Mycotoxins: The Hidden Threat of Mold to Our Bodies and Brains

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Mycotoxins are some of the most prevalent toxins in the environment. These molecules are secondary metabolites of fungi.[1] Most humans are exposed to mycotoxins through mold, which can be found growing in buildings, vehicles, and foodstuffs. Mold can grow on almost any surface, especially if the environment is warm and wet. Inner wall materials of buildings, wall paper, fiber glass insulation, ceiling tiles, and gypsum support are all good surfaces for mold to colonize. The mold can then release mycotoxins into the environment causing symptoms of many different chronic diseases. Diseases and symptoms linked to mycotoxin exposure include immune-suppression, fever, pneumonia-like symptoms, heart disease, rheumatic disease, asthma, sinusitis, cancer, memory loss, vision loss, chronic fatigue, skin rashes, depression, ADHD, anxiety, and liver damage.[2,3]

Mycotoxins are absorbed in the mucosal epithelia in the airways and the gut and can affect many immune-related organs and cell types.[4] These interactions suppress immune functions. Multiple types of mycotoxins can cause a decrease in B cells, white blood cells, and hematopoietic stem cells.[5,6] Exposure to mycotoxins decreases the amount of mature CD4+ cells and splenic T lymphocytes.[7] This exposure will also affect different groups of cytokines. IL-2 production and IL-2 receptors are decreased, but IL-17, IL-10, TGF-α, and MIP-1β are all elevated. These changes in cytokine expression can lead to enhanced tissue damage to multiple different tissues and organs.[8]

Mycotoxins and the Brain

One of the main organs affected by mycotoxins is the brain.[9] Mycotoxin inhibition of protein synthesis, damage to DNA, and increased production of inflammatory cytokines lead to damage of the central nervous system (CNS).[10] Mycotoxins also affect the proliferation and migration of neurons.[11] Neurotoxicity is most pronounced in the ventral mesencephalon, hippocampus, and striatum.[12] The blood brain barrier, which is a selective permeable barrier protecting the brain, can be damaged by mycotoxins. Trichothecenes can cause cytotoxic effects at the blood brain barrier, which will allow other harmful chemicals and pathogens to affect the brain.[13] In the brain, proinflammatory cytokine interleukin 1β is produced during mycotoxin exposure.[14] Damage caused by mycotoxin exposure can lead to depression, poor memory recall, Alzheimer's-like symptoms, and headaches.[15]

Introducing the GPL-MycoTOX Profile

At The Great Plains Laboratory, Inc., we have a primary focus on helping patients with chronic illnesses, including mental health disorders. We have developed tests that look at hundreds of different analytes and have worked with doctors to help them interpret how these data can be used to personalize treatment for patients. Our newest test, the GPL-MycoTOX Profile (a urine test), was developed to combat the pervasive problem of mold exposure. We have heard from our clients that the marketplace lacked an accurate and affordable test to measure mycotoxins. We decided to use our expertise in liquid chromatography mass spectrometry (LC/MS) to meet this need. Using this technology, we have a very sensitive test, which is important because mycotoxins can cause serious health issues even in small quantities. Other mycotoxin testing uses ELISA technology, which relies on antibodies. Utilization of LC-MS/MS technology gives us a precise identification of all of our analytes, which prevents having false positive errors. For many of our compounds we are able to detect amounts in the parts per trillion (ppt), which is about 100-fold better than any other test currently available.

