EDITORIAL

The Great Masquerader: Mycotoxins

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Mycotoxins can cause many diseases, and this is why the World Health Organization named it "The Great Masquerader" of the 21st century. Patients affected by mycotoxins present to their healthcare providers with a number of nonspecific clinical signs and symptoms, and mycotoxins are not routinely suspected. Many patients may be misdiagnosed with having chronic Lyme disease, Chronic Fatigue Syndrome, Fibromyalgia, autoimmune disorders, and others with psychiatric disorders such as adjustment disorder and depression.

Mold spores can be found in many indoor spaces; however, they are dormant until they come into contact with moisture or water and start producing spores and releasing them into the ambient air. Mold spores are like a packet of seeds: put them in a container with soil, water them, and you get results. The Environmental Protection Agency, the Centers for Disease Control and Prevention, and the National Institutes of Health all agree that molds start to grow and sporulate when they have been wet for 24 to 48 hours.

It has been well documented in the medical literature that water intrusion from leaky roofs, pipes, windows, poorly maintained flashings, and flooding from leaking washers, dishwashers, ice makers, etc., in the home as well as in the workplace cause mold growth with the subsequent exposure to mycotoxins. Reports of such exposures include homes, office buildings, courthouses, hospitals, hotels, schools, and university dormitories.

Mold spores carry with them mycotoxins. Mycotoxins have potent toxic effects on humans. To use an analogy, molds are the gun, and mycotoxins are the bullet. It is common that one mold produces a number of mycotoxins, and different molds make one mycotoxin.

Mycotoxins are what mold spores produce to weaken and destroy health. Mycotoxins are very strong and powerful and destructive to organs and systems. The alteration of immune responses due to mycotoxin exposure may also adversely affect the ability of the immune system to respond to other environmental challenges. This may explain why patients complain of increased sensitivity to chemical irritants. These patients may report more sensitivities to a number of foods, chemicals, odors, etc.

The adverse health effects of mycotoxins range from acute toxicity to long-term effects such as:

- Autism
- · Multiple sclerosis
- Alzheimer's disease
- Parkinson's, amyotrophic lateral sclerosis
- Postural Tachycardia Syndrome
- Chronic Fatigue Syndrome
- Fibromyalgia
- Small Intestinal Bacterial Overgrowth,
- Irritable Bowel Syndrome
- Inflammatory Bowel Diseases
- Mast Cell Activation Syndrome
- Autoimmune disorders
- Immune dysregulation
- Cancers

The effects of filamentous molds and mycotoxins on human health have been written about for centuries. An excellent protocol on what to do with a dwelling affected by mold can be found in chapter 14 of Leviticus in the Bible. An Assyrian table discusses a "noxious pustule in the ear of grain," referring to ergot. Consuming bread made from flour contaminated with ergot from the fungus Claviceps purpurea that infects rye and other cereals causes ergotism and its earliest reference is the Annales Xantenses for the year 857. In the Middle Ages, it became known as St. Anthony's Fire, and its symptoms include seizures, diarrhea, psychosis, headaches, dry gangrene of fingers and toes, nausea, and vomiting.

Molds produce toxins known as mycotoxins. Molds are always present in homes or workplaces that are water damaged and they are always producing mycotoxins.

It is well established in medicine and science that exposure to molds and mycotoxins indoors is hazardous, and more so in children and the elderly. How a person reacts to molds and mycotoxins depends on that person's health and nutritional status, if they have other medical conditions, how long is or was the exposure, the person's genetic makeup, and the nutritional status of the patient. There is no published scientific or medical evidence that genetics play a role.

Many people cannot see any indoor mold growth: the E.P.A. cautions that approximately 50% of the fungal growth can be hidden, i.e. hidden from view. When people smell something "musty", they are actually smelling VOC's (volatile organic compounds) produced by molds. Chronic exposure to even low levels of molds, mycotoxins, and VOC's, can cause serious health problems. Even small amounts of mold growth in the air conditioning or ducts will result in the occupants being chronically exposed, constantly breathing mold spores and their mycotoxins, causing illnesses.

Blood serum testing for mycotoxin antibodies have been used for the last 20 years and are currently the most accurate test available for mycotoxins. The specificity and sensitivity of blood serum testing for the presence of IgG and IgE antibodies to mycotoxins in the blood are of the highest degree. The other available testing is urine, which tests for mycotoxin metabolites and not mycotoxins themselves. A recent study by Garg stated that: "The variability of mycotoxin concentration in urine and its volume is based on daily intake and demands urine sampling at different time points during the day." Moreover: "The ELISA method to detect mycotoxins in human serum comes with significant accuracy, precision, and specificity." The laboratory that does this testing in the United States and internationally is Mymycolab.

