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Potential Effects of Fungal Contamination on Health

Bernard L. Fontaine, Jr., M.Sc., CIH, CSP
The Windsor Consulting Group Inc.
South River, NJ

Introduction

In recent years, the health effects from exposure to fungal growth within built environments have been a subject of intense public concern. Fungi can cause a number of infectious and noninfectious conditions. Several basic mechanisms are responsible for these health effects including, but not limited to, immunologic (IgE-mediated allergic response), infection, and toxic effects from ingestion, direct skin contact, inhalation of spores, and mycelial fragments.[1] It is common for several mechanisms to contribute toward the pathogenesis of a fungal-induced disease.

The type and severity of symptoms are related to the type of fungal spores, genera and speciation, and growth pattern. Susceptible individuals (e.g. people with allergic conditions or immuno-compromised) are more susceptible than healthy individuals. Fungi also produce a variety of volatile organic compounds; the most common being ethanol, which is responsible for musty odors associated with fungal growth. Exposure to microbial growth is associated with a variety of upper and lower respiratory tract symptoms.

Damp Indoor Spaces, Microbial Growth, and Human Health

Microbial growth will always be presented indoors. Exposure to a normal ecology of fungi can occur from outdoor sources and surfaces of skin, clothes, and shoes of people. These exposures are considered the normal mycoflora. When moisture problems occur inside residential, commercial, or institutional dwellings, the resulting fungal population can be quite different. Moisture in combination with nutrients and optimal environmental conditions can cause hyphal fragments to flourish and grow into a mycelial mass. As the mycelial mass grows, conidia are produced from the fungal population. The spores can become dispersed within the indoor environment by wind or air pressure differentials, insects, and sometimes by water droplets.[2, 3]

Fungal types are divided into distinct categories: common outdoor (CO) fungal species and those indoor species (IS) amplified by water or moisture intrusion in indoor environments. Some of the most common fungi found outdoors include species of *Cladosporium, Alternaria, Epicoccum,* yeast (*Rodotorula*), Ascospores, Basidiospores, *Paecilomyces, Pithomyces,* and *Ulocladium.* Indoor indicating species of fungi include: *Acremonium, Aspergillus, Aureobasidium, Chaetomium, Fusarium, Penicillium, Phoma, Stachybotrys,* and *Trichoderma*. Besides these fungi; gram-negative bacteria, streptomycetes, actinomycetes, and other thermophilic bacterial should be considered when evaluating the microbial growth within the interior envelope.

Under normal conditions, the mycoflora found in indoors is similar to the outdoor environment. Wind can cause the fungal spores, hyphal, and mycelial fragments in the soil, leaf litter, or

decaying vegetation to become airborne. Outdoor airborne concentrations, under these conditions, can be somewhat higher than indoor air concentrations. Alternatively, snow and heavy rain can dramatically decrease the outdoor airborne concentration of fungi. Caution should be used whenever comparing the outdoor to indoor air concentrations.

Much controversy has arisen on how damp indoor spaces and microbial growth affect human health. The Center for Disease Control (CDC) commissioned the Institute of Medicine (IOM) to perform a review of the scientific literature. The resulting report, *Damp Indoor Spaces and Health*, was published in 2004 and remains one of the most authoritative source of information on the subject.[4]

The IOM found sufficient evidence linking upper respiratory tract symptoms (such as nasal congestion, sneezing, runny or itchy nose, and throat irritation) to damp indoor environments and presence of microbial growth. Similarly, there was sufficient evidence to link lower respiratory tract symptoms of cough and wheeze. Sufficient evidence was also found for a link between damp indoor environments, microbial growth, and asthma symptoms in sensitized people with recurring asthma. Another link was made based upon sufficient evidence between fungal exposure and hypersensitivity pneumonitis in a small proportion of susceptible people with invasive respiratory and other fungal infections in severely immuno-compromised individuals, and fungal colonization of the respiratory tract in individuals with chronic pulmonary disorders.[5] IgE-mediated or allergic responses underlie the most common types of diseases associated with fungal exposure.

