022		
Volume (L):	30			7.5			75		
Sample Location:	Guest Bed Closet WC			Master Bath by toilet WC			Master Bath by sink WC		
Spore Types	Raw Count	Count/m³	% of Total	Raw Count	Count/m³	% of Total	Raw Count	Count/m³	% of Total
Alternaria	-	-	-	-	-	-	-	-	-
Ascospores	140	14800	28.2	5	2000	0.3	-	-	-
Aspergillus/Penicillium	345	36400	69.5	1650	696000	99.7	1550	65400	100
Basidiospores	2	200	0.4	-	-	-	-	-	-
Bipolaris++	-	-	-	-	-	-	-	-	-
Chaetomium	1	100	0.2	-	-	-	-	-	-
Cladosporium	5	500	1	-	-	-	-	-	-
Curvularia	-	-	-	-	-	-	-	-	-
Epicoccum	-	-	-	-	-	-	-	-	-
Fusarium	-	-	-	-	-	-	-	-	-
Ganoderma	-	-	-	-	-	-	-	-	-
Myxomycetes++	3	300	0.6						
Pithomyces	-	-	-	-	-	-	-	-	-
Rust	-	-	-	-	-	-	-	-	-
Scopulariopsis	-	-	-	-	-	-	-	-	-
Stachybotrys	-	-	-	-	-	-	-	-	-
Torula	-	-	-	-	-	-	-	-	-
Ulocladium	-	-	-	-	-	-	-	-	-
Unidentifiable Spores	-	-	-	-	-	-	-	-	-
Zygomycetes	-	-	-	-	-	-	-	-	-
Trichocladium	1	100	0.2	-	-	-	-	-	-
Total Fungi	**497**	**52400**	**100**	**1655**	**698000**	**100**	**1550**	**65400**	**100**
Hyphal Fragment	423	44600	-	-	-	-	1	40	-
Insect Fragment	273	28800	-	-	-	-	1	40	-
Pollen	-	-	-	-	-	-	-	-	-
Analyt. Sensitivity 600x	-	106	-	-	422	-	-	42	-
Analyt. Sensitivity 300x	-	33*	-	-	133*	-	-	13*	-
Skin Fragments (1-4)	-	2	-	-	1	-	-	1	-
Fibrous Particulate (1-4)	-	2	-	-	1	-	-	1	-
Background (1-5)	-	4	-	-	2	-	-	2	-

698,000!!!

Kelly K. McCann, MD

Testing and remediation

- The test is only as good as the sample collection.
- If the musty smell is in the bathroom, sampling in the living room may not reflect the full extent of the problem.
- Utilize an qualified inspector who will use the appropriate testing methods available, including ERMI or HERSTMI2, air samples and wall samples when indicated.
- Certified Indoor Environmental Professional
- Read the Consensus Statement for indoor environmental professional (IEP) on inspection and remediation. https://www.survivingmold.com/docs/IEP_CONSENSUS_04_12_16.pdf
- An inspector should never be the remediator. Often the remediator is not the contractor to repair the work. Some situations require plumbers and general contractors.
- Patients and health care practitioners need to advocate for themselves. Very few IEPs, remediators or contractors understand the level of remediation required for HLA susceptible persons.

Treatment of Mold Exposure

Get in your car and drive away! (although often the car is contaminated as well)

- Remediate the house or move.
- Test the new house, if able.
- Focus on healing the body.

- GET AWAY FROM THE MOLDY ENVIRONMENT!!
- Avoid other moldy environments.
- Avoid other environmental toxins; such as pesticides, formaldehyde, fragrances, plastics, chemicals, heavy Metals, EMR
- Leave any belongings that can't be cleaned. All cloth and porous surfaced materials will be difficult to clean.
- Any items kept, should be cleaned and placed in storage for several months to ensure no mold growth.
- Use High Quality HEPA Air filters and be sure to change out the filters after the mold/remediation

Mold Removing Options

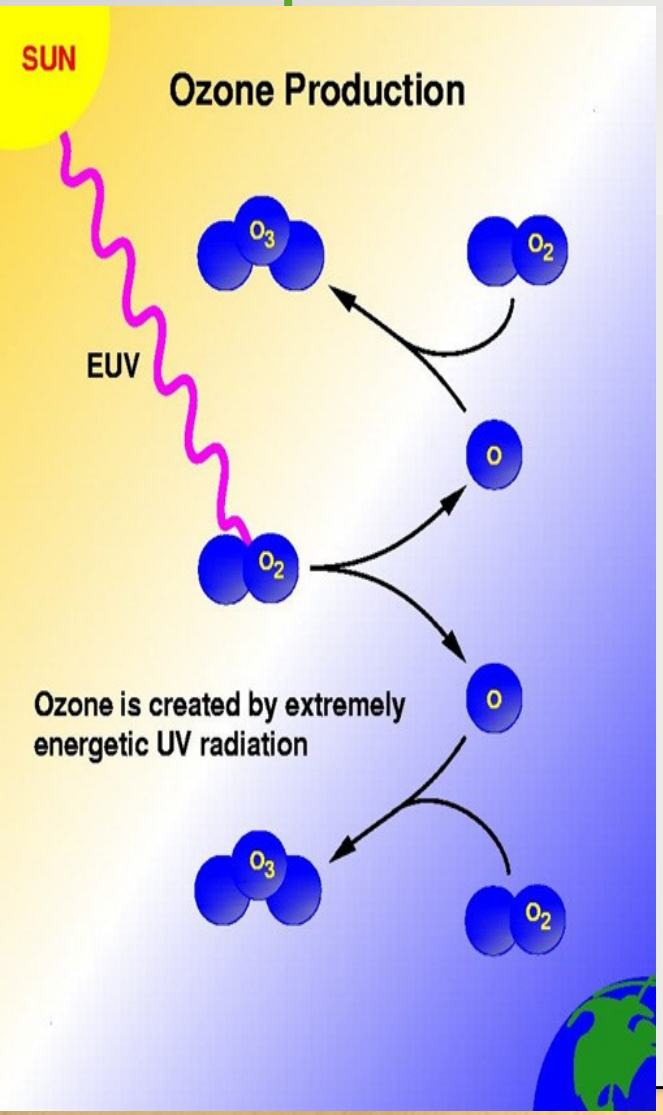
- Bleach
- Ethanol
- Vinegar
- Ammonia
- Hydrogen peroxide
- Detergent
- Baking soda
- Tea tree oil
- Grapefruit seed extract

Rogawansamy, et al. Evaluation of antifungal agents for the treatment of fungal contamination in indoor air environments. In J Environ Res Public Health 2015 June 2;12(6): 6319-32.

LOE: B

Kelly K. McCann, MD

What about Ozone?



- Used to disinfect by inactivating bacteria, viruses, fungi, yeast and protozoa
- Ozone used to treat contaminated grains, including wheat, maize, grapes, peanuts, sausages, cheeses by reducing mold and mycotoxins.
- Used in dental medicine and wound care

PMID: 22470237, 20477724, 26812055, 27287337, 26041242, 24982899, 24374809, 24282818

LOE: A

Kelly K. McCann, MD

Effect of Ozonation on Furniture Dust

- Furniture from 46 moisture-damaged sites totaling 73 sample pairs
- Ozone vs. steam clean plus ozone – not statistically different
- Assessed microbes in dust via DNA PCR and immunotoxic effects in vitro.
- Overall viable microbes decreased with both methods, with some persistence of fungal materials.
- Nitric oxide, Cytokines TNF alpha and IL-6 were lower after treatment.

- Huttunen, et al. The Effect of ozonation on furniture dust. Science of the otal Environment 408 (2010) 2305-11.

UV light /Air reactors

- www.hitechairsolutions.com
- www.airoasis.com
- The Molecules that it destroys are ALL organic matter, Viruses, Bacteria, Mold, Mildew, Odors, off gasses, formaldehyde, as well as many others.

- HOW THE AIR REACTOR WORKS

- "We use UV lighting (not to kill with) but to separate the light rays into different colors. What we have found with our research is that once the light rays are separated into different colors, different molecules attach to different color of light rays. We then developed a reactor pad, for these Molecules to travel through. While they are attached to different colors of light rays and travel through our specially designed reactor pad, it actually changes the molecular structure of that Molecule so that it is not what it was. Basically it implodes the molecule so that it does not exist as the molecule that it once was." - from the website…

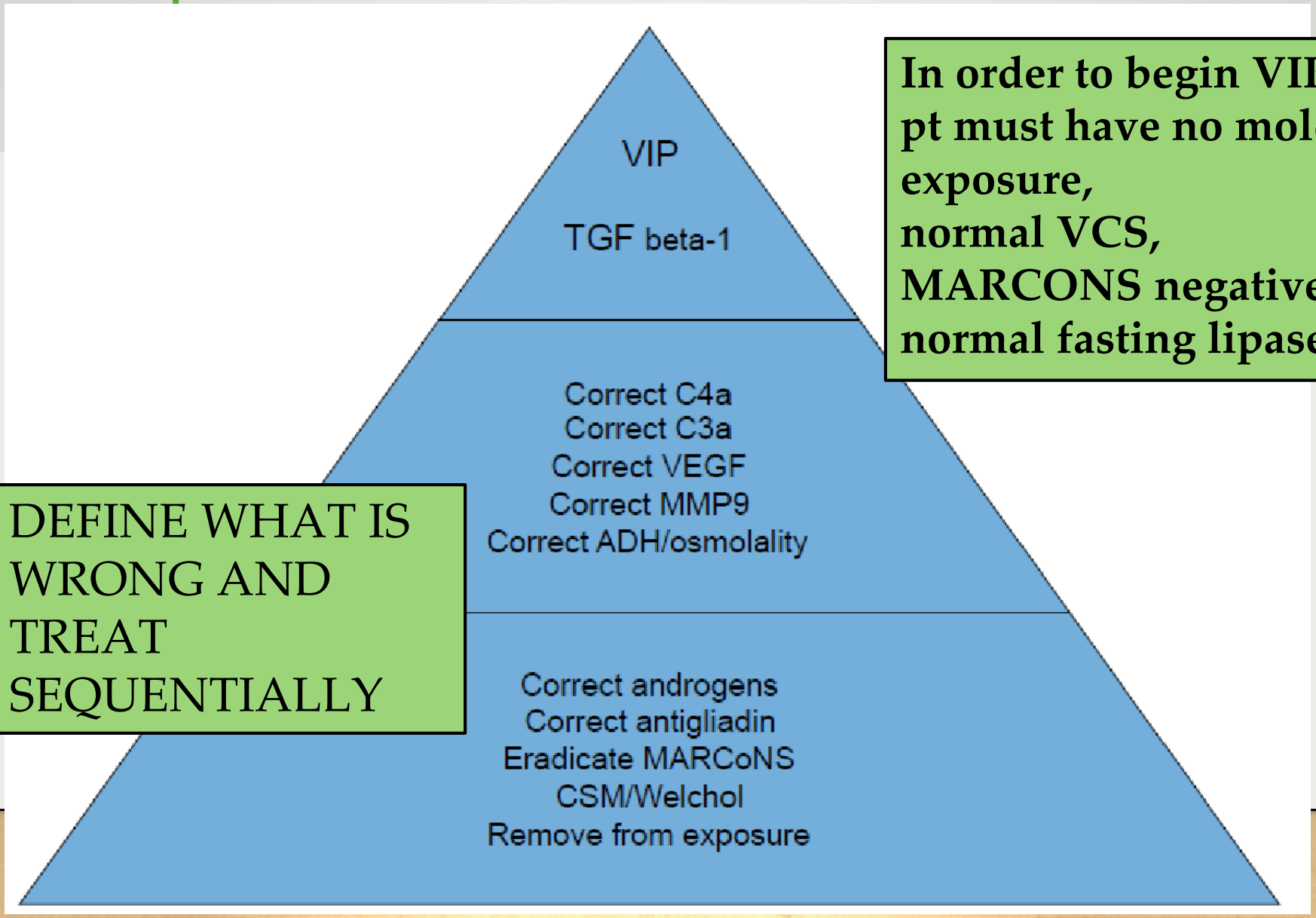
LOE: C

"How damp is this place?
Let me put it this way: I use mold and
mildew remover as a skin care product."

Mold and Mycotoxin Treatment Principles

- Reduce inflammation
- Detoxify - Remove the toxins
- Repair the gastrointestinal tract
- Correct cellular immune dysfunct
- Deal with autoimmunity
- Reduce colonization/ infection
- Rebuild mitochondria
- Restore the nervous system
- Improve hypoperfusion
- Balance hormones and adrenals
- Replenish nutrients
- Optimize Methylation
- Reset limbic system
- Foster healthy lifestyle choices

Shoemaker Treatment Protocol



In order to begin VIP, pt must have no mold exposure, normal VCS, MARCONS negative, normal fasting lipase.

DEFINE WHAT IS WRONG AND TREAT SEQUENTIALLY

Cholestyramine (CSM)

Cholestyramine– Insoluble quaternary ammonium exchange bile acid resin binder FDA approved for > 50 years to lower cholesterol. It is a long polystyrene chain with side groups. Positively charged, it binds to the mycotoxins which are ionophores containing both hydrophilic and hydrophobic aspects.

Off-label use of CSM. Consider informed consent.

- 4 grams four times daily. 30 minutes before fatty meal.
- Wait 90 minutes after eating. Mix in water or juice
- Start low and go slow with sensitive patients
- GI side effects include bloating, constipation
- Commercially available product contains aspartame. Compounding pharmacies can make alternatives.

Cholestyramine Evidence

Cholestyramine has been shown in studies to bind to:

- Cyanobacteria
- Dinoflagellates
- Clostridia Difficile toxin
- Borrelia burdorferi
- Babesia microti
- Ochratoxin A
- Fumonisins (mycotoxins)
- Helicobacter pylori

- Falsafi T, et al. Culture of Helicobacter pylori from stool samples in children. Can J Microbiol. 2007 Mar;53(3):411-6.
- Hope JH, Hope BE. A review of the diagnosis and treatment of Ochratoxin A inhalational exposure associated with human illness and kidney disease including focal segmental glomerulosclerosis. J Environ Public Health. 2012;2012:835059.
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Sequestering Agents

- These non-absorbable agents bind the mycotoxins and prevent them from entering the enterohepatic circulation, eventually lowering the total load. These need to be taken on an empty stomach away from food and supplements. Ideally 30-60 minutes before and 90+ minutes after.
- **Activated charcoal –** 2-3 caps once or twice daily. Build up dose slowly to avoid side effects. May bind aflatoxins, zearalenone and DON, and more effective for trichothecenes.
- **Bentonite Clay –** 2-3 caps once or twice daily. Can take liquid. Build up slowly. More drying and constipation inducing. Give adequate magnesium to soften stools. More effective for aflatoxins.

Sequestering agents

- **Chlorophyll-Chlorella –** Some practitioners have found helpful. 20 tabs three times daily 30 minutes before a meal.
- **Diatomaceous earth –** appears to bind aflatoxin, T-2 toxin, zearalenone and ochratoxin in vitro and in vivo in animal studies. Start 1 tsp once daily and work up to 1 tbsp TID

Denli M, et al. Efficacy of activated diatomaceous clay in reducing the toxicity of zearalenone in rats and piglets. J Anim Sci. 2015 Feb;93(2):637-45.

Bhatti SA, Comparative efficacy of Bentonite clay, activated charcoal and Trichosporon mycotoxinivorans in regulating the feed-to-tissue transfer of mycotoxins. J Sci Food Agric. 2017 Jul 11.

Dalie, et al. Lactic acid bacteria-Potential for control of mold growth and mycotoxins. Food Control 2010. 21(4) 370-80.

Del Pilar, et al. Activated carbons as potentially useful non-nutritive additives to prevent the effect of fumonisin B1 on sodium bentonite activity against chronic aflatoxicosis. Food Addit Contam Part A. 2016 May 31:1-10.

Kolosova. Substances for the reduction of the contamination of feed by mycotoxins. World Mycotoxin Journal 2011. 4(3): 225-56

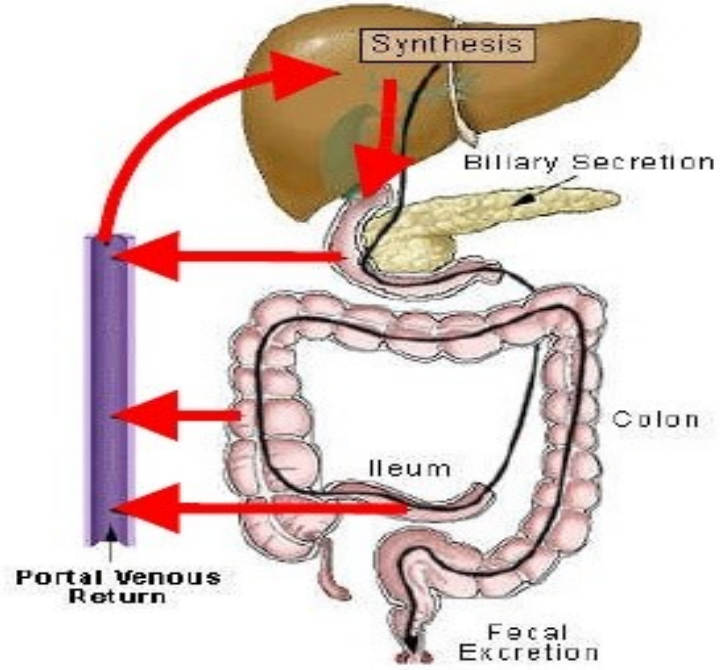
Pappas, et al. Role of bentonite binders in mycotoxins in chicken diets. Br Poult Sci 2016 May 12.

Enterohepatic Circulation

Stop Reabsorption

Accumulation

Enterohepatic Circulation

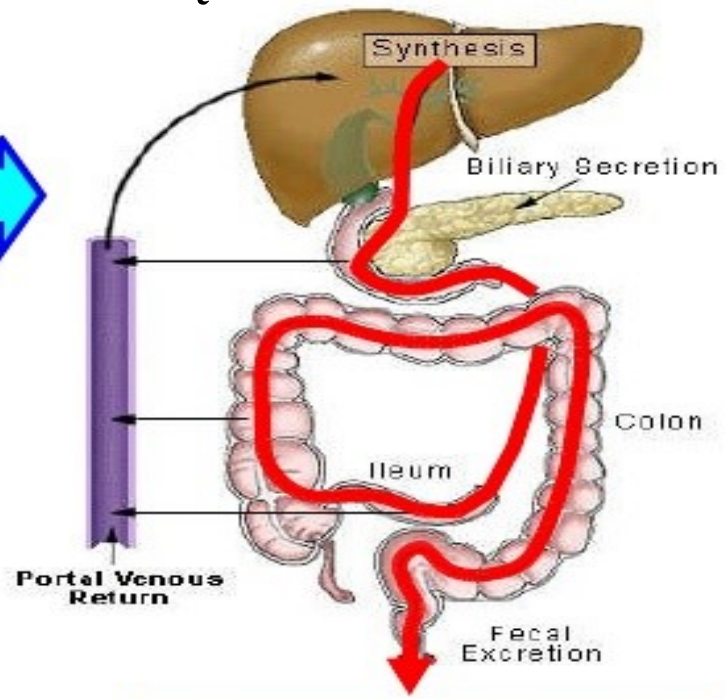


LOW EXCRETION

Binders

Inhibi t Re-

Enterohepatic Circulation



HIGH EXCRETION!

