

Fungal Hypersensitivity: Pathophysiology, Diagnosis and Therapy

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Introduction

Molds or fungi are everywhere in nature and their wind borne seeds (spores) make up the majority of the microscopic particles in the air at any time, even when pollen season is at its peak. Their value to the food industry is enormous while their contributions to medicine in the form of antibiotics, vitamins and other drugs is inestimable. But they can cause trouble.

Humans in good health can handle typical exposures to molds in the air, in their homes and in their workplaces without much difficulty. However, certain allergy-prone individuals may have symptoms during peak mold levels that include asthma, runny nose, sneezing fits and itchy noses and throats.

In the immunologically compromised patient, a single mold spore can initiate a deadly process. Patients on chemotherapy or immune suppression imposed for organ transplantation and those with chronic diseases such as AIDS, recurrent infections, cystic fibrosis and diabetes, are also at risk when exposed to molds at levels that healthy individuals can handle.

Exposure to high levels of mold can be a threat to anyone's health--as noticed in certain occupations. These conditions were given name such as farmer's lung, pigeon breeder's disease, malt workers disease, etc. They shared common symptoms, usually involving nose, sinuses and lungs and the consequences were serious, often leading to permanent breathing disorders and death. Over the last 30 years, non-occupational exposures have become recognized as dangerous in homes with moldy air conditioning or humidifiers, homes near composting facilities, and homes with water damage.

Exposure to high levels of fungi can be a health threat from inhalation, ingestion or skin contact involving tiny mold spores (invisible to the eye), mold toxins (mycotoxins) or mold bodies themselves. Initial symptoms seem to be the result of inhalation, such as sore throats, hoarseness, cough and nasal congestion. With time, symptoms can progress to include headaches, fatigue, rashes, dizziness, shortness of breath, sinus infections, ear pain, muscle and joint pain, and fever. These symptoms are the result of direct mycotoxin exposure and the effects of an overactive immune system trying desperately to overcome what it perceives to be an overwhelming infection. The immune system generates antibodies to the absorbed mold materials (antigens). These antibodies react with the antigens to form immune complexes, which is all part of the body's normal immune elimination function. When the immune clearance machinery is on overload, the complexes remain in the blood stream causing myriad symptoms, known to clinical immunologists as serum sickness, and appearing to the patient as a severe, unrelenting flu syndrome. Exposure to certain mycotoxins can result in brain damage seen as short-term memory loss, cognitive dysfunction, inability to concentrate and "fuzzy thinking". These changes seem to be reversible, at least in part, but they can take years to resolve.

Once the patient has become hypersensitive to the mold in their environment, they have also become overly reactive to all molds in their life including those they breathe elsewhere, those they eat and those that may be colonizing their tissues. Relief of symptoms can only come with a significant reduction in exposure including a mold free diet, avoidance of mold-ridden environments and treatment of mold colonization.

Some mold colonizations are well known, such as athlete's foot, vaginal yeast infections, ringworm, excessive dandruff, toenail fungus, etc. But molds are opportunistic and can become established on any tissue that has been previously damaged. This would include the sinuses of a patient who has had a sinus infection, the lungs of a patient with asthma, the nose of a patient with nasal congestion and the gastrointestinal tract of patients who have had chronic indigestion or abdominal discomfort. The patients' healthy, reactive immune system can prevent the mold from invading surrounding tissues and causing infection. However, it is not able to remove the mold from the mucosal or skin surfaces. The colonization continues, the patient continues to form immune complexes with the mold antigens, the overload continues, and the patient grows sicker. Once there is significant colonization, the symptoms continue even after the patient leaves the moldy workplace or home where the high exposures occurred.

Diagnosis

The diagnosis of fungal hypersensitivity syndrome rests on three criteria: an identified heavily contaminated source, appropriate symptoms temporally related to exposure, and high serum IgG antibody levels to molds. IgE antibodies are usually not involved and skin tests are, therefore, usually negative.

Specific IgG antibody levels to molds are helpful in supporting the diagnosis of fungal hypersensitivity. Everyone is exposed to some molds and, therefore, some antibody to mold is found in nearly everyone. But the levels are low. Individuals exposed to heavily moldy environments make great amounts of antibody. In mold hypersensitivity patients it is common to find antibodies to molds in class three or class four categories. Occasionally a patient with significant mold problems will present class two antibody levels.

