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Are You Missing Mold Illness?

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Are You Missing Mold Illness?

Online continuing education course for medical practitioners

Created & presented by Dr. Jill Crista

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Course Curriculum

1. Stuff You Need To Know First
2. Mold ~ A Formidable Foe
3. Scary Scary Mycotoxins
4. How To Spot Moldies
5. The Testing Conundrum
6. Peel The Orange
7. Protect & Repair
8. Fight
9. When Things Go Sideways
10. And The Environment

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Stuff You Need To Know First

How this course works

Certificates

Impacts

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How This Course Works

Over 10 hours - choose when to watch

CE/CME credit, ND Pharmacy

10 Modules ~
Lectures within each module

Quizzes ~
At end of each lecture

Case examples

Updates

Access for 1 year

A note on research…

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Where Are The RCTs?

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Respiratory research

OPEN ACCESS

ORIGINAL ARTICLE

Airway epithelial phosphoinositide 3-kinase-δ contributes to the modulation of fungi-induced innate immune response

Jae Seok Jeong,[1] Kyung Bae Lee,[1] So Ri Kim,[1,2] Dong Im Kim,[1] Hae Jin Park,[1] Hern-Ku Lee,[3] Hyung Jin Kim,[2,4] Seong Ho Cho,[5] Narasaiah Kolliputi,[5] Soon Ha Kim,[6] Yong Chul Lee[1,2]

International Journal of COPD

Dovepress

REVIEW

Lung inflammation caused by inhaled toxicants: a review

John Wong
Bruce E Magun
Lisa J Wood

School of Nursing, MGH Institute of Health Professions, Boston, MA, USA

This article was published in the following Dove
International Journal of COPD
23 June 2016
Number of times this article has been viewed

Abstract: Exposure of the lungs to
may lead to acute and chronic pulm
the leading cause of chronic obstr
areas of underdeveloped countries
Mycotoxins from fungal spores p
a health hazard to those living in
and silica (from building materia
of indoor air pollution that con
illness in experimental anima
extremely toxic yet relatively
different classes of toxic cher
and activation of macropha
protein synthesis, and prod
nanoparticles) or the produ
NOD-like receptor protein

Author Manuscript

Author Manuscript

toxin B_1 Promotes Influenza ication and Increases Virus ed Lung Damage via Activation Signaling

Su [1,2], Zixuan Liu [1,2], Dandan Liu [1,2], Fang Gan [1,2], Xingxiang Chen [1,2]

and Immunology, College of Veterinary Medicine, Nanjing Agricultural University, Nanjing
Metabolic Disorders in Domestic Animals and Foods, Nanjing Agricultural University,

alters immune responses to mammals, is one of the most
s and food. Swine influenza virus (SIV) is a major pathogen of
owever, there have been few studies about the
SIV replication.

HHS Public Access
Author manuscript
Toxicology. Author manuscript; available in PMC 2021 November 01.

Published in final edited form as:
Toxicology. 2020 November ; 444: 152582. doi:10.1016/j.tox.2020.152582.

Microphysiological System Modeling of Ochratoxin A-Associated Nephrotoxicity

Tomoki Imaoka[1], **Jade Yang**[1], **Lu Wang**[3], **Matthew G. McDonald**[2], **Zahra Afsharinejad**[3], **Theo K. Bammler**[3], **Kirk Van Ness**[1], **Catherine K. Yeung**[4,5], **Allan E. Rettie**[2], **Jonathan Himmelfarb**[5], **Edward J. Kelly**[1,5]

[1]Department of Pharmaceutics, School of Pharmacy, University of Washington, Seattle, Washington, 98195, USA

[2]Department of Medicinal Chemistry, School of Pharmacy, University of Washington, Seattle, Washington, 98195, USA

[3]Department of Environmental and Occupational Health Sciences, University of Washington, Seattle, Washington, 98195, USA

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Certificates

Mold-literate certification available to licensed primary care providers

View modules in order

Watch **entire** lecture before quiz

Quiz score >70%

Eligible practitioners are listed on DrCrista.com

CE/CME certificates up to 1 week

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Put Simply . . .

What are molds & mycotoxins

Who's impacted

How to test

What to do if you find it

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Impacts of Mold Illness

How Common Is It?

Threats of Indoor Mold

How Does It Get There?

Historical Perspective

Mold vs Yeast

Definition of Mold Illness

Do You Agree?

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Indoor Mold Occurence

More than a quarter of all buildings (OSHA)

Homes, apartments, schools, hospitals, workplaces, college housing, churches, hotels, summer camps, etc

66% of materials from WDB contain molds & mold toxins

Elevated fungal and microbial diversity in dust from WDB

Molds & mycotoxins persist - test positive at 5 months post WD event

PMID: 21531835, 19757292, 21585551

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Indoor Mold Threats

WDBs grow mold in biofilm

Creating superbugs via antifungals in paint

Negatively affects all living creatures

Mold harms via spores, spore fragments, mycotoxins, and chemicals

Increases the biologic and toxic load (biotoxins) on the inhabitants

PMID: 12781669, 22017920, 19191921

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Problematic Situations

Locations

- Humid climates, coasts, near water, poor drainage, river bottoms

Building specifics

- OSB/air tight combo in new construction, dirt crawl spaces, older run-down homes, finished basements, installation of moldy materials

Budget/Upkeep Issues

- Low-income housing, college housing, institutional buildings (schools, hospitals, churches)

During remediation

PMID: 22017920

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Water Intrusions

From The Outside-

- Roof Leaks
- Siding/Flashing Leaks
- Wall Cavities
- Floods
- Sewer Drain
- Shared Walls (condo, apt)
- Finished Basements
- Air Intake Filters

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Water Intrusions

From The Inside-

- Plumbing
- High Indoor Humidity
- Condensation
- Appliances
  - *esp Refrigerator
- Fish Tanks
- Pet Urine
- Plants
- Indoor Pools

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Historical Perspective

The Original Indoor Environmental Illness

Bible - physical & spiritual illness

Remediation guidance

Speaks to dangers to inhabitants *and* village

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Indoor Mold: Biblical Remediation

Leviticus 14: 33-45

34 “When you enter the land of Canaan, which I am giving you as your
possession, and I put a spreading mold in a house in that land, 35 the
owner of the house must go and tell the priest, ‘I have seen something
that looks like a defiling mold in my house.’ 36 **The priest is to order the
house to be emptied** before he goes in to examine the mold, so that
nothing in the house will be pronounced unclean. After this the priest is to
go in and inspect the house. 37 He is to examine the mold on the walls, and
if it has greenish or reddish depressions that appear to be deeper than the
surface of the wall, 38 the priest shall go out the doorway of the house and
close it up for seven days. 39 On the seventh day the priest shall return to
inspect the house. If the mold has spread on the walls, 40 he is to order that
**the contaminated stones be torn out and thrown into an unclean
place outside the town**. 41 He must have **all the inside walls of the
house scraped and the material that is scraped off dumped into an
unclean place outside the town.** 42 Then they are to take other stones to
replace these and take new clay and plaster the house.
43 “**If the defiling mold reappears** in the house after the stones have
been torn out and the house scraped and plastered, 44 the priest is to go
and examine it and, if the mold has spread in the house, it is a persistent
defiling mold; **the house is unclean.** 45 **It must be torn down—its
stones, timbers and all the plaster—and taken out of the town to
an unclean place.**

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Mold vs Yeast

Mold ~

- Multi-cellular fungi
- Grow in filamentous hyphae (branches)
- Reproduce via sexual & asexual methods
- Produce airborne spores
- Require organic matter for nutrition

Yeast ~

- Single-celled microscopic fungi
- Round, oval or budded
- Reproduce asexually
- Do not produce spores
- Used for fermentation
- Can be opportunistic infections (candida)

KEY POINT: Both contribute to total fungal load

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Spores, Spore Fragments & Mycotoxins

Occurrence ratio
500:1 ~ Fragment:Spore

Fragments ~ disrupted mold

Fragment size ~ nanoparticle-3 microns

Fragments ~ more allergenic (smaller size, ability to bypass lung clearance)

Fragments & spores secrete mycotoxins

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Mold Spore vs Mycotoxin

Mold Spores ~

- Large enough to trigger allergic-type reactions
- Trigger mucociliary clearance
- Recognized as causal for Type I Hypersens reactions
- Associated with the enigma 'Sick Building Syndrome'

Mycotoxins ~

- Too small to sound alarms
- Bypass mucociliary clearance
- Lipophilic adsorption into circulation via alveoli
- Arguments about source when illness ensues

MAKE NO MISTAKE: Both are implicated in human illnesses

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Scary Scary Mycotoxins: History

Middle Ages, St. Anthony's Fire

Salem Witch Trials

Ergotism ~ Rye & other grains

Ergot ~ mycotoxin from Claviceps purpurea

Ingest mycotoxin-infected grain

Symptoms ~ convulsive & gangrenous

Loss of digits/limbs (small vessel vasculitis), mania (CNS), GI convulsions

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The Current Definition of Mold Illness Do you Agree?

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Mold Illness Defined

"Spore illness"

Spores ~ large enough to trigger local resp system irritation & immune responses

NIOSH (Nat'l Inst for Occupational Safety & Health):
"health problems associated with excessive damp conditions and mold, to include: **allergies, hypersensitivity pneumonitis, and asthma**"

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Mold Illness Defined

WHO GUIDELINES FOR INDOOR AIR QUALITY: DAMPNESS AND MOULD

Sufficient epidemiological evidence is available from studies conducted in different countries and under different climatic conditions to show that the **occupants of damp or mouldy buildings, both houses and public buildings, are at increased risk of respiratory symptoms, respiratory infections and exacerbation of asthma**. Some evidence suggests **increased risks of allergic rhinitis and asthma**. Although few intervention studies are available, their results show that **remediation of dampness problems can reduce adverse health outcomes**.

There is clinical evidence that exposure to mould and other dampness-related microbial agents increases the risks of **rare** conditions, such as **hypersensitivity pneumonitis, allergic alveolitis, chronic rhinosinusitis and allergic fungal sinusitis**. Toxicological evidence obtained in vivo and in vitro supports these findings, showing the occurrence of diverse inflammatory and toxic responses after exposure to microorganisms – including their spores, metabolites and components – isolated from damp buildings.

While groups such as atopic and allergic people are particularly susceptible to biological and chemical agents in damp indoor environments, **adverse health effects have also been found in nonatopic populations**.

The **increasing prevalences of asthma and allergies** in many countries ***increase the number of people susceptible to the effects of dampness and mould in buildings***.

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Susceptibility

Does everyone exposed to a WDB react the same?

Predispositions

Polymorphisms ~ on the rise

HLA typing

In my experience, beware the non-allergic

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Missing Something In The Dx?

Being that spore illness is the only recognized mold illness

Being that spore fragments are formed 500:1 spores

Being that spores AND fragments secrete mycotoxins

Could we be missing symptoms and conditions that are in fact mold?

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Review

How this course works

Certification

Impacts

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Thank You

Dr. Jill Crista
Naturopathic Doctor
support@drcrista.com

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Are You Missing Mold Illness?

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Mold ~ A Formidable Foe

Are You Missing Mold Illness In Your Patients?

Dr. Jill Crista

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Mold ~ A Formidable Foe

Personality profile ~ a survivor

Mold's Specific Carbohydrate Diet

How mold creates harm

Mold, biofilm, and colonization

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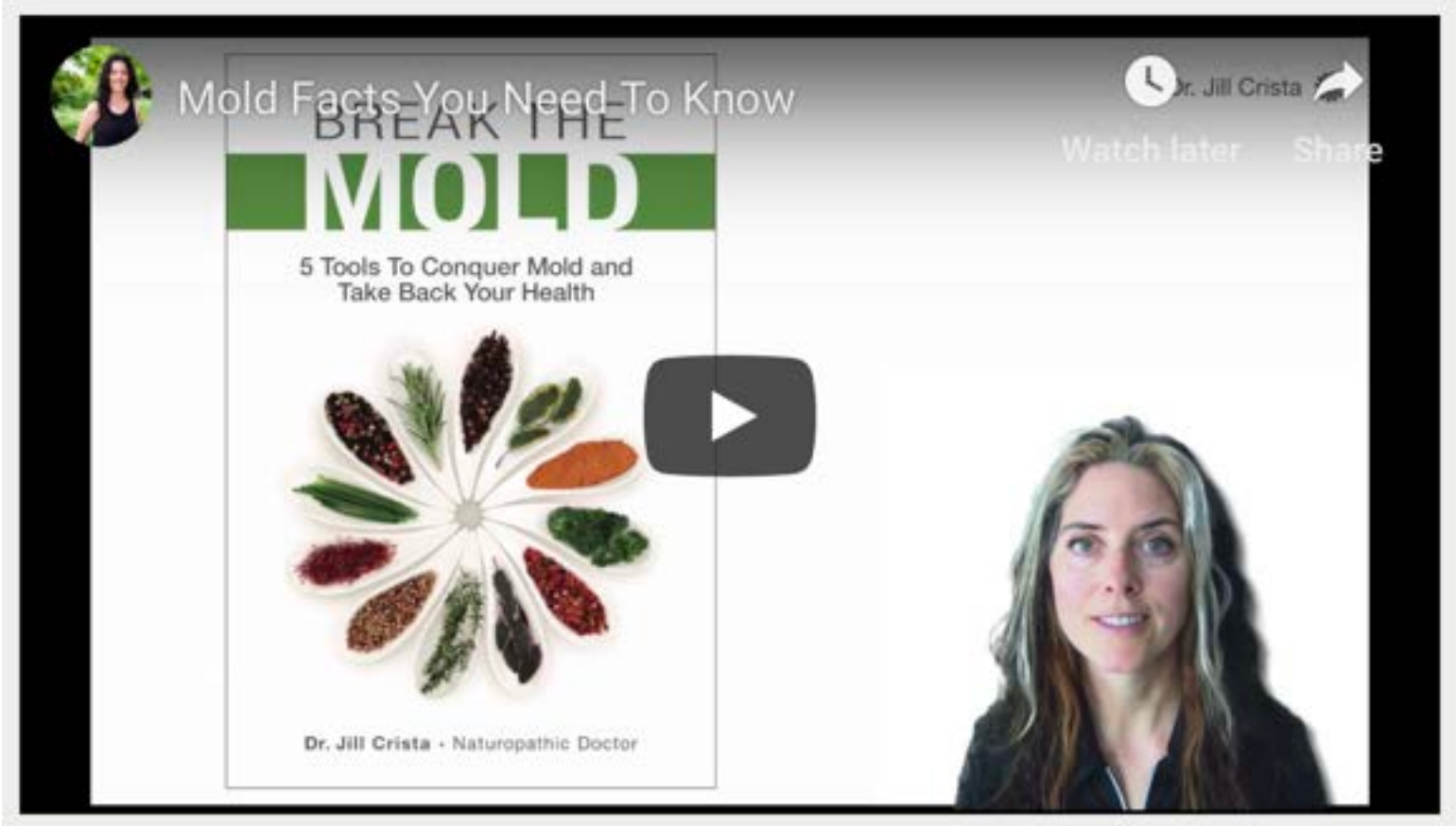
16 Mold Facts You Need To Know



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16 Mold Facts You Need To Know

MOLD...

1. is a survivor
2. has bad gas
3. is a bully
4. invades your body
5. causes toxic breath
6. won't go down without a fight
7. turns you into a wimp
8. causes cravings
9. can make you feel crazy, hazy and lazy
10. causes allergies
11. causes food sensitivities
12. makes you sensitive to chemicals
13. makes you sensitive to electromagnetic fields
14. sickness is hard to identify
15. sickness is often misdiagnosed
16. is part of a scandalous cover-up

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Mold Facts

Natural function ~ compost/recycle

Excrete 1° and 2° metabolites ~ inhaled, ingested, and absorbed

1° metabolites ~ nec for survival aldehydes, alcohols, odors, digestive enzymes, and structural elements (beta-glucans etc)

2° metabolites ~ competitive antimicrobials, mycotoxins

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Tenacious

Moisture ~ 1° element for growth,
2° is organic substrate

Obvious or visible water not necessary

High relative humidity is all that's required

Grows on WD surface within 24-48 hours

Difficult to kill

Spore formation and release increases
more when drying than when wet
(survival of species)

It's goal is to compost YOU

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Question

True or False?

Mold is an **old building** problem

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Answer

False!

Mold can grow in any building
within 48 hours
of the
water damage event,
no matter how old the
structure

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Mold's Specific Carbohydrate Diet

© Dr Jill Crista

Mold Types Found in WDBs

Penicillium chrysogenum

Aspergillus versicolor, A. fumigatus, A. melleus, A. niger, A. ochraceus

Chaetomium spp

Acremonium spp

Cladisporium herbarum

Ulocladium spp

Stachybotrys spp

Mucor racemosus, M. spinosus

Trichoderma spp

Arthrinium phaeospermum

Aureobasidium pullulans

Study limitation: only collection plates/flood conditions
Penicillium verrucosum, Alternaria, Fusarium missed

PMID: 21531835, 19191921

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Mold Types By Material

Wallpaper & Gypsum (drywall) ~
- Penicillium chrysogenum
- Acremonium spp
- Ulocladium spp
- Stachybotrys spp

Wood & “Was-Wood” ~
(plywood/modified wood products)
- Cladosporium herbarum
- Trichoderma spp
- Arthrinium phaeospermum
- Aureobasidium pullulans

PMID: 21531835

Attic

© Dr Jill Crista

APA
JUNE
20

Drywall

Photos courtesy of
Martine Davis
Certified Building
Biologist

Drywall

© Dr Jill Crista

Shower

© Dr Jill Crista

Mold Types By Material

Concrete & Flooring Materials ~

Aspergillus versicolor, A. fumigatus, A. melleus, A. niger, A. ochraceus

Chaetomium spp

Mucor racemosus, M. spinosus

Other ~

Penicillium verrucosum - ceiling tiles

Alternaria spp - carpets, textiles, horiz surfaces

Fusarium spp - HVAC, humidifiers

PMID: 21531835

Basement - Stachy + Chaetomium

© Dr Jill Crista

Air Duct

Flood

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Other Air Quality Considerations

VOCs and microbial VOCs

Dander

Allergens

Rodent feces

Gas (leaks, gas stove, sewer)

Formaldehyde (‘new’ smell)

Fiberglass

Fragrances

PCBs (candles)

Insecticides, pesticides

EMFs (WiFi, smart meters)

Radon (granite, foundation cracks)

Heavy metals (hunters/hobby, lead)

Endotoxins

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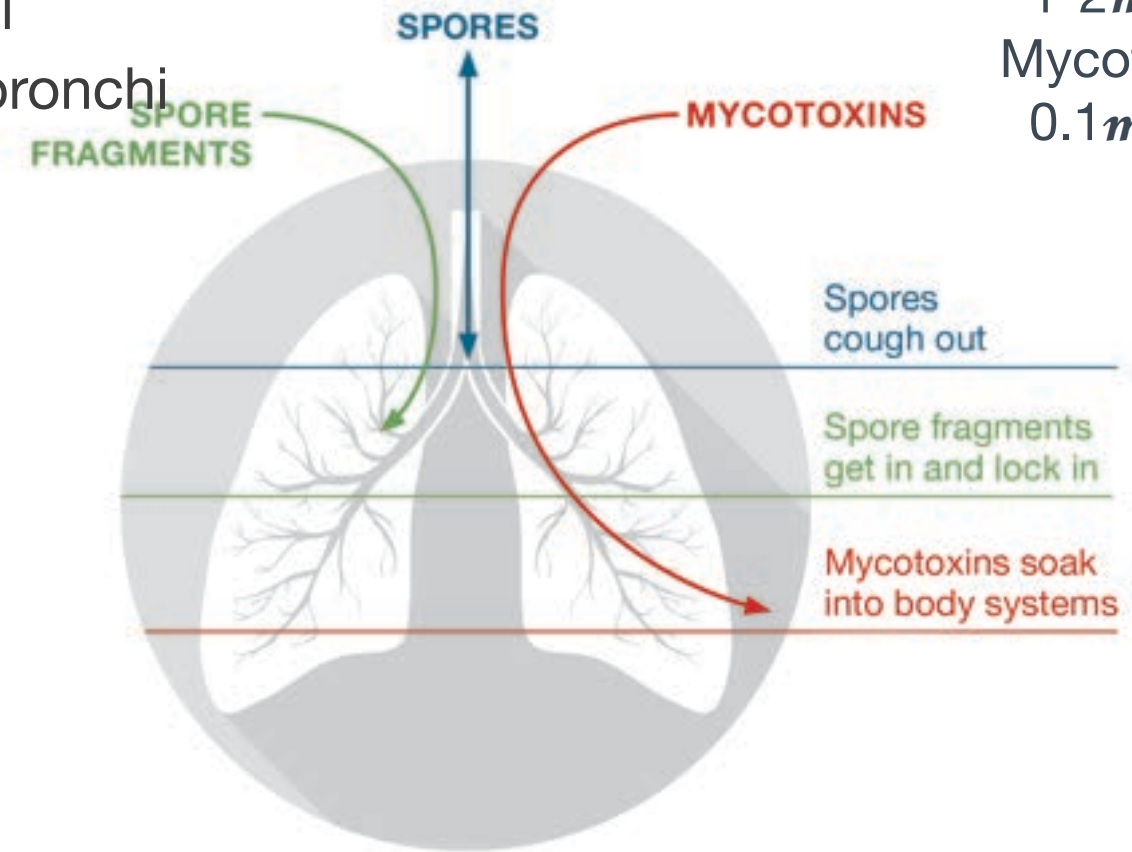
How Mold Creates Harm

© Dr Jill Crista

Respiratory System vs Mold

Respiratory System

- $>7m$ Nasal
- $5\text{-}7m$ Pharynx
- $3\text{-}5m$ Trachea
- $3\text{-}5m$ 1° Bronchi
- $2\text{-}3m$ 2° Bronchi
- $1\text{-}2m$ Terminal bronchi
- $<1m$ Alveoli



Mold

Spores-
- Cladosporium $3\text{-}5m$
- Aspergillus $2\text{-}5m$
- Penicillium $1\text{-}5m$

Fragments-
- $1\text{-}2m$

Mycotoxins-
- $0.1m$

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Spores

Immune responses are highly variable ~
- From allergic to life-threatening
- disseminated fungal infection (IFI)

General ROT ~
- Spores induce
- Mycotoxins suppress
- *but both deplete I/S with ongoing exposure

Mechanisms ~
- Induce inflammatory reaction
- Reduce respiratory mucosal ciliary function
- Adhesion
- Evasion
- Invasion

"*007*" analogy

PMID: 27623953, 26600019, 29371501, 27092126, 8463496, 19527167, 19201896

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Spores & Airways

First point of contact is most likely an airway epithelial cell (AEC)

First response by AEC is to “season it, then try to eat it”

If that doesn’t work, AEC’s next response is to send out gene intel to I/S, then commit suicide

Stachybotrys alters phospholipid synthesis related to surfactant ~
Keep the lungs hyperinflated for easier invasion

PMID: 25449202, 12221236, 26600019, 29371501, 27092126, 30589860

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NIH Public Access
Author Manuscript
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J Immunol. 2009 February 15; 182(4): 2416–2424. doi:10.4049/jimmunol.0801569.

IgE INFLUENCES THE NUMBER AND FUNCTION OF MATURE MAST CELLS BUT NOT PROGENITOR RECRUITMENT IN ALLERGIC PULMONARY INFLAMMATION[1]

Clinton B. Mathias[*,†], **Eva-Jasmin Freyschmidt**[*,†], **Benjamin Caplan**[*], **Tatiana Jones**[‡], **Dimitri Poddighe**[*,†], **Wei Xing**[‡], **Krista L. Harrison**[*], **Michael F. Gurish**[‡,†], and **Hans C. Oettgen**[2,*,†]

[*]*Division of Immunology, Children's Hospital Boston, Boston, MA 02115*

[‡]*Division of Rheumatology, Allergy and Immunology, Brigham and Women's Hospital, Boston, MA 02115*

[†]*Harvard Medical School, Boston, MA 02115*

Inhalation of A. fumigatus extract in mice induced a dramatic rise in IgE *accompanied by an increase in airway mast cells*, and signs indicating an elevated systemic mast cell load.

Analyses of potential cellular targets of IgE revealed that *IgE antibodies are not required for the induction of mast cell progenitors* in response to allergen but rather act by sustaining the survival of mature mast cells.

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Spore Effects

Allergic recruitment induction ~
- Influence mast cell homeostasis to enhance survival
- Induce pulmonary mast cell degranulation even in the absence of antigen-specific IgE
- Increased allergic responses to other respirable antigens (dust, grass, pollen, pet dander, exhaust)

Inflammation/irritation/degradation of respiratory mucosal linings over time (+gut/bladder)

Spore invasion/infection due to LT immune depletion

PMID: 27623953, 26600019, 29371501, 27092126, 8463496, 19527167, 19201896

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Respiratory research

ORIGINAL ARTICLE

Airway epithelial phosphoinositide 3-kinase-δ contributes to the modulation of fungi-induced innate immune response

Jae Seok Jeong,[1] Kyung Bae Lee,[1] So Ri Kim,[1,2] Dong Im Kim,[1] Hae Jin Park,[1] Hern-Ku Lee,[3] Hyung Jin Kim,[2,4] Seong Ho Cho,[5] Narasaiah Kolliputi,[5] Soon Ha Kim,[6] Yong Chul Lee[1,2]

"We used two in vivo models induced by exposure to *Aspergillus fumigatus* (*Af*) and *Alternaria alternata* (*Aa*), as well as an *Af*-exposed in vitro system. We also checked **NLRP3 expression** in lung tissues from patients with allergic bronchopulmonary aspergillosis (ABPA)."

What's the key question of this study?
"Phosphoinositide 3-kinase (PI3K)-δ isoform has been shown as an important mediator of allergic lung inflammation, including the fungi-induced form; however, a role of PI3K-δ in the modulation of innate immune response against fungal allergens has not been reported. "

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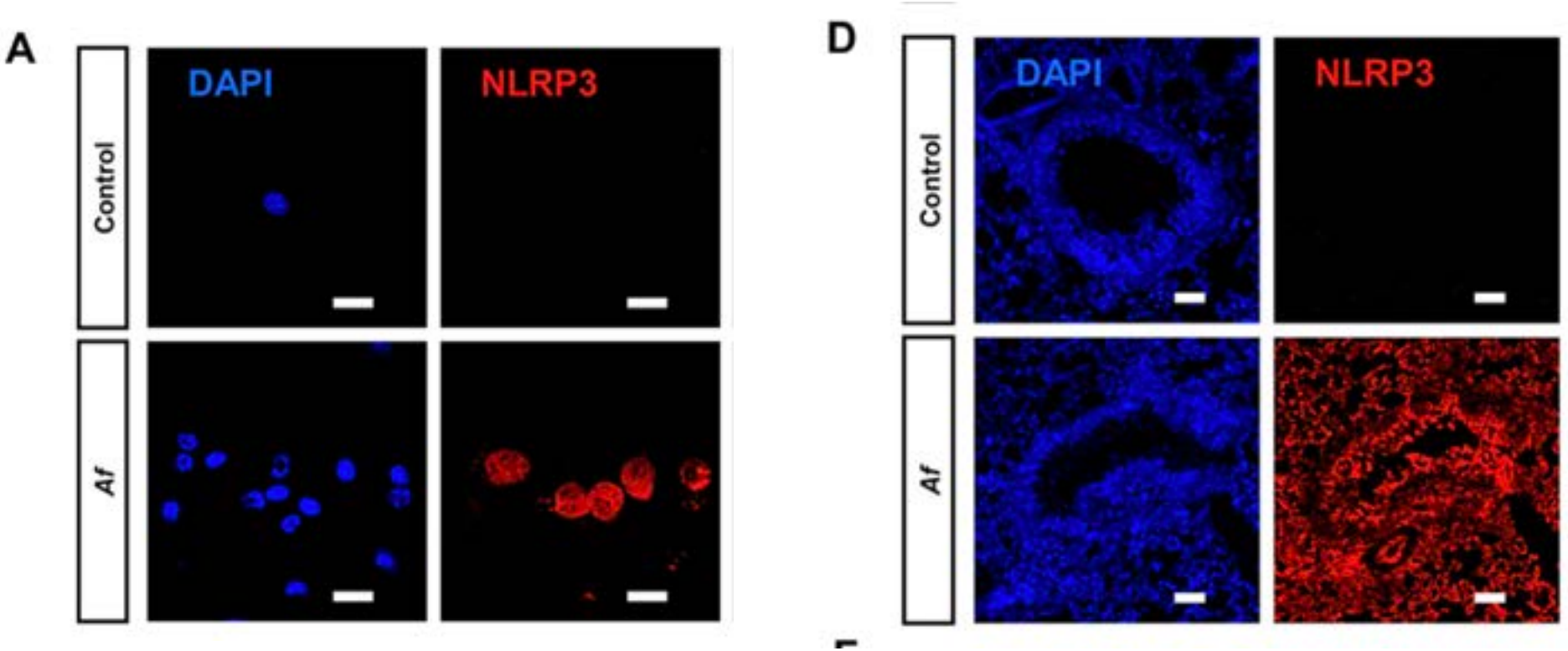

A: bronchoalveolar lavage D: lung tissue (DAPI stain=nuclear localisation)

Af-exposed mice: ↑**NLRP3 expression** (a limiting factor in NLRP3 inflammasome activation)

"NLRP3 is increased in lung tissues from patients with ABPA (allergic bronchopulmonary aspergillosis)"

"Elevation of NLRP3 inflammasome assembly/activation was also observed in Af-stimulated murine and human EpCs."

"NLRP3 inflammasome is implicated in *Af*-induced allergic lung inflammation"

"These data indicate that *Af* exposure may be related to the NLRP3 inflammasome activation in human lung disorder…"

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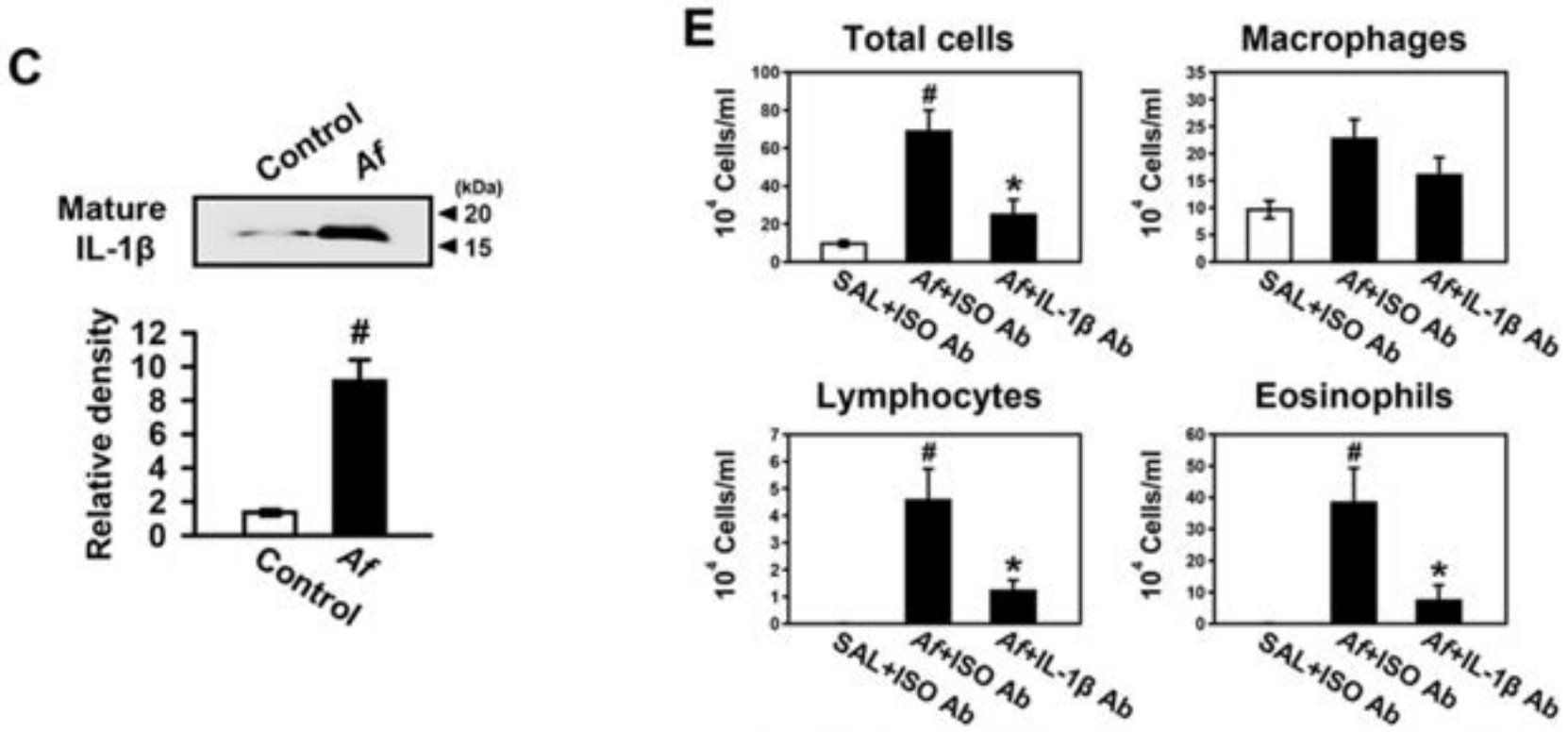

Af-exposed mice: ↑**IL-1β**

"NLRP3 inflammasome has been known to be implicated in allergic inflammatory processes as well as antifungal defence through IL-1β."

"Notably, selective inhibition of NLRP3 inflammasome led to the decrease of IL-1β in the lung of *Af*-exposed mice,…"

"…and neutralisation of IL-1β improved numerous features of *Af*-induced allergic lung inflammation."

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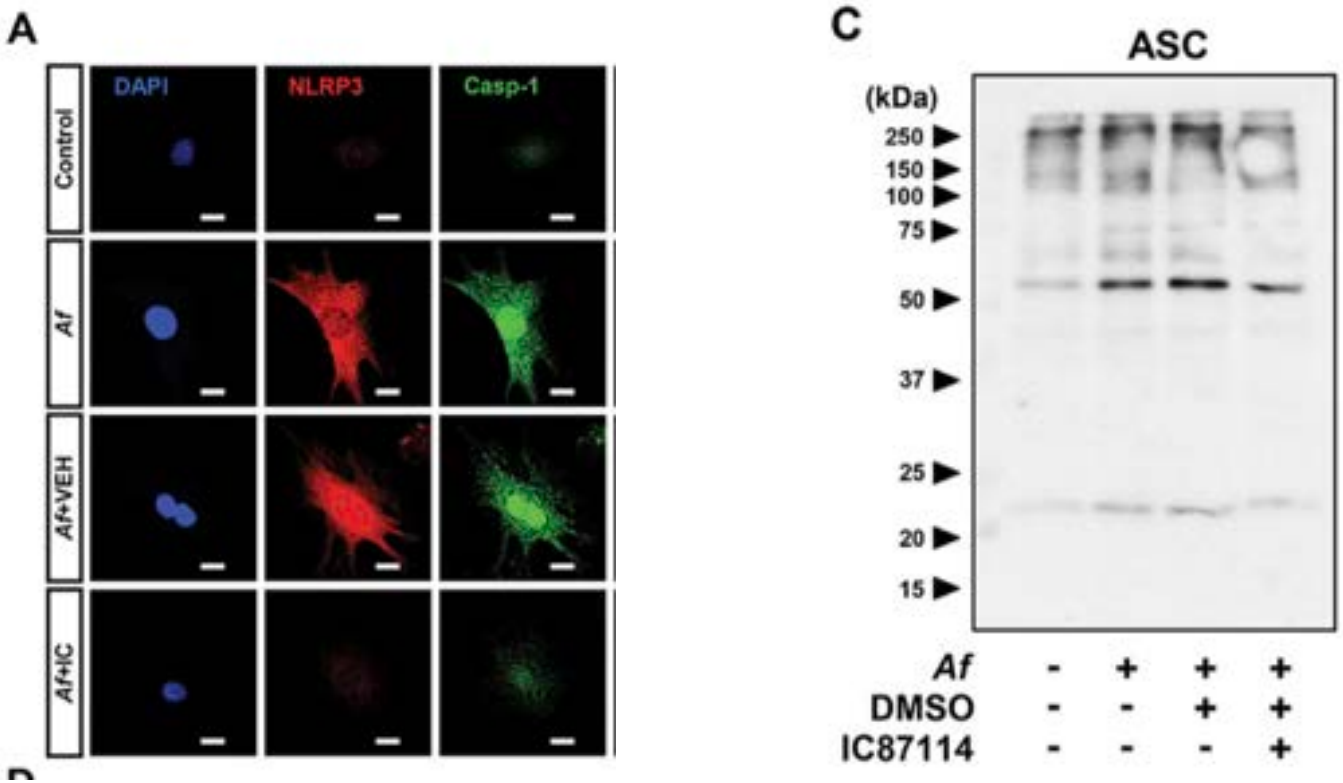

Af-exposed mice: ↑**PI3K-δ**

With admin of a selective inhibitor of PI3K-δ (IC87114, alpelisib & ..lisib Rx family)↓NLRP3

"PI3K-δ (phosphoinositide 3-kinase) plays a key role in regulation of immune processes through activating immune cells and trafficking inflammatory cells."

"PI3K-δ is also activated in response to fungal exposure and plays a role in the regulation of ER stress, thereby being crucially implicated in fungal allergic inflammation."

"Inhibition of PI3K-δ improves *Af*-induced allergic lung inflammation through regulation of NLRP3 inflammasome assembly/activation."

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international scientific meeting (the 22nd congress of the Asia Pacific Society of Respirology, 2017).

Received 28 March 2017
Revised 20 February 2018
Accepted 26 March 2018
Published Online First
5 April 2018

Results Assembly/activation of NLRP3 inflammasome was increased in the lung of *Af*-exposed mice. Elevation of NLRP3 inflammasome assembly/activation was observed in *Af*-stimulated murine and human epithelial cells. Similarly, pulmonary expression of NLRP3 in patients with ABPA was increased. Importantly, neutralisation of NLRP3 inflammasome derived IL-1β alleviated pathophysiological features of *Af*-induced allergic inflammation. Furthermore, PI3K-δ blockade improved *Af*-induced allergic inflammation through modulation of NLRP3 inflammasome, especially in epithelial cells. This modulatory role of PI3K-δ was mediated through the regulation of mitochondrial reactive oxygen species (mtROS) generation. NLRP3 inflammasome was also implicated in *Aa*-induced eosinophilic allergic inflammation, which was improved by PI3K-δ blockade.

Why read on?

- Inhibition of PI3K-δ signalling may have potential for treating fungi-induced severe allergic lung inflammation in humans.

between innate and adaptive immune response is central to airway inflammation.[1] Among many cells, airway epithelium which expresses various pattern recognition receptors (PRRs)[2] is the first line of defence on encountering allergens and an essential controller of immune responses.[3] Particularly, the nucleotide-binding domain, leucine-rich repeat containing receptors (NLRs) represent one important PRR family in the intracellular compartment.[4]

Several members of NLRs are involved in the

”These findings demonstrate that fungi-induced assembly/activation of NLRP3 inflammasome in airway epithelium may be modulated by PI3K-δ, which is mediated partly through the regulation of mtROS generation.”

“Inhibition of PI3K-δ may have potential for treating fungi-induced severe allergic lung inflammation.”

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Resveratrol attenuates experimental allergic asthma in mice by restoring inositol polyphosphate 4 phosphatase (INPP4A)

Jyotirmoi Aich [1], Ulaganathan Mabalirajan, Tanveer Ahmad, Kritika Khanna, Rakshinda Rehman, Anurag Agrawal, Balaram Ghosh

Affiliations + expand

PMID: 22986054 DOI: 10.1016/j.intimp.2012.08.017

”Oxidative stress has been shown to be strongly associated with most of the features of asthma and leads to accumulation of phosphatidyl inositol (3,4) bis-phosphate, which in turn activates PI3K pathway and contributes to oxidative stress.”

“Thus, there exists a vicious loop between oxidative stress and lipid phosphatase signaling.”

“These results suggest a novel mechanism of action of resveratrol in attenuating asthma phenotype by downregulating PI3K-Akt pathway via upregulating INPP4A.”

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Spore Fragments

500:1 Fragment:spore

Usu occurs when dead/dried mold is disrupted

Become ultrafine particulate in permanent suspension, even in lungs

Highly inflammatory to sinus & lung tissue ~
More potent than spores at inducing proinflam cytokines
Asp/Pen - enhance TLR2-dependent expression and release of IL-6 + IL-8 in human bronchial epithelial cells

Airway remodeling if persistent exposure

“Mold-othelioma” - mesothelioma-type LU condition related to mold fragment exposure vs asbestos: Shortness of breath, cough, pain in the chest or abdomen, fatigue, fever or night sweats, respiratory complications, muscle weakness, nausea or bloating

PMID: 30917597, 31116698

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International Journal of *Environmental Research and Public Health*

MDPI

Article

Pro-Inflammatory Responses in Human Bronchial Epithelial Cells Induced by Spores and Hyphal Fragments of Common Damp Indoor Molds

Elisabeth Øya [1,*], Rune Becher [1], Leni Ekeren [1], Anani K.J. Afanou [2], Johan Øvrevik [1,3] and Jørn A. Holme [1]

[1] Department of Air Pollution and Noise, Division of Infection Control and Environment and Health, Norwegian Institute of Public Health, P.O. Box 4404 Nydalen, N-0403 Oslo, Norway; Rune.Becher@fhi.no (R.B.); Leni.Ekeren@fhi.no (L.E.); Johan.Ovrevik@fhi.no (J.Ø.); JornAndreas.Holme@fhi.no (J.A.H.)