Shoemaker Protocol Steps

- 1. **Remove from mold exposure**
- 2. Perform **ERMI** testing
- 3. Treat with **Cholestyramine** (CSM) 4 grams 4 times daily or Welchol 2 tabs TID or 3 tabs BID with meals. Start slow and work up. Treat constipation! TAKE AWAY FROM FOOD AND SUPPLEMENTS.
- Treat for 1 month and then move on to step 4. Continue CSM.
- 4. Treat **MARCONS** with BEG nasal spray (Bacitracin/EDTA/Gentamycin) or BEC spray (Clindamycin) 2 sprays TID for 4-6 weeks. Or Silver and EDTA. Repeat test for cure. If persists, consider dental cavitation source, canine or close contact source or ongoing mold exposure. Ramp up slowly and support detox.
- Obtain BEG spray from Hopkinton Drug in Hopkinton, MA

Shoemaker RC, House DE. Sick building syndrome (SBS) and exposure to water-damaged buildings: time series study, clinical trial and mechanisms.
Neurotoxicol Teratol. 2006 Sep-Oct;28(5):573-88.

Shoemaker treatment protocol

- 5. **Correct anti-gliadin**, anti-cardiolipin ab. Eliminate gluten when warranted. Treat hypercoagulability.
- 6. **Correct androgens**. If estradiol levels too high, consider aromatase inhibitor. Inflammation and low VIP drives aromatase shunting testosterone to estradiol. Can support with DHEA. Androgens tend to self correct with toxin clearance. Testosterone replacement, in these patients, often causes more problems than it solves.
- 7. **Correct ADH.** Replete minerals when osmolality is low (<280) if ADH is low and osmolality high >295, consider DDAVP (vasopressin) with close supervision.
- 8. **Correct MMP-9 and VEGF.** Amylose-free diet and 2.4g EPA +1.8g DHA divided BID. Actos 15-45 mg was recommended previously.

Chaturvedi S, McCrae KR. Diagnosis and management of the antiphospholipid syndrome. Blood Rev. 2017 Jul 30.

Shoemaker treatment protocol

- 9. **Correct C4a.** Off-label treatment includes Procrit (Epogen) Has black box warnings.
- 10. **Correct TGF beta1**. Losartan increases a patient's T reg cells by slowing conversion of T reg into Th17 cytotoxic T cells, which in turn lowers TGF beta-1 levels. This is off label use.
- 11. **Replace VIP.** Ensure no exposure and no MARCONS. Check pre and post treatment labs in office.
- VIP nasal spray 50 mcg.
- One nasal spray - alternating nostrils -4 times daily.
- Obtain from Hopkinton Drug

Internal Medicine Review- Intranasal VIP safely restores volume to multiple grey matter nuclei in patients with CIRS- April 2017 Shoemaker, R., Katz, D., Ackerley, M., Rapaport, S., McMahon, S., Berndtson, K., Ryan, J.

Shoemaker R, House D, Ryan J. Vasoactive intestinal polypeptide (VIP) corrects chronic inflammatory response syndrome (CIRS) acquired following exposure to water-damaged buildings. Health 2013; 3: 396-401.

“You've got a real fungus problem. You'll have to move out until it's taken care of.”

Nutrient Supportive Treatments

- **Quercetin ameliorate Ochratoxin A toxicity in cell cultures.**
- **N-Acetyl Cysteine (NAC) 1800mg can lower TGF beta1 and protect intestinal barrier function.**
- **Liposomal glutathione - different formulations available.**
- **Co Q 10 100mg once or twice daily**
- **Methyl B12, methylfolate or folinic acid for methylation support**

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Berk M. Biol Psychiatry. 2008 Sep 15;64(6):468-75.

El Golli. Induction of Hsp 70 in Vero Cells in response to mycotoxins: Cytoprotection by Vitamin E. Toxicology letters 2006. 166(2): 122-130.

Guilford FT, Hope J. Deficient glutathione in the pathophysiology of mycotoxin-related illness. Toxins (Basel). 2014 Feb 10;6(2):608-23.

Raghubeer, et al. Resveratrol ameliorates OTA toxicity kidney cells. J Cell BioChem.2015 Dec;116(12):2947-55.

Ramyaa, et al. Quercetin modulate OTA-induced oxidative stress. BiochimBiophysActa.2014Jan;1840(1):681-92

Ranaldi. Intracellular zinc stores protect the intestinal epithelium from Ochratoxin A toxicity. Toxicology in vitro. 2009. 23(8): 516-21.

Speight,Neal. htttps://www.crcpress.com/Advancing-Medicine-with-Food-and-Nutrients-Secondedition/

Nutrient Supportive Treatments

- **Zinc – must balance with copper if given in high amounts**
- **Vitamin E – 400 iu daily**
- **Butyrate inhibits yeast and yeast biofilms, inhibits tumorigenesis, improves gut integrity**
- **Curcumin 1000mg twice daily or more to reduce inflammation and break down biofilms.**
- **Green tea polyphenol extract or green tea 2-5 cups daily has been shown in a number of trials to reduce MMP9.**

Nutrient Supportive therapies

- **Pterostibene has also been shown to lower MMP9.**
- **Resveratrol 100mg BID. Lowers TGFbeta1, Alters Treg/TH17.**
- **Taurine 1-2 grams/day. Taurine has anti-inflammatory and immunomodulatory activity.**

- Abrigo J, etal. Transforming growth factor type beta (TGF-β) requires reactive oxygen species to induce skeletal muscle atrophy. Cell Signal. 2016 May;28(5):366-76.
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- Park JW, et al. Green tea polyphenol (-)-epigallocatechin gallate reduces matrix metalloproteinase-9 activity following transient focal cerebral ischemia. J Nutr Biochem. 2010 Nov;21(11):1038-44.
- Shahahzad, M. Utilising polyphenols for the clinical management of Candida albicans biofilms. Int J Antimicrob Agents. 2014 Sep;44(3):269-73.
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Supportive Treatment of Mycotoxicosis

- Create a bedroom sanctuary
- Sauna – far infrared or traditional
- Epsom salt baths
- Body washes with charcoal or clay for itchy skin
- Sleep support
- Physical therapy and massage
- Colon hydrotherapy and coffee enemas
- "Bottoms Up" therapy
- Oxygen therapy
- Low Dose Naltrexone for immune dysregulation
- Phosphatidyl Choline – oral and IV forms

Kane. Detoxx
Rea, WJ. Treatment of patients with mycotoxin disease. Toxicol Ind Health. 2009 Oct-Nov;25(9-10):711-4.

Sauna

Compounds released in sweat

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

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

Membrane Stabilizing Diet: Modified Ketogenic Diet for Optimal Neurometabolic Health

Permitted foods

- Protein at every meal
- Raw, organic ground seeds and nuts and butters
- Free range eggs
- Lentils and legume pastas
- Paleo breads and wraps
- Limited starchy vegetables
- Organic ghee, butters and cheeses if tolerated
- Fruits – mostly berries, kiwi
- Veggies
- Bone Broths
- Cook foods in coconut oil or ghee

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Membrane Stabilizing Diet: Modified Ketogenic Diet for Optimal Neurometabolic Health

Omitted foods

- All grains, esp gluten
- No corn or rice
- No peanuts or peanut butter
- No mustard (often contaminated with molds and contain VLCFA)
- Avoid commercial oils extracted under heat such as canola oil
- No sugar or sweeteners, No sodas or diet drinks
- No hybridized oleic oils (olive)
- No moldy foods, No GMO foods
- No dried fruits, high sugar fruits
- NO fast food
- NO Kombucha, No mushrooms

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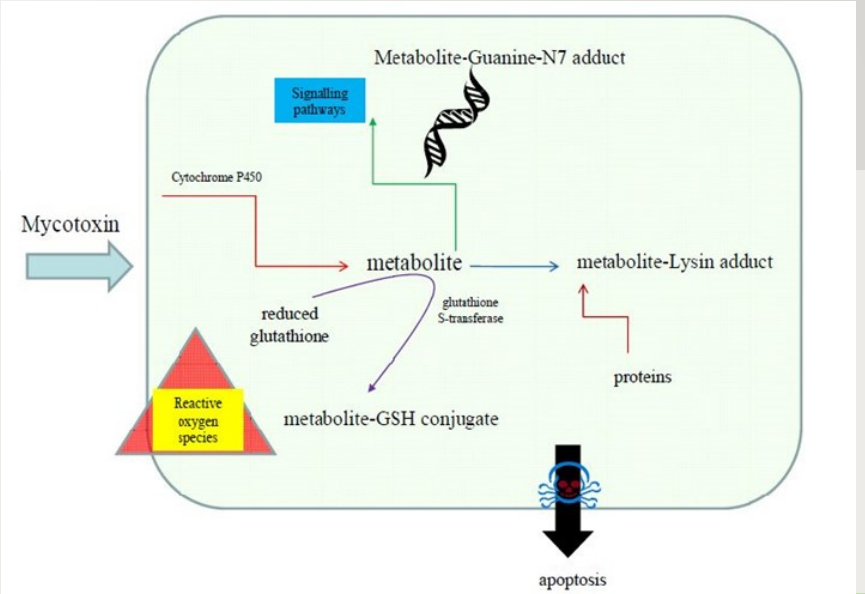
Mold and Mycotoxins Induce Oxidative Stress and Inflammation

- Chronic mold exposures induce changes in inflammatory and immune responses to specific mold and mycotoxin challenges.
- Mold exposed patients had different cytokine and chemokine profiles when their peripheral blood mononuclear cells (PBMCs) were exposed to mold vs non-exposed controls.



- ROS are cleared from the cell by the action of superoxide dismutase (SOD), catalase (CAT), or glutathione peroxidase (GPx). The main damage to cells results from the ROS-induced alteration of macromolecules such as polyunsaturated fatty acids in membrane lipids, proteins, and DNA.

Hossam El-Din M. Mycotoxins-Induced Oxidative Stress and Disease DOI: 10.5772/51806
Rosenblum Litchenstein. PloS one 2015 May; 10(5).

Mold and Mycotoxins Induce Oxidative Stress and Inflammation

- Mold toxins may suppress the immune system through a balance of cytotoxicity and altered Th1/Th2 balance, with increase Th1. The alteration of immune responses due to chronic mold exposures may also adversely affect the ability of the immune system to fight infections and other environmental challenges.
- This may explain patient complaints of concurrent susceptibility to infectious organisms and enhanced responses to chemical irritants.

Hossam El-Din M. Mycotoxins-Induced Oxidative Stress and Disease DOI: 10.5772/51806
Rosenblum Litchenstein. PloS one 2015 May; 10(5).

"They were my mother's microbes...
and now they're yours!"

Mold, Mycotoxin, Fungal Infections and the Mycobiome

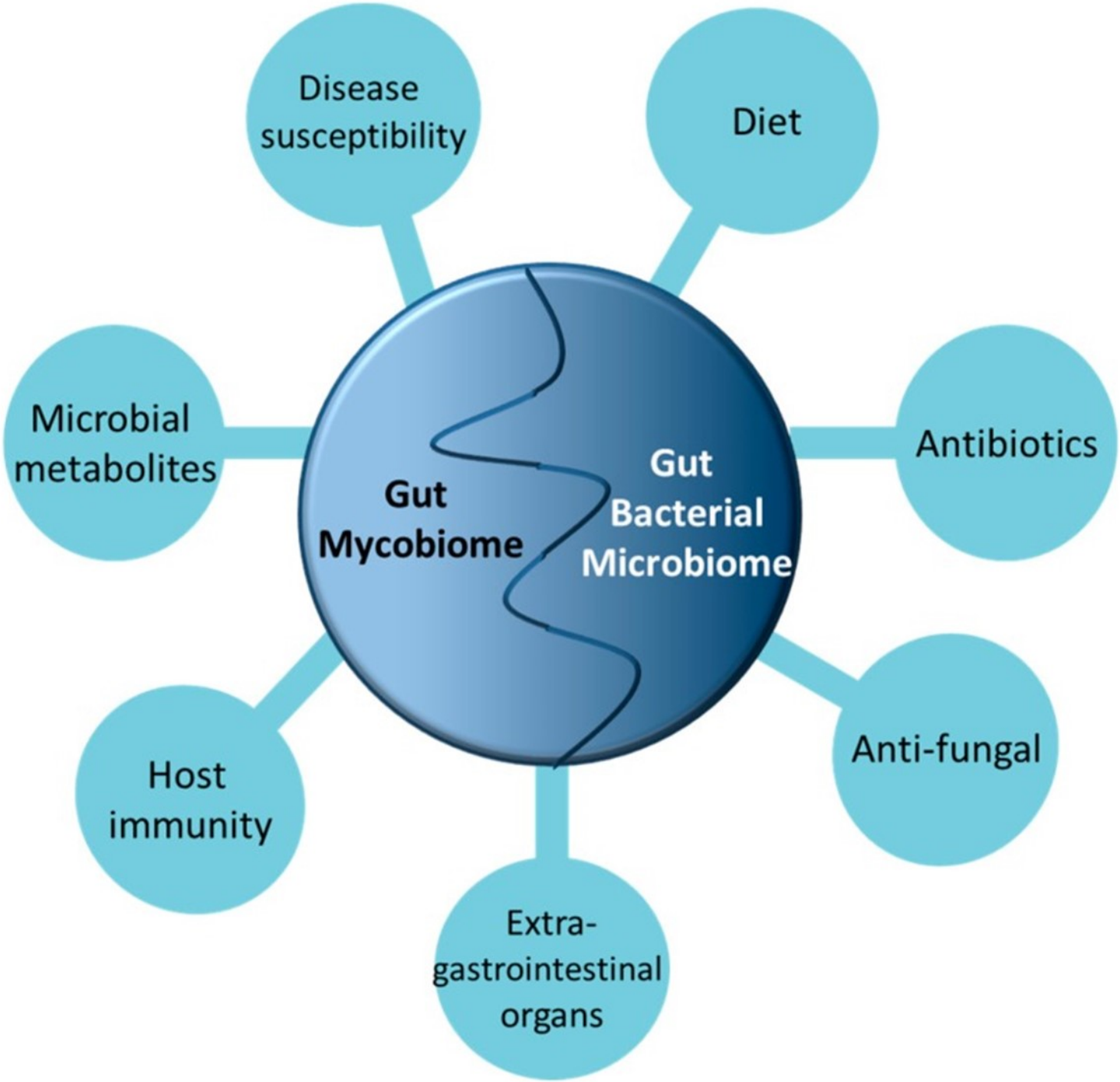
- **Mycotoxins (ingested or inhaled) in the GI tract**
  - **Affect regeneration and repair of intestinal epithelial cells**
  - **Increase intestinal mucosal permeability**
  - **Alter immune system response**
  - **Changes the composition of intestinal bacterial communities (and possibly the fungal mycobiome)**
  - **Are carcinogens in hepatocellular and esophagogastric cancers**
- **Commensal mycobiota may turn pathogenic**
- **Fungal pathogens elicit complex innate and adaptive immune responses**
- **Some genetic polymorphisms/predispositions increasing susceptibility to systemic fungal infections and induce chronic inflammation resulting in IBD colitis.**

Sam, QH, et al. The Fungal Mycobiome and its Interaction with the Gut Bacteria in the Host. Int J. Mol. Sci 2017; 18, 330.
Wang, 2014.

Fungal mycobiome

- **Fungal mycobiota important in GI tract**
- **70% of health adults have fungal organisms in GI tract**
- **Fungi also found in vagina, oral cavity, lungs, skin – intense research area**
- **Metagenomic analysis – only 0.1% of fecal microbial DNA was eukaryotic.**
- **Mycobiome affected similarly to microbiome. (age, BMI, birth circumstance, diet, geography, toxicants, tobacco, antibiotic usage, etc.)**
- **Some mycobiome from food sources**
- **Fungal-bacterial interactions very complex. Synergistic and antagonist**
- **Fungus as pathogen. Fungus as commensal perhaps not as clear cut as once assumed.**

Wang, ZK et al. Review article: fungal microbiota and digestive diseases. Aliment Pharmacol Ther 2014; 39:751-66.


Disease susceptibility
Diet
Microbial metabolites
Antibiotics
Gut Mycobiome
Gut Bacterial Microbiome
Host immunity
Anti-fungal
Extra-gastrointestinal organs

frontiers in Immunology

HYPOTHESIS AND THEORY
published: 09 January 2017
doi: 10.3389/fimmu.2016.00672

An Evolutionary-Based Framework for Analyzing Mold and Dampness-Associated Symptoms in DMHS

*Alvaro Daschner**

Instituto de Investigación Sanitaria, Hospital Universitario de la Princesa, Servicio de Alergia, Madrid, Spain

Among potential environmental harmful factors, fungi deserve special consideration. Their intrinsic ability to actively germinate or infect host tissues might determine a prominent trigger in host defense mechanisms. With the appearance of fungi in evolutionary history, other organisms had to evolve strategies to recognize and cope with them. Existing controversies around dampness and mold hypersensitivity syndrome (DMHS) can be due to the great variability of clinical symptoms but also of possible eliciting factors associated with mold and dampness. An hypothesis is presented, where an evolutionary analysis of the different response patterns seen in DMHS is able to explain the existing variability of disease patterns. Classical interpretation of immune responses and symptoms are addressed within the field of pathophysiology. The presented evolutionary analysis seeks for the ultimate causes of the vast array of symptoms in DMHS. Symptoms can be interpreted as induced by direct (toxic) actions of spores, mycotoxins, or other fungal metabolites, or on the other side by the host-initiated response, which aims to counterbalance and fight off potentially deleterious effects or fungal infection. Further, spores and components, unlike other bioaerosol particles, are more heterogeneous and biologically dynamic particles. Scientific advances have provided us with some analytic procedures to estimate

OPEN ACCESS

Edited by:
Kirsi Vaali,
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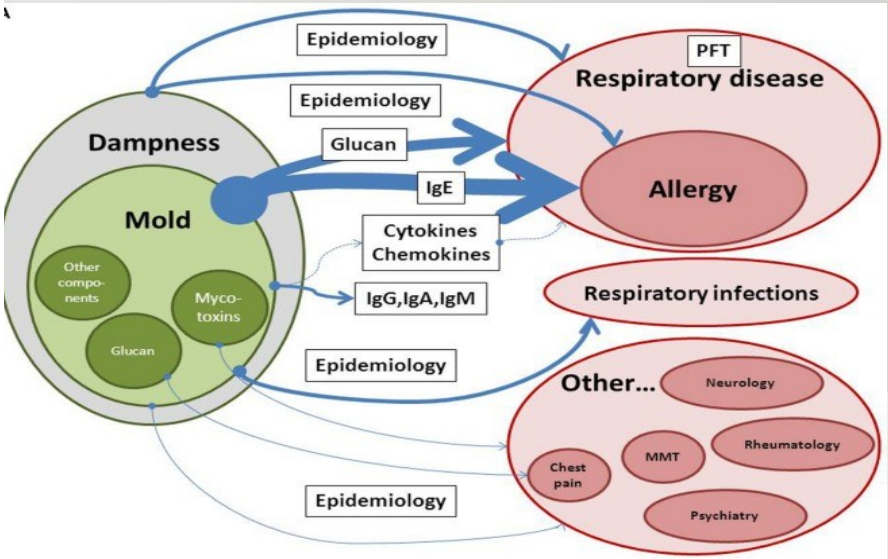
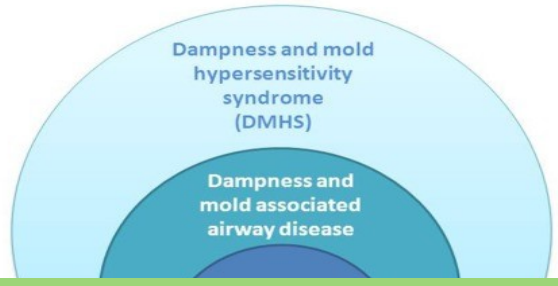




Relationship between humans and fungi denotes a paradox. Invasive fungal infections are rare…(but) the absence of a host-parasite relationship is associated with higher pathogenicity. Humans have a higher investment in prevention and elimination of these potential invaders, thus the pro-inflammatory response of the host is magnified.