According to the National Institute for Occupational Safety and Health (NIOSH), a part of the Centers for Disease Control and Prevention (CDC), low levels of mycotoxins are found in many foods. For that reason, they are routinely present in the urine of healthy people. Therefore, it does not mean the person suffers from any disease or disorder related to molds or mycotoxins. Please see:

"Use of Unvalidated Urine Mycotoxin Tests for the Clinical Diagnosis of Illness—United States, 2014." Centers for Disease Control and Prevention, Morbidity and Mortality Weekly Report, http://www.cdc.gov/mmwr/preview/ mmwrhtml/mm6406a7. htm

The most important point is that if you have mycotoxins in urine, it is a good thing: the body is doing its job of getting rid of mycotoxins from foods and beverages.

Urine levels of mycotoxins mean excretion; it does not mean pathology. Laboratories offering urine mycotoxin testing are measuring this minute quantity of metabolites of mycotoxins, <u>not the mycotoxins</u>. Furthermore, some mycotoxins, such as ochratoxin, cannot be measured in urine. Almost all, 99.8% of the body's ochratoxin is tightly bound to the body's main protein, albumin, so it cannot be excreted through the kidneys. It is reabsorbed from all parts of the nephron by active and passive transport and passive diffusion. Yet it is the most commonly found mycotoxin in urine, which raises a lot of questions on the accuracy of the testing.

HORMONES AND MYCOTOXINS

Mycotoxin toxicity can affect hormones in men and women. The enzyme aromatase is upregulated, which is responsible for the last steps of estrogen biosynthesis from androgens (i.e., testosterone), resulting in the increased conversion of testosterone to estrogen.

All estrogens need the appropriate function of the liver and of cytochrome P450 enzymes to enable them to be metabolized. Cytochrome P450 enzymes are essential for the body to detoxify.

T-2 mycotoxin, part of the trichothecene family, has been shown in studies to decrease testosterone biosynthesis and secretion. Alternariol mycotoxin is antiandrogenic, meaning it reduces the effects of testosterone, as does Ochratoxin A and deoxynivalenol (DON), aka vomitoxin.

All estrogens need the appropriate function of the liver and of cytochrome P450 enzymes to enable them to be metabolized. Cytochrome P450 enzymes are essential to the body to detoxify. Mycotoxins block P450 enzymes, making it much more difficult for the body to get rid of toxins and also affecting estrogen. This results in abnormal levels of estrogen and progesterone, leading to abnormalities in menstruation, abnormal uterine bleeding, and to infertility.

Treatment Guidelines:

It is very important to control and minimize environmental exposure to many toxicants:

- Pesticide exposure.
- Heavy metals.
- Living near golf courses, factories, agriculture areas where pesticides are regularly used.
- Processed foods.
- Artificial sweeteners.
- Artificial food flavorings, colorings, and preservatives.
- EMF exposures.

First and foremost: apply the first rule of toxicology: get the patient away from the toxin or the toxin away from the patient.

Second: simultaneously build up the immune system while killing the fungi.

Probiotics: use spore forming bacilli.

Boosting the immune system: immunotherapy with nutrients, vitamin D3 and B complex, omega 3's, CoQ10, zinc, melatonin, and others.

Anti-fungal treatment: itraconazole.

For cognitive issues: phosphatidyl serine and slow-release magnesium.

Infrared sauna: start low and go slow.

If a brain SPECT scan shows decreased perfusion, I recommend nitric oxide, specifically N_1O_1 , for its documented effects.

Eighty percent of the immune system is in the gut, so this is a primary place to begin. The main components are diet, supplements, and probiotics.

Diet: Try gluten free for 90 days. Avoid dairy, soy, and sugar.

Use: Broccoli, resveratrol, tomatoes for lycopene.

A publication from Reading University with the Food Safety Authority of the United Kingdom, in essence the FDA in England, showed that less than 10% of the usual commercial strains of Lactobacilli and Bifidobacterium in probiotics are able to get to the colon.

Studies in humans show the following benefits from Bacillus spores:

- Effective treatment for small intestinal bacterial overgrowth (SIBO).
- Reduced incidence of irritable bowel syndrome diarrhea.
- Improvement in pain scale in Rheumatoid arthritis patients.
- Immune modulation for childhood allergies.
- Immune stimulation of peripheral T-lymphocytes and B-lymphocytes.

