ERMI Mycotoxic Species and Clinical Presentation:

Mycotoxin Review

Acremonium strictum

Alternaria alternata

Aspergillus ochraceus

Aspergillus flavus/oryzae

Aspergillus fumigatus

Aspergillus niger

Aspergillus penicillioides

Aspergillus restrictus*

Aspergillus sclerotiorum

Aspergillus svdowii

Aspergillus unguis

Aspergillus ustus

Aspergillus versicolor

Aureobasidium pullulans

Chaetomium globosum

Cladosporium cladosporioides 1

Cladosporium cladosporioides 2

Cladosporium herbarum

Cladosporium sphaerospermum

Epicoccum nigrum

Eurotium (Asp.) amstelodami

Mucor amphibiorum*

Paecilomyces variotii

Penicillium brevicocompactum

Penicillium chrysogenum

Penicillium corlophilum

Penicillium crustosum*

Penicillium purpurogenum

Penicillium spinulosum*

Penicillium variabile

Rhizopus stolonifer

Scopulariopsis brevicaulis/fusca

Scopulariopsis chartarum

Stachybotrys chartarum

Trichoderma viridie*

Wallemia sebi

Eurotium (Asp.) amstelodami covers E. chevalieri, E. herbariorum, E. rubrum and E. repens.

Penicillium spinulosum covers P. glabrum, P. lividum, P. pupurescens, and P. thomii.

Trichoderma viride covers T. koningii and T. atroviride.

Aspergillus restrictus covers A. caesillus and A. conicus.

Mucor amphibiorum covers M. circinelloides, M. hiemalis, M. indicus, M. mucedo, M. racemosus, M. ramosissimus and Rhizopus zygosporus, R. homothalicus, R. microsporus, R.

^{*} Genetically closed-related species may be detected in the indicator assay:

oligosporus, R. oryzae. Penicillium crustosum covers P. camembertii, P. commune, P. echinulatum, P. solitum.

Mycotoxin Review

https://en.wikipedia.org/wiki/Mycotoxin

Myco (fungus) toxin (poison); these come in many types, flavors, & varieties of toxin produced from different families of fungi. One mold species may produce many different mycotoxins, and several species may produce the same mycotoxin. These toxins can affect the brain & nerves (neurotoxins), skin, respiratory/breathing system, gut and other parts of the body.

An important concept to understand about mold illness is that sometimes a fungus or mold can invade the human body and start growing there. Typically, this only happens to people who have weakened, or compromised immune systems, such as from AIDS, HIV, Cancer, Chemotherapy etc.

Toxins or poisons, released by the mold or fungus are another matter entirely! The mold does not need to invade and grow inside or on a person, it releases these poisons into the environment where they circulate in air currents, settle on surfaces and release Volatile Organic Compounds (VOC's) which can also produce toxic effects.

This is an extremely important concept in understanding how mold can make us sick!

Molds growing in buildings can be divided into three groups — primary, secondary, and tertiary colonizers. Each group is categorized by the ability to grow at a certain water activity requirement. It has become difficult to identify mycotoxin production by indoor molds for many variables, such as

- (i) they may be masked as derivatives
- (ii) they are poorly documented and
- (iii) the fact that they are likely to produce different metabolites on different building materials. Some of the mycotoxins in the indoor environment are produced by *Alternaria*, *Aspergillus* (multiple forms), *Penicillium*, and *Stachybotrys*. [21]

The negative health effects of mycotoxins are a function of the <u>concentration</u>, the duration of exposure and the subject's sensitivities. The concentrations experienced in a normal home, office or school are often too low to trigger a health response in occupants.

Stachybotrys is possibly an important contributing factor to DBRI. So far animal models indicate that airway exposure to *S. chartarum* can cause allergic sensitization, inflammation, and cytotoxicity (cell-toxicity or poisoning) in the upper and lower respiratory tracts. Trichothecene toxicity appears to be an underlying cause of many of these adverse effects. Recent findings indicate that lower doses (studies usually involve high doses) can cause these symptoms. [22]

Mycotoxicosis is the term used for poisoning associated with exposures to mycotoxins. The symptoms of mycotoxicosis depend on the type of mycotoxin; the concentration and length of exposure; as well as age, health, and sex of the exposed individual. [13] The synergistic effects associated with several other factors such as genetics, diet, and interactions with other toxins

have been poorly studied. Therefore, it is possible that vitamin deficiency, caloric deprivation, alcohol abuse, and infectious disease status can all have compounded effects with mycotoxins. [13] In turn, mycotoxins have the potential for both acute and chronic health effects via ingestion, skin contact, [37] and inhalation. These toxins can enter the blood stream and lymphatic system; they inhibit protein synthesis, damage macrophage systems, inhibit particle clearance of the lung, and increase sensitivity to bacterial endotoxin. [23]

Major Toxin groups

Aflatoxins are a type of mycotoxin produced by <u>Aspergillus</u> species of fungi, such as <u>A. flavus</u> and <u>A. parasiticus</u>. [8] The umbrella term aflatoxin refers to four different types of mycotoxins produced, which are B₁, B₂, G₁, and G₂. [9] Aflatoxin B₁, the most toxic, is a potent <u>carcinogen</u> and has been directly correlated to adverse health effects, such as <u>liver cancer</u>, in many animal species. [8] Aflatoxins are largely associated with <u>commodities</u> produced in the <u>tropics</u> and <u>subtropics</u>, such as <u>cotton</u>, <u>peanuts</u>, <u>spices</u>, <u>pistachios</u>, and <u>maize</u>. [8][9]

