Health effects of *Aspergillus* in food and air

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Abstract

This review summarizes the health aspects of the medically important fungal genus *Aspergillus*. The morphology and systematics of the genus are explained as well as its biogeography. Major mycotoxins, the aspergilli that produce them, affected crops, and symptoms of the toxicoses are summarized, as are the major mycoses caused by aspergilli. The current status of the relationship between *Aspergillus* in the indoor environment and health issues are discussed.

Keywords

Aspergillosis, mycotoxins, morphology, systematics

Introduction

Aspergillus is a large genus of filamentous fungi (molds). It is characterized by a unique spore-bearing structure (conidiophore, Figure 1) that reminded Micheli, the Catholic priest who named the genus in 1729, of the instrument used to sprinkle holy water, the aspergillum. It reproduces by forming mitotic spores (conidiospores) at the end of the conidiophore. Production of these spores is often prodigous – making *Aspergillus* one of the most common fungi on earth.

Over 250 species of *Aspergillus* have been described. These are organized into subgenera and sections, based on morphological, metabolic, and molecular characteristics. About 50 species have been described since the year 2000. A number of these result from changes in species concepts based on molecular and physiological data, and several of these new species cannot be differentiated morphologically. One newly described species of importance to clinicians is *Aspergillus lentulus*, a sibling species of the human pathogen *A. fumigatus. A. lentulus* is distinct phylogenetically, based on multilocus DNA sequences, and can be distinuished morphologically from *A. fumigatus* in that *A. lentulus* sporulates poorly and does not grow at 48°C, whereas *A. fumigatus* usually sporulates profusely and grows at 48°C (Balajee et al., 2005). Of clinical importance is the fact that *A. lentulus* has decreased in vitro susceptibility to antifungal agents (amphotericin B, itraconazole, voriconazole, and capsofungin) compared to *A. fumigatus* (Balajee et al., 2004).

One sometimes confusing aspect of *Aspergillus* is that some aspergilli have two acceptable Latin names (dual nomenclature). This is because some of the species produce sexual states (teleomorphs) and by definition *Aspergillus* is an asexual (anamorphic) genus, so the sexual state has a different genus name. For instance, *A. nidulans* has a sexual state called *Emericella nidulans*, and *A. fischerianus* has a sexual state called *Neosartorya fischeri*. When discussing both states, the teleomorph name takes precedence (McNeill et al., 2006).

Proper identification of aspergilli not only aids in selecting treatments for aspergillosis patients, it is necessary to determine etiology of both aspergilloses and allergies and for assessment of possible toxic metabolites. Morphologically based systems for identification are reliable and inexpensive, but take a week to perform and require that personnel undergo a short training period. Molecular methods can take less time and are becoming less expensive. Molecular

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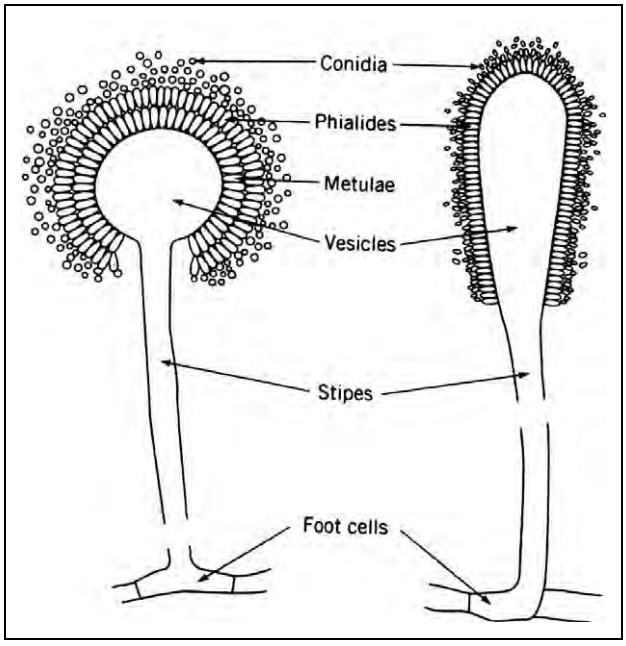

