Harmful fungi in both Agriculture and Medicine

Anthony J. De Lucca

Southern Regional Research Center, USDA, ARS, New Orleans, LA, USA

Summary Most fungi are saprophytic and not pathogenic to plants, animals and humans. However, a relative few fungal species are phytopathogenic, cause disease (e.g., infections, allergies) in man, and produce toxins that affect plants, animals and humans. Among such fungi are members of the *Aspergillus* and *Fusarium* genera as well as other genera (e.g., *Alternaria, Mucor*) comprising the "emerging pathogen" group in humans. These fungi present a common threat to both agricultural production and the health of healthy and immunocompromised individuals. Taken together, these relative few fungi can cause huge economic losses to agriculture, loss of food for consumption, and serious, often fatal diseases in humans and animals. Plants may be a source of antifungal compounds since they have had to develop compounds to resist infections by fungi present in their environment.

Key words Agriculture, Medicine, Pathogen, *Aspergillus*, *Fusarium*, *Alternaria, Mucor*

Hongos patógenos commúnes en la Agricultura y la Medicina

Resumen La mayoría de los hongos son saprobios y no patógenos de plantas, animales y humanos. Sin embargo, un número relativamente pequeño de especies fúngicas son fitopatógenas, causan efermedad humana (por ejemplo, infecciones, alergias), y producen toxinas que afectan a plantas, animales y humanos. Entre los hongos patógenos están los miembros de los géneros *Aspergillus* y *Fusarium* junto con otros géneros (por ejemplo, *Alternaria*, *Mucor*) que son denominados "patógenos fúngicos emergentes". Estos hongos representan una amenaza común tanto para la producción agrícola como para la salud de las personas sanas o inmunodeficientes. En conjunto, estos hongos pueden causar enormes pérdidas económicas en la agricultura, pérdidas alimenticias por deterioro, y enfermedades humanas y animales graves, a menudo fatales. Las plantas pueden ser origen de estos compuestos antifúngicos porque éstos necesitan desarrollarlos para resistir las infecciones por hongos presentes en su ambiente.

Palabras clave Agricultura, Medicina, Patógeno, *Aspergillus*, *Fusarium*, *Alternaria, Mucor*

Fungi are ubiquitous in nature and vital for recycling of nutrients contained in organic matter. The vast majority of the known fungal species are strict saprophytes, although there are a few capable of causing disease in plants or humans. However, there are several fungal genera containing species that cause disease (e.g., infections, allergies, toxicity) in plants, animals and man. These fungi can be categorized into two groups in regards to infection: (1) saprophytic fungi which can be opportunistic pathogens that enter via wounds or due to a weakened state of the host and (2) true pathogens that may depend on living plant or human tissues for nutrients but can also survive outside of the hosts. This review covers fungal species that cause not only disease in plants and but also in humans. These fungi include *Aspergillus* and *Fusarium* as well as other phytopathogenic fungi now considered members of the "emerging pathogen" group in humans.

Corresponding Author:
Dr. Anthony J. De Lucca
Southern Regional Research Center, USDA, ARS
1100 Robert E. Lee Blvd.
New Orleans, LA 70124 USA
Tel.: 01-504-286-4253
Fax: 01-504-286-4419
E-mail: adelucca@srrc.ars.usda.gov

1130-1406/01/10.00 €

Aspergillus

i) Plant pathogens

Plants have several levels of resistance (structural, innate, induced) to fungal infection. However, certain factors, such as heat stress insect damage and drought, weaken crop resistance to these fungi, and so play an important role in the fungal invasion of these crops and subsequent toxin production [3,41,137,179]. Moisture and seed nutrient content in the midrange of seed development provide optimum conditions for fungal development and toxin production [124].

The *Aspergillus* genus are saprophytes found worldwide in soil, forage products, food products, dust, organic debris and decomposing matter [82]. Although they are considered weak plant pathogens [82], there are two species, *Aspergillus flavus* and *Aspergillus parasiti-*

cus, which produce potent toxins (aflatoxins) on certain crops. Especially susceptible to these species are oilseeds and nuts such as peanuts, corn and cottonseed. *A. flavus* is the dominant of the two on corn and cottonseed [92,104]. In contrast, *A. parasiticus* is more prevalent on peanuts than on other crops [53] and, generally, constitute approximately 10 - 30% of the aflatoxin producing fungi on peanuts [92]. Corn hybrids having high oil content are at a greater risk for aflatoxin contamination than normal hybrids during some growing seasons [206].

ii) Aflatoxin risk to humans and animals

Death due to aflatoxins has been reported in humans, animals and birds [82,237]. Aflatoxins were discovered after groundnut meal contaminated with these toxins killed over 10,000 turkeys ("turkey X disease") in England [199]. They are potent heptatotoxic, teratogenic, mutagenic and carcinogenic secondary metabolites [42,169] that contaminate crops worldwide, rendering them unsafe for consumption [57,118,202,252,258]. The four main aflatoxins (B_1, B_2, G_1, and G_2) are produced by *A. flavus, A. parasiticus* and *Aspergillus nominus* [3]. The letters "B" and "G" refer to the blue and green colors produced by these toxins on thin layer chromatography plates illuminated by UV light, while the numbers 1 and 2 correspond to the major and minor compounds, respectively [82,179]. Aflatoxins M_1 and M_2 are oxidative metabolic products of aflatoxins B_1 and B_2, respectively, produced in animals and humans following ingestion of contaminated feed and appear in milk (animal and human), urine and feces [170].

Aflatoxin B_1, a group I carcinogen, is approximately 4,000 times more carcinogenic than the mycotoxin, fumonisin B_1 [96,110], produced by *Fusarium verticillioides* (formerly *Fusarium moniliforme*). Since corn is of global importance as a food and feed crop, aflatoxin B_1 (AFB_1) contamination of corn is considered the greatest mycotoxin health risk to humans [82,122]. In vitro, AFB_1 is biotransformed to the carcinogenic AFB_1-8,9 epoxide [164]. Aflatoxins (B_1, B_2 and M_1) are implicated in severe equine hepatic necrosis and primary hepatocellular carcinoma in humans which is estimated to cause 250,000 deaths annually worldwide, especially in developing countries [96,122,247].

Processing of infected grains results in the release of airborne particulate matter that is contaminated with aflatoxins, thereby exposing the lungs of agricultural workers to these toxins [134,135]. In humans, inhaled AFB_1 can cause inflammation and eventually irreversible, debilitating, pulmonary interstitial fibrosis, a scarring of the lung tissues between the air sacs [60,129]. AFB_1 has been found in lung samples from patients with this disease [60]. In vitro, human pulmonary microsomes activate AFB_1 to form the exo-AFB_1-8,9-epoxide [102]. It is possible that, under conditions in which the appropriate cytochromes are expressed in the lung, AFB_1 inhalation may increase the risk of lung cancer in exposed persons [234].

iii) Animal infections

Aspergillus fumigatus is the most common etiologic agent of avian pulmonary aspergillosis, although *A. flavus, Aspergillus niger*, *Aspergillus nidulans* and *Aspergillus terreus* have also been isolated during *Aspergillus*-caused epizootics [6,159]. Infection occurs in the lungs of birds when spores are inhaled [6]. Factors contributing to *Aspergillus* epizootics in hatcheries include heavy contamination of the air or feed, immunosuppression or stress [38,174]. *A. fumigatus* and *A. niger* have been isolated from the lungs and cerebellum of chickens with aspergillosis [7,159]. Pulmonary infections caused by Aspergillus in chickens, known as "brooder's pneumonia", can result in large economic losses for poultry farmers [6,158].

iv) Human infections

Though over 180 *Aspergillus* species are known, only four are commonly associated with invasive infection in humans [200,250]. These species include *A. fumigatus, A. flavus, A. terreus* and *A. niger*. Though saprophytic, they can cause infections in healthy individuals and, increasingly, are the causative agents of fatal opportunistic infections in immunocompromised patients. These fungi are ubiquitous worldwide and produce abundant amounts of asexual, haploid conidia, which are highly hydrophobic with very small diameters [15]. Their conidia are readily dispersed in air currents, thereby facilitating exposure [35,77,94]. Besides contacting the skin, eyes, and ears, these conidia are sufficiently small to be inhaled and lodge in all recesses of the lung, including the alveoli [15]. The innate immunity of healthy persons protects them from infection except in certain situations, such as trauma, where conidia may contaminate the wound. In cases where the immune system is weakened, the inhaled conidia can germinate and produce hyphae that invade the surrounding lung tissue, leading to the development of invasive pulmonary aspergillosis [13,227]. Invasive aspergillosis is a major cause of death in immunocompromised patients, with the associated mortality rate > 90% [48,180].