”Human bronchial epithelial cells were exposed to X-ray treated spores and hyphal fragments from pure cultures of Aspergillus fumigatus, Penicillum chrysogenum, Aspergillus versicolor and Stachybotrys chartarum.”

“Hyphal fragments of A. fumigatus and P. chrysogenum induced expression and release of the pro-inflammatory cytokines, *while none of the other hyphal preparations* had effects.”
[*Is this how the more toxigenic species like Stachy persist? By evading allergic detection?]

“Untreated A. fumigatus spores formed hyphae and **triggered expression of pro-inflammatory genes** with similarities to the effects of hyphal fragments.”

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Mycotoxin Immune Overview

Immunosuppressive via:
- Direct action on immune cells
- Epigenetic alterations to the immune response
- Direct genetic alterations

Inhibit host defense via:
- NK cell hypofunction
- T-/B-cell deficiency
- LT exposure - Ig subclass def (false neg allergy/ infection labs)

Leukopenia w relative lymphopenia, neutrophilia & eosinophilia

TGF-β1↑
- ↑ impairs T-reg fxn → immune overactivation/ asthma

Disordered GALT, affects nutrient absorption, intestinal apoptosis

PMID: 26474839, 27178040, 25449202, 12221236, 26600019

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frontiers in Immunology

ORIGINAL RESEARCH
published: 04 October 2018
doi: 10.3389/fimmu.2018.02297

Aflatoxin B_1 Promotes Influenza Replication and Increases Virus Related Lung Damage via Activation of TLR4 Signaling

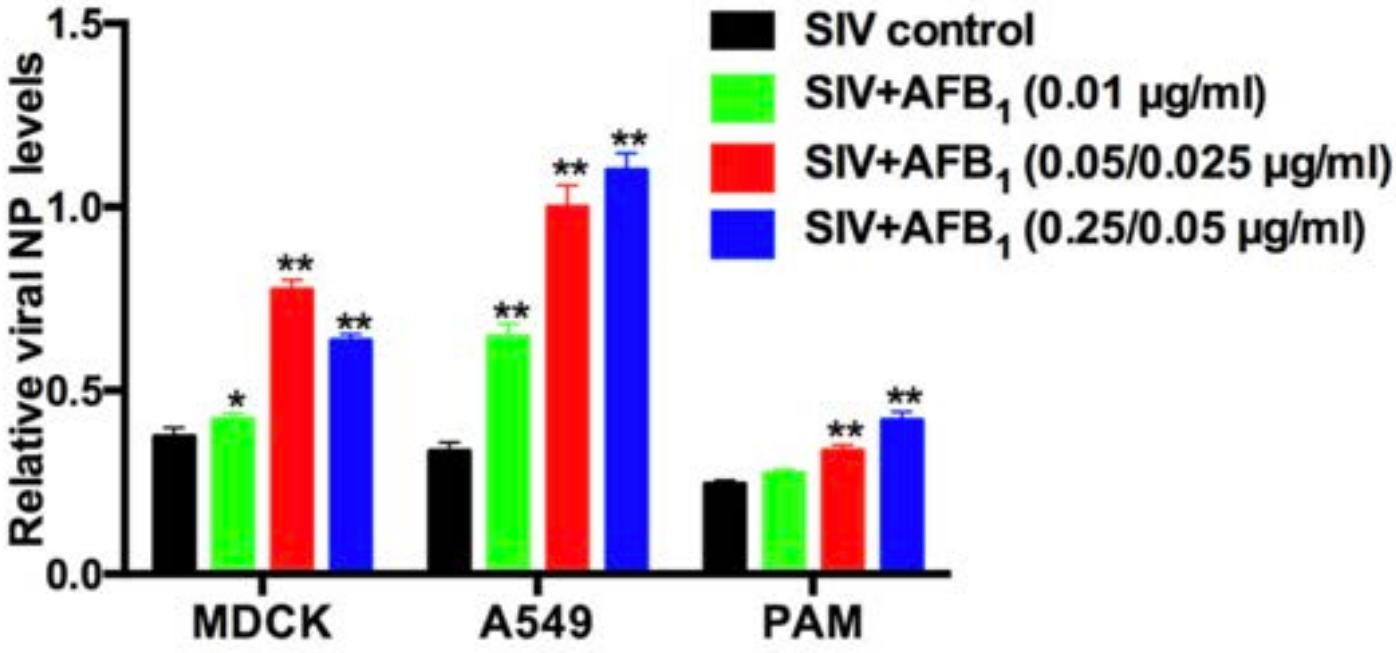
Yuhang Sun[1,2], *Jiarui Su*[1,2], *Zixuan Liu*[1,2], *Dandan Liu*[1,2], *Fang Gan*[1,2], *Xingxiang Chen*[1,2] *and Kehe Huang*[1,2*]

[1] *Department of Animal Nutrition and Immunology, College of Veterinary Medicine, Nanjing Agricultural University, Nanjing, China,* [2] *Institute of Nutritional and Metabolic Disorders in Domestic Animals and Fowls, Nanjing Agricultural University, Nanjing, China*

"Our results are the first to suggest that AFB1 promotes Swine Influenza Virus (SIV) replication and SIV-related lung damage by activating the TLR4-NFκB pathway.

This finding is supported by previous studies demonstrating that TLR4 antagonists or TLR4 knockout can prevent lethal influenza infection (20, 42). **Therefore, we infer that AFB1 might promote TLR4 overexpression and excessive inflammatory responses and reduce tolerance (43), thereby promoting SIV replication.**"

© Dr Jill Crista



Swine Influenza Virus (SIV) replication correlates to increasing concentrations of AFB1.

"Taken together, our results suggest that AFB1 exposure promotes SIV replication *in vitro*."

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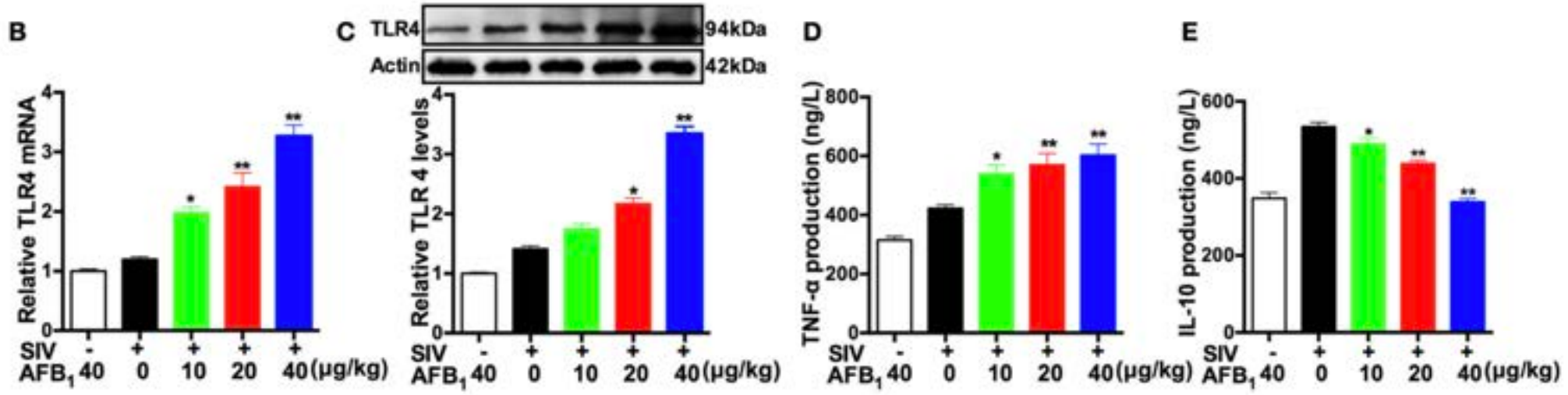

"In addition, the inflammatory response was quantified by the release of TNF-α and IL-10, and the results showed that AFB1 at doses of 10 to 40 μg/kg markedly increased TNF-α release but significantly decreased IL-10 release in sera (Figures 5D,E)."

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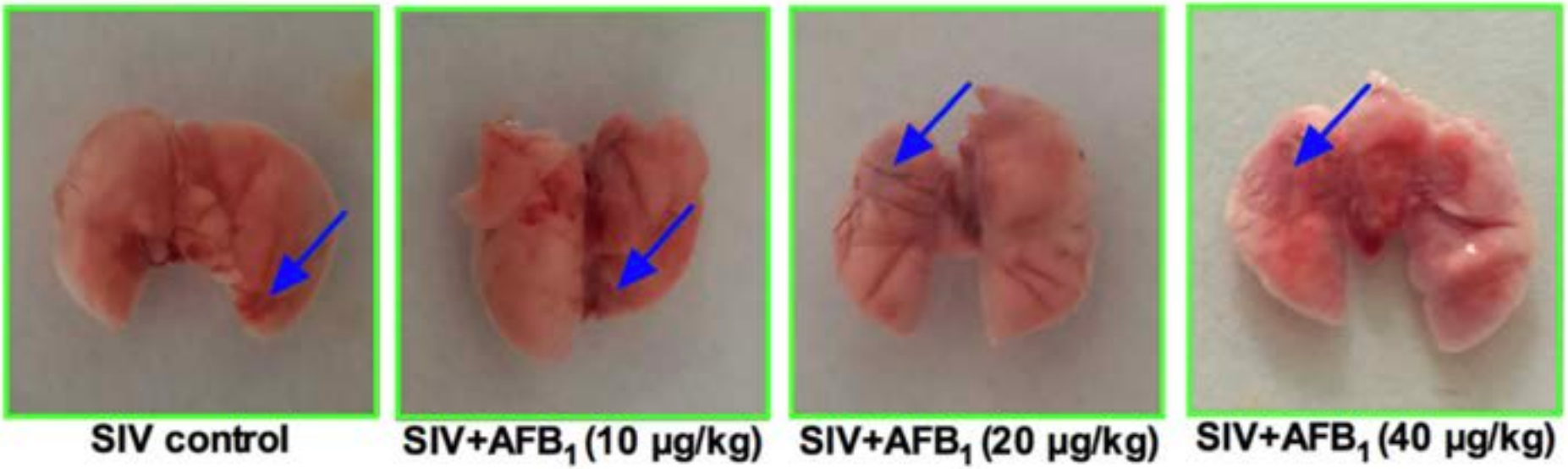

"To further verify the in vitro results, lung tissues were taken from SIV-infected mice exposed to AFB1 to assess viral replication…and histological damage.

The areas of hemorrhage are denoted with the blue arrows.

SIV-infected mice exhibited decreased weight gain, but enhanced… inflammatory cell infiltration compared with mice from the blank group, and these changes were aggravated following exposure to 10–40 µg/kg AFB1.

AFB1 promotes SIV **replication** and **lung damage** in mice."

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Cellular Physiology and Biochemistry

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Original Paper

Low-Level Aflatoxin B_1 Promotes Influenza Infection and Modulates a Switch in Macrophage Polarization from M1 to M2

Yuhang Sun[a,b] Zixuan Liu[a,b] Dandan Liu[a,b] Jin Chen[a,c] Fang Gan[a,b]
Kehe Huang[a,b]

[a]College of Veterinary Medicine, Nanjing Agricultural University, Nanjing, [b]Institute of Nutritional and Metabolic Disorders in Domestic Animals and Fowls, Nanjing Agricultural University, Nanjing, [c]National Research Center of Engineering and Technology for Veterinary Biologicals, Jiangsu Academy of Agricultural Sciences, Nanjing, China

"…given the differences in morbidity and mortality following SIV infection, we hypothesize that AFB1 promotes SIV infection.

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"...macrophages are the first line of defense against viral infection,…critical for the defense against influenza virus infection.

M1 macrophages produce proinflammatory cytokines, thus contributing to host defense against pathogens and tissue injury;

M2 macrophages produce anti-inflammatory cytokines, thus promoting tissue repair.

The phenomenon of the existence of the two contrasting M1/M2 phenotypes is referred to as 'macrophage polarization'.

Macrophage polarization can occur at any point in an inflammatory process;

multiple phenotypic markers, cytokines and growth factors, such as nitric oxide synthase (iNOS), TNF-α and IL-10, interact to determine the final polarization state.

Previous studies indicated that AFB was immunotoxic to porcine alveolar macrophages (PAMs) and that AFB leads to time- and dose-dependent *decreases in the viability and phagocytic activity of PAMs*;

furthermore, *AFB decreases proinflammatory cytokine levels and increases anti-inflammatory cytokine levels in macrophages*."

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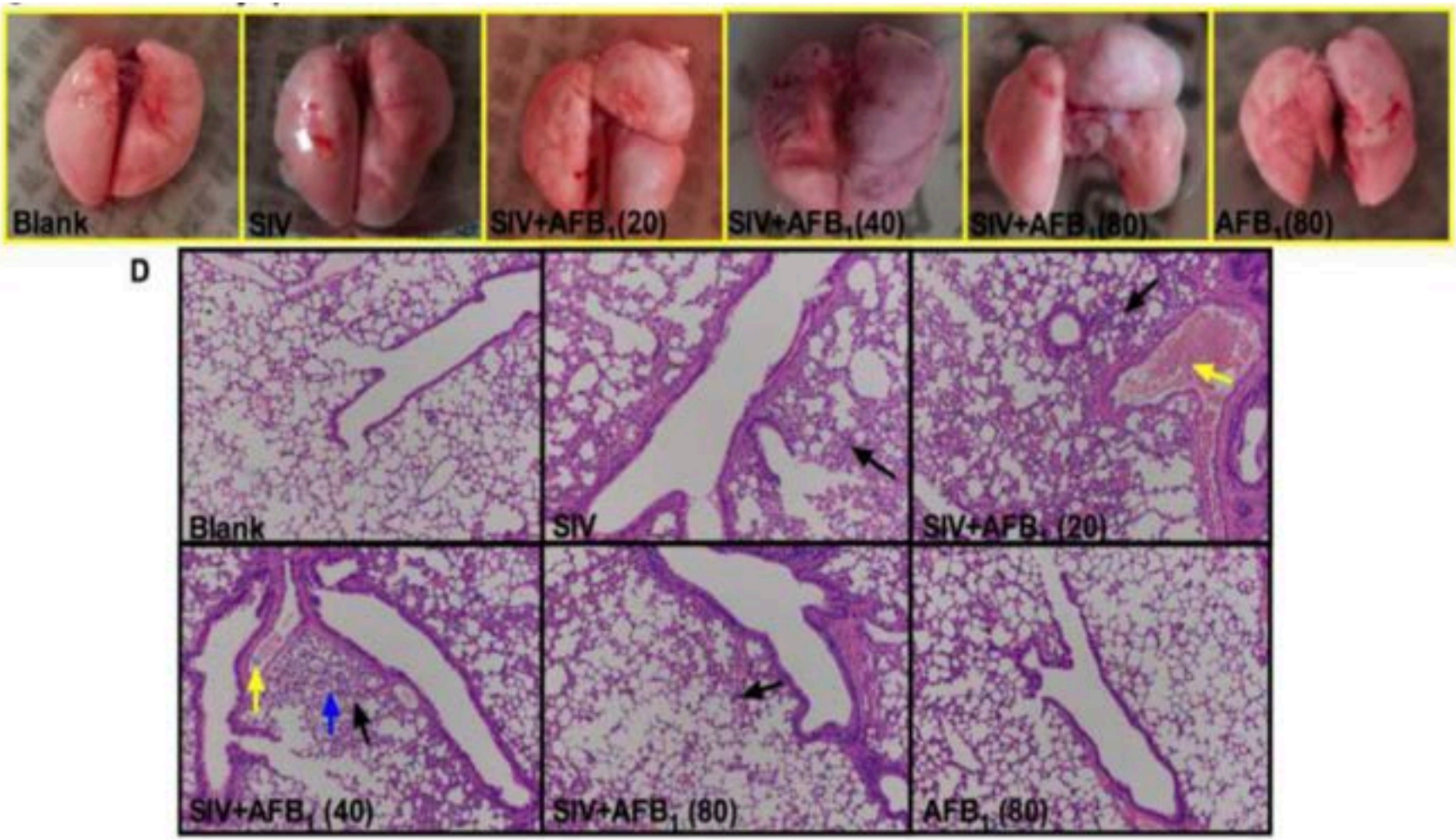

"Inflammatory cell infiltration, inflammatory cells in the bronchial lumen and areas of hemorrhage are denoted with the black, yellow and blue arrows, respectively.

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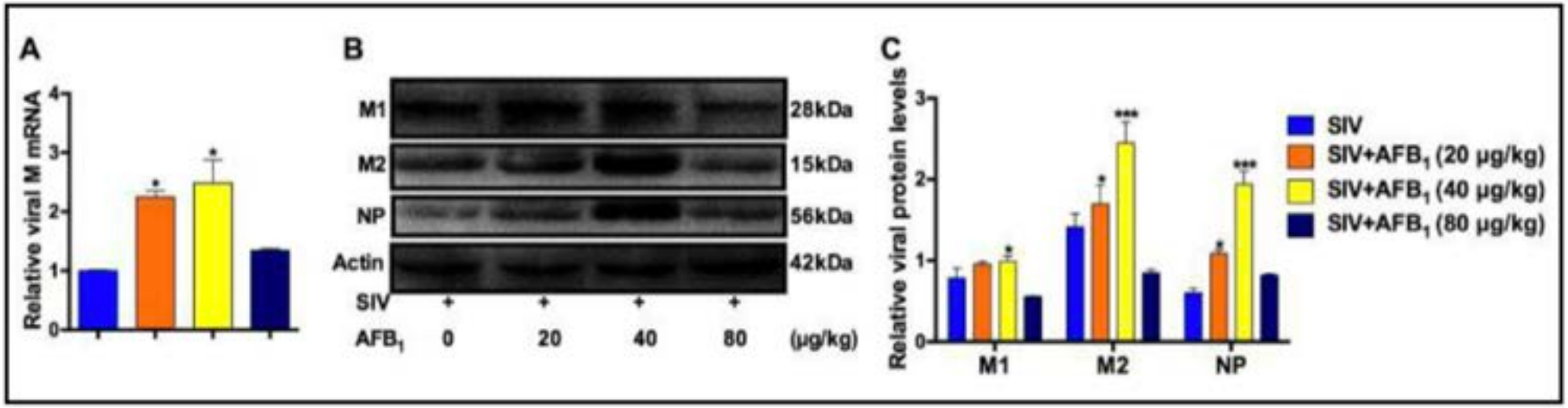

Low levels of AFB promote SIV infection, inflammatory responses, immune organ damage, induce a switch in alveolar macrophage polarization from M1 to M2, and confer poorer outcomes in SIV-infected in mice.

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Mold Wins

Breathing changes ~
- Shallow, airway constriction

Chronic inflammation ~
- All resp passages
- Nasal, sinus, lung

Airway remodeling ~
- Lower lobes of lungs
- Scarring

Immune deficiency ~
- Mucosal lining
- NK cell dysfunction
- T- and B-cell disorder

Neuroinflammation

Parallel GI tract inflammation

PMID: 23710148

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Recognized Human Impacts

Allergic (IgE-mediated) ~
- Allergic rhinitis
- Hypersensitivity Pneumonitis
- Asthma

Non-allergic (non IgE-mediated) ~
- Non-IgE mediated asthma exacerbation

Infection ~
- Aspergillosis

PMID: 24368325

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Mold: Mis*sed*Diagnoses

Seasonal Allergies
Chronic Sinusitis
Interstitial Lung Disease
Anxiety/Depression
Tinnitus
Sarcoidosis
T-cell Abnormality
Acquired Immunodeficiency
Chronic Fatigue Syndrome
Interstitial Cystitis
Nephritis
Insomnia/Sleep Apnea
Dysautonomia/Neuropathies
Mast Cell Activation Syndrome
Cancer

PMID: 26738372, 25616361, 25745963, 22253638

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STORY | Carpet Mushrooms

College friend invitation to see her carpet mushrooms

Three species of mushroom crops sprouting up through her carpet

Repurposed barn to a cottage

Initial ~ acne and fatigue

Next ~ nausea and decreased appetite

Cyclical vomiting syndrome

In 3 months, developed kidney disease

Too sick to go to school or work

No explanation for why this previously fit, healthy 20-yo woman was falling apart so quickly

A few weeks out of the cottage, she started to feel a little better

Her chiropractor asked about her living environment and made connection

More than a building issue, it was literally killing her

Took years to recover kidney function

* * *

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Mold, Colonization & Biofilm

© Dr Jill Crista

Colonization

Different than infection (Aspergillosis)

Sinuses of normal controls ~
- fungus, bacteria normal findings

So what's the big deal?

Only sick people's fungal colonies
- behave badly
- form mycotoxins

Colonization
- sinuses (>90%), lungs, GI tract

PMID: 24368325, 23710148

© Dr Jill Crista

Colonization, biofilm, or both?

Mycotoxins ~ competitive survival tactic

Other microbes in sinus to compete?

Culprits ~ MARCoNS, Pseudomonas, Klebsiella

Chronic rhinosinusitis patients
- endoscopic sinus surgery
- those w *biofilm* ~
- more severe disease preoperatively
- persistence of postoperative sxs
- ongoing mucosal inflammation
- increase infections

PMID: 20537281, 24368325, 23710148

© Dr Jill Crista

My Theory

Persistence despite Avoidance?

Normal controls: +fungus, -mycotoxins
Sick pts: +fungus, +mycotoxins

WDB exp is the key ∴ mycotoxins the trigger

If susceptible and/or sufficient exposure duration:
- Mycotoxins trigger protective mechanism
- Conversion of healthy microbiome to pathogenic biofilm
- Fungal overburden

Once recovered, mycotoxins can re-trigger old pattern

Theory explains persistence and flares

Rationale for effectiveness of antifungals w/o infection Dx

© Dr Jill Crista

Biofilm

In nature, is more the rule than the exception

Slime layer

Mixed microbial inhabitants

Matrix-like compound
- Protects & adheres inhabitants

Quorum sensing
- Share survival information
- Collectively survey host immunity
- Determine when to reproduce

Assist and compete (Mad Max)

Study | “microbiology of sinusitis is influenced by prev antimicrobial therapy, vaccinations & the presence of normal flora capable of interfering w growth of pathogens.”

PMID: 27086363

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The Key Is . . .

Exposure to a water-damaged building

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Review

Personality profile ~ a survivor

Mold's Specific Carbohydrate Diet

How mold creates harm

Mold, biofilm, and colonization

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Dr. Jill Crista
Naturopathic Doctor
support@drcrista.com

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Are You Missing Mold Illness?

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Scary Scary Mycotoxins

Are You Missing Mold Illness In Your Patients?

Dr. Jill Crista

© Dr Jill Crista

Mycotoxin Overview

What's a mycotoxin anyway?

Negative health impacts

Mycotoxin affinities & the body

Other than mycotoxins

© Dr Jill Crista

STORY | Stressed Out

Woman, Mid-40s, CFS & “stress”

Fatigue, sinus congestion, allergies, insomnia

Episodic unnerving feeling of dread, Dxd panic attacks

Incr freq, < work/travel

“High strung” at work, exhausted when not

Steroidal sinus spray qd-bid

Tylenol PM hs

Antianxiety Rx - s/e anxious/fatigue next day

Work~historic preserv in restored Victorian mansion

Bldg described as “musty” but had “gotten used to it”

Hobby ~ historic sites/historic B&Bs

Labs~ mult strains sinus fungus+hi urine mycotoxins

Work building had an invisible mold problem

Didn’t connect the dots that work caused her sinus issues/panic attacks bc neither happened immed

Moved locations for work/tx for mold

>fatigue, stress, panic attacks, allergies, sinuses, sleep

Steroid sinus spray/Tylenol PM d/c’d over time

Panic attacks dt mold, not an inability to handle stress

* * *

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What's A Mycotoxin Anyway?

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Mycotoxin Reminder

Ergotism - Middle Ages St. Anthony's Fire,
Salem Witch Trials

Ergot - mycotoxin from infected grain
caused convulsions
gangrene via small vessel vasculitis

Ergotamine - used in different Rx forms for
postpartum hemmorhage, migraine,
analgesia

Alcohol - brewer's yeast

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Mycotoxins Of Concern

Aflatoxin
Aspergillus flavus, A. parasiticus

Chaetoglobosin A,C
Chaetomium globosum

Citrinin
Aspergillus, Penicillium, Monascus

Enniatin B_1
Fusarium spp

Gliotoxin
Aspergillus fumigatus, Candida spp

Ochratoxin A
A. ochraseus, A. niger, Penicillium verrucosum, P. nordicum, P. chrysogenum

Patulin
Aspergillus spp, Penicillium spp, Mucor, Fusarium spp

Sterigmatocystin
Precursor of Aflatoxin, A. versicolor

Trichothecenes (Roridin, Verrucarin, Nivalenol, Deoxynivalenol, Diacetoxyscirpenol, Satratoxin)
Stachybotrys chartarum, Trichoderma viridae, Fusarium spp, Myrothecium

Zearalenone
Fusarium spp

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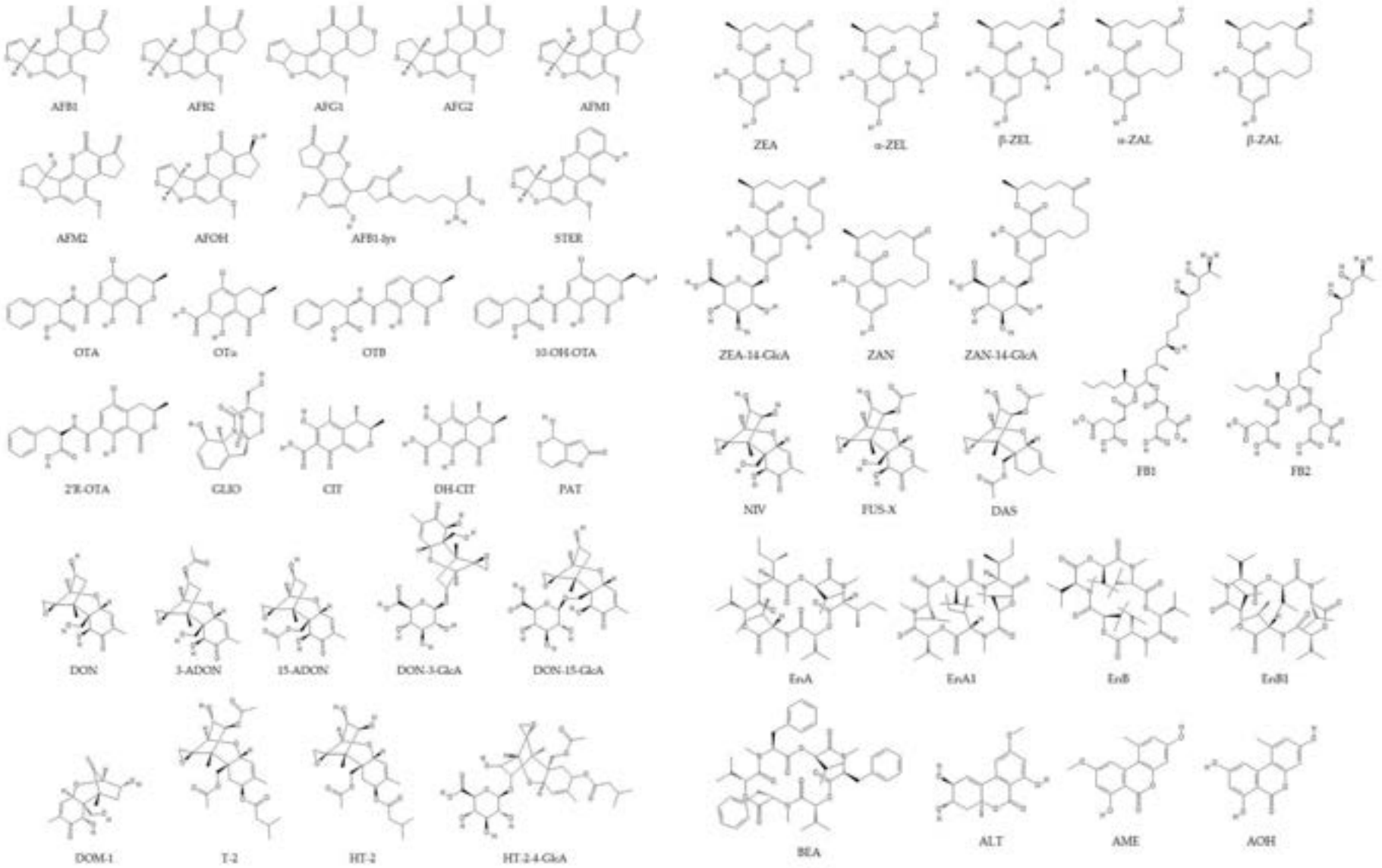
Wide Structural & Biosynthetic Diversity



PMID 32121036

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Mycotoxins

Produced by all fungal elements

Vary by mold species

Lipophilic molecules

Secreted onto substrate & aerosolized

Wide structural and biosynthetic diversity

Energetically expensive

Competitive inhibition of other microbes

Interfere with vital cellular processes
protein & RNA/DNA synthesis
∴ most are cytotoxic

Harmful to human health

Inhaled, ingested & absorbed

Commodified for oncology & weaponized

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Question

True or False?

You know you have a mold problem, because it **stinks**

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Answer

False!

Mycotoxins, the most toxic part of mold, which seep through building materials and poison indoor air, **have no scent**

Musty or moldy smells are from other mold chemicals, and need air exposure to stink. If it's trapped, **you can't smell it**

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Negative Health Impacts

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Mycotoxins ~ Health Impacts

Immunotoxic

Neurotoxic

Alimentary toxic

Dermatoxic

Nephrotoxic

Hepatotoxic

Hepatocarcinogenic

Genotoxic

Teratogenic

Carcinogenic

PMID: 26474839, 27178040, 25449202, 12221236, 26600019

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Mycotoxins ~ Health Impacts

Highly inflammatory to resp tissue

↓ ciliary clearance due to sm size

Airway remodeling if persistent

Some xBBB and reduce its integrity

Inhalation ~ olfactory n. to hippocampus,
frontal lobe

Many cross the placenta
bioactivate in utero

Found in breast milk

Implicated in neuropsych, ASD pathogenesis

PMID: 26474839, 27178040, 25449202, 12221236,
26600019, 19854819, 29880330

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Mycotoxins ~ Health Impacts

Induce apoptosis of intestinal epithelia

Induce bladder wall irritation/ulceration

Modified by multiple enzymes ~
Cyt P450s, glutathione S-transferases, UDP-glucuronosyltransferases, sulfur-transferases

Deplete glutathione

Cause mitochondrial damage

Nrf2 (“oxidant thermostat”) activation & depletion

PMID: 26474839, 27178040, 25449202, 12221236, 26600019

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Mycotoxins ~ Health Impacts

Interfere with protein synthesis:
DNA/RNA, actin/myosin(muscle/cardiac), keratin/elastin, enzymes, immune globulins, hemoglobin, albumin

Inhibit host defense

↓antibody-producing cells

↓antibody titres in blood serum

↓phagocytosis

Relative lymphopenia, neutrophilia, eosinophilia

PMID: 26474839, 27178040, 25449202, 12221236, 26600019, 7637687

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Mycotoxin Affinities & The Body

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Aflatoxin

Hepatocellular carcinoma
esp pre-existing Hep B

EBV-associated Burkitt's lymphoma

Desquamative Interstitial Pneumonitis

Immune impairment
decr lymphocytes & sIgA

Encourages viral replication with increased inflammation

Polymorphisms in CYP3A5 affect susceptibility

PMID: 27571469, 26424750, 15735246

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Chaetoglobosin

Crosses BBB

Oncology uses provide clues:

- CLL - induce apoptosis of leukemic cells via cytoskeleton
- Ovarian - induces apoptosis cisplatin-resistant CA cells
- Inhibits tumor angiogenesis via downregulation of vascular epithelial growth factor-binding *hypoxia-inducible factor* 1alpha.

Mouse study: necrosis of thymus/ spleen, spermatocyte degen

PMID: 24280868, 25304379, 23695013, 713122

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Citrinin

Toxic effects on the heart, liver, kidney, intestines, reproductive

Broad spectrum of bioactivities

Oxidative stress + mito dysfunction

Triggers endoplasmic reticulum (ER) stress

Intestines ~

↓ nmbr viable human intestinal cells
Induced apoptotic events via:
-mito membrane permeability
-activates programmed cell death enzyme
-elevated production of ROS

Inhibits oocyte maturation and early embryo development

PMID: 28993214, 29165056, 28404941

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Diacetoxyscirpenol (DAS)

Crosses BBB, neurotoxic

Developmental exposure “reversibly”
- disrupts hippocampal neurogenesis via ~
- Apoptosis of neural stem cells
- Induce oxidative cellular injury
- Suppress differentiation of granule cell lineages

Large bowel toxicity

Fertility ~ cytotoxic effects
- Decr male-related fertility, direct toxic effects on the testes

PMID: 10626642, 31836554, 31791183

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Enniatin

Crosses BBB, neurotoxic

Apoptotic

Brain carcinogenic ~
- Astrocytoma cells most sensitive
- Brain capillary endothelial cells
- Brain microvascular endothelial

Fertility ~ Cytotoxic effects
- Pre- + post-implant embryos
- Induce intracell oxidative stress and immunotoxicity in fetuses

PMID: 29768483, 30259633

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Gliotoxin

Not specific to brain. Named after fungi.

Disulfide bond ~ unique to other mycotoxins
(affects IgG subclass III preferentially bc of it's prevalence of disulfide bonds)

Immunosuppressive: T-lymph, PMNs, macrophages, monocytes, NK cells

Inhibits Nf-kB (cytokines) yet incr ROS

Mitochondria
reduced ATP
hyperpolarized membrane

Decreases rate of protein synthesis

Neurotoxic

Depletes glutathione

Inhibits histone methyltransferase (MCAS?)

PMID: 26445050, 26258781, 23278106, 22148349, 24039048

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Ochratoxin A

Kidneys ~ nephropathy, acute renal failure, chronic interstitial nephropathy, renal carcinogenicity

Renal fibrosis with chronic exposure

Inhib protein synthesis + energy prod

Depletes glutathione, incr intracell ROS

Immune ~ cytotoxic to neutrophils

Carcinogenic effects ~ combined direct and indirect mechanisms (genotoxicity, oxidative stress, epigenetic factors)

Male specific neurotox →mRNA changes poss trigger for autism & its male prev

PMID: 27384585, 27092524, 26095584, 27597255, 25597866

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Patulin

Damage to liver, kidney, spleen, intestines, I/S

Lung and brain edema

Retention sites - erythrocytes, blood-rich organs (spleen, kidney, lung and liver)

Mutagenicity, teratogenicity, chromosomal aberration, DNA strand damage

Affects the vital organs by damaging DNA

Classified as Category 3 human carcinogen

D/c'd past use chemo+Abs bc too toxic/carcinogenic

Protein synthesis inhibition ~
Binds to sulfhydryl group on AAs in proteins
Protein cross-linking w thiol groups, esp cysteine, lysine, histadine (think MCS, viral, MCAS)

Induces apoptosis via mitochondrial pathway

I/S ~

decr IFN-gamma-producing T-lymphs→Th2

dominance→allergies

Reduces macrophage fxn→reduced innate resistance to

pathogens→frequent infxns, autoimmunity, CA

Note: add yeast to patulin foods for adsorption (apples)

PMID: 30090541, 12112629, 26394380, 24931906

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Trichothecenes In General

Cell level ~

Potent protein synthesis inhibitor, incl DNA/ RNA; mito fxn, effects on cell division + membranes.

GI ~

N/V, intestinal epithelial blunting
Alimentary Toxic Aleukia

Lung Inflammation ~

Pulmonary Hemosiderosis

Immune deficiency ~

Compromised resistance to infxn, cancer - *Glioblastoma, Melanoma?

Haematotoxic ~ coagulation

Endocrine disrupter

PMID: 26572613, 15342083, 27198722, 22982764, 25542145

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Zearelanone

Endocrine disruptor → reproductive disorders, infertility

Non-steroidal estrogenic mycotoxin, but still binds to/lowers albumin (risk of C.diff)

ER binding affinity as potent as coumestrol and genistein, but ERβ is same as affinity for ERα → carcinogenic + immunotoxic

Arrhythmic (other Fusarium myco DON) 2nd-degree AV block, atrial brady, decr total power

PMID: 24632555, 28365492, 29868851, 27840141, 21804309

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Other Than Mycotoxins

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Mycophenolic Acid (MPA)

Not technically a mycotoxin

Part of "other chemicals" secreted by mold as part of normal metabolism

But mycotoxins formed in competition

∴ where there's mold, there's MPA, but not nec mycotoxins

Readily absorbed (w/in first few hrs)

Excreted quickly in bile IF liver can detox

Detox'd/excreted in Phase II as glucuronides

PMID: 4629779, 28327659

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Mycophenolic Acid (MPA)

Compromises intestinal membrane integrity → GI toxicity + leaky gut

Changes lipid-metabolizing proteins

Affects intracellular nucleotide levels, nucleotide-dependent processes, expression of structural proteins, fatty acid and lipid metabolism

Immunosuppressive

Rx transplant rejection, BRCA tx

PMID: 4629779, 28327659

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Endotoxins

Bacterial byproducts found in WDBs, humidifiers,

Highly inflam LPSs

Change inflam mediators in airways +/or blood ~
Eosinophils, IL-8, IL-1beta, TNFa, CRP

Reduce neutrophil count

SI ~↓ oxygenation enterocytes → hypermotility in attempt to reoxygenate

GI ~ genetic reduction in replication, energy production, absorption, immunity

Combo w mycotoxins ↑dmg to liver

Reduction improves steatohepatitis

PMID: 11409488, 17878567, 28477419, 26709789

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Review

What's a mycotoxin anyway?

Negative health impacts

Mycotoxin affinities & the body

Other than mycotoxins

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Dr. Jill Crista
Naturopathic Doctor
support@drcrista.com

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How To Spot Moldies

Are You Missing Mold Illness In Your Patients?