Daschner 2017

Front. Immunol. 7:672.
doi: 10.3389/fimmu.2016.00672

Kelly K. McCann, MD

www.nature.com/scientificreports

SCIENTIFIC REPORTS

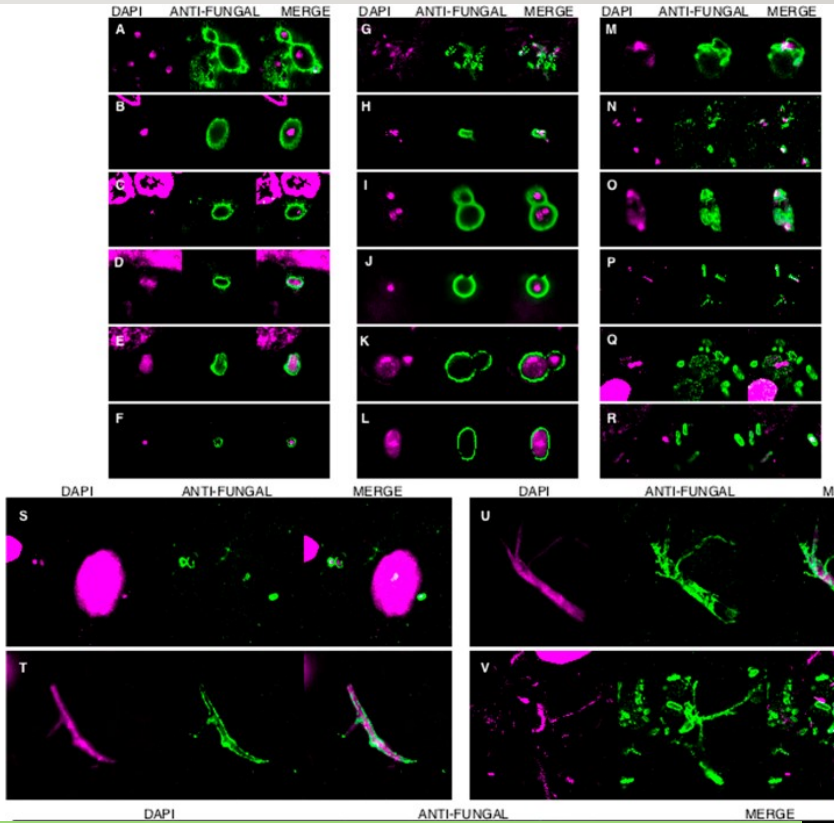
OPEN

Different Brain Regions are Infected with Fungi in Alzheimer's Disease

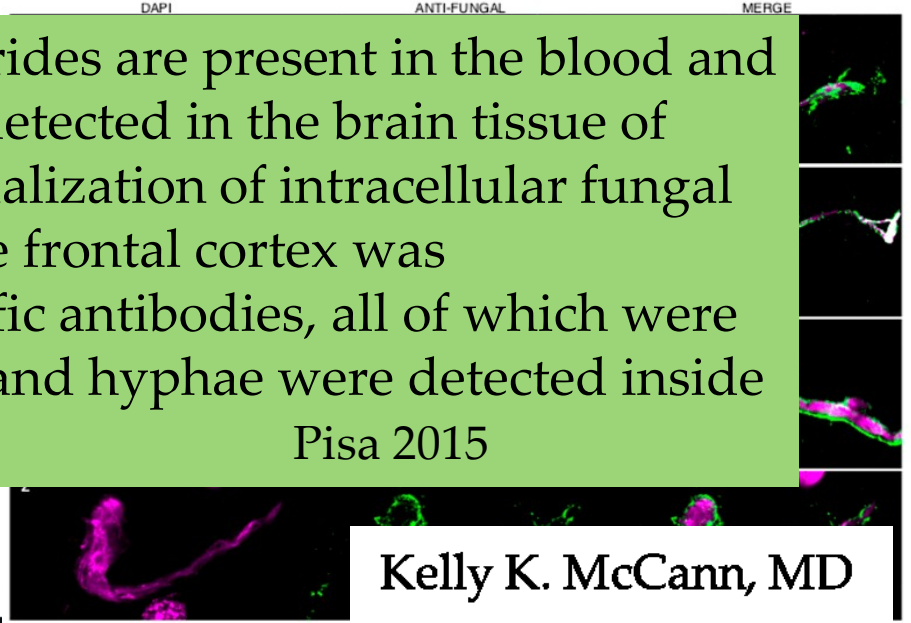
Received: 19 May 2015
Accepted: 15 September 2015
Published: 15 October 2015

Diana Pisa[1], Ruth Alonso[1], Alberto Rábano[2], Izaskun Rodal[2] & Luis Carrasco[1]

The possibility that Alzheimer's disease (AD) has a microbial aetiology has been proposed by several researchers. Here, we provide evidence that tissue from the central nervous system (CNS) of AD patients contain fungal cells and hyphae. Fungal material can be detected both intra- and extracellularly using specific antibodies against several fungi. Different brain regions including external frontal cortex, cerebellar hemisphere, entorhinal cortex/hippocampus and choroid plexus contain fungal material, which is absent in brain tissue from control individuals. Analysis of brain sections from ten additional AD patients reveals that all are infected with fungi. Fungal infection is also observed in blood vessels, which may explain the vascular pathology frequently detected in AD patients. Sequencing of fungal DNA extracted from frozen CNS samples identifies several fungal species. Collectively, our findings provide compelling evidence for the existence of fungal infection in the CNS from AD patients, but not in control individuals.



Fungal proteins and polysaccharides are present in the blood and fungal proteins and DNA was detected in the brain tissue of 100% of AD patients. Direct visualization of intracellular fungal infection in the neurons from the frontal cortex was demonstrated with fungal-specific antibodies, all of which were absent in controls. Fungal cells and hyphae were detected inside capillaries and blood vessels. Pisa 2015



necrosis factor α and interferon γ, are elevated in the brain of AD patients, suggesting an increased immune response[17–19]. These observations have led to the speculation that AD has an autoimmune aetiology[20]. Many investigators have also considered the idea that AD is an infectious disease, or at least that

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IVYSPRING INTERNATIONAL PUBLISHER

International Journal of Biological Sciences

2015; 11(5): 546-558. doi: 10.7150/ijbs.11084

Research Paper

Evidence for Fungal Infection in Cerebrospinal Fluid and Brain Tissue from Patients with Amyotrophic Lateral Sclerosis

Ruth Alonso[1], Diana Pisa[1], Ana Isabel Marina[1], Esperanza Morato[1], Alberto Rábano[2], Izaskun Rodal[2] and Luis Carrasco[1]✉

1. Centro de Biología Molecular "Severo Ochoa". c/Nicolás Cabrera, 1. Universidad Autónoma de Madrid. Cantoblanco. 28049 Madrid. Spain.
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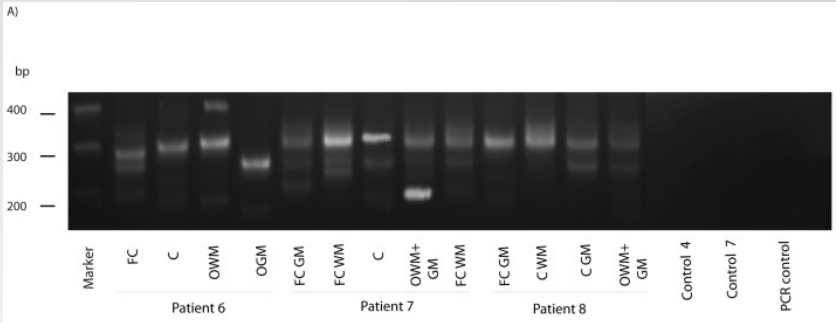
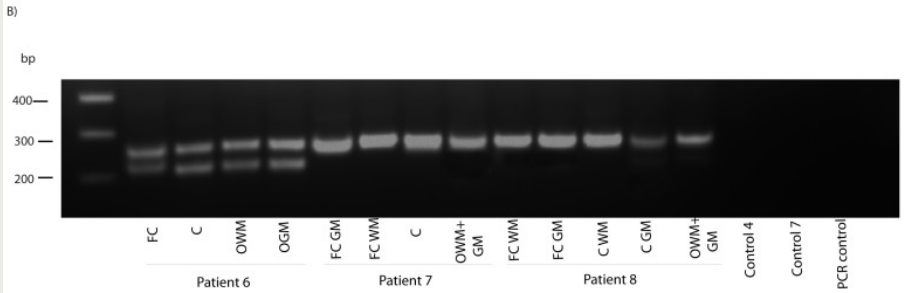
Received: 2014.11.17; Accepted: 2015.02.10; Published: 2015.04.02

Abstract

Among neurogenerative diseases, amyotrophic lateral sclerosis (ALS) is a fatal illness characterized by a progressive motor neuron dysfunction in the motor cortex, brainstem and spinal cord. ALS is th



Fungal species	Size	Patients number
Malassezia globosa	300	6FC,6C,6OWM,7FCWM,7FCGM,7C,7OWM,8FWG,8CWM,8CGM
Malassezia restricta	250	6FC,6OGM,7FCGM,7FCWM,7C ,8CGM ,8OWM
Candida albicans	200	6FC,7CGM,7C,7O,8FCGM
Cryptococcus neoformans	<200	7OWM



8CWG,8CGM,8OWMGM

Fungal antigens and DNA from several fungi were detected in the CFS of ALS patients. Fungal DNA was also detected in brain tissue using PCR analysis and proteomic analyses of brain tissue demonstrated with occurrence of several fungal peptides. In familial ALS, the most common gene mutation is of Cu/Zn superoxide dismutase (SOD1) which is an antioxidant defense gene involved in innate immune response to a number of pathogens, including fungi.

Alonso, et al 2015

Introducti

Amyotr
tating neuro
death within
neuromuscul
cated in the
rise to musc
motor neuro
is the most fr
vast majority of ALS cases are sporadic (about 95%),

hallmark for the classification of neurodegenerative

Kelly K. McCann, MD

Inhalational Alzheimer's disease

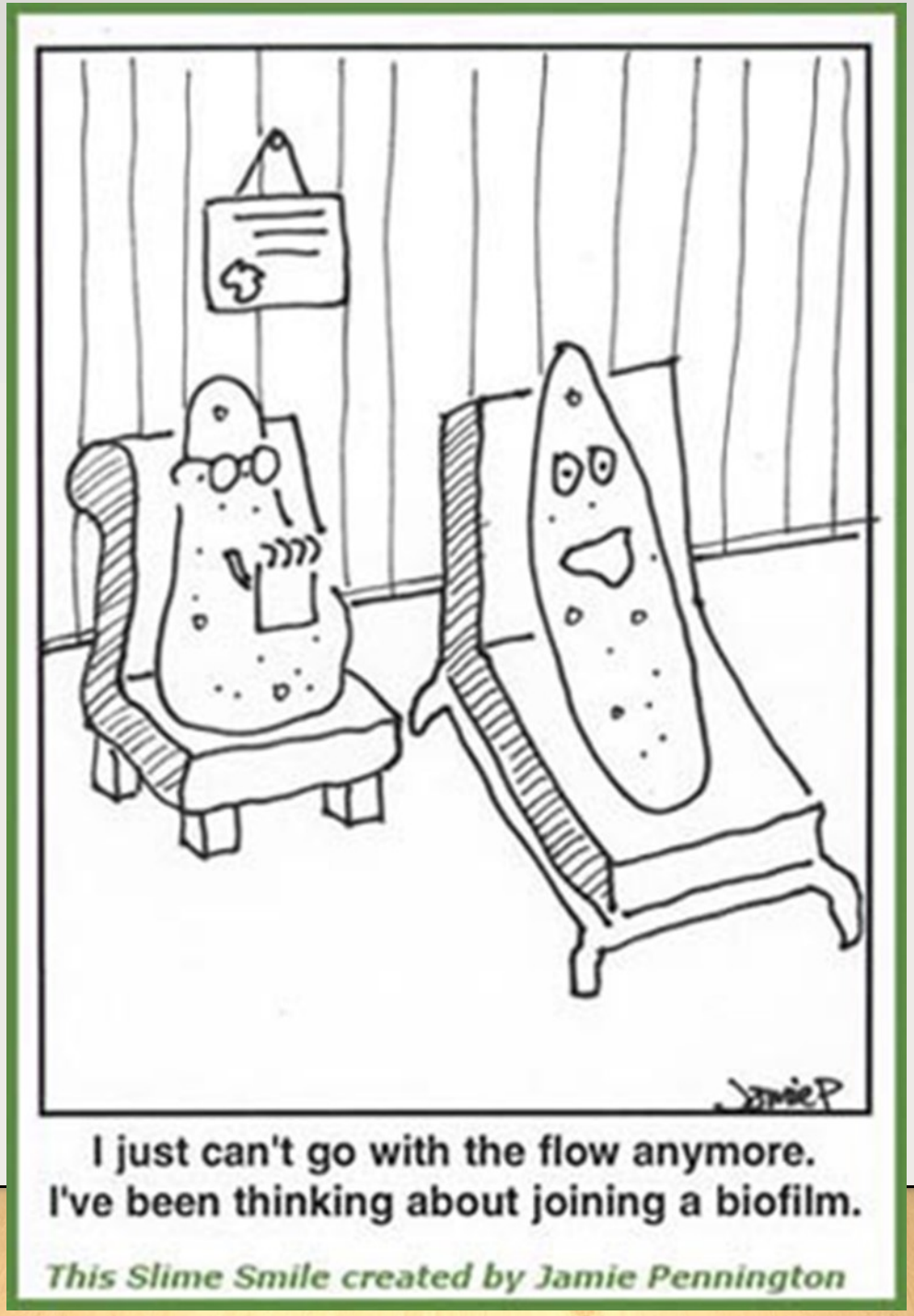
- **Three subtypes of AD**
- **1. Systemic inflammation**
- **2. Atrophic – often with hyperhomocysteine and insulin resistance**
- **3. CIRS type**
  - **Younger age (40-60 yrs)**
  - **APO E3/3, rather than APOE4**
  - **Onset following stress, menopause, surgery, trauma**
  - **Dyscalculia, executive dysfunction is neuro dysfunction**
  - **Preceded by depression**
  - **Treated with CIRS protocols**

Table 2. Symptoms, signs, and laboratory values suggestive of type 3 Alzheimer's disease.

Characteristic	Comment
Age at symptom onset less than 65 years.	Symptoms often begin in the 50s or late 40s.
ApoE ε4-negative genotype.	Typically ApoE3/3 unless there are other risk factors.
Negative family history or family history positive with symptom onset only in much older individuals than the patient.	
Symptom onset in association with menopause or andropause.	
Depression as a preceding or significant accompaniment of the cognitive decline.	
Headache as an early or preceding symptom.	
Atypical presentation, in which memory consolidation is not the initial and dominant characteristic.	Typical deficits include executive deficits, dyscalculia, paraphasias, or aphasia.
Precipitation or exacerbation by a period of great stress (e.g., loss of employment or marriage dissolution or family change) and sleep loss.	The degree of dysfunction is also markedly affected by stress and sleep loss.
Exposure to mycotoxins or metals (e.g., inorganic mercury via amalgams, or organic mercury via the consumption of large fish such as tuna) or both.	
Diagnosis of CIRS with cognitive decline.	Cognitive decline is common with CIRS.
Imaging suggestive of more than typical Alzheimer's involvement.	FDG-PET may show frontal as well as temporoparietal reductions in glucose utilization, even early in the course of the illness; MRI may show generalized cerebral and cerebellar atrophy, especially with mild FLAIR (fluid-attenuated inversion recovery) hyperintensity.
Low serum triglycerides or triglyceride:total cholesterol ratio.	Triglycerides are often in the 50s.
Low serum zinc (<75mcg/dl) or RBC zinc, or high copper:zinc ratio (>1.3).	
HPA axis dysfunction, with low pregnenolone, DHEA-S, and/or AM cortisol.	
High serum C4a, TGF-β1, or MMP9; or low serum MSH (melanocyte-stimulating hormone). Positive deep naso-pharyngeal culture for MARCoNS.	See reference 5.
HLA-DR/DQ associated with multiple biotoxin sensitivities or pathogen-specific sensitivity.	See reference 5.

Bredesen. Aging.Feb 2016; 8(2): 304-313.

Kelly K. McCann, MD


I just can't go with the flow anymore.
I've been thinking about joining a biofilm.
This Slime Smile created by Jamie Pennington

Do Mycotoxins Alter Phospholipids?

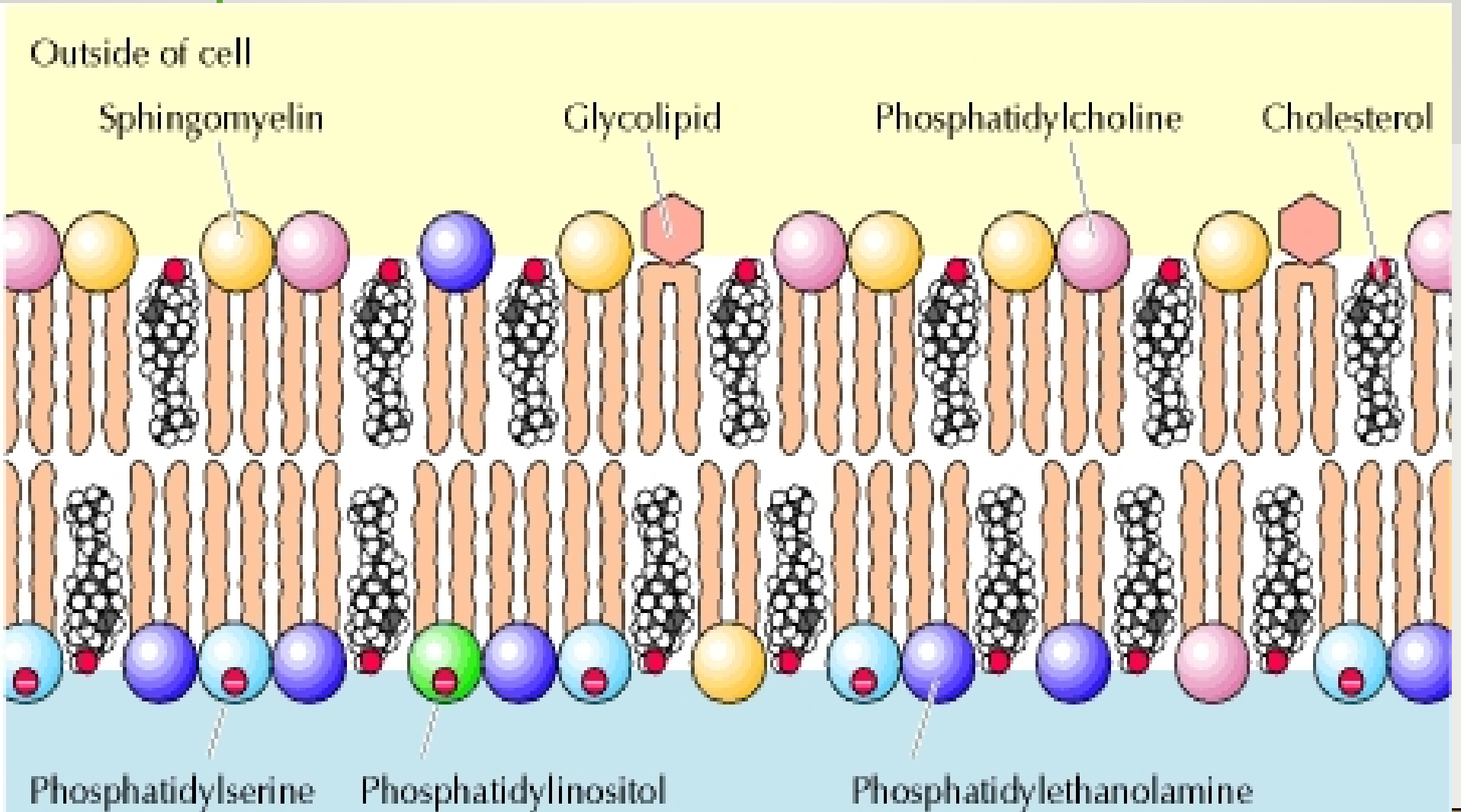
- **Stachybotrys chartarum mycotoxin reduces phosphatidylcholine enzyme synthesis in lung by 50%**
- **Fumonisin B1 disrupt membrane structure, enhances lipid oxidation leading to cell death.**
- **Fumonisin B1 in hepatocyte cultures changes to more rigid membrane structure by altering phospholipids**
- **Fumonisin B1 alters of lipid constituents of cellular membranes, and is a possible mechanism for hepatic cancer promotion and immunotoxicology**
- **Mushroom toxin phallolysin damages liposomes and phospholipid membranes**
- **Ochratoxin A is nephrotoxic, immunotoxic and carcinogenic, possibly by altering phospholipids.**

Hastings, C. et al. Toxicolo Sci 2005. Mar 84(1):186-94.
Yin, JJ. Biochim Biophys Acta. 1998. Apr 22;1371(1):134-42.
Buhring, HJ. Biochim Biophys Acta. 1983. Aug 24;733(1):117-23.
Burger HM. Lipids. 2007 Apr;42(3):249-61.
Hope. Jour Environ and Pub Health 2012. art ID 835059

Let's talk about Phosphatidyl choline, otherwise known as PC!