Ochratoxin is a mycotoxin that comes in three secondary metabolite forms, A, B, and C. All are produced by *Penicillium* and *Aspergillus* species. The three forms differ in that Ochratoxin B (OTB) is a nonchlorinated form of Ochratoxin A (OTA) and that Ochratoxin C (OTC) is an ethyl ester form Ochratoxin A. [10] *Aspergillus ochraceus* is found as a contaminant of a wide range of commodities including beverages such as beer and wine. *Aspergillus carbonarius* is the main species found on vine fruit, which releases its toxin during the juice making process. [11] OTA has been labeled as a carcinogen (causes cancer) and a nephrotoxin, (kidney poison) and has been linked to tumors in the human urinary tract, although research in humans is limited by confounding factors. [10][11]

<u>Citrinin</u> is a toxin that was first isolated from *Penicillium citrinum*, but has been identified in over a dozen species of *Penicillium* and several species of <u>Aspergillus</u>. Some of these species are used to produce human foodstuffs such as cheese (*Penicillium camembertii*), sake, <u>miso</u>, and <u>soy sauce</u> (<u>Aspergillus oryzae</u>). Citrinin is associated with <u>yellowed rice</u> disease in Japan and acts as a <u>nephrotoxin</u> in all animal species tested. Although it is associated with many human foods (<u>wheat, rice, corn, barley, oats, rye, and food colored with Monascus pigment) its full significance for human health is unknown. Citrinin can also act synergistically with Ochratoxin A to depress <u>RNA synthesis</u> in murine (mouse) kidneys.</u>

Ergot Alkaloids are compounds produced as a toxic mixture of alkaloids in the sclerotia of species of *Claviceps*, which are common pathogens of various grass species. The ingestion of ergot sclerotia from infected cereals, commonly in the form of bread produced from contaminated flour, cause ergotism the human disease historically known as St. Anthony's Fire. There are two forms of ergotism: gangrenous, affecting blood supply to extremities, and convulsive, affecting the central nervous system. Modern methods of grain cleaning have significantly reduced ergotism as a human disease, however it is still an important veterinary problem. Ergot alkaloids have been used pharmaceutically. [13]

<u>Patulin</u> is a toxin produced by the <u>P. expansum</u>, Aspergillus, Penicillium, and <u>Paecilomyces</u> fungal species. P. expansum is especially associated with a range of moldy <u>fruits</u> and <u>vegetables</u>, in particular rotting apples and figs. [14][15] It is destroyed by

the <u>fermentation</u> process and so is not found in apple beverages, such as <u>cider</u>. Although patulin has not been shown to be carcinogenic, it has been reported to damage the <u>immune system</u> in animals. In 2004, the <u>European Community</u> set limits to the concentrations of patulin in food products. They currently stand at 50 μ g/kg in all fruit juice concentrations, at 25 μ g/kg in solid apple products used for direct consumption, and at 10 μ g/kg for children's apple products, including apple juice. Italian

Fusarium toxins are produced by over 50 species of *Fusarium* and have a history of infecting the grain of developing cereals such as wheat and maize. They include a range of mycotoxins, such as: the fumonisins, which affect the nervous systems of horses and may cause cancer in rodents; the trichothecenes, which are most strongly associated with chronic and fatal toxic effects in animals and humans; and zearalenone, which is not correlated to any fatal toxic effects in animals or humans. Some of the other major types of *Fusarium* toxins include: beauvercin and enniatins, butenolide, equisetin, and fusarins.

Toxins that affect one species may or may not affect another. It's generally a good idea to avoid any poison that affects any species.

http://www.sciencedirect.com/science/article/pii/S1319562X1200040X

Wood is highly vulnerable to fungal attack. *Cladosporium* and *Penicillium (Penicillium brevicompactum* and *Penicillium expansum*) are reported to infest wooden building materials. Kiln dried wood surfaces are more susceptible to fungi (Sailer et al., 2010). Acylated wooden furnitures, wood polyethylene composites, plywood and modified wood products are susceptible to infestation by *Aspergillus*, *Trichoderma* and *Penicillium* (Thacker, 2004 and Doherty et al., 2011).

<u>List of Fungal Species associated with water-damaged buildings and human illness:</u> Acremonium strictum

https://en.wikipedia.org/wiki/Acremonium_strictum#Pathophysiology

Clinical presentation of an infection is ill-defined, but most individuals may present with a skin rash and flu like symptoms, such as elevated body temperature and fatigue. [1][3] In more severe infections, such as in immunodeficient individuals, peritonitis (inflammation of the abdominal cavity) and pleuritis (inflammation of the lung cavity), and may lead to multi-organ failure. [19][20] In the case of invasive infections, surgical intervention may be required to remove fungal mass from body tissues. [4] Due to limited, ill-defined cases and the variance in clinical presentation and species identification, no optimal treatments are available. [2] A. strictum and other Acremonium species are generally resistant to most antifungals, but antifungal susceptibility testing is recommended to select the most appropriate treatment for the strain of A. strictum that is the infection agent. [3] Amphotericin B therapy coupled with ketoconazole is usually recommended as the best available treatment. [2][3]

Alternaria alternata

http://www.moldbacteria.com/mold/alternaria.html

A. alternata is not commonly isolated from indoor building materials and in most instances spores found in indoor air environment may have originated from outdoor sources. A closely related mold, *Ulocladium chartarum*, which is very common in indoor environments is

frequently misidentified as *Alternaria alternata*. *Ulocladium chartarum* is common on wallpaper and drywall, and has been isolated from emulsion paint, polyurethane, plywood and manila fiber. *A. alternata* shows significant morphological variation and is believed to be a species complex meaning that it is an amalgam of closely related strains rather than a single homogeneous species.