Dr. Jill Crista

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How To Spot Moldies

It's All About The History

Symptoms

Questionnaire

Look Alikes & Comorbidities

Differential Diagnoses

Physical Exam Clues

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IT'S ALL ABOUT THE HISTORY

© Dr Jill Crista

Informed by History

Exposure to WDB *at any time* in life

Gestation fwd (bioactivate in utero)

Include neonatal exposure

Ask ~ schools, college housing, occupations, camp, vacation

Will forget, take them through space by space

No minimum duration required

Ask about water events, musty smell, *not only mold*

Toxic mold is commonly not visible

Building test results

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Onset of Symptoms

Onset timing varies

Start vague and nondescript

Tolerable and excusable

Mold canaries earlier

Women earlier

Assuming daily exp ~ 3-6 months

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Symptoms

© Dr Jill Crista

Recognized Human Impacts

Allergic (IgE-mediated) ~
- Allergic rhinitis
- Hypersensitivity Pneumonitis
- Asthma

Non-allergic (non IgE-mediated) ~
- Non-IgE mediated asthma exacerbation

Infection ~
- Aspergillosis

PMID: 24368325

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Respiratory System vs Mold

Respiratory System

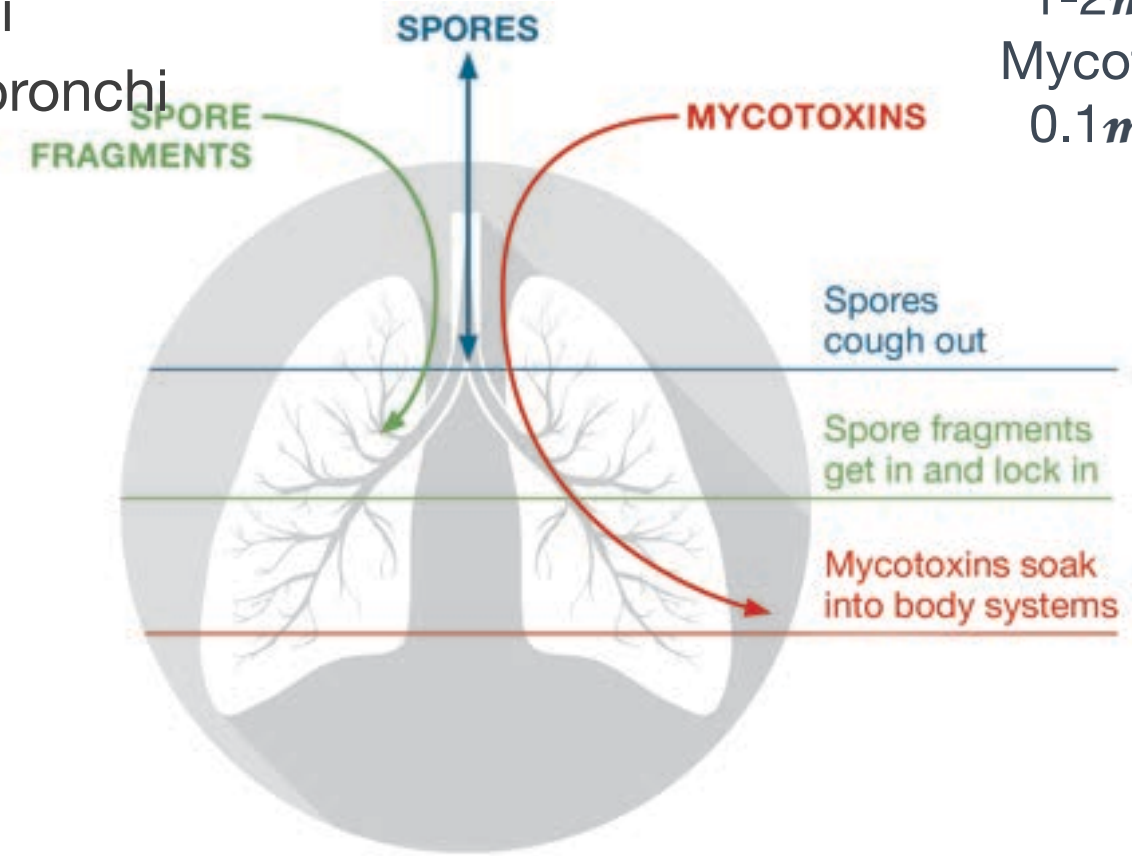
- $>7m$ Nasal
- $5\text{-}7m$ Pharynx
- $3\text{-}5m$ Trachea
- $3\text{-}5m$ 1° Bronchi
- $2\text{-}3m$ 2° Bronchi
- $1\text{-}2m$ Terminal bronchi
- $<1m$ Alveoli

Mold

Spores-
- Cladosporium $3\text{-}5m$
- Aspergillus $2\text{-}5m$
- Penicillium $1\text{-}5m$

Fragments-
- $1\text{-}2m$

Mycotoxins-
- $0.1m$



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Totality of Symptoms

Many systems

Many symptoms

No single diagnostic symptom

Genetic diversity

Individualized reactions

Symptoms abound

∴ Totality

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EENT (Eyes, Ears)

Dry eyes
Red, irritated eyes
Ocular pruritis
Floaters
Light sensitivity
Eye fatigue
Allergic shiners
Dark, sunken eyes
Blurry vision
Double vision
Frequently changing vision
Icterus

Pruritic ear canal
Sore inner ears
Ear fullness
Ear popping
Freq yawning to pop ears
Ear pain
Noise sensitivity
Tinnitus
Serous otitis media
Hearing loss

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EENT (Nose, Throat)

Sneezing
Runny nose
Blow nose often
Nose bleeds
Post-nasal drip
Nasal voice
Sinusitis
Blood-streaked mucous
Daily sinus spray/Neti
Nasal polyps
Allergies (esp not > tx)
Hayfever

Coated tongue
Thrush
Mouth sores
Palatal petechiae
Dry throat
Itchy throat
Sore throat
Back of throat feels full
Clears throat often
Globus hystericus
Cervical lymphadenopathy

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STORY | Student Athlete

College athlete

URI ↑ frequency & duration

→bacterial more often ~ sinuses or lungs

Require antibiotics

Affecting his ability to compete

Other sxs “tolerated” -insomnia, itchy ears,
“blow his throat” every am

Rarely had to blow his nose, even though nasal voice

PND at school, cleared up when home

Discovered living moldy building at school

Genetics not extreme sensitive

CMQ score only slightly probable for mold

Exercise routine helped him clear mycotoxins

Treated but refused move - grad soon

I/S strengthened - ↓ frequency of URIs + improved PND,
pruritis, sleep

Competitive again at his sport

When he left the moldy place to take a new job, he thrived

* * *

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Respiratory System

Dyspnea <exertion
Frequent yawn/sigh
Chronic dry cough
Episodic cough
Recurrent respiratory infxns
Colds go to lungs
Delayed recovery
Wheezing
Blood streaked sputum
Asthma
Incr need for inhaler meds

Burning lungs
Hemoptysis
Heaviness in chest
Non-obstructive sleep apnea
Lungs sensitive to inhaled particulates, exhaust, fragrances, musty spaces
Chronic respiratory illnesses
Fungal lung infection
Respiratory distress
Sarcoidosis of lungs

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STORY | Hay Fever

Man in 30s, healthy guy, gym rat

DIY finished basement for home office

Dev allergy to grass pollen - allergist said prob age

Allergy medication as recommended

Soon after, S/T, PND, dry irritated eyes, tinnitus

Followed by IBS not related to what he ate

Lack of focus worse when working

Desired nap rather than exercise

Hay fever progressed from grass season to any season when it wasn't frozen outdoors

Allergy medication starting to fail

Dev a faint wheeze when exercising

Doc rec asthma Rx - came to see me for alt's

Errors in basement buildout, mold behind outside walls

After remediation and tx, all sxs improved, but took longer than he had hoped

Suspect still being exposed to mycotoxins in belongings

* * *

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Cardiovascular System

Lightheaded
Low or reactive bp
Increased vascular fragility
Easy bruising
Spider veins/cherry angioma
Small vessel vasculitis
Vessel atonia
Varicose veins
Lower extremity edema
Heart palpitations
Irregular heartbeat

Arrythmia
Paroxysmal tachycardia
Postural tachycardia syndrome (PoTS)
Chest pain
Myocarditis
Hemorrhage into body tissue
Iron-deficiency anemia
Clotting issues
Atriovenous malformation
Coagulation abnormalities

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STORY | Myocarditis

Woman, mid-40s

Palpitations

Insomnia

Fatigue

DOE

Angina on exertion

“no pain no gain”

Self tx - CoQ10 + incr exercise

Angina became unbearable

Event of MI sxs → ER/referral for CV workup

Dx myocarditis

Mold discovered in basement below slow leaking refrigerator

After remediation & mold tx, all sxs remitted w occ palpitations after alcohol ingestion

* * *

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Digestive System

Appetite changes/anorexia
Crave sweets/alcohol
Food sensitivities
Peanut allergy
Abdominal pain
Gas/bloating
Constipation/Diarrhea
Consti-rrhea/IBS
Nausea
Reflux
Ulcer

SIBO
Vomiting
Cyclical vomiting syndrome
Histamine intolerance
Intestinal epithelial blunting
Hematochezia
Intestinal hemorrhage
Chemical sensitivity
Liver pain or congestion
Hepatocellular carcinoma

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STORY | Cook's Dilemma

30yo vegetarian cook & foodie

Nausea, generalized abd pn, IBS, urgent diarrhea alt w gas/ constipation

Wine - h/a, heartburn

ROS - neuropathy, poor circ, wt gain, sens skin, rash from fav lotions

Celiac, B12 tests N

Upper endoscopy - esophagitis

Colonoscopy - intestinal lining inflam/degradation wo ulceration

Suppressive med offered

Social life involved food and drink, socially isolated

Elimination-challenge - grains, wine, mushrooms, potatoes

Reintro only had a problem with nonorganic grains, and organic (yes, organic) wine

Presentation at wine club about ochratoxin in org wine cracked the code

Timing of wt gain and dig problems when took a new job

Leaky ceiling; trash cans to catch water during heavy storms

No mold seen, but was in ceiling tiles

* * *

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Nervous System

Anxiousness*
Easily overwhelmed
Low mood
Depression
Headache
Migraine
Drunken feeling
Dizziness/vertigo
Balance issues
Difficulty walking
Incoordination
Delayed reflexes
Internal vibrations
Parasthesias
Nerve pains
Tremors
Ataxia
Dementia
Atonia - central
Dysautonomia
Seizures

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STORY | Mold On The Mind

Woman mid-50s

Muscle twitches - sometimes so severe, wake her from sleep

Past 5 years - brain fog, insomnia, weak/easily fatigued muscles

Feared brain tumor but scan neg

PE revealed UMN lesion

Built their dream home, a log home in the country

Sxs started right after moving keepsakes from her mother's basement

Brought to her home for sorting bc her mother's house smelled terribly musty and made her feel strange

Unwittingly infected her pristine home

Removed from home, remediated and she started treatment

Despite a comprehensive plan, she couldn't move home for a very long time.

At that time, I wasn't aware of sinus colonies or mycotoxins, ∴ no sinus tx

Required extra time for her brain to rebuild the injured areas to stop the twitching

* * *

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Dermatological

Sensitive skin
Bothered by tags/seams
Frequent static shocks
Flushing
Hives
Dermatographism
Eczema/Rashes
Desquamation
Burning sensation
Pruritic skin
Photosensitivity

Recurrent fungal infections (jock itch, vaginal, athlete's foot, toenail, intertrigo)
Delayed wound healing
Skin reaction to antibiotics
Hair loss/thinning/slow growth
Raynaud's
Psoriatic lesions
Erythema nodosum (coccidioimycosis)

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STORY | Infant With Eczema

Infant covered with eczema from head to toe

So agitated, he couldn't sleep. Agitating autistic sibling

Cracking > topical steroids with antifungal

If missed one dose, break out to the point of cracking and bleeding

Feeling helpless, mom turned to the Internet. She read that other nursing moms noticed improvement with diet changes. She was a very proactive and educated mom. Her devotion to him was unending. She worked for three years to get pregnant. As a parent of another child, a four year old with autism, she understood sacrifice for a child.

She watched her baby son's reactions carefully and omitted foods that seemed to make things worse. She was down to lamb, rice, homemade organic bone broth, blueberries, and microgreens.

Other than the antifungal steroid cream, she put nothing on his skin. His clothes were washed in vinegar with an extra rinse, and diapers were organic cotton. There was little I could suggest to improve on this. We added a bath soak of calendula and chamomile tea, which soothed him enough to sleep. I recommended we test his stool for intestinal flora and conduct a full environmental assessment. These proactive parents hired a certified building biologist to check out their lakeside cottage home.

The indoor air inspector called aghast. There was black mold all over this cottage. It was behind the drywall of almost every wall in the house. The humidity was out of control because the house was essentially built on a bog by a lake. The inspector said the builder should never have been granted a building permit on that land.

Stool test - excessive yeast overgrowth.

He had fungus inside and out. With an autistic sibling, he likely had an inherited genetic susceptibility to environmental toxins. It turns out that everyone in the family was sick in their own way. They went to a hotel while remediation occurred and the little boy's skin cleared up.

Unfortunately in this case, the remediation had to be redone two more times to completely eradicate the mold. Each time they tried to come home, the baby would break out. Thankfully, the parents paid attention.

* * *

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Reproductive System

Unexplained menstrual cycle changes

Recurrent fungal vaginal infxns

Bacterial vaginosis

Chronic pelvic pain

Infertility - both genders

Low sperm counts

Immunotoxicity of fetus

Immune deficiency in surviving children

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STORY | Infertility

This story is about the mother of the infant boy with eczema mentioned earlier. She and her husband wanted very badly to get pregnant again. Because I didn't specialize in fertility, I referred her to colleagues. She apparently had a hard time getting pregnant with the little boy with eczema, her second child. Her first son was a four-year old with autism.

A year since finding the mold in their home, she and her husband still didn't have any luck getting pregnant. They remediated, but the mold didn't seem to want to go away. Their home required a total of three remediations. Each time they moved back, the baby boy, my patient, broke out in a rash. Mold toxins also interfered with the couple's fertility.

In this case, no one in the family felt well until they moved from the cottage with a moldy history. Even though they did the extra work of clearing mycotoxins and disposing of most of their belongings, they still couldn't get pregnant until they moved. Some people are simply too genetically sensitive to mold. There are times when the best action is to get out.

* * *

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Urinary System

Increased thirst
Frequent urination
Nocturnal polyuria
ADH resistance*
Burning in bladder
Pressure in bladder
UTI sxs with no infection
Hematuria
Interstitial cystitis
Electrolyte imbalance

Kidney or low back pain
Kidney swelling
Nephrotic syndrome
Nephritis

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STORY | Nephrotic Syndrome

This young man of 21 was living at home with his parents and one sibling. He came to see me for deep-seated fatigue, low-back pain, blood in his urine, and some libido challenges. I hadn't seen him in more than five years. I was struck by his appearance. He looked washed out with very dark circles under his eyes. He wasn't just pale, he was vampire pale.

Dark circles were a clue that he was depleting his health by not getting enough rest, exercise, hydration, or healthy food. He admitted that he wasn't treating his body well. His job and a new relationship consumed his schedule. He was definitely staying up too late zoning out to TV. At that appointment, I recommended lifestyle changes and ordered some labs.

At his follow-up, he had done a marvelous job adjusting lifestyle factors. He cleaned up his diet, drank water rather than soda, started walking to work, and dedicated himself to a sleep routine—whether he could fall asleep or not. He was motivated to improve his libido. But after a few months, he didn't feel much better and was still pale with dark circles under his eyes. There was an issue on his labs that I was concerned about.

A more in-depth test showed that his kidneys were in trouble. He was developing something called nephrotic syndrome—at 21! He followed adjustments to his treatment plan and we watched his labs carefully. He was very compliant and had improvements on both his tests and symptoms, but they were only mild. Normally in practice, I would've expected near complete recovery in someone so young, motivated, and otherwise healthy.

Then his mother came to see me for help with asthma attacks and fatigue. His sibling came in with fatigue, chronic sinusitis, and new food sensitivities. The whole family struggled with insomnia. There were other symptoms that led me to ask about their home environment. It turns out that they had mold in their home.

This young man chose to move out of the house in order to restore his kidney function. Within a few months, his kidneys recovered, back pain eased up, and energy improved. He no longer needed such a substantial treatment plan. At a follow-up visit, about five years after his move, he looked healthy. Libido issues were gone, and his relationship was going strong. He had no issues with fatigue unless he stayed up too late or worked too many hours—normal stuff.

Granted, initially he wasn't treating his body very well. But when someone makes positive lifestyle changes and doesn't see the benefits, more investigation is warranted. In his case, it was mold.

* * *

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Cognitive

Brain fog

Brain fatiguability

Difficulty word finding

Delayed cognition

Memory loss

Confusion

Difficultly thinking clearly

Disorientation

Cognitive impairment

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STORY | Tremor

A woman in her early 40s came to see me with her husband. She had a recent diagnosis of essential tremor, a condition similar to Parkinson's Disease. Prospects of recovery were not good. Her tremor was constant, affecting her balance and ability to sleep. She had heart palpitations that made her catch her breath. She also constantly felt like she had a bladder infection, even though no infection was found. The urinary frequency was so bad, she had to leave the appointment to urinate. Family said she'd become more weepy, which everyone understood considering her health issues.

Her husband seemed overly anxious about her health. While she was visiting the bathroom, he confided that he felt like he was getting more and more impatient and short with her. His sleep was interrupted with worry. This level of irritability didn't fit the kind and empathetic man in front of me.

On review, she had a tick bite about a year prior to the beginning of her first tremor. The tick was found, removed intact, and sent for testing. It was a Lyme-carrying tick. Even though many people who contract Lyme don't get a rash, she developed a growing red rash where the tick was. It was clear that she needed treatment for Lyme disease. She was given the standard of care at the time, which was later found to be insufficient at eradicating the bacteria.

It was evident to me that the Lyme bacteria might be persisting and affecting her nervous system. The tremor began in her hand on the same side as the tick bite. We started her on a chronic Lyme protocol. She only had minimal improvement. We tried a few tweaks, and still there wasn't much improvement with her tremor. I consulted with Lyme-literate colleagues to check my protocol or to spur ideas, and one mentioned checking into mold.

When I brought this idea up to the couple, the expressions on their faces looked as if I had just found them guilty of a crime. They had water damage in their home and with all that was going on with the wife's Lyme disease, they hadn't addressed it. They closed the door to the wet, musty basement to deal with it later. As mold expert Dr. Sandeep Gupta says, "If there's any part of you that you aren't addressing, eventually it will address you."

* * *

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Immune System

- Fungal overgrowth/infections
- Frequent viral infections
- Tendency toward bacterial sequelae
- Delayed healing infxns
- Increased susceptibility to infxn
- Herpes outbreaks
- Chronic EBV
- Mast cell activation syndrome
- Immune suppression
- Spleen / thymus underactivity
- Previous or current cancer dx

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STORY | Church Secretary

Widowed woman, mid-60's

Dx BV

Vaginal itching, burning, odor

Tx'd for yeast infxn but sxs persisted

Tx'd with 2 rounds of antibiotics, but s/e diarrhea

Wt gain, indigestion, gas/bloating, overwhelm, "snippy"

Sxs onset not long after "stressful roofing project" at church

Mold growing behind the paneling that lined her office from construction error during roofing project

No resp sxs bc spores were trapped behind paneling

Mycotoxin-induced dysbiosis & I/S def

Remediation and mold tx

BV improved, also wt gain, digestion, bloating, sense of overwhelm, mood

* * *

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Musculoskeletal

Decreased muscle mass

Decreased muscle tone

Exercise intolerant ~ EMFs, low oxygenation

Myositis

Soft-tissue prolapse

Soft-tissue injury

Delayed repair

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Constitutional

Chronic fatigue syndrome

Insomnia ~ maint > onset

Wake w anxious thoughts

Narcoleptic symptoms

Sxs worse temp extremes

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Typical Picture? 🤣

Many systems

Many symptoms

Genetic diversity

Individualized reactions

How to know it's mold?

Clues ~
New since water event
New onset since move/new job
Predispositions worsening
Not responding as expected
Inner unsettled feeling

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Crista Mold Questionnaire

Questionnaire

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CATEGORY 1

- ☐ Brain fog
- ☐ Feel tired all the time
- ☐ Frequent runny nose
- ☐ Blow your nose often
- ☐ Sneezing
- ☐ Sinusitis
- ☐ Post-nasal drip
- ☐ Nose bleeds
- ☐ Swollen glands
- ☐ Shortness of breath
- ☐ Frequent yawning or sighing
- ☐ Heart palpitations
- ☐ Headaches
- ☐ Hay fever
- ☐ Eye irritation
- ☐ Blurry vision
- ☐ Frequent change in vision
- ☐ Allergies
- ☐ Dark circles under eyes
- ☐ Sensitivity to sunlight
- ☐ Nervousness/can't settle
- ☐ Low mood or depressed
- ☐ Feeling overwhelmed
- ☐ Episodic/chronic dry cough
- ☐ Irritated lungs
- ☐ Blood-streaked mucous
- ☐ Nasal polyps
- ☐ Coated tongue
- ☐ Sores in the mouth
- ☐ Bumps on back of throat
- ☐ Thrush
- ☐ Sore or itchy ear canals
- ☐ Ringing in the ears
- ☐ Bothered by loud noises
- ☐ Skin rash
- ☐ Burning or itchy skin
- ☐ Easy bruising
- ☐ Spider veins
- ☐ Bothered by tags and seams on clothing
- ☐ Anemia
- ☐ Protruding veins on limbs
- ☐ Lower extremity edema
- ☐ Clear your throat often
- ☐ Sore throat
- ☐ Frequent colds
- ☐ Delayed recovery from colds
- ☐ Exhausted from exercise
- ☐ Frequent static shocks
- ☐ Increased thirst
- ☐ Trouble sleeping
- ☐ Feeling of internal vibration
- ☐ Dizziness
- ☐ Vertigo
- ☐ Drunken feeling
- ☐ Frequent urination
- ☐ Yeast infection
- ☐ Change in appetite
- ☐ Intestinal gas
- ☐ Nausea
- ☐ Feeling bloated
- ☐ Constipation
- ☐ Crave sweets
- ☐ Crave alcohol

TOTAL **CATEGORY 1** BOXES MARKED: _____

0-4 boxes marked = Score 0
5-9 boxes marked = Score 1
10-15 boxes marked = Score 2
16+ boxes marked = Score 3

CATEGORY 1 SCORE _____

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Questionnaire

CATEGORY 2

- ☐ Wheezing
- ☐ Asthma
- ☐ Burning lungs
- ☐ Recurrent respiratory infections
- ☐ Migraine
- ☐ Allergies aren't well controlled by medication
- ☐ Voice sounds nasally
- ☐ Plugged or clogged ears
- ☐ Chronic sinusitis
- ☐ Vomiting
- ☐ Alternating constipation/ diarrhea
- ☐ Diarrhea
- ☐ Irritable bowel
- ☐ Food sensitivities
- ☐ Chemical sensitivities
- ☐ Abnormal reaction to antibiotics
- ☐ Epstein-Barr virus
- ☐ Recurrent yeast infections
- ☐ Bacterial vaginosis
- ☐ Recurrent athlete's foot, jock itch, or toenail fungus
- ☐ Peeling/sloughing skin
- ☐ Episodes of fast heart rate
- ☐ Chest pain
- ☐ Raynaud's syndrome
- ☐ Non-obstructive sleep apnea
- ☐ Difficulty thinking clearly
- ☐ Disorientation
- ☐ Balance Issues
- ☐ Slow reflexes
- ☐ Incoordination
- ☐ Numbness or tingling
- ☐ Nerve pains
- ☐ Unexplained menstrual changes
- ☐ Overactive bladder
- ☐ Bladder infection
- ☐ React to musty spaces

TOTAL **CATEGORY 2** BOXES MARKED: _____

0-2 boxes marked = Score 0
3-5 boxes marked = Score 1
6-9 boxes marked = Score 2
10+ boxes marked = Score 3

CATEGORY 2 SCORE _____

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Questionnaire

CATEGORY 3

- ☐ Daily use of sinus spray, sinus prescription, or Neti pot
- ☐ Sinus surgery at any time in your life
- ☐ Chronic inflammatory response syndrome (CIRS)
- ☐ MARCoNS
- ☐ Peanut allergy
- ☐ Chronic fatigue syndrome
- ☐ Difficulty walking
- ☐ Dysautonomia
- ☐ Postural Tachycardia Syndrome (PoTS)
- ☐ Hearing loss
- ☐ Confusion
- ☐ Dementia
- ☐ Memory loss
- ☐ Tremors
- ☐ Sarcoidosis
- ☐ Asthma that's difficult to control with medication
- ☐ Idiopathic pneumonitis
- ☐ Lung scarring or nodules
- ☐ Respiratory distress
- ☐ Aspergillosis
- ☐ Arrhythmia
- ☐ Coagulation abnormalities
- ☐ Atriovenous abnormalities
- ☐ Churg Strauss Syndrome
- ☐ Histamine intolerance
- ☐ Erythema nodosum
- ☐ Eosinophilic esophagitis
- ☐ Ulcer
- ☐ Non-celiac intestinal disease
- ☐ Blood in stool
- ☐ Cyclical vomiting syndrome
- ☐ Liver pain or swelling
- ☐ Fatty liver
- ☐ Non-alcoholic steatohepatitis (NASH)
- ☐ Interstitial cystitis
- ☐ Kidney pain or swelling
- ☐ Kidney disease
- ☐ Nephritis
- ☐ Chronic pelvic pain
- ☐ Infertility
- ☐ Hepatocellular carcinoma
- ☐ Previous or current cancer diagnosis
- ☐ Mast cell activation syndrome (MCAS)
- ☐ Exposure to water-damaged building any time in your life
- ☐ Exposure to mold
- ☐ Positive Shoemaker tests

TOTAL **CATEGORY 3** BOXES MARKED: _____

Score 1 for each box marked
Boxes marked and score will
be the same for this category

CATEGORY 3 SCORE _____

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Questionnaire

TOTAL MOLD RISK **RESULTS**

Gather your Category scores
from the 3 previous pages

CATEGORY 1 SCORE: _____ +
CATEGORY 2 SCORE: _____ +
CATEGORY 3 SCORE: _____ = TOTAL MOLD RISK _____

TOTAL MOLD RISK
RESULTS

0-4 = Not Likely Mold Sickness
5-9 = Possible Mold Sickness
10+ = Probable Mold or Biotoxin Sickness

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Take A Moment

What's your score?

Of your most stuck patient?

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Look-Alikes, Comorbidities, Differentials

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Look-Alikes & Comorbidities

Tick-borne diseases ~
Persisters dt immune deficiency
Distinguishing characteristic ~ migrating

SIBO ~
Myenteric plexus neurotoxicity interrupts peristalsis
Intestinal epithelium blunting
Biofilm promoter

MCAS ~
Dysfunctioning mast cells, differently differentiated dep on tissue →many diff sx pictures
Inflammation in multiple systems
Wax/wane pattern

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Differential Diagnoses

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Differential Diagnoses

Clue ~ CMQ Category III

B12 deficiency

Lyme & co-infections

Lung CA/Mesothelioma

GI ~ UC/Crohn's

Liver/kidney CA

Other autoimmune dzs

- Celiac
- SLE
- Scleroderma
- Sjogren's

MCAS

Alzheimer's, Parkinson's

Glaucoma

Alcoholism

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Physical Exam Clues

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Physical Exam Clues

Gross ~
hypotonia (rounded shoulders, pronation, pronounced veins), sunken eyes, pale or reddish complexion, “puffy”, diffuse lymphadenopathy, sighs through interview, pretzeling, adventitious movements

Skin ~
rashes, eczema, flushing, dermatographism, ecchymoses, desquamation

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Physical Exam Clues

Vitals ~
shallow breathing, usu low bp but reactive,
usu temp low-N but mb incr temp (infxn),
reactive HR (POTS)

Orthostatic Intolerance: NASA Lean Test
Lie quietly x5 min beforehand, no talking, no phone. Take baseline HR.
Stand w feet 6-8 in from wall, and lean back against the wall w shoulders touching.
Test at 1, 5, 10 mins.
HR
>30 bpm from supine to standing (10 min)
If under 18yo >40 bpm from supine
to standing (10 mins)

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Physical Exam Clues

Neuro ~
+Rhomberg, +heel-toe, can't toe-stand eyes closed, altered DTRs - usu delayed, but if hyperreflexive screen for UMN lesion (+Rhomberg, +Babinski, clonus, m.weakness w incr tone, rigidity flexors arms, extensors legs), +CN I (anosmia)/III (convergence)/VII (Bell's palsy)/XIV+XII (palate/tongue), parasthesias (h/c, vibration, sharp/dull), twitches, tremors

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Physical Exam Clues

Eyes ~
sunken eyes, infraorbital darkness medial half, Dennies lines, edema at base of eyelashes, injected conjunctiva, icterus, sensitive to light challenge, convergence insufficiency (eyes drift outward at near vision/while reading), report floaters/white ceiling test, edema around optic nerve, retina-cotton wool spots, VCS fail

Ears ~
external canal flaking/sloughing/excoriations, poss tragus sign, TM orange-peel consistency &/or retracted, hearing loss, usu (-)Weber (no lateralization, but dulled/req lower tone tuning fork) with (-)Rinne, +Schwabach (b/l sensorineural loss), vestibular eval (caution Dix-Hallpike, alt side-lying head up 45°)

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Physical Exam Clues

Nose ~ salute sign, clear or blood-streaked coryza, boggy nasal mucosa, enlarged turbinates, polyps (teardrop/grape), sinuses TTP

Mouth/Throat ~ dental occlusions w high arched palate (children/allergic facies), palatal petechiae, coated tongue, mouth sores, post pharynx l/a "cobblestoning", hypertrophic/injected tonsils/**adenoids**, w poss tonsillids/stones, uvula enlarged

Cervical/tonsillar + cervical chain lymphadenopathy

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Physical Exam Clues

LU ~
ausc-harsh bronchial breath sounds, b/l fine crackles in dependent regions not cleared by cough but >leaning fwd (discontinuous high-pitched, low-amplitude, short duration, velcro-like mid-late inspir), expiratory wheeze (continuous high pitched), b/l lower lobe (+)egophany w (-) whispered pectoriloquy

CV ~
spider veins, cherry angiomas, lower limb veins collapse when elevated, delayed capillary refill, decr intensity of 1st HT sound, isolated S4 (pause bw ventricles)

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Physical Exam Clues

GI ~
delayed bowel sounds, doughy abdomen TTP &/or bloated, +GB sign, liver TTP/enlarged/scarred, kidneys TTP

M/S ~
myopenia (unmatched to age), prolapse, synovitis, ganglions TTP, chiro adjustments don't hold

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Review

It's All About The History

Symptoms

Questionnaire

Look Alikes & Comorbidities

Differential Diagnoses

Physical Exam Clues

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Dr. Jill Crista
Naturopathic Doctor
support@drcrista.com

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Are You Missing Mold Illness?

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The Testing Conundrum

Are You Missing Mold Illness In Your Patients?

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Testing Conundrum

Diagnostic Assessments

Mycotoxin Discussion

Shoemaker Panel Highlights

Colonization, Allergy, Infection

Advances In Imaging

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DIAGNOSTIC ASSESSMENTS

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Conundrum ~ Which? When? Reliability?

Decision points ~

Info req'd to guide tx

Baseline

Pt request

Buy-in ~ pt/fam

"Proof" ~ Ins/occup/landlord

Comfort w existing models

Accuracy

Cost

Reassess tx progress

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Diagnostics ~ Tier 1

Tier 1 purpose - is it mold?

DIRECT

Urine mycotoxin - LC/MS

Comprehensive stool test

INDIRECT+HIGH CORRELATION

Visual Contrast Sensitivity (VCS)

Serum mycotoxin antibody

Urine mycotoxin - ELISA

Organic acids test

NK cell f*unction* (diff than total)

- Lytic units, <7 abn
- Quest

NK cell total (freq normal)

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VCS APTitude© Screening Test

www.survivingmold.com

VCS Left Eye

	A	B	C	D	E
9	✗	✗	✗	✗	✗
8	✗	✗	✗	✗	✗
7	✗	✗	✗	✗	✗
6	✓	✓	✗	✗	✗
5	✓	✓	✗	✗	✗
4	✓	✓	✗	✓	✗
3	✓	✓	✗	✓	✗
2	✓	✗	✓	✗	✗
1	✓	✓	✓	✗	✗

VCS Right Eye

	A	B	C	D	E
9	✗	✗	✗	✗	✗
8	✗	✓	✗	✗	✗
7	✗	✗	✗	✗	✗
6	✗	✗	✗	✗	✗
5	✓	✗	✗	✗	✗
4	✓	✗	✗	✗	✗
3	✓	✓	✗	✗	✗
2	✓	✓	✗	✗	✗
1	✓	✓	✓	✓	✗

Result: Fail

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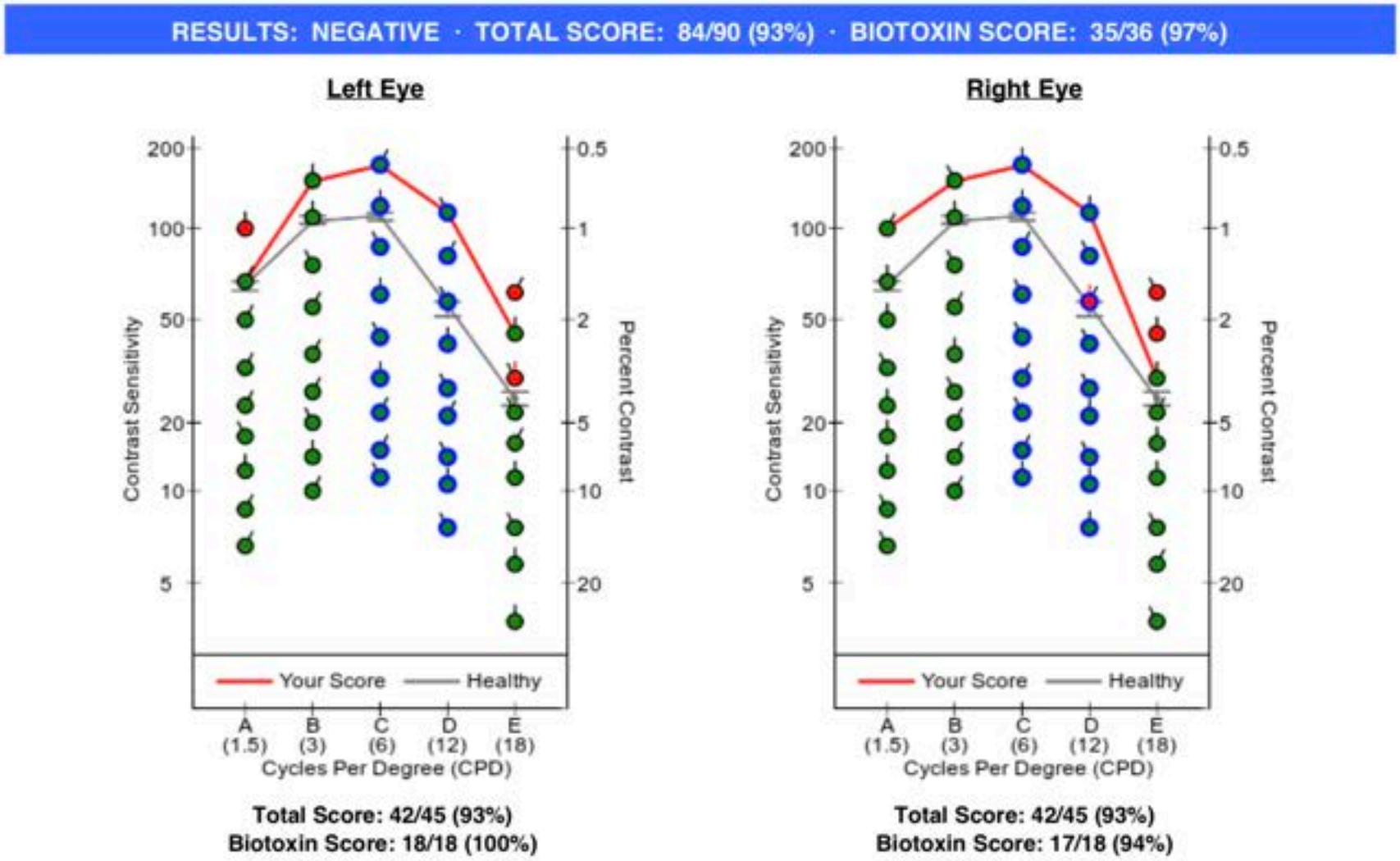

VCStest.com *calibrate screen first!* Technically pass/fail but the higher the score the better.

The maximum biotoxin score is 18 in each eye and 36 for both eyes.

Columns A, B, - green is good, red means lack of ability to see the contrast (nutritional, glyphosate, SIBO)

Columns C, D - blue is good (mold/biotoxin illness, insect venom, cyanobacteria, dinoflagellates-esp Pfiesteria and Ciguatera, Lyme+coinfections, parasites, tobacco use*, some VOCs)

Column E - green is good (biotoxin, metals, tobacco use*, alcohol, lead, VOCs, age, low socioeconomic status)

Columns D, E - worse with Herx, detox

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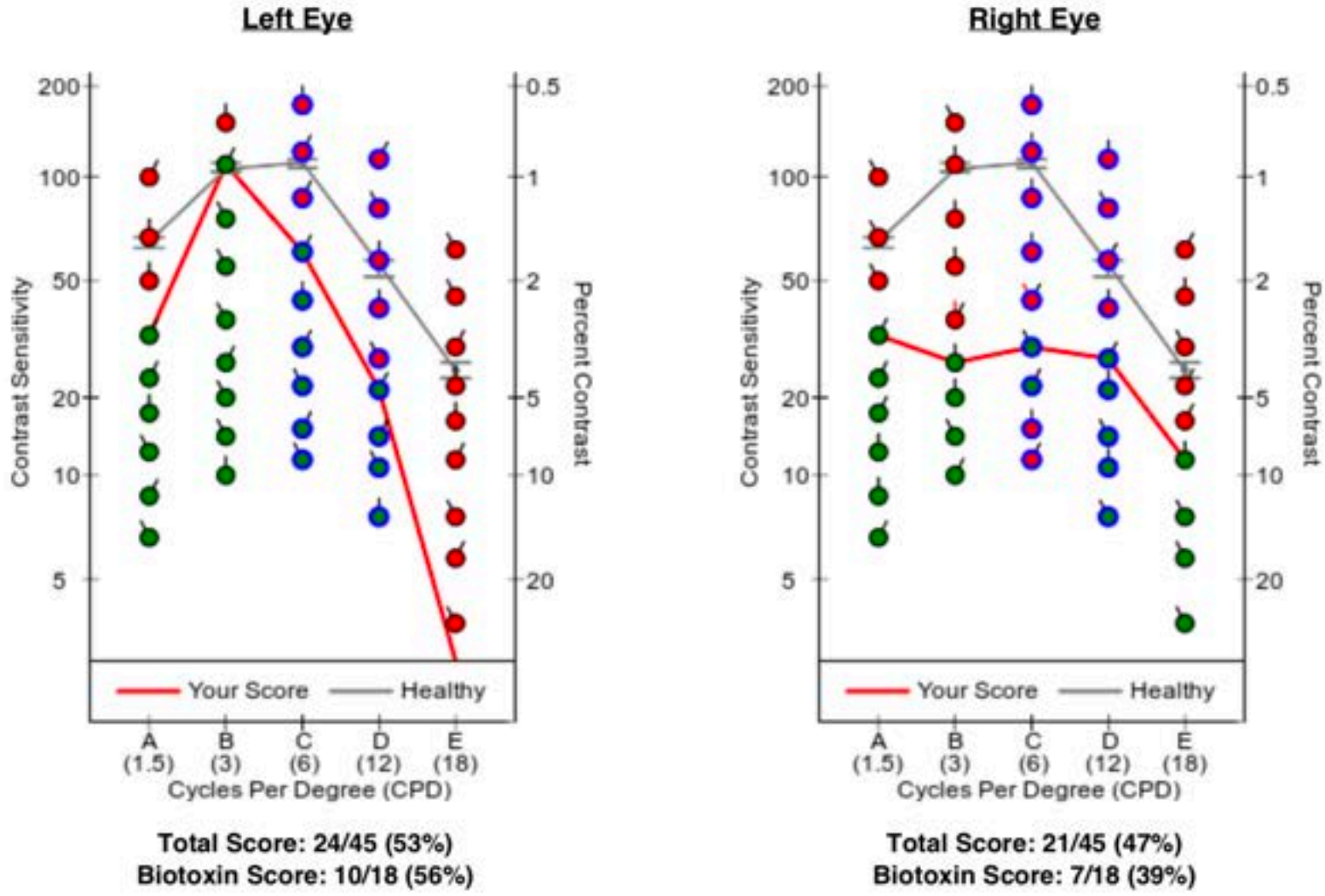
RESULTS: POSITIVE · TOTAL SCORE: 45/90 (50%) · BIOTOXIN SCORE: 17/36 (47%)



Mold-Lyme combo at Dx

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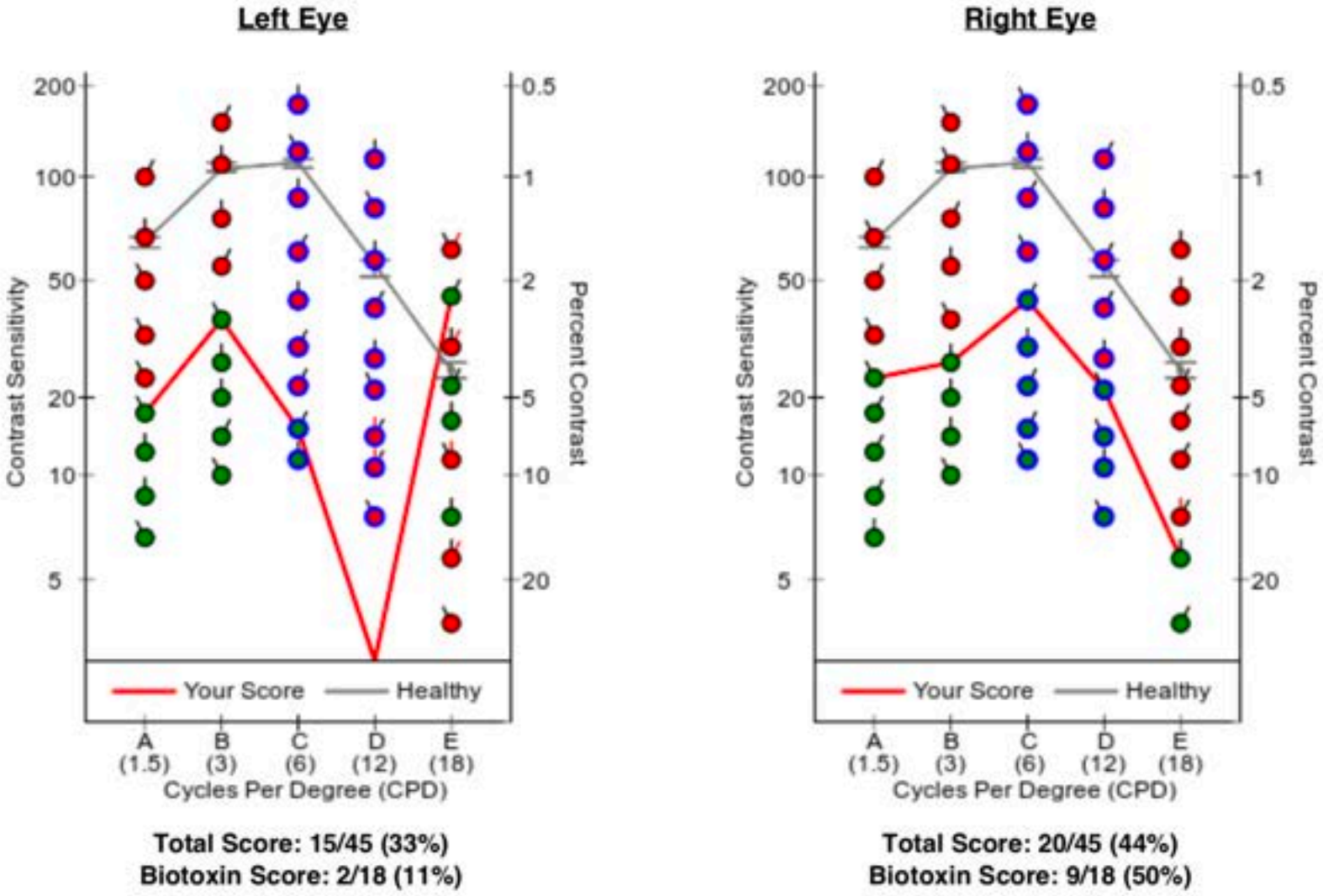
RESULTS: POSITIVE · TOTAL SCORE: 35/90 (39%) · BIOTOXIN SCORE: 11/36 (31%)



Lyme pt Herxed and d/c every antibiotic round. We then found mold.