Atopy, or the genetic predisposition to form IgE responses to allergens, is an important risk factor. Clinical conditions associated with allergy include rhinitis and asthma. Allergic rhinitis is often associated with allergic conjunctivitis and sinusitis. Symptoms of allergic rhinitis include sneezing, itching of the nose, eyes, mouth, or throat; nasal stuffiness; clear rhinorrhea; and, if associated with allergic conjunctivitis, red, itchy eyes.[6] Individuals with sinusitis may complain of sinus fullness or post-nasal drip, often purulent. Examination of the nasal septum shows eosinophilic inflammation and allergy skin tests demonstrate specific IgE-sensitization to causative allergies.[7] Unfortunately, skin testing reagents and blood tests to document IgE-sensitization to fungi, are poorly standardized and the results are unclear regarding the sensitivity and specificity.

Asthma is a disease characterized by episodic, reversible airway obstruction and eosinophilic airway inflammation. Over time, chronic asthma can lead to an irreversible airway obstruction. People with asthma experience chest tightness, wheezing, dyspnea, or cough, which be reversed using a bronchodilator. People with asthma exhibit normal bronchial hyperactivity to a methacholine challenge test; however, false positive results have occurred in a substantial number of individuals with no etiology or known history of asthma. Besides spirometry to document pulmonary obstruction during and asthmatic attack and evaluating sputum-induced eosinophils from the nasal cavity, nitric oxide can be measured from the individual's exhaled breath. These tests are not performed in a standard clinical setting.

Allergic Diseases Associated with Airway Colonization

The general consensus appears to indicate that allergy is the most common clinical response to fungal exposure in contaminated indoor environments.[8] Allergic reactions can range from mild, transitory responses, to severe, chronic illness. The Institute of Medicine (1993) estimated that twenty percent of Americans suffer from allergic rhinitis (Type I response) or flu-like illness

(Type III response), the single most common chronic disease experienced by humans. These clinical conditions could represent the early manifestations of hypersensitive pneumonitis.

In Type I allergy, the over-reaction of the immune system will occur after massive and long exposure to the offending agent, ranging from months to years. Once the immune system has been triggered, the allergic reaction will be elicited upon exposure to small amounts of the specific allergen. The frequency of Type 1 allergy is not as high as other inhaled allergens. It is estimated that 8 percent of the population and 20-25 percent of children experience a Type 1 airway allergy. As a result, the body produces IgE-mediated antibodies to protect the body from the offending antigen.

The causative agents in respiratory allergy are usually proteins. Water soluble proteins from fungal spores become soluble in bodily fluids by means of the mucosa as the fungal spores deposit themselves in the upper airway. Extraction of the protein molecules – antigens – takes about 30 seconds. After deposition and extraction, macrophages engulf and degrade the protein. Some of the allergen binds to T-cells and B-cells to form a specific complex. Interlukins along with T-cells and B-cells produce IgE antibodies. The amount of IgE-antibody produced depends upon the amount and duration of exposure. Histamine is a potent mediator substance produced during exposure by the mast cells (tissue) and basophil cells (blood). Histamine production can contract smooth muscles around the bronchioles resulting in asthma; secrete mucous from the lung tissue resulting in infection and inflammatory reactions; secrete nasal fluids and tears from the eyes resulting in congestion of the nose and itchy/watery eyes; and finally histamine will influence the vascular permeability of the blood vessels resulting a decline in blood pressure

A Type III allergic reaction is caused by inhalation of microbial growth resulting in extrinsic allergic alveolitis. This antigen-antibody reaction does not produce an IgE-mediated response. The allergic reaction is mediated by other antibodies, mainly IgG, which form complexes with the inhaled antigen. The complexes will initiate different inflammatory response and sometimes trigger the complement system, which may result in asthma. The symptoms are elicited between 6-8 hours after exposure. These symptoms include malaise, flu-like symptoms, elevated temperature, muscle and joint pain, dyspnea, weight loss, and later asthma. Cessation of exposure before the onset of fibrosis will normally lead to a return of the individual to a healthy state.