Species of Mold

We are currently measuring seven different markers in our test from multiple species of mold. This makes the GPL-MycoTOX Profile the most comprehensive mycotoxin test on the market. It is also the most cost-effective. Here are four of the genuses of mold we

are evaluating: *Aspergillus, Penicillium, Stachybotrys,* and *Fusarium.*

Aspergillus is the most prevalent mold group in the environment. It has caused billions of dollars in damage to crops and livestock. The most common *Aspergillus* mycotoxins are aflatoxin, ochratoxin, patulin, and fumagillin. The main target of these toxins is the liver. These toxins have been found in all major cereal crops including peanuts, corn, cotton, millet, rice, sorghum, sunflower seeds, wheat, and a variety of spices. They are also found in eggs, milk, and meat from animals fed contaminated grains. Diseases caused by *Aspergillus* are called aspergillosis. The most common route of infection is through the respiratory system. *Aspergillus* can cause severe asthma when the mold colonizes the lung, forming a granulomatous disease.[16]

There are over 200 species of *Penicillium* that have been discovered. It is often found in indoor environments and is responsible for many allergic reactions. *Penicillium* is also a known contaminate in many different food items. Several different types of citrus fruits can become contaminated with *Penicillium*, but it can also contaminate seeds and grains. One reason that *Penicillium* is so common is because of its ability to thrive in low humidity. In the home, Penicillium can be found in wallpaper, carpet, furniture, and fiberglass insulation. The most common mycotoxin produced by Penicillium is ochratoxin. Ochratoxin is nephrotoxic, which means that it damages the kidneys. It is also carcinogenic.[17]

Stachybotrys is a greenish-black mold. This mold can grow on materials with high cellulose and low nitrogen content such as gypsum board, paper, fiberboard, and ceiling tiles. *Stachybotrys* is known for its production of the highly toxic macrocyclic trichothecene mycotoxins, which can be extremely neurotoxic. Two of the more common mycotoxins produced by *Stachybotrys* are roridin E and verrucarin. In addition to these mycotoxins, the fungus produces nine phenylspirodrimanes, as well as cyclosporine, which are potent immunosuppressors. These immunosuppressors, along with the mycotoxin trichothecenes, may be responsible for the high toxicity of *Stachybotrys*.[16]

Fusarium's major mycotoxins are zearalenone (ZEN) and fumonisin. *Fusarium* fungi grow best in temperate climate conditions. They require lower temperatures for growth than *Aspergillus*. *Fusarium* grows worldwide on many different types of grains including corn and wheat. Exposure to mycotoxins from *Fusarium* can lead to both acute and chronic effects. These symptoms can include abdominal distress, malaise, diarrhea, emesis, and death. ZEN possesses estrogenic effects and has been implicated in reproductive disorders.[18]

Markers in the GPL-MycoTOX Profile

The seven different markers for mycotoxins in our GPL-MycoTOX Profile provide extensive coverage, allowing us to catch most mold exposures.

Aflatoxin M1: Aflatoxin M1 (AFM1) is the main metabolite of aflatoxin B1, which is a mycotoxin produced by the mold genus *Aspergillus*. Aflatoxins are some of the most carcinogenic substances in the environment. Aflatoxin susceptibility is dependent on multiple different factors such as age, sex, and diet. Aflatoxin can be found in beans, corn, rice, tree nuts, wheat, milk, eggs, and meat. In cases of lung aspergilloma, aflatoxin has been found in human tissue specimens. Aflatoxin can cause liver damage, cancer, mental impairment, abdominal pain, hemorrhaging, coma, and death. Aflatoxin has been shown to inhibit leucocyte proliferation. Clinical signs of aflatoxicosis are non-pruritic macular rash, headache, gastrointestinal dysfunction (often extreme), lower extremity edema, anemia, and jaundice. The toxicity of aflatoxin is increased in the presence of ochratoxin and zearalenone.[19]

Ochratoxin: Ochratoxin A (OTA) is a nephrotoxic, immunotoxic, and carcinogenic mycotoxin. This chemical is produced by molds in the *Aspergillus* and *Penicillium* genuses. Exposure is primarily through contaminated foods such as cereals, grape juices, dairy, spices, wine, dried vine fruit, and coffee. Exposure to OTA can also come from inhalation exposure in water-damaged buildings. OTA can lead to kidney disease and adverse neurological effects. Studies have shown that OTA can cause significant oxidative damage to multiple brain regions and the kidneys. Dopamine levels in the brain of mice have been shown to be decreased after exposure to OTA.[20]

