EDITORIAL

Molds and Mycotoxins: A Brief Review

In the second book of the Bible, in Chapter 14 of Leviticus, Moses describes what needs to be done to a dwelling in which there is an eruptive plague on the wall. It is a wise and correct protocol for the remediation for mold growing indoors that still holds true in our modern times. It also shows that the issue of molds causing disease is as old as the Bible itself.

Diseases caused by ergot alkaloids from the mold *Claviceps purpurea* have been recognized since ancient times. It grows on rye, barley, and other grains; when made into flour then bread and eaten, the ergot alkaloids cause the symptoms. A reference to a "noxious pustule in the ear of grain" on an Assyrian tablet from 600 BCE is one of the first writings about ergot.[1] In the middle ages, people suffered from hallucinations and "madness" from ergotism: It was called St Anthony's fire. As late as in 1951, this same "fire" killed several people in a village in France.[2] There were 132 epidemics of ergotism in Europe between the sixth and 18th centuries documented by the 3-volume work by August Hirsch titled *Handbook of Geographical and Historical Pathology*, published in London in 1886.[3] There are many instances of molds triggering diseases throughout history, as well as causing a number of epidemics. For example, an epidemic of alimentary toxic aleukia killed approximately 100 000 in Russia in 1944 when people ate moldy bread. The culprit was a mycotoxin known as trichothecene.[4] Today, with modern technological methods used to clean grain, ergotism has been almost eliminated in humans.

There are two basic forms of ergotism: one that affects circulation of blood causing a dry gangrene of the extremities, and the other affecting the central nervous system and causing convulsions. It is known to cause painful seizures, diarrhea, paresthesias, mania, psychosis, and headaches. I've personally asked a number of neurologists if molds can cause seizures, and they all said that they have never heard of that; then, I ask them if they have ever read about ergotism, and their eyes light up.

In past times, midwives used ergot alkaloids either to induce uterine contractions for women in labor or to bring about abortions.[5] More recently, methylergonovine maleate was prescribed to stop postpartum hemorrhage and migraine headaches were sometimes treated with ergotamine. Lysergic acid diethylamide (LSD) got its start at Sandoz Laboratories in Switzerland during research on ergot alkaloids. It was named Delysid and touted as a treatment for schizophrenia.[6]

There are more than 100 000 species of molds; approximately 2 dozen can cause health problems in humans. Mycoses are when fungi grow on and in us and are either aggravating, such as athlete's foot, or critical, such as invasive aspergillosis. Molds can be found everywhere on this planet. Cold or warm, wet or dry environments, mold spores are omnipresent, and they can grow on anything once wet. They are like seeds in a packet that one buys in a store: without water, they do very little. Once they get wet and remain wet for 24 to 48 hours, molds start to multiply and sporulate. Attached to these spores is a secondary metabolite, mycotoxins. Mycotoxins are there for survival of the fittest: When you pull out that plastic bag from the back of your refrigerator with the heel of a loaf of bread left in it, with various colored spots on it, these are bacteria and molds feeding on the bread. The mycotoxins destroy the bacteria so that the food remains only for the molds. This effect of mycotoxins on bacteria was the inadvertent finding of Sir Alexander Fleming when, after returning from a vacation, he noticed that one of the petri dishes with staphylococci was contaminated by the mold *Penicillium notatum* and that the colonies of staphylococci surrounding the fungus had been destroyed. From this he eventually developed the first antibiotic, penicillin, and it is estimated that more than 200 million lives were saved as a result of patients being given this antibiotic.[7] Today, when patients get a bone marrow transplant, they are given a potent immune suppressant derived from mycotoxins: cyclosporine. The toxic and immunogenic byproducts of molds are not limited to mycotoxins; they include 1,3-α-D glucans, extracellular polysaccharides, and volatile organic compounds (VOCs).

Occupants of dwellings and workplaces affected by mold growth due to leaks or water intrusion can develop one or all of the following, some due to mycotoxins:

1. Mycotic infections (mycoses).
2. Fungal rinosinusitis.
3. Immunoglobulin E (IgE)-mediated sensitivity and asthma.
4. Hypersensitivity pneumonitis and related inflammatory pulmonary diseases.
5. Cytotoxicity.
6. Immune suppression/modulation.
7. Mitochondrial toxicity.
8. Carcinogenicity.
9. Nephrotoxicity.
10. The formation of nuclear and mitochondrial DNA adduct.