a) *Aspergillus* infections in healthy individuals. As with members of the genus *Fusarium*, some of the Aspergilli can cause infections in immunocompetent persons who may, or may not, suffer trauma. For example, *Aspergillus* can cause chronic sphenoid sinusitis, as well as the usually fatal intracranial invasive aspergillosis originating in the sphenoid sinus in healthy individuals [34,255]. Agricultural workers, especially in the third world, whose eyes are injured with subsequent contamination by organic matter, may develop corneal infections by *Aspergillus* species [22,226,253]. Trauma to nails may lead to infection (onychomycosis) by environmental, especially soil, fungi. Onychomycoses by nondermatophytic molds are considered uncommon although *Aspergillus* species are known to cause this disease worldwide [140,228]. The ear is another location of *Aspergillus* infections in the healthy individual. Local lesions in both the external and middle ear, as well as in postoperative cavities, can create favorable conditions for fungal growth and subsequent otomycosis caused by *A. flavus, A. fumigatus* and *A. niger* [101,112,156,168,235].

b) *Aspergillus* infections of immunocompromised patients. The immunocompromised host can also confront serious, often lethal, invasive and disseminated aspergillosis [116]. Invasive aspergillosis is a progressive, increasingly common and often fatal opportunistic infection particularly in severely neutropenic patients [45,47,250]. Ecologically, *A. fumigatus* is commonly found in countries with a temperate climate, whereas *A. flavus* is more prevalent in hot, tropical climates [37]. Although it is the least isolated of all airborne saprophytic fungal conidia [250], *A. fumigatus* is responsible for approximately 90% of all cases of pulmonary fungal infections [45,46]. *Aspergillus flavus* is less commonly found in pulmonary aspergillosis cases but does cause invasive disease at other sites [200]. *Aspergillus terreus* is another *Aspergillus* which can cause infections in immunocompromised patients. A molecular epidemiology study has implicated potted plants, present near patients in a hospital, as a source of *A. terreus* which

caused lethal infections in nine patients undergoing myeloblative chemotherapy [114].

In addition to pulmonary involvement, *A. fumigatus* can also colonize other areas of immunocompromised hosts. Sino-orbital aspergillosis is a progressive, relentless, and usually fatal opportunistic infection in AIDS patients. In one study, all five patients studied developed sino-orbital aspergillosis caused by this fungus with intracranial extension development in four of them [100]. Mortality was eighty per cent.

The preponderance of *A. fumigatus* in such infections may be due to a genetic "reprogramming" that induces expression of specific genes required to change from a saprophyte to a human pathogen [82]. Melanin present in the conidia also plays a role in the evasion of host defense, by quenching oxidative metabolites produced by granulocytes that assist in the elimination of the conidia [91]. In addition, several virulence factors have been identified that could mediate *A. fumigatus* adherence to host tissues, invasion, and protection from host immune responses [116,149,183].

vi) Allergic responses to *Aspergillus*

Aspergillus species cause four distinct forms of respiratory hypersensitivity disorders; allergic bronchopulmonary aspergillosis, allergic *Aspergillus* sinusitis, IgE-mediated asthma and hypersensitivity pneumonitis [135,208]. Allergic bronchopulmonary aspergillosis patients were found to elicit a strong immediate-type reactivity to *A. niger, A. fumigatus, A. flavus, A. terreus,* and *Aspergillus tamarii* [19,135,209,213]. *Aspergillus flavus* is also known to cause allergic rhinosinusitis [222]. Sensitivity to these fungi commonly occur in both the natural environment [135] and working locations such as bakeries were large amounts of grain flour becomes airborne [212].

Fusarium

i) Plant pathogens

The genus *Fusarium* consists of septate filamentous fungi common in soil, marine or river environments, and on plants throughout the world [87]. Some are soil saprophytes while others are true plant pathogens. The phytopathogens of this genus are the most important toxigenic fungi on crops in the northern temperate regions [86,87]. They are responsible for several important plant diseases including vascular wilt, and pre- and post emergence blight, as well as root and stem rots [201]. *Fusarium* head blight (FHB) of small grain cereals and ear rot in maize cause significant loss of crops worldwide [97,166,182]. In wheat, this disease is caused by several *Fusarium*, species including *Fusarium avenaceum, Fusarium graminearum, Fusarium culmorum* and *Fusarium poae* [62,97]. *Fusarium avenaceum, Fusarium sporotrichioides, F. poae* as well as *Fusarium oxysporum* are the causative agents of FHB in barley and often lead to significant grain loss worldwide [36,216]. Infection of the grain results in economic loss due to shrunken grain heads, with loss of milling and malting quality. Infected grains are also contaminated by potent toxic secondary metabolites (described below) produced by these fungi [36,197,216].

Fusarium oxysporum and *Fusarium solani* cause wilt and root rot [78] in a number of crops including peas [150], cotton [50,215,244], as well as ornamentals, small fruits and cucurbits [65,154,245]. *Fusarium solani* is considered the major plant pathogen of its genus though it can also cause disease in humans [217,261]. This fungus causes sudden death syndrome in soybeans and green beans [79]. The major symptoms of this disease include root rot, crown and leaf necrosis, pod abortion, and vascular discoloration of roots and stems [153,193,194].

ii) *Fusarium* toxins: affect on human and animal health

Fusarium species are commonly found on cereal grains where growth of these fungi, in addition to contamination by their toxins, can render these grains unsafe for consumption [108,141,195].

Fusarium mycotoxins are considered one of the five major mycotoxin groups affecting human health [179]. *F. oxysporum* and *F. verticillioides* (formerly known as *F. moniliforme*) produce fumonisins that are cytotoxic to several mammalian cell lines [2,205]. Fumonisins are found in corn and corn-based foods worldwide [30] and their production is directly correlated to climate and rainfall [8] especially where drastic changes in rainfall and relative humidity patterns can result in physiological stress [3,157,231,239]. Their mode of action may involve competition with sphingosine in sphingolipid metabolism [185]. The disruption of sphingolipid metabolism by fumonisins, as well as folate transport and neural tube development in embryo culture, suggests that these mycotoxins play a role in diseases affecting human neural tube development in populations consuming fumonisin-contaminated maize [32,132]. They are reported to induce equine leukoencephalomalacia and pulmonary edema in swine [70,71,89,131]. Fumonisins are also implicated in esophageal cancer after being found in homegrown maize in an area of the Transkei region of South Africa which has a high-incidence of this disease [220].

Certain *Fusarium* species produce the types A and B trichothecenes [62]. The type A trichothecenes include T-2, HT-2, T-2 triol, T-2 tetraol, neosolaniol, di- and 15-monoacetoxyscirpenol (DAS, MAS), and scirpentriol. T-2 is the most important toxin of the group since it inhibits eukaryotic protein synthesis and is very toxic to leucocytes, resulting in immunosuppression [86,256].

Type B trichothecenes include nivalenol, deoxynivalenol (DON), 3- and 15-acetylDON, fusarenon-X, zearalanone and its two derivatives, α- and β-zearalanone [201]. These toxins affect the immune system of laboratory animals, resulting in increased susceptibility to various microbial diseases [176]. Fumonisin B_1 is immunotoxic to swine alveolar macrophages, as shown by a dramatic decrease in mRNA content [126]. *Fusarium graminearum* produces DON (also known as vomitoxin) which causes vomiting and feed refusal in swine [51,179]. DON disrupts normal cell function by inhibiting protein synthesis via binding to the ribosome and by activating critical cellular kinases involved in signal transduction related to proliferation, differentiation and apoptosis [176]. In humans, the symptoms of DON toxicity include anorexia, nausea, vomiting, headache, abdominal pain, diarrhea, chills, giddiness, and convulsions [259]. DON is also known to be a potent inducer of human lymphocyte cytokine production [138]. In vitro, DON, fusarenol-X, nivalenol and T-2 exert an immunosuppressive effect on human peripheral blood mononuclear cells [21]. T-2 toxin, in vitro, is also cytotoxic to human B and T lymphoid cell lines [142]. Ingestion of type A and B trichothecenes present in contaminated grains may lead to secondary infections due to their immunosuppressive properties [21].