Figure 1. *Aspergillus* conidiophores with structures labelled.

identification relies heavily on 'matching' DNA sequences of the unknown fungus with those in a database. One of the major problems with this approach is that genetic databases are not always properly curated. Inaccurate sequences may be put into the databases, leading to inaccurate identifications. Physiological data is also useful in fungal identification, but cannot be used as a sole method because isolates vary widely in the metabolites they produce. For instance, aflatoxin B_1 is one of the 'characteristic' metabolites of *A. flavus*, but it is produced by fewer than half the isolates (Klich and Pitt, 1988). For the most accurate possible identification, it is generally recommended that one use more than one method. (Geiser et al., 2007)

Aspergillus. species are very common in both indoor and outdoor environments. This is in part due to the fact that aspergilli produce vast numbers of small, air-borne spores, and in part due to the fact that aspergilli are metabolic olympians. They have been isolated on everything from penguin dung in the antarctic to sea fans in tropical coral reefs (Ellis, 1980; Geiser et al., 1998). They produce enzymes capable of degrading a great variety of organic substrates (Fogarty, 1994). A number of species are xerophilic and can thrive in relatively low moistures. In indoor environments, they are found growing on wood, paper, paint, glue, and even dirty metal doors when the humidity is high.

In soils, aspergilli tend to occur in subtropical to warm temperate climates, but several of the pathogenic species are truly ubiquitous (Klich, 2002). They are generally reported less frequently from latitudes above 45° north or south. The most frequently reported species in soil are *A fumigatus, A. niger, A. flavus*, and *A. terreus*. It is probably not a coincidence that these are also the most frequently reported species in human disease. All four of these species are evenly distributed in all biomes, except *A. terreus*, which is reported at greater than expected frequencies in cultivated soils (Klich, 2002).

Aspergillus mycotoxins

Many organisms produce metabolites that are not necessary for their survival (secondary metabolites). Hundreds of such metabolites are produced by fungi. *Aspergillus* has been the source of a number of useful metabolites including antibiotics and the cholesterol lowering drug lovastatin (Lipitor). Lovastatin is produced by *A. terreus*, an organism that also causes human mycoses. Small molecular weight secondary metabolites produced by filamentous fungi that are toxic to vertebrates in low concentrations are called mycotoxins. Most of the major mycotoxins are produced by members of three genera; *Aspergillus, Penicillium*, and *Fusarium*. The US Food and Drug Adminstration (FDA) estimates that the economic costs of crop losses from mycotoxins is close to a billion dollars a year (Council for Agricultural Science and Technology [CAST], 2003). It is estimated that 25% of the world's agricultural products are contaminated with mycotoxins (CAST, 2003).

Sixty toxic secondary metabolites have been reported from *Aspergillus* species (www.aspergillus.org.uk). It is generally believed that most mycotoxicoses result from ingestion of the toxins in foods. There is mounting evidence, however, that toxins may be inhaled or form *in situ* in patients with mycoses (see below). A sampling of the *Aspergillus* mycotoxins, the fungi that produce them and the wide array of symptoms they cause is listed below (summarized from Bennett and Klich, 2003; CAST, 2003; Committee on Damp Indoor Spaces and Health, 2004; www.aspergillus.org.uk).

Aflatoxins

Produced by: *A. arachidicola, A. bombycis, A. flavus, A. minisclerotigenes, A. nomius, A. ochraceoroseus, A. parasiticus, A. pseudotamarii, A. rambellii, Emericella astellata, Em. venezuelensis*, and *Em. olivicola* (Frisvad et al., 2007; Pildain et al., 2008;