Sterigmatocystin (STC): STC is a mycotoxin that is closely related to aflatoxin. STC is produced from several genuses of mold such as *Aspergillus*, *Penicillium*, and *Bipolaris*. It is considered to be carcinogenic, particularly in the cells of the GI tract and liver. STC has been found in the dust from damp carpets. It is also a contaminant of many foods including grains, corn, bread, cheese, spices, coffee beans, soybeans, pistachio nuts, and animal feed. In cases of lung aspergilloma, STC has been found in human tissue specimens. The toxicity of STC affects the liver, kidneys, and immune system. Tumors have been found in the lungs of rodents that were exposed to STC. Oxidative stress becomes measurably elevated during STC exposure, which causes a depletion of antioxidants such as glutathione, particularly in the liver.[21]

Zearalenone (ZEN): ZEN is a mycotoxin that is produced by the mold *Fusarium*, and has been shown to be hepatotoxic, haematotoxic, immunotoxic, and genotoxic. ZEN is commonly found in several foods in the US, Europe, Asia, and Africa including wheat, barley, rice, and maize. ZEN has estrogenic activity and exposure to ZEN can lead to reproductive changes. ZEN's estrogenic activity is higher than that of other non-steroidal isoflavones (compounds that have estrogen-like effects) such as soy and clover. ZEN exposure can result in thymus atrophy and alter spleen lymphocyte production as well as impair lymphocyte immune response, which leads to patients being susceptible to disease.[22]

Roridin E and Verrucarin A: Roridin E and verrucarin A are macrocyclic trichothecenes produced by the mold genuses *Fusarium*, *Myrothecium*, and *Stachybotrys* (i.e.

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black mold). Trichothecenes are frequently found in buildings with water damage but can also be found in contaminated grain. These are very toxic compounds, which inhibit protein biosynthesis by preventing peptidyl transferase activity. Trichothecenes are considered extremely toxic and have been used as biological warfare agents. Even low levels of exposure to macrocyclic trichothecenes can cause severe neurological damage, immunosuppression, endocrine disruption, cardiovascular problems, and gastrointestinal distress.[23]

Enniatin B: This is a fungal metabolite categorized as a cyclohexa depsipeptides toxin produced by the fungus *Fusarium*. This fungus is one of the most common cereal contaminants. Grains in many different countries have recently been contaminated with high levels of enniatin. The toxic effects of enniatin are caused by the inhibition of the acyl-CoA cholesterol acyltransferase, depolarization of mitochondria, and inhibition of osteoclastic bone resorption. Enniatin has antibiotic properties, and chronic exposure may lead to weight loss, fatigue, and liver disease.[24]

Summary

Mycotoxins from mold are some of the most common and toxic compounds we are exposed to, and they can be incredibly harmful to our mental and physical health. The neurotoxicity caused by mycotoxins can lead to a variety of neurological and neuropsychiatric problems including depression, memory loss, and Alzheimer's-like symptoms. Mycotoxins also cause many other health problems and can be carcinogenic. The Great Plains Laboratory, Inc. offers cutting-edge diagnostic tools that help identify underlying causes of symptoms like these and provides recommendations for treatment based on test results. The new GPL-MycoTOX Profile is a highly accurate and affordable urine test for mycotoxin exposure that can be run with our other urine tests including the Organic Acids Test (OAT), GPL-TOX (Toxic Non-Metal Chemical Profile), and the Phospholipase A2 Activity Test (PLA2). All of these tests are incredibly clinically useful in the assessment of underlying contributors to mental health and neurological disorders. Utilizing this combination of tests will help practitioners discover the underlying causes of many of their patient's symptoms, whether neurological, psychiatric, or otherwise.

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