NUTRITION

An important component of treatment is not to add more substances that cause the immune system to react, especially chemicals or foreign substances in foods and beverages. Artificial coloring, artificial flavoring, artificial sweeteners, chemical preservatives, should be eliminated from the diet. Organic foods are preferred. Healthiest cooking methods are boiling, oven cooked meals, and broiling. Coated pans and cooking utensils should not be used. Plastic bottles and canned foods may contain bisphenols which are endocrine disruptors, and should be avoided. Liquids should be limited to water from glass bottles or containers.

BOOSTING THE IMMUNE SYSTEM

This is best done with supplements and depends on each patient's immune status. Choosing a supplement from a reputable supplier is paramount: over-the-counter supplements are discouraged, as their origin is unknown. Melatonin, vitamin D3, vitamin C, and B complex vitamins are all very helpful. Zinc is an essential nutrient of the immune system.

ANTI-FUNGAL MEDICATION

A broad-spectrum anti-fungal medication such as itraconazole is part of the treatment. It may be necessary to use such an anti-fungal for longer periods of time, depending on each patient's response. The most effective antifungal is itraconazole, and it is well tolerated. Fluconazole does not work against multicellular fungi such as Aspergillus, Penicillium, Stachybotrys, etc.; it only works against singlecell fungi, which are yeasts, such as Candida.

Binders are not recommended for the following reasons: a study by Rogawska and colleagues showed that binders rely on the absorption of mycotoxins from the gut, preventing them from getting into the bloodstream. These binders include kaolinite, clays, activated charcoal, zeolite, bentonite, and aluminosilicates. They are effective in neutralizing aflatoxin, which is rarely found in indoor environments. They are ineffective in all other mycotoxins. In addition, this study showed how they bind vital vitamins and macro- and micro-elements.

1. Cholestyramine cannot be taken by patients with the following conditions:

- Patients with hypothyroidism
- Diabetes
- Nephrotic syndrome
- Liver disease
- Kidney disease
- Alcoholism
- Dysproteinemia

2. Binders interfere with the absorption of the following medications:

- · Estrogens and progestins
- Thyroid medication
- Oral diabetes drugs
- Penicillin G
- Phenobarbital
- Spironolactone
- Tetracycline
- Thiazide-type diuretic pills
- Warfarin
- Leflunomide
- Digitalis

Satratoxin is a trichothecene mycotoxin mainly produced by Stachybotrys, also known as "black mold". It causes fatigue, headaches, nosebleeds, pulmonary hemorrhage, chest pain, moist dermatitis, and fever. It is neurotoxic and causes neurocognitive symptoms.

Verrucarin and Verrucarol are trichothecene mycotoxins mainly produced by Fusarium and Aspergillus species and are known to cause tremors, immune toxicity, and inflammation, they are cytotoxic and are potent protein synthesis inhibitors.

Ochratoxin: causes immune suppression, lung disease, and urinary tract tumors, and is nephrotoxic (kidneys), hepatotoxic (liver), genotoxic (genes), and carcinogenic (causes cancer). This is due to its ability to form DNA adducts and inhibit protein synthesis. Ochratoxin can potentiate the effects of IL-1 β on IL-8 secretion with a range of 35% to 138% increase and augments the transepithelial passage of commensal bacteria with a 12- to 1522-fold increase. Ochratoxin's major targets are:

- 1. Liver
- 2. Kidney
- 3. Brain

4. Skeletal muscle

5. Fat tissue

6. Ochratoxin crosses the placenta.

The highest Ochratoxin levels is found in breast milk.

Studies have shown it causes leaky gut syndrome and changes the nutrients that are absorbed from foods.

T2 Toxin: are trichothecene mycotoxins and are the only mycotoxins that have been used in biological warfare. They can cause diarrhea, vomiting, and intestinal hemorrhage, as well as changes in reproductive cycles and infertility. This mycotoxin is known to decrease testosterone.

Vomitoxin aka Deoxynivalenol: are trichothecene mycotoxins that destroys intestinal barrier function, resulting in anorexia, inflammatory bowel disease and celiac disease. They are able to increase IL-8 secretion with a 10- to 15-fold increase. This mycotoxin adversely affects both estrogen and testosterone.

Cladosporium Toxin: The airborne spores of Cladosporium species are significant allergens, and they can severely affect asthmatics and people with respiratory diseases. Cladosporium also produce volatile organic compounds (VOCs), which are neurotoxic.

Alternaria Toxin: Alternariol is cytotoxic (toxic to cells), mutagenic (causes mutations), genotoxic (genes), and causes immune suppression. This mycotoxin is also known to form reactive oxygen species (ROS) and to lower testosterone.