Table 1. Mold, Mycotoxins, and Their Effects[8]

Mold	Mycotoxins	Effects
Stachybotrys chartarum	Satratoxins, verrucarin; trichothecene	Pulmonary hemosiderosis; induce proinflammatory cytokines; neurotoxic; immune suppression
Aspergillus flavus	Aflatoxin B_1	Carcinogenesis, aspergillosis
Aspergillus fumigatus	Fumitoxins; gliotoxins	Tremors and CNS injury; immune dysregulation; aspergillosis
Aspergillus niger	Ochratoxin	Nephropathy
Aspergillus versicolor	Sterigmatocystin	Carcinogenesis; aspergillosis
Chaetomium globosum	Chaetoglobosin	Cytotoxicity; inhibition of cell division
Penicillium brevicompactum	Mycophenolic acid	Toxic: mutagenic
Penicillium expansum	Patulin, citrinin	Immune toxicity; tremorgenic
Penicillium polonicum	Verrucosidins; nephrotoxic glycopeptides	Tremors; cytotoxicity, nephropathy
Trichoderma species	Trichothecenes; gliotoxins	Neurotoxic; immune suppression

Abbreviation: CNS, central nervous system.

Slightly less than 1 year after Hurricane Katrina struck New Orleans and the surrounding areas, the Centers for Disease Control and Prevention (CDC)[9] published its findings in *Morbidity and Mortality Weekly Report* in an article titled "Mold Prevention Strategies and Possible Health Effects in the Aftermath of Hurricanes and Major Floods." The CDC concluded that "excessive exposure to mold-contaminated materials can cause health effects in susceptible persons regardless of the type of molds or the extent of contamination."[9] A few years later, in 2009, the World Health Organization published in its *Guidelines for Indoor Air Quality*:

> Sufficient epidemiological evidence is available from studies conducted in different countries and under different climactic conditions to show that the occupants of damp or moldy buildings, both houses and public buildings, are at increased risk of respiratory symptoms, respiratory infections and exacerbation of asthma …
>
> Toxicological evidence obtained in vivo and in vitro support these findings showing the occurrence of diverse inflammatory and toxic responses after exposure to microorganisms including their spores, metabolites, and components isolated from damp buildings.[10]

The symptoms of indoor mold exposure depend on the length of time of the exposure and the amount as well as the types of molds. They are general and nonspecific: fatigue, unusual headaches, confusion, palpitations, shortness of breath, blurred vision, muscle and joint aches and pains, short-term memory loss, tremors, mood swings, and sleep disturbance are the most common.[8] Patients affected by molds and mycotoxins are frequently shuttled from one specialist to another, with their diagnoses being more of symptoms than disease. I have treated many that were told they had chronic fatigue syndrome, fibromyalgia, intractable Lyme's disease, and so forth.

Treatment starts once the first rule of toxicology is achieved: Get the patient away from the toxin or the toxin away from the patient. If the water intrusion is in the home and has lasted a few days, then it is likely that all in the home may be contaminated: bedding, curtains, fabrics on living room furniture, towels, etc. Here again, Moses told us what to do. In public buildings or schools, remediation must be started as soon as possible, preferably before the spread of mold spores through the heating/ventilation/air conditioning (HVAC) system. However, the needed rapidity of remediation is rarely achieved due to delays.