Kelly K. McCann, MD

The Lipid Bilayer



Yechiel E, Barenholz Y. Relationships between membrane lipid composition and biological properties of rat myocytes. Effects of aging and manipulation of lipid composition. J Biol Chem 1985 Aug 5;260(16):9123-31.

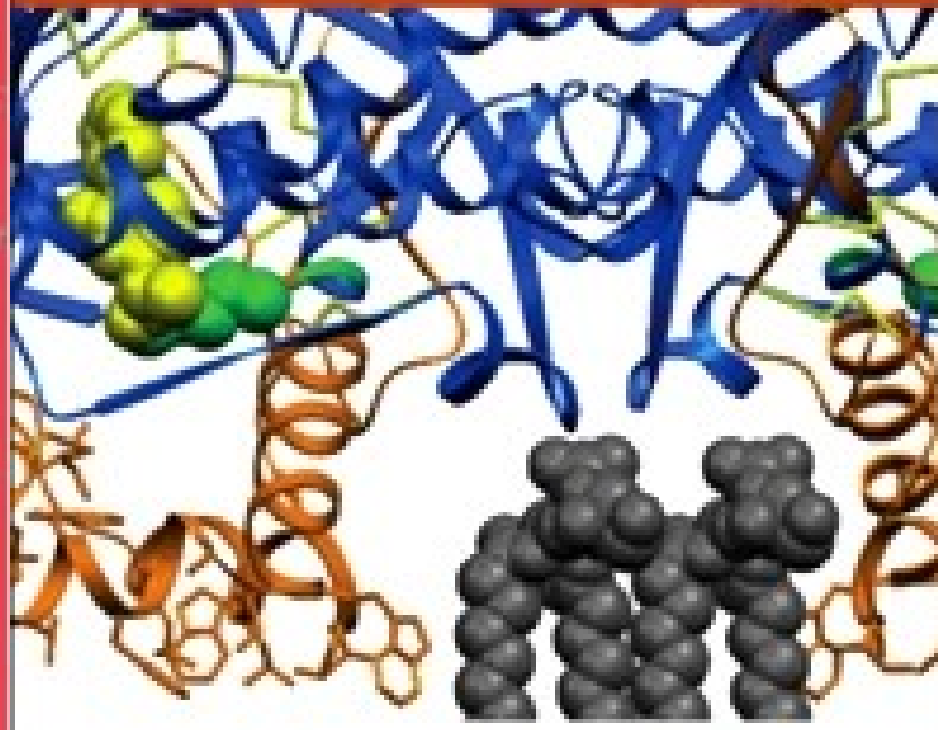
M.I. Gurr
J.L. Harwood
K.N. Frayn

LIPID BIOCHEMISTRY

An Introduction
5th Edition

Blackwell Publishing

6th Edition



Biochemistry of Lipids, Lipoproteins and Membranes

Edited by
Neale Ridgway and Roger McLeod

AP

Clinical Indications for use of Phosphatidylcholine

- Acute and chronic hepatitis
- Fatty liver
- Toxic liver damage
- Cirrhosis of the Liver
- Prevention gallstones
- Renal insufficiency
- Hyperemesis gravidarum
- Dyslipidemia
- Atherosclerosis
- Circulatory problems
- Angina pectoris
- Hypertension
- Gastrointestinal inflammation
- Dementia
- Multiple sclerosis
- Headache
- Insomnia
- Psoriasis
- Any Inflammatory condition

Gunderman. Essential Phospholipids.1993.
https://www.bodybio.com/BodyBio/docs/PC-Phosphatidylcholine-Fountain-of-Health.pdf
PhosChol monograph; http://www.phoschol.com/prescribing_information/PhosCholPrescribing.pdf

Kelly K. McCann, MD

Changing the 'In-Vironment' for Therapy

Digestive Diseases

Dig Dis 2012;30(suppl 3):85–91
DOI: 10.1159/000342729

Mucosal Protection by Phosphatidylcholine

Wolfgang Stremmel Robert Ehehalt Sabine Staffer Sabine Stoffels
Andrea Mohr Max Karner Annika Braun

Department of Gastroenterology, University Hospital Heidelberg, Heidelberg, Germany

Key Words
Mucus · Phosphatidylcholine · Ulcerative colitis

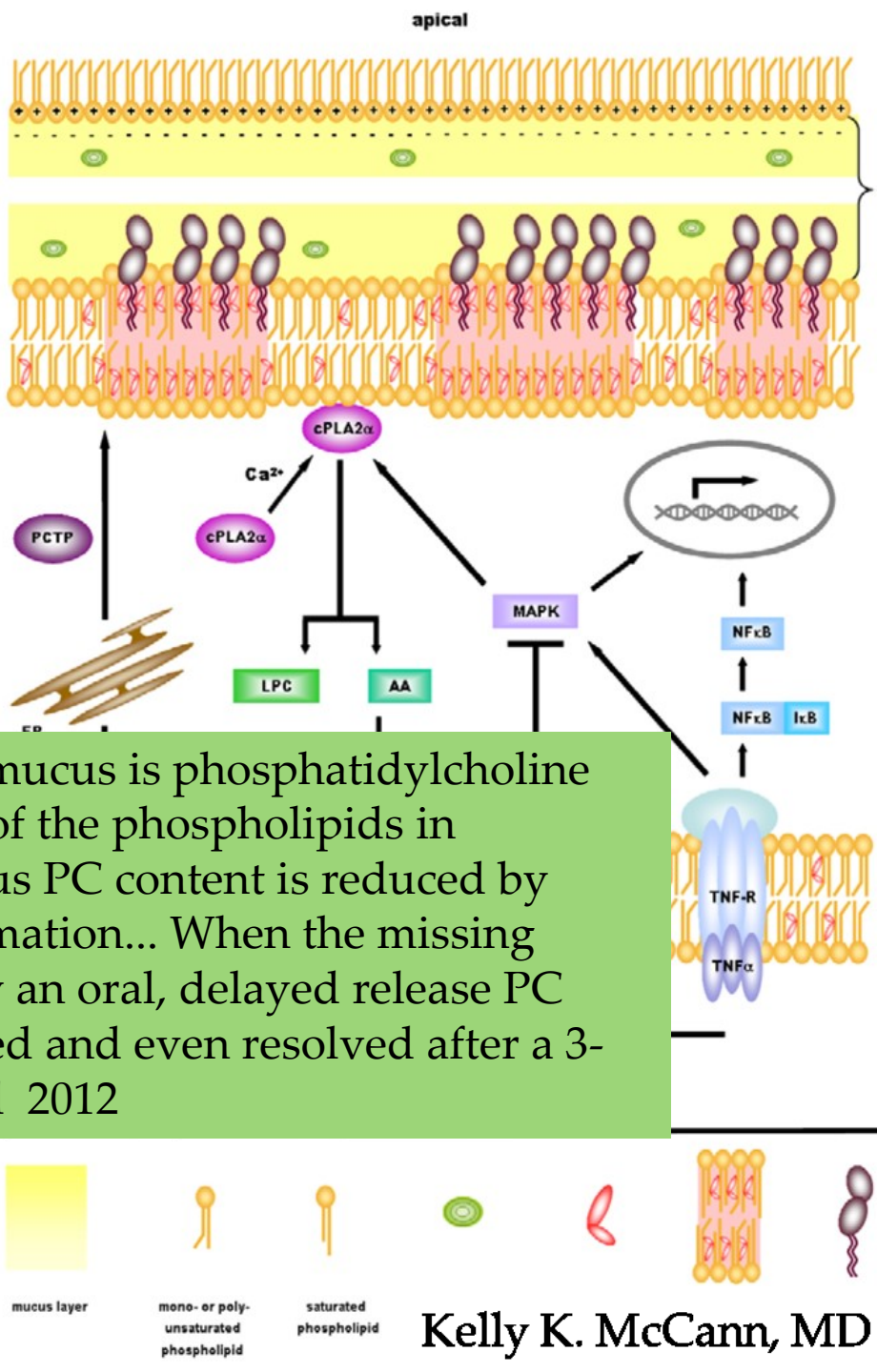
Abstract
The colonic m
commensal ba
essential com
choline (PC) w
pholipids in m
into this comp
surfactant-like
face on top of
sion of bacter
(UC), the muc
of the state of
trinsic primary
terial invasion
PC was shown to be mainly secreted by the ileal mucosa from where it is assumed to move distally to the colon, the PC content along the colonic wall towards the rectum gradually thins, with the least PC content in the rectum. This explains the start of the clinical manifestation of UC in the rectum and the expansion from there to the upper parts of the colon. In three clinical trials, when missing mucus PC in UC was supplemented by an oral, delayed release PC prepara-

tion, the inflammation improved and even res
3-month treatment course. The data indicate
role of the mucus PC content for protection ag

during bowel movements.

The etiology of UC is unknown. Based o
logical examinations, it is surmised that alon
netic disposition environmental factors trig
ease. A disturbed mucosal barrier is thought
tiating factor of the disease and subsequent a
the colonic commensal bacterial flora resul
mation of the mucosa [1–3].

One essential component of intestinal mucus is phosphatidylcholine (PC) which represents more than 90% of the phospholipids in mucus…. In ulcerative colitis, the mucus PC content is reduced by 70%, irrespective of the state of inflammation... When the missing mucus PC in UC was supplemented by an oral, delayed release PC preparation, the inflammation improved and even resolved after a 3-month treatment course. Stremmel 2012



Kelly K. McCann, MD

Am J Cardiovasc Dis 2013;3(1):17-26
www.AJCD.us /ISSN:2160-200X/AJCD1211005

Review Article

Interaction between sphingomyelin and oxysterols contributes to atherosclerosis and sudden death

Fred A Kummerow

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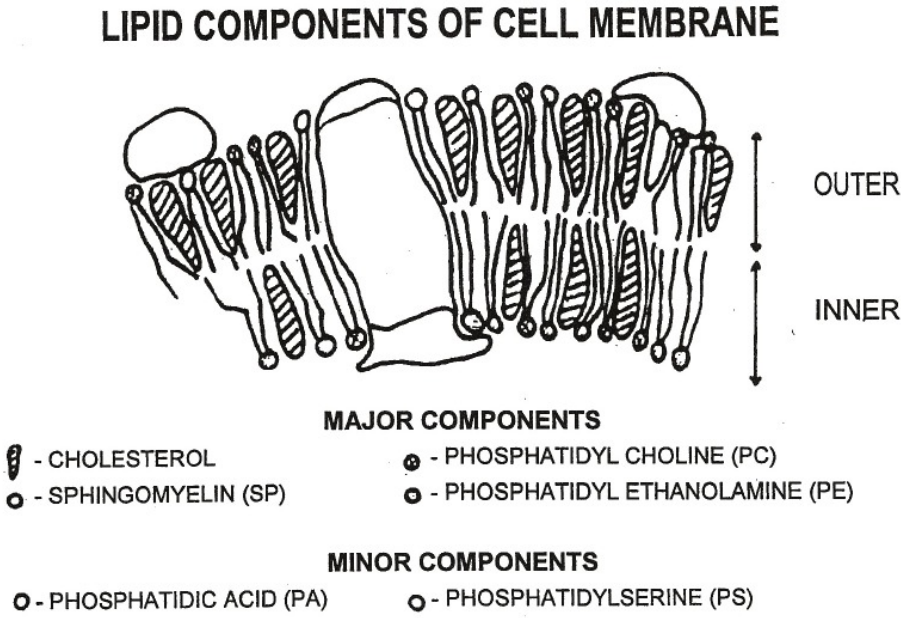
Received November 26, 2012; Accepted January 23, 2013; Epub February 17, 2013; Published February 27, 2013

Abstract: Despite major public health efforts, coronary heart disease continues to be the leading cause of death in the United States. Oxidized lipids contribute to heart disease both by increasing deposition of calcium on the arterial wall, a major hallmark of atherosclerosis, and by interrupting blood flow, a major contributor to heart attack and sudden death. Oxidized cholesterol (oxysterols) enhances the production of sphingomyelin, a phospholipid found in the cellular membranes of the coronary artery. This increases the sphingomyelin content in the cell membrane, which in turn enhances the interaction between the membrane and ionic calcium (Ca^{2+}), thereby increasing the risk of arterial calcification. Patients undergoing bypass surgery had greater concentrations of oxysterols in their plasma than cardiac catheterized controls with no stenosis, and had five times more sphingomyelin in their arteries than



Despite major public health efforts, coronary heart disease continues to be the leading cause of death in the United States. Oxidized lipids contribute to heart disease both by increasing deposition of Ca++ on the arterial wall, a major hallmark of atherosclerosis, and by interrupting blood flow, a major contributor to heart attack and sudden death.

Oxidized cholesterol (oxysterols) enhances the production of sphingomyelin (SM), a phospholipid found in the cellular membranes of the coronary artery. This increases the SM content in the cell membrane, which in turn enhances the interaction between the membrane and ionic calcium (Ca++), thereby increasing the risk of arterial calcification.

Thanks to Edward Kane for this info

Kelly K. McCann, MD

LIPIDS IN HEALTH AND DISEASE

RESEARCH Open Access

DL- and PO-phosphatidylcholines as a promising learning and memory enhancer

Tetsu Nagata, Takahiro Yaguchi, Tomoyuki Nishizaki*

Abstract

In the water maze test, oral administration with 1,2-dilynoleoyl-*sn*-glycero-3-phosphocholine (DLPhtCho)(5 mg/kg) alone or DLPhtCho (5 mg/kg) plus 1-palmitoyl-2-oleoyl-*sn*-glycero-3-phosphocholine (POPhtCho)(5 mg/kg) significantly shortened the prolonged acquisition latency for rats intraperitoneally injected with scopolamine, with more efficient effect than (POPhtCho)(5 mg/kg) alone, arachidonic acid (AA)(5 mg/kg) alone, docosahexaenoic acid (DHA)(5 mg/kg) alone, or 1-palmitoyl-2-linoleil-*sn*-glycero-3-phosphoserine (PLPhtSer)(5 mg/kg) alone. POPhtCho (5 mg/kg) alone or DLPhtCho (5 mg/kg) plus POPhtCho (5 mg/kg) also significantly shortened the prolonged retention latency for rats intraperitoneally injected with scopolamine, but otherwise no significant effect was obtained with DLPhtCho (5 mg/kg) alone, AA (5 mg/kg) alone, DHA (5 mg/kg) alone, or PLPhtSer (5 mg/kg) alone. Oral co-administration with DLPhtCho (5 mg/kg) and POPhtCho (5 mg/kg) significantly shortened the acquisition latency for rats untreated with scopolamine as compared with the latency for administration with polyethylene glycol (PEG), DLPhtCho alone at doses of 5 and 10 mg/kg, or POPhtCho alone at doses of 5 and 10 mg/kg, while no efficient effect on the retention latency was obtained. To assess the effect of DLPhtCho and POPhtCho on cognitive functions for humans, Mini Mental State Examination (MMSE) test was performed in subjects with cognitive disorders (the average MMSE score, 15). Oral co-intake with DLPhtCho (50 mg) and POPhtCho (45 mg) once after breakfast everyday raised the score to over 20, corresponding to normal cognitive functions, throughout 5 months after intake, and the increase in the score was significantly greater than that for oral intake with DLPhtCho (100 mg/day) alone or POPhtCho (90 mg/kg) alone. Taken together, the results of the present study show that co-intake with DLPhtCho and POPhtCho could enhance learning and memory ability and improve cognitive disorders for both the animals and humans with a promising efficacy.

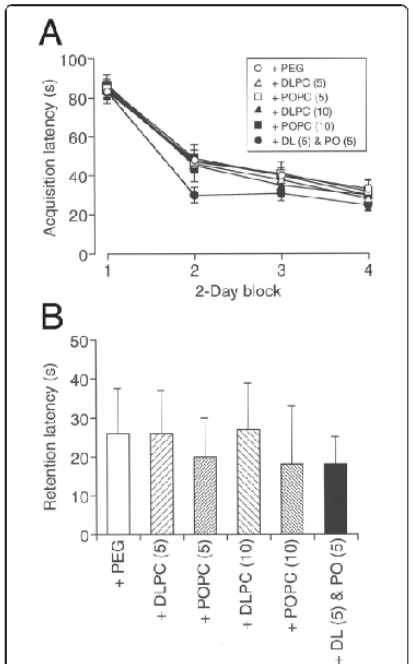


Figure 2 Effect of DLPhtCho and/or POPhtCho on spatial learning and memory for normal rats. Rats were orally administered with PEG, DLPhtCho (DLPC), POPhtCho (POPC), or DLPhtCho plus POPhtCho (DL & PO) everyday throughout experiments from 7 days prior to the beginning of water maze test. **(A)** Each point represents the mean (± SEM) acquisition latency from consecutive 2 days (n = 6). **(B)** Each column represents the mean

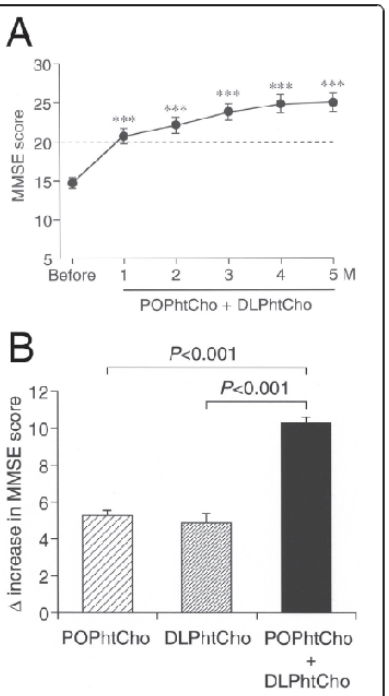


Figure 3 Effect of DLPhtCho and/or POPhtCho on cognitive disorders for humans. MMSE test was carried out once a month before and after oral intake with DLPhtCho, POPhtCho, and DLPhtCho plus POPhtCho once after breakfast every day. **(A)** Each point represents the mean (± SEM) MMSE score at the periods as indicated for 75 subjects with oral intake with DLPhtCho (50 mg/kg/day). $^{**}P < 0.001$ as compared with the paired *t*-test. **(B)** An MMSE score rise was

Introduction

Accumulating evidence has pointed to a role(s) of lipids as a regulatory mediator(s) turated free fatty acids su nic, and DHA, that are p catalyzed hydrolysis of serve as a retrograde me term potentiation (LTP), memory [2]. Those free f synaptic transmission by ACh receptors under th (PKC) [3,4]. This accou fatty acids to LTP forma fatty acids, accordingly memory ability.