Mold antigens are highly cross-reactive, which means that an antibody response on exposure to mold A may show significant reactivity on the IgG panel test to mold B as well. Sometimes the molds to which the patient shows highest antibody levels are not identified in an environment survey. This reflects the difficulty of getting the mold growing happily on wet sheet rock to grow on an agar culture dish.

Therapy

Therapy is based on avoidance. The contaminated environment must be remediated or abandoned, a mold-free diet is very helpful, and colonization must be eliminated by the appropriate use of antifungals. The most common colonization sites are the nose, nasopharynx and esophagus. A compounded nasal spray containing two percent Nizoral in saline used four times daily with thorough wetting of the nose and nasopharynx is extremely effective. For colonization of lungs or sinuses, Sporanox at 200 to 400 mgm per day is useful. For primarily gastrointestinal symptoms, miconazole or econazole in 250 mgm capsules can be very effective. This is given twice daily. If candida antibodies are highest, candida may be the offending organism. Nystatin capsules (500,000u) are helpful given 1,000,000 units three times daily. All use of antifungals can evoke a flu-like Herxheimer reaction in the hypersensitive patient at the initiation of therapy. This is presumed to be due to massive die-off of the colonizing fungi with an overloading release of fungal antigens and toxins onto the mucosal surface. To prevent such flu-like reactions, therapy should begin at a quarter to an eighth the final dose and advanced, as tolerated, over a two to few week period. Once therapeutic doses

are achieved, treatment needs to continue for six months or more although the patient will report symptom reduction after a few weeks. The need for prolonged therapy is presumed to be due to the presence of frugal spores that cannot be killed until they germinate.

Conclusion

The diagnosis of fungal hypersensitivity is difficult for most physicians because mycology is not a strong subject in medical school. Most colonizations are not life threatening and such conditions as athlete's foot and yeast vaginitis are often self-treated with over-the-counter medications. At the other extreme are life threatening fungal infections in the immune compromised patient, which are usually treated by oncologists with help from infectious disease specialists. In this article fungal hypersensitivity and colonization is occurring in healthy individuals who have been exposed to excessive fungal contamination in their homes or work places. They experience symptoms which are usually attributed to viruses such as an upper respiratory tract infection or the flu. As time goes by and the symptoms persist, the patient may come to realize the basic problem is heavy fungal exposure from having read about someone else's affliction in a newspaper or magazine. It now behooves the physician to recognize the problem and know what to do to help his/her patients.

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Appendix: Foods Rich in Fungal (Mold) Protein-Allergies.
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Dried Fruit	Raisins, apricots, prunes, figs, etc.
Aged Cheese	Some cheeses are okay if milk is not a problem, e.g., cottage cheese, mozzarella, provolone, ricotta and farmer's cheese.
Mushrooms	
Over-Ripe Fruits and Vegetables	Check ingredients. <i>Malted</i> means moldy. Dough conditioners are moldy. Sourdough is worse (sometimes labeled <i>yeast-free</i>). Bread develops surface mold after a day. Tortillas, biscuits, muffins, cakes and cookies are usually yeast free.
Tomato Products	Juice, sauce, paste, ketchup, etc., are made from moldy tomatoes.
Beer	The darker the brew, the more mold it contains.
Wine and Wine Vinegar	White wine is least moldy; clear vinegar may be tolerated.
Most Liquors	Vodka, tequila, clear rums are least moldy.
Multi-B Vitamins	Contain either yeast or mold (rice hulls are moldy).
Processed Meats	Hot dogs, sausage, salami, bologna, etc. Solid preserved meats such as ham, turkey, pastrami may be okay.
Hamburger	Beware! Often from aged meat; eat within a day of grinding.
Products of Aspergillus Fermentation	Soy sauce, chocolate, black tea, malt extract (bread, cereals), lactaid (milk additive), citric acid (common food additive - not derived from citrus fruit), fruit juice (commercial juices often made from moldy fruit; may contain mold enzymes added in processing), digestive enzymes (pancreatic are okay), cholesterol-lowering enzymes.

Notes:

All food will become moldy with time. Organic foods are most likely to mold.

Shop frequently, buy in small quantities, and when in doubt, ask the vendor about the freshness of his foods.

Read labels.

Molds thrive on sugar – control your intake.

Do not store food in frost-free freezers for more than one to two weeks because of the automatic thaw cycle several times a day.

A moldy environment (home, office, school, church, car) can be an additional problem.