Aspergillus Toxin: Aspergillus Hemolysin: causes immune dysregulation and is carcinogenic.

Auto-Toxin: Aspergillus Sterigmatocystin: carcinogenic (causes cancer), mutagenic (causes mutations), and teratogenic (causes malformations of the fetus), hepatotoxic (liver); can cause autoimmune diseases.

Penicillium Toxin (mycophynolic acid): causes immune suppression.

Aspergillus/Penicillium Neuro Auto-Toxin (Gliotoxin): causes immune suppression, neurotoxicity, has been linked to multiple sclerosis, immune toxicity.

Stachybotrys Toxin (Trichothecene): is a trichothecene mycotoxin that can cause the following:

- Vascular system: increased vascular fragility (blood vessels), pulmonary hemorrhage or hemorrhage into body tissues.
- Nervous system: tremors, headaches, seizures, sleep disturbance, incoordination, and depression. It can also cause demyelination of nerves leading to Chronic Inflammatory Demyelinating Polyneuropathy (CIDP).
- Digestive system: vomiting, diarrhea, liver toxicity, intestinal hemorrhage, and anorexia. It is a cause of intestinal permeability
- Cutaneous (skin) system: rash, photosensitization, sloughing of skin, burning sensation.
- Endocrine system: decrease in testosterone in men and women; increase in estrogens in men and women.

In conclusion, the World Health Organization has given mycotoxins a well deserved name: The Great Masquerader of the 21st Century.

REFERENCES

Akbari P, Braber S, Gremmels H, et al. Deoxynivalenol: a trigger for intestinal integrity breakdown. FASEB J. 2014;28(6):2414-2429. doi:10.1096/fj.13-238717

- Andersson MA, Nikulin M, Köljalg U, et al. Bacteria, molds, and toxins in water-damaged building materials. Appl Environ Microbiol. 1997;63(2):387-393. doi:10.1128/aem.63.2.387-393.1997
- Anyanwu E, Campbell AW, High W. Brainstem auditory evoked response in adolescents with acoustic mycotic neuroma due to environmental exposure to toxic molds. Int J Adolesc Med Health. 2002;14(1):67-76. doi:10.1515/IJAMH.2002.14.1.67
- Anyanwu EC, Campbell AW, Vojdani A. Neurophysiological effects of chronic indoor environmental toxic mold exposure on children. Scientific WorldJournal. 2003;3:281-290. doi:10.1100/tsw.2003.22
- Anyanwu E, Campbell AW, Jones J, Ehiri JE, Akpan AI. The neurological significance of abnormal natural killer cell activity in chronic toxigenic mold exposures. Scientific World Journal. 2003;3:1128-1137. doi:10.1100/tsw.2003.98
- Anyanwu E. The validity of the environmental neurotoxic effects of toxigenic molds and mycotoxins. Int J Toxicol. 2008;5(2). doi:10.5580/2099b
- Anyanwu E, Ehiri J, Akpan AI. Application, effectiveness, and limitations of the electrophysiological diagnosis of neurotoxic effects of chronic environmental mycotoxins in humans. Int J Adolesc Med Health. 2004;16(2):107-118. doi:10.1515/IJAMH.2004.16.2.107

Anyanwu EC, Morad M, Campbell AW. Metabolism of mycotoxins, intracellular functions of vitamin B12, and neurological manifestations in patients with chronic toxigenic mold exposures. A review. Scientific WorldJournal. 2004;4:736-745. doi:10.1100/tsw.2004.133