Zalar et al., 2008). Health effects: carcinogen, mutagen, teratogen, hepatotoxin, nephrotoxin, immunosuppressant, and hemorrhage of intestinal tract and kidneys. These are perhaps the most important mycotoxins in the world. Aflatoxins are the best known mycotoxins and aflatoxin B_1 is the only one currently regulated by the FDA. Aflatoxin B_1 is also the most potent naturally-formed carcinogen. Crops may become contaminated with the fungus (usually *A. flavus*) in the field or in storage. Oilseed crops such as peanuts, cottonseed, tree nuts, and corn are most susceptible to field contamination in drought years. The increase during drought may be due in part to competitive displacement since *A. flavus* can grow at higher temperatures and with less available water than many filamentous fungi. The chemistry and genetics of the biosynthetic pathway of this polyketide are fairly well delineated and the pathway has approximately 25 steps. Aflatoxicosis takes two forms, chronic and acute. Acute aflatoxicosis results in rapid death with liver and kidney damage. Chronic aflatoxicosis results in cancer, immune suppression, and other symptoms. The liver is the primary organ affected. In spite of strong regulatory controls, aflatoxin still occasionally infests food and feed in developed countries. A recent outbreak in the US killed many dogs when contaminated corn was an ingredient in dog food marketed along the eastern seaboard. In developing countries, aflatoxicosis is much more common in humans and other animals.

Ochratoxins

Produced by: *A. albertensis, A. alliaceus, A. auricomus, A. carbonarius, A. citricus, A. flocculosus, A. fonsecaeus, A. lanosus, A. melleus, A. niger, A. ochraceus, A. ostianus, A. petrakii, A. pseudoelegans, A. roseoglobulosus, A. sclerotiorum, A. steynii, A. sulphureus, A. westerdijkiae*, and, *Neopetromyces muricatus* (Samson et al., 2006). Health effects: nephrotoxin, hepatotoxin, immunosuppressant, teratogen, and urinary tract tumors. Ochratoxins are major mycotoxins worldwide. Ochratoxin A is primarily a nephrotoxin. *Penicillium verrucosum* is responsible for most of the ochratoxin in crops in cool climates where it forms in small grains such as wheat and barley. Ochratoxin A was initially isolated from *A. ochraceus*, and most of the ochratoxin-producing species are related to *A. ochraceus* (*Aspergillus* section *Circumdati*). Two black aspergilli (*Aspergillus* section *Nigri*) are known to produce ochratoxin, *A. carbonarius* and *A. niger*. Ochratoxin from aspergilli affects crops such as tree nuts, coffee, and wine grapes. Ochratoxin produced by *A. carbonarius* is predominantly a problem in the warmer grape-growing areas. The major ochratoxin, ochratoxin A, has been implicated in the human disease endemic Balkan nephropathy, but not all studies concur. Ochratoxin will form at fairly high temperatures and may be a virulence factor in mycoses caused by the fungi in *Aspergillus* section *Circumdati* (Klich et al. in preparation). Ochratoxin production is usually very low in the *A. niger* isolates that produce it, however, it is a major concern because *A. niger* is used to produce food products such as citric acid and amylase.

Sterigmatocystin

Produced by: *A. flavus, A. multicolor, A. nidulans, A. parasiticus, A. rambellii, A. ustus, A. versicolor, Em. nidulans, Em. quadrilineata, Em. rugulosa, Em. venezuelensis*. Health effects: hepatotoxin, nephrotoxin, carcinogen, mutagen, and immunosuppressant. Sterigmatocystin is one of the precursors of aflatoxin in the biosynthetic pathway of aflatoxin. As a carcinogen, sterigmatocystin is only slightly less toxic than aflatoxin. Many sterigmatocystin-producing fungi are common indoor air molds and will be discussed in more detail under that topic. Sterigmatocystin is not a common toxin in foods, but has been reported from barley and other grains, green coffee, and hard cheese rinds (Abramson, 1991).

Cyclopiazonic acid

Produced by: *A. flavus, A. lentulus, A. minisclerotigenes, A. oryzae, A. pseudotamarii, A. versicolor*. Health effects: calcium transport disrupter, hepatic cell necrosis, intestinal hemorrhage and edema, muscle necrosis, and immunosupressant. This toxin is found in corn, peanuts, and cheese.