Less than one percent of the total population suffers from more serious chronic diseases like allergic bronchopulmonary aspergillosis (ABPA). This disease occurs when the airways of individuals with obstructive pulmonary diseases like asthma, cystic fibrosis, or chronic obstructive pulmonary disease (COPD) become colonized with *Aspergillus fumigatus* or other species of *Aspergillus* fungi.[9] Inflammatory responses lead to additional airway damage. Marked exacerbation of existing asthma is a typical clinical presentation of ABPA. Symptoms include recurrent episodes of bronchial obstruction, fever, malaise, expectoration of brownish mucous plugs, peripheral blood eosinophilia, hemoptysis, and asymptomatic pulmonary consolidation.

Other clinical features are immediate skin test reactivity to *Aspergillus* antigens, precipitating serum antibodies to *A. fumigatus*, markedly elevated serum total IgE, fleeting lung infiltrates, and central bronchiectasis. Airway colonization with other fungal species can result in a similar clinical picture. Allergic fungal sinusitis (AFS) is noninvasive and typically occurs in allergic, immuno-suppressed patients, which have existing asthma and nasal polyps. Fungal colonization is characterized by mucous containing a high level of eosinophils. The mere presence of fungi inside the nasal passages is not indicative of an active infection.

Hypersensitivity Pneumonitis

Hypersensitivity pneumonitis (HP), also known as extrinsic allergic alveolitis, is a granulomatous interstitial lung disease. A wide range of materials, including fungi, can be inhaled by people who are sensitized or susceptible and inducing both antibody and cell-mediated immune responses. The presence of HP can be either acute or chronic. The symptoms from the acute HP can be confused with the onset of pneumonia. These symptoms include chills, fever, malaise, cough, and dyspnea appearing 4-8 hour after exposure. Chronic HP is thought to be induced by continuous low-level exposure.[10] Symptoms occur without any chills, fever, or malaise; and these symptoms are characterized by a progressive shortness of breath with weight loss. Examining physicians should obtain a clinical and exposure history to determine if patients have been exposed to damp and water-damaged building materials, farms, birds, hot tubs, and other environment factors related to HP. Chronic HP can be confused with idiopathic pulmonary fibrosis.

Inhalation Fever

Inhalation fever is a general term given to a variety of flu-like, self-limiting syndromes that may be caused by a variety of environmental stimuli. Humidifier fever (HF) is characterized by fever, respiratory symptoms, and fatigue within hours after exposure to a contaminated humidification system. Thermophilic actinomycetes; and other gram-negative bacteria, including species of *Legionella* and *Pseudomonas*; and protozoa have been associated with HF.[11] Aerosolized endotoxins from gram-negative bacteria have been implicated in this condition. Although humidifier fever can be confused with acute HP, it is a short-term illness and removal from exposure is an effective treatment.

Fungal Infections

Fungi can act as causative agents for adverse health effects in different ways. They can cause airway allergy, irritation of the eyes, nose, and throat, and cause toxic effects on many different body organs. Some moulds cause skin irritation after direct contact. Like other microorganisms, fungi can be pathogenic and result in infection. Mycoses may be divided into opportunistic or non-opportunistic infections. Opportunistic infections occur in patients with lowered resistance to infection by disease, therapy, or medication. Non-opportunistic infections are caused by direct response to toxigenic fungi such as *Cryptococcus neoformans*.

Infection from microbial contaminated building materials is an important concern. In general, individuals with impaired host defenses suffer the most severe types of fungal infections. However, invasive fungal infections can occur in individuals with normal host defenses, and become life threatening. Any impairment of cell-mediated immunity or neutropenia (human immunodeficiency virus (HIV) infection, leukemia, lymphoma, diabetes mellitus, increase the risk for fungal infection. Severely immuno-suppressed patients, such as solid organ or stem cell transplant recipients, or those receiving cancer chemotherapy, corticosteroids, or agents inhibiting immune function are a much higher risk for locally invasive infections of the lungs, sinuses, skin, and systemic infection. *Aspergillus* and *Fusarium* species are particularly important problems in these patients.