- Bin-Umer MA, McLaughlin JE, Basu D, McCormick S, Tumer NE. Trichothecene mycotoxins inhibit mitochondrial translation--implication for the mechanism of toxicity. Toxins (Basel). 2011;3(12):1484-1501. doi:10.3390/toxins3121484
- Bondy GS, Pestka JJ; Genevieve S. Bondy, James J. Pestka. Immunomodulation by fungal toxins. J Toxicol Environ Health B Crit Rev. 2000;3(2):109-143. doi:10.1080/109374000281113
- Boonen J, Malysheva S, et al. Human skin penetration of selected model mycotoxins. Toxicology, vol. 301, no. 1-3, pp. 21-32, 2012.
- Bouslimi A, Ouannes Z, et al. Cytotoxicity and oxidative damage in kidney cells exposed to the mycotoxins Ochratoxin A and citrinin: individual and combined effects. Toxicology Mechanisms and Methods, vol. 18, no. 4, pp. 341-349, 2008.
- Brasel T, Martin J, et al. Detection of airborne Stachybotrys chartarum macrocyclic trichothecene mycotoxins in the indoor environment. Appl Environ Microbiol. 2005 Nov; 71(11):7376-88.
- Brasel T, Campbell A, et al. Detection of trichothecene mycotoxins in sera from individuals exposed to Stachybotrys chartarum in indoor environments. Archives of Environmental Health, vol. 59, no. 6, pp. 317-323, 2004.
- Campbell AW. Lyme Disease and Mycotoxicosis: How to Differentiate Between the Two. Altern Then Health Med. 2019;25(4):8-10.
- Campbell A, Anyanwu E, et al. Combination of High-dose Intravenous Immunoglobulins and Itraconozole in Treating Chronic Mycotic Demyelinating Optic Neuritis. Scientific World Journal, 3:640-646, 2003.
- Campbell A. Thrasher J. et al. Mold and Mycotoxins: Effects on the Neurological and Immune Systems in Humans. Advances in applied microbiology, 2004. 55:375-406.
- Campbell A, Thrasher J, et al. Neural autoantibodies and neurophysiologic abnormalities in patients exposed to molds in water-damaged buildings. Arch Environ Health. 2003 Aug 58(8):464-74.
- Casula G, Cutting S, Bacillus Probiotics: Spore Germination in the Gastrointestinal Tract. Appl Environ Microbiol. 2002;(May):2344-2352.
- Clark H, Snedeker S. Ochratoxin A: its cancer risk and potential for exposure. J Toxicol Environ Health B Crit Rev. 2006;9(3):265-296. doi:10.1080/15287390500195570
- Creasia D, Thurman J, et al. Acute inhalation toxicity of T-2 mycotoxin in mice. Fundamental and Applied Toxicology 1987: 8: 230-235.
- Creasia D, Thurman J, et al. Acute Inhalation toxicity of T-2 Mycotoxin in the Rat and Guinea Pig. Fundamental and Applied Toxicology, vol. 14, no. 1, pp. 54-59, 1990.
- Dearborn D, Smith P, et al. Clinical profile of 30 infants with acute pulmonary hemorrhage in Cleveland. Pediatrics 2002, 110(3):627-37.
- De Santis B, Raggi M, et al. Study on the Association among Mycotoxins and other Variables in Children with Autism. Toxins 2017, 9, 203.
- Doi K, Uetsuka K. Mechanisms of mycotoxin-induced neurotoxicity through oxidative stress-associated pathways. Int J Mol Sci. 2011;12(8):5213-5237. doi:10.3390/ijms12085213
- Empting LD. Neurologic and neuropsychiatric syndrome features of mold and mycotoxin exposure. *Toxicol Ind Health*. 2009;25(9-10):577-581. doi:10.1177/0748233709348393
- Etzel RA, Montaña E, Sorenson WG, Kullman GJ, Allan TM, Dearborn DG. Acute pulmonary hemorrhage in infants associated with exposure to Stachybotrys atra and other fungi. Arch Pediatr Adolesc Med. 1998;152(8):757-762. doi:10.1001/archpedi.152.8.757 Etzel R, Rylander R. Indoor Mold and Children's Health. Environ Health Perspect. 1999;107(suppl
- 3):463. doi:10.1289/ehp.107-1566224
- Etzel, R. Toxic Effects of Indoor Molds. American Academy of Pediatrics, Committee on Environmental Health, Vol 101, No. 4, April 1998.
- Etzel, R. What the Primary Care Pediatrician Should Know about Syndromes Associated with Exposures to Mycotoxins. Curr Probl Pediatr Adolesc Health Care. 2006;(September):282-305. Etzel RA. Mycotoxins. JAMA. 2002;287(4):425-427. doi:10.1001/jama.287.4.425