Gliotoxin

Produced by: *A. flavus, A. fumigatus, A. niger, A. terreus, Eurotium chevalieri, Eu. rubrum, Neosartorya pseudofischeri*. Health effects: immunosuppressant, apoptosis. Gliotoxin is not a common toxin in crops. It is, however, a probable virulence factor in human mycoses caused by *A. fumigatus* (Bok et al., 2005). It has been found in the sera of animals with natural and induced *A. fumigatus* infections, and in human cancer patients suffering from invasive aspergillosis (Lewis et al., 2005). It inhibits phagocytosis by

human neutrophils (Comera et al., 2007) and apoptosis in macrophages (Waring et al., 1988). In a mouse model of aspergillosis, gliotoxin was a potent virulence factor in mice receiving repeated doses of cortisone acetate (Kupfahl et al., 2006; Sugui et al., 2007).

Patulin

Produced by: *A. clavatus, A. longivesica, A. terreus*. Health effects: pulmonary and cerebral edema, nausea, gastritis, paralysis, convulsions, capillary damage, and carcinogenic. This toxin is found in moldy feed and apples. The toxin in apples (and apple juice) is caused by a *Penicillium* species.

Citrinin

Produced by: *A. candidus, A. carneus, A. flavipes, A. niveus, A. terreus*. Health effects: nephrotoxin, hepatotoxin, fetotoxin. Citrinin is usually associated with cereal grains.

Penicillic acid

Produced by: *A. melleus, A. ochraceus, A.ostianus*. Health effects: tremorigen, liver and kidney damage, dilates blood vessels, and antidiuretic. It is found in stored corn, cereal grains, and beans.

Diseases caused by *Aspergillus*

Of the 250 described species of *Aspergillus*, only about 40 are considered to be clinically important, but the list is growing (Klich, 2006). The most important clinical species are *A. fumigatus, A. flavus, A. terreus*, and *A. niger*. Most, but not all, clinically important species grow well at 37°C and have relatively small spores. Unlike mycotoxicoses, the primary infection route for aspergilloses is through inhalation. The diseases caused by aspergilli represent a continuum of symptoms from mild sneezing to fatal systemic infections. Many books and articles have been written on *Aspergillus* diseases (see www.aspergillus.org.uk). Here, I will attempt a brief summary of some of the more important diseases.

Allergies

Aspergilli are well-known allergens that are present in both indoor and outdoor environments. Allergic reactions can range from the irritations such as rhinitus, conjunctivitis, and coughing to life-threatening pulmonary airway obstruction or anaphylaxis. *A. fumigatus, A. Flavus*, and *A. niger* are commonly involved in fungal allergies. *A. oryzae*, a relatively uncommon fungus, has been shown to be indirectly involved in allergic reactions. This fungus is used to produce amylases used in the baking industry. Baker's asthma is caused by an allergen from *A. oryzae* in the amylase (Baur et al., 1994; Kurup et al., 2000). Hypersensitivity pneumonitis (allergic alveolitis) results from inhalation of large numbers of spores, and causes flu-like symptoms, coughing and chest tightness 4-6 hours after exposure. These include malt worker's lung (*A. clavatus* and *A. fumigatus)*, air-conditioning disease (*A. fumigatus)* (Stevens, 1987), and farmer's lung (*A. umbosus* and others, Kaukonen et al., 1994).

Allergic bronchopulmonary aspergillosis (ABPA) is characterized by moderate to severe asthma, bronchial obstruction, eosinophilia, and may mimic tuberculosis (Stevens, 1987; Greenburger, 2005). This disease usually affects patients with asthma or cystic fibrosis. *A. fumigatus* is usually the allergen (Greenberger, 2005).

Fungal sinusitis

Invasive *Aspergillus* sinusitis is not a common form of aspergillosis, but may be fatal (Lin et al., 2001; Teh et al., 1995). It has been hypothesized that most cases of chronic rhinosinusitis are fungal in origin, and that aspergilli are frequently the causal agent, but this hypothesis is still controversial (Lanza et al., 2006; Ponikau et al., 1999).