MYCOTOXINS

Mycotoxicoses differ from mycoses in that these are toxins and are, therefore, similar to the health problems caused by heavy metal exposures or pesticides or other toxins. Mycotoxins usually enter the body by inhalation, ingestions, or dermal absorption. Studies have shown that when *Stachybotrys chartarum* is present in an indoor environment, mycotoxins are also present in the sera of the exposed individuals.[11]

Symptoms vary depending on the mycotoxin, the amount of mycotoxin and the duration of the exposure, as well as the general health of the exposed person.[12] A number of mycotoxins are known to affect the neurological system, causing cognitive function problems, tremors, and inflammatory neuropathies. Several papers have demonstrated chronic inflammatory demyelinating neuropathy caused by exposure to elevated levels of molds in the environment and, therefore, mycotoxins. Many mycotoxins induce tremors as a neurological effect.[13]

AFLATOXINS

Exposure to aflatoxins in the diet is considered an important risk factor for the development of primary hepatocellular carcinoma, particularly in individuals already exposed to hepatitis B. Extrahepatic neoplasms of the lungs are also associated with aflatoxin. The International Agency for Research on Cancer (IARC) has classified aflatoxin B1 as a group I carcinogen, the worse group, causing liver cancer.

Acute aflatoxicosis results in death; chronic aflatoxicosis results in cancer, immune suppression, and other "slow" pathological conditions. Exposure to aflatoxins can result in hepatocellular carcinoma, especially in a person already affected by hepatitis B.[14]

FUMONISINS

The mycotoxins known as fumonisins are associated with esophageal cancer. Charleston, South Carolina, has the highest incidence of esophageal cancer in African Americans in the United States. This has been linked to elevated levels of fumonisins in corn meal and corn grits, and 7 samples from a supermarket there were found contaminated.[15] As fumonisins can cause the development of neural tube defects in experimental animals, it has been suggested that a cluster of anencephaly and spina bifida in southern Texas along the Mexican border may have been caused by contaminated corn products.[16] The IARC has classified fumonisins as group 2B: probably carcinogenic.[17]

OCHRATOXINS

Animal studies show that ochratoxin A is an immune suppressant, a carcinogen, a potent teratogen, and hepatoxic.[18] It has been detected in human milk and is regularly found in pork for human consumption.[19] Porcine nephropathy is endemic in Denmark, and it would behoove the medical community to consider ochratoxin toxicity in patients presenting with symptoms of renal disorders.[20] IARC has classified ochratoxin 2B, a possible human carcinogen.[21]

TRICHOTHECENES

Trichothecenes are produced by the molds *Stachybotrys*, although *Myrothecium* and *Trichothecium* species can produce them as well. The Trichothecenes produced by *Stachybotrys chartarum* include satratoxins, roridins, verrucarins, and atranones.[22] Molds, chiefly *Stachybotrys*, easily grow on numerous building materials that have high cellulose content: ceiling tiles, wood fiber boards, and gypsum boards, among others. Dust-lined heating, air conditioning, and ventilations ducts (HVACs) are also areas where *Stachybotrys* has been found and, therefore, also Trichothecenes. Presence of these has been linked to pulmonary bleeding in infants.[23] In another link to the Bible, it has been proposed that the 10th plague of Egypt was *Stachybotrys* infestation.[24]

INDOOR AIR QUALITY AND SICK-BUILDING SYNDROME

Sick-building syndrome is used when there is no etiology identified to cause symptoms; when there is a causal factor, then the term *building-related illness* applies.[25,26,27] Most homes in the United States are built by homebuilders and not by architects, increasing the likelihood of problems related to construction that allow for water intrusion. Respiratory problems including asthma and allergies are known to be exacerbated by dirty HVAC ducts, vents, and filters, dust stirred up during reconstruction, and in the aftermath of water intrusion to interiors of dwellings or buildings due to broken water pipes, faulty installation of clothes washers, refrigerators with ice makers and water dispensers, roofs, windows, and chimney leaks, poor flashing placements, and floods, among others.

SUMMARY

It is an uncontested medical and scientific fact that molds and mycotoxins cause diseases in humans. Both are health hazards, and both are often overlooked and not part of clinicians' differential diagnosis. Molds produce metabolites such as mycotoxins and solvents, shed antigenic materials such as spores, hyphae, extracellular polysaccharides, and enzymes, which are toxic and cause immunologic responses. Forgacs[28] called mold mycotoxicosis "the neglected disease." Clinicians should include molds and mycotoxins in their evaluation of patients and help this become "the accepted disease."[28] (*Altern Ther Health Med.* 2016;22(4):8-11.)

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