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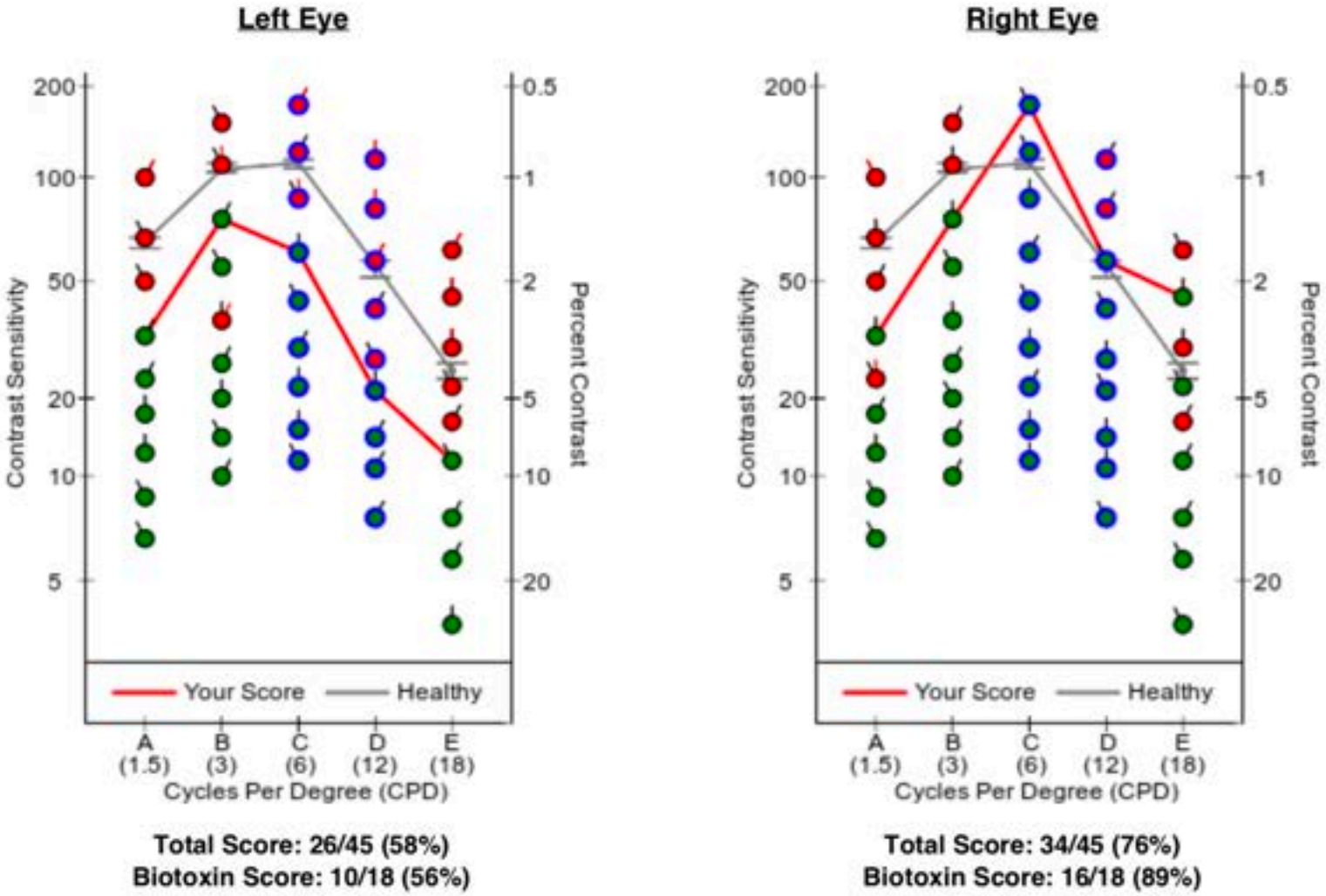
RESULTS: POSITIVE · TOTAL SCORE: 60/90 (67%) · BIOTOXIN SCORE: 26/36 (72%)



Same pt 4 months after treating mold and added Lyme herbs.

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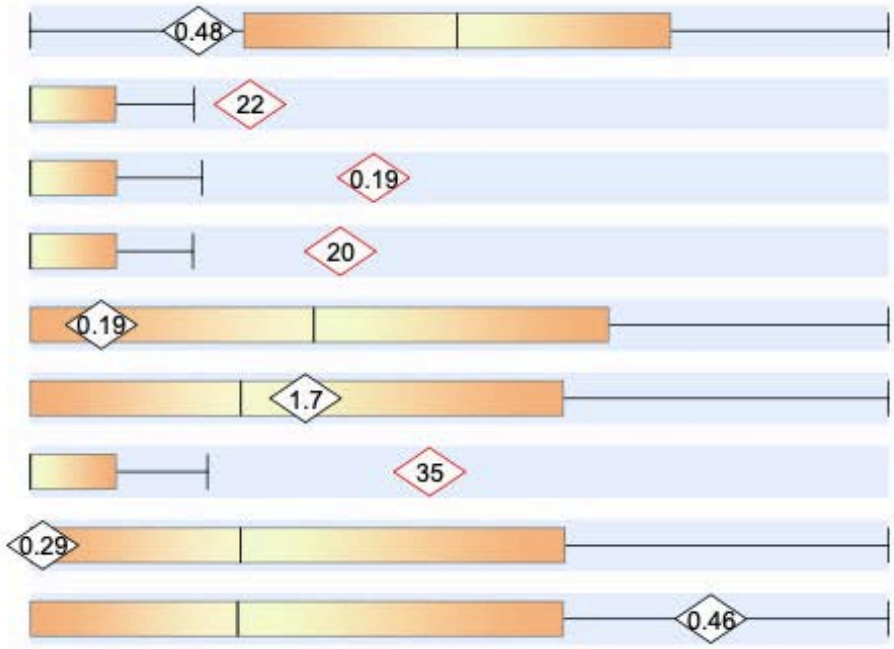
Organic Acids Test - Nutritional and Metabolic Profile

Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)	Patient Value	Reference Population - Males Age 13 and Over
Intestinal Microbial Overgrowth			
Yeast and Fungal Markers			
1 Citramalic	0.11 - 2.0	0.48	
2 5-Hydroxymethyl-2-furoic *(Aspergillus)*	≤ 18	H 22	
3 3-Oxoglutaric	≤ 0.11	H 0.19	
4 Furan-2,5-dicarboxylic *(Aspergillus)*	≤ 13	H 20	
5 Furancarbonylglycine *(Aspergillus)*	≤ 2.3	0.19	
6 Tartaric *(Aspergillus)*	≤ 5.3	1.7	
7 Arabinose	≤ 20	H 35	
8 Carboxycitric	≤ 20	0.29	
9 Tricarballylic *(Fusarium)*	≤ 0.58	0.46	



2,4,5 ~ Aspergillus

4,5 ~ Colonization

6 ~ Aspergillus & Candida

9 ~ Fusarium

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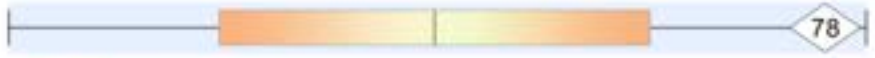
Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)	Patient Value	Reference Population - Males Age 13 and Over
Oxalate Metabolites			
19 Glyceric	0.21 - 4.9	3.4	
20 Glycolic	18 - 81	78	
21 Oxalic	8.9 - 67	H 76	

19, 20, 21 ~ Incr oxalate metabolites - yeast, mold, food

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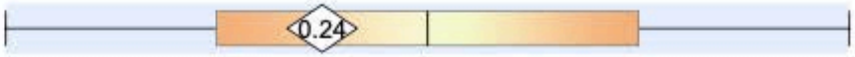
Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)	Patient Value	Reference Population - Females Age 13 and Over
Indicators of Detoxification			
Glutathione			
58 Pyroglutamic ✱	10 - 33	22	
Methylation, Toxic exposure			
59 2-Hydroxybutyric ✱✱	0.03 - 1.8	H 13	
Ammonia Excess			
60 Orotic	0.06 - 0.54	0.24	
Aspartame, salicylates, or GI bacteria			
61 2-Hydroxyhippuric	≤ 1.3	0.37	

✱ ***A high value for this marker may indicate a Glutathione deficiency.***

✱✱ ***High values may indicate methylation defects and/or toxic exposures.***

58 ~ Glutathione status

59 ~ Methylation ability

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Diagnostics ~ Tier 2

Tier 2 purpose - how bad is it?

CBC

Fe-def anemia

↓WBC~relative↓lymph↑neutr↑eos

CMP

↑ALT, AST, GGT(↓GSH), ↑bilirubin,

↓GFR, ↓albumin, creatinine>1.0

Vit D (25-OH)↓

Vit D (1,25)↑ (↓Intracellular GSH?)

hs-CRP↑

RBC glutathione↓

Urinalysis

+blood, yellow-brown/yellow-green(bili),

(-)leuko, ↑urobilinogen

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Diagnostics ~ Tier 2

IgE mold + IgG/M/A candida
    *not useful for mycotoxins

IgG/IgA total & subclasses
    IgG subclass III def
    - potent pro-inflam aby
    - first to respond to viral infxn
    - gliotoxin (disulfide bonds)

Lymphocyte Subset Panel
    T- and B-cell total↓

IL-6↑ → IL-10↑, TNF↑

ANA↑

BDG (Fungitell) Quant*↑

Galactomannan*↑

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Diagnostics ~ Tier 2

Food allergy
- IgG/IgA (yeasts, peanuts, coffee, mushrooms, corn, potatoes, grains)

Kidney health
- microalbumin/creatinine ratio>30
- combo w creatinine>1=concern

ADH <1

Copeptin 4-14

EKG
- 2nd-degree AV block, atrial brady, supraventricular extrasystole, ventricular extrasystole

Genetic mold canary
- HLA DR/DQ
- DRB1, DQB1,DRB3-5
- Detoxification snps

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Diagnostics ~ Tier 3

Tier 3 purpose ~ clarification

Shoemaker labs (next section)

SIBO breath test

Ferritin & clotting ~ mixed results

Venous blood gasses (no tourniquet!)

MCAS labs

- Mayo ~ Urine 24-hr
- MUST be chilled to certain temp asap
- -Methylhistamine or MIA
- -PGD-2
- -17-Beta-PGF-2-alpha
- Diff to get right, pre-arrange w lab
- Not all have this capacity
- First r/o mastocytosis w tryptase

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Diagnostics ~ Differentials

B12 & MMA (B-12 def)

Lyme & co-infections*

Lung CA/Mesothelioma

GI ~ UC/Crohn's

Liver/kidney CA

Other autoimmune dzs

- Celiac
- SLE
- Scleroderma
- Sjogren's

MCAS

Alzheimer's, Parkinson's

Glaucoma ~ eye exam

Alcoholism

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STORY | Not An Alcoholic

Man late 50s

Dr suspects alcoholism

Hi GGT, AST/ALT on the rise

BS on the rise, chol dropping 115

Onset RUQ pain

Episodes N/V

Obese, pre-diabetic

Worsening lethargy

No alcohol ingestion, verified by wife

Wife says lazy after kids moved out & got his man-cave

Close door & use window air conditioner “always hot”

Cool sanctuary, often falls asleep at his desk

Window air conditioner was full of mold

Mycotoxins mimicked alcohol

* * *

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Mycotoxin Discussion

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The Path of the Mycotoxin

In WDB exposure ~
- Inspiration
- Absorption - sinus mucosa to lung alveoli
- Carried via blood
- Liver & Kidney
- Kidney - filtration
- Liver - bound to bile and delivered to lumen
- Left-over absorbed into lipid-rich tissue for later mgmt

Why test urine?
- Filtrate of blood

Why test serum?
- Blood & serum antibody reactions

Note 1: Ingested mycotoxins may remain unbound in lumen

Note 2: No data on mycotoxin secretion in sweat

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Mycotoxin Detection Methods

The question is not which - it's if, when and how

Methods currently in use in US ~
- Urine ELISA (enzyme-linked immunosorbent assay)
- Urine LC-MS (liquid chromatrography with mass spectrometry)
- Serum antibody (IgE, IgG)

Considerations ~
- Which mycotoxins are tested?
- Pt's immune status
- Pt's liver & kidney health
- Pt's supplementation
- Cost, coverage
- Compare to previous test
- Practitioner comfort
- Lab - certifications, ongoing independent validations, and willingness to share validation results

PMID 32121036

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Mycotoxin Controversy

Mostly driven by insurance companies

Source ~

- Food - studies are mixed
- Fat stores
- Lifestyle - ie: smoking, coffee, alcohol
- *Certainly not WDBs*

Except, levels have been shown to decrease with removal from WDB

Inducible ~

- Independent case study
- Urinary mycotoxins ↑10 fold, 4-6 hrs after sauna tx

Courtesy Dr. Joseph Brewer

PMID: 28240164

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International Journal of *Environmental Research and Public Health*

MDPI

Review

Occurrence, Toxicity, and Analysis of Major Mycotoxins in Food

Ahmad Alshannaq [1,2] and Jae-Hyuk Yu [2,3,*]

1 Department of Food Science, University of Wisconsin-Madison, 1550 Linden Drive, Madison, WI 53706, USA; alshannaq@wisc.edu
2 Food Research Institute, University of Wisconsin-Madison, 1550 Linden Drive, Madison, WI 53706, USA
3 Department of Bacteriology, University of Wisconsin-Madison, 1550 Linden Drive, Madison, WI 53706, USA
* Correspondence: jyu1@wisc.edu; Tel.: +1-608-262-4696

Academic Editor: Marcello Iriti
Received: 15 May 2017; Accepted: 6 June 2017; Published: 13 June 2017

"Members of three fungal genera, Aspergillus, Fusarium, and Penicillium, are the major mycotoxin producers [in food].

While over 300 mycotoxins have been identified, six (aflatoxins, trichothecenes, zearalenone, fumonisins, ochratoxins, and patulin) are regularly found in food, posing unpredictable and ongoing food safety problems worldwide.

In addition to concerns over adverse effects from direct consumption of mycotoxin-contaminated foods and feeds, there is also public health concern over the potential ingestion of animal-derived food products, such as meat, milk, or eggs, containing residues or metabolites of mycotoxins."

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Table 1. Major mycotoxins and US and EU limits on food and animal feed levels.

Mycotoxin	Fungal Species	Food Commodity	US FDA (μg/kg)	EU (EC 2006) (μg/kg)
Aflatoxins B1, B2, G1, G2	*Aspergillus flavus* *Aspergillus parasiticus*	Maize, wheat, rice, peanut, sorghum, pistachio, almond, ground nuts, tree nuts, figs, cottonseed, spices	20 for total	2–12 for B1 4–15 for total
Aflatoxin M1	Metabolite of aflatoxin B1	Milk, milk Products	0.5	0.05 in milk 0.025 in infant formulae and infant milk
Ochratoxin A	*Aspergillus ochraceus* *Penicillium verrucosum* *Aspergillus carbonarius*	Cereals, dried vine fruit, wine, grapes, coffee, cocoa, cheese	Not set	2–10
Fumonisins B1, B2, B3	*Fusarium verticillioides* *Fusarium proliferatum*	Maize, maize, products, sorghum, asparagus	2000–4000	200–1000
Zearalenone	*Fusarium graminearum* *Fusarium culmorum*	Cereals, cereal products, maize, wheat, barley	Not set	20–100
Deoxynivalenol	*Fusarium graminearum* *Fusarium culmorum*	Cereals, cereal products	1000	200–50
Patulin	*Penicillium expansum*	Apples, apple juice, and concentrate	50	10–50

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Mycotoxin Study

Sample ~
Urine, sputum, tissue biopsy (lung/liver/brain)

Mycotoxins tested ~
Aflatoxin, Ochratoxin, Trichothecenes, Gliotoxin

Findings ~
Normal controls ~ no detectable mycotoxins in tissues or fluids
WDB pts ~ detectable mycotoxins, varying degrees in tissues and fluids

Why urine?
Adequate and reliable method to detect mycotoxins (though may underreport tricothecenes)
Least invasive
Lowest cost

Study limitation - author's possible conflict of interest

PMID: 19468319

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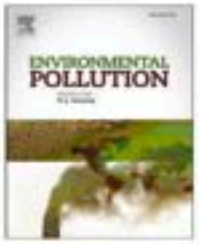
Contents lists available at ScienceDirect

Environmental Pollution

journal homepage: www.elsevier.com/locate/envpol



Determination of multiple mycotoxins in paired plasma and urine samples to assess human exposure in Nanjing, China☆

Kai Fan [a, 1], Juanjuan Xu [b, 1], Keqiu Jiang [a], Xing Liu [a], Jiajia Meng [a], José Diana Di Mavungu [c], Wenbo Guo [a], Zhiqi Zhang [a], Jun Jing [b], Hongru Li [b], Bing Yao [b], Hui Li [d], Zhihui Zhao [a], Zheng Han [a, *]

[a] Institute for Agro-food Standards and Testing Technology, Shanghai Key Laboratory of Protected Horticultural Technology, Shanghai Academy of Agricultural Sciences, Shanghai, 201403, China
[b] Reproductive Medical Center, Nanjing Jinling Hospital, Nanjing University, School of Medicine, Nanjing, Jiangsu, 210002, China
[c] Laboratory of Food Analysis, Department of Bio-analysis, Faculty of Pharmaceutical Sciences, Ghent University, Ottergemsesteenweg 460, 9000, Ghent, Belgium
[d] Department of Plant, Soil and Microbial Sciences, Michigan State University, East Lansing, MI, 48824, USA

"This study was conducted to investigate mycotoxin exposure in 260 rural residents (age 18-66 years; mean age 36.9 years, average BMI was 23.0kg/m2) in Nanjing, China. All participants were healthy and free from chronic diseases.

Paired plasma and first morning urine samples were analyzed for 26 mycotoxin biomarkers, including 12 parent mycotoxins and 14 mycotoxin metabolites, by an ultra-high-performance liquid chromatography tandem mass spectrometry (UHPLC-MS/MS) method.

Individuals with previous medical records indicating liver, kidney or other metabolic problems were excluded from this study. "

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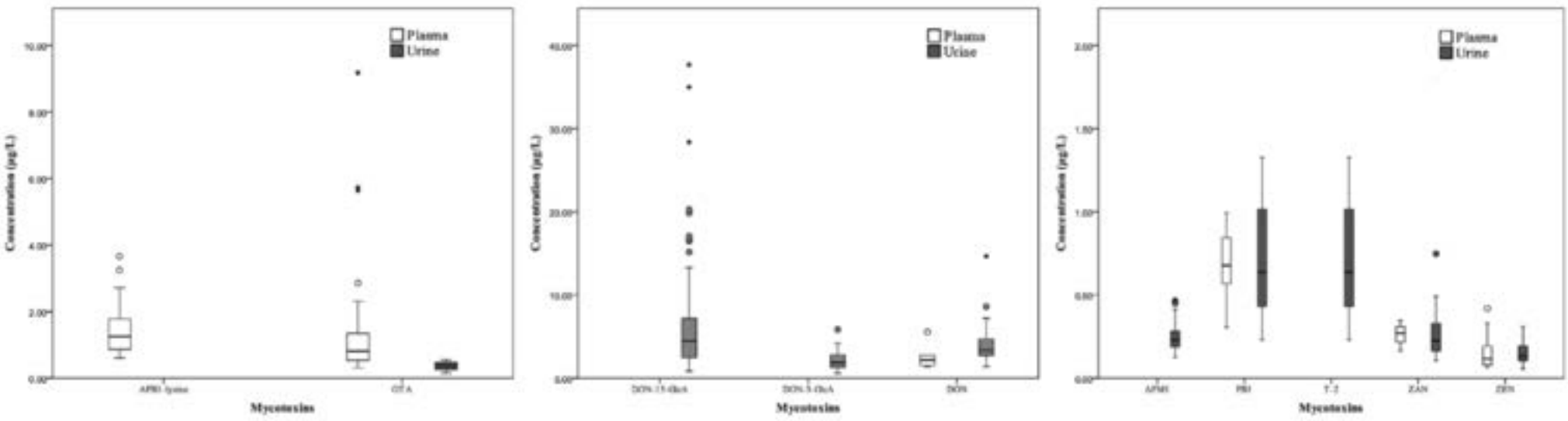

"In the *plasma* samples, [95 out of 260] 36.5% of samples were found to contain mycotoxins.

OTA was the most prevalent one (incidence of 27.7%) and its concentration ranged from 0.312 to 9.18mg/L.

AFB1-lysine, FB1, DON, ZEN and ZAN were also detected in plasma with incidences of 19.6%, 2.7%, 2.3%, 6.5% and 1.2%, respectively."

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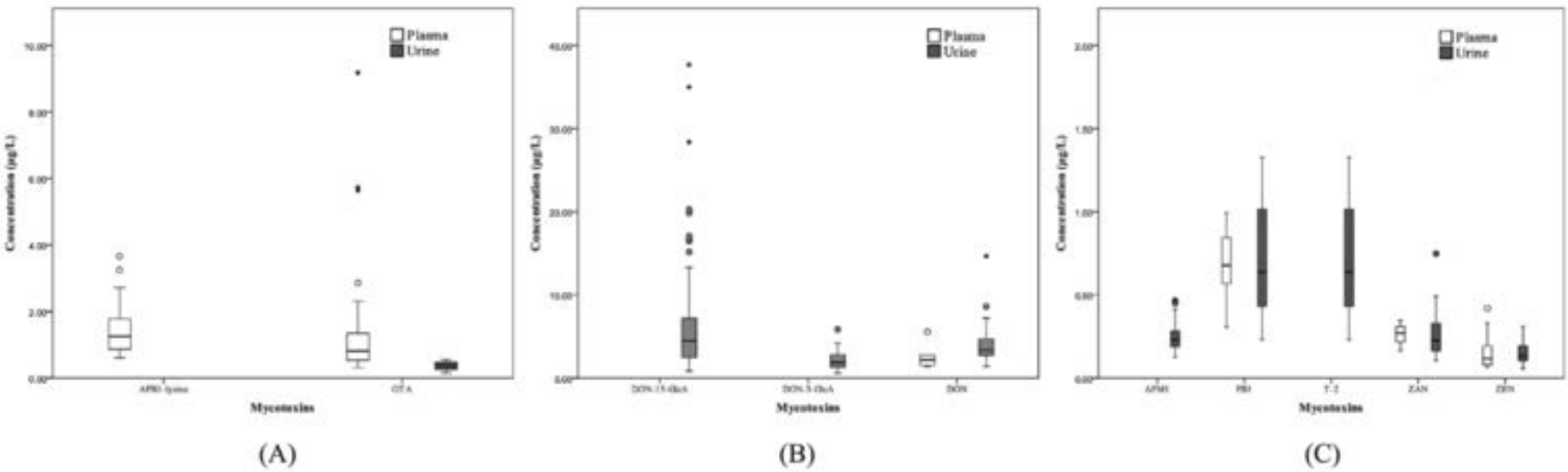

"In the *urine* samples, one or more mycotoxins were detected in144 out of 260 (55.4%) participants.

DON-15-GlcA (incidence of 43.8%), a urinary metabolite of DON, was the most abundant mycotoxin in urine samples; its concentration ranged from 0.828 to 37.7mg/L(0.694e37.3mg/g Cr).

AFM1,OTA,FB1, T-2, DON, DON-3-GlcA, ZENand ZAN were detected in 10.4%, 1.2%, 3.1%, 2.3%, 10.0%, 15.8%, 6.9% and 7.7% of the urine samples, respectively.

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Does Gender Matter?

"42.7% were female and 57.3% were male. There was no significant difference in age and BMI between males and females ($p > 0.05$).

The incidence and concentration of mycotoxins in males and females were slightly different.

Compared to females, males presented higher levels of plasma FB1, plasma DON, urinary T-2, urinary DON-3-GlcA, urinary DON-15-GlcA, and urinary ZEN,

but lower levels of plasma AFB1-lysine, plasma ZEN, urinary OTA, urinary DON and urinary ZAN.

However, the differences of the mean mycotoxin concentrations between male and female were not significant ($p>0.05$)."

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Urine ELISA Mycotoxin

Established use for 15 years

Indirect measure

The idea - due to the body's ability to modify mycotoxins, antigen detection vs molecular matching will catch more metabolites and give a better view of body burden

Strengths ~

- Detect both the mycotoxin in pure form and metabolites of mycotoxins due to common antigens on most modified forms
- Levels correlate to symptoms in majority of my patients ("bell-curve")

Challenges ~

- Not controlled for creatinine
- Antigen selection by lab
- Non-specific reactions (aka background noise) w poss false-positives
- Varying accuracy for pts w issues detoxing and excreting
- Doesn't help answer the question of whether currently being exposed
- Unknown degree of contamination via ingestion

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Urine LC-Mass Spect Mycotoxin

Gold standard for small molecules

Direct measure

The idea - molecular identification as direct detection of the presence in the urine

Strengths ~
- Controlled for creatinine
- Specific metabolites of mycotoxins can be tested and reported as an individual finding, then grouped for a bigger picture
- Levels correlate to symptoms in majority of my patients (“bell-curve”)

Challenges ~
- Some of the molecules are similar in structure, peak together, leading to possible cross-reporting
- May miss metabolites if not specifically identified as a structure to monitor
- Extraction method to prep sample varies
- Varying accuracy for pts w issues detoxing and excreting
- Doesn’t help answer the question of whether currently being exposed
- Unknown degree of contamination via ingestion

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Serum Mycotoxin Antibody

New kid on the block commercially

Indirect measure

The idea - the meer presence of a mycotoxin not as important as knowing what the body thinks about it

Strengths ~
- Not an excretion test
- Detection of metabolites of mycotoxins that share common antigens
- IgE helps to answer whether it's a current exposure

Challenges ~
- Antigen selection by lab
- May miss metabolites if antigens have been modified
- Immune status of the pt
- IgG remains positive for up to 6 months
- Unknown degree of contamination via ingestion

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toxins

MDPI

Article

Mycotoxin Analysis of Human Urine by LC-MS/MS: A Comparative Extraction Study

Laura Escrivá, Lara Manyes, Guillermina Font and Houda Berrada *

Laboratory of Food Chemistry and Toxicology, Faculty of Pharmacy, University of Valencia, Av. Vicent Andres Estelles s/n, 46100 Burjassot, Spain; laura.escriva@uv.es (L.E.);lara.manyes@uv.es (L.M.); guillermina.font@uv.es (G.F.)

* Correspondence: houda.berrada@uv.es; Tel.: +34-963-544-117

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"Three extraction methods, namely salting-out liquid–liquid extraction (SALLE), miniQuEChERS (quick, easy, cheap, effective, rugged, and safe), and dispersive liquid–liquid microextraction (DLLME), were evaluated and compared based on analytical parameters for the quantitative LC-MS/MS measurement of 11 mycotoxins (AFB1, AFB2, AFG1, AFG2, OTA, ZEA, BEA, EN A, EN B, EN A1 and EN B1) in human urine.

DLLME was selected as the most appropriate methodology, as it produced better validation results for recovery (79–113%), reproducibility (RSDs < 12%), and repeatability (RSDs < 15%)

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Random Urine Adequate?

Comparison study, in-house

LC-MS method

Creatinine controlled

3 variations ~
- First-morning, 6 hour, 24 hour

Results ~
- Positives remained positive
- Negatives remained negative
- Values not necessarily the same, varied by mycotoxin

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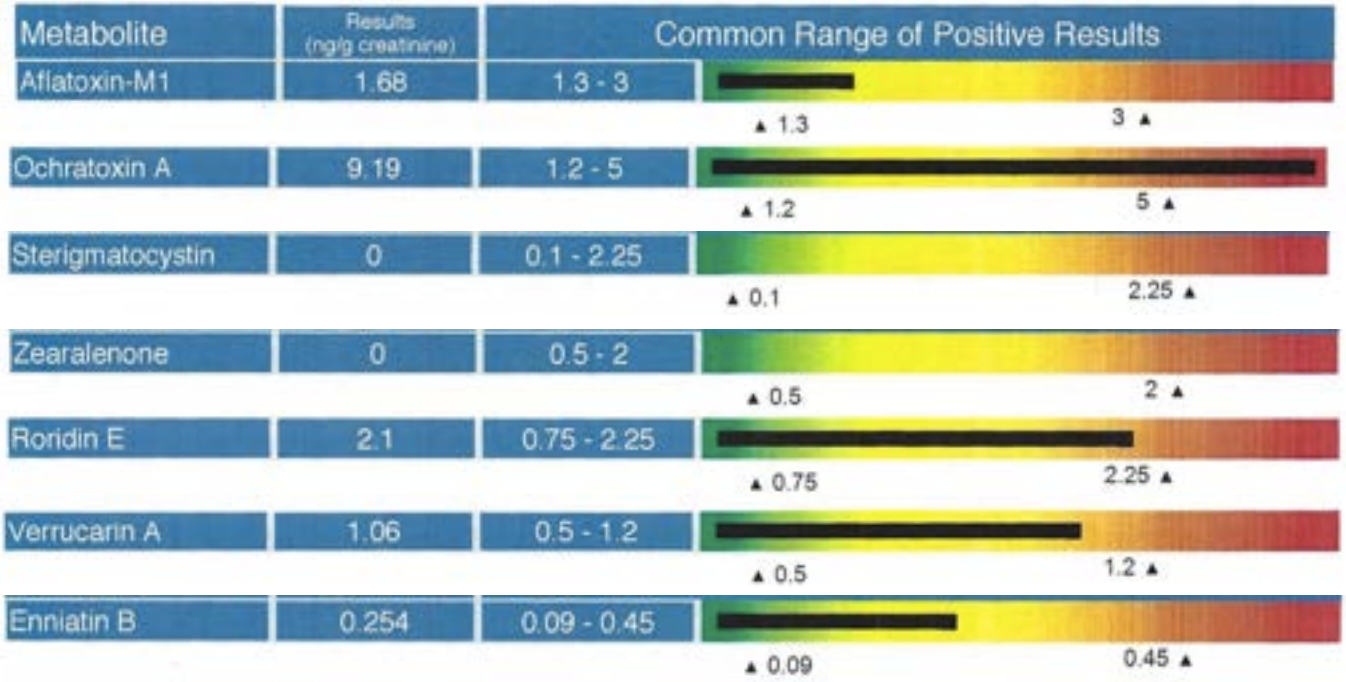
Split Sample - Mass Spect vs ELISA



K Code	Test	Specimen	Value	Result	Not Present if less than	Equivocal if between	Present if greater or equal
E8501	Ochratoxin A	Urine	1.10000 ppb	Not Present	1.8 ppb	1.8-2.0 ppb	2.0 ppb
E8502	Aflatoxin Group (B1,B2,G1.G2)	Urine	1.07600 ppb	Present	0.8 ppb	0.8-1.0 ppb	1.0 ppb
E8503	Trichothecene Group (Macrocyclic)	Urine	0.07400 ppb	Present	0.02 ppb	0.02-0.03 ppb	0.03 ppb
E8510	Gliotoxin Derivative	Urine	1.62100 ppb	Present	0.5 ppb	0.5-1.0 ppb	1.0 ppb

More symptomatic identical twin. No glutathione. No sweating. No creatine.

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Split Sample - Mass Spect vs ELISA

Code	Test	Specimen	Value	Result	Not Present if less than	Equivocal if between	Present if greater or equal
E8501	Ochratoxin A	Urine	1.51000 ppb	Not Present	1.8 ppb	1.8-2.0 ppb	2.0 ppb
E8502	Aflatoxin Group (B1,B2,G1,G2)	Urine	1.02700 ppb	Present	0.8 ppb	0.8-1.0 ppb	1.0 ppb
E8503	Trichothecene Group (Macrocyclic)	Urine	0.08100 ppb	Present	0.02 ppb	0.02-0.03 ppb	0.03 ppb
E8510	Gliotoxin Derivative	Urine	1.83100 ppb	Present	0.5 ppb	0.5-1.0 ppb	1.0 ppb

Less symptomatic identical twin. Taking glutathione + creatine. Exercises.

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Questions Raised

Controlling for creatinine ~
Does this explain the differences in OTA results?
To what degree does creatine supp affect creatinine clearance?

Sweating/exercise ~
Was twin 2 more detoxed bc of exercise?
Are the results of mass spect falsely lower bc of "detox bolus" the night before when worked out?…OR…

Glutathione administration ~
Falsely lower the mass spect results?

Is the bigger issue "normal ranges"? How are these determined?
ie: OTA 1.10 (1.8-2.0) vs 9.19 (1.2-5.0)
ie: OTA 1.51 (1.8-2.0) vs 5.27 (1.2-5.0)

Is there such a thing as a test with all zeros?
(answer - YES!)

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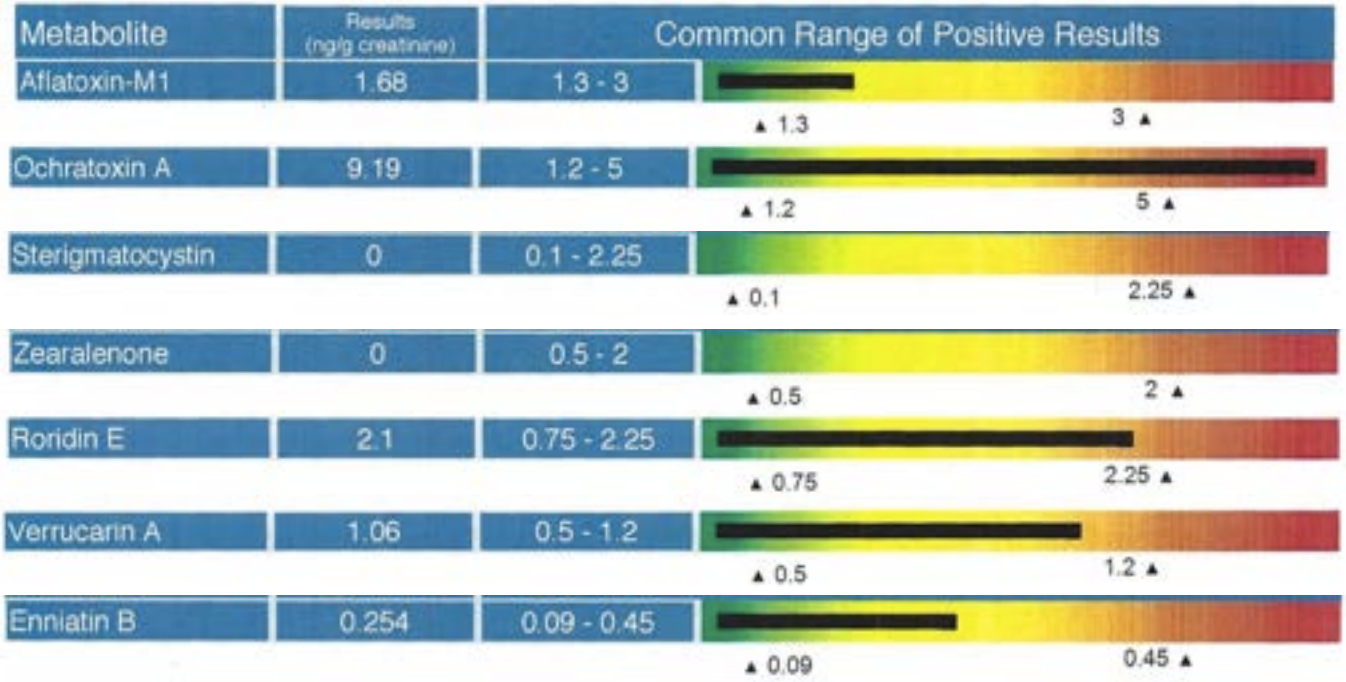
Split Sample - Baseline Twin 1



K Code	Test	Specimen	Value	Result	Not Present if less than	Equivocal if between	Present if greater or equal
E8501	Ochratoxin A	Urine	1.10000 ppb	Not Present	1.8 ppb	1.8-2.0 ppb	2.0 ppb
E8502	Aflatoxin Group (B1,B2,G1.G2)	Urine	1.07600 ppb	Present	0.8 ppb	0.8-1.0 ppb	1.0 ppb
E8503	Trichothecene Group (Macrocyclic)	Urine	0.07400 ppb	Present	0.02 ppb	0.02-0.03 ppb	0.03 ppb
E8510	Gliotoxin Derivative	Urine	1.62100 ppb	Present	0.5 ppb	0.5-1.0 ppb	1.0 ppb

More symptomatic identical twin. No glutathione. No sweating. No creatine.

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Split Sample - Mass Spect Methods

Creatinine Value: 125.97 mg/dl

Metabolite	Results (ng/g creatinine)	Normal Range *	Abnormal Range
Aspergillus			
Aflatoxin-M1	0.00	< 0.5	▲ 0.5
Ochratoxin A	10.93	< 7.5	▲ 7.5
Gliotoxin	0.00	< 200	▲ 200
Penicillum			
Sterigmatocystin	0.00	< 0.4	▲ 0.4
Mycophenolic Acid	0.00	< 37.4	▲ 37.4
Stachybotrys			
Roridin E	0.00	< 0.2	▲ 0.2

More symptomatic identical twin. 1 year later.

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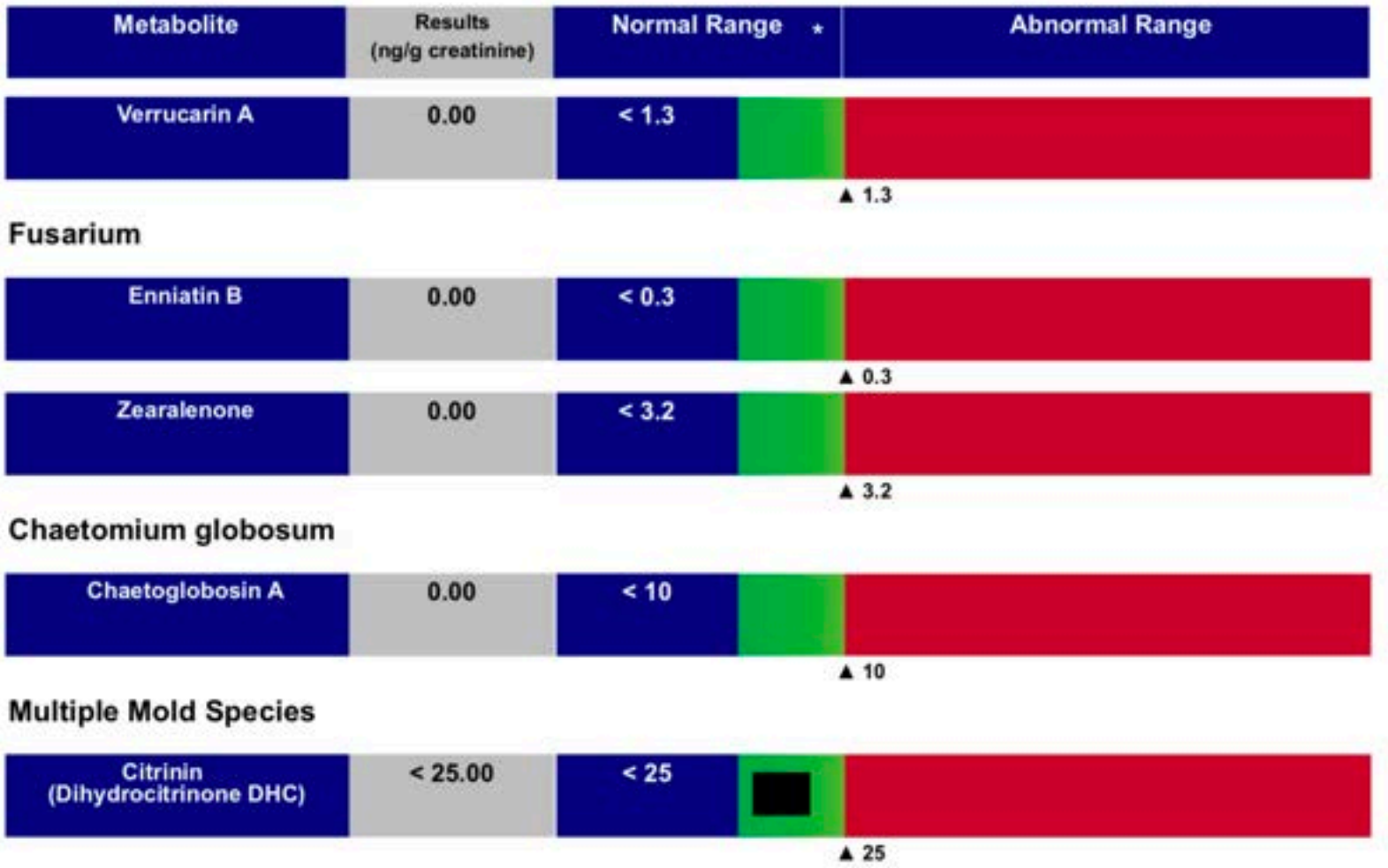
Split Sample - Mass Spect Methods



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Split Sample - Mass Spect Methods

Mycotoxins - High

Test Name	Species Name	In Control	Moderate	High	Current Level	Previous Level
diacetoxyscirpenol (DAS) (ng/g)	Fusarium	≤3.20	3.21–6.40	≥6.41	14.07	

Mycotoxins - Moderate

Test Name	Species Name	In Control	Moderate	High	Current Level	Previous Level
Ochratoxin A (ng/g)	Aspergillus, Penicillium	≤5.10	5.11–10.20	≥10.21	7.55	
Dihydrocitrinone (ng/g)	Aspergillus, Penicillium, Monascus	≤12.40	12.41–24.80	≥24.81	23.30	
Roridin A (ng/g)	Stachybotrys chartarum	≤5.70	5.71–11.40	≥11.41	6.37	

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Building Test Results

ALL CLEAR currently!