A. alternata is recognized as an important allergen (causing allergic reactions) with airborne spores and mycelial fragments being responsible for the allergic symptoms in individuals with rhinitis (nasal inflammation) or bronchial asthma. Alternaria sensitivity can also lead to severe and potentially fatal asthma. Studies have shown that up to 70 % of mold-allergic patients have skin test reactivity to Alternaria. It has also been shown that prolonged heavy exposure to A. alternata spores and mycelial fragments mimics that of other allergens such as cat dander and dust mites. It has also been recorded as an opportunistic pathogen causing skin diseases particularly in immunocompromised patients such as the bone marrow transplant patients.

Note: The presence of Stachybotrys, Chaetomium, Trichoderma, Aureobasidium and also actinomycetes and other bacteria in an indoor environment is generally indicative of wet conditions, not just high humidity or condensation on indoor surfaces.

Aspergillus ochraceus

See Mycotoxin Review; Grows well in "middle-wet" conditions, Produces Ochratoxin

Aspergillus flavus/A. oryzae

See <u>Mycotoxin Review</u>; Grows well in "middle-wet" conditions, Produces <u>Aflatoxin http://cmr.asm.org/content/16/3/497.full</u>

Originally isolated from *Penicillium cyclopium* (now *Penicillium aurantiogriseum*), cyclopiazonic acid is an indole tetramic acid. This mycotoxin is a specific inhibitor of calcium-dependent ATPase and induces alterations in ion transport across cell membranes (214). It is produced by many other species of *Penicillium* as well as several species of *Aspergillus*, including *Aspergillus flavus*. Calcium transport affects nerve, muscle and other cellular functions.

Aspergillus fumigatus Grows well in "middle-wet" conditions http://cmr.asm.org/content/16/3/497.full

There is relatively little evidence that mycotoxins enhance the ability of fungi to grow in vertebrate hosts. *Aspergillus fumigatus* is case in point. It is the major species associated with aspergillosis and produces gliotoxins (inhibitors of T-cell activation and proliferation as well as macrophage phagocytosis which *weaken the immune system*). However, gliotoxin is not known to be produced in significant amounts by *Aspergillus fumigatus*. This may be another example of the difference between invasive fungal disease and fungal toxin production harming the host.

Aspergillus niger Grows well in "middle-wet" conditions, See Mycotoxin Review; Produces Ochratoxin

Aspergillus penicillioides Grows well in "middle-wet" conditions, Is able to grow across a wide range of moisture indices from very dry to quite damp.

Aspergillus restrictus* Grows well in "middle-wet" conditions,

See Mycotoxin Review;

Aspergillus sclerotiorum Grows well in "middle-wet" conditions,

See Mycotoxin Review;

Aspergillus sydowii Grows well in "middle-wet" conditions,

https://en.wikipedia.org/wiki/Aspergillus_sydowii

Aspergillus sydowii has been implicated in the <u>pathogenesis</u> of several human diseases, including <u>aspergillosis, onychomycosis</u>, and <u>keratomycosis</u>. [4] as an invasive disease, not as a mycotoxin.

See Mycotoxin Review;

Aspergillus unguis

Grows well in "middle-wet" conditions See Mycotoxin Review

Aspergillus ustus

See Mycotoxin Review

Aspergillus versicolor

https://en.wikipedia.org/wiki/Aspergillus_penicillioides

Like other members of its species, A. versicolor is an opportunistic pathogen (usually harms people who are already ill or weak) and is considered to be an important causative agent of <u>aspergillosis</u>. ^[6] There have been reported cases of the fungus causing <u>onychomycosis</u>, (nail infection) which is often treated with topical azoles. However, A. versicolor is insensitive to these treatments and the infection can persist even after months or years of treatment. Studies have shown that like other Aspergillus species, A. versicolor is highly sensitive to terbinafine, which has in vitro fungicidal activity. ^[16]

There are more than 20 <u>allergens</u> that have been identified from *A. versicolor*, with the most abundant being glyceraldehyde-3-phosphate dehydrogenase. Other proteins include sorbitol reductase, catalase, enolase, malate dehydrogenase, and Asp v 13. It is common in developed countries to measure IgG responses in humans.

Additionally, mycotoxins can act as immunosuppressant's, which likely explains the association of increased prevalence of frequent infections among inhabitants of damp buildings. [19]

Aureobasidium pullulans

https://en.wikipedia.org/wiki/Aureobasidium_pullulans

Chronic human exposure to *A. pullulans* via humidifiers or air conditioners can lead to hypersensitivity <u>pneumonitis</u> (lung inflammation, extrinsic allergic alveolitis) or "<u>humidifier lung</u>". This condition is characterized acutely by <u>dyspnea</u> (shortness of breath), cough, fever, chest infiltrates, and acute inflammatory reaction. The condition can also be chronic, and <u>lymphocyte</u>-mediated. The chronic condition is characterized radiographically by reticulonodular infiltrates in the lung, with apical sparing. The strains causing infections in humans were reclassified to *A. melanogenum*. [5]

http://www.rightdiagnosis.com/a/aureobasidium_pullulans_exposure/intro.htm

It can cause infection in just about any part of the body depending on the nature of the exposure (inhalation, wound, ingestion etc.) and as such the type and severity of symptoms can vary considerably.

- Pneumonia
- Asthma
- Dermatitis
- Keratitis
- Respiratory system irritation
- Digestive symptoms
- Respiratory symptoms
- Skin symptoms
- <u>Urinary symptoms</u>
- Allergy symptoms
- Sinusitis
- Peritonitis
- Skin infection
- Fungal infection
- Hypersensitivity pneumonitis
- more information...»

Chaetomium globosum

Grows well in "wet-wet" conditions

http://www.moldlab.com/wp_moldlab/black-mold-symptoms-chaetomium/

<u>www.mold-help.org</u> describes C. globosum as allergenic and an agent of onychomycoses (nasal infection), peritonitis, cutaneous (skin) lesions and potential agent in fatal systemic mycoses. It is also says "No toxic diseases have been documented to date"

Chaetomium globosum grows on damp cellulosic materials indoors and can adversely affect human health through allergic and toxic reactions. To study allergic response, exposure assessments must be done by measuring human allergens or antigens.

