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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

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Mycotoxin Overview

What's a mycotoxin anyway?

Negative health impacts

Mycotoxin affinities & the body

Other than mycotoxins

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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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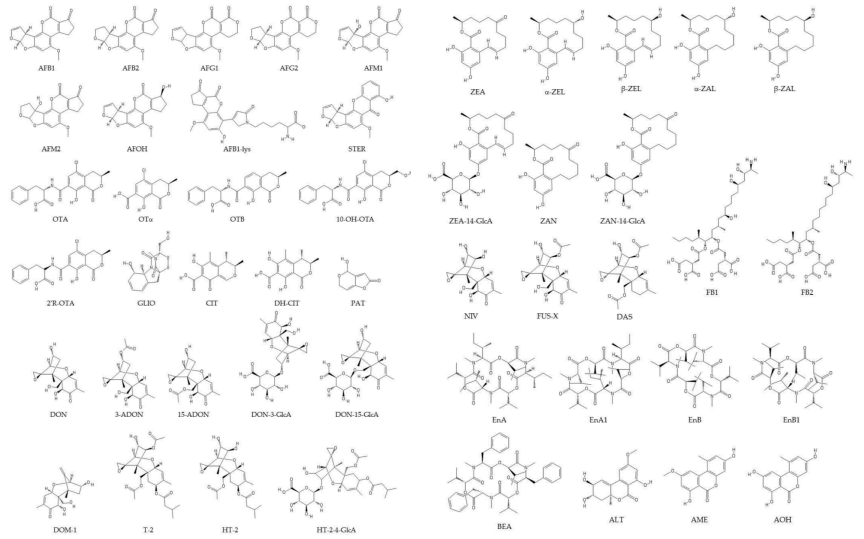
Wide Structural & Biosynthetic Diversity



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?

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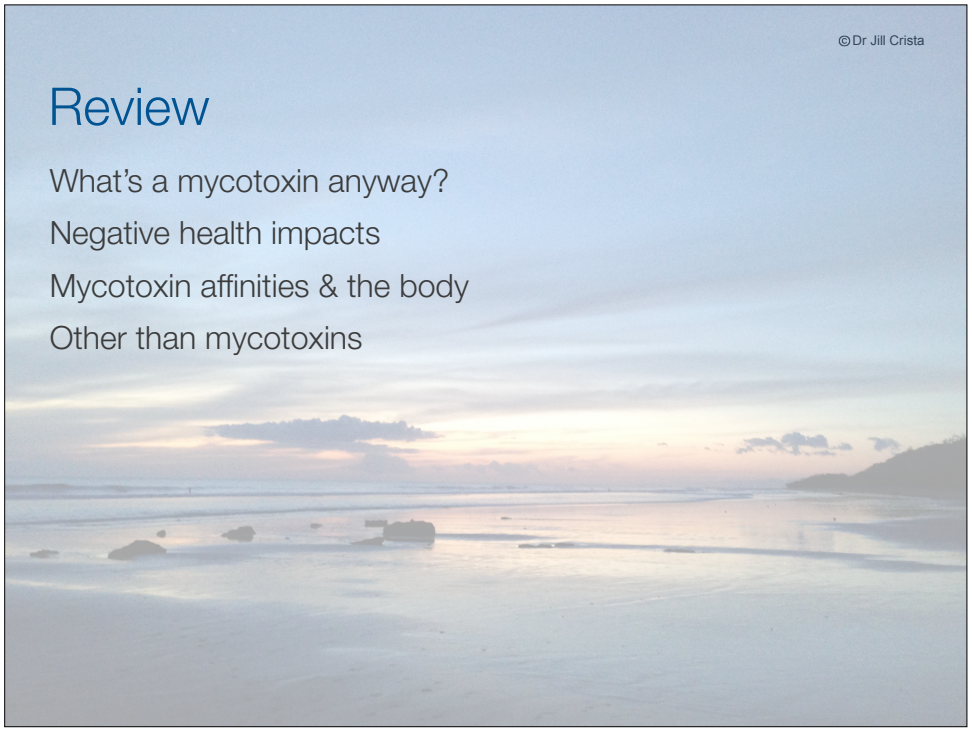
Other than mycotoxins



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Dr. Jill Crista
Naturopathic Doctor
support@drcrista.com