But had moved 4 mo prior from place with Fusarium in HVAC.

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Split Sample - Baseline Twin 2

Code	Test	Specimen	Value	Result	Not Present if less than	Equivocal if between	Present if greater or equal
E8501	Ochratoxin A	Urine	1.51000 ppb	Not Present	1.8 ppb	1.8-2.0 ppb	2.0 ppb
E8502	Aflatoxin Group (B1,B2,G1,G2)	Urine	1.02700 ppb	Present	0.8 ppb	0.8-1.0 ppb	1.0 ppb
E8503	Trichothecene Group (Macrocyclic)	Urine	0.08100 ppb	Present	0.02 ppb	0.02-0.03 ppb	0.03 ppb
E8510	Gliotoxin Derivative	Urine	1.83100 ppb	Present	0.5 ppb	0.5-1.0 ppb	1.0 ppb

Less symptomatic identical twin. Taking glutathione + creatine. Exercises.

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Split Sample - Mass Spect Methods

Creatinine Value: 184.83 mg/dl

Metabolite	Results (ng/g creatinine)	Normal Range *	Abnormal Range
Aspergillus			
Aflatoxin-M1	0.00	< 0.5	▲ 0.5
Ochratoxin A	15.31	< 7.5	▲ 7.5
Gliotoxin	0.00	< 200	▲ 200
Penicillum			
Sterigmatocystin	0.00	< 0.4	▲ 0.4
Mycophenolic Acid	59.77	< 37.4	▲ 37.4
Stachybotrys			
Roridin E	0.00	< 0.2	▲ 0.2

Less symptomatic identical twin. 1 year later. But now new sxs.

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Split Sample - Mass Spect Methods

Metabolite	Results (ng/g creatinine)	Normal Range *	Abnormal Range
Verrucarin A	0.00	< 1.3	▲ 1.3
Fusarium			
Enniatin B	0.00	< 0.3	▲ 0.3
Zearalenone	0.00	< 3.2	▲ 3.2
Chaetomium globosum			
Chaetoglobosin A	0.00	< 10	▲ 10
Multiple Mold Species			
Citrinin (Dihydrocitrinone DHC)	0.00	< 25	▲ 25

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Split Sample - Mass Spect Methods

Mycotoxins - Moderate

Test Name	Species Name	In Control	Moderate	High	Current Level	Previous Level
Ochratoxin A (ng/g)	Aspergillus, Penicillium	≤5.10	5.11~10.20	≥10.21	7.03	
Fumonisins B1 (ng/g)	Fusarium	≤4.60	4.61~9.20	≥9.21	7.71	

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Building Test Results

Fusarium in HVAC

Asp/Pen in flooring around bathroom shower

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More Questions Raised

MPA ~

Not only from Pen. Also from Asp.
Reporting on both labs confusing
linkage to only Pen.
Why high on one but not the other?
What is the population norm for MPA?

Is second method catching more
because of expanded metabolites?

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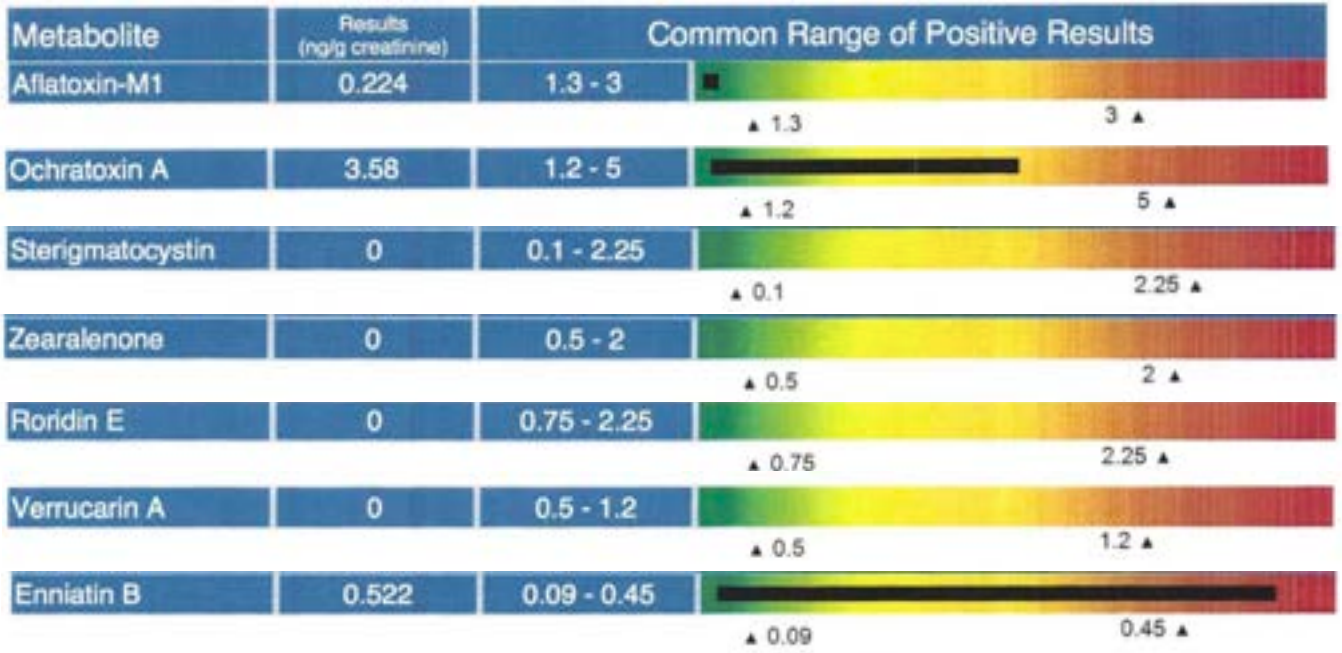
Urine Mycotoxin Split Sample



Results:

J Code	Test	Specimen	Value	Result	Not Present if less than	Equivocal if between	Present if greater or equal
E8501	Ochratoxin A	Urine	1.55300 ppb	Not Present	1.8 ppb	1.8-2.0 ppb	2.0 ppb
E8502	Aflatoxin Group (B1,B2,G1,G2)	Urine	0.80500 ppb	Equivocal	0.8 ppb	0.8-1.0 ppb	1.0 ppb
E8503	Trichothecene Group (Macrocyclic)	Urine	0.07200 ppb	Present	0.02 ppb	0.02-0.03 ppb	0.03 ppb
E8510	Gliotoxin Derivative	Urine	1.42100 ppb	Present	0.5 ppb	0.5-1.0 ppb	1.0 ppb

+Candida on stool testing. Taking EFAs+curcumin+resveratrol+milk thistle.

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Questions Raised

To what degree does Candida overgrowth alter urine mycotoxin labs?

Gliotoxin also formed from Candida

Are Candida/Rhodotorula cause or protective effect of mold exposure?

Which mycotoxins are detoxed with which natural remedies?

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Mycotoxin Negative but Mold-Sick

Not testing all mycotoxins

Confounding factors before sample~

- Random urine
- Exercise
- Sauna
- Glutathione admin
- Acute viral challenge

Exposure duration too limited

Intimate contact/parental toxification

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Glutathione Pre-Assessment

Organic Acids Test (OAT)

Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)		Patient Value	Reference Population - Females Age 13 and Over
Indicators of Detoxification				
Glutathione				
58 Pyroglutamic *	10	- 33	22	
Methylation, Toxic exposure				
59 2-Hydroxybutyric **	0.03	- 1.8	H 13	
Ammonia Excess				
60 Orotic	0.06	- 0.54	0.24	
Aspartame, salicylates, or GI bacteria				
61 2-Hydroxyhippuric		≤ 1.3	0.37	

* ***A high value for this marker may indicate a Glutathione deficiency.***

** ***High values may indicate methylation defects and/or toxic exposures.***

RBC Glutathione (not whole blood)

Glutathione; Erythrocytes

	Within	Outside	Reference Range	
Glutathione*		1093	> 1100	µmoles/L

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Urine Mycotoxin Pre-Testing Guidelines

2 days minimum before test ~

- Avoid ingestion of mold/mycotoxin containing foods, bevs, supps, meds
- Avoid binders
- To provoke or not? If so, how?

Do not fast more than physiological

Morning of test ~

- Collect first-morning's urine
- Avoid food/water prior
- Avoid exercise
- Avoid intercourse
- Avoid sauna and hot shower

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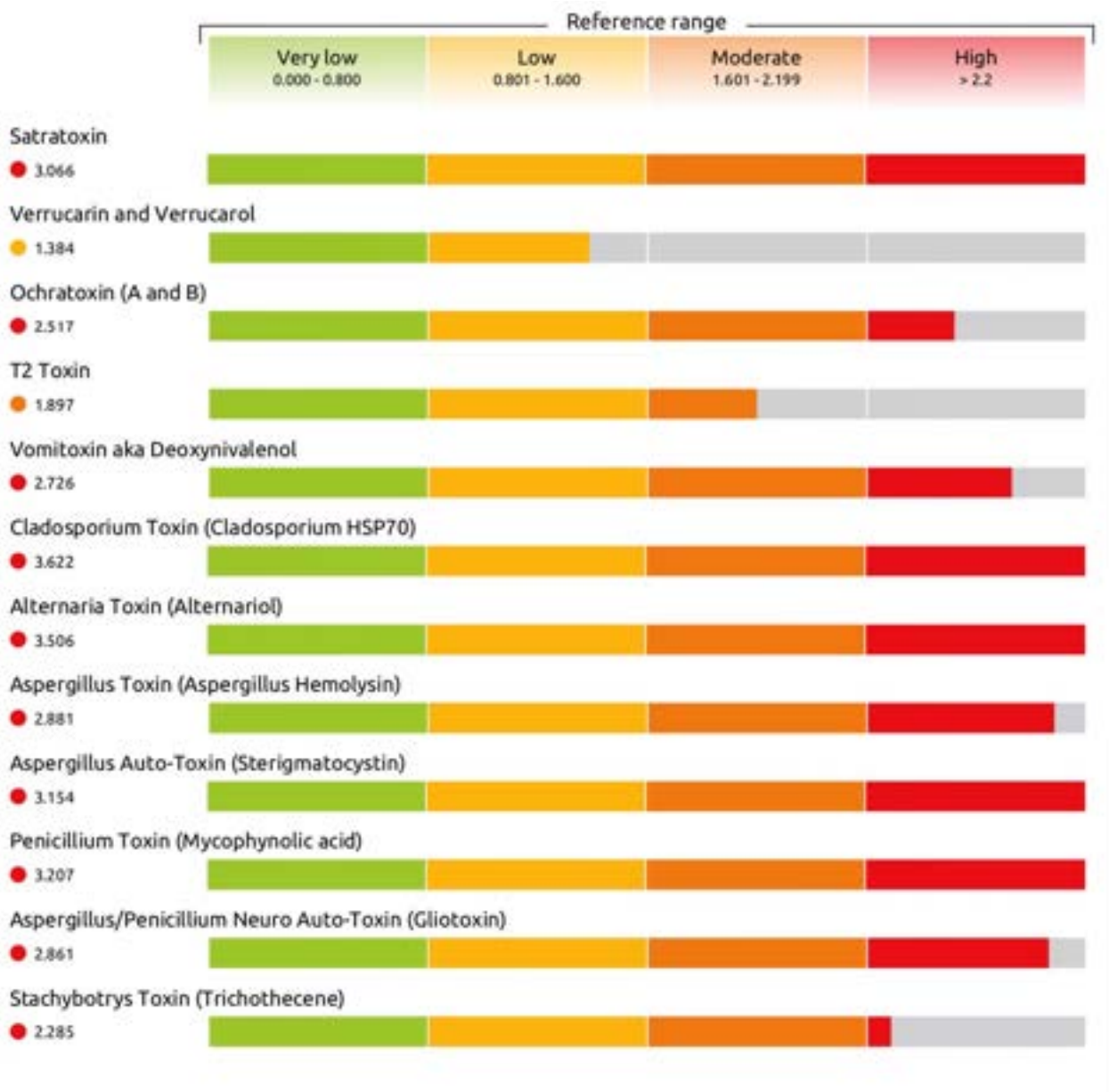
Serum Mycotoxin Antibody



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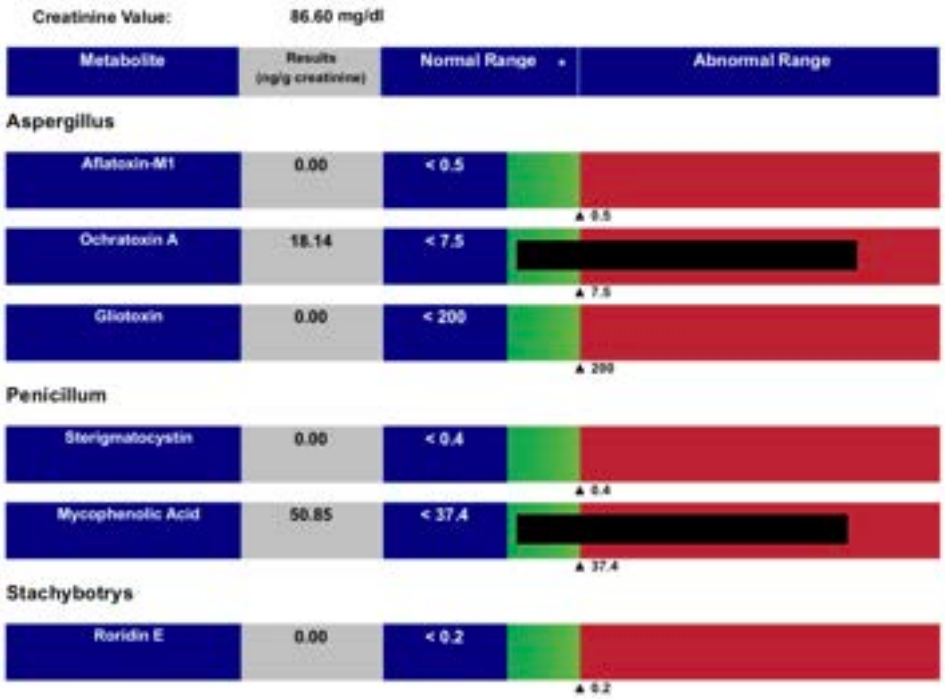
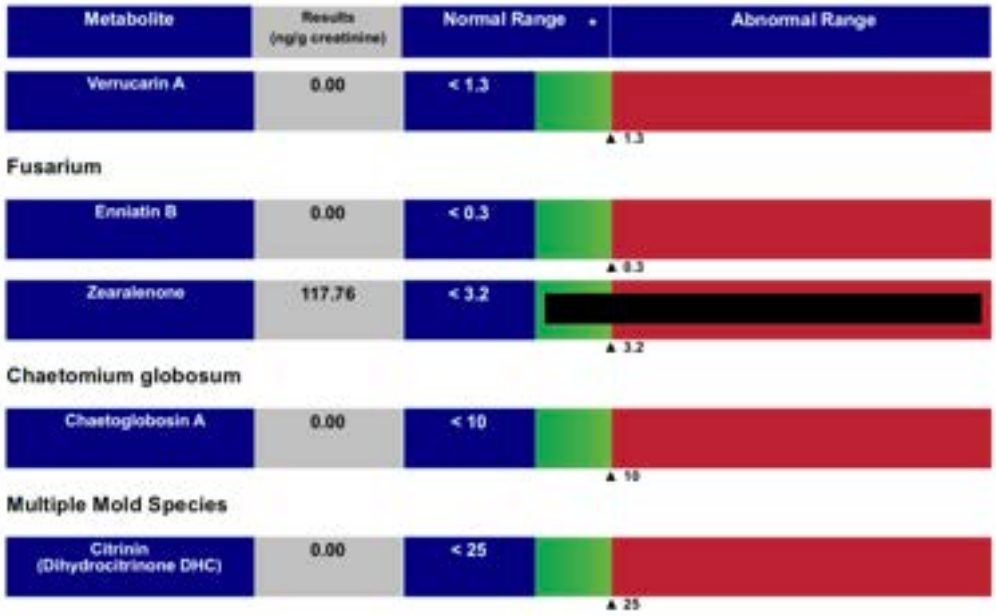
Serum Mycotoxin - Urine Mycotoxin LC-MS



Creatinine Value: 86.60 mg/dl

Metabolite	Results (ng/g creatinine)	Normal Range	Abnormal Range
Aspergillus			
Aflatoxin-M1	0.00	< 0.5	▲ 0.5
Ochratoxin A	18.14	< 7.5	▲ 7.5
Gliotoxin	0.00	< 200	▲ 200
Penicillum			
Sterigmatocystin	0.00	< 0.4	▲ 0.4
Mycophenolic Acid	50.85	< 37.4	▲ 37.4
Stachybotrys			
Roridin E	0.00	< 0.2	▲ 0.2



Metabolite	Results (ng/g creatinine)	Normal Range	Abnormal Range
Verrucarin A	0.00	< 1.3	▲ 1.3
Fusarium			
Enniatin B	0.00	< 0.3	▲ 0.3
Zearalenone	117.76	< 3.2	▲ 3.2
Chaetomium globosum			
Chaetoglobosin A	0.00	< 10	▲ 10
Multiple Mold Species			
Citrinin (Dihydrocitrinone DHC)	0.00	< 25	▲ 25

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Serum Mycotoxin Antibody

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Serum Mycotoxin Antibody

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Anal Bioanal Chem (2017) 409:3369–3382
DOI 10.1007/s00216-017-0279-9

RESEARCH PAPER

Multi-mycotoxin analysis using dried blood spots and dried serum spots

Bernd Osteresch[1] · Susana Viegas[2,3] · Benedikt Cramer[1] · Hans-Ulrich Humpf[1]

"HPLC-MS/MS detection was used for the analysis of dried serum spots (DSS) and dried blood spots (DBS).

Detection of aflatoxins (AFB1, AFB2, AFG1, AFG2, AFM1), trichothecenes (deoxynivalenol, DON; DON-3-glucoronic acid, DON-3-GlcA; T-2; HT-2; and HT-2-4-GlcA), fumonisin B1 (FB1), ochratoxins (OTA and its thermal degradation product 2'R-OTA; OTα; 10- hydroxychratoxin A, 10-OH-OTA), citrinin (CIT and its urinary metabolite dihydrocitrinone, DH-CIT), zearalenone and zearalanone (ZEN, ZAN), altenuene (ALT), alternariols (AOH; alternariol monomethyl ether, AME), enniatins (EnA, EnA1, EnB, EnB1) and beauvericin (Bea) was validated for two matrices, serum (DSS), and whole blood (DBS).

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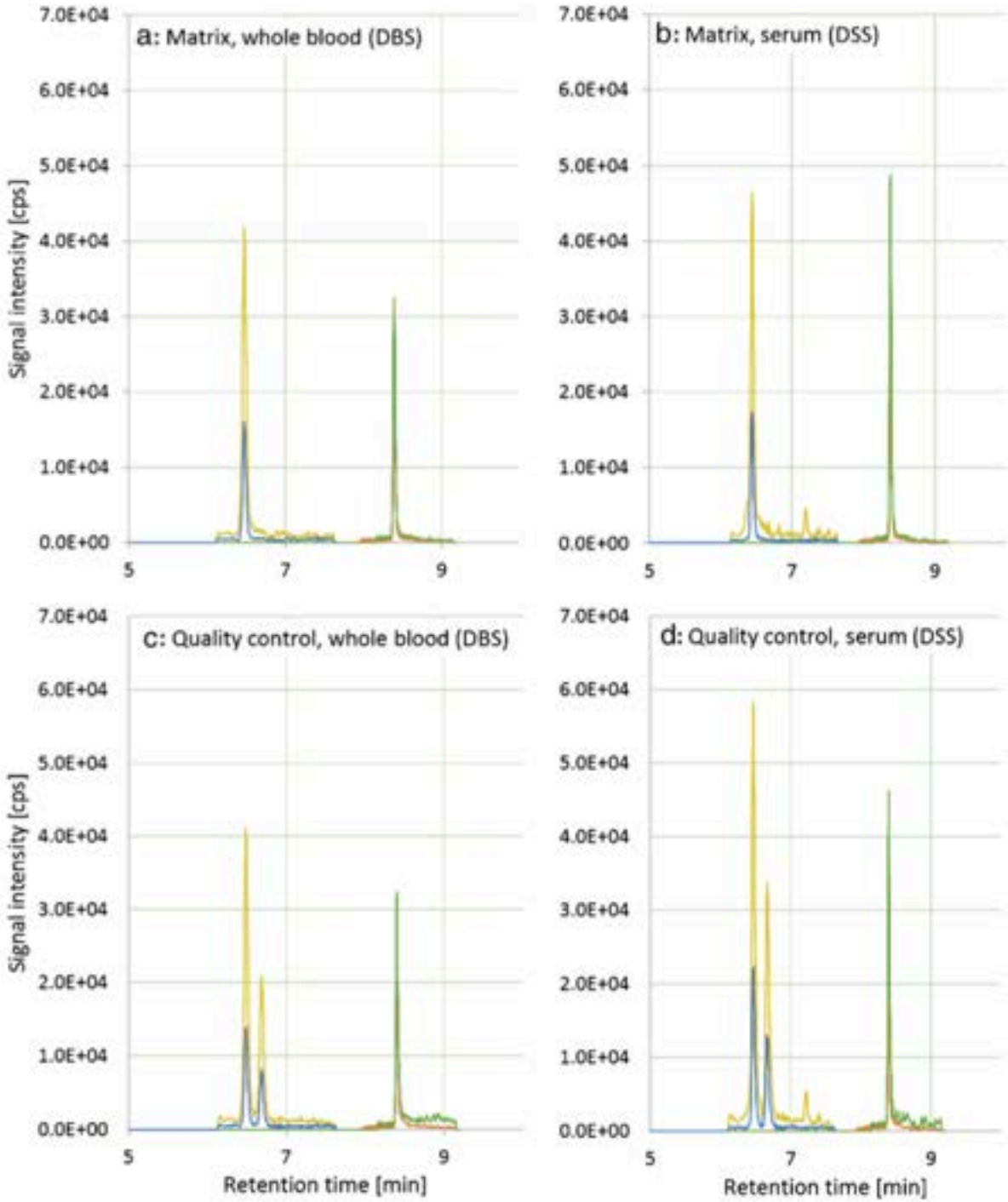

Fig. 2 Extracted ion chromatograms of OTA/2'*R*-OTA (*yellow transition m/z* 404.1 → 239.0, *blue transition m/z* 404.1 → 102.0) and EnB (*green transition m/z* 640.4 → 196.2, *orange transition m/z* 662.4 → 336.3) in whole blood (**a** and **c**) and serum (**b** and **d**). **a**, **b** Analyte signals for the used matrix solutions containing 0.291 ng/mL OTA and 0.0349 ng/mL EnB. **c**, **d** A real sample which was used as quality control sample containing 0.283 ng/mL OTA, 0.193 ng/mL 2'*R* OTA, and 0.0366 ng/mL EnB

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For most analytes, LOQs (limit of quantitation) in the lower pg/mL range and excellent recovery rate were achieved using matrix-matched calibration.

Besides validation of the method, the analyte stability in DBS and DSS was also investigated. Stability is a main issue for some analytes when the dried samples are stored under common conditions at room temperature.

This methodical study establishes a validated multi-mycotoxin approach for the detection of 27 mycotoxins and metabolites in dried blood/serum spots based on a fast sample preparation followed by sensitive HPLC-MS/MS analysis.

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ELSEVIER

Journal of Chromatography B

Volume 1020, 1 May 2016, Pages 158-164

Analysis of ochratoxin A in dried blood spots – Correlation between venous and finger-prick blood, the influence of hematocrit and spotted volume

Bernd Osteresch, Benedikt Cramer, Hans-Ulrich Humpf

The use of capillary blood from finger-pricks versus venous blood was evaluated. The analyte levels correlate indicating that the less invasive finger-prick sampling gives also reliable results.

No significant hematocrit effect was observed.

In this experiment, finger-prick samples typically consist of about 90 µL blood. Therefore spots of 75, 100 and 125 µL blood were prepared and analyzed. Similar to the hematocrit effect, no considerable influence was observed.

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Mol. Nutr. Food Res. 2015, *59*, 1837–1843 DOI 10.1002/mnfr.201500220

RESEARCH ARTICLE

Biomonitoring using dried blood spots: Detection of ochratoxin A and its degradation product 2'R-ochratoxin A in blood from coffee drinkers*

Benedikt Cramer[1], *Bernd Osteresch*[1], *Katherine A. Muñoz*[2], *Hartmut Hillmann*[3], *Walter Sibrowski*[3] *and Hans-Ulrich Humpf*[1]

[1] Institute of Food Chemistry, Westfälische Wilhelms-Universität Münster, Münster, Germany
[2] Universität Koblenz-Landau, Institute for Environmental Sciences, Research Group of Environmental and Soil Chemistry, Landau in der Pfalz, Germany
[3] Institut für Transfusionsmedizin und Transplantationsimmunologie, Universitätsklinikum Münster, Münster, Germany

"The results of this study revealed for the first time a high exposure of coffee consumers to 2'R-OTA, a compound formed from OTA during coffee roasting.

Since little information is available regarding toxicity and possible carcinogenicity of this compound, further OTA monitoring in blood including 2'R-OTA is advisable."

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Mycotoxin Testing - Yes? No? How?

Above all, be mindul of cost ~
 If you know it's mold, skip the test and tx
 And/or consider methods validated/ins coverage ie:
 Neuroquant

ELISA Urine ~
 Immune deficient, able to detox, body burden, track tx

LC-MS Urine ~
 Immune deficient, able to detox, body burden, track tx, liv/kidney creatinine clearance

Serum antibody ~
 Excretion/detox-challenged, liv/kidney dz, IgE - is it a "now" issue?

Be mindful of supplement use ~
 Binders, glutathione, creatine

To provoke or not? Depends more on your pt than agent

OR…maybe use a clinical questionnaire

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Shoemaker Highlights

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Shoemaker ~ Diagnostic Indicators

Visual Contrast Test at VCStest.com
- Convergence disorder
- L/R eye visual processing in brain+eye
- m impairment

TGF-β1 (transforming growth factor beta-1)↑
- Cytokine
- ↑ impairs T-reg fxn → immune overactivation/asthma
- Range <2380 pg/ml
- (Quest→Cambridge Biomedical)

MMP-9 (matrix metallopeptidase 9) ↑
- Tissue repair enzyme induces I/S stim
- Range ~ 85-332 ng/ml
- Drs. Patel/Farshchian - link to MCAS
- (Labcorp)

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Shoemaker ~ Diagnostic Indicators

ADH (vasopressin) ↓

- Range ~ 1.0-13.3 pg/ml;
- Test in conjunction with blood osmolality ~ 280-300 mosmol

VIP (vasoactive intestinal polypeptide) ↓

- Neuro and cardioreg hormone with receptors in the hypothalamus
- Range 23-63 pg/ml

MSH (melanocyte stim hormone) ↓

- Pituitary hormone w neurohormonal and anti-inflammatory actions
- Range 35-81 pg/ml

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Colonization, Allergy, Infection

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Culture Nares

2” depth

Pediatric swab

Off all nasal tx for 3 days

+MRSA/+MARCoNS common

Consider false neg if positive urine mycotoxins

Specific lab (MARCoNS)

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Colonization

Posterior Nasal Culture
- Req posterior nasal wash
- Fungus tenaciously adhered
- Consider false neg if positive urine mycotoxins
- PCR/DNA better yield
- +MARCoNS

Opthalmology
- Freq changing vision w sinus colonies
- (empirical exper)

BDG (Fungitell) Quantitative (<60 pg/mL)
- (1,3)-Beta-D-glucan
- Invasive Fungal Infection (IFI)
- Note: not present in Mucorales, Cryptococcus, Blastomyces
- Note: false + if taking Beta-lactam antibiotic

Galactomannan - (<0.5 index)
- Less sensitive than BDG (81% vs 49%)
- Charting tx of known Aspergillosis
- BDG option if on Beta-lactams

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Allergy

Skin Testing

- RAST limitations
- Update ~ Intradermal
- Provocation Neutralization
- Training req'd
- Caution: ↑ potential of harm
- Off all antihistamines* incl supp

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Infection

Swab

- Oral, vaginal/groin, perianal, intertrigo

Tissue sample

- Skin, scalp, toenail

Biopsy/culture

- Culture
- Tissue biopsy (sinus, lung)
- Varying yields
- Flexible laryngoscopy ~ sinus
- Transthoracic CT ~ fine needle aspirate lung nodules

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Advances In Imaging

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Imaging

- Sinus
  - X-ray
  - CT
- Chest
  - XRay
    - (may not be abn in
    - pulm fibrosis→CT)
  - High-res CT
  - Fiberoptic bronchoscopy

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Imaging

- Abdomen
  - Upper endoscopy
  - Colonoscopy
- Brain
  - MRI NeuroQuant
  - SPECT - volumetric

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Review

Diagnostic Assessments

Mycotoxin Discussion

Shoemaker Panel Highlights

Colonization, Allergy, Infection

Advances In Imaging

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Thank You

Dr. Jill Crista
Naturopathic Doctor
support@drcrista.com

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Are You Missing Mold Illness?

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Peel The Orange

Are You Missing Mold Illness In Your Patients?

Dr. Jill Crista

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Peel The Orange

Avoidance

Air Filtration

Food ~ Do's & Dont's

Beverage ~ Do's & Dont's

Med/Supp Cautions

Fundamentals

Health Hokey Pokey

Emunctories

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How Mold Makes Your Job Harder

"Sensitive" patients~minute doses

Counter-intuitive reactions

Detox organs~drug clearance

Immune depletion~chronicity

Inflammatory reactions

Sm vessel vasculitis & coagulation abnormalities~remedy delivery

Cardiac~fatigue

Neuro~"mold brain"

Sleep

∴ Don't/can't stick to tx plan

AND spiritually/energetically depleted

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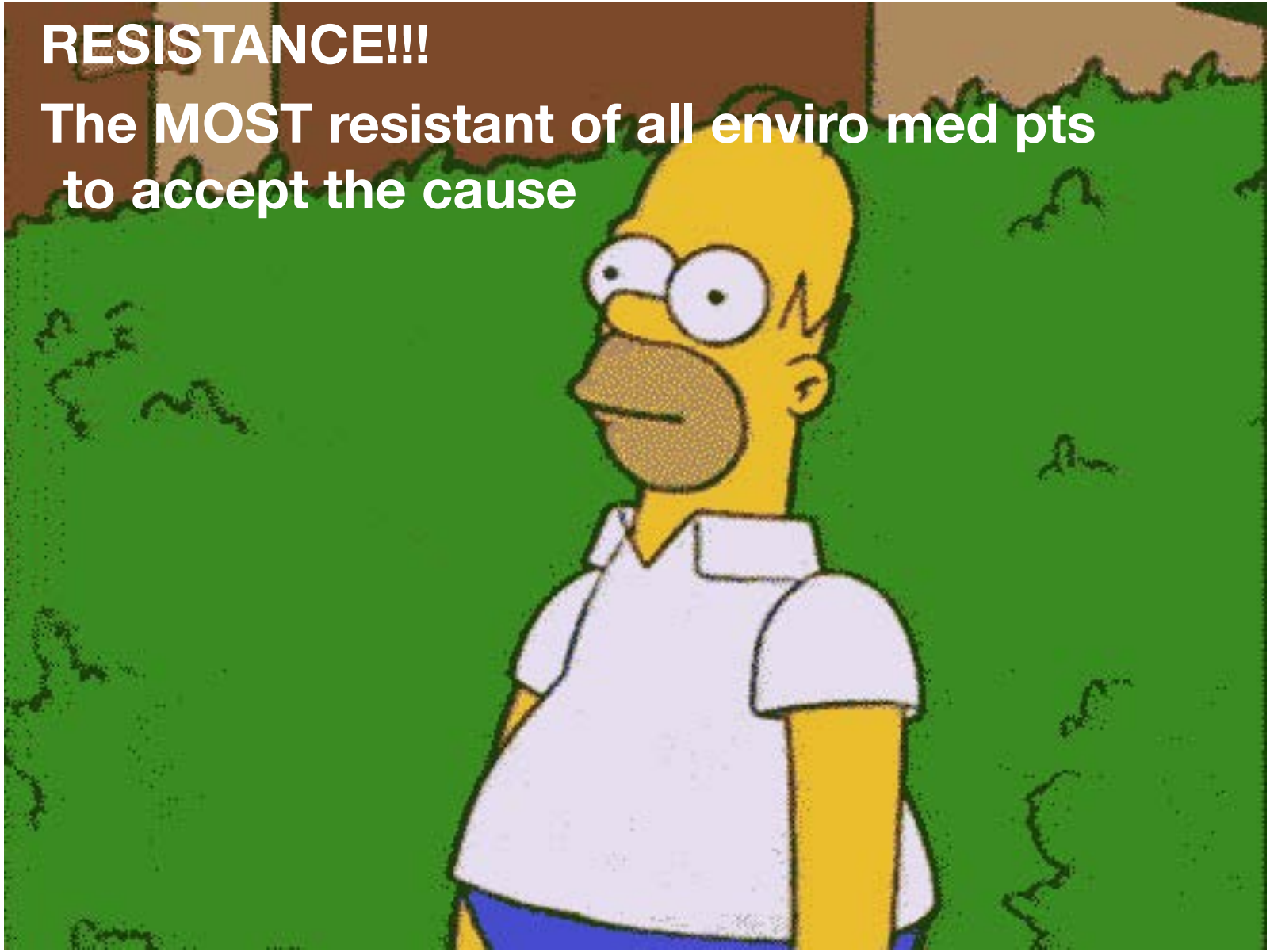
How Mold Makes Your Job Harder



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Peel The Orange

1 AVOIDANCE~critical/hardest

2 FUNDAMENTALS~BTGs

3 PROTECT~mycotoxins/die-off

4 REPAIR~gene/cell/organ/system

5 FIGHT~last step

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First 3 Rules of Toxic Exposure

1) Avoidance

2) Avoidance

3) Avoidance

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Avoidance ~ Easy To Say . . .

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Avoidances

1. Habitat
2. Air Quality
3. Foods To Avoid
4. Beverages To Avoid
5. Supplement & Medication Cautions
6. Hobbies & Habits

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Avoidance of WDB

The most difficult part of tx plan

Sick, fatigued, cognitively impaired, financially strapped

More questions about this than other parts of tx plan

Build referral base

Use online resources/guidance

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Get Out & Take Little With You

Relocate w open-ended duration

Usu must leave possessions behind

Mold toxic patients are **the most** resistant of all enviro toxic pts to accept that mold is the issue

Jedi mind trick? neuroinflam?

The key to my success?

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Relocation During Remediation

Occupational study - no resp sx improvement after remediation

Possible contributing factors:

- Fragment formation
- Mycotoxin increase
- Contamination
- Internal Colonization

All above!

PMID: 21413053

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Counsel Against DIY

…testing *and* remediation

Mold gets more toxic when bugged

Aspergillus exposed to amphotericin B ↑ Gliotoxin prod

Too much addt'l toxin burden for already symptomatic pt

Guaranteed way to have aggrav

PMID: 15272057

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And What About Hobbies?

Baker

Brewmaster

Cheese connoisseur

Somelier

Antiquer

Historian

Mushroomer

Rare book collector

Love it? or beholden to it?

*cannabis ~ storage issue

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Air Filtration

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STORY | C-PAP Dementia

Late 70s F, concerned adult kids ~ mom's safety

Beg signs of dementia, garage door open overnight

Dev confusion, balance issues, req cane

HTN, C-PAP for insomnia dt RLS

Large historic home, "bad about dusting"

Stopped using C-PAP bc forgetful

Readded C-PAP, kids dusted, air filter in bedroom

Husband's insomnia improved. Hers worsened.

High anxiety, worry, forget where she is, night wandering

Nap ok in recliner ~ too far from her C-PAP to use

Tested C-PAP machine ~ high Aspergillus + endotoxins

Wasn't maintaining adequate cleaning sched

Replaced tubing, cleaned machine appropriately

Dementia sxs improved to no longer an issue

* * *

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Air Filtration

Ionizing:

- Sanitizing = ionized oxygen (O_2^-)
- Not making ozone (O_3)
- Filters mycotoxins at 0.007 microns

Filtration:

- HyperHEPA
- Ultrafine particles to 0.003 microns
- Traps mycotoxins

Incineration:

- In-home Incinerator
- Incinerates at 400°F, removes 99% airborne microbiological contaminants

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Air Filtration

NOT a replacement for remediation!!!

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Food ~ Do's & Dont's

© Dr Jill Crista

Avoidance Foods ~ First Tier

Fermented & mold-containing. May need LT avoidance:

Sweets of any kind
Dried fruits
Leavened bread
Yeast
Simple carbohydrates
Baked goodies
Mushrooms
Corn
Potatoes
Pickles & pickled foods
Vinegar
Soy sauce
Cantaloupe
Grapes
Aged cheese
Moldy cheeses
Peanuts
Peanut butter

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Avoidance Foods ~ Second Tier

Mold and yeast target. Usually ST avoidance.

All fruit

Starchy vegetables

All grains

Fermented foods

Shelled nuts

Condiments made w vinegar or sugar

Sour cream

Soured milk products

Mass-produced cocoa*

PMID: 5723973, 24287569

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Effects of Cooking

Netherlands study 2016

Pasta infected with ~
Enniatin
Deoxynivalenol (DON)
(tricothecene aka vomitoxin)

Cooked in duplicate on diff days,
under stndized conditions,
simulating house-hold preparation

Tested post-cooking

83-100% enniatin retained

60% tricothecenes retained

PMID: 27451245

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What To Eat?

- Rainbow of color
- Veggies rule (veggies>fruit)
- Feed the guts
- Say yes to good fats
- Eat stinky foods
- Adequate protein

Bioflavonoids (polyphenols)

Inhibition of NF-κB signaling

↓ expression of proinflam markers

PMID: 21432698

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Protective Foods

Colorful vegs ~
Beets, artichoke, asparagus, radishes (liver)
Broccoli, Brussel sprouts (sulfurophanes)
Tomatoes (lycopene neutralizes mycotoxins)
Cabbage, okra (enterocytes, mucosa)
Celery, cucumber (kidney fluid balance)
Bitter greens (cholagogue) arugula, broccoli rabe, endive, watercress, kale, dandelion greens

Colorful fruits (1 serving/d)

Organic beef liver (choline)

EFAs
Avocado, olive oil, fresh seeds/nuts (refrig), cage-free eggs, wild fish

Yogurt (probiotics)

Butter (butyrate enterocyte)

Turmeric-curry (liver/kidney/brain anti-inflam)

Bitter chocolate, artisanal (cholagogue)

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Mold Combat Foods/Spices

Eat stinky!

- Garlic
- Onions
- Scallions
- Chives
- Leeks

Use spices with **wild abandon**

- Ginger (hepatoprotective)
- Clove (mycotoxin neutralizer)
- Cumin
- Rosemary
- Sage
- Thyme
- Oregano
- Basil
- Bay leaf

PMID: 28475920

© Dr Jill Crista

Beverage ~ Do's & Dont's

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Avoidance Beverages

Fermented, contain mycotoxins, add fungal burden:

ANY sweetened beverage

Fruit juice

Oolong and black tea

Moldy coffee

Mass-produced cocoa

Alcoholic beverages
esp org wine/grain-based

Fermented cider

Kombucha*

Fermented bev avoidance maybe LT

PMID: 5723973, 24287569, 22372472, 29117141, 19610336

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What To Drink?

Spring water
- RO w sea salt
- bioplasma cell salts
- colloidal trace minerals

Green tea (polyphenols)
- anti-inflam
- hepatoprotective ~ aflatoxin
- cytoprotective ~ fusarium
- myoprotective ~ citrinin
- glucuronidation ~ MPA

Coffee
- cholagogue
- indep verified mycotoxin free

PMID: 17195249, 23410590, 27539359

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Med/Supp Cautions

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Supplement Cautions

Are actual fungus ~
- Medicinal mushrooms
- Nutritional yeast
- Sacch B…? (more next)

Grown on fungus ~
- "Aspergillus-activated"
- B-vitamins
- Digestive enzymes

Contaminated with mycotoxin ~
- Red yeast rice ~ citrinin
- Resveratrol
- Bee propolis

Companies that don't test for mycotoxin contamination

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Sacch B

Literature ~

In vitro 24-hr culture to prevent mycotox during yeast ferm/beer prod/feed additive

Min animal studies

↓ mycotoxin effect on Hgb

No control group/all got Sacch B

What I see ~

Aggravations

Yeast “control” but incr body burden

Is yeast protective from biofilm?