In our earlier studies, DLPhtCho potentiated α7 nico-

Both rat and human studies showed administration of Phosphatidyl choline led to improvements in memory and performance. Pre-test MMSE scores averaged at 15. Five months later, MMSE scores rose to over 20 after daily intake of combination PC of 90-100mg/kg/day.

Nagata 2011.

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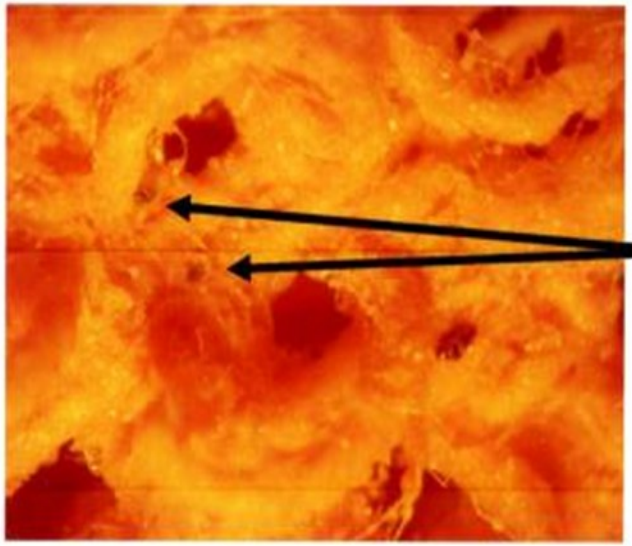
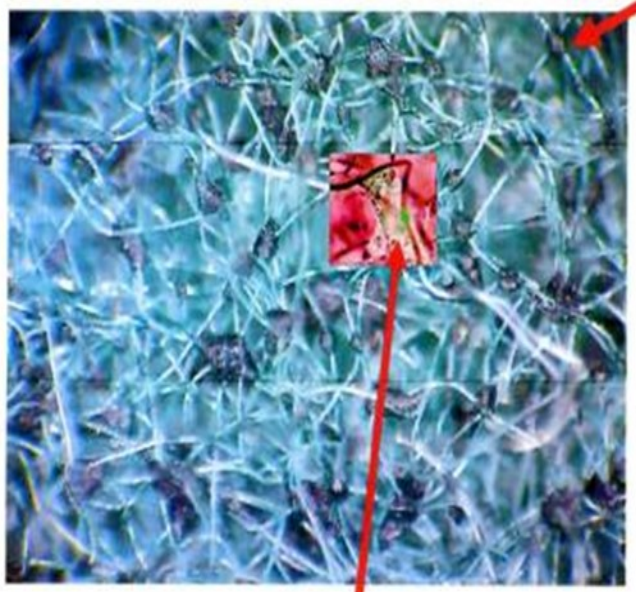
Kelly K. McCann, MD



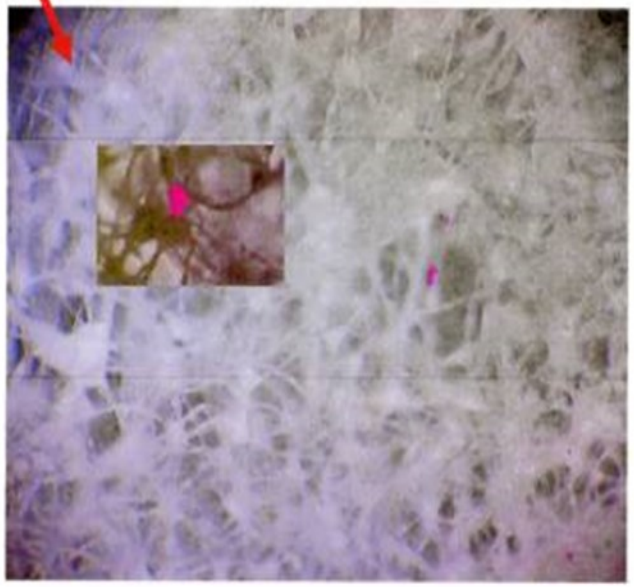
Very high magnification fluorescence
Arachidonic acid/other fatty acids

There are traces of **fungal metabolite** (brown probe) ***within*** the fatty acid structure

The cytoskeleton (layered fluorescence)
actin fibrils & mitochondria



Inset area: **Phenoxyethanol** on a mitochondrial membrane (green probe)



Inset area: **Aflatoxin B**, fungal metabolite (red probe)

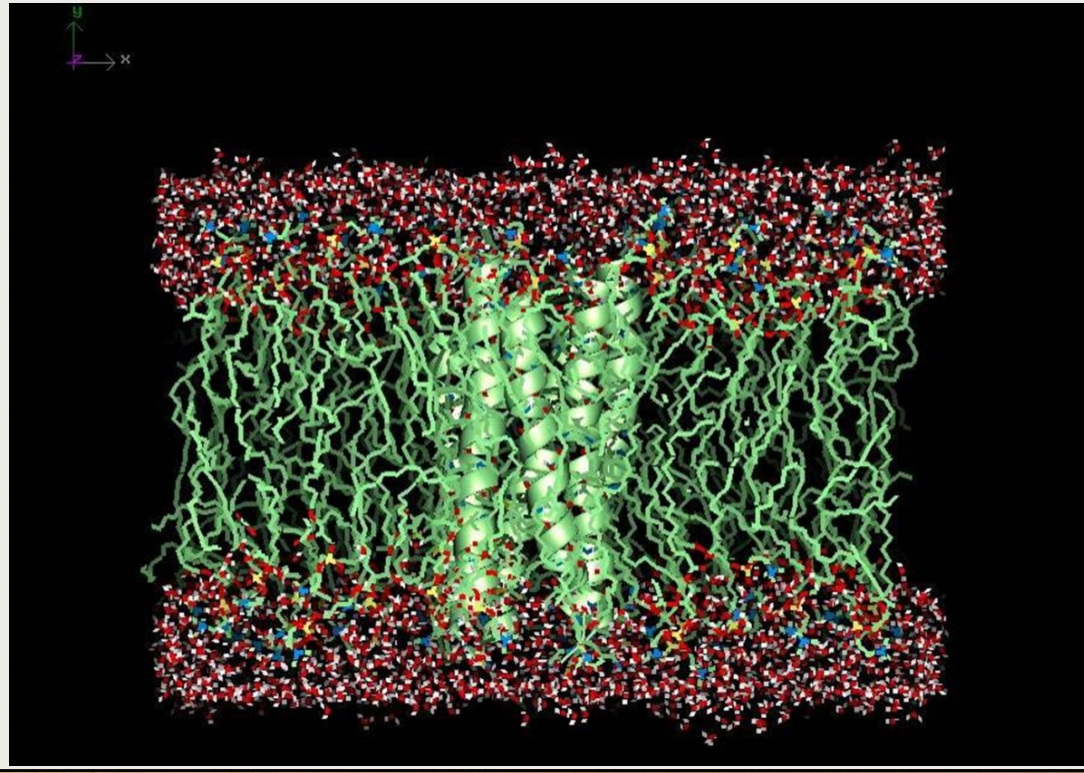
Mycotoxin Insult

- Patient with Rheumatoid Arthritis
- Fungus and its metabolites embedded in her cell membranes and mitochondria

Kelly K. McCann, MD

Assessing RBC fatty acid content

- Kennedy Krieger Institute Peroxisomal Laboratory at Johns Hopkins University



- Body Bio Assessment

Case 1 continued

Tel. 443-923-2788 FAX 443-923-2755

Laboratory Report

Red Blood Cell Membrane Total Lipid Fatty Acid Profile

Kelly K. McCann, MD
1831 Orange Ave Suite C

Costa Mesa
CA 92627

PATIENT
DOB
HOSPITAL
HISTORY #
HOSP. SAMPLE #
PDL TEST # 138808
PHYSICIAN
SAMPLE DATE 11/17/2014 RUN DATE 11/27/201
REPORT DATE 12/3/14 12:20:00
PRINTED ON 12/03/2014

	Patient Results ug/ml	Patient Results % of Total	Adult Control Values* Mean (n=143)	Adult Control Values* Standard Deviation	high/low = > or < 2 Std. Dev.
C10:0 Capric	0.100	0.007%	0.003%	0.001%	high
C12:0 Lauric	0.400	0.029%	.34%	0.007%	
C14:0 Myristic	3.720	0.273%	.26%	0.054%	
C15:0 Pentadecanoic	1.100	0.081%	0.113%	0.022%	
C16:0 Palmitic	239.930	17.592%	19.615%	1.075%	
C17:0 Heptadecanoic	3.150	0.231%	.336%	0.045%	low
C18:0 Stearic	172.900	12.677%	15.603%	1.030%	low
C20:0 - Arachidic	3.930	0.288%	0.411%	0.047%	low
C22:0	17.710	1.299%	1.705%	0.194%	low
C23:0 Tricosanoic	2.610	0.191%	0.292%	0.035%	low
C24:0	61.520	4.511%	5.066%	0.461%	
C25:0 Pentacosanoic	1.120	0.082%	0.110%	0.015%	
C26:0 Hexacosanoic	3.390	0.249%	0.261%	0.038%	
C28:0 - Octacosanoic	0.070	0.005%	0.004%	0.001%	
C30:0	0.020	0.001%	0.001%	0.000%	
C10:1 Caproleic	0.000	0.000%	0.000%	0.000%	
C12:1 Dodecaenoic	0.010	0.001%	0.001%	0.000%	
C16:1(n-9)	0.870	0.064%	0.062%	0.012%	
C17:1 - Heptadecaenoic	0.220	0.016%	0.025%	0.006%	
C18:1(n-9) Oleic	186.020	13.639%	11.305%	0.832%	high
C20:1(n-9) - Eicosenoic	4.030	0.295%	0.200%	0.040%	high
C20:3(n-9) Mead	0.660	0.048%	0.035%	0.010%	
C22:1(n-9) - Erucic	0.830	0.061%	0.053%	0.010%	
C24:1(n-9) Nervonic	82.260	6.031%	3.747%	0.519%	high
C26:1	2.840	0.208%	0.223%	0.050%	
C14:1(n-5) Myristoleic	0.010	0.001%	0.002%	0.001%	
C16:1(n-7) - Palmitoleic	2.270	0.166%	0.144%	0.053%	
C18:1(n-7) - Vaccenic	12.570	0.922%	0.728%	0.104%	
C18:1(n-5)	0.560	0.041%	0.127%	0.066%	
C20:3(n-7)	0.720	0.053%	0.050%	0.014%	
C14:2 - Myristolenic	0.000	0.000%	0.000%	0.000%	
C16:2 - Palmitolenic	0.020	0.001%	0.001%	0.000%	
C18:2(n-6) - Linoleic	142.680	10.462%	9.191%	1.461%	
C18:2(N-6)Conj - Rumenic	0.220	0.016%	0.054%	0.014%	low
C18:3(n-6) - Gamma Linolenic	0.500	0.037%	0.032%	0.010%	
C20:2(n-6) - Eicosadienoic	3.770	0.276%	0.233%	0.045%	

Page 1

Kennedy Krieger Institute
PATIEN

Red Blood Cell Membrane Total Lipid Fatty Acid Profile
DOB 12/28/1968 PDL TEST #138808

	Patient Results ug/ml	Patient Results % Total	Adult Control Values Mean	Adult Control Values Std. Dev.	high/low = > or < 2 Std. Dev.
C20:3(n-6) - Dihomo-g-linolenic	16.930	1.241%	1.274%	0.285%	
C20:4(n-6) - Arachidonic	159.690	11.709%	12.042%	1.270%	
C22:2(n-6) - Docosadienoic	0.890	0.065%	0.061%	0.015%	
C22:4(n-6) - Adrenic	35.540	2.606%	2.462%	0.580%	
C22:5(n-6) - Docosapentaenoic	6.880	0.504%	0.551%	0.192%	
C24:2(n-6)	6.540	0.480%	0.554%	0.121%	
C26:2 - Hexacosadienoic	1.060	0.078%	0.119%	0.052%	
C18:3(n-3) - Alpha Linolenic	1.240	0.091%	0.107%	0.032%	
C20:5(n-3) - Eicosapentaenoic	6.420	0.471%	0.598%	0.429%	
C22:5(n-3)	24.970	1.831%	1.813%	0.356%	
C22:6(n-3) - Docosahexaenoic	64.000	4.693%	3.703%	1.008%	
Pristanic Acid	0.010	0.001%	0.000%	0.0001%	
Phytanic Acid	0.010	0.001%	0.002%	0.001%	low
Sum C16:1 Trans FA	0.330	0.024%	0.056%	0.016%	
Sum C18:1 Trans FA	3.720	0.273%	0.748%	0.282%	
Sum C18:2 Trans FA	0.580	0.043%	0.098%	0.025%	low
16:0DMA	23.674	1.736%	1.557%	0.221%	
18:0DMA	39.790	2.917%	2.905%	0.357%	
Total 18:1 DMA	18.841	1.381%	0.905%	0.167%	high
Total Saturates	511.670	37.517%	43.781%	1.505%	low
Total W9 (n-9)	277.740	20.364%	15.592%	1.674%	high
Total W7&5 (n-7&n-5)	16.130	1.183%	1.064%	0.165%	
Total W6 (n-6)	374.720	27.475%	26.615%	2.033%	
Total W3 (n-3)	96.630	7.085%	6.143%	1.503%	
Total Branched Chain FA	0.020	0.001%	0.003%	0.001%	
Total Trans Fatty Acids	4.630	0.339%	0.887%	0.285%	
Total DMA's	82.305	6.035%	5.310%	0.915%	
Total Fatty Acids (ug/ml)	1363.845	100.000%	1604	187	
Arachidonic/DHA Ratio	2.495	%	3.502	1.139	
16DMA/16:0	0.099	%	0.077	0.018	
18DMA/18:0	0.230	%	0.179	0.040	

Method: Capillary gas chromatography/mass spectroscopy of pentafluorobenzyl bromide fatty acid esters. References: Lagerstedt SA et al. Quantitative Determination of Plasma C8-C26 Total Fatty Acids for the Biochemical Diagnosis of Nutritional and Metabolic Disorders. Mol. Gen. Metabol. 73, 38-45, 2001. This clinical test was developed by the CLIA regulated Genetics Laboratories, The Kennedy Krieger Institute and has not been cleared by the FDA. *Adult Controls: Age (Mean +/- Std. Dev.) = 49.5 +/- 17.0 years; range 19-82 years. N=143

INTERPRETATION:
Recv'd 11/18/14: The percentage of the total saturated fatty acids is lower than normal range. The percentage of the total w9 fatty acids is increased. The percentage of C18:1DMA is higher than normal range.

Carol Tiffany, M.S.
Lisa E. Kratz, Ph.D.

Ann B. Moser
Richard O. Jones, Ph.D.

Kelly K. McCann, MD

Case 1: RBC Fatty Acid

Red Cell Lipid Biomarkers

Specimen Draw Date: 11/17/2014
Practitioner: Dr. Kelly K. McCann (19062)

The % Status is the weighted deviation of the lab result and will show no graph when the research does not support negative values.

	% Status		Result	Low	High
16 DMA	**40.70**	H	1.74	1.34	1.78
18:0 DMA	1.68		2.92	2.55	3.26
18:1 DMA	**142.51**	H	1.38	0.74	1.07
C14:0 Myristic	12.04		0.27	0.21	0.31
C14:1w5 Myristoleic	**-50.00**	L	0.0010	0.001	0.003
C15:0 Pentadecanoic	**-73.26**	L	0.08	0.09	0.13
C16:0 Palmitic	**-94.09**	L	17.59	18.54	20.69
C16:1w7 Palmitoleic	20.75		0.17	0.09	0.20
C16:1w9 Hexadecanoic	8.33		0.06	0.05	0.07
C17:0 Heptadecanoic	**-115.56**	L	0.23	0.29	0.38
C17:1 Heptadecaenoic	**-75.00**	L	0.02	0.02	0.03
C18:0 Stearic	**-141.76**	L	12.68	14.57	16.63
C18:1w5 Octadecanoic	**-65.15**	L	0.04	0.06	0.19
C18:1w7 Vaccenic	**92.58**	H	0.92	0.62	0.83
C18:1w9 Oleic	**140.38**	H	13.64	10.47	12.14
LA **C18:2w6 Linoleic**	**44.18**	H	10.48	7.73	10.65
C18:2w6 Conj Rumenic	**-130.00**	L	0.02	0.04	0.07
ALA **C18:3w3 Alpha Linolenic**	**-25.00**	L	0.09	0.07	0.14
GLA **C18:3w6 Gamma Linolenic**	**28.95**	H	0.04	0.02	0.04
C20:0 Arachidic	**-130.85**	L	0.29	0.36	0.46
C20:1w9 Gondoic	**118.75**	H	0.29	0.16	0.24
C20:2w6 Eicosadienoic	**45.56**	H	0.28	0.19	0.28
DGLA C20:3w6 Dihomo-y Lino.	-5.79		1.24	0.99	1.56
C20:3w9 Mead	**65.00**	H	0.05	0.03	0.04
AA C20:4w6 Arachidonic	-13.14		11.71	10.77	13.31
EPA C20:5w3 Eicosapenta.	-14.80		0.47	0.17	1.03
C22:0 Behenic	**-104.50**	L	1.30	1.51	1.90
C22:1w9 Erucic	**35.00**	H	0.06	0.04	0.06
C22:2w6 Docosadienoic	13.33		0.07	0.05	0.08
C22:4w6 Adrenic	12.41		2.61	1.88	3.04
C22:5w3 Docosapenta.	2.46		1.83	1.46	2.17
C22:5w6 Osbond	-12.14		0.50	0.36	0.74
DHA **C22:6w3 Docosahexa.**	**49.11**	H	4.69	2.70	4.71
C23:0 Tricosanoic	**-144.29**	L	0.19	0.26	0.33
C24:0 Lignoceric	**-60.21**	L	4.51	4.61	5.53
C24:1w9 Nervonic	**412.72**	H	8.03	3.23	4.27
C24:2w6 Tetracosadienoic	**-30.50**	L	0.48	0.43	0.67
C25:0 Pentacosanoic	**-88.71**	L	0.08	0.09	0.13
C26:0 Hexacosanoic	-16.23		0.25	0.22	0.30
C26:1 Lumequic	-15.66		0.21	0.17	0.27
C26:2 Hexacosadienoic	**-39.42**	L	0.08	0.07	0.17
C28:0 Octacosanoic	**50.00**	H	0.0050	0.003	0.005
C30:0 Triacontanoic	**50.00**	H	0.0010	0.000	0.001
Phytanic	**-50.00**	L	0.0010	0.001	0.003
Pristanic	**950.00**	H	0.0010	0.000	0.000
Sum C16:1 Trans FAs	**-88.71**	L	0.02	0.04	0.07
Sum C18:1 Trans FAs	**-84.46**	L	0.27	0.47	1.03
Sum C18:2 Trans FAs	**-110.00**	L	0.04	0.07	0.12
Total Lipid Content	**-64.31**	L	1363.85	1417.24	1790.28
Total Saturates	**-208.11**	L	37.52	42.28	45.29
Total w3's	**31.34**	H	7.08	4.64	7.65
Total w6's	21.14		27.48	24.58	28.65