Nivalenol is reported to be genotoxic in the mouse gastrointestinal tract [230]. This toxicity is attributed to its ability to inhibit protein biosynthesis in eukaryotic cells by

interfering with ribosomal functions [28]. Nivalenol toxicity is considered to be similar to, or somewhat greater than, DON [177].

Zearalenone is an estrogenic toxin produced by *F. graminearum* and related species [179]. On wheat, *F. graminearum* produces zearalenone which causes genital problems in domestic farm animals, especially pigs [179]. This toxin has a serious affect on livestock reproduction due to its estrogenic activity [51] and is implicated in precocious pubertal changes in children [109].

iii) Allergic and immunotoxic diseases due to *Fusarium*

During harvesting and handling of grains, aerosolized grain dusts are produced which may contain *Fusarium* species as well as their toxins [108]. *Fusarium avenaceum, F. culmorum, F. graminearum, F. poae* and *F. sporotrichioides* and their toxins (DON, moniliformin, nivalenol, vomitoxin, zearlanone, T-2) can be present in the airborne dusts of contaminated cereal grains [4,18,43,63,97,119,178]. Inhalation of these toxins by agricultural workers may lead to the development of debilitating diseases such as bronchial asthma, allergic alveolitis, allergic rhinitis, atopic conjunctivitis, organic dust toxic syndrome, and chronic fatigue-like syndrome [108,113]. In addition to these toxins, *Fusarium* allergens are most likely present. *Fusarium solani* contains several allergens of different molecular weights that react to the serum of patients sensitive to many fungi [160,236].

iv) *Fusarium* infections in humans

Several *Fusarium* species are opportunistic pathogens in patients who are immunocompetent but with superficial or deep tissue injury, or, immunocompromised with hematologic malignancies, aplastic anemia or undergoing chemotherapy treatment [40,115]. Disseminated *Fusarium* infection is almost exclusively encountered in immunocompromised individuals, particularly in neutropenic cancer patients submitted to intensive cytotoxic treatment and/or to bone marrow transplantations [133].

a) *Fusarium* infections in immunocompetent patients. *Fusarium* infections occur in healthy individuals as a result of tissue damage due to direct trauma or the presence of a foreign object. *Fusarium* infections are the most common cause of fungal keratitis worldwide [52,55,80,148,152,221] followed by *Aspergillus* [33,49,59,111,165,218,232] and *Candida* [192,221]. *Fusarium* keratitis is a suppurative, usually ulcerative, disease that may also occur in immunodepressed patients [80,225]. The epidemiological pattern of *Fusarium* keratitis varies by country, with climate appearing to play a crucial factor in determining the predominance of certain species [55]. *Fusarium dimerum*, a plant rot pathogen (e.g. figs), is known to cause keratitis [241]. One study noted that members of the *F. solani* group were the predominant agents of *Fusarium* keratitis followed by *F. verticilliodies, F. dimerum* and members of the *F. oxysporum* group [152]. In vitro, 76% of these isolates produced the mycotoxins fusaric acid and moniliformin [152]. In vitro cytotoxicity data suggests that these mycotoxins may play a role in the pathogenesis of *Fusarium* keratitis infections [152]. *F. moniliforme*, which produces fumonisin B_1, is another member of this genus reported to cause keratitis [217]. *Fusarium* keratitis is difficult to treat, especially that caused by *F. solani*, has a worse prognosis than keratitis produced by other fungi, and often results in rapid corneal sloughing and serious vision loss [184].

Fusarium may infect the nails and skin of healthy persons. *Fusarium* onychomycosis occurs when nails are dystrophic, have been traumatized, or already infected with dermatophytes [14]. However, *Fusarium* onychomycosis is uncommon, with the most common reported species being *F. oxysporum*, and *F. solani* [74,76,83]. *Fusarium* infections also occur in burn patients where it is sometimes fatal [115]. One source of these fungi may be in water used by the patients. One study indicated that the water system of a hospital served as the reservoir for *F. oxysporum* and *F. solani* found causing infections in the resident patients [9].

b) *Fusarium* infections of immunocompromised patients. *Fusarium* species cause disseminated disease in severely immunocompromised patients and have emerged in some centers as the second most common pathogenic mold after *Aspergillus* in high-risk patients with haematological cancer, recipients of solid organ and allogenic bone marrow or stem cell transplants (26,52,107,155,198]. Disseminated fusariosis is a life-threatening disease whose outcome is highly influenced by immune status [52].

In general, invasive fusariosis is caused by three species, *F. solani*, *F. oxysporum* and *F. verticillioides* (formerly *F. moniliforme*), although in approximately one-third of invasive fusariosis cases the species was unidentified [80,133,171,204]. *Fusarium solani* infections may become disseminated in stem cell transplantation patients [210]. Although rare, the cereal pathogens *F. dimerum* and *F. chlamydosporum,* are reported to cause localized and disseminated infection in immunocompromised patients [12,17,121,204].

The most important risk factor for the development of disseminated fusariosis is profound and prolonged aplasia [80]. Symptoms of disseminated *Fusarium* infection include persistent fever refractory to antibiotics, skin lesions, and pneumonia. This is a highly fatal infection that merges fungemia with multiple organ injuries such as in the lung, liver, spleen, kidney, and heart [99,210]. Mortality of immunocompromised patients having fusariosis ranges from 50% to 80% [26,52,99,155].

The incidence of fungal pneumonias, where *Fusarium* is the etiologic agent, has increased greatly in recent years. Inhalation of *Fusarium* spores can lead to pulmonary infections in immunocompromised individuals [80,249]. Leukemia is, by far, the most frequent underlying disease leading to *Fusarium* pneumonia [80,133]. *Fusarium solani* is the most common isolate in such cases [242] followed by *F. oxysporum* and *F. verticilliodies*. Other *Fusarium* species are rarely involved, although *F. chlamydosporum, F. proliferatum*, and *F. anthophilum* have been reported involved in fungal pneumonia [133,200]. Clinical isolates of *F. solani* produce cyclosporin A, an immunosuppressive compound, which may a role in the pathogenesis of this fungus [217].

Dematiaceous fungi

Dematiaceous fungi are characterized by the presence of pale brown to dark melanin-like pigments in the cell wall [68]. Some dematiaceous fungi are considered emerging pathogens in man, where they cause morbidity and mortality in an expanding immunocompromised patient population [243]. This group includes species of *Alternaria*, *Curvularia*, and *Cladosporium* which are phytopathogens, causing rots and seed damage, and produce a number of phytotoxic metabolites that also affect mammalian cells. They produce a wide range of diseases including

phaeohyphomycosis, chromoblastomycosis, and eumycotic diseases [27]. These fungi are the third most common cause of keramycosis after *Aspergillus* and *Fusarium* [69,251]. Melanin, as mentioned above, also plays an important role in their evasion of host defenses [243].

Alternaria

i) Phytopathogenicity

Alternaria alternata is a seed pathogen of cereals, such as sorghum and wheat, where fungal growth causes surface discoloration initially, followed by breakdown of the seed components [90,123,246]. This reduces the grain yield, viability, and quality as well as nutritional and economic values [188]. *Alternaria tenuis*, *Alternaria brassicola* and *Alternaria oleracea* are recognized as spoilage organisms causing rot of vegetables such as tomatoes, peppers, cucurbits and leafy crucifers [229].

ii) *Alternaria* mycotoxins

Alternaria species produce mycotoxins belonging to three different structural groups: (1) dibenzopyrone derivatives of alternariol, alternariol methyl ether and alternuene; (2) the perylene derivatives alteroxins (ATX-I and II); and (3) the tetramic acid derivative, tenuazonic acid [123]. These toxins contaminate grains, sunflower seeds and decayed fruits worldwide [10,44,123,203,219,248]. The *Alternaria* toxins are cytotoxic, in vitro, to mammalian and bacterial cells and are fetotoxic and teratogenic in mice and hamsters [240]. These toxins are known to block synthesis of sphingolipid by inhibiting the rate-limiting enzyme, ceramide synthase though they are not as active as fumonisin B_1 in this regard [233].