- Garg K, Villavicencio-Aguilar F, Solano-Rivera F, Gilbert L. Analytical Validation of a Direct Competitive ELISA for Multiple Mycotoxin Detection in Human Serum. Toxins (Basel). 2022;14(11):727. doi:10.3390/toxins14110727
- Gharbi A, Trillon O, et al. Some effects of ochratoxin A, a mycotoxin contaminating feeds and food, on rat testis. Toxicology. 1993 Oct 25;83(1-3):9-18. Gordon K, Masotti, R. et al. Tremorgenic encephalopathy: a role of mycotoxins in the production of CNS
- disease in humans? Can J Neurol Sci. 1993 Aug;20(3):237-9.
- Gordon WA, Cantor JB. The diagnosis of cognitive impairment associated with exposure to mold. Adv Appl Microbiol. 2004;55:361-374. doi:10.1016/S0065-2164(04)55014-1
- Gordon W, Cantor J, et al. Cognitive impairment associated with toxigenic fungal exposure: a replication and extension of previous findings. *Applied Neuropsychology* 2004, 11 (2), 65-74. Gottschalk C, Bauer J, et al. Detection of satratoxin G and H in indoor air from a water-damaged
- building. Mycopathologia. 2008 Aug;166(2):103-7.
- Gray M, Thrasher J, et al. Mixed mold mycotoxicosis: immunological changes in humans following exposure in water-damaged buildings. Arch Environ Health, 2003 Jul; 58(7):410-420.

Hong, H, Duc, L, et al. The use of bacterial spore formers as probiotics. *FEMS Microbiol.* 2005, Rev. 29, 813-835.