Toxic Effects of Fungi and Moulds

Many fungi and moulds produce metabolites with a wide range of toxicity such as antibiotic (penicillin), immuno-suppressive (cyclosporine), carcinogenic (aflatoxins), emetic, and hallucinogenic (ergot alkaloids).[13] Mycotoxins are natural products produced by fungi that act

like poison to humans and animals alike. Although ingestion is the most common route of exposure, inhalation and dermal contact can also cause adverse health effects. Mycotoxin production is dependent not only on fungal species and strain, but also environmental conditions (temperature, water activity, light), and growth substrate. Some of the adverse effects from exposure to mycotoxins include skin irritation, skin necrosis, cough, rhinitis, and bloody nasal exudates after inhaling or touching materials with heavy microbial contamination. Fungi also can secrete exodigestive enzymes that can cause tissue destruction, angioinvasion, thrombosis, infarction, and other manifestations of mycosis.

Table 1 illustrates some of the toxic effects elicited by selected environmental fungi and moulds. The discovery of aflatoxin-B[1] – the most carcinogenic biological substance known today – initiated worldwide interest in the isolation and characterization of mycotoxins. Acute reactions to ingestion of aflatoxins in humans were tragically demonstrated in India in 1974, where a severe drought was followed by heavy rain before harvest. The harvested corn was infected with *A. flavus* and caused more than 100 people to die after eating the mouldy corn. In 1981, 12 people in Kenya died under similar circumstances. The toxic metabolite, ochratoxin A, was isolated from *A. ochraceus* and *Penicillium verrucosum* in swine and poultry.

Another similar case involving humans is known as the Balkan endemic nephropathy. Both *P. aurantiogriseum* and *P. polonicum* produced the nephrotoxic glycopeptides involved with this disease. Other toxigenic moulds include species of *Stachybotrys* and *Fusarium*, which produce the macrocyclic trichothecenes with potent effects on the immune system and protein synthesis. *F. moniliforme*, in particular, produces a series of mutagenic compounds called moniliformin and fusarin, which may be responsible for esophageal cancer in humans.[13] Recent research has focused more on the respiratory route and direct skin contact with respect to the toxic metabolites since mycotoxins are produced inside as well as on the surface of fungal spores. Croft et al. (1986) reported an airborne outbreak of trichothecenes toxicosis. Therefore, inhalation and direct skin contact becomes more important route of exposure than ingestion when occupants are exposed to active microbial growth from various sources of water or moisture intrusion. Today approximately 3,000 metabolites have been characterized and produced by about 600 different mould species.[14]

Mixed Microbial Mycotoxicosis

Potentially toxic and immunogenic byproducts of microbial growth include mycotoxins; 1,3-α-D-glucans; extracellular polysaccharides (EPS); enzymes; and solvents. Occupants of affected structures can develop symptoms in multiple organ systems, including the upper and lower respiratory tract, central and peripheral nervous systems, skin, gastrointestinal tract, urinary tract, connective tissue, and musculoskeletal system. Human illness may result in mycotic infections or mycoses; immunoglobulin (IgE)-mediated sensitivity and asthma; hypersensitivity pneumonitis and related inflammatory pulmonary diseases; cytotoxicity; immune system suppression, mitochondrial toxicity, carcinogenicity, nephrotoxicity, and the formation of both nuclear and mitochondrial deoxyribonucleic acid adducts.

After studying 209 patients with multiple organ system symptoms, individuals exposed to mixed colonies of microbial growth in water-damaged buildings have several abnormalities among their immune system parameters.[15] The study population complained of excessive fatigue, headache, nasal symptoms, memory problems, spaciness and disorientation, sinus discomfort, coughing, watery eyes, throat discomfort, slurred speech, lightheadedness, dizziness, weakness, bloating, insomnia, spasms, coordination problems, vision disturbances, rash, chest tightness, and wheezing.