Cladosporium cladosporioides 1

https://en.wikipedia.org/wiki/Cladosporium_cladosporioides#Animals

Cladosporium cladosporioides rarely causes infections in humans, although superficial infections have been reported. [4][24]

It can occasionally cause pulmonary (lung)^[25] and cutaneous^[26] phaeohyphomycosis^{[4][27]} and it has been isolated from cerebrospinal fluid in an immunocompromised patient. ^[24]

This species can trigger <u>asthmatic reactions</u> due to the presence of allergens and <u>beta-glucans</u> on its <u>spore</u> surface. [28]

In mice, living *C. cladosporioides* spores have induced <u>hyperresponsiveness of the lungs</u>, as well as an increase in <u>eosinophils</u>, which are <u>white blood cells</u> typically associated with <u>asthmatic</u> and <u>allergic</u> reactions. [28]

Cladosporium cladosporioides can also induce respiratory inflammation due to the up-regulation of macrophage inflammatory protein (MIP)-2 and keratinocyte chemoattractant (KC), which are cytokines involved in the mediation of inflammation. [29]

A case of <u>mycotic encephalitis</u> (brain inflammation) and <u>nephritis</u> (kidney inflammation) due to *C. cladosporioides* has been described in a dog, resulting in altered behavior, depression,

abnormal reflexes in all 4 limbs and loss of vision. [30] Post-mortem examination indicated posterior brainstem and cerebellar lesions, confirming the causative involvement of the agent. [30]

http://www.mold-help.org/content/view/414/0/

Most commonly identified as an outdoor fungus. The outdoor numbers are reduced in the winter. The numbers are often high in the summer. Often found indoors in numbers less than outdoor numbers. Indoor Cladosporium may be different than the species identified outdoors. It is commonly found on the surface of fiberglass duct liner in the interior of supply ducts. A wide variety of plants are food sources for this fungus. It is found on dead plants, woody plants, food, straw, soil, paint and textiles. Produces greater than 10 antigens. Antigens in commercial extracts are of variable quality and may degrade within weeks of preparation.

http://www.moldunit.com/cladosporium.html

What are the symptoms?

Symptoms most common to Cladosporium mold are: congested or runny nose, sinus problems, red and watery eyes, skin irritation, fatigue, sore throat, cough and hoarseness. Over time, more serious symptoms may develop such as, ear inflammation; nose bleeds and joint pain, without swelling.

Cladosporium cladosporioides 2

Cladosporium herbarum

http://www.moldunit.com/cladosporium.html

Symptoms most common to Cladosporium mold are: congested or runny nose, sinus problems, red and watery eyes, skin irritation, fatigue, sore throat, cough and hoarseness. Over time, more serious symptoms may develop such as, ear inflammation; nose bleeds and joint pain, without swelling.

http://mycota-crcc.mnhn.fr/site/specie.php?idE=102#ancre1

C. herbarum is implicated in cases of allergies, rhinitis and asthma.

C. herbarum parasites living plants followed by a saprophytic phase during which it continues to sporulate on dead tissues. Its parasitism phase is short (3-5 months in average) then decreases.

Cladosporium sphaerospermum

https://microbewiki.kenyon.edu/index.php/Cladosporium_sphaerospermum#Pathology

C. sphaerospermum is one of the most commonly isolated airborne contaminants. Some of the strains of the fungus are not pathogenic to humans and animal; they are, however, detrimental to plants. Some of the species, can cause cerebral and cutaneous phaehyphomycoses, sinusitis, and peritonitis in humans [3]. In 2003 a case was reported of a woman who developed intrabronchial lesion due to C. sphaerospermum [22]. In animals, skin and lungs are the most affected by the fungus organs. For example, exposed to the fungus mice showed systemic and subcutaneous infections and even death in immunocompromised mice [21]. C. sphaerospermum can also cause erratic behavior in red snappers following infection of the bladder and kidney [20]. Eledone cirrhosa, the lesser octopus, is also not immune to infection by this fungus [8].

Epicoccum nigrum

http://ispub.com/IJTO/3/1/12980

Chronic Exposure To Alternaria Tenuis, Pullularia Pullulans, And Epicoccum Nigrum May Lead To Symptoms Of *Neuropsychological Illnesses*: Evidence From A Comprehensive Evaluation Results: Abnormal antibodies to Alternaria tenuis, Pullularia pullulans, and Epicoccum nigrum antigens were found in all the subjects' serum. EEG examination was abnormal all the subjects with 10 Hz posterior dominant activities in 6 out of 12, which were synchronous, symmetrical and attenuated on eye opening and eye-closure. There was an evidence of tremor of the extremities in 3 subjects.

Gross neuropsychological abnormalities including those observed in the brain-damaged population and significantly below non-brain damaged functioning were observed. These findings seem to indicate that chronic exposures to Alternaria tenuis, Pullularia pullulans, and Epicoccum nigrum might have neuropsychological effects, and that most likely, only one abnormal antibody to toxigenic mold antigen could have the most dominant adverse toxic exertion leading to the observed neuropsychological effects.