Take-away ~

Use it to rebal prn after solidly on antifungals

Use it to prevent C. Diff w ABs

PMID: 15613821, 30721525

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Probiotics

Not “a given” w mold illness

Gentrification

Correlation w SIBO

Empirically ~ start w greens
sm dose of probiotics in
presence of chlorophyll

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Probiotics

L. plantarum C88/MON03 ~
source fermented tofu
adhesion of aflatoxin in lumen
upreg antiox enzymes
↑GST expression via Nrf2 pathway
protects CYP3A4

L. rhamnosus GAF01~
binds aflatoxin in solution
counteracts RBC, WBC, lymph immunotox effects

PMID: 28129335, 24738739, 23030351

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Probiotics

L. casei strain Shirota~
strain is impt!
some strains control vs cause histamine
source fermented dairy
hepatoprotective
chlorophyllin ↑ efficacy

Props Dr. Lauren Tessier ISEAI

PMID: 21816119

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Medication Cautions

Antibiotics ~

Some are literal mycotoxins

Penicillium~penicillin, amoxicillin

"allergic to penicillin"

Acremonium~cephalosporins

Actinomycetes/actinobacteria~ tetracyclines, macrolides, aminoglycosides, rifamycins

Antivirals ~

Actinobacteria~Ivermectin

Antifungals ~

↑aggressive when threatened

Incr mycotoxin formation

Die-off

DO NOT d/c suppressive meds!

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Fundamentals

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Circadian Rhythm

- Wake within the same hour every day
- Go to sleep within the same hour every day
- Adjust sleep/wake time by seasonal variation in light
- Eat meals at nearly the same times every day. Aim to eat most of your food earlier in the day versus later.
- Exercise within the same hour every day—the earlier in the day the better
- Go to bed with a little room left in your tummy
- Allow time every morning for regular bowel evacuation. 10 min minimum. Schedule it.

BACK TO NATURE, back to health.

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Health Hokey Pokey

Air in 😗

Air out 🌳

Air moved all about 🚶‍♀️

Water in 💦

Water out 🚽

Water moved all about 💃

Food in 🥦

Food out 💩

Food moved all about 🌀

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Emunctories

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Emunctories

Methods used to excrete waste

Breath ~ caution contamination of self, others, and “stuff”

Bowels ~ minimum 2 BMs/d

Urine ~ caution ADH resistance

Sweat ~ exercise, FIR Sauna

Menses ~ clots

Ejaculate ~ “allergic” to semen

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Emunctories

From outside in/large to small

system→organ/gland→blood→
ECM→cell→gene

If can't exercise:
Lymphatic massage
Peat mud/peloid therapy (my fav!)

To aid detox:
Frequency-specific microcurrent
COPs over the liver/gut
Acupuncture

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Review

Avoidance

Air Filtration

Food ~ Do's & Dont's

Beverage ~ Do's & Dont's

Med/Supp Cautions

Fundamentals

Health Hokey Pokey

Emunctories

Thank You

Dr. Jill Crista
Naturopathic Doctor
support@drcrista.com

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Are You Missing Mold Illness?

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Mycotoxins ~ Protect & Repair

Are You Missing Mold Illness In Your Patients?

Dr. Jill Crista

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Mycotoxin Protect & Repair

Binders

Homeopathy

Physical Medicine

Nutrients

Botanical Champs

Mycophenolic Acid

Endotoxins

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Only Mycotoxins?

What about spores?

Almost everything you do to
Protect & Repair from mycotoxins
treats spore-induced damage…

…BUT don't forget to Fight mold…

…otherwise eventually, the
damage will be irreversible

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Peel The Orange

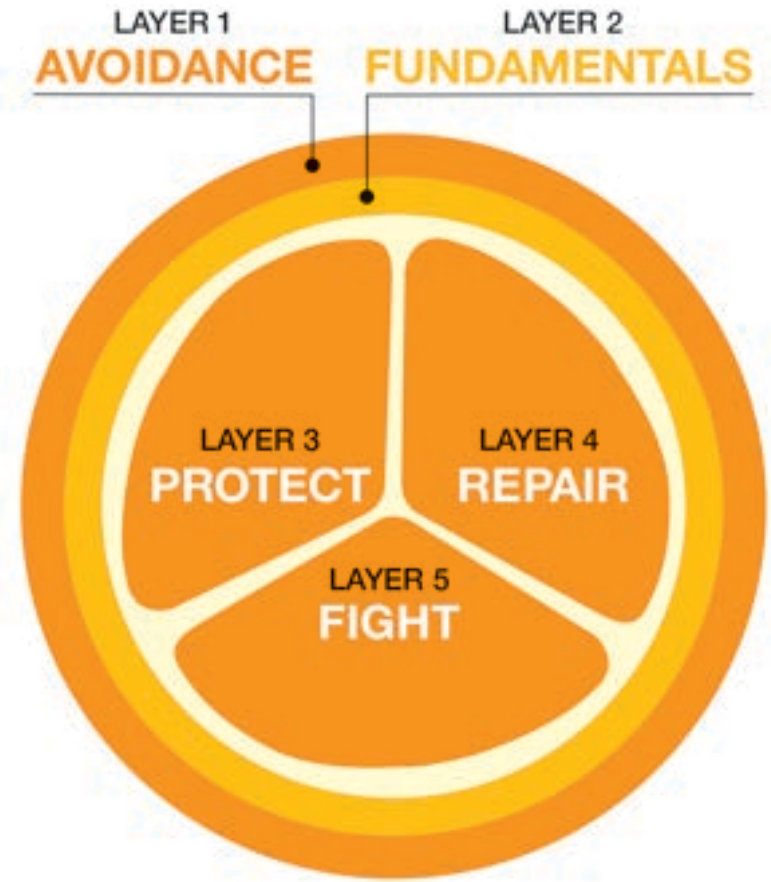
1 AVOIDANCE

2 FUNDAMENTALS

3 PROTECT

4 REPAIR

5 FIGHT



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Essence of Protect

Prevention avoidance

Mucosal linings (resp/GI/GU)

Prevent intestinal absorption/bile recirc

Organs of detoxification

Lipophilic tissues (brain/nerve/eye)

Gut/brain barriers

Membranes cell/mito

Immune suppression

Genetic recoding

Pre-emptive dosing

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Essence of Repair

Immune modulation (NK, T-cells)

Inflammation (Nrf-2)

Neuroinflammation

Gut repair (epithelium, myenteric plexus)

Restore detox pathways (glutathione)

Mitochondrial repair
(core 'economic' recession reducing energy output/power to heal)

Epigenetic expression, gene repair

Limbic retraining (fear, biochem sickness behavior pattern reversal)

Effects from meds (psych/LT steroids)

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Mycotoxin Review

Immunotoxic, neurotoxic, alimentary, dermatoxic, nephrotoxic, hepatotoxic, hepatocarcinogenic, genotoxic, teratogenic, carcinogenic

Reduced ciliary clearance due to small size

Highly inflammatory to lung tissue

Modified by multiple enzymes ~
Cyt P450s, glutathione S-transferases, UDP-glucuronosyltransferases, sulfur-transferases

Deplete glutathione

Nrf2 (“oxidant thermostat”) activation/depletion

Cause mitochondrial damage

Inhibit host defense

Induce apoptosis of intestinal epithelial cells

Induce bladder wall irritation/ulceration

Some cross BBB and reduce its integrity

Olfactory nerve to hippocampus, frontal lobe

x-placenta, bioactivate in utero, found in breast milk

PMID: 26474839, 27178040, 25449202, 12221236, 26600019

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Treatment Ideas

Not an exclusive list

And based on my selection bias

Encourage you to:

Understand mechanisms

Know your patient

Use your reasoning skills to match the remedy to your patient

Teach me & others as you learn

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Binders

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A Treatise on Bile

A detergent, cleanses fat

1° fxn ~ emulsify fats

2° fxn ~ eliminate toxins

3° fxn ~ non-liver

GI: ↑sIgA, probiotic adherence, lipase, enterocytes

Anti-apoptotic for neurodegen dz's

Reduce prion conversion & neuronal loss

Protects retinal cells

↓ER stress assoc w↑glucose in DM

ongoing studies re: anti-apoptosis ~ obesity, stroke, acute MI, spinal cord injury

PMID: 24891994, 25972546

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A Treatise on Bile

Stimulated by secretin, which is stim'd by acidic chyme (hypochlorhydria)

Produce ~1L/d, 95% water (dehydration)

~93% is recycled via hepatic portal vein (alcoholism/cirrhosis)

10:1 PC:cholesterol (methylation snps)

Bile salts ~ bile acids conjugated by glycine & taurine

Courier of detoxed/pkg'd mycotoxins in micelles

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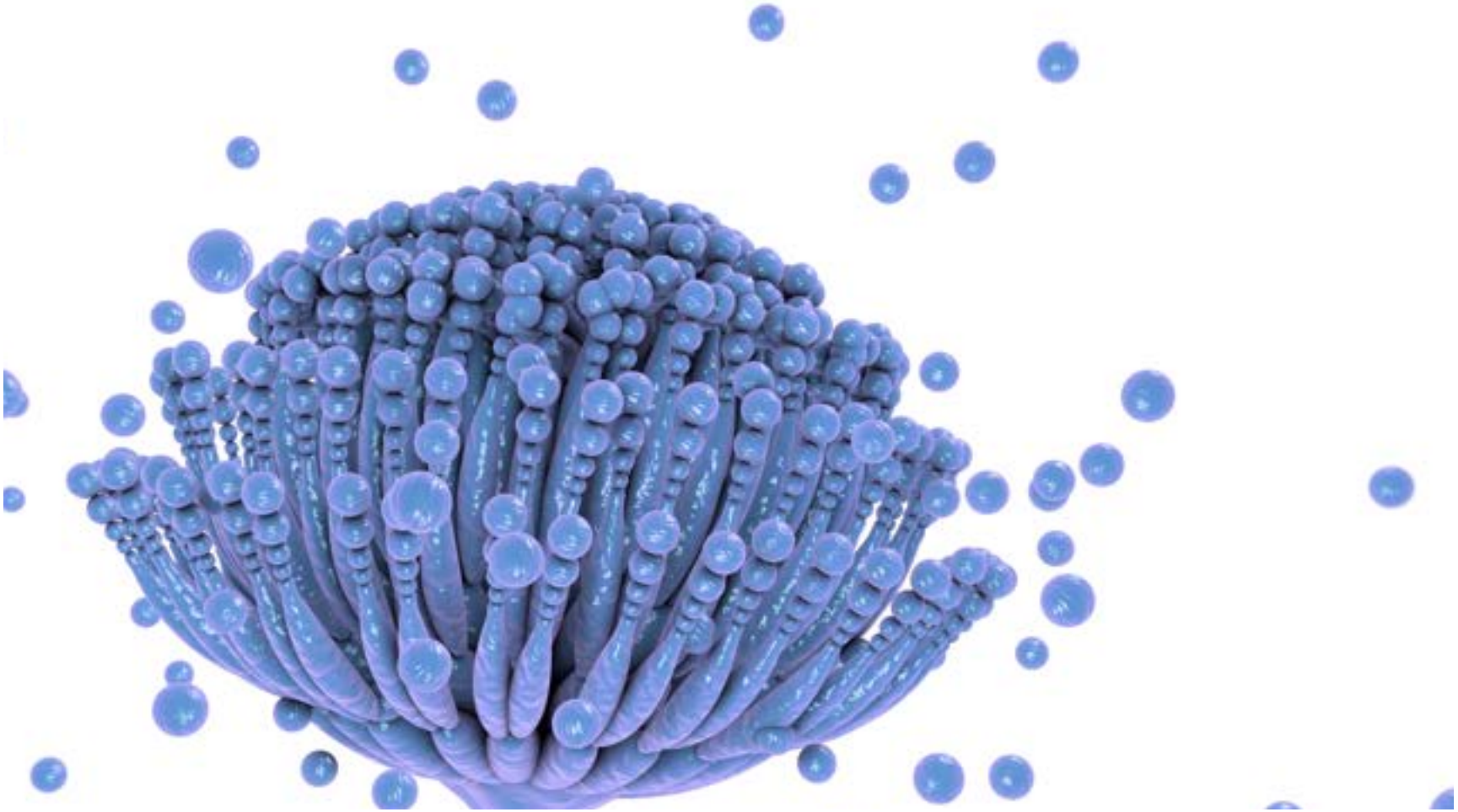
Understanding Bile Emulsification

Amphipathic ~ hydrophobic/philic poles

Bile breaks up lipids to↑exp to colonic lipase



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Bile & Binders

Lipase shown to degrade mycotoxins* (pancreatic insufficiency)

Micelles transport contents to intestinal epithelium, unbind and resorb

Occurs at terminal ileum (motility/SIBO)

Excretes sIgA & stim innate I/S in lumen

Sequestered by “binders” to interrupt bile recirc

Liver & bile duct forced to make new, clean bile IF nec components avail

A**d**sorption = !! Weak bond !!

PMID: 29686653

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Thoughts on Binders

What are we binding? Bile or toxin or both?
- Bile-laden toxin - insoluble fiber
- Mycotoxin contamination of food-toxin dependent

Based on my selection bias ~
- Over-emphasis on binders in tx
- Biases vs data, dt lack of human studies (incl myself!)
- Mycotoxins are morphologically diff
- Most studies in vitro
- Done to find feed additives, not bioremediation of human bodies
- Big Ag trying to convince us to use ag by-products (biomass) as binders

Real solutions ~
- Better building practices
- Better farming/storage practices

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Binder Cautions

LT use → nutrient depletion
- PC (membranes, <“snp rich”)
- Cholesterol (hormones, HDL:VLDL)
- Fat-soluble nut’s (CoQ, A, E, D, K)
- Glycine (component of GSH, NTs)
- Taurine (retina, CNS, osmoreg)

Constipation ~ intestinal epithelial damage when bond breaks

Necessary component of tx?
- Or should focus be dilution?
- Or both?

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Pre-Binders

Cholaretics ~

Stimulate production of bile in hepatocytes

Regulate metabolism of hepatocytes

Cholagogues ~

Stimulate bile secretion & flow

↑sIgA

↑probiotic mucosal adherence

Trigger pancreatic lipase secretion

Protect against intestinal barrier bkdown by promoting enterocyte migration via bile acids

*AND both induce peristalsis

Lipase ~ can supplement

PMID: 29672156

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"Cholagogues"

Botanicals ~
Matricaria, Taraxacum, Inula, Solidago, Curcuma, Chelidonium, Gentiana, Ceanothus, Bitter orange peel e.o.
(usu mix w carminatives, demulcents)

Forms ~
liquid > pill (open 1 cap in bottle)
tincture, glycerite, liposomal

Bitters ~
5 drops on tongue 10-15 min *ac*

Nutrients ~
Choline, taurine, glycine

Bile salts ~
Cholecystectomy, cholelithiasis
200mg Ox bile extract with meals
Caution: bile duct blockage

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Rx Cholagogue Options

Ursodeoxycholic acid (Actigall, Ursodiol) ~

↓absorption of chol
Rx'd to dissolve chol-based gallstones
First line alternative to surgery
Dose: 300mg bid-tid cc
S/E: GI upset
Cautions: bile duct blockage

Tauroursodeoxycholic acid (TUDCA generic) ~
Taurine conjugate of ursodeoxycholic acid
Internationally avail

Deoxycholic Acid (Kybella) ~
"For improvement in appearance of mod-severe fullness [from] submental fat."
Injectable to submentum, double chin
Thought question: clearing fat or toxin?

Taurochenodeoxycholic acid, glycochenodeoxycholic acid ~
Bile salts currently only avail for research

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Coffee Enema

Concept ~
- Induces bile release
- Unique action on lacteals

Overview ~
- First trial with water enema
- Tepid temp retention enema
- Left-side lying <15 min
- (Gerson says right-side)
- Strengths vary ~ 1-3 Tbsp/quart distilled

Cautions ~
- Sensitive to caffeine
- Colon/iliocecal valve laxity
- Used as detox, not for daily use
- Use only organic coffee
- Some debate over bag material

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Botanical Binders

Advice for cholecystectomy pts ~
- Steamed > raw veg bind more easily to bile acids

Kale study (*in vitro) ~
- Verified mycotoxin binder
- Steamed > raw
- Binding effect > lettuce, so not nec any greens will do

Okra ~
- Adsorption of chol (micelles?)
- Flavonoid donor - the bigger contributor to efficacy?
- Both effects stronger after superfine grinding

Aloe ~ discussed later

PMID: 30187492, 19083431, 26359588

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Fiber Binders

Insoluble fiber ~ proven toxin removers

Rice bran fiber ~ high in insoluble fiber
(Clean, Green & Lean; Dr. Walter Crinnion)
2-5gm/d

Empirically ~
- Best success with blends
- Least→most constip ~
- Flax
- Chia
- Rice
- Oat
- Psyllium

Dose ~
- Start low & go slow
- 1/8 tsp qd with largest meal
- Titrate up to 2-5gm/day

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Binders

Activated charcoal ~
- Trichothecenes *ad*sorption
- In vivo/pigs “superactivated” effective - all exposure routes (1985, Buck)
- In vivo/pigs - no transfer to plasma detection when fed DON bolus
- In vivo/chks - minimal benefit 21-day feed exp
- Dose: 500-1000mg bid-tid

Bentonite clay ~
- Effective binder - aflatoxin enterosorbent
- Human study - LT use didn’t deplete A,E, most mins
- Poss heavy metal contamination, incr strontium

Zeolite ~
- Aflatoxin - simulated GI in vitro

Chlorella ~ mixed results

On the horizon ~
- Carbon-based nanomaterials (Graphene)
- Polymeric nanoparticles

PMID: 2590872, 25337799, 18569006, 9276881, 30469366, 30223519

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Taurine - A Binder?

Cytoprotective amino acid

"Master osmolyte in the body" (IIVNTP)

Plays an important role as a basic factor for maintaining cellular integrity homeostasis

Nephroprotective, neuroprotective, retinal component

Decreases OTA-induced cytotoxicity + attenuates apoptosis in kidney

Blocks ROS-dependent autophagy via inhibiting AMPK/mTOR signaling pathway

Acts as a "pre-binder"
If on a high fat diet (the dilute pollutants solution diet), taurine inhibits bile acid absorption in the colon.

PMID: 32371067, 30332612, 19239159

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Rx Binders ~ Colesevelam

Rarely need to use IF…
Avoidance & Pre-Binders

Welchol ~ generic avail

Uses: hyperlipidemia, DM2

Dose: 625mg tab, 2-3 po q12 hrs
With meals + plenty of liquid
Oral suspension avail for peds, but contains phenylalanine, caution PKU
Chewable bar: 3.75 g (1 bar) po qd (PKU)

S/E: constip, dyspepsia, h/a, nasopharyngitis

Interactions:
"Monitor closely" drugs for DM, warfarin, seizure
Impacts absorption of co-admin therapies - diuretics, CVD, Abx

Admin 4 hrs prior to colesevelam:
Rxs w known intrxns/narrow therapeutic index
Fat-soluble vitamins
Oral HRT & contraception

Pregnancy category: "no adequate and well-controlled studies of colesevelam HCl use in pregnant women"

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Rx Binders ~ Cholestyramine

Questran ~ generic avail

*Compounded, excipient-free

4 gms of anhydrous cholestyramine resin in:
- 9 gms of Questran powder
- 5 gms Questran Light powder (PKU)

Dosing based on resin not pwder

Dose: 4-8 gm po q12 hrs
Start at 2 gm qd and titrate
Not over 24 gms over 24 hours
CIRS 4 gm qid

Admin 4 hrs prior to colesevelam:
Rxs w known intrxns/narrow therapeutic index
Fat-soluble vitamins
Oral HRT & contraception

Uses, S/Es, Interactions, Cautions, Pregnancy risk ~ all the same as Colesevelam, plus:
(+) also binds endotoxins
(-) slight increased risk intestinal tumors, alimentary system cancers

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Homeopathy

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Nosodes & Isopathics

Isopathy ~ “myco” formulas
- Homeopathic prep of various mycotoxins
- Esp useful for hypersensitive pts
- Start - 1 drop in water daily

Isopathy ~ “mold” formulas
- Homeopathic prep of mold itself
- Caution early in tx & if/when still exposed

Nosode ~
- Homeopathic prep of affected tissue
- Consider for deep lung remodeling/ asthma, bladder, brain, nerve plexus

Homeopathic vasopressin ~
- Tinnitus
- PoTS
- CHF w pulmonary HTN

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Common Rubrics

Anxiety ~
Mind, Anxiety/Restlessness, Dyspnea, in
Mind Forgetful/Confusion
Sleep, Sleeplessness, Liver complaints, during

Allergy/Sinusitis/Asthma ~
Nose, Catarrh/Coryza, Extending to frontal sinuses
Nose, fullness, Sensation, from inflammation
Eye pain, Extending to frontal sinuses
Respiration, Difficult/Impeded
Respiration, Wheezing

Skin ~
Skin, Eruptions, Eczema
Skin, Itching

Liver ~
Abdomen, Liver, Affections of
Abdomen, Inflammation/Enlarged, Liver

Bladder ~
Bladder, Pain, Burning/Stitching, Urination, before, during, after

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Physical Medicine

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Physical Medicine

Topical castor oil

Lymphatic massage

Peloid therapy

Frequency-Specific Microcurrent

Sauna

Cold laser*

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Topical Castor Oil

Application ~
 Packs, rubs - *organic source
 Timing varies 5-45 min

MOA ~
 Lymphagogue
 Liver - lacteals
 Upper cervicals -glymphatics

Cautions/Reactions ~
 Abd cramping, nausea, diarrhea
 h/a

PMID: 21168117

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Lymphatic Massage

Patient education ~
- Different than deep tissue
- Pressure of a nickel
- Ok to stop to use bathroom

Cautions ~
- Cardiac insufficiency
- All kidney diseases
- Start with one limb and observe

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Peloid Therapy

Moor mud ~
- “dirty water bath”
- Kept liquid to retain enz activity
- Source is critical for purity

Concept ~
- Nourishing detoxification
- Exchange of enzymes/probiotics

How to ~
- Fill bath comfortably warm, temp will rise
- Fully mush & mix mud into bath
- Submerge up to 20 mins
- Cool rinse <1min
- Lie down loosely wrapped, no drafts

Safe for septic ~
- Not clay
- Rinse down the drain, sponge wipe

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Peloid Therapy

Patient prep ~
- Well hydrated
- Empty stomach
- If light-headed, ice on chest, get out

Plan ahead ~
- Ice pack near bath for first
- Assistance getting out of bath
- Lie down for 1 hour after
- Copious sweating*
- Hydrate - tepid electrolytes by bed

Cautions ~
- Open skin wound
- Cardiac - hypotension, CHF
- All kidney diseases, urolithiasis
- Not while pregnant

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Frequency-Specific Microcurrent

Concept ~
- Each tissue has unique, innate “beat”
- Morbid influences derange tissue’s beat
- Restore innate beat via specific balancing/ countering frequencies
- Tissue-specific balancing
- Morbid influence-specific countering
- Tissue gets back on beat

The art ~
- Picking the right frequencies

Cautions ~
- Metal implants
- Pace-maker
- Any active cancer
- Pregnancy

*Different than TENS

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Frequency-Specific Microcurrent

Set-up ~
FSM machine - no contact with metal, wood/plastic ok

Patient Prep ~
No contact with metal
No electronic devices
Remove watches, metal jewelry
Well hydrated

Observe ~
Needed freq - sleepy, softening

Tissue resistance ~
Towels not wet enough
Not the right freq
Right freq but need cofactors

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Frequency-Specific Microcurrent

*WAIT to use mold frequencies
(23,95)
It's too much in the early phases

Target Conditions ~ "A" frequencies
9 Allergy reactions
18 Hemorrhage, leaking
40, 284 Inflammation
87 Active toxins
57, 920, 900* Toxicity
115 Skin eruptions
49 Vitality

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Frequency-Specific Microcurrent

Target tissues ~ “B” frequencies

132 Mucous membrane
25, 75 Sinuses
44 Inner ear
17 Lungs
22 Small Intestine
35 Liver
23 Kidney
37 Bladder
21 Heart muscle
396 Nerves
116 Immune system
985 Deep Limbic system

Combinations ~

880/7.4 Hypoxia
40/00 General inflammation

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Sauna

Sweat content vs radiator effect

Dry heat ~
- Temp: 150-175°F / 75-100°C
- Duration: 30-45 min
- Follow w short, cold rinse <1min

Far Infrared (FIR) ~
- Temp: 125-130°F / 52-55°C
- Duration: 25-30 min
- Wrap up after until sweating stops, then rinse w short, cold <1min

Cautions ~
- Saunas that emit EMFs
- Mold in sauna if steam used
- Dehydration
- HTN, CHF
- All kidney diseases

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Nutrients

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Immune Modulation - Vitamin D3

Role in both innate & adaptive immunity
- T-cell regulator
- Upregulates monocyte genes

Vit D receptor in intestine & kidney significantly
- down-modulated after aflatoxin exp

Promote LU tissue repair in *particle-induced pulmonary injury* ~
- Repress TGFβ1 signaling pathway
- Upreg MMP9 expression
- Activation of Nrf2 transcription factor

Dose ~ to lab levels
- Goal 25-OH Vit D >60 ng/mL
- Emulsified best, esp if cholecystectomy
- Oral (daily-weekly), IM

PMID: 30698894, 25483621, 25912039, 26404359,18569389

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Mold Is A Big FAT Problem

The **solution** to **pollution** is **dilution**!

Mycotoxins are lipophilic

∴ dilute toxins with **C**opious **C**lean **C**orrect fats

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Mycotoxin Nutrients - DHA

ω-3 fatty acid

1° structural component in brain

Neuroprotective

Protects against aflatoxin-induced hepatocellular carcinoma

Attenuates mycotoxin-induced IgA nephropathy

Suppresses MMP-9

Potentiates effects of cerebral VEGF-repair BBB

Dose ~
- Acute/rescue: 6-10gm/d
- Chronic: 2gm/d

Mouse study - 30g/kg safe w no AE
- Translation to humans? Empirically 10gm/d safe LT

PMID: 27513579, 27435775, 15570035, 24794156

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Mycotoxin Nutrients - EFAs

Multiple biochem fxns ~
- Synthesis of inflammatory mediators
- Cell membrane fluidity
- Intracellular signaling
- Gene expression

Modulate aspects of inflam, immunity, cell growth and tissue repair

CNS inflam modulation ~
- Direct impact on neuronal membrane fluidity and receptor fxn

Restore mitochondrial function

Dose: 1gm/d mixed EFAs: EPA (350mg), DHA (300mg), 6's: GLA (100mg), 9's: OA (150mg)

PMID: 27651257, 22248591

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Mycotoxin Nutrients - Phospholipids

Phosphatidyl choline/serine ~
- Lipid raft constituent (cell/mito)
- Membrane stability/integrity
- Major component of pulmonary surfactant
- Bile component

Optimal PC membrane ratio→
- Inhibits cell proliferation
- Induction of apoptosis
- Implications for cancer promotion

Fumosinin ↓PC ratio of hepatocyte lipid rafts

Stachybotrys “spore extract" alters surfactant-related phospholipid synthesis

Dose ~
- Oral liposomal 1-3gms daily
- Lipid Resuscitation (Dr. Rea)
- PTC-IV
- Patricia Kane protocol

PMID: 15574675, 29510220

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Mycotoxin Nutrients - Bioflavonoids

Pigmenting plant compounds with wide ranging biological & pharmacological actions

Cytoprotective via Nrf2, ↓TGF-β1

Protective against Aflatoxin-induced cell injury

Counteract Ochratoxin-induced toxic ox stress on renal cells

Preserve GSH, SOD after Ochra exp

Daily Dose ~
Eat 5-7 servings of colorful vegs
NO SUPP TOPS REAL FOOD

PMID: 27279697, 26798045, 17195249, 26571153

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Mycotoxin Nutrients - Quercetin

Polyphenolic compound

Potent antiox, anti-inflam, antigenotoxic

Pretreatment before mycotoxin exp cytoprotective

Modulates Ochratoxin-induced ox stress via Nrf2 expression, NF-kB and COX-2

Protects peripheral blood PMNs from OTA-induced ox stress, genotoxicity & inflam

Reduces Alternaria mycotoxin damage to human adenocarcinoma cells

Protects cells from Zearalenone-induced (Fusarium) apoptosis

Dose: 300-600mg bid-tid, consider liposomal

PMID: 24161694, 25532488, 26802676, 26134454

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Mycotoxin Nutrients - Lycopene

"Vitamin Red" - carotenoid

Protection against Aflatoxin-induced nephrotoxicity and cardiotoxicity

↓Aflatoxin-induced kidney lesions via attenuation of ox stress, GSH

Restores trace element levels in ochratoxin-exposed rats

Pretreatment preserves Nrf2+ downstream target gene translation/protein expression

Dose ~
5mg/kg/day x 15d in rat myco study.
Humans?
Dose-response study 30mg/d x 8 weeks
- Signif ↓ DNA damage ($p = 0.007$)
- Signif ↓ urinary 8-OHdG (ox stress biomarker)

PMID: 30059796, 28665799, 30462120, 18689558

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Mycotoxin Nutrients - Melatonin

Nephroprotective, hepatoprotective

Hepatoprotective against aflatoxin ~
- Enhance hepatic antiox/detox system
- ↓apoptotic rate & necrobiotic changes

Protective effect against ochratoxin ~
- Inhibits oxidative damage
- Stimulates GST activities

Rat study - liver protection augmented by addition of CoQ10

Dose ~
- Rat myco study 5-10mg/kg/d. Humans?
- Caution: excess may create central regulatory hormone issues
- Dose per oncology SOPs - 20mg qd hs

PMID: 11781538, 11701387, 17365150

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Mycotoxin Nutrients - CoQ10

"Heart antioxidant", mitochondrial fxn

Ochratoxin ~
- Hepatoprotective
- Significantly ↓ severity of kidney lesions

Trichothecenes ~
- Cytoprotective, hepatoprotective
- Antiox effect via GSH preservation
- Decr DNA damage in combo w tocopherols

Pretreatment in combo > CoQ alone ~
- [CoQ10 + L-carnitine + α-tocopherol + Se]
- Decr DNA damage
- Decr activation of liver enzymes
- Slight ↑GSH compared to myco-exp control

Dose ~
- 100mg prn up to 600mg qd
- Dissolve "chewables" in buccal mucosa

PMID: 21793342, 17365150, 9266532, 10660942

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Mycotoxin Nutrients - Vitamin E

Tocopherols/tocotrienols

Hepatoprotective, nephroprotective

Cyotoprotective against Trichothecenes

Attenuates Aflatoxin-induced toxicity & ox stress

Preservation of renal cell viability & tight junctions

Preservation of G6PD *IVC implications

Protective effect on hepatocytes not seen with alpha-tocopherol alone

Dose ~
Mixed tocopherols/tocotrienols
400mg qd-bid

PMID: 29068590, 28251704, 9266532, 16008110

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Mycotoxin Nutrients - Alpha-Lipoic Acid

Hepatoprotective, anti-inflammatory, genoprotective

Engages molecular mechanisms against liver oxidative damage & inflam responses after aflatoxin exp

Inhibits NF-κB expression after aflatoxin exp

Alleviates Aflatoxin-induced ox stress & immune changes

Modulates inflam response partly through changes in the expression of proinflam cytokines such as IL6 and TNFα

Dose ~
- Oral 300mg bid, R+ allele
- Take with food reduces reflux SE
- Also consider IV administration

PMID: 26694462, 24699046, 20390578

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Mycotoxin Nutrients - Selenium

Protective effects on aflatoxin-induced mitochondrial permeability and DNA damage

Protects against T-2 toxin-induced cytotoxicity and oxidative stress

Exhibited protective effects on aflatoxin-induced kidney toxicity

Critical component of glutathione-peroxidase enzyme

Supp as Selenomethionine
Activated w yeast, test myco-free

Dose: 200mcg bid

PMID: 25431300, 26371027, 30261313

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One Antioxidant To Rule Them All

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Glutathione

Pros ~
- Straight to the end game
- Brain fog
- Lung function
- Kidney sparing

Cons ~
- Too intense for many
- Cofactor/coenzyme depletion

Dosing ~
- Form matters & is very individual
- Start low & titrate
- Dose to lab values
- Schedule - debate daily vs pulsed

PMID: 1676780, 10852775

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Glutathione

Oral ~
- Liposomal only*
- Dose 210-420mg qd-bid
- Caution - tastes like rotten eggs

Nebulized ~
- Compounding pharmacy
- Idiopathic Pulm Fibrosis study
- 600mg bid x 3d
- Best responses 600mg qd or greater

Freq - begin 1-2x/week for 4-6 weeks, working towards a maintenance treatment plan of 1-2x/mo

Caution - active asthmatic, can increase bronchoconstriction

PMID: 1676780, 10852775

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Glutathione

Rectal suppositories ~
- Bypass first-pass effect
- Target brain, lung (asthmatic)
- Prev radiated renal CA
- “Skin lightening”

Pharmacokinetics ~
- Hydrolysis in the ECM
- 2 metabolites: γ-glutamylcysteine, glycine

Dose ~
- 225, 450, 500, 1500mg per suppository
- Up to 2000mg liposomal - skin
- Add NAC, taurine, C
- Start low, hs x 14d, then pulse 2-3x/wk

Cautions ~
- Rectal irritation
- Easily dose too high
- Ship on ice

PMID: 11409324

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Glutathione

Intravenous Push ~
Most direct delivery to liver/kidney
'May deactivate Gliotoxin' per research
Amelioration of resp sxs noted as incidental finding - Parkinson's study

Caution ~
Sulfite sens, nasal swab before IV admin
Don't mix w other nut's in same bag

Lower dose~
5cc of 200mg in 10cc HNS; total 1000mg

Higher dose ~
6.5cc of 300mg in 23.5 HNS; total~2000mg

Up to 3000mg given safely

Push rate ~ 1mL/30 seconds

S/E ~
light-headed, nausea, diarrhea, anxiety

PMID: 1676780, 10852775

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Which To Choose?

Use all for greater effect?

No!

Burdened systems

Start w food, fill in cracks

Treat specific deficiencies/sxs

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Botanical Champs

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Mycotoxin Botanicals - Milk Thistle

Silybum marinarum (silymarin, silybinin)

Strengthens & stabilizes cell membranes

Blocks penetration into hepatocytes

Protects from free rad ox by ↑SOD enzyme activity & intracellular glutathione

Inhibits synth of prostaglandins assoc w lipid peroxidation

Promotes regen of liver via stim of protein synthesis

Significant reduction in liver-related mortality

Amel of Ochratoxin-induced immunotoxic effects

↓genotoxic effect of Aflatoxin w pre- and simultaneous exposure

PMID: 23243923, 22734832, 20032005, 19156713, 19841158, 19303273

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Mycotoxin Botanicals - Milk Thistle

Dose ~
Min therapeutic-700mg, up to 1500mg seed powder/extract, best divided <2.1 gms/day in Hep C study well tolerated w no AE

Cautions ~
Inhibits cytP450*

*A heme-based enzyme!
So already impaired by mold

PMID: 23243923, 22734832, 20032005, 19156713, 19841158, 19303273

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Mycotoxin Botanicals - Green Tea

Camellia sinensis

Polyphenols ~ postharvest inactivation of phenol oxidases via steaming & drying prevents ox of catechins vs fermented tea prods

Antifungal, antibacterial, antiviral, antitoxin

Protective against aflatoxin-induced cell injury

Protects against ochratoxin-induced cytotoxicity in kidney

Cytoprotective to macrophages against DON (Fusarium) in a dose-response manner

Daily Dose ~
4-6 cups green tea
Double steep to extract polyphenols

Cautions ~ cytP450 inhibitor

PMID: 23410590, 23605930, 17195249, 17548142, 27518169

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Mycotoxin Botanicals - Turmeric

Curcuma longa

Antioxidant, hepatoprotective, nephroprotective, epigenetic protection

Amel of aflatoxin-induced effects via ~
- Up-reg of antiox enzyme gene expression
- Activation of the expressed genes
- Increase in the availability of GSH

Provides protection against toxic effects of aflatoxin on liver & kidney

In study on chickens, protective dose was 5mg/kg, translational dose?

Dose: 350mg qd-tid, start low, titrate slowly

Cautions: inhibits cytp450

PMID: 25639897, 26450181

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Mycotoxin Botanicals - Artichoke

Cynara scolymus

Polyphenol-rich antiox, hepatoprotective, nephroprotective, immunoprotective, prevents lipid peroxidation, choleretic

Reduces N/V, flatulence, abd pn

Prevents swelling & granular degen in epithelium (more than skin - eyes, organ coverings/linings, etc)

Genoprotective to endothelium via eNOS (antithrombotic, anti-atherosclerotic)

Protects against mycotoxin-induced oncogenic effects in liver & kidney (angiogenesis & mononuclear cell proliferation)

Prevents ochratoxin-induced degen changes & depletion of lymphoid cells in lymphoid organs (thymus, spleen)

PMID: 9194411, 15123766, 15609872, 12738088

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Mycotoxin Botanicals - Artichoke

Cynara scolymus

Dose ~

500-750 leaf extract bid-tid (extract highest in phenolics)

Cautions ~

Mixed activity on cytp450 (in vitro slight inhib CYP3A4, GGT, GPX2, GSR and GST, mild stim CYP1A2)

SOURCE: LOHR, Gesine; DETERS, Alexandra and HENSEL, Andreas. In vitro investigations of Cynara scolymus L. extract on cell physiology of HepG2 liver cells. Braz. J. Pharm. Sci. [online]. 2009, vol.45, n.2 [cited 2019-07-07], pp.201-208. Available from: <http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1984-82502009000200003&lng=en&nrm=iso>. ISSN 2175-9790. http://dx.doi.org/10.1590/S1984-82502009000200003.

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Mycotoxin Botanicals

Would any “liver herb” do?

Maybe!

Limited budget/supply

Consider ~
- Taraxacum
- Arctium
- Rumex
- Raphenus
- Corydalis

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Mycotoxin Botanicals - Resveratrol

Nrf2 restorative, nephroprotective,

neuroprotective, anti-oxidant, reduces TGF-β1

Anti-cancer effect on Ochratoxin affected cells

Dose: Repeated daily doses of 1g/d trans-resveratrol yielded the desired plasma concentration 25microM

150mg extract trans-resveratrol = 60 bottles red wine

CAUTION: Most Resveratrol extracted by fermenting Japanese Knotweed (plant source) **with Aspergillus**

Better to take Japanese Knotweed?

PMID: 26095584, 24089405, 30901941

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Mycotoxin Botanicals - Japanese Knotweed

Polygonum cuspidatum

Tenacious ‘invasive’ hedge row plant

Potent anti-oxidant, antimicrobial,
antiinflammatory, neuroprotective,
multiple CV benefits

Dose ~
CVD clinical trial 5.33mg/kg extract
Alcohol tincture - 1tsp tid

Cautions ~
Resveratrol & Japanese knotweed inhibit
cytp450

PMID: 24956862, 26968677

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Mycotoxin Botanicals - Aloe

Aloe vera barbedensis (*usu)

Anti-inflam to mucosa

Boosts humoral immunity

Adsorptive binding of aflatoxin

Dose ~
Low daily dose most effective vs "chase the burn"

*Note: earthworms (Alma millsoni) matched aloe's efficacy, plus helps anemia, biofilm

PMID: 26648773, 30469366

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Mycotoxin Botanicals - Chromolaena

Chromolaena odorata (synonym Eupatorium odoratum L.)

East-Asia/Africa as nature's wound healer, historical use for gastric ulcers

Antipyretic, analgesic, antimicrobial, hemostatic

Anti-ox & anti-inflam against aflatoxin-induced alterations in pro-inflam cytokines

Mitigated rise in serum IL-1β, correlated with hemorrhages of intestines & liver

Reduced intestinal leukocytic & lymphocytic infiltration induced by aflatoxin exp

Protects against epithelial apoptosis

Suppresses MMP-9

Dose ~
Tea 1/2 cup bid. Tincture 10-15 drops bid.

Caution ~ liver damage in high doses (pyrrolizidine alkaloids), photophobia

PMID: 26798045, 23984087, 23535395, 28112383

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Mycotoxin Botanicals - CBD

Cannabis sativa (agricultural hemp)

Cannabinadiol - non-psychogenic hemp-derived endocannabinoid

Neuroprotective, anti-inflamm, reduces BBB leakage

Use only pharmaceutical grade, organic products
- Mycotoxin contamination found in non-controlled cannabis products.