The subjects in the study exhibited a high risk for producing autoimmune antibodies to nuclei, smooth muscle, central and peripheral nervous system myelin, and neurofilament. The presence of these autoimmune antibodies has been reported in the literature following exposure to other xenobiotics. High titers of nucleic acids/nucleoproteins (ANA) have been associated with various types of connective tissue injury and/or connective tissue diseases. ASM (against smooth muscle) autoimmune antibodies are generally non-specific but occur in S variety of other diseases, including autoimmune hepatitis, vascular events, rheumatoid arthritis, bronchial suppuration, autoimmunity, and asthmatic bronchitis.[16] The antimyelin autoimmune antibodies, which have been initially identified in Guillian–Barre syndrome may be related to several different neuronal antigens, including various gangliosides, tubulin, chondroitin sulfate, and sulfatide, found in neuropathies.

Conclusions

Health effects following exposure to microbial contaminated environments include: irritation, allergic reactions, infection, neurological disorders, autoimmune diseases, cancer, and intoxication. The toxicological effects of mycotoxins and toxic chemical substances on human health remain most controversial. The preponderance of reports suggests that inhalation and direct contact may be of most importance. In addition, mixed colonies of microbial growth may indeed have similar importance on occupant health. Well designed and objective scientific research is needed to determine the clinical and sub-clinical effects from both inhalation and direct contact to various fungal species as well as mixed fungal biota containing mycotoxins and other toxic chemical substances.

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Table 1 – Toxic Effects of Environmental Fungi and Moulds [13,17]

Fugal Genera	Allergy	Infection	Mycotoxins
Alternaria sps.	Type I allergies (hay fever, asthma) and Type III allergies (hypersensitivity pneumonitis)	Phaeohyphomycosis (causing cystic granolomas in the skin and subcutaneous tissue). Colonizes in immuno-compromised patients causes paranasal sinuses and leads to chronic hypertrophic sinusitis. A. alternate is associated with oesophageal cancer in Linxian, China. Tenuazonic acid has been implicated in onyalai, a blood disease among people in South Africa.	Alternariol (AOH) Alternairol monomethylether (AME) Tenuazonic acid (TeA) Altenuene (ALT) Altertoxins (ATX) - mutagenic
Arthrinium sps.	Not commonly regarded as problem mould	Single case of skin infection and a single post-surgical ear infection. Rare occurrences as a pathogen in immunocompromised patients	None reported in the literature
Aspergillus sps.	Type I allergies (hay fever, asthma)	*A. flavus* may cause infection of the ear and eye. Infections of the lung, heart, and bladder are rare. *A niger* can infect the human ear. *A. tereus* has been isolated from patients with cystic fibrosis and ear and able to attack skin and nails	Aflatoxin B, B_2, G_1, G_2 Cyclopiazonic acid Kojic acid Aspergillic acid Some metabolites of *A. terreus* are neurotoxins and nephrotoxins
Aureobasidium sps.	Type I allergies (hay fever, asthma)	Pulmonary and cutaneous infections, peritonitis, and invasive mycosis have been rarely reported Isolated from patients whose immune system has been compromised by injury, disease, or medical therapy.	None reported in the literature
Basidiomycetes	Type I allergies (hay fever, asthma) and Type III allergies (hypersensitivity pneumonitis)	Depends on species. At least 25 different species have been tested and found to be allergenic. *Lentiun edodes* (shiitake), *Pleurotus ostreatus*, and *Merulius lacrymans* can cause hypersensitivity pneumonitis.	Amanitins Monomethyl-hydrazine Muscarine Ibotentic acid Psilocybin
Beauveria sps.	Type I allergies (hay fever, asthma) and Type III allergies (hypersensitivity pneumonitis)	*B. bassiana* isolated from pulmonary cavity of 22 year old patient	None reported in the literature
Blastomyces sps.	Not reported in the literature	Blastomycosis is a disease of both humans and animals caused by inhalation of spores from *B. dermatitidis.* Clinical manifestations include acute, sub-acute, and chronic pulmonary disease. Infection involves skin, bone, genitourinary tract, and central nervous system	None reported in the literature