The *A. alternata* group also produces plant specific phytotoxins [162]. Perhaps the most interesting of this toxin group is AAL-toxin produced by *Alternaria alternata* f. sp. *lycopersici*. This toxin, structurally similar to fumonisin B_1, causes necrotic lesions in genetically susceptible tomato lines [75,144].

iii) *Alternaria* in human infections

As with *Aspergillus* and *Fusarium*, the members of the *Alternaria* genus are widespread in the environment worldwide [27]. However, *Alternaria* is not as commonly found in infections of healthy individuals as are *Aspergillus* and *Fusarium*. *Alternaria alternata* and *Alternaria tenuissima* are the most frequent agents of human infection, although six other species have been implicated [27].

Alternaria alternata is known to produce onychomycosis in healthy individuals [11,73,190,214]. However, the most common *Alternaria* infections occur in immunocompromised patients. In such patients, *A. alternate* and *A. tenuissima* can cause skin infections [5,136,172,187,190,191], keratomycosis [260], and sinonasal infections [147].

iv) Sensitization caused by *Alternaria*

Alternaira alternata is one of the molds most frequently observed to produce type I allergies in both an indoor or outdoor environment, especially in warm climates [127]. This mold, as well as *A. tenuis*, is known to produce asthma and allergic conjunctivitis worldwide [93,125,143]. Several epidemiological studies have shown that sensitization to *A. alternata* is widespread, with between three and four percent of assayed patients in the United States and Scandinavia having a positive reaction upon challenge [72,128].

Curvularia

i) Phytopathogenicity

The genus *Curvularia* is comprised of 40 saprophytic members. Of these, only a few are phytopathogenic. *Curvularia lunata* infects grains such as sorghum, wheat (kernel smudge), and corn (leaf spot). As with *Alternaria, Curvularia* reduces yield, seed quality, and deterioration of the endosperm and embryo [151]. This genus produces a number of cytotoxic mycotoxins including the brefeldins and curvulins which are discussed below.

ii) *Curvularia* infections in man

Curvularia lunata may infect healthy persons upon trauma to the eye or skin, resulting in fungal corneal keratitis [251], onychomycosis, skin ulcerations and subcutaneous mycetoma [66,254]. *Curvularia* species are the most common group of dematiaceous fungi isolated from patients with mycotic keratitis in the southern United States [251]. The onset of *Curvularia* induced keratitis is clustered in warm, humid months [251]. In comparison, *Curvularia* keratitis is less severe and of slower progression, than that caused by *Fusarium* [224]. *Curvularia* may also infect the paranasal sinus [61,98]. Systemic infections are rare in immunocompetent persons [189]. However, in immunocompromised individuals, various *Curvularia* species can cause often serious and systemic infections with dissemination being common [196]. Infections may develop into phaeohyphomycosis [196], mycetoma [27], and a rapid form of invasive sinusitis [186].

Brefeldin and curvularin, toxins produced by *Curvularia*, affect several mammalian metabolic processes. Nitric oxide (NO) plays an important role in the immune response as a regulatory and cytotoxic effector molecule [24,103]. Brefeldin-A, a 13-carbon macrolide lactone, is known to disrupt intracellular protein transport in animal cells [173]. In vitro, brefeldin-A selectively and reversibly interferes with the generation of endothelial-derived hyperpolarizing factor in native and cultured endothelial cells [16]. S14-95 and S-curvularin, toxins produced by *Curvularia* as well as several other fungi, inhibit in vitro production of a synthase (inducible NO synthase) responsible for NO production in human cells [257].

iii) Hypersensitivity to *Curvularia*

Members of the *Curvularia* genus contain allergens that are highly reactive in humans. *Curvularia lunata* is considered a major problem in respiratory allergic disorders [84,181]. The clinical and pathologic features of allergic sinusitis caused by *C. lunata* are identical to those of allergic *Aspergillus* sinusitis [130]. Many *C. lunata* sensitive patients show positive skin tests with allergens of other fungi, such as the six other *Curvularia* species, *A. alternata* and *Epicoccum nigrum*, whose allergenic proteins have strong cross-reactivity with *C. lunata* proteins [84,85].

Cladosporium

Members of the *Cladosporium* genus are ubiquitous in the environment and can be isolated from many sources, including dead organic matter, woody plants soil, straw, paint and textiles. One species, *Cladosporium cladosporioides*, can be pathogenic in both plants and humans.

i) Phytopathogenicity

Cladosporium species cause spoilage of freshly harvested vegetables, resulting in great economic losses [229]. They enter plant tissue after mechanical or chilling injuries or after the plant skin barrier has been compromised by other organisms [229]. *Cladosporium cladosporioides* causes decay in fruits, vegetables and other agricultural products, especially after harvesting. In addition to post harvest infection, *C. cladosporioides* can cause grape rot in the vineyard [39].

ii) Human infections

C*ladosporium cladosporioides* can cause the cutaneous form of phaeohyphomycosis in healthy and immunocompromised individuals [58,81,238]. Phaeohyphomycosis is characterized by the presence of dematiaceous septate hyphae, sometimes yeasts, or a combination of both in tissues such as the skin, brain or bone. Generally, phaeohyphomycosis can be controlled by surgical excision and drugs (amphotericin B, itraconazole, or 5-fluoroctyosine).

iii) Allergic response to *Cladosporium*

Positive skin tests have linked patients, suffering from allergic rhinitis and asthma, to *C. cladosporioides* [23,223]. Hypersensitivity to this fungus is IgG, not IgE, mediated and involves the outer wall layer of the spores [20,167].

Other fungi

Colletotrichum

i) Phytopathogenicity

Colletotrichum is distributed worldwide and is considered one of the most serious phytopathogenic fungal genera [31]. Genus members cause field anthracnose, resulting in major economic losses of many crops such as cereals, legumes, coffee and rubber [117]. Two of the phytopathogenic species are also human pathogens. One of these, *Colletotrichum gloeosporioides*, affects many crops of agricultural importance throughout the world. It is the etiological agent of anthracnose, resulting in serious economic and crop losses of strawberry [95,211], yams [1], and mango [56].

The other phytopathogen of this group affecting human health is *Colletotrichum coccodes*, an increasingly important potato pathogen. This fungus causes tuber blemish (black dot disease) and foliar disease [120]. Losses from this disease occur in potatoes destined for the growing market for fresh, prepackaged potatoes, which demands tubers with a high quality appearance [120]. The majority of the disease reports originate in North America, Europe and Australia [88,145]. This fungus is also pathogenic on several plants in the *Solanaceae* and *Curcurbitaceae* groups [54].

ii) *Colletotrichum* infections in humans

Colletotrichum infections mainly occur in immunocompromised patients, although healthy persons are also infected when the skin barrier is compromised [31]. *Colletotrichum gloeosporioides* can cause keratitis in both healthy and immunocompromised persons [67]. Both *C. gloeosporioides* and *C. coccodes* can induce phaeohyphomycosis in patients with hematologic malignancies and iatrogenic immunosuppression [161].

Mucorales

i) Phytopathogenicity

Mucor and *Rhizopus* are members of the Mucorales group containing pathogens of both plants and humans. They are found throughout the world and in many types of climates and terrain. These fungi cause rot in fruits both in the field and post harvest. Mechanical injury during harvesting and post harvest handling provide a site of infection by these fungi [29]. *Mucor piriformis* causes decay of cherries on the tree as well as rot of apples stored under humid conditions [25,139]. *Rhizopus arrhizus* causes a wet, juicy rot of grapes in warm, wet climates [39]. In humid weather the fungus can spread to other berries in the grape cluster causing bunch rot.

ii) Human infections

Rhizopus, Absidia, Rhizomucor and *Mucor* are harmless to persons in good health, but cause opportunistic infections in immmunosuppressed patients or those suffering from trauma, such as wounds and burns [105]. In recent years, the clinical importance of mucormycosis has significantly increased [64]. Mucormycosis is a filamentous fungal infection most frequently arising in patients with hematologic malignancies [106,146,163]. Various species of *Mucor* and *R. arrhizus* are the predominant members of this group causing mucormycosis although other species are occasionally involved.

Patients having prolonged and profound neutropenia secondary to the myeloablative treatments used for the underlying hematologic malignancy are susceptible to mucormycosis [163]. It is most common in acute leukemia rather than in patients with other types of hematologic malignancies. Infection occurs when either those undergoing immunosuppression inhale conidia or when traumatized areas are contaminated. Rhino-cerebral, maxillofacial and pulmonary infections are the most common, although neutropenic patients are also at a high risk of developing a disseminated infection from these fungi [163]. The major blood vessels can be invaded where the fungus grows on the walls and lumen, causing thromboembolism, ischemia and necrosis of the tissues [207]. The infection is usually acute and progresses rapidly and has a mortality rate of about 70% [163].