- Indoor Environmental Quality: Dampness and Mold in Buildings. National Institute for Occupational Safety and Health. August 1, 2008.
- International Agency for Research on Cancer (IARC) RE: Ochratoxin A. Monographs on the Evaluation of Carcinogenic Risks to Humans. International Agency for Research on Cancer. IARC; 1993.
- Islam Z, Amuzie C, et al. Neurotoxicity and inflammation in the nasal airways of mice exposed to the macrocyclic trichothecene mycotoxin roridin A: kinetics and potentiation by bacterial lipopolysaccharide coexposure. *Toxicological Sciences*, vol. 98, no. 2, pp. 526–541, 2007.
- Islam Z, Pestka JJ. Role of IL-1 (beta) in endotoxin potentiation of deoxynivalenol-induced corticosterone response and leukocyte apoptosis in mice. *Toxicol Sci.* 2003;74(1):93-102. doi:10.1093/toxsci/kfg119
- Islam Z, Harkema J, et al. Satratoxin G from the black mold Stachybotrys chartarum evokes olfactory sensory neuron loss and inflammation in the murine nose and brain. *Environ Health Perspect*. 2006 Jul; 114(7):1099-107.
- Islam Z, Hegg C, et al. Satratoxin G-induced apoptosis in PC-12 neuronal cells is mediated by PKR and caspase independent Toxicol Sci. 2008 Sep;105(1):142-52. Epub 2008 Jun 4 Center for Integrative Toxicology, Michigan State University, East Lansing, Michigan 48824-1224, USA.
- Islam Z, Nagase M, et al. Structure-function relationship of T-2 toxin and its metabolites in inducing thymic apoptosis in vivo in mice. *Biosci Biotechnol Biochem*. 1998 Aug;62(8):1492-7.
- Islam Z, Amuzie C, et al. Neurotoxicity and inflammation in the nasal airways of mice exposed to the macrocyclic trichothecene roridin A: Kinetics and potentiation by bacterial lipopolysaccharides. *Toxicol Sci* 2007; 98:526-41.
- Jarvis BB, Miller JD. Mycotoxins as harmful indoor air contaminants. Appl Microbiol Biotechnol. 2005;66(4):367-372. doi:10.1007/s00253-004-1753-9
- Jedrychowski W, Maurgeri U, et al. Cognitive impairment of 6-year old children exposed to moldcontaminated homes in early postnatal period. Prospective birth cohort study in Poland. *Physiology* and Behavior 2011 204:989-95.
- Jørgensen K. Survey of pork, poultry, coffee, beer and pulses for ochratoxin A. Food Addit Contam. 1998;15(5):550-554. doi:10.1080/02652039809374680
- Kankkunen P, Rintahaka J, et al. Trichothecene mycotoxins activate inflammatory response in human macrophages. *Journal of Immunology*, vol. 182, no. 10, pp. 6418–6425, 2009.
 Karunasena E. The mechanisms of neurotoxicity induced by a Stachybotrys chartarum trichothecene
- Karunasena E. The mechanisms of neurotoxicity induced by a Stachybotrys chartarum trichothecene mycotoxin in an in vitro model. A dissertation in microbiology and immunology, submitted to the graduate faculty of Texas Tech University Health Sciences Center for the degree of Doctor of Philosophy. i-ix, 1-114.
- Karunasena E, Larranaga M, et al. Building-associated neurological damage modeled in human cells: a mechanism of neurotoxic effects by exposure to mycotoxins in the indoor environment. *Mycopathologia* 2010;170:377-390.
- Kilburn K. Role of molds and mycotoxins in being sick in buildings: neurobehavioral and pulmonary impairment Adv Appl Microbiol. 2004; 55:339-59. University of Southern California Keck School of Medicine Environmental Sciences Laboratory Alhambra, California 91803, USA.
- Kilburn KH. Indoor mold exposure associated with neurobehavioral and pulmonary impairment: a preliminary report. Arch Environ Health. 2003;58(7):390-398. doi:10.1080/00039896.2003.11879139
- Kilburn KH. Neurobehavioral and pulmonary impairment in 105 adults with indoor exposure to molds compared to 100 exposed to chemicals. *Toxicol Ind Health.* 2009;25(9-10):681-692. doi:10.1177/0748233709348390
- Kilburn K, Thrasher J, el al. Do terbutaline- and mold-associated impairments of the brain and lung related to autism? *Toxicol Ind Health*. 2009;25:681-692.
- Kosalec F, Klaric M, et al. Verruculogen production in airborne and clinical isolates of Aspergillus fumigatus. *Acta Pharm.* 2005 Dec;55(4):357-64.
- Kőszegi T, Poór M. Ochratoxin A: Molecular Interactions, Mechanisms of Toxicity and Prevention at the Molecular Level. Toxins (Basel). 2016;8(4):111. doi:10.3390/toxins8040111
- Kouadio J, Dano S, et al. Effects of combinations of Fusarium mycotoxins on the inhibition of macromolecular synthesis, malondialdehyde levels, DNA methylation and fragmentation, and viability in Caco-2 cells. *Toxicon* 2007; 49(3): 306-317.
- Kouadio J, Mobio T, et al. Comparative study of cytotoxicity and oxidative stress induced by deoxynivalenol, zearalenone or fumonisin B1 in human intestinal cell line Caco-2. *Toxicology* 2005; 213(1-2): 56-65.
- Lichtenstein J, et al. Environmental Mold and Mycotoxin Exposures Elicit Specific Cytokine and Chemokine Responses. PLOS ONE doi:10.1371/journal.pone.0126926 May 26, 2015.
- Lieberman A, Curtis L, et al. Development of new-onset chronic inflammatory demyelinating polyneuropathy following exposure to a water-damaged home with high airborne mold levels: a report of two cases and a review of the literature. J Neurol Res, 2017, 7(3), 59-62.
- Liu J, Wang Y, et al. Ochratoxin A induces oxidative DNA damage and G1 phase arrest in human peripheral blood mononuclear cells in vitro. Toxicology Letters, vol. 211, no. 2, pp. 164–171, 2012. Malir F, Ostry V, et al. Ochratoxin A: 50 years of research. *Toxins*, 2016, 8, 191; doi:10.3390/toxins8070191.
- Mandel D, Eichas K, et al. Bacillus coagulans: a viable adjunct therapy for relieving symptoms of rheumatoid arthritis according to a randomized, controlled trial. *BMC Complement Altern Med.* 2010 [an 12:10:1.
- Marseglia G, Tosca M, et al. Efficacy of Bacillus clausii spores in the prevention of recurrent respiratory infections in children: a pilot study. *Ther Clin Risk Manag.* 2007 Mar;3(1):13-7.
- Martin L, Doebler J, et al. Scanning cytophotometric analysis of brain neuronal nuclear chromatin changes in acute T-2 toxin-treated rats. *Toxicol Appl Pharmacol* 1986; 85(2): 207-214.
- Martin LJ, Morse JD, Anthony A. Quantitative cytophotometric analysis of brain neuronal RNA and protein changes in acute T-2 mycotoxin poisoned rats. *Toxicon*. 1986;24(9):933-941. doi:10.1016/0041-0101(86)90093-0
- Meloche JL, Smith TK. Altered tissue amino acid metabolism in acute T-2 toxicosis. Proc Soc Exp Biol Med. 1995;210(3):260-265. doi:10.3181/00379727-210-43947
- Mor F, Kilic MA, et al. The effects of orchidectomy on toxicological responses to dietary ochratoxin A in Wistar rats. *Exp Toxicol Pathol.* 2014 Aug;66(5-6):267-75.
- Nagase M, Alam M, et al. Apoptosis induction by T-2 toxin: activation of caspase-9, caspase-3, and DFF-40/CAD through cytosolic release of cytochrome c in HL-60 cells. *Biosci Biotechnol Biochem*. 2001 Aug; 65(8):1741-7.
- Omar R, Gelboin H, et al. Effect of cytochrome P450 induction on the metabolism and toxicity of ochratoxin A. *Biochemical Pharmacology*, vol. 51, no. 3, pp. 207–216, 1996.
- Peraica M, et al. Bulletin of the World Health Organization (WHO). Toxic Effects of Mycotoxins in Humans. 1999.
- Pfohl-Leszkowicz, A.; Petkova-Bocharova, T, et al. Balkan Endemic Nephropathy and associated Urinary tract tumours: A review on aetiological causes and the potential role of mycotoxins. *Food Addit. Contam.* 2002, 19, 282–302.
- Ponikau E, Frigas J, et al. The diagnosis and incidence of allergic fungal sinusitis. Mayo Clinic Proceedings, vol. 74, no. 9, pp. 877–884. 1999.