Red Cell Lipid Biopsy

Specimen Draw Date: 11/17/2014
Practitioner: Dr. Kelly K. McCann (19062)

BURN IT

TRANS ISOMERS

VLCFA'S

Erucic	35.00	H
Triacontanoic	50.00	H

SATURATED ODD

RENEGADES

Vaccenic	92.58	H
Mead	65.00	H
Eicosanoic	65.00	H
Pristanic	950.00	H
Gondoic	118.75	H

BUILD IT

MYELINATION

STRUCTURAL

Palmitic	-94.09	L
Stearic	-141.76	L

SUMMATION

Total Saturates	-208.11	L
Total Lipid Cont	-64.31	L

BALANCE IT

OMEGA 6

Linoleic	44.18	H
Gamma Linolenic	28.95	H
Dihomo-y Linolenic	-5.79	
Arachidonic	-13.14	
Adrenic	12.41	

OMEGA 3

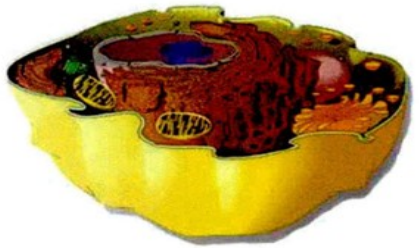
Alpha Linolenic	-25.00	L
Eicosapentaenoic	-14.80	
Docosapentaenoic	2.46	
Docosahexaenoic	49.11	H

INDEXES

Fluidity Index	50.00	H
MR Index	51.48	H
PR Index	293.93	H
Myelination Index	0.00	
Trans Isomer Index	0.00	
Odd Chain Index	-37.50	L

STABILIZE IT

18:1 DMA	142.51	H	PR Index	293.93	H



Kelly K. McCann, MD

Red Cell Lipid Biopsy

Kelly McCann, MD Female / Age: 45
Patient ID: (41262) Request: K0000000000

Specimen Draw Date: 11/17/2014
Practitioner: Dr. Kelly K. McCann (19062)

BURN IT

TRANS ISOMERS			
	VLCFA'S		
	Erucic	35.00	H
	Triacontanoic	50.00	H
SATURATED ODD	RENEGADES		
	Vaccenic	92.58	H
	Mead	65.00	H
	Eicosanoic	65.00	H
	Pristanic	950.00	H
	Gondoic	118.75	H

BUILD IT

MYELINATION			
	STRUCTURAL		
	Palmitic	-94.09	L
	Stearic	-141.76	L

SUMMATION		
Total Saturates	-208.11	L
Total Lipid Cont	-64.31	L

BALANCE IT

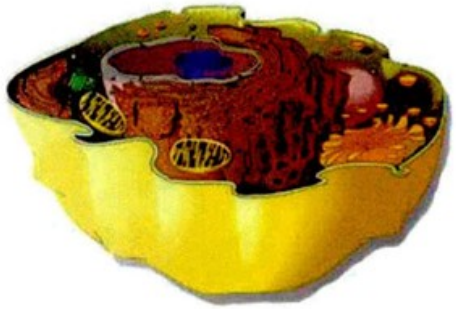
OMEGA 6			OMEGA 3		
Linoleic	44.18	H	Alpha Linolenic	-25.00	L
Gamma Linolenic	28.95	H	Eicosapentaenoic	-14.80	
Dihomo-y Linolenic	-5.79		Docosapentaenoic	2.46	
Arachidonic	-13.14		Docosahexaenoic	49.11	H
Adrenic	12.41				

INDEXES

Fluidity Index	50.00	H	Myelination Index	0.00	
MR Index	51.48	H	Trans Isomer Index	0.00	
PR Index	293.93	H	Odd Chain Index	-37.50	L

STABILIZE IT

18:1 DMA	142.51	H	PR Index	293.93	H



7/6/20

Accumulation of VLCFA and Renegrade Fatty acids

Saturated fats 200% low! Low lipid content at 65%

Imbalanced Omega3s

Elevated DMA which is a marker of overmyelination. High SM and low PC

Kelly K. McCann, MD


KIRUNAL
fish oil supplement
240 capsules • 500 mg
PC
PHOSPHATIDYL CHOLINE
Complex of Omega 6 to Omega 3 at a 4:1 Ratio
8 fl. oz.
237 mL
Balance Oil
Omega 6: Omega 3
4:1 Ratio
Organic Sunflower & Flax Seed Oil Blend
Rich in Essential Omega 6 and Omega 3 Oils
16 fl. oz. / 473 ml.
EVENING PRIMROSE
10% GLA
8 fl. oz
237 mL
Dietary Supplement

Oral Protocol for Case 1

- Phosphatidylcholine 1 tbsp or 14 caps daily = 9 grams or more if tolerated
- Sodium/potassium Butyrate 2 caps twice daily =500mg butyric acid/cap
- E'lyte solution – can give up to ½ bottle daily in severe fasciculations
- Evening primrose oil 1000mg daily
- Fish in the form of caviar or small fish
- Balance oil 4:1 mixture of Omega6:omega3 – 4-6 tbsp daily

Membrane Stabilizing Protein Drink

- Protein powder
- Phosphatidylcholine 1 tbsp
- E'lyte 1 tbsp or more
- Body Bio Balance Oil 2 tbsp
- Evening primrose oil 1 tbsp = 1000mg
- Trace minerals
- Can add coconut, almond or sheep milk kefir
- Organic seeds, nuts can be soaked and blended and added
- Berries to taste

Nutrients **2011**, *3*, 858-876; doi:10.3390/nu3100858

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Review

Regulation of Inflammation by Short Chain Fatty Acids

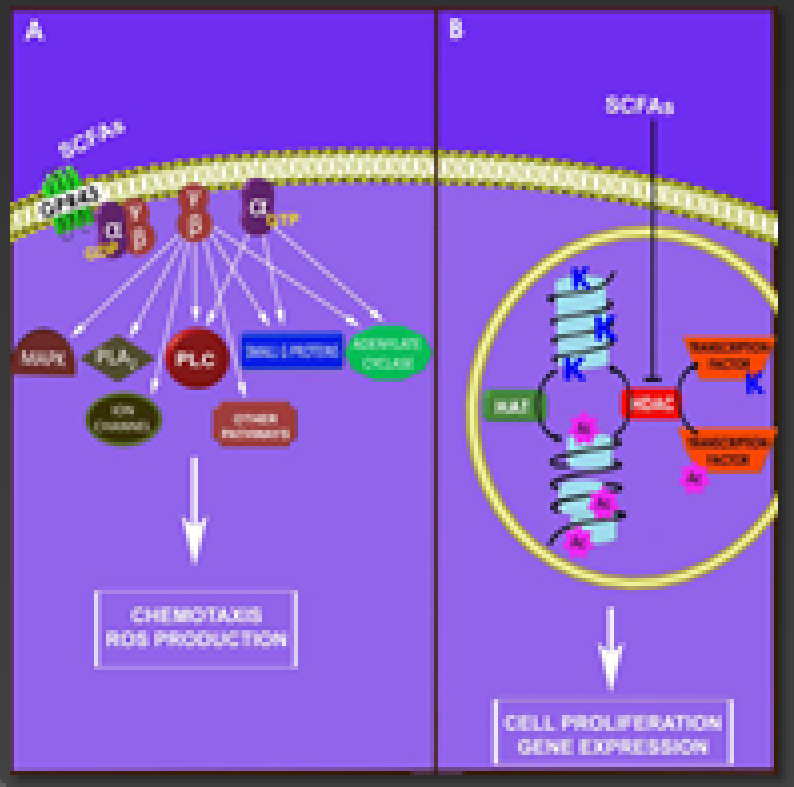
Marco A.R. Vinolo *, Hosana G. Rodrigues, Renato T. Nachbar and Rui Curi

Department of Physiology and Biophysics, Institute of Biomedical Sciences—ICB-I, Sao Paulo University, Brazil; E-Mails: hosanagr@icb.usp.br (H.G.R.); nachbar@icb.usp.br (R.T.N.); ruicuri@icb.usp.br (R.C.)

* Author to whom correspondence should be addressed; E-Mail: mramirez@icb.usp.br; Tel.: +55-11-3091-7245; Fax: +55-11-3091-7285.

Received: 18 July 2011; in revised form: 21 September 2011 / Accepted: 8 October 2011 / Published: 14 October 2011

Abstract: The short chain fatty acids (SCFAs): acetate (C_2), propionate (C_3) and butyrate (C_4) are the main metabolic products of anaerobic bacteria fermentation in the intestine. In addition to their important role as fuel for intestinal epithelial cells, SCFAs modulate different processes in the gastrointestinal (GI) tract such as electrolyte and water



Butyrate, a short chain fatty acid, modulates gene expression by activation of GPCRs and inhibition of histone deacetylase (HDAC) activity but its effects are far reaching in modulating inflammatory mediators, modifying lipid metabolism as stimulating the production of resolvins/protectins and having a CNS protective aspect in neurological disease including reduction in brain infarct volume.

Vinolo MA et al. 2011

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Butyrate

- Butyrate may be anti-atherogenic and antioxidant effects on glutathione production
- Butyrate reduces inflammation in shigellosis
- Modulates gene expression
- Butyrate decreases proinflammatory expression via inhibition of NFκB activation in Crohn's
- Must be used with PC and lipids

- Butyrate protects mice from NASH by reducing inflammation
- Phenylbutyrate is a histone deactylator and breaks up VLCFA and has indications in spinal muscle atrophy, ALS, ischemia, urea cycle defects, sickle cell, Cystic fibrosis and Huntington's disease

Omana, P. Pharmaceuticals (Basel). 2014 Nov; 7(11): 1008–1027.
Johannes J. Immunology. 2013 Jul; 139(3): 395–405.
Rubhana. BMC Infect Dis. 2012; 12: 111.
Tan, J. Adv Immunol. 2014;121:91-119.
Vinolo. Nutrients. 2011 Oct; 3(10): 858–876.
Segain JP. Gut. 2000;47:397–403.
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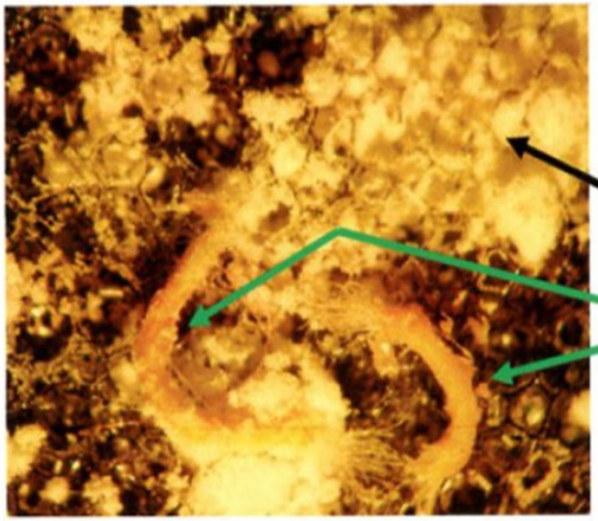
BEFORE (AUGUST 2010)

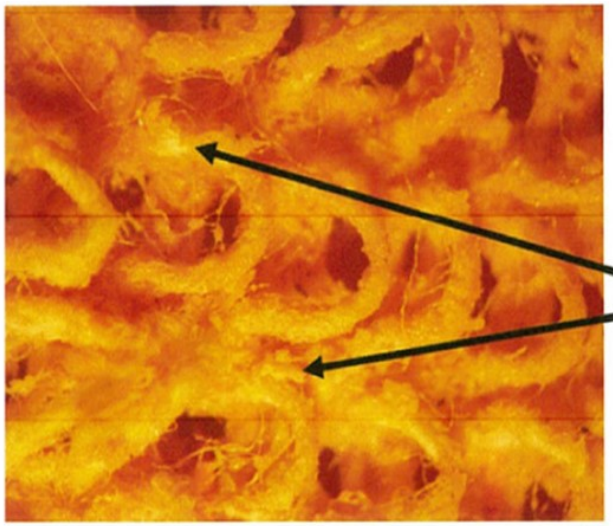


Layered polarization/fluorescence image
Outer surface of the plasma membrane
(x15 *higher magnification than usual)*

Marked oxidative damage

Diolein or similar toxic lipid(s)

AFTER IV PK TREATMENT (DECEMBER 2011)



Very high magnification fluorescence
Arachidonic acid/other fatty acids

Essentially normal but some very **small areas** that still shows **oxidative damage**

- Research lab in the UK/ Germany
- Not currently available for most clinicians

NEUROLIPID RESEARCH FOUNDATION

Amount of Essentiale-PC Required to Clear Toxicity

At the International Phospholipid conference in London November 12-13, 2010 physicians Katrin Bieber and Meinrad Milz (oncologist) presented their extensive biostatistical analysis of their patients' cellular toxicity status from repeat blood analyses from Acumen research laboratory that the amount of Essentiale-PC in the IV PK Membrane Stabilizing Protocol required to clear toxins adducted to the nuclear and mitochondrial DNA, normalize test results and note improvement in clinical presentation is the following.

The amount of PC required to clear DNA adducts and stabilize patient:

0.5 to 1.2 grams of PC per kg of body weight

quantity of PC required to clear DNA adducts,
normalize cell membranes and stabilize patient
Bieber K and Milz M 2010

per biostatistical analysis at the University of Ulm in Germany working with Dr. Meinrad Milz and Dr. Katrin Bieber

Example:

Requirement of Essentiale is 2 to 5 vials per kg body wt
For a 50 kg female this equals 100 to 250 vials
At 8 vials per treatment would equate to 12 to 32 treatments.

The Membrane Stabilizing IV Protocol is initiated with a phospholipid exchange or bolus phospholipid drip followed by IV folinic acid (Leucovorin or Fusilev) to support methylation. In the last step of the protocol reduced glutathione (diluted with sterile H_20, not saline) is infused to support sulfation. In administering glutathione with PC we are attempting to achieve a lipid-soluble glutathione to clear numerous toxins and to chelate heavy metals bound to the peptide metallothionein, (which binds heavy metals), support immune function, and suppress PLA2, thereby stabilizing the phospholipids in the membrane. Glutathione can form metal complexes via nonenzymatic reactions and is a versatile and pervasive metal-binding ligand. The sulfhydryl group of the cysteine moiety of glutathione has a strong affinity for mercury, silver, cadmium, arsenic, lead, gold, zinc, and copper. Glutathione, however, is not lipid soluble and cannot penetrate the membrane of blood brain barrier without the 'drug delivery system' effect of Essentiale Phosphatidylcholine. Thus the infusion of Essentiale precedes the administration of glutathione so that it is 'lipid soluble' and can penetrate the cell membrane.

The cellular impact of toxic burdens can result in disturbed prostaglandin synthesis, poor cellular integrity, increased cytokine release, decreased glutathione levels, suppression of omega-6 arachidonic and linoleic acids, and marked elevation of renegade fats. Our clinical recourse is to address cellular derangement with PC, both orally and by infusion, to potentially offset the accumulation of ceramides, influence membrane fluidity, clear neurotoxins from the nuclear and mitochondrial DNA, and stabilize the integrity of the lipid mitochondrial cardiolipin based inner membrane and plasma membrane leaflets.

Case 1: follow up

- She received 0.5g/kg of IV PC so far.
- Patient relocated to a mold-free house.
- She got rid of ALL her soft furniture items including her mattress, sofa, chairs, dining room chairs, carpets, lamps
- She dry cleaned or washed with the mold laundry additive her absolute favorite clothes and put them in storage to see if mold would grow after several months.
- She wiped down and stored all her wood furniture for 2 months.
- And repeated her labs….
- TGFbeta1 2300 pg/mL (<2382) down from 9800+
- MMP9 368 ng/mL (<332) down from 900+
- VIP 26.6 pg/mL (23-63) up from <16
- MSH <8 pg/mL, unchanged

Case 5: September 2016

- **48 yr old woman came in with multiple medical problems and a long history of not feeling well for the past 7-8 years. She complained of:**
- **Joint pains, Fatigue**
- **Brain fog**
- **Muscle tightness and twitches**
- **Chemical sensitivities**
- **Food sensitivities - only 5 foods**
- **Flushing, Voice hoarseness**
- **Mouth pain**
- **Irritable bowel symptoms**
- **Burning eyes, Dizziness**
- **Adrenal fatigue on Cortef**

- **Tick bit in Orange County, CA 2 ½ years prior, then developed bronchitis requiring steroids and antibiotics, then 2 weeks later a cellulitis on her Great toe, in another 2 weeks had an eye infection and recurrent rashes.**
- **Igenex lyme test was equivocal but 31 epitope test was negative.**
- **Current house and work environment are both moldy.**

Is it Lyme or mold? Could it be both?