Chronic mycetoma

This lung disease, also called aspergilloma or fungus ball, is usually associated with preexisting lung cavities caused by tuberculosis, histoplasmosis, blastomycosis, and activomycosis. It is usually benign. Hemoptysis (often mild) is the most common symptom, but chronic cough, weight loss and, rarely, fever may occur (Pennington, 1993).

Invasive aspergillosis

Aspergillosis has become more common as the immunosuppressed population has grown over the past 30 years (Denning, 1996). This often fatal disease usually affects immunosuppressed patients, most frequently those being treated for hematological cancers (Vonberg and Gastmeier, 2006). Other risk factors include solid organ transplant, chronic

granulomatous disease, neutropenia, advanced AIDS, and long-term use of immunosuppressants (Pursell et al., 1992; Segal and Walsh, 2006). It is frequently a nosocomial disease. These infections are difficult to diagnose, yet prompt diagnosis is essential for survival, so antifungals are often given to cancer patients prophylactically, which has improved survival (Pennington, 1993; Grigg, 2002).

The most common fungi involved are *A. fumigatus* and *A. flavus*, with *A. niger* and *A. terreus* accounting for fewer cases, however, *A. terreus* has a higher fatality rate than the others, probably due to its resistance to amphotericin B (Steinbach et al., 2004; Vonberg and Gastmeier, 2006).

Not all aspergilloses are a result of apparent severe immunosuppression, however, many are rare enough that individual case studies are still published. Some examples follow. Chronic cavitary pulmonary aspergillosis (CCPA) develops slowly in patients and is associated with lower frequency of several alleles but no overt disease (Sambatakou et al., 2006). Acute pulmonary aspergillosis has been reported from immunocompetent men after spreading bark chippings (Arendrup et al., 2007). Invasive aspergillosis with a brain lesion was found in an apparently immunocompetent, non-neutropenic patient who was brought to the hospital after experiencing a seizure (Garcia et al., 2006). *A. terreus* infective endocarditis was found in a patient with no immunosuppression and no known heart disease (Piens et al., 1995).

Aspergillus in indoor environments

Like all fungi, aspergilli need water and a carbon source in order to grow. In indoor environments, fungal problems are usually associated with flooding, leaky pipes or roofs, condensate in HVAC systems or windows, or damp basements and bathrooms. The water source must be eliminated or remediation would be useless. In walls, the carbon source for fungi can be greatly reduced by use of non-cellulosic wallboard. It is generally believed that mold problems have become more abundant as modern air-tight buildings have been built. Nosocomial aspergillosis is most frequently reported from hospitals undergoing renovation/construction (Vonberg and Gastmeier, 2006). Solving a mold problem involves two steps, assessment and remediation.

Sometimes mold problems are obvious while others are more subtle. In many cases of mold problems in buildings, professional assessment is not necessary, as in the case of major flooding (Figure 2). However, if there are health problems potentially due to mold exposure, if there is potential for litigation resulting from the mold problem, or if the mold problem is not obvious, professional assessment should be conducted. Tools of the professional will range from very low-tech, a roll of clear tape and some microscope slides, to high-tech calibrated air samplers. The tape is used to sample potential problem areas. Even professionals cannot always tell whether a wall smudge is a scuff mark or fungal colony, so the tape is pressed onto the affected area, placed on a microscope slide, and then observed under high power on a compound microscope. If fungi are visible under the microscope, the area in question has been colonized.

Figure 2. Obvious mold contamination in the author's home after Hurricane Katrina.