Conclusion: It is concluded therefore, that *chronic exposures to certain toxigenic molds might lead to neuropsychological manifestations* and that although, it is acknowledged that the contaminations of the indoor environment by toxigenic molds are directly related to the adverse health effects on the occupants, there could be a situation where such relationship does not exist.

https://en.wikipedia.org/wiki/Epicoccum_nigrum#Epidemiology

Epicoccum nigrum is associated with respiratory fungal allergies, including allergic asthma, rhinitis, hypersensitivity pneumonitis, and allergic fungal sinusitis. [16][31] Two pediatric cases of <u>hypersensitivity pneumonitis</u> caused by *E. nigrum* were reported in children living in a damp and moldy home, with daily exposure to *E. nigrum* in the shower. [32]

Eurotium (Asp.) amstelodami

http://www.lmaleidykla.lt/publ/0235-7224/2006/3/Eko_042_047.pdf

Five mycotoxins were found in the mycelium of A. amstelodami 724 and two in the medium. There were identified patulin, ochratoxin A (OTA) and sterigmatocystin. The ability of A. amstelodami 724 to produce one of these mycotoxins – OTA – was confirmed quantitatively growing the fungi on grains. The greatest amount of OTA was estimated after 21 days of growing.

This fungus produces echinulin, preechinulin, neoechinulins, cryptoechinulin (Cole, Cox, 1981). OTA exhibited carcinogenic, nephrotoxic, teratogenic (birth defects), neurotoxic and immunotoxic effects in experimental rodents and other animals (IPCS, 2001). OTA has been identified as a causative factor in the human disease called Balkan endemic nephropathy. It evokes an acute hepatic injury, fatty infiltration, and focal necrosis in livers of laboratory animals.

In most species of animals OTA affects such organs as liver, myocardium, gastrointestinal tract, lymphoid organs, skeletal system, hemopoietic tissues and reproductive organs. Tests on laboratory animals indicated the capability of this substance to trigger immunomodulation (immune system alterations) even at levels far below the toxicity threshold (Muller et al., 1999). The present study revealed the effects of OTA in the model cell cultures derived from the potent OTA-target organs – blood and liver. During the experiments there were made quantitative

analyses of the effect of OTA treatment on the viability and proliferation of hemopoietic and hepatic (MH-22A) cell lines.

Contradictory reports on DNA-damaging activity and on the carcinogenity of mycotoxins have appeared. It was shown that OTA may activate different cellular processes involved in the degradation of various kinds of cells. One species of fungi produces a range of mycotoxins which have different targets and different mechanisms of action.

Mucor amphibiorum*

http://medical-dictionary.thefreedictionary.com/mucormycosis

Mucormycosis is caused by fungi of several different species, including *Mucor*, *Rhizopus*, *Absidi* a, and *Rhizomucor*. When these organisms gain access to the mucous membranes of the patient's nose or lungs, they multiply rapidly andinvade the nearby blood vessels. The fungi destroy soft tissue and bone, as well as the walls of blood vessels.

The early symptoms of rhinocerebral mucormycosis include fever, sinus pain, <u>headache</u>, and <u>cellulitis</u>(skininfection). As the fungusreaches the eye tissues, the patient develops dilated pupils, drooping eyelid, a bulging eye, and eventually hemorrhageof the blood vessels in the brain, causi ng convulsions, partial paralysis, and <u>death</u>.

The symptoms of pulmonary mucormycosis include fever and difficulty breathing, with eventual bleeding from the lungs.

The symptoms of gastrointestinal mucormycosis are not unique to the disease, which may Complicate diagnosis.

Patients typically complain of pressure or pain in the abdomen, nausea, and vomiting.

Paecilomyces variotii

http://www.mold-help.org/content/view/423/

Paecilomyces species can cause various infections in humans. These infections are occasionally referred to as paecilomycosis. Corneal ulcer, keratitis (corneal inflammation), and endophthalmitis (inner eye inflammation) due to Paecilomyces may develop following extended wear contact lens use or ocular surgery. Paecilomyces is among the emerging causative agents of opportunistic mycoses in immunocompromised hosts. Direct cutaneous inoculation may lead to these infections. These infections may involve almost any organ or system of human body. Soft tissue, pulmonary, and cutaneous infections, cellulitis onychomycosis, sinusitis, otitis media, endocarditis, osteomyelitis, peritonitis and catheter-related fungemia have all been reported. Paecilomyces species can also cause allergic disorders, such as allergic alveolitis.

Penicillium brevicompactum

(*Penicillium spp.* do have the ability to produce mycotoxins.)

http://www.dynamiclist.com/export/static_html.aspx?node=53687436-2e3a-4aec-9f29cc878ce9974d

Mycophenolic acid is produced by Penicillium brevicompactum. Health effects: blocks inosine monophosphate dehydrogenase, it acts as an immunosuppressive.

http://www.moldbacteria.com/mold/indoor-molds-that-produce-known-mycotoxins-on-building-materials.html

Penicillium brevicompactum is common on damp walls and building materials e.g., gypsum board; floor, carpet, mattress and upholstered-furniture dust. *P. brevicompactum* produces

mycophenolic acid. *P. brevicompactum* can grow at -2 and 30 °C with an optimum at 25 °C. Its water activity requirements are a minimum of 0.75 and an optimum at 0.96.

http://www.sciencedirect.com/science/article/pii/S0040403900002239

(+)-Brevione A. The first member of a novel family of bioactive spiroditerpenoids isolated from *Penicillium brevicompactum*Dierckx

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4556995/

Three new breviane spiroditerpenoids, breviones I–K (104–106), and the known breviones (107–110) (Figure 17) have been isolated from the crude extract of the deep-sea fungus *Penicillium* sp. and display strong cytotoxic effects against MCF-7 cells (IC₅₀: 7.44–28.4 μ M). Compound 106 exhibits cytotoxic activity against A549 cells with IC₅₀ of 32.5 μ M [46]. Similar compounds, Breviones F–H (111–113) (Figure 17), have been isolated from the same fungal species by Li *et al.* (2009) [61]. These compounds (111–113) show 25.2%–44.9% cytotoxicity against HeLa at 10 μ g/mL. Particularly, compound 111 displays a very strong cytotoxicity to HIV-1 replication in C8166 cells with an EC₅₀ of 14.7 μ M [61].