Conclusion

Fungi often infect crops either in the field after harvesting resulting in considerable economic losses to farmers and producers worldwide. When food and feed contaminated with fungi, and the toxins they may produce, are ingested by humans and/or animals, a wide variety of debilitating diseases can occur with some leading to death. Some of the major phytopathogens affecting food production also cause serious, and very often lethal, infections in man. Taken together, this rather small group of fungi affect the health and well being of millions of persons worldwide. Enormous economic losses can occur, both from agricultural losses and medical care costs. Research is needed to develop a series of novel antifungals targeted specifically for particular members of this multi-disease producing group. Successful development of such antifungal compounds could prove eventually useful in combating infectious and toxin-producing fungi in both the agricultural and medical fields. Plants may be a good source of such compounds since they have had to develop compounds to resist fungal infections.

References

1. Abano MM, Hoffmann P, Winter S, Green KR, Wolf GA. Vegetative compatibility among isolates of *Colletotrichum gloeosporioides* from yam (*Dioscorea* spp.) in Nigeria. J Phytopathol 2004; 152: 21-37.
2. Abbas HK, Shier WT, Seo J-A, Lee Y-W, Musser SM. Phytotoxicity and cytotoxicity of the fumonosin C and P series of mycotoxins from *Fusarium* spp. fungi. Toxicon 1998; 36: 2033-2037.
3. Abbas HK, Williams WP, Windham GL, Pringle HC 3rd, Xie W, Shier WT. Aflatoxin and fumonisin contamination of commercial corn (*Zea mays*) hybrids in Mississippi. J Agric Food Chem 2002; 50: 5246-5254.
4. Abramson D, Clear RM, Gaba D, Smith DM, Patrick SK, Saydak D. Trichothecene and moniliformin production by *Fusarium* species from western Canadian wheat. J Food Protect 2001; 64: 1220-1225.
5. Acland KM, Hay RJ, Groves R. Cutaneous infection with *Alternaria alternata* complicating immunosuppression: successful treatment with itraconazole. Br J Dermatol 1998; 138: 354-356.
6. Ainsworth GC, Austwick PKC. Fungal Diseases of Animals. 2 Ed. Slough, Commonwealth Agricultural Bureau, 1973.
7. Akan M, Haziroglu R, Ihan Z, Sareyyupoglu B, Tunca R. A case of aspergillosis in a broiler breeder flock. Avian Dis 2002; 46: 497-501.
8. Almeida AP, Fonseca H, Fancelli AL, Direito GM, Ortega EM, Corrêa B. Mycoflora and fumonisin contamination in Brazilian corn from sowing to harvest. J Ag Food Chem 2002; 50: 3877-3882.
9. Anaissie EJ, Kuchar RT, Rex JH, Francesconi A, Kasai M, Müller F-MC, Lozano-Chiu M, Summerbell RC, Dignani MC, Chanock SJ, Walsh TJ. Fusariosis associated with pathogenic *Fusarium* species colonization of a hospital water system: a new paradigm for the epidemiology of opportunistic mold infections. Clin Infect Dis 2001; 33: 1871-1878.
10. Ansari AA, Shrivastava AK. Natural occurrence of *Alternaria* mycotoxins in sorghum and ragi from North Bihar, India. Food Addit Contam 1990; 7: 815-820.
11. Arrese JE, Piérard-Franchimont C, Piérard GE. Onychomycosis and keratomycosis caused by *Alternaria* spp. Am J Dermatopathol 1996; 18: 611-613.
12. Austin B, McCarthy H, Wilkins B, Smith A, Duncombe A. Fatal disseminated *Fusarium* infection in acute lymphoblastic leukaemia in complete remission. J Clin Pathol 2005; 54: 488-490.
13. Balloy V, Huerre M, Latgé J-P, Chignard M. Differences in patterns of infection and inflammation for corticosteroid treatment and chemotherapy in experimental invasive pulmonary aspergillosis. Infect Immun 2005; 73: 494-503.
14. Baran R, Tosti A, Piraccini BM. Uncommon clinical patterns of *Fusarium* nail infection: report of three cases. Br J Dermatol 1997; 136: 424-427.
15. Bart-Delabesse E, Latge J-P. Ecology and genetic diversity of *Aspergillus fumigatus*. In: Domer JE, Kobayashi GS (Eds.) The Mycota. XII. Human Fungal Pathogens. Berlin, Springer-Verlag 2004: 25-36.
16. Bauersachs J, Fleming I, Scholz D, Popp R, Busse R. Endothelium-derived hyperpolarizing factor, but not nitric acid, is reversibly inhibited by brefeldin A. Hypertension 1997; 30: 1598-1605.
17. Bigley VH, Duarte RF, Gosling RD, Kibber CC, Seaton S, Potter M. *Fusarium dimerum* infection in a stem cell transplant recipient treated successfully with voriconazole. Bone Marrow Transplant 2004; 34: 815-817.
18. Birzele B, Prange A, Kramer J. Deoxynivalenol and ochratoxin A in German wheat and changes of level in relation to storage parameters. Food Addit Contam 2000; 17: 1027-1035.
19. Bauer X, Dexheimer E. Hypersensitivity pneumonitis concomitant with acute airway obstruction after exposure to hay dust. Respiration 1984; 46: 354-361.
20. Bergen MS, Yang TJ, Collins RP. Involvement of the outer wall layer of *Cladosporium cladosporioides* in and IgG-mediated hypersensitivity. Int Arch Allergy Appl Immunol 1988; 85: 20-26.
21. Berek L, Petri IB, Mesterházy Á, Téren J, Molnár J. Effects of mycotoxins on human immune functions *in vitro*. Toxicol in Vitro 2001; 15: 25-30.
22. Bharathi MJ, Ramakrisnan R, Vasu S, Meenakshi R, Palaniappan R. Epidemiological characteristics and laboratory diagnosis of fungal keratitis. A three-year study. Indian J Ophthalmol 2003; 51: 315-321.
23. Black PN, Udy AA, Brodie SM. Sensitivity to fungal allergens is a risk factor for life-threatening asthma. Allergy 2000; 55: 501-504.