To establish a relationship between a house mold and human disease, it must be demonstrated that the person has potentially been in contact with the mold or spores. There are several kinds of sampling devices. All must be volumetric and carefully calibrated to provide useful information (Levetin and Horner, 2002). A vacuum device may be used to collect dust from carpets or furniture. This will give an assessment of potential exposure over a relatively long period of time, but is not quantitative in the sense that the exact amount of time the dust has been accumulating cannot be determined. There are two general types of quantitative air samplers, viable and non-viable. Non-viable air samplers work by blowing air over a sticky surface. Only a small part of the surface is exposed at any one time. The advantage of the non-viable samplers is that they can run for a long period of time, and provide information on the daily 'pattern'

of spores in the air. The disadvantage is that spores of *Aspergillus* and other genera such as *Penicillium* cannot be identified to the species level. Viable air samplers blow air onto the surface of a growth medium. The medium is removed from the sampler and incubated. The colonies that form are counted, giving an estimate of the number of viable particles per unit of air. The colonies may be subcultured and identified to the species level. The disadvantage of this method is that a sampler can only run for a short period of time. Generally, results from indoor samples are compared to those of outdoor samples, with the assumption that indoor counts higher than outdoor counts are indicative of a potential indoor mold problem. Results obtained using different methods do not necessarily correlate (Chew et al., 2003). At present, there is no standarized procedure for assessing indoor fungi. Without such procedures, it is very difficult to assess the effects of indoor fungi on health (Portnoy et al., 2004, Straus, this volume).

Another source of variability in assessing indoor air fungi is the medium used for isolation of the fungi. Common media include, Rose Bengal Agar, Malt Extract Agar (MEA), Dichloran Glycerol Agar (DG18), and Potato Dextrose Agar (for formulae see Klich, 1992). Individual laboratories have modified these for their own use. The medium used can result in major differences in the mycobiota recovered. For instance, in a study of dust samples on either MEA or DG18, three species of aspergilli were among the 30 most abundant species on MEA and eight species were among the 30 most abundant species on DG18 (Horner et al., 2004). Chao et al. (2002) also compared recovery of different genera on DG18 and MEA. Recovery frequency for *Aspergillus* was higher on DG18, but recovery of some fungi was equal with the two media and for others, recovery was greater on MEA.

Remediation involves reducing or eliminating the moisture source and cleaning or removing colonized materials. According to the EPA (http://www.epa.gov/mold), small areas may be remediated by lay people taking safety precautions, but larger areas should be professionally remediated. The CDC also provides information and advice on dealing with indoor mold problems (http://www.cdc.gov/mold). These recommendations are in a state of flux, so I would strongly recommend checking these websites prior to remediation.

Almost every published study of indoor air fungi reports the presence of *Aspergillus* or its teleomorphs. In their book on food and indoor fungi, Samson et al. (2000) listed 14 species of aspergilli as indoor environment fungi. Table 1 summarizes the reports of aspergilli from 15 primary studies of indoor fungi from around the world. *A. flavus, A. fumigatus, A. niger, A. ochraceus*, and *A. versicolor* were the most commonly reported species, both in the number of studies reporting their presence and the dominance of the species within the study.

In a large study examining 9619 indoor air samples from 1717 buildings across the United States, *Aspergillus* species were among the most common culturable fungi (Shelton et al., 2002). Throughout, they used a 6-stage viable air sampler and one of two media. The most common aspergilli reported were *A. flavus, A. fumigatus, A. niger* and *A. versicolor*. Of these, only *A. versicolor* was reported at higher levels indoors than outdoors through all the seasons of the year. In a comparison of samples submitted for health-related reasons verses samples submitted for reasons other than health, mold presence or water damage, *A. versicolor* had the second highest odds ratio (after *Curvularia)* of being associated with health problems.

It is difficult to establish a cause-effect relationship between health problems and mold in the indoor environment. The presence of mold in the indoor environment does not necessarily correlate with personal exposure (Toivola et al., 2004). Fungi interact with other organisms that may cause health problems. For example, there is an association between dust mite populations and *Aspergillus* populations in beds (Andersen, 1985). Testing potentially harmful substances on humans is not possible, and extrapolations from animal models may not be valid. Case reports cannot establish a cause-effect relationship, but do establish evidence of an association between the health problems and mold. The literature on damp indoor air and health was evaluated by a committee commissioned by the National Research Council, National Academy of Science, and other highly reputable organizations (Committee on Damp Indoor Spaces and Health, 2004). They concluded that there is sufficient evidence of an association between indoor mold presence and upper respiratory tract symptoms, cough, wheeze, asthma symptoms in sensitized people, and severe respiratory infections in immunocompromised people, but insufficient evidence to establish a relationship between indoor mold and dyspnea, fungal sinusitis, airflow obstruction in otherwise healthy people, mucous membrane