Penicillium chrysogenum

http://www.mold-survivor.com/symptoms.html

(*Penicillium spp.* do have the ability to produce mycotoxins.)

The genus Penicillium has several species. The most common ones include Penicillium chrysogenum, Penicillium citrinum, Penicillium janthinellum, Penicillium marneffei, and Penicillium purpurogenum.

This fungus has been isolated from patients with keratitis, ear infections, pneumonia, endocarditis (heart-lining infection), peritonitis (abdominal cavity inflammation), and urinary tract infections. Penicillium infections are most commonly exhibited in immunosuppressed individuals. For example, P. marneffei is a fungus abundant in Southeast Asia that typically infects patients with AIDS in this area. Infection with P. marneffei is acquired via inhalation and initially results in a pulmonary infection and then spreads to other areas of the body (lymphatic system, liver, spleen, and bones), and is often fatal. An indication of infection is the appearance of papules that resemble acne on the face, trunk, and extremities.

Penicillium spp. do have the ability to produce mycotoxins.

The mycotoxin known as Ochratoxin A, which is nephrotoxic and carcinogenic, may be produced by Penicillium verrucosum.

Verrucosidin is another mycotoxin produced by this fungus that exhibits neurotoxicity. Penicillic acid is another mycotoxin that is nephrotoxic (causes kidney and liver damage). Permanent problems sometimes associated with fungal exposure after treatment:

- Balance
- Short term memory
- Hearing
- Sight

See Associated Illnesses after Fungal Exposure

Penicillium corlophilum

http://www.mold-survivor.com/symptoms.html

(*Penicillium spp.* do have the ability to produce mycotoxins.)

Penicillium crustosum*

http://www.mold-survivor.com/symptoms.html

(*Penicillium spp.* do have the ability to produce mycotoxins.)

http://www.sciencedirect.com/science/article/pii/S0041010112007714

Neurotoxicity of *Penicillium crustosum* secondary metabolites: Tremorgenic (causes tremors) activity of orally administered penitrem A and thomitrem A and E in mice. It produces a neurotoxin called penitrem A.

Several cases of neurological disease in dogs after poisoning by food- and feed-borne *Penicillium* toxins.

http://www.moldbacteria.com/mold/penicillium.html

Some species are known to produce toxic compounds (mycotoxins). The spores can trigger allergic reactions in individual's sensitive to mold.

Penicillium chrysogenum is the most common species in indoor environment. It is widespread and has a wide range of habitats. In indoor environment, it is extremely common on damp building materials, walls and wallpaper, floor, carpet mattress and upholstered furniture dust. It produces a number of toxins of moderate toxicity. It is allergenic (i.e., it can trigger allergic reactions).

Some species of *Penicillium* can also infect immunocompromised individuals. For example, *P. marneffei* is pathogenic particularly in patients with AIDS and its isolation from blood is considered as an HIV marker in endemic areas. It has emerged as the third most common opportunistic pathogen among HIV-positive individuals in Southeast Asia where it is endemic and infects bamboo rats which serve as reservoirs for human infections.

Penicillium as A Producer of Mycotoxins

Penicillium species other than *P. marneffei* are commonly considered as contaminants but they are also known to produce mycotoxins. For example, *P. verrucosum* produces a mycotoxin, ochratoxin A, which is damaging to the kidney (nephrotoxic) and could be cancer causing (carcinogenic). The production of the toxin usually occurs in cereal grains at cold climates but has been isolated in buildings contaminated with *Penicillium*. Other mycotoxins include patulin, citrinin, and citroviridin among others.

Penicillium purpurogenum

http://www.mold-survivor.com/symptoms.html

(*Penicillim spp.* do have the ability to produce mycotoxins.)

http://www.sciencedirect.com/science/article/pii/S1319562X1200040X

Grows well on paper (drywall)

https://books.google.com/books?id=ywtaAgAAQBAJ&pg=PA352&lpg=PA352&dq=Penicillium+purpurogenum++health+effects&source=bl&ots=616lBH-

 $\frac{bE4\&sig=k6reWOUpciWWaQdzG7Vc8MKedK0\&hl=en\&sa=X\&ved=0ahUKEwjFkoSlpezNA}{hWMMyYKHYfFDXIQ6AEIUDAG#v=onepage\&q=Penicillium%20purpurogenum%20%20he}{alth%20effects\&f=false}$

Is frequently found in water-damaged buildings that have been associated with adverse health effects.

Penicillium spinulosum*

http://www.mold-survivor.com/symptoms.html

(Penicillim spp. do have the ability to produce mycotoxins.)

http://www.architecturaldiagnostics.com/pdf/Fungi%20Paper.pdf

Tolerates dry conditions and causes inflammatory problems in the respiratory tract.

Penicillium variabile

http://www.mold-survivor.com/symptoms.html

(*Penicillim spp.* do have the ability to produce mycotoxins.)

http://www.sanair.com/Fungi/742-Penicillium-variabile/View-details.html

It may cause hypersensitivity pneumonitis and allergic alveolitis in susceptible individuals. It is reported to be allergenic (skin). Common cause of extrinsic asthma (immediate-type hypersensitivity: type I). Acute symptoms include edema and bronchospasms, chronic cases may develop pulmonary emphysema.

Often found in aerosol samples. Commonly found in soil, food, cellulose, and grains. It is also found in paint and compost piles. Commonly found in carpet, wallpaper, and in interior fiberglass duct insulation. Both Penicillium and Aspergillus spores share similar morphology on

non-viable analysis and therefore are lumped together into the same group. Only through the visualization of reproductive structures can the genera be distinguished.

Rhizopus stolonifera

http://www.mold.ph/rhizopus.htm

Rhizopus species are among the fungi causing the group of infections referred to as <u>zygomycosis</u>. Zygomycosis is now the preferred term over mucormycosis for this angio (vascular) – invasive disease. *Rhizopus arrhizus* is the most common cause of zygomycosis and is followed by *Rhizopus microsporus var. rhizopodiformis*.