24. Bogdan C. Nitric oxide and the immune response. Nat Immunol 2001; 2: 907-916.
25. Børve J, Stensvand A. Use of a plastic rain shield reduces fruit decay and need for fungicides in sweet cherry. Plant Dis 2003; 87: 523-528.
26. Boutati EI, Anaissie EJ. *Fusarium*, a significant emerging pathogen in patients with hematologic malignancy: ten years' experience at a cancer and implications for management. Blood 1997; 90: 999-1008.
27. Brandt ME, Warnock DW. Epidemiology, clinical manifestations, and therapy of infections caused by dematiaceous fungi. J Chemother 2003; 15 (Suppl 2): 36-47.
28. Bretz M, Knecht A, Göckler S, Humpf H-U. Structural elucidation and analysis of thermal degradation products of the *Fusarium* mycotoxin nivalenol. Mol Nutr Food Res 2005; 49: 309-316.
29. Bruton BD. Mechanical injury and latent infections leading to postharvest decay. Hort Sci 1994; 29: 747-749.
30. Bullerman LB. Occurrence of *Fusarium* and fumonisins on food grains and in foods. Adv Exp Med Biol 1996; 392: 27-38.
31. Cano J, Guarro J, Gené J. Molecular and morphological identification of *Colletotrichum* species of clinical interest. J Clin Microbiol 2004; 42: 2450-2454.
32. Carratù MR, Cassano T, Coluccia A, Borracci P, Cuomo V. Antinutritional effects of fumonisin B_1 and pathophysiological consequences. Toxicol Lett 2003; 140-141: 459-463.
33. Chander J, Sharma A. Prevalence of fungal corneal ulcers in northern India. Infection 1994; 22: 207-209.
34. Chakrabarti A, Sharma SC. Paranasal sinus mycoses. Indian J Chest Dis Allied Sci 2000; 42: 293-304.
35. Chazalet V, Debeaupuis J-P, Sarfati J, Lortholary J, Ribaud P, Shah P, Cornet M, Vu Thien H, Gluckman E, Brücker G, Latge J-P. Molecular typing of environmental and patient isolates of *Aspergillus fumigatus* from various hospital settings. J Clin Microbiol 1998; 36: 1494-1500.
36. Choo TM, Martin RA, Ho KM, Shen Q, Fedak G, Savard M, Voldeng H, Falk DE, Etienne M, Sparry E. *Fusarium* head blight and deoxynivalenol accumulation of barley in Eastern Canada: cultivar response and correlation analysis. Plant Dis 2004; 88: 837-844.
37. Christensen M, Tuthill D. *Aspergillus*: an overview. In: Samson R, Pitt J (Eds.) Advances in *Penicillium* and *Aspergillus* systematics. New York, Plenum Press, 1985: 195-209.
38. Chute HL, Richard JL. Fungal infections. In: Calnek BW, Barnes HJ, Beard CW, McDougald LR, Saif YM. (Eds.) Diseases of Poultry. 10th ed. Ames, Iowa State University Press, 1997: 351-365.
39. Compendium of Grape Disease. Pearson RC, Goheen AC (Eds.) 4th printing. St. Paul, American Phytopathological Press, 1998.
40. Connolly JE Jr, McAdams HP, Erasmus JJ, Rosado-de-Christenson ML. Opportunistic fungal pneumonia. J Thorac Imaging 1999; 14: 51-62.
41. Cotty PJ, Bayman P, Egel DS, Elias KE. Agriculture, aflatoxin and *Aspergillus*. In: Powell KA, Reenwick A, Peberdy JF (Eds.) The Genus *Aspergillus*. New York, Plenum Press, 1994: 1-28.
42. Council for Agricultural Science and Technology. Aflatoxin and Other Mycotoxins: An Agricultural Perspective. Report 80. Ames, Council for Agricultural Science and Technology 1979.
43. Dacero A, Torres A, Etcheverry M, Chulze S, Varsavsky E. Occurrence of deoxynivalenol and *Fusarium graminearum* in Argentinean wheat. Food Addit Contam 1997; 14: 11-14.
44. David BS, Seitz LM, Burroughs R, Mohr HE, West JL, Milleret RJ, Anthony HD. Toxicity of *Alternaria* metabolites found in weathered sorghum grain at harvest. J Agric Food Chem 1978; 26: 1380-1383.
45. De La Rosa GR, Champlin RE, Kontoyiannis DP. Risk factors for the development of invasive fungal infections in allogenic blood and marrow transplant recipients. Transpl Infect Dis 2002; 4: 3-9.
46. Denning DW. Invasive aspergillosis. Clin Infect Dis 1998; 26: 781-805.
47. Denning DW, Marinus A, Cohen J, Spence D, Herbrecht R, Pagano L, Kibber C, Kcrmery V, Offner F, Cordonnier C, Jehn U, Ellis M, Collette L, Sylvester R. An EORTC multicentre prospective survey of invasive aspergillosis in haematological patients: Diagnosis and therapeutic outcome. J Infect 1998; 37: 173-180.
48. Denning DW, Stevens DA. Antifungal and surgical treatment of invasive aspergillosis: review of 2,121 published cases. Rev Inf Dis 1990; 12: 1147-1201.
49. Deshpande SD, Koppikar GV. A study of mycotic keratitis in Mumbai. Indian J Pathol Microbiol 1999; 42: 81-87.
50. DeVay JE. Half a century dynamics and control of cotton diseases: *Fusarium* and *Verticillium* wilts. In: Brown J (Ed.) 1986 Proc. Beltwide Cotton Conf. Memphis, National Cotton Council of America, 1986, 35-41.
50. Diekman MA, Green ML. Mycotoxins and reproduction in domestic livestock. J Anim Sci 1992; 70:1615-1627.
52. Dignani MC, Anaissie E. Human fusariosis. Clin Microbiol Infect 2004; 10 (Suppl. 1): 67-75.
53. Diener UL, Cole RJ, Sanders TH, Payne GA, Lee LS, Klich MA. Epidemiology of aflatoxin formation by *Aspergillus flavus*. Annu Rev Phytopathol 1987; 25: 249-270.
54. Dillard HR. The pathogen and its hosts. In: Baily JA, Jeger MJ (Eds.) *Colletotrichum:* Biology, Pathology, and Control. Wallingford, CAB International, 1992: 225-236.
55. Dóczi I, Gyetvai T, Kredics L, Nagy E. Involvement of *Fusarium* spp. in fungal keratitis. Clin Microbiol Infect 2004; 10: 773-776.