Form-specific individualization
- Try all forms before aborting this therapy
- Gold > tincture > capsule > butter/food

Initial dose ~
- 1mg/day, titrate to 50mg/day
- Maintenance dose ~
- Common is 10-50mg/day qd-bid, high anxiety/hs

Cautions ~
- Less is more: lower doses more effective in mold
- Too high can cause anxiety/nausea
- Indep mycotoxin testing

PMID: 24854329, 27534533, 27543109

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Mycotoxin Botanicals - Hawthorn

Crataegus spp (oxyacantha*)

Cardiotonic MOA ~
+inotropic/-chronotropic

↑ coronary blood flow and exercise tolerance
Enzyme inhibition (ACE + phosphodiesterase)
Anti-inflamm, improves status of antiox enzymes
Antihyperlipidemic effects

Est cardiac uses ~
CHF Stages I&II-NY HT Assoc classification
Angina pectoris, HTN w myocardial insuff,
mild alt's of cardiac rhythm, atherosclerosis

Hepatoprotective ~
Reduces elev liver enz + ox stress on liver
Improves NAFLD

Attenuates airway inflam by modulation of MMP-9
induced asthma

Dose ~
Active sxs: 1000mg qid
Maintenance: 500mg bid
Solid extract - 1/2-1 tsp bid-qid
Tincture 4:1 - 1 tsp tid-qid

PMID: 27655074, 30058501, 29719880, 23029210

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Mycotoxins - Bee Pollen

Protects against immunotoxicological aspects of Aflatoxin ~
Restores normal neut/lymphocyte ratio

↑neutrophil phagocytic activity

↑lymphocyte proliferative capacity
Induced lymphocytic hyperplasia after Aflatoxin-induced lymphocyte depletion

Helps maintain protein and globulin levels during Aflatoxin exposure

Increases glutathione

CAUTIONS ~
Commonly contains mycotoxins
Ask for independent testing
Sustainability issues

Dose: 500mg qd-bid

PMID: 26930797

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Mycophenolic Acid

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MPA - Mycophenolic Acid

Quickly absorbed & excreted in bile within first few hours of exp so use small freq doses

Intestinal lining damage

Phenolic substances detoxed/excreted in Phase II as glucuronides

Tx focus on glucuronidation

EGCG from green tea ~ 500mg bid green tea (~75%EGCG)

Calcium-D-glucarate ~ 150mg qd-bid

Curcumin, Quercetin, Resveratrol

Don't forget co-factors/substrates (grape seed extract, glutathione)

PMID: 21049395

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Endotoxins

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Endotoxins

Smilax glabra (Sarsaparilla) ~
Anti-inflam polysaccharides

Signif ↓NO, TNF-α, IL-6 via:
-suppression of release from LPS-induced macrophages
-downreg mRNA expression
Effect not observed w isolated extracts
∴ use whole root
Dose: whole root extract-100mg cc
"Tincture forte" 1:2/1:3 - 1/2 tsp cc

Green tea ~
protection against virulent bacterial protein toxins

PMID: 25817687, 25569518, 17195249

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Review

Binders

Homeopathy

Physical Medicine

Nutrients

Botanicals

Mycophenolic Acid

Endotoxins

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Thank You

Dr. Jill Crista
Naturopathic Doctor
support@drcrista.com

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Are You Missing Mold Illness?

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Fight

Are You Missing Mold Illness In Your Patients?

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Fight

Fighting Spirit

Systemic Antifungals

Herb-Rx Combinations

Intranasal Antifungals

Essential Oils & Hydrosols

Ozone

Intranasal Biofilm

Topical Antifungals

Pregnancy & Ped's

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Fighting Spirit

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Energetics of the Moldie

Conquer mold first on the inside

Energetic trend - unsafe/involuting

Fill with light

Guide mold to compost pile

Thank and release it

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Systemic Antifungals

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Peel The Orange

1 AVOIDANCE

2 FUNDAMENTALS

3 PROTECT

4 REPAIR

5 FIGHT

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Systemic + Intranasal Antifungals

Reduces recalcitrance

Reduces drug resistance

Systemic treatment factors ~
- Health status of patient
- Infection vs colonization
- Location

Botanical medicines can offer
- effective but less harmful systemic treatment options

BUT don't be afraid to combine

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Yeast vs Mold

Do antifungal tx's work for mold?

Fungal burden

Many/most ~ yeast biofilm

↑mycotoxin production

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Botanical Antifungals - Holy Basil

Ocimum sanctum/basilicum

Ayurvedic - Tulsi, taken traditionally as tea

Antifungal, antibiotic, antioxidant, antiparasitic

Affinity for lungs & mind*

Signif inhibited cell adhesion/invasion

Shown to detox aflatoxin

Signif inhibited activities of MMP-9

Action against fluconazole resistance

Dose ~
Tea: 4 cups daily
Steep covered to retain e.o.'s
Extract: 550mg leaf extract qd-bid

PMID: 20233602, 27471501, 20161958, 27274752

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Botanical Antifungals - Pau D'Arco

Hydroanthus impetiginous/Tabebuia spp

Central/S. America forest tree known as lapacho

Taheebo tea - traditional tea from inner bark

Antifungal ~ MICs similar to those of amphotericin B

Antimicrobial ~ activity against MRSA

Immunomodulator, antitumor, adaptogen

Expectorant to deeply embedded mucous & contaminants

Not cytotoxic to normal cells at concentrations that were active against fungi and bacteria

Dose ~
Tea: 2-4 cups, simmer 10 min
Capsule: 1gm qd-bid
Tincture: 1 tsp bid-qid

*Avoid during pregnancy

PMID: 9517956, 23778660, 16553949

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Botanical Antifungals - Thyme

Thymus vulgaris

Reliable broad-spectrum antifungal, antibacterial

Down-reg effect on growth, gene expr in Fusarium

Action against fluconazole resistance
(A. fumigatus, Trichophyton rubrum/athlete's foot, Candida spp)
Effective against both the macro and arthroconidia growth (MIC 72 µg/mL) in fluconazole-resistant fungi
>80% reduction in elastase activity

Inhibitory effects on Aflatoxin prod found at lower doses than required for antifungal activity

High safety profile - nontoxic even up to concentration 2x higher than their respective MFCs

Dose ~
Capsule (oil extract) - up to 50mg bid
Tincture - 1/4-1/2 tsp bid-tid
Essential oil - 10 drops in water, per 24 hours

PMID: 25466118, 28062283, 25242937, 31359292

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Botanical Antifungals - Garlic

Allium sativum

Bioactive sulfur-containing compounds (allicin, alliin)

Antifungal - Aspergillus & Penicillum species
Mouse study-Efficacy against Candida slightly less than fluconazole (fungal burden reduction, host survival time at 1mg/kg/d)

Ethanol prep effective against MDR candida (fluconazole, clotrimazole, Amphotericin B, itraconazole, ketoconazole, miconazole, nystatin)

Antimicrobial - Staph aureus, E coli, Pseudomonas, Bacillus

Antiox, anti-inflam, immunomod, CV protective, anticancer, hepatoprotective, nephroprotective, neuroprotective , GI protective, anti-diabetic, anti-obesity

Dose ~
Eat it! Goal 4 cloves daily
Tincture: 1/8-1/4 tsp bid-tid

Cautions ~
Gastritis
Co-admin with antithrombotics (delays aPTT)

PMID: 27259073, 31284512, 30345234, 28584446, 30319862

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Botanical Antifungals - Neem

Azadirachta indica

Antifungal - Aspergillus spp, Candida, Microsporum

Antimicrobial, antiviral, antiparasitic (malaria/Babesia)

Ethanol prep effective against MDR candida (fluconazole, clotrimazole, Amphotericin B, itraconazole, ketoconazole, miconazole, nystatin)

Antiox, anti-inflam, immunomod, hepato/ nephroprotective, neuroprotective, antidiabetic, anticancer, vulnerary

↓ Nf-kB, VEGF, c-Myc(oncogene)

Dose ~
Capsules: 500mg qd-bid, pulsed
Tincture: 1tsp qd-bid
Use whole plant, nimonol extract alone not effective

Cautions ~
“Strong” antifungal
Nontoxic at low doses, poss lymphocyte suppression at high doses (in vitro)

PMID: 28584446, 27034694, 24031718, 26491309

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Botanical Antifungals - Olive Leaf

Olea europaea, O. africana

Oleuropein - biophenol, bitter

Antifungal, antiviral, antibacterial

Antifungal ~
Potency against Aspergillus niger, A. fumigatus (MIC: 12.5-25 mg/ml)
Activity against Candida albicans (MIC of 24 mg/ml, MFC of 48 mg/ml)

Antiox ~
Radical scavenging activity >2x that of Green tea

Anti-inflam, immunomodulatory, anticonvulsant, gastroprotective, cardioprotective, hypocholesterolemic, hypoglycemic

Antiviral - virucidal effect in dose-dep manner (VHSV, rotavirus) so consider for concom EBV

Mild activity against Pseudomonas aeruginosa

Dose ~
Extract/tincture most effective
500mg bid-qid

PMID: 28681004, 28681003, 27383889, 26577343, 25802541, 15869811, 30897691

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Botanical Antifungals - Oil of Oregano

Origanum vulgare

Volatile oil extract

Antifungal - Candida spp, Aspergillus, Penicillium

Antimycotoxic - Aflatoxin

Antibiotic - E.Coli, Staph aureus, Enterococcus

Antioxidant, antiproliferative

Combine safely w fluconazole & cipro ~

↓drug resistance

↓free-rad formation+S/E

Dose ~

150mg of 10:1 extract (equiv to 1500mg oregano)

Cautions ~

Dyspepsia (tx's & causes)

PMID: 27222835, 28176439, 29402621, 29846575, 29987237, 25364204, 25952773

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Botanical Antifungals - Old Man's Beard

Usnea spp

Lichen

Antifungal - Aspergillus, Trichophyton rubrum, Candida spp

Antibacterial - Staph aureus

Antiviral, anticancer, antiox, anti-inflam, antithrombosis

Dose ~
Tea: 2 Tbsp C/S in 2-3 c boiled water daily
Tincture: 1/2-1 tsp qd-tid, pulsed x 3-5 days

Cautions ~
Poss hepatotoxicity if LT use of isolated extracts
2001-liver tox assoc w LipoKinetix supp
Usnea blamed
2008-"At present, a toxicological evaluation of usnic acid is being conducted by the Nat'l Toxicology Program"
Results still pending? Yet patent pending for CA tx

PMID: 30676068, 27186821, 29718734, 23713280, 19034791

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Systemic Antifungals - Triazoles

Fluconazole, Itraconazole, Voriconazole, Posaconazole, Isavuconazole

- Available oral and IV
- Tolerated reasonably well but there are AE
- Documented success with clinical infections (invasive aspergillosis)

Above courtesy of Dr. Joseph Brewer

Pros ~
- Favorable safety profiles

Cons ~
- Spectrum of activity somewhat limited
- Increasing resistance

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Systemic Antifungals

Fluconazole ~ (Diflucan)

- Fungistatic w dose-dep fungicidal activity
- Candida albicans, Cryptococcus neoformans
- Dose: 100-200mg qd
- 200mg Day 1, then 100mg x 14d
- S/E: diarrhea, h/a, QT prolongation
- Cautions: potent inhibitor cytP450

PMID: 29393017, 16278744

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Systemic Antifungals

Itraconazole ~ (Sporanox, Onmel, Tolsura)
- Most effective against Aspergillus & resistant Candida strains
- Blastomycosis, pulmonary + extrapulmonary
- Histoplasmosis, incl chronic cavitary pulmonary dz and disseminated, non-meningeal histoplasmosis
- Expensive!
- Dose: 200mg qd-bid x
- Loading dose common 200mg tid
- S/E: diarrhea, h/a, QT prolongation, hepatotoxicity
- Cautions: CI in pregnancy, inhibits cytP450

PMID: 29393017, 16278744

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Systemic Antifungals

Voriconazole ~

- Structure related to Fluconazole
- Spectrum of activity comparable to Itraconazole
- Invasive aspergillosis
- Refractory Scedosporium apiospermum & Fusarium spp
- Dose: 200mg q12h, ic
- Duration: min 14d + for at least 7d following resolution of sxs
- S/E: N/V, h/a, QT prolongation, hepatotoxicity
- Cautions: inhibits cytP450, many Rx-Rx interactions, CI in pregnancy

PMID: 19029318

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Systemic Antifungals

Nystatin ~
- Fungistatic
- Cutaneous/mucocutaneous Candidal infxns
- Not absorbed systemically

Dose: Oral tablets:
- 500,000-1,000,000 units every 8 hours until infxn clears+48h

S/E: N/V, diarrhea, ab pn

*Use w caution in pregnancy

© Dr Jill Crista

Systemic Antifungals

Ecchinocandins ~
Micafungin, Caspofungin

- IV only
- Generally well tolerated
- Documented success with clinical infections

Above courtesy of Dr. Joseph Brewer

Amphotericin B ~

- IV only
- Fungistatic
- Tx of progressive and potentially life-threatening fungal infxns
- High incidence of toxicity

© Dr Jill Crista

Herb-Rx Antifungal Combos

© Dr Jill Crista

Herb-Rx Antifungal Combos

Herbs to reduce Rx resistance ~

- Holy Basil
- Thyme
- Garlic
- Neem
- Oil of Oregano

Choose at least 1 of these and combine w other botanical antifungals for best efficacy

© Dr Jill Crista

How Long To Tx?

Until ALL of the following:

- Nasal treatment is complete
- Resolution of sx's*
- Negative mycotoxins

Fungi are tenacious!

Fumes can restart the issue

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Herb-Rx Antifungal Combo Example

Step 1:
Thyme tincture ~
Loading dose x 1 week before Rx
1 tsp tincture bid

Step 2:
Add pulsed Fluconazole ~
200mg x 3d/wk

Step 3:
Add pulsed antifungal botanical on
alt days (ie Pau D'Arco)

Step 4:
Finish with botanicals x 1 addtnl mo
Thyme tincture ~ 1 tsp qd
Pau D'Arco ~ 500mg caps qd-bid

© Dr Jill Crista

Intranasal Antifungals

© Dr Jill Crista

Sinus Treatment

6mo's MINIMUM - diff compliance

SIG min qd, up to qid

Treat both nostrils

Prevent swallowing w positioning

Rinse mouth with water after use

Warn epistaxis common, esp when add chelating agent

Temporarily d/c chelator if severe nasal reactions

Test mycotoxins at 3mo's. If no ↓ in mycotoxins, change Rx

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Sinus Treatment

Devices ~

Hand-held atomizing nasal device

Nasal (“vertical”) sprays

Neti pots

Clean device/tip after each use with essential oils to prevent biofilm

Use 15% H2O2 or blend of essential oils:

E.O. Sterilizer Solution - 15 drops each of 3-4 e.o. in 1 oz purified water. Spray after each use. Air dry.

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DIY Sinus Treatments

Essential oils*

Ozone*

NAC*

Xylitol

Probiotics - open cap & snuff

Manuka honey - $^{1}/_{16}$-$^{1}/_{8}$ tsp per 100mL

Propolis

Colloidal silver

Lauricidin/monolaurin - 10% solution

Allicin - 8 drops in 100mL

CYA - mix with sterile water ONLY
(per pharmacist)

PMID: 24999540,

© Dr Jill Crista

Intranasal Antifungal Rx Combos

Amphotericin B (5mg)/3mL sterile water (NOT saline)

Levofloxacin(100mg)+Itraconazole(40mg) +Budesonide(0.6mg)/5ml saline

Ceftriaxone(500mg)+Itraconazole(40mg) +Budesonide(0.6mg)/5ml saline

Nystatin(50,000IU)/10mL saline bid (per Dr. Brewer-reduced AE)

Nystatin(50,000IU)+Tobramycin(100mg)/ 10mL (Klebsiella)

Tobramycin(100mg)+Fluticasone(3mg)/ 10mL saline

NOTE: Off-label use of above med's

© Dr Jill Crista

Intranasal Multi-Targeted

Nasal Spray Application ~
0.1% Amphoterecin B
0.2% Fluconazole
0.2% Mupirocin
0.03% Triamcinolone
#30mL
SIG: 1 nasal instillation each nostril qid
*with permission -
Dr. Paul Anderson of
ConsultDrAnderson.com*

Compounding ~
Sterile water, saline
Loxasperse powder
XyliFos
MucoLox (polymer-oral,rectal,vag)

© Dr Jill Crista

Essential Oils & Hydrosols

© Dr Jill Crista

Essential Oils

Shown to reduce fungal growth, reduce mycotoxin production, and safe to inhale long-term:

- Cedar leaf (Thuja plicata) - broad spectrum antimicrobial
- Rosemary leaf (Rosmarinus officinalis)
- Ajwain seed (Trachyspermum copticum L.) thyme-anise-oregano
- Holy Basil leaf (Ocimum sanctum, O. basilicum)
- Cumin seed (Cuminum cyminum L.)
- Tea tree (Maleleuca alternifolia)
- Thyme leaf (Thymus vulgaris)
- Black cumin (Nigella sativa)
- Clove (Syzygium aromaticum)

Use ONLY inhalation grade

PMID: 22408584,18190993, 27275253, 24624154, 27211664, 17209812, 31006459, 15856529, 26042369, 28811611

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Essential Oils - Rx Resistance

Thyme ~
Inhibitory effects on Aflatoxin prod
found at lower doses than needed
for antifungal activity
Action against fluconazole-resistant
fungi and Candida spp

Ajwain ~
Caraway, can be used
interchangeably with Thyme (recipes)
Action against fluconazole-resistant
fungi

PMID: 28584446

© Dr Jill Crista

Essential Oils - Safety

Safety ~

Oregano, Thyme, Clove, Thuja

Very strong activity against Chaetomium globosum, Penicillium chrysogenum, Cladosporium cladosporoides, Alternaria alternata, and Aspergillus fumigatus, also Pseudomonas

Effective at full strength & reduced conc

Genotoxic effect eval on human embryo lung cells showed none of the oils induced significant DNA damage in vitro after 24 h

*But they do contain aldehydes

PMID: 28811611

© Dr Jill Crista

Essential Oils - How To

Titrate ~

From 1 drop per 1 ounce liquid

To 25 drops per 1 ounce liquid

How-To Video ~

© Dr Jill Crista

Hydrosols

Aka aromatic waters, floral waters, distillates

Water-soluble volatile components

Vital essence of medicinal plants

Formed in the distillation process of e.o.

Safe to use LT, less harsh than e.o.

More than 50 marketed in Iran

Persian hydrosols for hyperlipidemia ~
Thyme, Holy Basil, Artemisia, Garlic,
Barberry, Aloe, Dill

Drink, spritz, nasal spray, bathe

Caution ~ many mixed w sweeteners

PMID: 29228785

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Ozone

© Dr Jill Crista

Intranasal Ozone

In-office ‘cold corona discharge’ ozone generator, fill capped syringe

Carefully insufflate directly into sinus - DO NOT inhale

Hold for 20-30 seconds, then blow out through nose

CAUTION—prevent inhalation into the lungs

Dose: 2cc of 11 gamma per nostril, can incr by 1cc up to 10cc

Frequency: 1-2 times/week

Normal reaction - increased mucous production in 15 min, self-lt

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Intranasal Ozone

Oil-trap - “safer” method

Ozone discharged through oil bubbler, 35 gamma through 15 mL olive oil at 125 cc/min

Nasal cannula - 10 minutes max

89% of the irrigated patients recovered faster than conventionally treated controls. Study of 102 chronic purulent frontal sinusitis pts

Be in a clean space! Co-exposure of airway toxicants with ozone significantly amplifies the damage of those toxicants

PMID: 12501776, 9163213, 555470, 12773774

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Intranasal Biofilm

© Dr Jill Crista

Intranasal Biofilm

EDTA 15mg/2mLs

EDTA + Polysorbate 80 (surfactant)

2mL of solution (2mL vials)
- Polysorbate 80
- Glacial acetic acid
- Benzalkonium chloride
- 0.9% sterile sodium chloride

Xylitol

Mupirocin (S.aureus)

NAC (next slide)

Must use something to break up biofilm for complete resolution

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Intranasal NAC

Compounded NAC (N-Acetyl Cysteine)

200mg qd-bid

Similar to the idea of Mucomyst, mucolytic

Can add 1 drop inhalation-grade mint e.o. to mask sulfur smell

PMID: 25843257, 23307410, 24799199, 26386189

© Dr Jill Crista

Treatment Caution

Be mindful of Herx “die-off” sxs

In vitro Aspergillus exposed to amphotericin B increased Gliotoxin production - a possible explanation

PMID: 15272057

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Topical Antifungals

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Topicals

Mycotoxins ~
- Plantain (Plantago lanceolata)
- Yarrow (Achillea millifolium pannonica*)
- Anti-aflatoxin in vitro

Antifungal ~
- Clove - oil, oral, analgesic
- Pau D'Arco - non-irritant dermal application for fungal/MRSA
- Thyme - oral, intertrigo. Can irritate
- Coconut - shell extract (MIC>3Rx)

Artemesinin cream for rashes of undetermined cause

PMID: 30127827, 23015356, 16553949, 28930122, 22290952

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Pregnancy & Peds

© Dr Jill Crista

Pregnancy & Nursing

AVOIDANCE!!!

Stability and reduction of myco's vs "win the fight"

Focus on protective things, esp in 1st trimester
- DHA
- Bioflavonoids
- Fiber

May use gentle nasal treatments to prevent fungus in the sinuses - esp since sinus congestion so common in pregnancy
- Eucalyptus essential oil is a nice option

For systemics,"fungistatic" vs fungicidal
- Avoids excess spillage of mycotoxins

Daily garlic bid, either as food or tincture if adding it to food is too hit-and-miss or upsets the stomach

Add oregano, thyme, rosemary, and sage to cooking

Tincture of sage + thyme
- Dose at a very low daily dose in the 2nd/3rd trimester

Holy Basil, Pau D'arco, and Oregano Oil are NOT recommended in pregnancy

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Breastfed Infant

Challenge - administration

Via mom & skin

Mom-good fats, bioflavonoids, bitters, fiber

Systemic antifungals, via mom ~
holy basil, rosemary, thyme
(Avoid garlic+oregano oil if gas, pau d'arco not proven safe)

Intranasal antifungal ~
breastmilk

Calendula Bath ~
Flower infusion: emolient vulnerary, soothing antiinflam/ flavonoids, lymphagogue
Leaf tincture: antifungal
Boil 32 oz water, add 1 cup flowers, steep x 10 mins. Strain, cool to tepid. Add to bath.
AND add 1 tsp tincture to 8 oz water, bring to boil to burn off alcohol. Remove from heat, let cool to tepid. Add to bath. Soak baby 10 min's minimum.

Cocunut milk/oil rubs

PMID: 29484986

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Ped's

Challenge - taste, texture

Prep 2-3 different things that work in case of refusal

Good fats, bioflavonoids

Insoluble fiber *if doesn't cause constipation*
If it does, work on liver/bile sluggishness
Curcuma - nice option bc is a bitter, anti-inflammatory, and protective against mycotoxins
Golden Milk, or liposomal mixed w resveratrol
Then try adding fiber (flax seed powder)

Definitely tx intranasal plus systemic antifungals
Propolis good option for ped's (antifungal and neutralizes mycotoxins) *health food stores

For systemic, pau d'arco, holy basil, thyme
Ok daily and LT with peds

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Adolescent

Challenge - compliance, added toxicants, circ rhythm

Clean body care - perfumes, lotions, acne txs,
mouthwashes (tip for parental adulteration)

Stinky foods reduce stinky body. Molybdemum for garlic
intolerance.

Circ rhythm enforce w supps ~
Vit D - early am
Melatonin - at dinner time
*caution dose <3mg dt ability to delay puberty

Detox ~
Consider plants vs specific nutrients
Caution your effect on puberty - monitor carefully, esp if
using glutathione

Intranasal ~
Options for compliance issue w nasal spray:
e.o. diffuser in bedroom running all night

For systemic ~
Ok daily and LT: olive leaf, thyme, spilanthes, pau d'arco
Pulse: neem, oil of oregano, usnea
Discuss with parents about use of alcohol tinctures, CBD

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Review

Fighting Spirit

Systemic Antifungals

Herb-Rx Combinations

Intranasal Antifungals

Essential Oils

Ozone

Intranasal Biofilm

Topical Antifungals

Pregnancy & Ped's

© Dr Jill Crista
Thank You
Dr. Jill Crista
Naturopathic Doctor
support@drcrista.com

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Are You Missing Mold Illness?

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When Things Go Sideways

Are You Missing Mold Illness In Your Patients?

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When Things Go Sideways

Herx

Exposure plan

Travel tips

Reintroduction

Fortification

What If's

Cases

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How Mold Makes Your Job Harder

"Sensitive" patients~minute doses

Counter-intuitive reactions

Drug clearance~detox organs

Immune depletion~chronicity

Inflammatory reactions

Sm vessel vasculitis & coagulation abnormalities~remedy delivery

Cardiac~fatigue

Neuro~"mold brain"

Sleep

∴ Don't/can't stick to tx plan

AND spiritually/energetically depleted

© Dr Jill Crista

Peel The Orange

1 AVOIDANCE

2 FUNDAMENTALS

3 PROTECT

4 REPAIR

5 FIGHT

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Orange Half Peeled?

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Herx

© Dr Jill Crista

The True Herx

Jarisch-Herxheimer reaction

Described over a century ago re: syphilis, *induced by antibiotic tx*

Transient immunological phenomenon seen commonly in pts tx'd for spirochetal infxns

Considered an adverse effect from antibiotic treatment

Rarely fatal: neonates, LBW pregnancy

"Complex interplay of its underlying patho-physiological mechanisms continues to elude modern medicine."

PMID: 23632012, 28077740

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The True Herx

"Experimental evidence indicates it is caused by nonendotoxin pyrogen and spirochetal lipoproteins."

Pro-inflam cytokines: TNF, IL-6, IL-8

Accel phagocytosis of spirochetes by PMN leukocytes *before* rise in cytokines, but *after* antibiotic initiation

Sxs ~

Onset 24-hrs after initiating Abx
Constitutional sxs resolve within hours
Fever, chills, h/a, myalgias, exacerbation of existing cutaneous lesions

PMID: 23632012, 28077740

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Today's "Herx"

Loosely defined & broadly applied

Sx onset anywhere from hrs to days after initiating tx

Self-resolves in 2-5 days

Sxs ~
Fatigue, h/a, cognitive/neuro, myalgias, n/v/d, exacerbation of existing skin sxs, rarely low-grade fever

If longer than 2-3 days ~
Tx too aggressive for pt
Something else is going on

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Mold “Herx"

Induced by antifungals vs antibiotics

Inhibit fungal sterol synth (impt fungal cell membrane component) vs intracellular Abs

↓accel of phagocytosis→slower onset rxn

↑ROS

↑MC (metacaspases) -“executioners”
Apoptosis, cytokine maturation
Neurodegen & autoinflammatory disorders

If mold senses↑threat→↑mycotoxin prod

Mycotoxin vs nonendotoxin pyrogen

∴ think toxicity > microbial “guts"

∴ tx target is detox

PMID: 10515900, 28983298, 18298652, 24415839

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Herx Helpers

1st: Ask if tx needs adjusting
Most common cause is iatrogenic

2nd: Fast

3rd: Take a salt bath

4th: Mega bioflavonoids

5th: Bamboo binding

6th: Consider fats & alkalization

7th: Consider enzymes

Prep the tools and plan ahead

Executive fxn during Herx = ⓪

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Fasting

12-24hrs minimum

Fuel switch to fat-derived ketone bodies & free fatty acids

"Induces adaptive cellular responses~
Reduce ox damage & inflam
Optimize energy metabolism
Bolster cellular protection"

↓inflammasomes in steroid-naïve asthmatics, diminish airway epithelial cell cytokine prod

Start immed at first sign of Herx

During first 2-3 days of antifungal therapy for unstable pts or if need antifungals before you can fully peel the orange

PMID: 24440038, 30021766

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Epsom salts

Prep by the tub, pre-arrange at supportive helper's home w/tub

Bath ~
- 2-4 cups per bath x 20-30 min
- End w cool shower
- Caution: dehydration, abd cramping, bile duct spasm

Poultice ~
- Mix 1 cup per 2 qts warm water
- Apply soaked towel to entire abdomen
- Cover w heat x 30 min
- End w cold scrub

Practice before begin antifungals

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Bioflavonoids

ROS ~
- Less activity in mammals than plants, but still shown to be effective

Protein kinases ~
- Substrates of active caspases
- Bioflavs inhibit

SO pick a color, any color, make it liquid

Lemon juice ~
- REAL lemons, squeezed & bluntly smash peel in container

Tart dark cherry juice

Carrot juice

Wheat grass juice

Onion soup broth

Beiler's broth

PMID: 23580885, 23434657

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Beiler's Broth

RECIPE

BIELER'S BROTH

Ingredients (use only organic ingredients)

4 cups spring water
3 medium zucchini, coarsely chopped
4 stalks celery, coarsely chopped
1 pound string beans, tipped
1 bunch parsley, stems removed

THE END OF DR. BIELER'S INGREDIENTS

Optional additions for mold recovery:

Up to ¼ cup each of nettles, beet greens, or dandelion leaves.
(NOTE: Handle raw nettles with gloves to prevent stinging. Once cooked, they no longer sting.)
1-2 cloves garlic or 1/4 cup chopped onions, or both (optional)
1/4 cup olive oil or butter (optional)

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Beiler's Broth

In a large pot, sauté celery, zucchini, string beans, garlic, and onions in oil or butter for 5-7 minutes.

Add water, nettles, beet greens, and **dandelion greens**, and bring to a boil.

Boil for about 10 minutes or until all vegetables are bright green and tender.

Remove from heat and **add parsley**.

Use an immersion blender or food processor to blend until smooth.

Spice to taste using salt, pepper, or other desired spices.

Quoting Dr. Jillian Stansbury, **"use spices with wild abandon."**

Another version of this recipe can be found in Nourishing Traditions by Sally Fallon.

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Carbonized Bamboo

Well known in Japan

Mild antifungal + antibacterial

Porous nature ~ thirsty absorber (up to 10x moreso than wood treated similarly)

Research from Japan claims it emits ~
FIR rays (thus improving circulation)
Negative ions (shields from EMF's)

Natural source of minerals (macro and trace)
∴alkalizing

Aborts the reaction, quicker return to normal

Shown to be effective at binding aflatoxins* (poss heavy metals)

Contraindications ~
Variegate porphyria

PMID: 25014194

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Fats, Alkalizers & Enzymes

Lipid Rescue ~
- DHA 5-10 grams
- GLA 3 grams

Alkalizers ~
- Alka-Seltzer Gold
- Tonic water

Enzymes ~
- Lipase, protease
- Take away from meals

Try any and all until better

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Herx or New Exposure?

Watch for signature trends

Determine effect on ultimate survival of the being

Hering's Law of Cure ~
Revisit old symptoms

Herx ~
Better deep, worse surface
Better mental, worse physical

New exposure ~
May look similar to Herx, BUT doesn't clear w Herx tx &/or reduction or d/c of tx

© Dr Jill Crista

Doc, What's Happening?

Developed a **terrible rash** & **sinus congestion**, but **anxiety** is a little better.

Is your patient getting better or was there a new exposure?

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Rationale

What is the “deeper" issue, or the one which is more detrimental to wellbeing…

skin rash or **anxiety?**
sinus infection or **anxiety?**

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Anxiety!

May see skin rash or sinus infection at the resolution of deep-seated anxiety

Most likely a “Herx”

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Exposure Plan

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Exposures Will Happen

Cars, restaurants, shopping,
school, church, travel

What to have along ~
- Nasal spray
- Bioflavonoid of choice
- Cholagogue
- Antifungal (if pt strong enough)
- Posse ready to support

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Travel Tips

© Dr Jill Crista

Travel Tips

Rental cars ~

A/C - turn on, off, on, watch for reaction, then don't use if poss

Take time to be in car w closed windows before driving away

Hotel ~

Tell them mold sensitive at check-in

Room inspection - water stains on ceiling, below A/C unit, below sink

Request new filter for your room, BE THERE to avoid deodorizer

Then don't use HVAC if poss

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Reintroduction

© Dr Jill Crista

Reintroduction

Yes, you can get your life back after mold!

Typical timeframe (selection bias) is 2 years to pre-mold norm

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Diet Reintroduction

All foods tolerated before mold s/b tolerated after mold

Add back slowly, q4-7 days

1st: Begin with Tier II foods if removed

2nd: Fermented foods/bevs

3rd: Foods that get moldy from growing/storing techniques

4th: Foods/bevs that promote yeast overgrowth

5th: Foods that are actual fungus

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Fortification

© Dr Jill Crista

Fortification

Myco-Remediation ~
Agarikon, Maitake, Shitake, Reishi, Ganoderma, Hericium, Trametes, Cordyceps (rebirth), etc…

Paul Stamets, Mycologist

Mycelium hyper-accum Se

"Mycelial networks are the foundation of the food web, the interface organisms between life and death, and build soil."
Interview on WPR's To The Best of Our Knowledge

Imagine what they do for our soil

© Dr Jill Crista

Immune Modulation

Many well-researched immune modulating botanicals which also have anti-fungal action ~ Pau D'arco, Garlic, Holy Basil, Cordyceps

Botanical immune modulators ~ Astragalus, Codonopsis, Eleutherococcus, Ligustrum, Panax ginseng, P. quinquefolius, Rhodiola, Schisandra, Withania

PMC3915757, PMC3874089, PMC3909570

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What If's

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What If… Can't Leave the Mold?

Is it even worth treating?

YES!

Protect tissues/cellular invasion ~
- DHA
- Bioflavonoids
- Milk thistle, turmeric, artichoke
- Green tea

Protect genes ~
- [CoQ10 + L-carnitine + α-tocopherol + Se]

Minimize colonization ~
- Nasal spray

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What If… Only MPA + But Symptomatic

Key points, pt is symptomatic + not testing every mycotoxin

Variables to note - duration of WDB exp & sx level/type

Taking glutathione? ~

May create false neg myco's
(does exactly what we want it to do - detox)

Neg test doesn't confirm no myco's bc symptomatic
(note that MPA alone can still make pt sick - usually GI)

If no glutathione ~

1st: still being exposed?
Remediation didn't address "stuff" contamination

2nd: pt too toxic to detox myco's & dump in urine

3rd: processed myco's well, but has genetic snp impairing MPA clearance (Green tea & ECGC)
BUT that's only probable if pt feeling overall much better

Plan ~

Proceed with the full mold tx until improvement in sxs, including systemic + nasal txs

Don't be surprised on subsequent myco testing, start spilling mycotoxins

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What If… Reaction to Antifungals

Question your tx ~
- Too much?
- Too soon?
- Wrong choice?

Prep done aka "peel the orange”?

Still being exposed?

Plan ~
- Impress on pt - no exposure!
- Reduce or pause antifungals
- Support weak system

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What If… Can't Tolerate Binders?

What do you mean by binders?
- Pharmaceutical
- Fiber
- Clay/charcoal
- Food

Why can't tolerate?

Provoking bile?

Plan ~
- Start with steamed kale & bitters
- Add 5-7 servings veg
- Try charcoal
- Try rice brain fiber
- *Binders are not necessary to getting better

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What If… Can't Tolerate Glutathione?

Not uncommon!

Unsupported detox ~
- Not pooping
- Need cofactors/coenzymes

Other ways to boost GSH ~
- NAD, B-vitamins
- Selenium
- ALA
- Milk thistle
- Turmeric

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What If… Not Better Despite Full Avoidance?

Are you sure there's 100% avoidance???

Consider viral load
EBV, HHV-6, Coxsackie

Consider opportunists
Lyme, co-infections

Consider other enviro toxins

Consider food sensitivities

Mitochondrial dysfunction

Genetic snp support

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Cases

© Dr Jill Crista

Aspects of a Comprehensive Plan

Avoidance avoidance avoidance

Diet diet diet

Bioflavonoids

Good fats

Bile movement

Fiber binding

Detox + mito support

Immune support

Antifungals

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CASE | CPAP Dementia

Late 70s F, LT pt

Concerned adult kids ~ mom's safety

Beg signs of dementia, garage door open overnight

Progressing confusion, balance issues, requiring cane

HTN, constipation, C-PAP for RLS insomnia

Sinusy voice normal for her

Large historic home, "bad about dusting"

Stopped using C-PAP "bc forgetful"

© Dr Jill Crista

CASE | CPAP Dementia

Kid intervention - Monitor (aka force) C-PAP use, major dust/declutter & air filter in bedroom, found a little mold in basement - cleaned with bleach

Husband's insomnia improved. Hers worsened, but naps ok in recliner ~ too far from her C-PAP to use

Worsening sxs overall: High anxiety, fears, worry, night wandering, personality change, worsening confusion, forgetful

Having new food reactions, so "forgets"/avoids eating

BP on the rise, takes at home in am

Kids have scheduled another sleep study, long wait time

© Dr Jill Crista

CASE | CPAP Dementia

P/E ~

Vitals - bp 158/90, HR 104, RR 16, temp N

Eczematous rash b/l ear canal, b/l pedal onychomycosis

Arthritis - ankles, fingers/toes

Blepharitis, anosmia, enlarged turbinates, pharyngeal cobblestoning

Delayed capillary refill, dermatographism

LU - harsh bronchial breath sounds

HT - RRR, no adventitious sounds

Abd - delayed BSAQ, bloating

Neuro - all wnl

Labs ~

↑hs-CRP if not taking B-complex, B-12

↑LDL

Vit D 25-OH - 23

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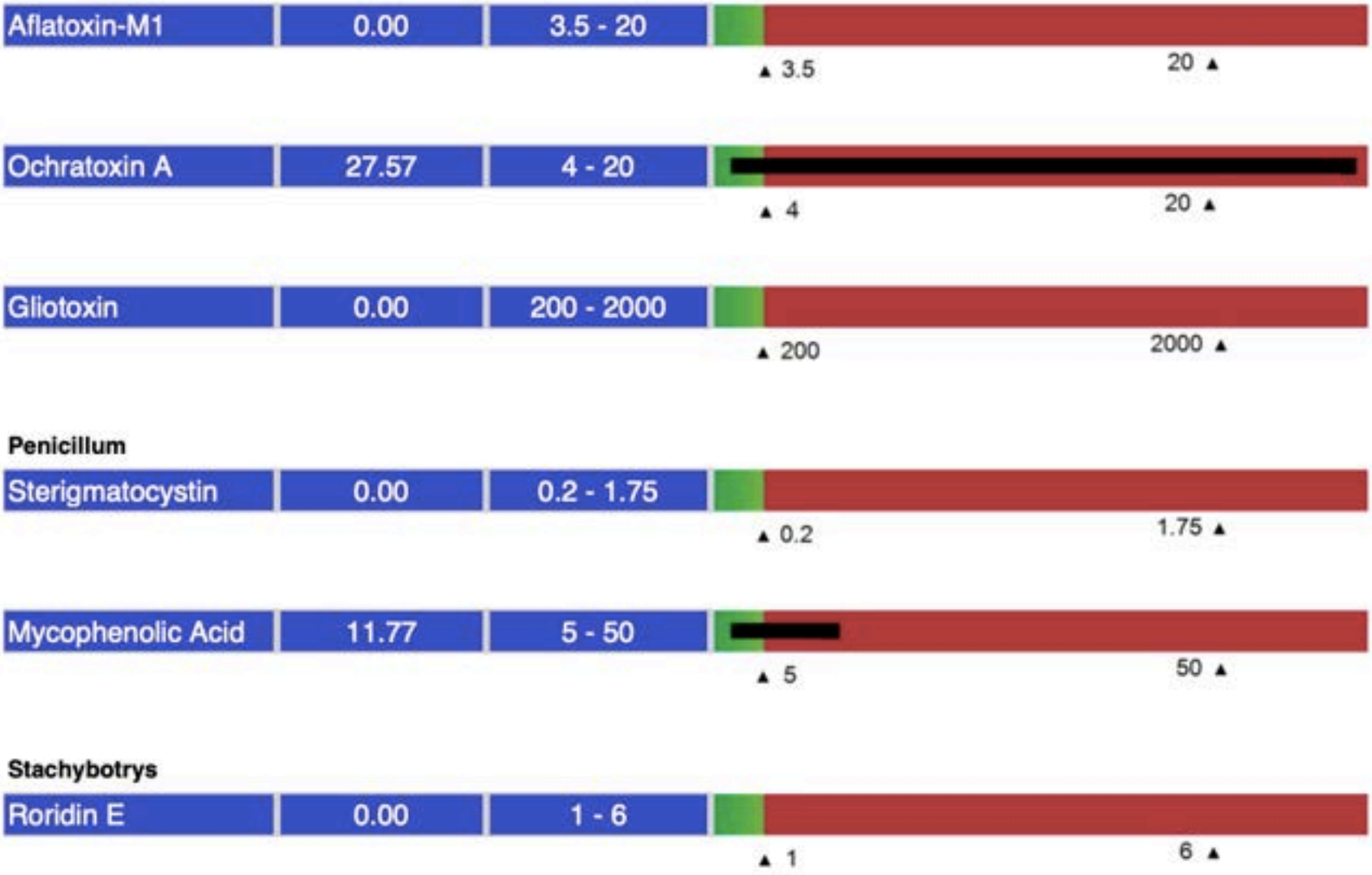
MycoTox Profile

Metabolite	Results (ng/g creatinine)	Common Range of Positive Results
Aspergillus		
Aflatoxin-M1	0.00	3.5 - 20
Ochratoxin A	27.57	4 - 20
Gliotoxin	0.00	200 - 2000
Penicillum		
Sterigmatocystin	0.00	0.2 - 1.75
Mycophenolic Acid	11.77	5 - 50
Stachybotrys		
Roridin E	0.00	1 - 6



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Metabolite	Results (ng/g creatinine)	Common Range of Positive Results
Verrucarin A	0.00	1 - 10

Fusarium

Enniatin B	0.00	0.07 - 1

Zearalenone	23.27	0.5 - 10

Chaetomium globosum

Chaetoglobosin A	0.00	20 - 80

Multiple Mold Species

Citrinin	29.21	10 - 50

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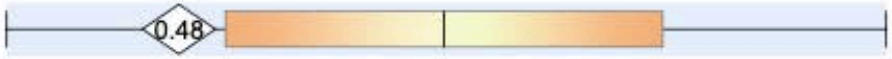
Organic Acids Test - Nutritional and Metabolic Profile

Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)		Patient Value	Reference Population - Males Age 13 and Over
Intestinal Microbial Overgrowth				
Yeast and Fungal Markers				
1 Citramalic	0.11 - 2.0		0.48	
2 5-Hydroxymethyl-2-furoic *(Aspergillus)*	≤ 18	H	22	
3 3-Oxoglutaric	≤ 0.11	H	0.19	
4 Furan-2,5-dicarboxylic *(Aspergillus)*	≤ 13	H	20	
5 Furancarbonylglycine *(Aspergillus)*	≤ 2.3		0.19	
6 Tartaric *(Aspergillus)*	≤ 5.3		1.7	
7 Arabinose	≤ 20	H	35	
8 Carboxycitric	≤ 20		0.29	
9 Tricarballylic *(Fusarium)*	≤ 0.58		0.46	