Table 1 – Toxic Effects of Environmental Fungi and Moulds (cont'd) [13,17]

Bipolaris sps.	Type I allergies (hay fever, asthma)	*B. hawaiiensis* was isolated from a fatal case of meningoencephalitis and brain tissue of a patient	None reported in the literature
Botrytis sps.	Type I allergies (hay fever, asthma)	None reported in the literature	Botrydial Botryllin
Chaetomium sps.	Type I allergies (hay fever, asthma)	Onychomycosis (nail infection). *C. perfucidum* recognized as a new agent of cerebral phaeohyphomycosis *C. atrobrunneum, C. funicola*, and C. globosum have been implicated in mycotic infections of the skin, nails, brain, and as agents of peritonitis	Chaetomin Chaetoglobosins A,B, D, and F are produced by *C. globosum* Sterigmatocystin is produced in rare species
Cladosporium sps.	Type I allergies (hay fever, asthma)	Exposure can result in edema, keratitis, onychomycosis (nail infection), pulmonary infections (allergic alveolitis), sinusitis	Cladosporin Emodin
Chrysosporium sps.	Not reported in the literature	*C. tropicum* was isolated from skin lesions. *C. pannicola* causes skin infections	Not reported in the literature
Cryptococcus sps.	Not reported in the literature	C. neoformans causes cryptococcosis in humans and animals. Disease initiated by infectious particles in air causing subacute, chronic, and fatal meningitis. Skin may show lesions, ulcers, and subcutaneous tumor-like masses. Potentially life-threatening in AIDS patients.	Not reported in the literature
Curvularia sps.	Type III – (allergic sinusitis)	Occasionally infects heart, lung, and central nervous system. Responsible for mycotic keratitis (fungal infection of the cornea) in patients with underlying, debilitating diseases, or immunosuppressive chemical or radiation therapies	Not reported in the literature
Epicoccum sps.	Type I allergies (hay fever, asthma)	Not important in human medicine. May cause allergies but spore counts are seldom at elevated concentrations for long periods of time	Flavipin, Ferricrocin, Coprogen Epicorazine A, B Indole-3-acetonitrile Phenylalaine anhydride Trioricin, and α-naphtopyran

Table 1 – Toxic Effects of Environmental Fungi and Moulds (cont'd) [13,17]

Exophiala sps.	Not reported in the literature	Species can cause phaeohyphomycosis. *E. dermatitidis* has been implicated as an agent in dermatitis and pneumonia, especially in patients with traumatic injury or underlying disease. Neurotropic symptoms reported in children. *E. jeanselmei* cause phaeohyphomycotic cysts or black grain mycetomes besides skin infection	Not reported in the literature
Fusarium sps.	Type I allergies (hay fever, asthma)	Esophageal cancer related to *F. moniliforme* infected corn. Other infections include keratitis, endophalmitis, onychomycosis, cutaneous infections, mycetoma, sinusitis, pulmonary infection, endocarditis, peritonitis, central venous catheter infection, septic arthritis, and neurological and respiratory disease in animals	Trichothecenes Zearalenone Fumonisins
Geotrichum sps.	Type I allergies (hay fever, asthma)	G. candidum rarely casues human infection known as geotrichosis. Infections of oral cavity, respiratory system, and skin have been reported.	Not reported in the literature
Histoplasm var.	Not reported in the literature	H. capsulatum is initially a pulmonary mycosis that becomes systemic. Infection may have different clinical forms – asymptomatic infection, acute, benign symptoms that involve mild repiratory illness, muscle pain and cough, acute symptoms of debilitating fever, gastronintestinal illness, and involvement of other body organs, chronic disseminated disease including low grade fever, weight loss, and liver and blood disorders, and chronic pulmonary disease resembling tuberculosis	Not reported in the literature
Monocillium sps.	Not reported in the literature	Monocillium speices are not known to be pathogenic	Sterigmatocystin
Mucor sps.	Type I allergies (hay fever, asthma) and Type III allergies (hypersensitivity pneumonitis)	Heavy exposure cause specific airway allergy. Initiate disease referred to as zygomycosis. Opportunistic pathogen in patients with leukemia	Not reported in the literature
Nigrospora sps.	Not reported in the literature	Rare but implicated in skin and eye infections	Not reported in the literature
Paecilomyces sps.	Type I allergies (hay fever, asthma) and Type III allergies (hypersensitivity pneumonitis)	*P. variotti* and other species of Paecilomyces are agents of allergic alveolitis and humidifier fever. Speices are considered opportunistic pathogens and have been solated from heart inflammation and lachrymal sacs.	Ferrirubin Viriditoxin Indole-3-acetic acid Fusigen, Variotin Patulin formed by some strains