56. Dodd JC, Estrada AB, Matcham J, Jeffries P, Jeger MJ. The effect of climatic factors on *Colletotrichum gloeosporioides*, causal agent of mango anthracnose, in the Philippines. Plant Pathol 1991; 40: 568-575.
57. Dorner JW. Simultaneous quantitation of *Aspergillus flavus/A. parasiticus* and aflatoxin in peanuts. J AOAC Int 2002; 85: 911-916.
58. Drabick JJ, Gomatos PJ, Solis JB. Cutaneous cladosporiosis as a complication of skin testing in a man positive for human immunodeficiency virus. J Am Acad Dermatol 1990; 22: 135-136.
59. Dunlop AA, Wright ED, Howlader SA, Nazrul I, Husain R, McClellan K, Billson FA. Superative corneal ulceration in Bangladesh. A study of 142 cases examining the microbiological diagnosis, clinical and epidemiological features of bacterial and fungal keratitis. Aust NZ J Ophthalmol 1994; 22: 105-110.
60. Dvoraková I, Pichová V. Pulmonary interstitial fibrosis with evidence of aflatoxin B_1 in lung tissue. J Toxicol Environ Health 1986; 18: 153-157.
61. Ebright JR, Chandrasekar PH, Marks S, Fairfax MR, Aneziokoro A, McGinnis MR. Invasive sinusitis and cerebritis due to *Curvularia lunata* in an immunocompetent adult. Clin Infect Dis 1999; 28: 687-689.
62. Edwards SG. Influence of agricultural practices on *Fusarium* infection of cereals and subsequent contamination of grain by trichothecene mycotoxins. Toxicol Lett 2004; 153: 29-35.
63. Escola M, Parikka P, Rizzo A. Trichothecenes, ochratoxin A and zearalone contamination and *Fusarium* infection in Finnish cereal samples in 1998. Food Addit Contam 2001; 18: 707-718.
64. Eucker J, Sezer O, Graf B, Possinger, K. Mucormycoses. Mycoses 2001; 44: 253-260.
65. Farias GM, Griffin GJ. Roles of *Fusarium oxysporum* and *F. solani* in Essex disease of soybean in Virginia. Plant Dis 1989; 73: 38-42.
66. Fernandez M, Noyola DE, Rossman SN, Edwards MS. Cutaneous phaeohyphomycosis caused by *Curvularia lunata* and a review of *Curvularia* infections in pediatrics. Pediatr Infect Dis J 1999; 18: 727-731.
67. Fernandez V, Dursun D, Miller D, Alfonso EC. *Colletotrichum* keratitis. Am J Ophthalmol 2002; 134: 435-438.
68. Fleming RV, Walsh TJ, Anaissie EJ. Emerging and less common fungal pathogens. Infect Dis Clin North Am 2002; 16: 915-933.
69. Garg MS, Gopinathan U, Choudhary K, Rao GN. Keratomycosis - clinical and microbiologic experience with dematiaceous fungi. Ophthalmology 2000; 107: 574-580.
70. Gelderblom WCA, Jaskiewicz K, Marasas WFO, Thiel PG, Horak RM, Vleggaar R, Kriek NPJ. Fumonisins – Novel mycotoxins with cancer-promoting activity produced by *Fusarium moniliforme*. Appl Environ Microbiol 1988; 54: 1806-1811.
71. Gelderblom WCA, Snyman SD, Abel S, Lebepe-Mazur S, Smuts CM, Van der Westuizen L, Marasas WFO, Victor TC, Knasmuller S, Huber W. Hepatotoxicity and carcinogenicity of the fumonisins in rats. A review regarding mechanistic implications for establishing risk in humans. In: Jackson LS, De Vries JW, Bullerman LB (Eds.) Fumonisins in Food. New York, Plenum Press, 1996: 279-296.
72. Germen PJ, Turkeltaub PC, Kovar MG. The prevalence of skin test reactivity to eight common aeroallergens in the US population: results from the second National Health and Nutrition Examination Survey. J Clin Immunol 1987; 80: 669-679.
73. Gianni C, Cerri A, Crosti C. Ungual phaeochomycosis caused by *Alternaria alternata*. Mycoses 1997; 40: 219-221.
74. Gianni C, Cerri A, Crosti C. Unusual clinical features of fingernail infection by *Fusarium oxysporum.* Mycoses 1997; 40: 455-459.
75. Gilchrist DG, Ward B, Moussata V, Mirocha CJ. Genetic and physiological response to fumonisin and AAL-toxin in intact tissue of a higher plant. Mycopathologia 1992; 117: 57-64.
76. Godoy P, Nunes E, Silva V, Tomimori-Yamashita J, Zaror L, Fischman O. Onychomycosis caused by *Fusarium solani* and *Fusarium oxysporum* in Sao Paulo, Brazil. Mycopathologia 2004; 157: 287-290.
77. Goodley J, Clayton Y, Hay R. Environmental sampling for aspergilli during building construction on a hospital site. J Hosp Infect 1994; 26: 27-35.
78. Gordon TR, Martyn RD. The evolutionary biology of *Fusarium oxysporum*. Ann Rev Phytopathol 1997; 35: 111-128.
79. Gray LE, Achenbach LA, Duff RJ, Lightfoot D. Pathogenicity of *Fusarium solani* sp. *glycines* isolates on soybean and green bean plants. J Phytopathol 1999; 147: 281-284.
80. Guarro J, Gene J. Opportunistic fusarial infections in humans. Eur J Clin Microbiol Infect Dis 1995; 14: 741-754.
81. Gugnani HC, Sood N, Singh B, Makkar R. Case report. Subcutaneous phaeohyphomycosis due to *Cladosporium cladosporioides*. Mycoses 2000; 43: 85-87.
82. Gugnani HC. Ecology and taxonomy of pathogenic aspergilli. Front Biosci 2003; 8: S346-S357.
83. Gupta AK, Baran R, Summerbell RC. *Fusarium* infections of the skin. Curr Opinion Infect Dis 2000; 13: 121-128.
84. Gupta R, Singh BP, Sridhara S, Gaur SN, Kunar R, Chaudhary VK, Arora N. Identification of cross-reactive proteins amongst different *Curvularia* species. Int Arch Allergy Immunol 2002; 127: 38-46.
85. Gupta R, Singh BP, Sridhara S, Gaur SN, Kumar R, Chaudhary VK, Arora N. Allergenic cross-reactivity of *Curvularia lunata* with other airborne fungal species. Allergy 2002; 57: 636-640.
86. Gutleb AC, Morrison E, Murk AJ. Cytotoxicity assays for mycotoxins produced by *Fusarium* strains: a review. Environ Toxicol Pharmacol 2002; 11: 309-320.
87. Guy St-Germain BS, Summerbell R. Identifying filamentous fungi. Belmont, Star Publishing Co, 1999.
88. Harrison DE. Black dot disease of potato. J Agri Victoria 1963; 61: 573-576.
89. Harrison LR, Colvin BM, Greene JT, Newman LE, Cole JR. Pulmonary edema and hydrothorax in swine by fumonisin B_1 a toxic metabolite of *Fusarium moniliforme*. J Vet Diagn Invest 1990; 2: 217-221.
90. Hasan HAH. Phytotoxicity of pathogenic fungi and their mycotoxins to cereal seedling viability. Mycopathologia. 1999; 148: 149-155.
91. Hasse G, Brakhage AA. Melanized fungi infecting humans: Function of melanin as a factor in pathogenesis. In: Domer JE, Kobayashi GS (Eds.) The Mycota XII. Human Fungal Pathogens. Berlin, Springler-Verlag, 2004: 67-87.
92. Hill RA, Wilson DM, McMillian WW, Widstrom NW, Cole RJ, Sanders TH, Blankenship PD. Ecology of the *Aspergillus flavus* group and aflatoxin formation in maize and groundnut. In: Lacey J (Ed.) Trichothecenes and Other Mycotoxins. Chichester, John Wiley and Sons, 1985: 79-95.
93. Halomen M, Stern DA, Wright AL, Taussig LM, Martinez FD. *Alternaria* as a major allergen for asthma in children raised in a desert environment. Am J Respir Crit Care 1997; 155: 1356-1361.
94. Hospenthal DR, Kwon-Chung KJ, Bennett JE. Concentrations of airborne *Aspergillus* compared to the incidence of invasive aspergillosis: Lack of correlation. Med Mycol 1998; 36: 165-168.
95. Howard CM, Albregts EE. Black leaf spot phase of strawberry anthracnose caused by *Colletotrichum gloeosporioides* (= *C. fragariae*). Plant Dis 1983; 67: 1144-1146.
96. IARC. The Evaluation of the Carcinogenic Risk of Chemicals to Humans. IARC monograph Supplement 4. Lyon, International Agency for Research on Cancer, 1984.
97. Ioos R, Belhadj A, Menez M. Occurrence and distribution of *Microdochium nivale* and *Fusarium* species isolated from barley, durum and soft wheat grains in France from 2000 to 2002. Mycopathologia 2004; 158: 351-362.
98. Ismail Y, Johnson RH, Wells MV, Pusavat J, Douglas K, Arsura EL. Invasive sinusitis with intercranial extension caused by *Curvularia lunata*. Arch Intern Med 1993; 153: 1604-1606.
99. Jensen TG, Gahrn-Hansen B, Arendrup M, Bruun B. *Fusarium* fungaemia in immunocompromised patients Clin Microbiol Infect 2004; 10: 499-501.
100. Johnson TE, Casiano RR, Kronish JW, Tse DT, Meldrum M, Chang W. Sino-orbital aspergillosis in acquired immunodeficiency syndrome. Arch Ophthalmol 1999; 117: 57-64.
101. Kaur R, Mittal N, Kakkar M, Aggarwal AK, Mathur MD. Otomycosis: a clinicomycologic study. Ear Nose Throat J 2000; 79: 606-609.
102. Kelly JD, Eaton DL, Guengerich FP, Coulombe RA. Aflatoxin B_1 activation in human lung. Toxicol Appl Pharmacol 1997; 144: 88-95.
103. Kleinert H, Boissel JP, Schwartz PM, Förstermann U. Regulation of the expression of nitric oxide synthase isoforms. In: Ignarro LJ (Ed.) Nitric Oxide: Biology and Pathobiology. New York, Academic Press, 2000: 105-128.
104. Klich MA. Mycoflora of cottonseed from the southern United States: a three-year study of distribution and frequency. Mycologia 1986; 78: 706-712.
105. Kobayashi M, Hiruma M, Matsushita A, Kawai M, Ogawa H, Udagawa S. Cutaneous zygomycosis: a case report and review of Japanese reports. Mycoses 2001; 44: 311-315.
106. Kontoyiannis DP, Wessel VC, Bodey GP, Rolston KV. Zygomycosis in the 1990s in a tertiary care cancer center. Clin Infect Dis 2002; 30; 851-856.
107. Krcmery V Jr, Jesenska Z, Spanik S, Gyarfas J, Nogova J, Botek R, Mardiak J, Sufliarsky J, Sisolakova J, Vanickova M, Kunova A, Studena M, Trupl J. Fungaemia due to *Fusarium* spp. in cancer patients. J Hosp Infect 1997; 36: 223-238.
108. Krysinska-Traczyk E, Kiecana I, Perkowski J, Dutiewicz J. Levels of fungi and mycotoxins in samples of grain and grain dust collected on farms in Eastern Poland. Ann Agric Environ Med 2001; 8: 269-274.