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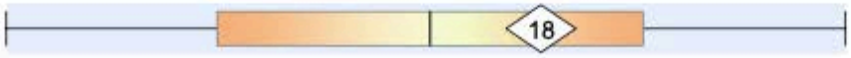
Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)	Patient Value	Reference Population - Males Age 13 and Over
Indicators of Detoxification			
Glutathione			
58 Pyroglutamic *	5.7 - 25	18	
Methylation, Toxic exposure			
59 2-Hydroxybutyric **	≤ 1.2	0.88	
Ammonia Excess			
60 Orotic	≤ 0.46	0.21	
Aspartame, salicylates, or GI bacteria			
61 2-Hydroxyhippuric	≤ 0.86	0.53	

* ***A high value for this marker may indicate a Glutathione deficiency.***

** ***High values may indicate methylation defects and/or toxic exposures.***

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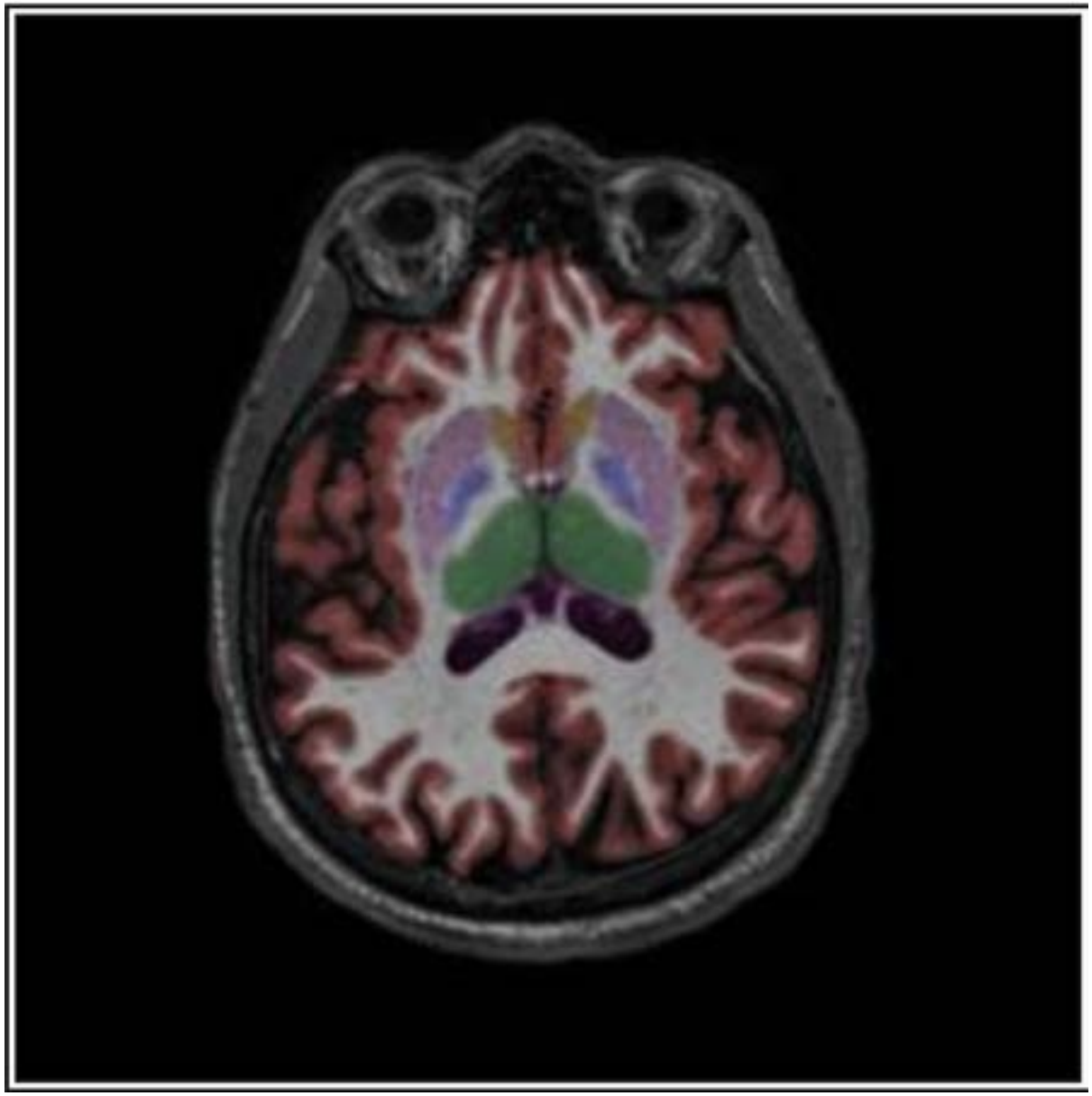
Glyphosate Profile

Metabolite	Result ug/g creatinine	Reference Range
Glyphosate	1.2	LLOQ 0.38 — 75th 1.8 — 95th 2.5

© Dr Jill Crista



NeuroQuant
Triage Brain Atrophy Report (TBAR)

- Compressed 3rd ventricle
  surrounded by inflamed thalamus
- Assymetry
- Thalamus inflam
  Site of mast cells MCAS
  Limbic activation

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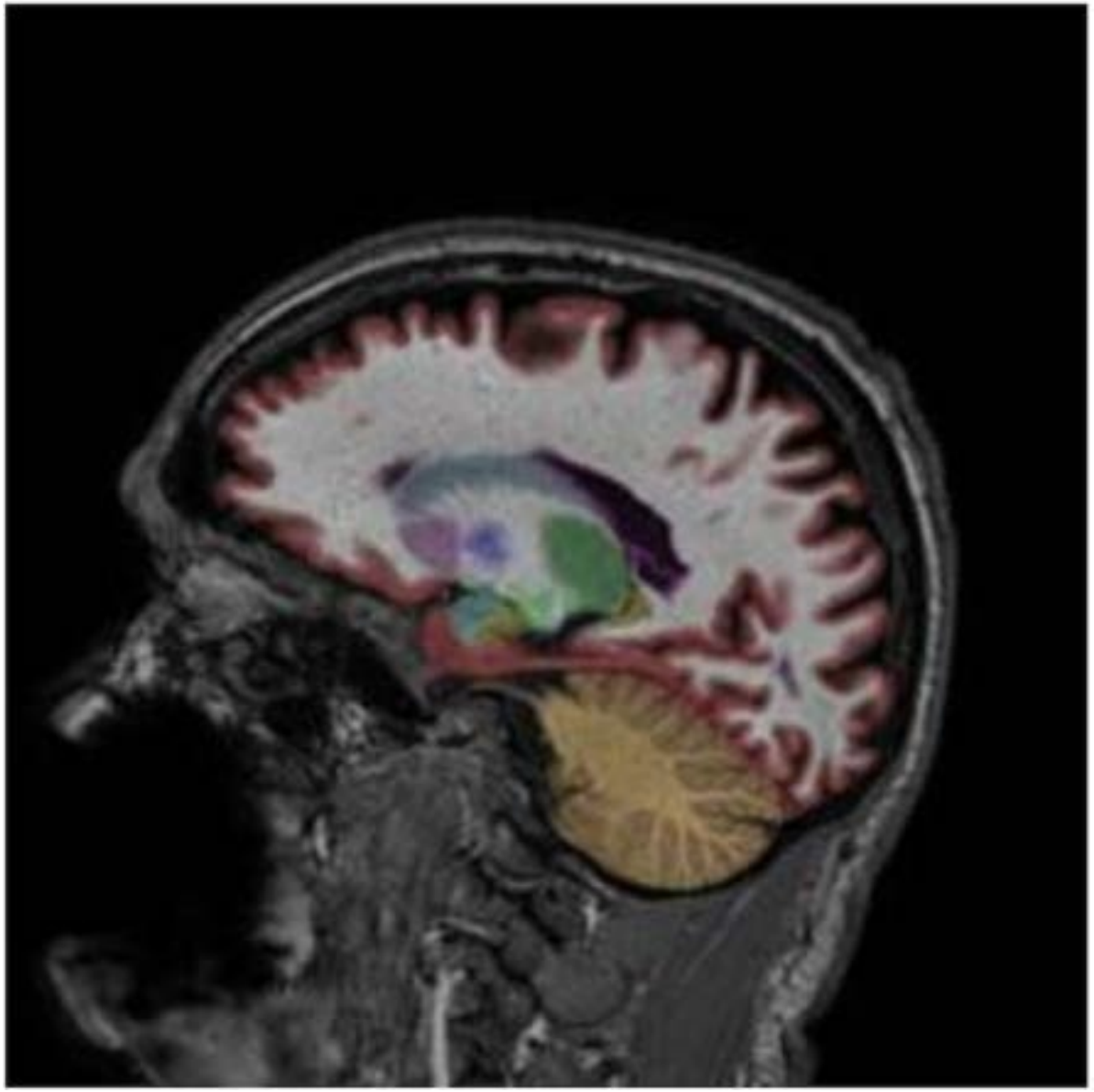

NeuroQuant Triage Brain Atrophy Report (TBAR)

- Cingulate inflammation
- Frontal atrophy

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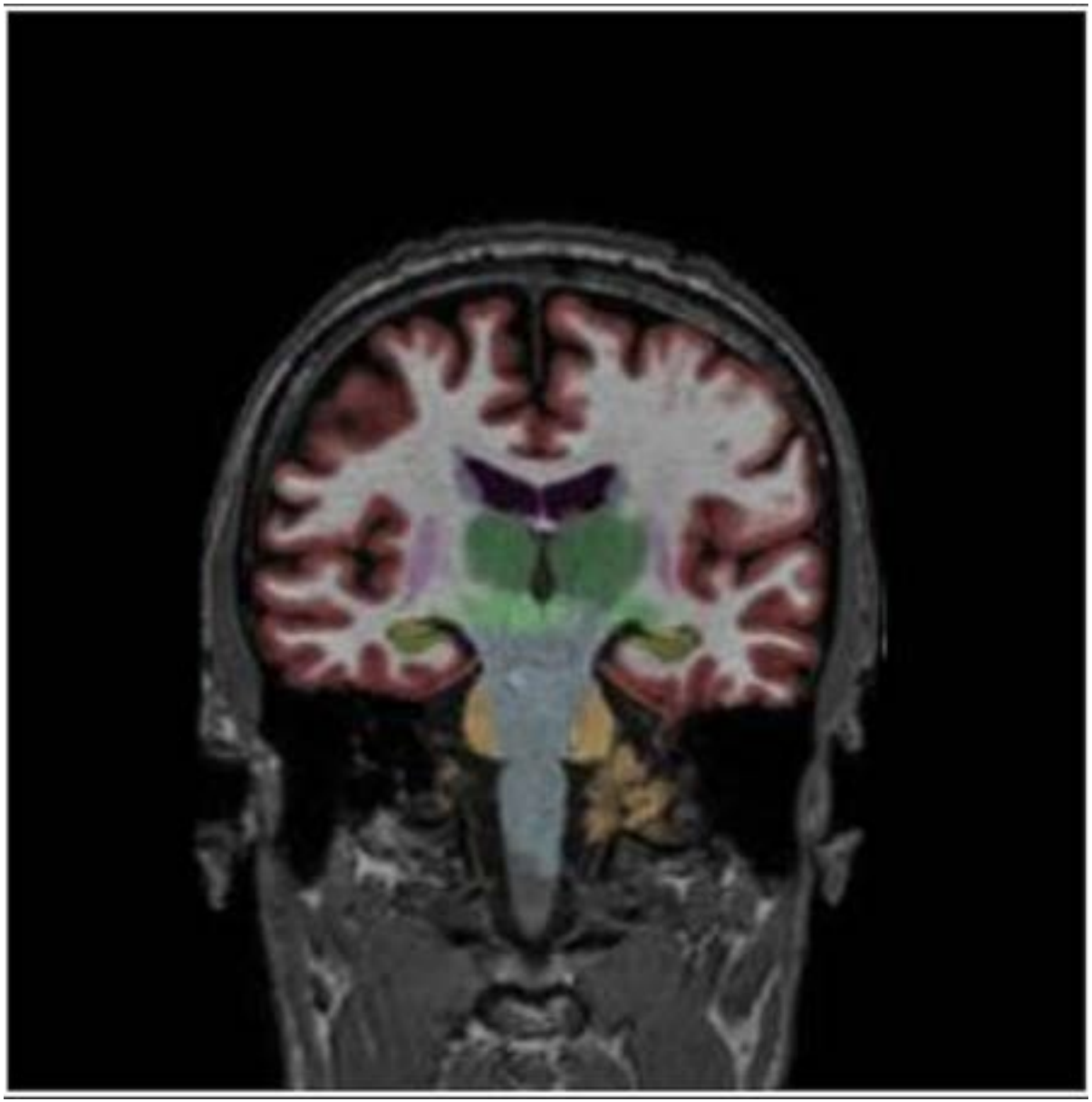

NeuroQuant
Triage Brain Atrophy Report (TBAR)

- Ventricular asymmetry (TBI?)
- Patchy asymmetry Inflammation, infection

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CASE | CPAP Dementia

"Oh yeah, mom had a fall" - many years prior

Mold inspector ~ Minor fragments in basement. No obvious water intrusion. Issues with clutter, cardboard storage, humidity, dust.

Recommended remediation - HEPA vac + wipe down surfaces, air filtration, replace all cardboard storage containers, better dust & humidity mgmt, duct cleaning

Tested C-PAP machine ~ extremely high Aspergillus, +Endotoxins

Wasn't maintaining adequate cleaning schedule or replacing tubing

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CASE | CPAP Dementia

Tx ~

CPAP: Cleaned machine appropriately, replaced tubing, SoClean ozone system. Home changes took a little longer, done by kids.

Nat sulph 200c

DHA 3gms daily, divided

GLA 1 gm daily, divided

Liposomal phosphatidyl choline 500mg bid

Melatonin 3mg hs + 3mg sustained release

Green drink - bid

Resveratrol - 1gm divided

Liposomal curcuma/resveratrol 400mg/150mg bid

F/U in 3-4 weeks

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CASE | CPAP Dementia

1st F/U ~

Improved sleep, anxiety, confusion, joint pain

Worsened constipation, food reactions

Sinuses cleared at first, now congesting again

Reduce DHA 2gms daily, divided

Reduce GLA 500mg daily

D/C added resveratrol, replaced with quercetin 600mg tid

Cont greens, PC, curcuma/resveratrol, melatonin

Add: Garlic tincture with Thymus & Holy Basil alternating 1 tsp bid-tid

Intranasal ozone daily x 1 week, then 3-4x/week

F/U 6 weeks, sooner if poor reaction to antifungals

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CASE | CPAP Dementia

2nd F/U ~
Marked improvement in RLS, sleep maintenance, sinus congestion, BMs, food rxns

Improvement in all dementia sxs, bp

Anxiety still an issue, desires easier nasal tx

Continue DHA, GLA (found a combo prod) - 2 gms divided

Reduce PC 500mg daily

Cont curcuma/resv, greens

Reduce quercetin 600mg bid

Cont melatonin 3mg hs, but d/c added 3mg sustained release

Cont Garlic tincture with Thymus & Holy Basil alternating 1 tsp bid

Replace Intranasal ozone with propolis nasal spray

Limbic retraining via FSM

F/U 3 months

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CASE | CPAP Dementia

3rd F/U ~
Sustained improvement in dementia sxs, RLS, sleep maintenance, sinus congestion, BMs, food rxns, bp

Anxiety - reducing but not as fast as desired

Alternate DHA/GLA with PC

Reduce quercetin 400mg bid, over time wean, watch sinus congestion

Cont greens, curcuma/resv (may wean over time, watch joints)

Use melatonin 3mg hs prn

Cont Garlic tincture with Thymus & Holy Basil alternating 1/2 tsp bid (wean over time)

Cont nasal spray hs

Limbic retraining via DNRS

F/U 3 months

Over time, dementia sxs continued to improve & now no longer an issue. Anxiety improved.
Better about managing dust/humidity

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CASE | Breathless & Anxious

Early 50s M, outwardly calm, conscientious, but suppressed

Executive, accustomed to high pace & high functioning

Remodeled a Frank Lloyd Wright home in “choice” neighborhood

Relationship problems “this house killed my marriage”, divorce

Beginning breathing troubles around same time

Describes “broken heart pain”

Anxiety, insomnia, weeping

Dx allergies, asthma, anxiety

Rx steroid nebulizer, rescue inhaler, anxiolytic

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CASE | Breathless & Anxious

Worsening resp sxs

Various specialists, no answers

Worsening insomnia, new onset reflux, jock itch

Allergist confirms mold allergy

Rx antifungal cream w steroids, proton-pump inhibitors, statins*

* * *

All sxs worsening esp breathing issues, very distressing

New onset tinnitus, pelvic pain, constip, jock itch wakes from sleep

* * *

In desparation, comes to see the woo-woo doctor in town

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TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
Allergen Profile, Mold					
Class Description					01

Levels of Specific IgE	Class	Description of Class
< 0.10	0	Negative
0.10 - 0.31	0/I	Equivocal/Low
0.32 - 0.55	I	Low
0.56 - 1.40	II	Moderate
1.41 - 3.90	III	High
3.91 - 19.00	IV	Very High
19.01 - 100.00	V	Very High
>100.00	VI	Very High

M001-IgE Penicillium chrysogen	<0.10		kU/L	Class 0	01
M002-IgE Cladosporium herbarum	<0.10		kU/L	Class 0	01
M003-IgE Aspergillus fumigatus	<0.10		kU/L	Class 0	01
M004-IgE Mucor racemosus	<0.10		kU/L	Class 0	01
M005-IgE Candida albicans	<0.10		kU/L	Class 0	01
M006-IgE Alternaria alternata	**0.84**	**Abnormal**	kU/L	Class II	01
M008-IgE Setomelanomma rostrat	**0.25**	**Abnormal**	kU/L	Class 0/I	01
M009-IgE Fusarium proliferatum	**0.11**	**Abnormal**	kU/L	Class 0/I	01
M012-IgE Aureobasidi pullulans	**0.18**	**Abnormal**	kU/L	Class 0/I	01
M013-IgE Phoma betae	**0.16**	**Abnormal**	kU/L	Class 0/I	01
M014-IgE Epicoccum purpur	**0.30**	**Abnormal**	kU/L	Class 0/I	01
M010-IgE Stemphylium herbarum	**0.27**	**Abnormal**	kU/L	Class 0/I	01

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TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
Lower Respiratory Culture					
Lower Respiratory Culture					
Final report					01
Result 1					
Routine respiratory flora					01

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Sample	Time	ppm H2	ppm CH4	ppm H2 + CH4	% CO2	Correction	Symptoms
#0 - 0	9:00 AM	3	5	8	4.3	1.27	
#1 - 20	9:20 AM	5	6	11	4.6	1.19	
#2 - 40	9:40 AM	8	8	16	4.2	1.3	
#3 - 60	10:00 AM	9	9	18	4.4	1.25	
#4 - 80	10:20 AM	6	7	13	4.6	1.19	
#5 - 100	10:40 AM	6	8	14	4.3	1.27	
#6 - 120	11:00 AM	4	5	9	4.2	1.3	
#7 - 140	11:20 AM	2	5	7	4.6	1.19	
#8 - 160	11:40 AM	1	4	5	4.5	1.22	
#9 - 180	12:00 PM	1	4	5	4.5	1.22	

© Dr Jill Crista

Glutathione; Erythrocytes

	Within	Outside	Reference Range	
Glutathione*		1093	> 1100	µmoles/L

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Results:

Code	Test	Specimen	Value	Result	Not Present if less than	Equivocal if between	Present if greater or equal
E8501	Ochratoxin A	Urine	1.55300 ppb	Not Present	1.8 ppb	1.8-2.0 ppb	2.0 ppb
E8502	Aflatoxin Group (B1,B2,G1.G2)	Urine	0.80500 ppb	Equivocal	0.8 ppb	0.8-1.0 ppb	1.0 ppb
E8503	Trichothecene Group (Macrocyclic)	Urine	0.07200 ppb	Present	0.02 ppb	0.02-0.03 ppb	0.03 ppb
E8510	Gliotoxin Derivative	Urine	1.42100 ppb	Present	0.5 ppb	0.5-1.0 ppb	1.0 ppb

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CASE | Breathless & Anxious

Labs ~

Fe-def anemia, ↓WBC, ↑IgE, rising liver enzymes,

↓Vit D 25-OH

Stool test - +Candida, (-)SIBO

Nares Culture +MRSA

Tx ~ (pt request - “give me everything”)

Home mold inspection

Already pristine diet, organic veggies, low animal protein

EVOO 1 Tbsp qid

Quercetin 600mg qid

Hawthorn solid extract 1/2 tsp tid

Lung tincture blend 1/2 tsp tid (Symplocarpus, Asafoedita, Eriodictyon, Verbascum)

Aloe juice 1 cup tid before meals

Bile salts with dinner, trial Betaine HCl

Emulsified vit D - 10,000 IU daily

Allicin swab nares bid

F/U 3 weeks after home report available

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CASE | Breathless & Anxious

1st F/U ~

Home loaded with mold, covered over by remodelers

Mild improvement in asthma, reflux, constipation. HCl too burny.

Excited, first sign of possibility of improvement

Request retest and antimicrobials

Tx ~

Move out while home remediated

Cont EVOO, Quercetin, Hawthorn, Lung formula, Aloe, Bile salts, D

Add psyllium husk fiber 1 Tbsp daily

Add Nebulized GSH (compounded) bid

Intranasal allicin bid

D/C statin

F/U 3 months, unless downturn, retest 2.5mo

Antifungal combo as follows…

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CASE | Breathless & Anxious

Step 1:

Thyme tincture ~

Loading dose x 1 week before Rx

1 tsp tincture bid

Step 2:

Add pulsed Fluconazole - 200mg x 3-4d/wk

Step 3:

Add pulsed antifungal botanical on alt days (ie Pau D'Arco, Oil of Oregano)

Step 4:

Continue with botanicals x 1 addtnl mo, d/c fluconazole

Thyme tincture ~ 1 tsp qd

Pau D'Arco ~ 500mg caps qd-bid, pulsed varied (Neem, Monolaurin)

Step 5:

Continue pulsed rotating antifungals x 6-12mo or until neg mycotoxins

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CASE | Breathless & Anxious

2nd F/U ~

Marked improvement resp, GI, HT, jock itch

Anxiety, mood issues, bloating, sweet cravings persist

Tx ~

Stay the course on supps, neb, intranasal

Increase animal protein

Replace steroid-containing antifungal w pure antifungal

Alternate nostril breathing qd

Retest mycotoxins, OAT, nares in time for appt

F/U 3-4 mo unless downturn

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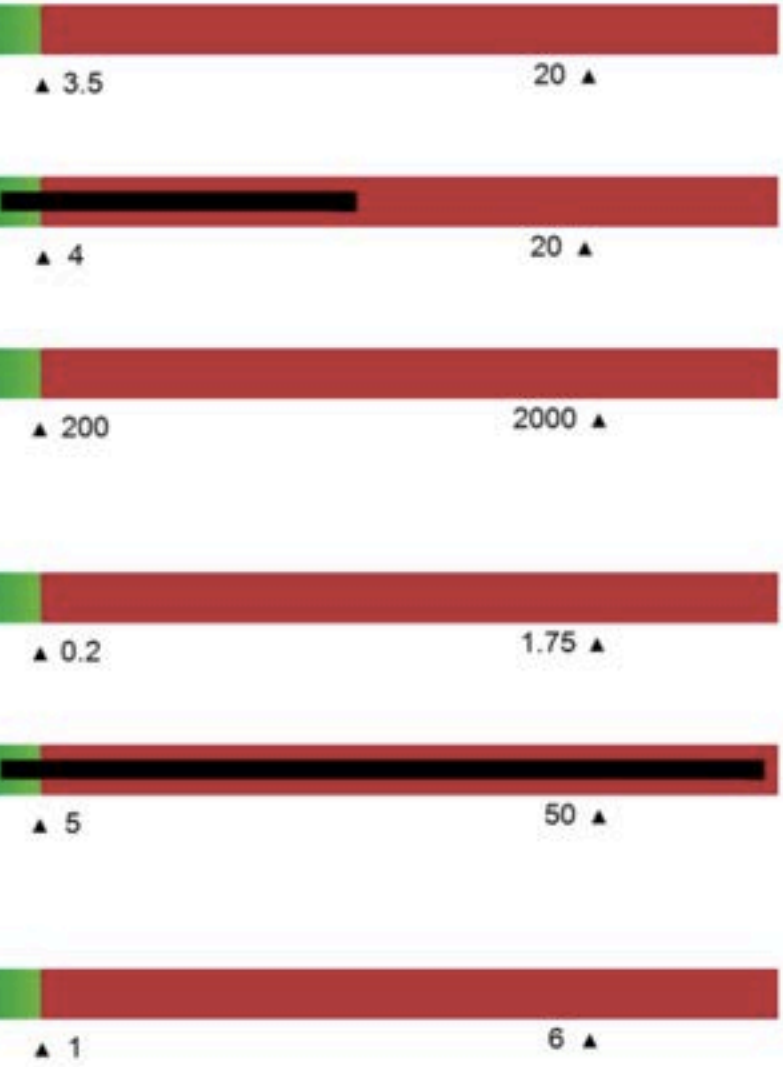
MycoTox Profile

Metabolite	Results (ng/g creatinine)	Common Range of Positive Results
Aspergillus		
Aflatoxin-M1	0.00	3.5 - 20
Ochratoxin A	12.97	4 - 20
Gliotoxin	0.00	200 - 2000
Penicillum		
Sterigmatocystin	0.00	0.2 - 1.75
Mycophenolic Acid	438.03	5 - 50
Stachybotrys		
Roridin E	0.00	1 - 6



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Metabolite	Results (ng/g creatinine)	Common Range of Positive Results
Verrucarin A	0.00	1 - 10

Fusarium

Enniatin B	0.00	0.07 - 1

Zearalenone	0.00	0.5 - 10

Chaetomium globosum

Chaetoglobosin A	0.00	20 - 80

Multiple Mold Species

Citrinin	0.00	10 - 50

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Organic Acids Test - Nutritional and Metabolic Profile

Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)		Patient Value	Reference Population - Males Age 13 and Over
Intestinal Microbial Overgrowth				
Yeast and Fungal Markers				
1 Citramalic	0.11	- 2.0	1.3	
2 5-Hydroxymethyl-2-furoic *(Aspergillus)*		≤ 18	11	
3 3-Oxoglutaric		≤ 0.11	H 0.13	
4 Furan-2,5-dicarboxylic *(Aspergillus)*		≤ 13	7.1	
5 Furancarbonylglycine *(Aspergillus)*		≤ 2.3	0.19	
6 Tartaric *(Aspergillus)*		≤ 5.3	0.52	
7 Arabinose		≤ 20	H 27	
8 Carboxycitric		≤ 20	0.46	
9 Tricarballylic *(Fusarium)*		≤ 0.58	0.18	

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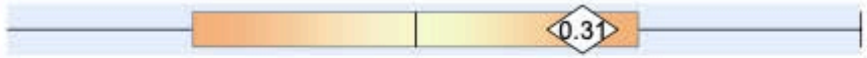
Metabolic Markers in Urine	Reference Range (mmol/mol creatinine)	Patient Value	Reference Population - Males Age 13 and Over
Indicators of Detoxification			
Glutathione			
58 Pyroglutamic *	5.7 - 25	20	
Methylation, Toxic exposure			
59 2-Hydroxybutyric **	≤ 1.2	0.69	
Ammonia Excess			
60 Orotic	≤ 0.46	0.31	
Aspartame, salicylates, or GI bacteria			
61 2-Hydroxyhippuric	≤ 0.86	H 0.94	

* *A high value for this marker may indicate a Glutathione deficiency.*

** *High values may indicate methylation defects and/or toxic exposures.*

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CASE | Breathless & Anxious

3rd F/U ~

Persistent MRSA, Candida on labs but asx

Flaring when home, better work travel

Tx ~

Retest home, more to remediate?

Cut all oral supps in half, one at a time, divided by 1-2 weeks, watch sxs

Reduce nebulized GSH to qd

Replace Intranasal allicin with e.o. blend, add intranasal xylitol

Wean lung tincture, add NAC

Cont antifungal combo plan, slow wean after neg mycotoxins

Cont rotating biofilm txs, watch reactions

Talk to gastroenterologist for plan to wean PPI

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CASE | Breathless & Anxious

Resolved ~
Acute breathing issues, allergies, “heart pain”, weeping, reflux, jock itch

Improved anxiety, insomnia, asthma

D/c'd steroid nebulizer, proton-pump inhibitors, statins

Retaining rescue inhaler

Anxiolytic prn for occasional insomnia

Residual tinnitus, pelvic pain lasted up to 2 additional years

Asthma eventually resolved but keeps rescue inhaler on my request

Remediation took 3 tries

* * *

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Review

Herx

Exposure plan

Travel tips

Reintroduction

Fortification

What If's

Cases

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Thank You
Dr. Jill Crista
Naturopathic Doctor
support@drcrista.com

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Are You Missing Mold Illness?

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And The Environment

Are You Missing Mold Illness In Your Patients?

Dr. Jill Crista

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And The Environment

Canaries ~ Just Don't

Inspectors & Remediators

Building Assessment Basics

Endotoxins

Remediation Tips

What To Do About "Stuff"

Prevention

© Dr Jill Crista

Canaries ~ Just Don't

© Dr Jill Crista

Who Should Keep Out

Ok, EVERYONE!

But certainly, people who are ~

- Pregnant
- Breastfeeding
- Young children
- Respiratory conditions
- Liver disease
- Kidney disease
- Immune deficiency
- Cancer
- Genetically mold sensitive (canaries)

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Dorks Stay Healthy

Protective gear ~

Disposable Tyvek suit with hood
Toss after each exposure

Safety glasses
Clean with bleach after each use

Silicone respirator w disposable filters
Clean with bleach after each use

P100 respirator filters
Toss after each exposure

Double gloves
Toss after each exposure

Shoe booties
Toss after each exposure

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Inspectors & Remediators

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Inspectors

Why need?
- More than mold
- Advocacy
- Select remediators
- Guide remediation plan
- Post inspection

Inspector Qualifications ~
- Sensitive pts

Certifying organizations ~
- BBEC (Building Biology Institute)
- ACAC certified
- IICRC certified

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Inspectors

Questions to vet inspectors ~

Patient handout courtesy of
Corey Levy, CMI, CIE, WELL AP
YesWeInspect.com

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Conflicts of Interest

Inspectors test
Remediators remediate

🚩 - remediation co that says they'll do the post-test instead of inspector
(illegal in some states)

Post-rem testing by remediators is done ~
For internal QC
Usu only air sampling
*Not a thorough inspection

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Remediators

Chosen by inspector

Know how & be willing
to work w sensitive ppl

Understand inspector will post-test

Provide written plan in detail, costs
itemized, meet, sign-off

Is the norm to find more as they
open up (water source, more
mold)

Make sure any alterations are in
writing and cost estimate given,
agreed upon before proceeding

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Building Assessment Basics

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Know Your Lane

Are you a building expert?
- Plumbing, roofing, attics, crawl spaces, grading, partial pressures, etc

Even experienced, certified inspectors
- miss mold on occasion

Costly mistakes ~
- False sense of security
- Ruin the chances of getting ins coverage

Chain of Custody
- By Certified Inspector
- Submit w any sampling
- Must have in place legally, ins
- Dr can submit *but must be the sampler/ defend in court*

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Purpose Of This Section

Know enough to protect your pt from bad actors & guide them through the process

NOT to take this part on

You're their body Dr not bldg Dr

Highly recommend doing the work to find your go-to inspectors in your area, then REFER

But if you're itching for more ~ Mold Masterclass by Brian Karr

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Inspections

Goals ~

1) Determine the sources of the contamination
   W/o eliminating the sources the problem will persist

2) Determine how the sources have impacted the occupied living spaces & HVAC system

Allows inspector to provide a holistic & comprehensive remediation strategy

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Inspections

Thorough history ~

- Not only about areas that are currently wet
- Hx of water events very important!
- Water-impacted areas that are now dry have a significant impact on contamination
- Dried colonies easily break apart into ultra-fine fragments & particulate

Time ~

- Should last >2hrs, typical is 4hrs
- Attic, crawlspaces, outdoor, roof

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Sampling Limitations

Just like testing bodies ~
 Each method has strengths & weaknesses

Goal ~
 Maximize strengths
 Minimize weaknesses

Solution ~
 Multiple testing strategies

Looking for ~
 Moisture, staining, rusting, spores, fragments, DNA, mycotoxins

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Sampling Tools & Methods

Tools ~
- Eyes - visual inspection* most important
- Infrared camera (moisture)
- Moisture meter, humidistat
- Sterile swabs
- Spore trap vacuum
- On-location microscope

Methods ~
- Plates (controversial)
- Air sampling (cavities/isolated spaces)
- Spore trap (cavity)
- Dust sampling
- Tape lift
- Bulk (textile, carved sill plate, filter, etc)
- On-location microscopy

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ERMI/EMMA

Environmental Relative Mold Index

EPA std: DNA-based MSqPCR method. ID & quantify spore/fragment DNA

26 mold species known to thrive in WDB + 10 species "found in all homes, with or without water damage"***

Dust sample using HEPA filter trap. Vacuum specific area of a carpet (or other material) in LR + main BR

Compare to national database of US homes. Reported as percentiles, then scored via algorithm, with EPA's opinion that "every home in US has mold" (bc of improper selection criteria imho)

Don't go by the "score" only!

Per certified inspectors - flawed scoring system

Look at species & quantitative findings. Can still be high mold burden with a "normal" ERMI score.

Some species indicative of long-standing issue

EMMA adds mycotoxins

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HERTSMI-2

Health Effects Roster of Type Specific Formers of Mycotoxins and Inflammagens - 2nd Version

DNA-based MSqPCR method. Score based on qty detected.

Swiffer or vacuum collection

The big 5 - the bad actors
- Aspergilus Penicilloides
- Aspergillus Versicolor
- Chaetomium Globosum
- Stachybotrys Chartarum
- Wallemia Sebi

“Indicator” species correlated both w WDB & MARCoNS incidence

Score <10

Cost savings

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Spore Trap

Specific, focused air sample

Cavities

Disrupt then let dust settle

Specialized HEPA vacuum

Vacuum for 5 min, no less

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Mycotoxin

Current or forensic, no surety

Furnace filter - 3” square after 3 mo continuous use

Aggregated dust sample from tops of ~
picture frames
tall shelves
books
kitchen cabinets
trim around closets

Avoid sampling near windows/ doors to the outside

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Bulk

My clinical experience

Kitchen ceiling ~
- Spore trap: mild Aspergillus
- Bulk: mod Chaetomium

Bathroom subfloor ~
- Swab: mod Asp & Pen
- Bulk: mild Stachy

Lessons ~
- There are no perfect tests
- Toxic species are gooey
- Test everything that is removed

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Other Sources

CPAPs

Keurig

Refrigerator: coils, water filter

Bath toys

Mattresses

Dehumidifiers

Saunas

Car cabin filters

Furnace coils!

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Endotoxins

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Endotoxins

Usu where there's mold,
there's bacteria

Story of the vegetative framing
member

Humidifiers/CPAPs ~
Tap water: bacterial count
Causes aerated endotoxins
Only use distilled water

© Dr Jill Crista

What To Do About “Stuff”

© Dr Jill Crista

What To Take

Depends on extent

First ~ GET YOURSELF OUT!

“The best things in life are not things” Hawaiian Rules To Live By

Take only the bare minimum

The primary reason for chronicity

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Storage Solutions

Buys time/space for better decision-making

Plastic bins, sealed w tape

Caution: many storage units are also toxic ~
Rat poison
Pesticides
Critters, feces
Neighboring units
Many are moldy (roof leaks)

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Cross-Contamination Risk

Caution ~ car contamination

Wipe down everything 3x before it
leaves sick envir w new cloths~
First at the front door/garage
Second midway to car
Third just before place in car

My story ~ 2x not enough

© Dr Jill Crista

What Might Be Remediated

Metal & glass

Maybe 100% real wood furniture,
BUT many many asterisks****
*how hard is the wood?
*how close to mold?
*how long?
*how old is the piece?
*how well maintained?
*how many crevices?

© Dr Jill Crista

What About Clothing?

Reminder abt research re: pasta cooking
- mycotoxins retained despite heat

Posited solution (no data!) ~
High heat wash
100 drops e.o. per load
High heat dry
Sunshine exposure daily x 1 wk every surface
Borax

Cautions ~
False sense of security
Dermal absorption
Contaminated washer

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Remediation Tips

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Remediation Pressures

Remediators ~

Least force options

Building owner ~

Rush to rebuild

Insurance company ~

Mitigate losses

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Remediation Tips

1. No spray & pray
2. No seal & deal
3. When in doubt, cut it out
4. Take out more than you think

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Remediation Formulas

All-Purpose Cleaning Formula ~
- Non-porous - glass/metal
- Real wood - witch hazel>water
- *Essential oils theoretical workhorse

Peroxide 15% or Bleach ~
- Concrete

Carpet cleaner ~
- *Essential oils theoretical workhorse

Ozone & Enzyme treatments ~
- What happens in pathogenic biofilm envir?

WE REALLY DON'T KNOW!
- Must post-test!
- Only keep what's worth testing

© Dr Jill Crista

Mycotoxins & Particulate

Foggers ~
Not considered remediation, but rather cleanup
May use as a final step to control ultra-fine particulate

Air filters ~
Also not remediation!

-HyperHEPA (mycotoxins=0.1m)

-Sanitizing
-Incinerating

*Change filters early to avoid pass-through effect

© Dr Jill Crista

Prevention

© Dr Jill Crista

Mold's Weaknesses

Dryness

Sunlight

Air movement

Dust-free spaces

Lack of clutter

Mold-killing essential oils

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Preventive Measures

Don't water it

- Manage humidity ~
- Indoor humidity <50%
- Humidistat in each room
- Run fans before steam

Don't feed it

- Manage dust ~
- Dust with gusto!
- Reduce clutter
- No cardboard box storage
- Central vacuum system

Don't help it find a new home

- Change filters regularly ~
- Home at least 2x/year
- Car at least annually
- Air filters maintain as rec
- CPAP as rec

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Prevention Tips

Dry every moist thing

Quantify humidity in each room

Dehumidify if needed, by location

No water to refrigerator

Drain/pan under washing machine

Reduce carpeting

No finished basements

Cabinets with feet

Air movement indoors

Air out closets, e.o. cotton balls

Showers/windows vinegar

Manage cracked grout

Paper towel test toilets routinely

Check attic after big rain or snow melt

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Before Buying/Renting

Always test in advance

Offer must allow to buyer to completely w/d from offer

No “right to cure” - seller/leasor will cover up the problem rather than remediate

Unfortunately most sellers/leasors will demand notification of testing methods, some will adulterate

Mycotoxin dust sampling often adequate - inside ductwork

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Other Air Quality Considerations

VOCs and microbial VOCs

Dander

Allergens

Gas leaks

Formaldehyde (‘new’ smell)

Fiberglass

Fragrances

PCBs (candles)

EMFs - WiFi, smart meters

Endotoxins

Heavy metals (hobbyists-lead solder)

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Review

Canaries ~ Just Don't

Inspectors & Remediators

Building Assessment Basics

Endotoxins

Remediation Tips

What To Do About "Stuff"

Prevention

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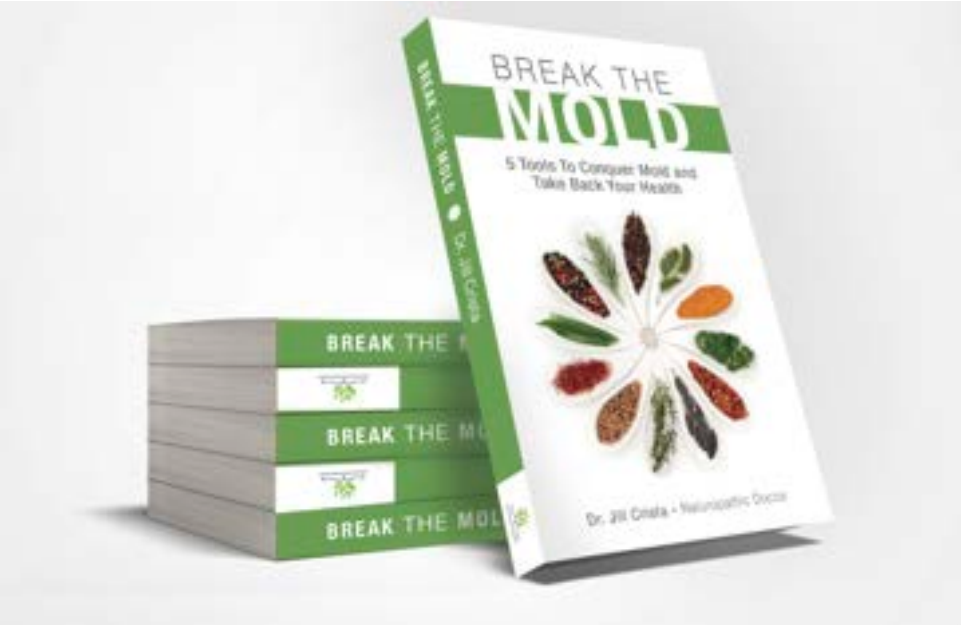
Survey

DrCrista.com

- Patient resources
- Short video blogs

Break The Mold

Mentorship

Stay in the light ✨