Lyme symptoms
Fatigue
Fevers
Rashes
Sweats
Hair loss
Swollen lymph nodes
Sore throat
Chest pain
Shortness of breath
Heart palpitations
Nausea or vomiting
Difficulty eating
Constipation
Diarrhea
Bladder dysfunction
Cystitis
Dizziness
Balance problems
Tremor

Joint pain
Myalgias
Joint swelling
Back pain
Neck stiffness
TMJ pain
Headaches
Muscle twitching
Neurological sensations of tingling burning or stabbing
Increased motion sickness
Vision changes
Hearing changes
Hypotension
Disturbed sleep
Memory loss
Confusion
Difficulty concentrating

Mold symptoms
Fatigue
Weakness
Decreased assimilation of new knowledge
Myalgias
Headaches
Memory impairment
Word finding problems
Decreased concentration
Light sensitivity
Joint pains
Morning stiffness
Red eyes
Tearing eyes
Blurred vision
Vertigo
Aches
Ice pick pain

Tingling
Tremors
Unusual pain
Shortness of breath
Sinus congestion
Cough
Excessive thirst
Confusion
Appetite swings
Temperature regulation issues
Increased urinary frequency
Nocturia
Abdominal pain
Numbness
Disorientation
Metallic taste
Static shocks
Sweats (esp night sweats) Skin sensitivity/rashes

CLUSTER ANALYSES. Give 1 point for any or all symptoms in a category. 6 or more points for children. 8 or more teens and adults. Circle any that apply

- **Fatigue**
- **Weakness, difficulty assimilating new information, muscle aches, headaches, light sensitivity**
- **Memory problems, word finding difficulties**
- **Problems with Concentration**
- **Joint pains, morning stiffness, muscle cramps**
- **Unusual skin sensations, tingling**
- **Shortness of breath, sinus congestion or nasal drainage**
- **Cough, increased thirst, confusion**
- **Appetite swings, body temperature regulation, urinary frequency/urgency**
- **Red eyes, blurred vision, excessive or nighttime sweating, mood swings, unusual pains esp. "ice pick pains"**
- **Abdominal tenderness or pain, diarrhea or loose stools, numbness**
- **Eye tearing, disorientation, metallic taste**
- **Static shocks, vertigo**

Total number:

Kelly K. McCann, MD

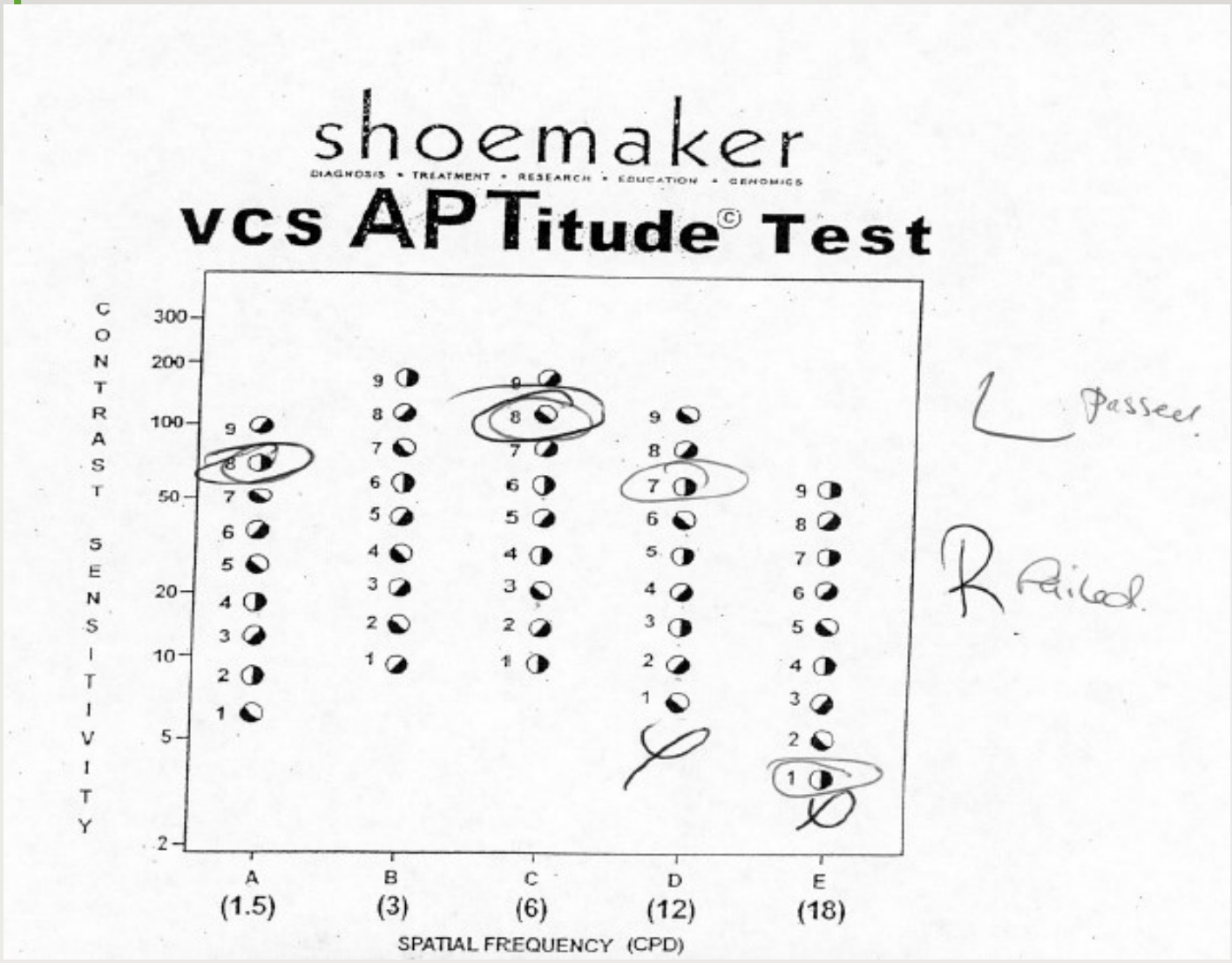
Case 5

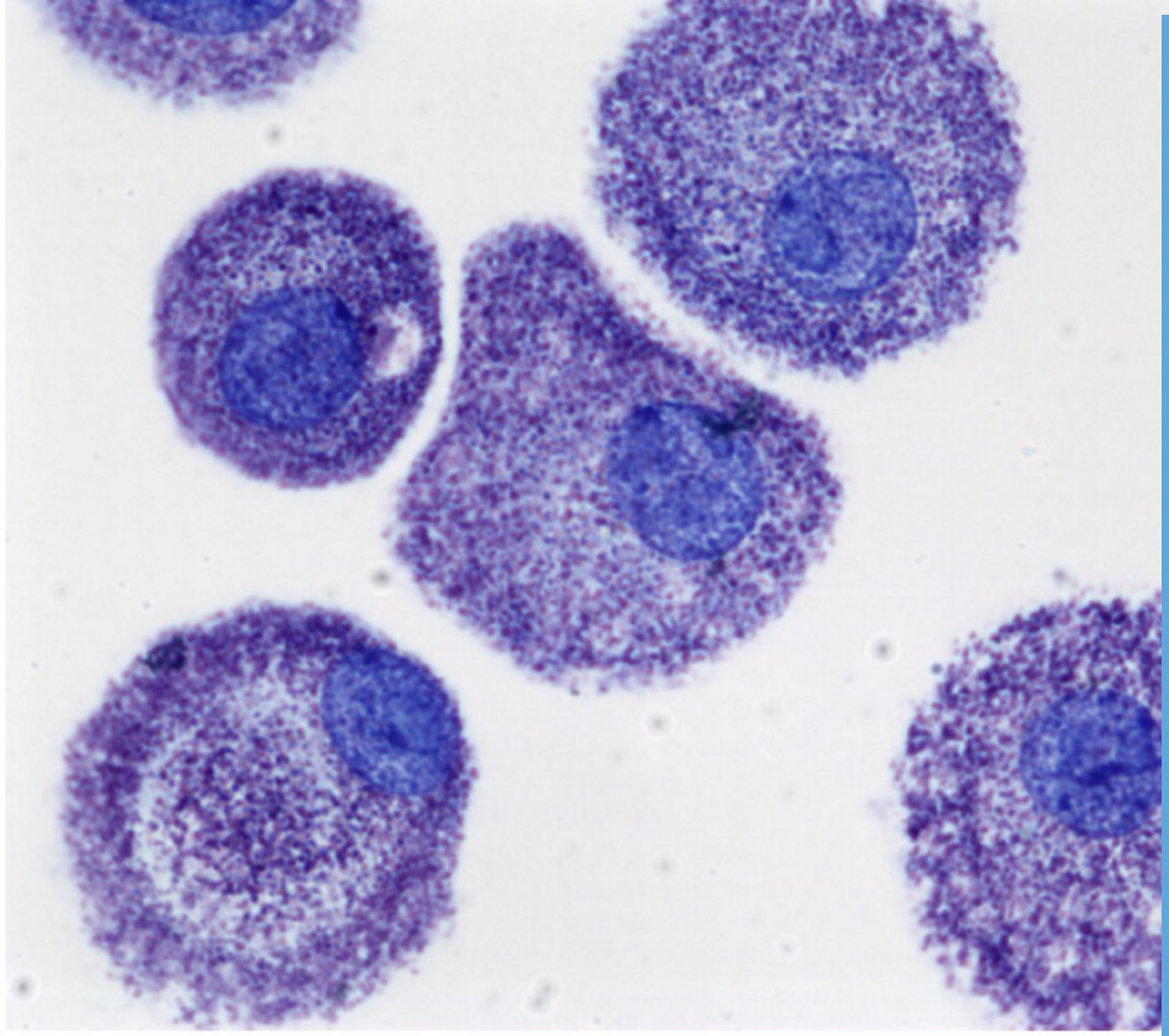
- PMHx: hyperlipidemia, tinnitus, CFS, fibromyalgia, hypothyroidism, IBS, insomnia, GERD, +RF, depression, anxiety, osteopenia, metabolic syndrome perimenopausal, recurrent hives, mast cell activation syndrome, Multiple Chemical Sensitivity
- PSHx: uterine ablation 2015

LABS: HLA DR 1-5 low MSH, 13-6-52C mold susceptible

- MSH 17 pg/mL (nl 35-81)
- VIP 48.8pg/mL (nl 23-63)
- TGFBeta1 5623 pg/mL H (<2382)
- C4a 14,043ng/mL H (<2830)
- MMP9 766 ng/mL H (<332)
- VEGF 53 pg/mL (nl 31-86)
- MARCONS +large amount
- RF 177 IU/mL H
- antiCCP<1 U/mL
- hs CRP 3.45mg/dL = 32.86 nmol/L

Case 5


shoemaker
DIAGNOSIS • TREATMENT • RESEARCH • EDUCATION • GENOMICS
vcs APTitude© Test
CONTRAST SENSITIVITY
300
200
100
50
20
10
5
2
A (1.5)
B (3)
C (6)
D (12)
E (18)
SPATIAL FREQUENCY (CPD)
L passed
R failed



Mast Cells: Laboratory of Allergic Diseases, National Institute of Allergy and I
Diseases, National Institutes of Health (LAD/NIAID/NIH)

What are Mast Cells?
Mast cells are type of white blood cells, specifically, granulocytes derived from myeloid stem cell that is part of the immune and neuroimmune system. Each mast cell contains secretory granules (storage sacs), each containing powerful biologically active molecules called mediators, like histamine and heparin. These can be secreted when mast cells are triggered, leading to allergic and inflammatory diseases.

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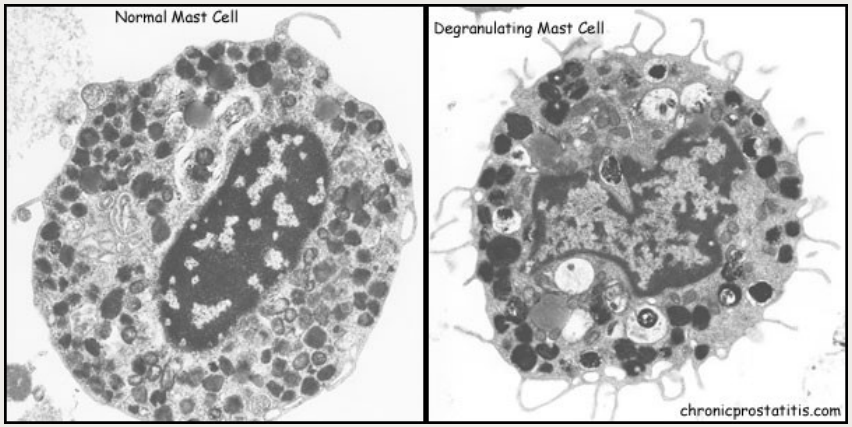
Classification of mast cell disorders

Primary mast cell disorders
Mastocytosis (systemic and cutaneous)
Monoclonal mast cell activation syndrome
Secondary mast cell disorders
Allergic disorders
Physical urticarias
Mast cell activation associated with chronic inflammatory or neoplastic disorders
Idiopathic mast cell disorders
Idiopathic anaphylaxis
Idiopathic urticaria
Idiopathic histaminergic angioedema
Idiopathic mast cell activation syndrome

Table 3 Frequent signs and clinical symptoms ascribed to episodic unregulated release of mast cell mediators (modified from [12]; further references therein; an exhaustive survey is given in [50])

Signs and Symptoms	
Abdominal	abdominal pain, intestinal cramping and bloating, diarrhea and/or obstipation, nausea, non-cardiac chest pain, Helicobacter pylori-negative gastritis, malabsorption
Oropharyngeal	burning pain, aphthae
Respiratory	cough, asthma-like symptoms, dyspnea, rhinitis, sinusitis
Ophthalmologic	conjunctivitis, difficulty in focusing
Hepatic	splenomegaly, hyperbilirubinemia, elevation of liver transaminases, hypercholesterolemia
Splenomegaly	
Lymphadenopathy	
Cardiovascular	tachycardia, blood pressure irregularity (hypotension and/or hypertension), syncope, hot flush
Neuropsychiatric	headache, neuropathic pain, polyneuropathy, decreased attention span, difficulty in concentration, forgetfulness, anxiety, sleeplessness, organic brain syndrome, vertigo, lightheadedness, tinnitus
Cutaneous	urticaria pigmentosa, hives, efflorescences with/without pruritus, telangiectasia, flushing, angioedema
Abnormal bleeding	
Musculoskeletal	muscle pain, osteoporosis/osteopenia, bone pain, migratory arthritis
Interstitial cystitis	
Constitutional	fatigue, asthenia, fever, environmental sensitivities

Mast Cell Activation Syndrome (MCAS)



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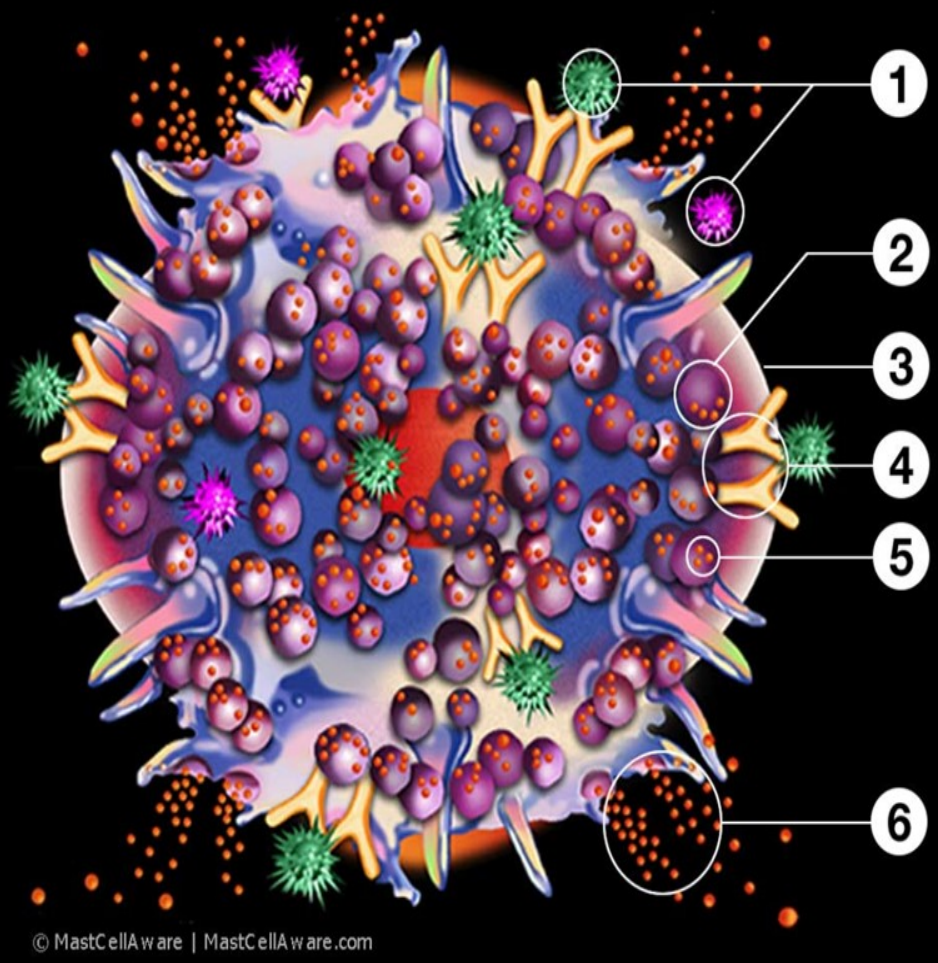
Mast Cells In Activation



Click the links to learn more about the parts of a mast cell. (Links open in new window)

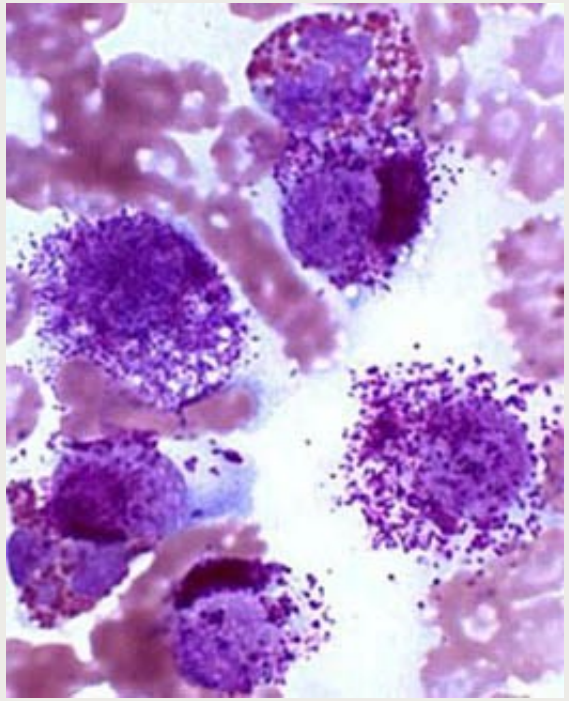
1. Allergens & Triggers
2. Storage Granules
3. Mast Cell
4. IgE Antibodies
5. Histamine & Tryptase
6. Degranulation

In this illustration, the mast cell, similar in appearance to a white blood cell (white/blue areas), contains many storage granules (purple spheres) rich in histamine and tryptase (small orange granules).When allergens, drugs, toxins, etc. (green & pink spiked shapes) are binding & cross-bridging the antibodies (yellow Y-shaped pairs), a mast cell reaction is triggered, releasing histamine, tryptase and other mediators into the system (represented by the release of orange granules).

Thanks to Theoharis C. Theoharides, MS, PhD, MD, FAAAAI for his guidance with this visual interpretation of mast cells in activation.

Testing for Mast cell Activation Syndrome

Must stop all NSAIDS, aspirin or other salisylates and all PPIs 5 days prior to testing. It is ok to continue H2 blockers like zantac or pepcid or other histamine blockers such as bendaryl, zyrtec or Claritin if necessary. If at all possible, stop these.



1. Chilled serum trypase
2. Chromogranin A
3. Plasma prostaglandin D2
4. Histamine
5. Heparin
6. Random urine N-methylhistamine
7. Random urine Leukotriene E4
8. 24-hour urine prostaglandin D2

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Testing for Mast cell Activation Syndrome

9. **24-hour urine N-methylhistamine**
10. **24-hour urine leukotriene E4**
11. **24-hour urine 2,3-dinor-11beta-prostaglandin F2 alpha**
12. **Anti-IgE IgG (define autoimmunity)**
13. **Anti-IgE-receptor antibody testing (define autoimmune urticaria)**

- All blood tests must be collected on ice, spun down in the cold centrifuge, and sent frozen.
- For random urine collections, they must be kept cold (either on ice or in the refrigerator) until they are processed in the Reference lab, and then sent frozen.
- For 24 hour urine collections, they must be kept refrigerated during collection (as usual), and sent frozen.