Zygomycosis infection includes mucocutaneous, rhinocerebral, genitourinary, gastrointestinal, pulmonary, and disseminated infections. The most frequent predisposing factors for zygomycosis include diabetic ketoacidosis and immunosuppression due to various reasons, such as organ transplantation and other factors such as desferoxamine treatment, renal failure, extensive burns, trauma, and intravenous drug use which may also predispose to development of zygomycosis. Heatstroke has been described as a risk factor for disseminated zygomycosis as well. Contaminated adhesive tapes and wooden tongue depressors have been reported to lead to nosocomial outbreaks of zygomycosis. Vascular invasion that causes necrosis of the infected tissue, and perineural invasion are the most frustrating features of these infections. Zygomycosis is frequently considered as fatal infection.

Scopulariopsis brevicaulis/fusca

http://www.moldbacteria.com/mold/scopulariopsis.html

In indoor environments it is found on damp walls, cellulose board and wallpaper; wood; floor and mattress dust. Species of *Scopulariopsis* has also been isolated from carpets, hospital floors, swimming pools; wooden food packing, shoes and wood pulp. *Scopulariopsis* species are sometimes encountered growing on meat in storage.

Health effects associated with Scopulariopsis species

A number of species of *Scopulariopsis* are of importance in the medical field, having been implicated in infection of nails. Many species of *Scopulariopsis* can liberate arsenic gas from substrates containing that element; this may be noticed as a garlic-like odour. In the past, there have been a few serious poisoning incidents due to the growth

of *Scopulariopsis brevicaulis* on dyes used in wallpaper production. There were also suggestions that the infant cot death syndrome (SIDS) may in some cases be caused by *Scopulariopsis* but these have largely been refuted.

Scopulariopsis brevicaulis

Of the group, *Scopulariopsis brevicaulis* is by far the most common species encountered in an indoor environment. It is found growing on all kinds of decomposing organic matter, and flourishes on materials containing a high level of protein, such as meat and ripening cheese. It decomposes cotton, textiles and paper products and causes deterioration of paints. It is also implicated as a human pathogen (causing illness in people).

Other common species include: *Scopulariopsis acremonium*, *S. halophilica*, and *S. fimicola*. *S. acremonium* has been reported as causing the spoilage of free fatty acids in stored barley. *S. halophilica* is particularly resistant to high concentrations of salt, and causes spoilage of salt fish in various Asian countries. *S. fimicola* causes the "white plaster mould" of commercial mushroom growing.

The Scopulariopsis group of molds are commonly associated with skin and nail problems.

Scopulariopsis chartarum

Se above, S. brevicaulis which has many similar effects.

Stachybotrys chartarum

Grows well in "wet-wet" conditions

 $\underline{http://www.moldbacteria.com/mold/can-stachybotrys-chartarum-black-mold-affect-pregnancy.html}$

Stachybotrys chartarum or <u>black mold</u> as it's commonly called by the general public has been associated with numerous health issues some of which have not been scientifically proven. Among the many concerns is that exposure to Stachybotrys chartarum during pregnancy can cause pregnancy loss or stillbirth.

This article briefly explains what Stachybotrys chartarum is, how one can get exposed to it, what currently is known about its effect on pregnancy and how one can easily test for this mold. *Stachybotrys chartarum*

<u>Stachybotrys chartarum</u> is a toxigenic mold often found in buildings with moisture problems. It is a greenish-black mold that grows on materials that contain cellulose such as:

- drywall
- wallpaper
- cotton fabrics/textiles
- cellulose based ceiling tiles
- paper products
- carpets made of natural fibers
- paper covering on insulated pipes
- insulation material
- wood and wood paneling
- general organic debris (when material is subject to prolonged wetting)

Since it is a slow grower and poorly competes with other indoor molds, *Stachybotrys chartarum* is seen several months later after the initial water damage.

Exposure to Stachybotrys chartarum

When *Stachybotrys chartarum* is actively growing, a wet slime covers and holds the spores together, preventing them from becoming airborne. Therefore, inhalational exposure only occur when the mold has dried up and disturbed thus releasing the spores into the air. As such, finding *Stachybotrys chartarum* in a building does not necessarily mean that the building occupants had been exposed to this mold.

Can exposure to Stachybotrys chartarum affect pregnancy?

A link between <u>inhalational exposure to molds</u> such as *Stachybotrys* and *Aspergillus* and pregnancy loss has not been proven. It is very unlikely for the unborn baby to be directly exposed to inhaled spores.

However, numerous unreliable reports exist supporting a link between mold toxins (mycotoxins) and pregnancy loss in humans. However, animal studies using mice indicate that mold toxins can disrupt fetal development. For example, oral ingestion of contaminated feed or partially purified toxin of *Stachybotrys chartarum* was shown to cause a decrease in the number of pregnant mice; an increased frequency in dead, resorbed or stunted fetuses; and decreased average litter size. While currently there is no scientific evidence supporting that mold exposure during pregnancy can cause miscarriage or stillbirth it doesn't mean it's safe to expose yourself. If inhaled in large

quantities, spores of *Stachybotrys* can cause health problems such as <u>allergic reactions similar to hay fever</u>, breathing difficulties, eye irritation, skin rashes and occasionally, more serious symptoms. It is known that people at greatest risk of health effects associated with mold exposure are those with respiratory conditions such allergies, asthma, and sinusitis, as well as infants and children, elderly people, individuals with a weakened immune system and pregnant women.

http://cmr.asm.org/content/16/3/497.full

Trichothecenes produced by *Stachybotrys atra* (*Stachybotrys chartarum*) have received the most attention. The poisons produced include satratoxins (Fig. 9), roridins, verrucarins, and atranones (116).

