Health Consequences of Mold and Mycotoxin Exposure
Part 2: Toxicity and Laboratory Testing

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In Part 1 of this article series titled Health Consequences of Mold and Mycotoxin Exposure, I discussed different aspects of immune reactivity to mold and related fungus. As a quick review, a mold compared to a yeast (e.g., candida) is defined as “A fungus that grows in the form of multicellular filaments called hyphae. In contrast, fungi that can adopt a single-celled growth habit are called yeasts” (1). Candida is a type of yeast. One of the most common mold species – Aspergillus – is not a yeast, but a fungus.

It is well established that molds can produce chemical compounds called mycotoxins (myco = of fungal origin). These mycotoxins, as secondary metabolites (2), have various adverse health effects and can cause severe disease and death in animals and humans (3). This article will discuss commonly encountered mycotoxins and the use of urine assessment to detect certain mold toxins produced by Aspergillus, Penicillium, and Fusarium species, as well as Stachybotrys chartarum (toxic black mold). The specific mycotoxins outlined below are Ochratoxin A, Gliotoxin, Mycophenolic, Verrucarin A, and Zearalenone. This list represents a cross-section of commonly encountered mycotoxins produced from the previously mentioned molds.

**Ochratoxin A**

Ochratoxin A (OTA) is produced by Aspergillus (and certain Penicillium) mold (4, 5). It has various health-associated toxic properties, including being carcinogenic and immunotoxic (6). Exposure to OTA can occur when Aspergillus mold contaminates foods such as cereal grains, coffee, dairy products (from cow’s eating mold contaminated hay), and certain fruits. OTA is also produced by Aspergillus molds that grow in water-damaged material found in homes, office buildings, and schools.

There are many physiological disturbances that can occur from OTA exposure, including kidney damage (7) and neurologic reactivity to the cerebellum, basal ganglia, and hippocampus (8). Alzheimer’s and Parkinson’s are two neurodegenerative disorders that are linked to problems in the hippocampal and basal ganglia areas of the brain, respectively. The destruction of dopaminergic producing cells from OTA (9) has links to Parkinson’s as well.

**Gliotoxin**

Gliotoxin (GTX) is another commonly encountered mycotoxin produced from Aspergillus mold (10). GTX has various immunotoxic properties that allow it to evade the host immune system. For example, GTX can suppress various cells of the innate immune system, including neutrophils, eosinophils, and macrophages (11). GTX also impairs T-cell activation compromising lymphocyte proliferation and antibody production (12).

A major problem with GTX is its ability to damage cell membrane integrity and function (11). This not only affects membrane function with regard to cellular activities, i.e., protein transport, second messenger signaling, but also mitochondrial membrane integrity. The mitochondria contain two membranes, inner and outer, and it’s the inner mitochondrial membrane which houses the electron transport chain linked to robust adenosine triphosphate (ATP) production. GTX through its effects on cellular membrane activity can lead to mitochondrial damage (12) compromising ATP output.
**Mycophenolic**

Mycophenolic (MPA) has been used as an immunosuppressive compound in pharmaceutical medications for transplant patients (e.g., kidney). This mycotoxin, produced by *Penicillium* fungus, is often associated with exposure to the mold in water-damaged building material (13). One of its primary modes of activity for immune suppression is the blocking of guanosine nucleotide production in lymphocytes (14). This leads to a selective inhibition of DNA replication in T cells and B cells. Because of its adverse effects on T cells and B cells there is increased risk for secondary infections (e.g., viral), and reduced production of antibodies from B cells.

Secretory IgA, which is derived from plasma cell (coming from B cells) production of systemic IgA, is the main antibody produced along the mucosal surface of the digestive and upper respiratory systems. Immunotoxic mycotoxins such as MPA can lead to poor mucosal immune function and subsequent gut pathogen overgrowth.

MPA is also associated with various autoimmune conditions such as Bechet’s (affecting various parts of the body, including the eyes, mouth, and joints), psoriasis, and small vessel vasculitis (15). Finally, MPA can affect a normal pregnancy in women exposed to this toxic compound. Congenital malformations and miscarriages are associated with MPA toxicity (16).

**Verrucarin A**

Verrucarin A (VRA) is included in a group of mycotoxins called trichothecenes. This family of chemically related compounds are linked to various species of molds such as *Cephalosporium, Fusarium, Stachybotrys*, and *Trichoderma*. Certain molds that produce trichothecene mycotoxins, such as *Stachybotrys chartarum*, can grow in damp indoor environments. It has been found that trichothecenes produced by *S. chartarum* can become airborne and contribute to health problems among occupants in buildings (17).

The toxicity mechanisms of action of trichothecenes, including VRA, are broad and complex. However, they primarily interfere with protein synthesis (18). This protein synthesis interference occurs at the level of the ribosome and has wide spreading effects throughout the cell. For example, the mitochondria are dependent on protein synthesis. If mitochondrial protein synthesis is disrupted, there is increased risk for reactive oxygen species production damaging mitochondrial DNA and affecting membrane stability and function (19).