Table 1. Summary of aspergilli in 15 indoor air studies

Species	Location of study	Citation
Aspergillus candidus	Cleveland, USA	Kuhn and Ghannoum (2003)
	India	Adhikari et al. (2000)
A. caespitosus	Austria	Rainer et al. (2000)
A. carbonarius	Uganda	Ismail et al. (1999)
A. clavatus	Uganda	Ismail et al. (1999)
A. flavipes	Finland	Tuomi et al. (2000)
	Uganda	Ismail et al. (1999)
A. flavus	**USA**[a]	**Shelton et al. (2002)**
	Slovakia	**Pieckova and Kunova (2002)**
	India	**Adhikari et al. (2000)**
	Uganda	**Ismail et al. (1999)**
	Japan	**Takahashi (1997)**
	Kuwait	**Khan et al. (1999)**
	UAE	Jaffal et al. (1997)
A. fumigatus	**USA**	**Shelton et al. (2002)**
	Austria	**Rainer et al. (2000)**
	Cleveland, USA	**Kuhn and Ghannoum (2003)**
	India	**Adhikari et al. (2000)**
	Uganda	**Ismail et al. (1999)**
	Japan	Takahashi (1997)
	Kuwait	**Khan et al. (1999)**
	UAE	Jaffal et al. (1997)
A. glaucus	**Slovakia**	**Pieckova and Kunova (2002)**
	India	Adhikari et al. (2000)
	Japan	**Takahashi (1997)**
A. japonicus	**India**	**Adhikari et al. (2000)**
A. melleus	Uganda	Ismail et al. (1999)
A. niger	**USA**	**Shelton et al. (2002)**
	Atlanta, USA	**Horner et al. (2004)**
	Cleveland, USA	**Kuhn and Ghannoum (2003)**
	Slovakia	**Pieckova and Kunova (2002)**
	Finland	Tuomi et al. (2000)
	Austria	Rainer et al. (2000)
	India	**Adhikari et al. (2000)**
	Uganda	**Ismail et al. (1999)**
	Japan	**Takahashi (1997)**
	Korea	**Kwon et al. (1984)**
	Kuwait	**Khan et al. (1999)**
	UAE	**Jaffal et al. (1997)**
A. ochraceus	**Slovakia**	**Pieckova and Kunova (2002)**
	Atlanta, USA	**Horner et al. (2004)**
	Cleveland, USA	Kuhn and Ghannoum (2003)
	Finland	Tuomi et al. (2000)
	Austria	Rainer et al. (2000)
	India	**Adhikari et al. (2000)**
	Korea	Kwon et al. (1984)
	Uganda	Ismail et al. (1999)
A. oryzae	Uganda	Ismail et al. (1999)
A. parasiticus	Austria	Rainer et al. (2000)
A. penicillioides	Austria	Rainer et al. (2000)
A. restrictus	Slovakia	Pieckova and Kunova (2002)
	Japan	Takahashi (1997)

(continued)

Table 1 (continued)