Table 1 – Toxic Effects of Environmental Fungi and Moulds (cont'd) [13,17]

Penicillium sps.	Type I allergies (hay fever, asthma)	Important clinical pathogens of humans and animals. Some strains are opportunistic pathogens, causing infection of the eyes, ears, lung, urinary tract, and lining of the heart (endocarditis). *P. aurantiogriseum* produces nephrotoxc glycopeptides which can cause keryomegaly of the kidneys and a neurotoxin verrucosidin. P. marneffie can cause life-threatening infections in HIV-positive individuals	Nephrotic glycopeptides Verrucosidin Verrucofortine 3-methyloxyviridicatin Penicillin and Penicillic acid Cyclopiazonic acid Cyclopaldic acid Palitantin Fumigaclavine A, B Ergot alkaloids Roquefortine C Chyrsogine, Citronin Citromycetin (hepatotoxin) Isofumigaclivine A, B Mycophenolic acid PR toxin and marcfortins Brevianamide A, and Decumbin
Rhinocladiella sps.	Not reported in the literature	Rarely causes chromoblastomycosis, a chronic skin and lymph disease of the lower extremeties and sometimes of the hands, head, or trunk. Disease characterized by warty nodules, tumor-like masses, cauliflower-like lesions. Infections of the central nervous system and foot have been documented in the literature.	Not reported in the literature
Rhizopus sps.	Type I allergies (hay fever, asthma) and Type III allergies (allergic alveolitis)	*Rhizopus* are opportunistic pathogens causing zygomycosis primarily in individuals compromised physically, physiologically, immunologically, or who have suffer trauma. Disease can become systemic with invasion of the central nervous system, blood, lungs, and gastrointestinal tract	Rhizonin A
Scopulariopsis sps	Type III allergies (allergic alveolitis)	Potential pathogenic fungus. *S. holsaticus* may cause infection of the skin and, even more common, infection of the nails	Deacetoxycephalosporin C

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Stachybotrys sps.	Type I allergies (hay fever, asthma)	*S. chartarum* produces mycotoxins that are toxic by ingestion and strongly inhibit protein synthesis, RNA and DNA synthesis. Anecdotal evidence of symptoms ranging from chronic fatigue syndrome to pulmonary hemorrhage in infants. Other reported symptoms are dermatitis, burning sensation of the mouth and nasal passage, and mucosal irritation such as cough, phlegm. Inhalation of conidia may cause pneumomycotoxicosis	Macrocyclic trichothecenes Roridin E Satratoxin H Sporidesmin G Trichoverrins Verrucarol
Trichoderma sps.	Type I allergies (hay fever, asthma)	Inhalation of conidia or the volatile components of this mould may cause symptoms similar to *Stachybotrys.*	6-phenyl-α- pyrone Pachybasin Chrysophanol Emodin Trichodermin Trichotoxin A Trichoriazines
Ulocladium sps.	Type I allergies (hay fever, asthma)	*U. chartarum* reported to cause subcutaneous infection in a patient	Not reported in the literature
Wallemia sps.	Type I allergies (hay fever, asthma)	Allergy was reported from exposure to *W. sebi*	Walleminol
Verticillium sps.	Not reported in the literature	Not recognized as human pathogen. Rare agent of keratitis	*V. albo-atrum* produces a wilt toxin which is a phytotoxic mycotoxin