**Zearalenone**

Zearalenone (ZEA) is a *Fusarium* mold-associated mycotoxin. It has a wide array of toxicities, including being hepatotoxic, hemotoxic, and immunotoxic. Its immunotoxic effects are linked to atrophy of the thymus gland, compromising T-cell formation and release. The spleen can be affected too.

*Fusarium* species can produce various toxins which can be detrimental to livestock, but also to humans. ZEA is associated with spontaneous abortions, infertility, and through its estrogenic properties it can interact with estrogen receptors (20). There is concern for early female development with chronic exposure to ZEA (21).

ZEA is found in contaminated foods such as barley, corn, rice, and wheat (22). Because it is heat stable it has a strong ability to resist degradation, which is why it is a worldwide mycotoxin found in so many different food sources and supplies (23).
Review of Examples of Immune Reactions to Mold

Because molds are environmentally ubiquitous and mold spores are a common component of soil, certain food products, and dust particles in our homes and workplaces, exposure to mold is not uncommon.

When it comes to common indoor molds, the grouping of Alternaria, Aspergillus, Cladosporium, and Penicillium are most common (24). Fusarium and Stachybotrys are more common with significant water damage. When mold spores are present in large quantities, they can trigger allergic reactions which include nasal congestion, itching, sneezing, as well as respiratory problems such as coughing and wheezing (25).

A mold allergy is an abnormal immune reaction mediated through immunoglobulin E (IgE) production in response to exposure to mold spores or cellular components of the mold. This IgE antibody, which binds with mast cells, can initiate a cascade of chemicals such as histamine, eicosanoids, and cytokines (e.g., interleukin 6) which drive inflammatory reactions. These reactions can be mild (sneezing, coughing) or more severe such as reactive airway disease (26).

When mold spores are inhaled intact, they can embed in lung tissue and begin to grow as an infection. This is particularly serious for anyone already immunocompromised. This type of infection is called aspergillosis and can ultimately lead to invasive aspergillosis (27).

Sick building syndrome (28) is a type of sensitivity where people have heightened symptoms and health problems when they encounter environments known to have mold exposure. There have been multiple papers written on this subject, including a 2018 review of 16 associated studies evaluating sick building syndrome. This study concluded that individuals exposed to molds and associated mycotoxins had “symptoms affecting multiple organs, including the lungs, musculoskeletal system, as well as the central and peripheral nervous systems” (29).

The symptoms associated with sick building syndrome could occur in almost anyone with mold illness and is likely associated with mycotoxin exposure and toxicity. Not everyone experiences mold exposures in the same way. Some people have primarily allergic and immune sensitivity reactions to mold spore exposure, while others can have associated health conditions brought about by mycotoxin induced cellular damage that may manifest as cancer.

It is critical for any practitioner working with a mold-exposed individual to have a broad understanding of the various reactivity mechanisms and adverse health effects of mold and mold toxins.

Mycotoxin Testing

There are various methods for analyzing the existence of mycotoxins in the body. Two popular methods used by many laboratories is the enzyme-linked immunosorbent assay (ELISA) and liquid chromatography-mass-spectrometry (LC-MS). Both methods can detect the presence of mycotoxins that have accumulated in the body from ongoing or previous mold exposure:

ELISA – specific antigens (a substance that can stimulate the production of an antibody) are attached to a binding surface (typically a polystyrene microtiter plate). A matching antibody (immune protein) is applied over the surface of the binding plate to allow the antibody a chance to bind to the antigen. The specific binding antibody is linked to an enzyme which then reacts with an added enzyme substrate. The substrate-enzyme reaction produces a color change signal indicating a positive match and identified antigen, i.e., a specific mycotoxin.
LC-MS – this method is popular in chemical analysis because each technique (both the liquid chromatography and mass spectrometry) is synergistically enhanced. The liquid chromatography separates multiple chemical components, while the mass spectrometry provides structural identity of the individual components with high molecular specificity and chemical detection sensitivity. In essence, this method provides high accuracy of chemical detection of seemingly similar appearing compounds.

In the context of mycotoxin detection, both methods help to identify the existence of various mycotoxins. The ELISA method tends to work off a “lock and key” mechanism. There may be more false positive results (depending on certain variables within the testing method) that can occur if two antigens have a similar structure and bind an enzyme-linked antibody. The LC-MS method seems to have enhanced abilities to analyze specific chemical configurations and greatly reduces the false positive detection of similar appearing compounds.

My preference in clinical practice is to use a laboratory that provides the liquid chromatography-mass spectrometry method of detection.

In the third and final part of this series, I will explore various intervention options for mold and mycotoxin exposure, both from a conventional medicine and integrative medicine standpoint, as it is important to understand the pros and cons of each.

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REFERENCES