Species	Location of study	Citation
A. sclerotiorum	Austria	Rainer et al. (2000)
A. sparsus	UAE	Jaffal et al. (1997)
A. sydowii	**Atlanta, USA**	**Horner et al. (2004)**
	Finland	Tuomi et al. (2000)
	Uganda	Ismail et al. (1999)
	Korea	Kwon et al. (1984)
A. tamarii	Kuwait	Khan et al. (1999)
	UAE	Jaffal et al. (1997)
A. terreus	Austria	Rainer et al. (2000)
	Uganda	Ismail et al. (1999)
	Kuwait	Khan et al. (1999)
	UAE	Jaffal et al. (1997)
A. unguis	**Atlanta, USA**	**Horner et al. (2004)**
	Austria	Rainer et al. (2000)
A. ustus	**Slovakia**	**Pieckova and Kunova (2002)**
	Finland	Tuomi et al. (2000)
	Austria	Rainer et al. (2000)
A. versicolor	**USA**	**Shelton et al. (2002)**
	Atlanta, USA	**Horner et al. (2004)**
	Slovakia	**Pieckova and Kunova (2002)**
	Finland	**Tuomi et al. (2000)**
	Austria	**Rainer et al. (2000)**
	Uganda	Ismail et al. (1999)
	Japan	Takahashi (1997)
	Korea	**Kwon et al. (1984)**
	UAE	Jaffal et al. (1997)
A. wentii	Austria	Rainer et al. (2000)
Emericella nidulans[b]	India	Adhikari et al. (2000)
	Uganda	Ismail et al. (1999)
	Kuwait	Khan et al. (1999)
	Korea	Kwon et al. (1984)
Eurotium amstelodami	**Atlanta, USA**	**Horner et al. (2004)**
E, herbariorum	Atlanta, USA	Horner et al. (2004)
E. niveoglaucum	Uganda	Ismail et al. (1999)
Neosartorin fischeri	**Slovakia**	**Pieckova and Kunova (2002)**

[a] Bold indicates that the species was a common species in the study. The Shelton et al. study included samples from all over the United States.
[b] Teleomorph abbreviations: E*m., Emericella*; *Eu., Eurotium*; *Neo, Neosartorya*.

irritation syndrome, chronic obstructive pulmonary disease, development of asthma, or respiratory illness in otherwise healthy adults or children. Research is ongoing on the relationship between mold and these health problems. For instance, a study in 2005 added strong evidence to the relationship between the presence of mold odor in the home and development of childhood asthma (Jaakkola et al., 2005).

Mycotoxins and indoor air

A number of *Aspergillus* species common in indoor environments produce mycotoxins on substrates other than food. Summarizing from an excellent review on the topic by Nielsen (2003): *A. flavus, A. niger*, and *A. ustus* do not appear to produce their toxins on building materials; *A. fumigatus* is capable of producting gliotoxin and tremorgenic agents on building materials; and *A. versicolor* produces sterigmatocystin and a related compound, 5-methoxy-sterigmatocystin on building materials.

Ochratoxin A, produced by *A. ochraceus sensu latu*, is known to be carried on spores, but it is not known whether or not *A. ochraceus* produces the toxin on building materials (Skaug et al., 2000). One of the few published papers demonstrating

probable human mycotoxicosis from indoor air contamination involved ochratoxin (Richard et al., 1999). The residents of a house complained of increased thirst, polyuria, edema, skin rash, and lethargy. The pets also had increased water intake and polyuria. These symptoms are known to result from ochratoxicosis in farm animals. Dust samples were taken from the heating ducts in the house and assayed for ochratoxin. One sample contained over 1500 ppb of ochratoxin A. The symptoms of all the mammals in the house disappeared when the heating ducts were cleaned. Unfortunately, the 'smoking gun', presence of ochratoxin A in the sickened individuals, was not established.

Sterigmatocystin produced by *A. versicolor* has been isolated from carpet dust in homes of people with health problems potentially related to mold in their homes (Engelhart et al., 2002). The spores of *A. versicolor* have been shown to cause inflammation and toxicity in mouse lungs (Jussila et al., 2002). In my experience, in a workshop setting, a participant who was an indoor air professional developed facial flushing when exposed to a toxigenic strain of *A. versicolor*, but not when exposed to a non-toxigenic strain. Reactive strain also had a different volatile profile than the non-reactive strain (unpublished data). This information, combined with the high odds ratio of *A. versicolor* being associated with human health problems (Shelton et al., 2002), indicates that this may be a dangerous house mold. Further research is needed to establish the exact effects of *A. versicolor* on human health.

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