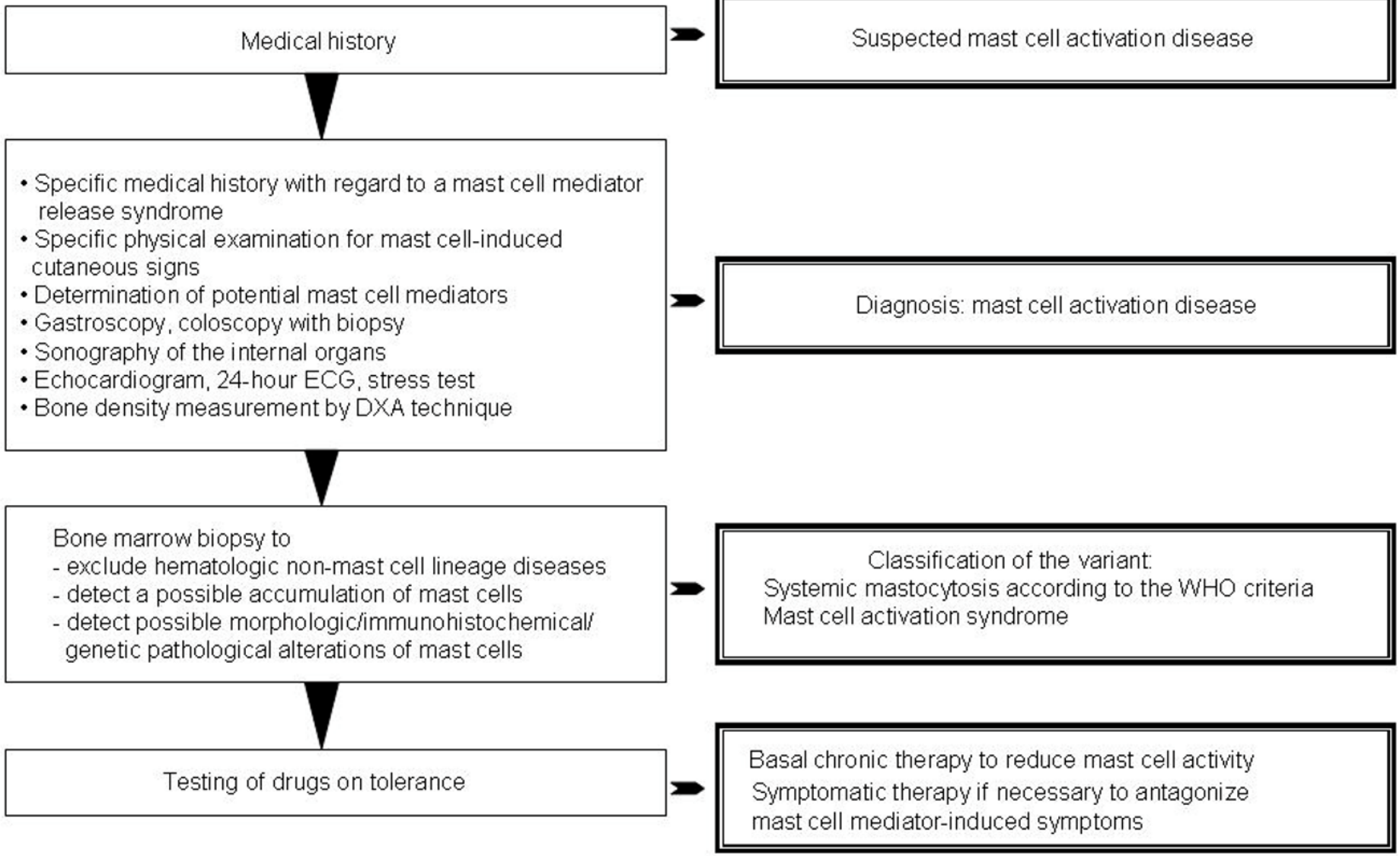


Figure 1 Diagnostic algorithm.

Molderings et al. Journal of Hematology & Oncology 2011, 4:10 http://www.jhoonline.org/content/4/1/10

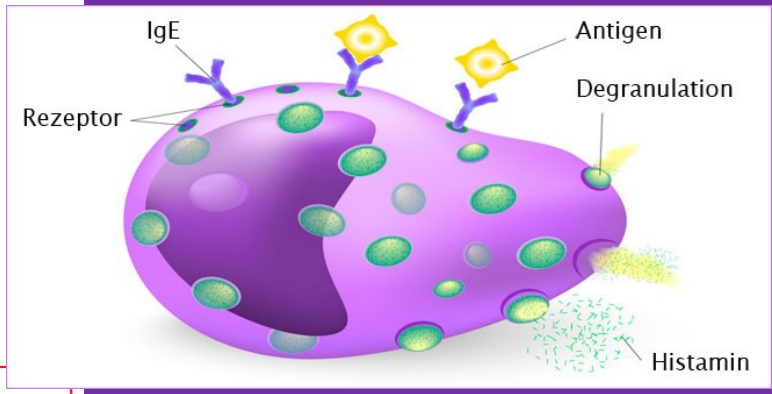
Molderings et al. Journal of Hematology & Oncology 2011, 4:10
http://www.jhoonline.org/content/4/1/10

JOURNAL OF HEMATOLOGY & ONCOLOGY

REVIEW Open Access

Mast cell activation disease: a concise practical guide for diagnostic workup and therapeutic options

Gerhard J Molderings[1*], Stefan Brettner[2], Jürgen Homann[3], Lawrence B Afrin[4]



Abstract

Mast cell activation disease comprises disorders characterized by accumulation of genetically altered mast cells and/or abnormal release of these cells' mediators, affecting functions in potentially every organ system, often without caus
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MCAS typically presents as chronic, persistent or recurrent, waxing and waning or slowly progressive multisystem polymorbidity generally, but not necessarily, of an inflammatory theme. It is usually acquired early in life via unknown mechanisms; interaction of environmental factors with inheritable risk factors is one possibility. Variable and numerous mutations in MC regulation lead to heterogeneity of presentations. Afrin, 2011

Introduction

The term *ma*
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subclass termed *systemic mastocytosis* (SM) includes disorders characterized by certain pathological immunohistochemical and mutational findings (the WHO criteria; Table 2; [1,2]) which are divided into several subtypes (Table 1). On the other hand, *mast cell activation syn-*

organs. The bone marrow typically shows a diffuse, dense infiltration with mast cells. In typical MCL, mast cells account for more than 10% of blood leukocytes. In a smaller group of patients, pancytopenia occurs and mast cells account for less than 10% (aleukemic variant

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Table 2 Criteria proposed to define mast cell activation disease (for references, see text)

Criteria to define *mast cell activation syndrome*	WHO criteria to define *systemic mastocytosis*
Major criteria	**Major criterion**
1. Multifocal or disseminated dense infiltrates of mast cells in bone marrow biopsies and/or in sections of other extracutaneous organ(s) (e.g., gastrointestinal tract biopsies; CD117-, tryptase- and CD25-stained)	Multifocal dense infiltrates of mast cells (>15 mast cells in aggregates) in bone marrow biopsies and/or in sections of other extracutaneous organ(s) (CD117-, tryptase- and CD25-stained)
2. Unique constellation of clinical complaints as a result of a pathologically increased mast cell activity (mast cell mediator release syndrome)	
Minor criteria	**Minor criteria**
1. Mast cells in bone marrow or other extracutaneous organ(s) show an abnormal morphology (>25%) in bone marrow smears or in histologies	1. Mast cells in bone marrow or other extracutaneous organ(s) show an abnormal morphology (>25%) in bone marrow smears or in histologies
2. Mast cells in bone marrow express CD2 and/or CD25	2. Mast cells in bone marrow express CD2 and/or CD25
3. Detection of genetic changes in mast cells from blood, bone marrow or extracutaneous organs for which an impact on the state of activity of affected mast cells in terms of an increased activity has been proved.	3. c-kit mutation in tyrosine kinase at codon 816 in mast cells in extracutaneous organ(s)
4. Evidence of a pathologically increased release of mast cell mediators by determination of the content of • tryptase in blood • N-methylhistamine in urine • heparin in blood • chromogranin A in blood • other mast cell-specific mediators (e.g., leukotrienes, prostaglandin D_2)	4. Serum total tryptase >20 ng/ml (does not apply in patients who have associated hematologic non-mast-cell lineage disease)

The diagnosis *mast cell activation syndrome* is made if both major criteria or the second criterion and at least one minor criterion are fulfilled. According to the WHO criteria [1], the diagnosis *systemic mastocytosis* is established if the major criterion and at least one minor criterion or at least three minor criteria

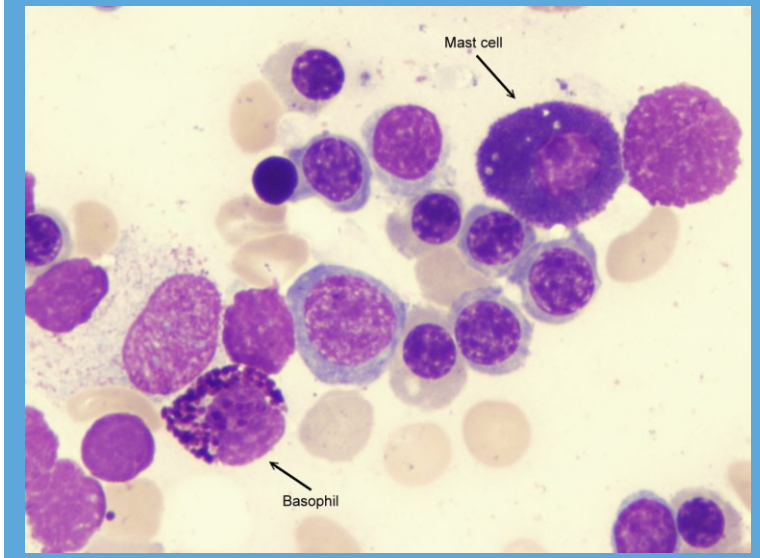

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Table 5 Treatment options for mast cell activation disease

Basic therapy (continuous oral combination therapy to reduce mast cell activity)	• H_1-histamine receptor antagonist (to block activating H_1-histamine receptors on mast cells; to antagonize H_1-histamine receptor-mediated symptoms) • H_2- histamine receptor antagonist (to block activating H_2-histamine receptors on mast cells; to antagonize H_2-histamine receptor-mediated symptoms) • Cromolyn sodium (stabilising mast cells) • Slow-release Vitamin C (increased degradation of histamine; inhibition of mast cell degranulation; not more than 750 mg/day) • If necessary, ketotifen to stabilise mast cells and to block activating H_1-histamine receptors on mast cells
Symptomatic treatment options (orally as needed)	• ***Headache***⇒ paracetamol; metamizole; flupirtine • ***Diarrhea***⇒ colestyramine; nystatin; montelukast; 5-HT_3 receptor inhibitors (eg. ondansetron); incremental doses (50-350 mg/day; extreme caution because of the possibility to induce mast cell degranulation) of acetylsalicylic acid; (in steps test each drug for 5 days until improvement of diarrhea) • ***Colicky abdominal pain***due to distinct meteorism ⇒ metamizole; butylscopolamine • ***Nausea***⇒ metoclopramide; dimenhydrinate; 5-HT_3 receptor inhibitors; icatibant • ***Respiratory symptoms***(mainly increased production of viscous mucus and obstruction with compulsive throat clearing) ⇒ montelukast; urgent: short-acting ß-sympathomimetic • ***Gastric complaints***⇒ proton pump inhibitors (de-escalating dose finding) • ***Osteoporosis, osteolysis, bone pain***⇒ biphosphonates ([51]; vitamin D plus calcium application is second-line treatment in MCAD patients because of limited reported success and an increased risk for developing kidney and ureter stones; [52]) • ***Non-cardiac chest pain***⇒ when needed, additional dose of a H_2-histamine receptor antagonist; also, proton pump inhibitors for proven gastroesophageal reflux • ***Tachycardia***⇒ verapamil; AT1-receptor antagonists; ivabradin • ***Neuropathic pain and paresthesia***⇒ α-lipoic acid • ***Interstitial cystitis***⇒ pentosan, amphetamines • ***Sleep-onset insomnia/sleep-maintenance insomnia***⇒ triazolam/oxazepam • ***Conjunctivitis***⇒ exclusion of a secondary disease; otherwise preservative-free eye drops with glucocorticoids for brief courses • ***Hypercholesterolemia***⇒ (does not depend on the composition of the diet) therapeutic trial with HMG-CoA reductase inhibitors (frequently ineffective) • ***Elevated prostaglandin levels, persistant flushing***⇒ incremental doses of acetylsalicylic acid (50-350 mg/day; extreme caution because of the possibility to induce mast cell degranulation)

All drugs should be tested for tolerance in a low single dose before therapeutic use, if their tolerance in the patient is not known from an earlier application.

Case 5: SIM (similar to ERMI)

Sample ID: BK081916-7-1 (SIM 1-3)

Description: Home Screen: Kitchen, Living Room, Master

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Species Detected	Cells/Sample	Relative Abundance (%)
Acremonium strictum	ND	0.000
Alternaria alternata	2,858	0.243
Anigr*	208	0.018
Aspergillus flavus / oryzae	ND	0.000
Aspergillus fumigatus, Neosartorya fischeri	329,459	28.026
Aspergillus ochraceus / ostianus	ND	0.000
Aspergillus penicillioides	ND	0.000
Aspergillus restrictus / caesillus / conicus	ND	0.000
Aspergillus sclerotiorum	ND	0.000
Aspergillus sydowii	ND	0.000
Aspergillus unguis	ND	0.000
Aspergillus ustus	ND	0.000
Aspergillus versicolor	ND	0.000
Aureobasidium pullulans	1,948	0.166
Chaetomium globosum	ND	0.000
Cladosporium cladosporioides svar. 1	72	0.006
Cladosporium cladosporioides svar. 2	98	0.008
Cladosporium herbarum	ND	0.000
Cladosporium sphaerospermum	ND	0.000
Eamst*	ND	0.000
Epicoccum nigrum	1	0.000
Muc1*	508,107	43.223
Paecilomyces variotii	332,023	28.244
PenGrp2*†	Absent	
Penicillium brevicompactum / stoloniferum	ND	0.000
Penicillium chrysogenum	ND	0.000
Penicillium corylophilum	ND	0.000
Penicillium purpurogenum	ND	0.000
Penicillium variabile	741	0.063
Pspin2*	ND	0.000
Rhizopus stolonifer	ND	0.000
Scopulariopsis brevicaulis / fusca	ND	0.000
Scopulariopsis chartarum	32	0.003
Stachybotrys chartarum	ND	0.000
Trichoderma viride / atroviride / koningii	ND	0.000
Wallemia sebi	ND	0.000

Total Spores 1,175,546

1,175,546

*These assays detect four or more species.

Eamst *Eurotium (Aspergillus) amstelodami / chevalieri / herbariorum / rubrum / repens*
Anigr *Aspergillus niger / awamori / foetidus / phoenicis*
PenGrp2 *Penicillium crustosum / camemberti / commune / echinulatum / solitum*
Pspin2 *Penicillium glabrum / lividum / purpurescens / spinulosum / thomii*
Muc1 *Mucor amphibiorum / circinelloides / hiemalis / indicus / mucedo / racemosus / ramosissimus and Rhizopus azygosporus / homothalicus / microsporus / oligosporus / oryzae*

†Due to the design of the Primer and Probe by the EPA ERMI study quantifications based on this assay may lead to erroneous and/or misleading counts. Due to this, PenGrp2 assay is reported as present or absent

Sample ID: BK081916-7-2 (A)

Description: HVAC Supply Ducts/Register, Return Vent

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Species Detected	Cells/Sample	Relative Abundance (%)
Acremonium strictum	ND	0.000
Alternaria alternata	43	0.001
Anigr*	1,255	0.040
Aspergillus flavus / oryzae	10	0.000
Aspergillus fumigatus, Neosartorya fischeri	1,583	0.051
Aspergillus ochraceus / ostianus	382,601	12.289
Aspergillus penicillioides	47	0.002
Aspergillus restrictus / caesillus / conicus	20	0.001
Aspergillus sclerotiorum	1	0.000
Aspergillus sydowii	ND	0.000
Aspergillus unguis	ND	0.000
Aspergillus ustus	12	0.000
Aspergillus versicolor	ND	0.000
Aureobasidium pullulans	18,925	0.608
Chaetomium globosum	1	0.000
Cladosporium cladosporioides svar. 1	2,259	0.073
Cladosporium cladosporioides svar. 2	387	0.012
Cladosporium herbarum	15,460	0.497
Cladosporium sphaerospermum	61	0.002
Eamst*	1,856	0.060
Epicoccum nigrum	1	0.000
Muc1*	109,621	3.521
Paecilomyces variotii	2,576,074	82.741
PenGrp2*†	Absent	
Penicillium brevicompactum / stoloniferum	23	0.001
Penicillium chrysogenum	203	0.007
Penicillium corylophilum	ND	0.000
Penicillium purpurogenum	13	0.000
Penicillium variabile	12	0.000
Pspin2*	2,406	0.077
Rhizopus stolonifer	149	0.005
Scopulariopsis brevicaulis / fusca	150	0.005
Scopulariopsis chartarum	1	0.000
Stachybotrys chartarum	19	0.001
Trichoderma viride / atroviride / koningii	12	0.000
Wallemia sebi		0.007

Total Spore

3,113,410

*These assays detect four or more species.

Eamst *Eurotium (Aspergillus) amstelodami / chevalieri / herbariorum / rubrum / repens*
Anigr *Aspergillus niger / awamori / foetidus / phoenicis*
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CASE 5: Gentle Detox support

- For sensitive patients who can't tolerate binders consider starting:
- **Homeopathic detox** (*Pekana Detox Kit*– Itires, Apo-hepat, Renelix) – start 1-2 drops once or twice daily and can work up to 15 drops of each in glass water bottle and drink throughout the day.
- *Pekana* – Mucan – cleanses the extracellular matrix but mildly provocative so use later in the case
- Takesumi Supreme by *Supreme Nutritionals* is a bamboo charcoal that can be used as a generalized binder. 1 scoop or ¼ tsp 2-3 times per day.

Herbal Mold/Fungal Treatment options

- *Beyond Balance* – ToxEase GL – 1-2 drops once or twice daily
- *Beyond Balance* – Pro-MYCO – assist against mold and mycotoxins. Start 1-2 drops BID and work up to 10 drops BID
- *Beyond Balance* – MycoRegen -guard against fungal issues (more potent) Start 1-2 drops 2 times daily and work up to 8-10 drops 2 times daily. Some may have to use very small doses.
- *Beyond Balance* – ENL-BT for biotoxins 1-2 drops 1-2 times daily. Don't exceed 8-10 drops three times daily.
- *Research Nutritionals* – Transfer Factor Enviro for mold. Intended to help against Penicillium, Fusarium, Aspergillus, Cladosporium and Candida sp. Start 1 cap daily away from food and supplements. Can increase to 2 or higher. Can take with Transfer Factor Multi Immune.

MCAS treatments

- Treat her Mast Cell Activation Syndrome – Quercetin, DAO enzymes, NeuroproTek, Allqlear, Perimine as herbal options
- Mast Cell pharmaceutical options – H1 and H2 blockers (Pepcid or Zantac and Zyrtec or Clairitin) Ketotifen or Cromolyn.
- Lawrence Afrin, MD ***Never Bet Against Occam*** book on MCAS
- Theo Theoharides, MD, PhD has written a number of articles http://mastcellmaster.com/

Moldy Recap

1. **Get patients to a safe, mold free environment. Including home, work, car and mold-free belongings**
2. **Differential diagnosis. Consider underlying chronic infections and chemical toxicant burdens**
3. **Do a thorough history and complete lab evaluations, if able**
4. **Begin binders – charcoal, clay, chlorella, takesumi, CSM**
5. **Begin Phosphatidyl choline to begin healing cellular membranes**
6. **Begin Butryate to break up VLCFA and other deleterious fatty acids.**
7. **Address nasal and GI colonizations and mycobiome disruption with antifungals and biofilm busters**
8. **Restore nutrients, hormones**
9. **Apply Naturopathic and functional medicine tools for healing**

Final Notes

- These patients are complicated and sensitive. They often know what they need and can tolerate, so listen to them and devise an individualized plan to address their issues.
- www.retrainingthebrain.com – Dynamic Neural Retraining System by Annie Hopper
- Must address emotional, psychological and even spiritual issues to get these patients to a place of healing.
- Trust your clinical judgement

Contact information

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