- Rea W, Pan Y, et al. The Treatment of Patients with Mycotoxin-induced Disease. Toxicology and Industrial Health 25(9-10) 711-714.
- Reijula K, Tuomi T. Mycotoxins of aspergilli: exposure and health effects. *Front Biosci*. 2003;8(5):s232-s235. doi:10.2741/978
- Rogowska A, Pomastowski P, Sagandykova G, Buszewski B. Zearalenone and its metabolites: effect on human health, metabolism and neutralisation methods. *Toxicon*. 2019;162:46-56. doi:10.1016/j. toxicon.2019.03.004
- Rosenblum Lichtenstein J, Hsu Y-H, et al. Environmental Mold and Mycotoxin Exposures Elicit Specific Cytokine and Chemokine Responses. 2015. PLoS ONE 10(5): e0126926. doi:10.1371/journal. pone.0126926.
- Sava, V.; Reunova, O. et al. Acute neurotoxic effects of the fungal metabolite Ochratoxin A. Neurotoxicology 2006, 27, 82–92.
- Schoental R. Fusarial mycotoxins and behaviour: possible implications for psychiatric disorder. Br J Psychiatry, 1985;146(2):115-119. doi:10.1192/bjp.146.2.115
- Skaug M, Eduard W, et al. Ochratoxin A in airborne dust and fungal conidia. *Mycopathologia* 2001; 151(2): 93-98.
- Smoragiewicz W, Cossette B, et al. Trichothecene mycotoxins in the dust of ventilation systems in office buildings. Int Arch Occup Environ Health 1993; 65: 113-117.
- Sohaug A, Eriksen G, et al. Mechanisms of Action and Toxicity of the Mycotoxin Alternariol: Review A. Basic Clin Pharmacol Toxicol. 2016;119:533-539. doi:10.1111/bcpt.12635
- Sorenson W, Frazer D, et al. Trichothecene mycotoxins in aerosolized conidia of Stachybotrys atra. Applied and Environmental Microbiology 1987; 53(6): 1370-1375.
- prando R, Collins TF, et al. Characterization of the effect of deoxynivalenol on selected male reproductive endpoints. *Food Chem Toxicol.* 2005 Apr;43(4):623-35.
 Stypuła-Trębas S, Minta M, et al. Nonsteroidal mycotoxin alternariol is a full androgen agonist in the
- yeas reporter androgen bioassay. Environ Toxicol Pharmacol. 2017 Oct;55:208-211.
- U.S. Army Medical Research and Development Command with the College of Veterinary Medicine, University of Illinois. Toxicologic and Analytical Studies with T-2 and Related Trichothecene Mycotoxins. August 20, 1985.
- Vojdani A, Thrasher J, et al. Antibodies to molds and satratoxin in individuals exposed in waterdamaged buildings. Archives of Environmental Health, An International Journal 08/2003; 58(7):421-32.
- Wang J, Fitzpatrick D, et al. Effects to the trichothecene T-2 toxin on neurotransmitters and metabolites in discrete areas of the rat brain. *Food & Chemical Toxicol*. 1998, 36:947-953.
- Wang J, Fitzpatrick D, et al. Effects to the trichothecene T-2 toxin on blood-brain barrier permeability monoamine oxidase activity and protein synthesis in rats. *Food & Chemical Toxicol*.1998, 36,955-961.Wannemacher RW, Wiener SL. Trichothecene Mycotoxins. Textbook of Military Medicine: Medical Aspects of Chemical and Biological Warfare: Chapter 34.
- Yang JY, Zhang YF, et al. Effects of T-2 toxin on the regulation of steroidogenesis in mouse Leydig cells. Toxicol Ind Health. 2016 Oct;32(10):1801-7.
- Yike I, Distler A, et al. Mycotoxin adducts on human serum albumin: biomarkers of exposure to Stachybotrys chartarum. Environmental Health Perspectives 2006; 114(8): 1221-1226.