PERSPECTIVE

Understanding Mycotoxin-induced Illness: Part 1

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Molds are an ubiquitous type of fungus in our environment, with filaments that grow into hyphae. As a protection, these hyphae release spores called mycotoxins, which are the compounds that trigger the immune system and cause disease in humans. One mold can release multiple types of mycotoxins that can be toxic to different organs in the body. Because of this, mycotoxin illness can create multiple symptoms and be difficult to identify.

Awareness that mycotoxins from mold can cause systemic illness is increasing among practitioners who treat chronic disease. As early as 1994, research showed water damage in up to 50% of US households.[1] With climate change and the increase in storms, estimates are now higher.[2] Water-damaged buildings contain molds together with toxic bacteria, endotoxins, protozoa, and volatile chemicals from deterioration of building materials.[3] The primary mycotoxins that have been found in water-damaged buildings include aflatoxins, ochratoxins, and trichothecenes.[4]

Worldwide, mycotoxin exposure can also be from food. Six mycotoxins are regularly found in food, including aflatoxins, trichothecenes, zearalenone, fuminisins, ochratoxins, and patulin.[5] The mycotoxin aflatoxin from Aspergillus is estimated to contaminate 25% of the world's food supply.[6] This impact seems to be the greatest in developing countries. Aflatoxin exposure alone can contribute to poor outcomes in pregnancy and in children, in addition to chronic adult illness.[6]

TYPES OF MOLDS AND MYCOTOXINS

Molds exist in all environments, and our exposure can occur in many ways, from food to indoor and outdoor air. Molds can grow anywhere with moisture and oxygen, which is why humid, moist environments and water damage are risk factors. The molds themselves are easy to eradicate, but their mycotoxins are in the form of spores that can survive dry conditions where mold can't. These spores become airborne, where they can be inhaled and ingested and cause illness. This is a survival mechanism similar to that used by bacterial spores.

Multiple types of molds exist that create mycotoxins, but the majority of mycotoxins are not harmful to human health. Currently, more than 300 mycotoxins have been identified.[5] The three primary mycotoxin producers include the mold species Aspergillus, Fusarium, and Penicillium, which all produce multiple mycotoxins.[5] Even a single type of mold, such as Aspergillus, can produce multiple mycotoxins, such as ochratoxins, aflatoxins, and gliotoxins.[7]

ASPERGILLUS MOLD

Aspergillus is one of the most researched molds because its mycotoxins can harm the food supply. This mold grows in decaying plants and soil, where its mycotoxins can contaminate crops and stored food. The aflatoxins, which are the primary mycotoxins in Aspergillus, can lead to illness in both animals and humans. Humans, upon consumption of animals, have an additional exposure from the animals. Mycotoxins in food are difficult to eliminate because they are in a spore form that is resistant to heat and physical and chemical treatments.[5]

Aflatoxins can cause both acute and chronic toxicity. They are known to bind to DNA, causing mutations and leading to cancers.[8] They are a leading cause of liver cancer in many developing countries.[9] Aflatoxin B1 is one of the most potent carcinogens known.[9] In addition, aflatoxins are teratogenic, mutagenic, and toxic to the immune system and the liver.8 The mechanisms of action of aflatoxins are the negative impacts on DNA, peptide-chain modification, protein methylation, and production of free radicals.[8]

Unlike aflatoxins that target the liver, ochratoxins are primarily damaging to the kidneys.[10] They are also carcinogenic and damaging to the immune and nervous systems and to a developing fetus.[10] One of the unique features of ochratoxins is their structural similarity to the essential amino acid

phenylalanine. Because of this, they can interfere with phenylalanine-hydroxylase activity in both the kidney and the liver, causing an inhibition of normal protein synthesis.[11]

Gliotoxins are another potent mycotoxin that is from the species Aspergillus Fumigatus. This specific Aspergillus is often found in invasive aspergillosis. Gliotoxins create reactive oxygen species that can damage tissues and cause apoptosis of mitochondria.[12] They also have significant immunosuppressive effects on the macrophages and monocytes, therefore inhibiting phagocytosis.[13]

STACHYBOTRYS MOLD

Stachybotrys chartarum, often called toxic black mold, is another mold found in water-damaged buildings. It produces a group of mycotoxins that are grouped together as trichothecenes. The trichothecenes include mycotoxins such as roridin E and verrucarin. Other mold species, such as Fusarium, can also produce trichothecenes, which are considered to be extremely toxic and have been used in biological warfare.[14] Their primary toxicity is thought to be from the inhibition of protein synthesis.[15] These mycotoxins impact many organ systems. A range of symptoms can be seen, including neurological changes, immunosuppressive effects, and respiratory and gastrointestinal illnesses.[15] Respiratory symptoms can be acute, with a specific acute pulmonary illness being seen in children.[14]

HEALTH IMPACTS

Genetics

While all people are exposed to molds, not all people will develop acute or chronic symptoms based on this exposure. The human leukocyte antigen (HLA) is one of the most important determinants of autoimmune and inflammatory disorders.[16] The HLA antigen is the protein expressed by the HLA-DR gene, which is found on most cells in the body. It signals to the immune cells, indicating which cells they should use to respond, and if it's functioning properly, it will activate an immune response to a foreign threat to the body, including molds and other biotoxins.