A cluster of eight cases of idiopathic pulmonary hemorrhage among infants in Cleveland, Ohio (36). Stachybotrys chartarum was implicated in the outbreak. The mold was found more frequently in the houses of affected babies than in control houses (58). A case-control study identified water damage (leaks and flooding) and smoking as risk factors for developing the infant pulmonary hemorrhage (183). Other evaluations and a second report from the Centers for Disease Control and Prevention were more equivocal and concluded that a cause-and-effect relationship had not been proven (37, 86, 134). Nevertheless, the Committee on Public Health of the American Academy of Pediatrics issued a statement on the toxic effects of indoor molds, alerting pediatricians to the possibility that idiopathic pulmonary hemorrhage may be associated with molds (3). Strains of the fungus isolated from the Cleveland outbreak produced a number of highly toxic macrocylic trichothecenes (130). Stachybotrys chartarum was also shown to produce the hemolysin stachylysin (272). Although there is no method for testing for Stachybotrys mycotoxins in humans, PCR methods for evaluating the presence of Stachybotrys chartarum have been developed (271).

http://www.johanningmd.com/images/Johanning_et_al_1996_art_10.1007_BF00381430.pdf

Abstract There is growing concern about adverse health effects of fungal bio-aerosols on occupants of water damaged buildings Accidental, occupational exposure in a nonagricultural setting has not been investigated using modern immunological laboratory tests The objective of this study was to evaluate the health status of office workers after exposure to fungal bioaerosols, especially Stachybotrys chartarum (atra) (S chartarum) and its toxigenic metabolites (satratoxins), and to study laboratory parameters or biomarkers related to allergic or toxic human health effects Exposure characterization and quantification were performed using microscopic, culture, and chemical techniques The study population (n = 53) consisted of 39 female and 14 male employees (mean age 34 8 years) who had worked for a mean of 3.1 years at a problem office site; a control group comprised 21 persons (mean age 37 5 years) without contact with the problem office site Health complaints were surveyed with a 187-item standardized questionnaire A comprehensive test battery was used to study the red and white blood cell system, serum chemistry, immunology/antibodies, lymphocyte enumeration and function Widespread fungal contamination of water-damaged, primarily cellulose material with S chartarum was found S chartarum produced a macrocyclic trichothecene, satratoxin H, and spirocyclic lactones Strong associations with exposure indicators and significant differences between employees (n = 53)and controls (n = 21) were found for lower respiratory system symptoms, dermatological symptoms, eye symptoms, constitutional symptoms, chronic fatigue symptoms and several

enumeration and function laboratory tests, mainly of the white blood cell system The proportion of mature T-lymphocyte cells (CD 3 %) was lower in employees than in controls, and regression analyses showed significantly lower CD 3 % among those reporting a history of upper respiratory infections Specific S chartarum antibody tests (Ig E and Ig G) showed small differences (NS) It is concluded that prolonged and intense exposure to toxigenic S chartarum and other atypical fungi was associated with reported disorders of the respiratory and central nervous systems, reported disorders of the mucous membranes and a few parameters pertaining to the cellular and humoral immune system, suggesting a possible immune competency dysfunction.

Trichoderma viridie* Grows well in "dry-wet" conditions

http://www.mold.ph/trichoderma.htm

Trichoderma viride has been reported as a causative agent of pulmonary infection, <u>peritonitis</u> in a dialysis patient, and perihepatic infection in a liver transplant patient. *Trichoderma* infections are opportunistic in nature and develop in immunocompromised patients, such as neutropenic cases and transplant patients, as well as those with chronic renal failure, chronic lung disease, or amyloidosis. Disseminated infections due to *Trichoderma* have also been reported.

https://en.wikipedia.org/wiki/Trichoderma#Causal_agent_of_disease

The common house mold, *Trichoderma longibrachiatum*, produces small toxic peptides containing amino acids not found in common proteins, like alpha-aminoisobutyric acid, called trilongins (up to 10% w/w). Their toxicity is due to absorption into cells and production of nano-channels that obstruct vital <u>ion channels</u> that ferry potassium and sodium ions across the <u>cell membrane</u>. This affects in the cells <u>action potential</u> profile, as seen in <u>cardiomyocytes</u> (heart muscle cells), <u>pneumocytes</u> (lung cells) and <u>neurons</u> leading to electrical <u>conduction</u> <u>defects</u>. Trilongins are highly resistant to heat and <u>antimicrobials</u> making <u>primary prevention</u> the only management option. [11][12][13]

Wallemia sebi Grows well in "dry-wet" conditions

https://microbewiki.kenyon.edu/index.php/Wallemia_sebi#Pathology

[2] W. Sebi has been found to cause hay fever symptoms which include coughing, sneezing, itchy and watery eyes, itchy nose, and sinus pressure. W. Sebi has on rare occasions colonized human abscesses. There is one documented case of W. Sebi infecting an ulcer on the foot of a patient in northern India. The patient was treated with an antifungal, Itraconazole, but the patient neglected to attend follow up appointments so it is unknown if the treatment was successful.

http://www.moldbacteria.com/mold/wallemia.html

Wallemia sebi has a world-wide distribution. It is common in indoor environments and has been isolated from jams, dates, bread, cakes, salted beans and fish, bacon, fruits, soil, hay, and textiles. It is also common in agricultural environments where it is suspected to be one of the causes of farmer's lung disease and other human allergies.

Wallemia sebi produces extremely tiny spores (even smaller than spores of some species of Penicillium or Aspergillus) that are reported to be highly allergenic. Their small size would certainly allow for efficient invasion of the respiratory system. Some strains of Wallemia produce the mycotoxins walleminol and walleminon and may cause subcutaneous infections and allergic reactions (farmer's lung disease) in humans.