Approximately 90% of people with illness from mold exposure have a genetically abnormal response on some of their HLA-DR genes, causing them to have an ineffective immune response.[17] This abnormal response causes a misprocessing of antigens that inhibit the immune system from producing the proper antibodies to remove mycotoxins from the body. These mycotoxins are then stored and create an autoimmune and inflammatory response seen in chronically-ill, mold-exposed patients. These HLA-DR gene mutations are present in roughly 25% of the population worldwide, leading to approximately one in four people being at increased risk of illness from mycotoxin exposure. Acute illness from mold can also be associated with the increasing susceptibility of HLA-DR genes. Children with moderate-to-severe asthma with the HLA-DRB1*13 and HLA-DRB1*03 gene have shown increased sensitivities to Aspergillus and Alternaria.[18]

Mechanisms of Action

Multiple mechanisms of action interact in the development of symptoms from mycotoxins in susceptible individuals. When mycotoxins are inhaled, they often travel to the digestive system, where they alter the microbiome by decreasing beneficial bacteria and increasing gut pathogens.[19] Since the intestinal microbiome contains a large percentage of the immune system, a mycotoxin-induced dysbiosis can be the first step in developing immune dysfunction and inflammation.[19]

Inflammation leads to oxidative stress, which is one of the most significant pathologies in mycotoxin-induced illness.[20] This oxidative stress can also be created by infection, toxicity, and autoimmune and allergic responses to mycotoxins as well as the other bacteria and toxins that result when human exposure is from water-damaged buildings.[15] Oxidative stress causes damage to both the nuclear and the mitochondrial DNA, leading to DNA adducts and mutations with an increased risk of carcinogenicity.[20]

Understanding the mechanisms of action from mycotoxin-induced illness can help in the development of treatment protocols. Since oxidative stress is an important mediator, addressing it with antioxidants, such as glutathione, becomes important. Additional treatment should target inflammation and mitochondrial dysfunction while also addressing patient's symptoms and the removal of mycotoxins from the body.

GENERAL SIGNS AND SYMPTOMS

Acute Illness

While people with HLA-DR-gene weaknesses can develop chronic inflammatory issues resulting in systemic illness, people with allergic tendencies and asthma can suffer acute symptoms.

These symptoms are often respiratory when the mold is inhaled. Mold exposure can increase the risk of developing asthma and worsen existing asthma. When children are exposed at home to molds, their risk of developing asthma increases 2.4 times.[21] In workplace exposure, mold can also increase the risk of respiratory infections in adults, such as rhinitis and sinusitis, 4.6 times.[22] Allergic respiratory reactions are common with mold exposure from water-damaged buildings. Unlike other allergic conditions, the allergic and sensitivity reactions to mold are often not immunoglobulin E (IgE)-mediated.[15] Acute reactions to mold are more easily identified and recognized by the medical community.

Chronic Illness

Increasingly, people are being recognized who have symptoms involving all body systems after exposure to water-damaged buildings. These people are often in the 25% group who have the weak genetics for the HLA-DR receptor. Their symptoms are often nonspecific but can be debilitating. Symptoms can include significant fatigue, muscle and joint pain, headaches, mood issues, neurocognitive symptoms,

sleep disturbance, gastrointestinal issues, tremors, autonomic dysfunction, balance disturbance, cardiac issues including palpitations and vasculitis, and angioedema.[23,24]

Chemical sensitivity is a more specific sign of mycotoxin illness.[24] The neurological cognitive symptoms can mimic psychiatric disorders, movement disorders, and dementia, and those may be the presenting symptoms from exposure.[25] This group of symptoms from mycotoxins and other biotoxins has been termed chronic inflammatory response syndrome (CIRS) by Dr. Shoemaker.[26] This has helped practitioners to recognize the chronic issue of mycotoxin illness, to be able to identify it better with laboratory markers, and to develop treatment plans.

When practitioners have patients with multiple nonspecific symptoms, the presentation of mycotoxin illness can look like many chronic diseases, such as Lyme disease, fibromyalgia, chronic fatigue syndrome, or autoimmune disease. In my experience, patients can have chronic infections with mycotoxin illness, together with autoimmune disease and mast-cell activation. This is why identifying the pathology underlying the symptoms is so important, because many of the above diseases overlap and have similar underlying mechanisms. All of these disease can cause chronic inflammation, oxidative stress, and immune dysfunction that need to be treated, in addition to the treatment of other symptoms whether they are from mycotoxins, other toxins, or infections.

CONCLUSION: PART 1

With our changing climate, risks of mold-contaminated buildings and food supply will continue to increase. It's important to understand the significant health impacts of mycotoxins, which can begin in utero with lasting effects on children. Identifying mycotoxin illness using exposure risks and symptoms is a good start. While acute allergic and respiratory symptoms are commonly recognized, it's important to not miss people with potentially debilitating chronic illness from mycotoxins.

In part 2, I will discuss both testing options and comprehensive treatment plans.

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