109. Kuiper-Goodman T, Scott PM, Watanabe H. Risk assessment of the mycotoxin zearalenone. Reg Toxicol Pharmacol 1987; 7: 253-306.

110. Kuiper-Goodman T. Prevention of human mycotoxicoses through risk assessment and risk management. In: Miller JD, Trenholm HL (Eds.) Mycotoxins in Grains, Compounds Other than Aflatoxins. St. Paul, Eagan Press, 1994: 439-469.

111. Kumari N, Xess A, Shahi SK. A study of keratomycosis: our experience. Indian J Pathol Microbiol 2002; 45: 299-302.

112. Kurnatowski P, Kilipiak A. Otomycosis: prevalence, clinical symptoms, therapeutic procedure. Mycoses 2001; 44: 472-479.

113. Lacey J, Dutkiewicz J. Bioaerosols and occupational lung disease. J Aerosol Sci 1994; 25: 1371-1404.

114. Lass-Florl C, Rath P, Niederwieser D, Kofler G, Wurzner R, Krezy A, Dierich MP. *Aspergillus terreus* infections in haematological malignancies: molecular epidemiology suggests association with in-hospital plants. J Hosp Infect 2000; 46: 31-35.

115. Latenser BA. *Fusarium* infections in burn patients: a case report and review of the literature. J Burn Care Rehabil 2003; 24: 285-288.

116. Latge JP. *Aspergillus fumigatus* and aspergillosis. Clin Microbiol Rev 1999; 12: 310-350.

117. Latunde-Dada AO. *Colletotrichum*: tales of forcible entry, stealth, transient confinement and breakout. Mol Plant Pathol 2001; 2: 187-198.

118. Leitao J, De Saint Blanquat G, Baily JR, Paillas Ch. Quantitation of aflatoxins from various strains of *Aspergillus* in foodstuffs. J Chromatogr 1988; 435: 229-234.

119. Lee US, Jang HS, Tanaka T, Hasegawa A, Oh YJ, Ueno Y. The coexistence of the *Fusarium* mycotoxins nivalenol, deoxynivalenol and zearalenone in Korean cereals harvested in 1983. Food Addit Contam 1985; 2: 185-192.

120. Lees AK, Hilton AJ. Black dot (*Colletotrichum coccodes*): an increasingly important disease of potato. Plant Pathol 2003; 52: 3-12.

121. Letscher-Bru V, Campos F, Waller J, Randriamahazaha R, Candolfi E, Herbrecht R. Successful outcome of treatment of a disseminated infection due to *Fusarium dimerum* in a leukemia patient. J Clin Microbiol 2002; 40: 1100-1102.

122. Li FQ, Yoshizawa T, Kawamura O, Luo X-Y, Li Y-W. Aflatoxins and fumonisins in corn from the high-incidence area for human hepatocellular carcinoma in Guangxi, China. J Agric Food Chem 2001; 49: 4122-426.

123. Li FQ, Yoshizawa T. *Alternaria* mycotoxins in weathered wheat from China. J Agric Food Chem 2000; 48: 2920-2924.

124. Lillehoj EB, Wall JH, Bowers EJ. Preharvest aflatoxin contamination: Effect of moisture and substrate variation in developing cottonseed and corn kernels. Appl Environ Microbiol 1987; 53: 584-586.

125. Lin RY, Williams KD. Hypersensitivity to molds in New York City in adults who have asthma. Allergy Asthma Proc 2003; 24: 13-18.

126. Liu BH, Yu FY, Chan MH, Yang YL. The effects of mycotoxins, fumonisin B_1 and aflatoxin B_1 on primary swine alveolar macrophages. Toxicol Appl Pharmacol 2002; 180: 197-204.

127. Lizaso MT, MartÍnez A, Asturias JA, Algorta J, Madariaga B, Labarta N, Tabar AI. Biological standardization and maximum tolerated dose estimation of an *Alternaria alternata* allergenic extract. J Investig Allergol Clin Immunol 2006; 16: 94-103.

128. López M, Salvaggio JE. Mold sensitive asthma. Clin Rev Allergy 1985; 3: 183-196.

129. Lougheed MD, Roos JO, Waddell WR, Munt PW. Desquamative interstitial pneumonitis and diffuse alveolar damage in textile workers. Chest 1995; 108: 1196-1200.

130. MacMIllan RH 3rd, Cooper PH, Body BA, Mills AS. Allergic fungal sinusitis due to *Curvularia lunata*. Hum Pathol 1987; 18: 960-964.

131. Marasas WFO, Kellerman TS, Gelderblom WCA, Coetzer JAW, Thiel PG, van der Lugt JJ. Leukoencephalomalacia in a horse induced by fumonisin B1 a toxic metabolite of *Fusarium moniliforme*. Onderstepoort J Vet Res 1988; 55: 197-203.

132. Marasas WFO, Riley RT, Hendricks KA, Stevens VL, Sadler TW, Gelineau-van Waes J, Missmer SA, Cabrera J, Torres O, Gelderblom W CA, Allegood J, Martinez C, Maddox J, Miller JD, Starr L, Sullards MC, Roman AV, Voss KA, Wang E, Merrill AH Jr. Fumonisins disrupt sphingolipid metabolism, folate transport, and neural tube development in embryo culture and *in vivo*: A potential risk factor for human neural tube defects among populations consuming fumonisin-contaminated maize. J Nutr 2004; 134: 711-716.

133. Martin P, Gastaldi R, Raccah R, Girmenia C. Clinical patterns of *Fusarium* infections in immunocompromised patients. J. Infect 1994; 28(Suppl 1): 7-15.

134. Massey TE. The 1995 Pharmacological Society of Canada Merck Frosst Award. Cellular and molecular targets in pulmonary chemical carcinogenesis: Studies with aflatoxin B_1. Can J Physiol Pharmacol 1996; 74: 621-628.

135. Maurya V, Gugnami HC, Sarma PU, Madan T, Shah A. Sensitization to *Aspergillus* antigens and occurrence of allergic bronchopulmonary aspergillosis in patients with asthma. Chest 2005; 127: 1252-1259.

136. Mayser P, Nilles M, de Hoog GS. Case Report. Cutaneous phaeohyphomycosis due to *Alternaria alternata*. Mycoses 2002; 45: 338-340.

137. McMillian WA, Wilson DM, Widstrom NW. Insect damage, *Aspergillus* ear mold, and aflatoxin contamination in south Georgia corn field in1977. J Environ Qual 1978; 7: 565.

138. Meky FA, Hardie LJ, Evans SW, Wild CP. Deoxynivalenol-induced immunomodulation of human lymphocyte proliferation and cytokine production. Food Chem Toxicol 2001; 39: 827-836.

139. Michailides TJ, Spots RA. Postharvest diseases of pome and stone fruits caused by *Mucor piriformis* in the Pacific Northwest and California. Plant Dis 1990; 74: 537-543.

140. Midgley G, Moore MK. Nail infections. Dermatol Clin 1996; 14: 41-49.

141. Miller JD. Epidemiology of *Fusarium* ear diseases of cereals. In: Miller JD, Trenholm HL (Eds.) Mycotoxins in Grains, Compounds other than Aflatoxins. St. Paul, Eagan Press, 1994: 19-36.

142. Minervini F, Fornelli F, Lucivero G, Romano C, Visconti A. T-2 toxin immunotoxicity on human B and T lymphoid cell lines. Toxicology 2005; 210: 81-91.

143. Mimura T, Yamagami S, Amano S, Funatsu H, Arimoto A, Usui T, Ono K, Araie M Okamoto S. Allergens in Japanese patients with allergic conjunctivitis in autumn. Eye 2005; 19: 995-999.

144. Mirocha CJ, Gilchrist DG, Shier WT, Abbas HK, Wen Y, Versonder RF. AAL toxins, fumonisins (biology and chemistry) and host-specificity concepts. Mycopathologia 1992; 117: 47-56.

145. Mordue JEM. *Colletotrichum coccodes*. CMI Descriptions of Pathogenic Fungi and Bacteria, no. 131. Kew, Commonwealth Agricultural Bureau, 1967.

146. Morrison VA, McGlave PB. Mucormycosis in the BMT population. Bone Marrow Transplant 1993; 11: 383-388.

147. Morrison VA, Weisdorf DJ. *Alternaria*: a sinonasal pathogen of immunocompromised hosts. Clin Infect Dis 1993; 16: 265-270.

148. Mselle J. Fungal keratitis as an indicator of HIV infection in Africa. Trop Doct 1999; 29: 133-135.

149. Muhlschlegal F, Fonzi W, Hoyer L, Payne T, Poulet FM, Clevenger J, Latge J-P, Calera J, Beauvais A, Paris S, Monod M, Sturtevant J, Ghannoum M, Nozawa Y, Calderone R. Molecular mechanisms of virulence in fungus-host interactions for *Aspergillus fumigatus* and *Candida ablicans*. Med Mycol 1998; 36(Suppl 1): 238-248.

150. Navas-Cortés JA, Hau B, Jiménez-Diaz RM. Yield loss in chickpeas in relation to development of *Fusarium* wilt epidemics. Phytopathology 2000; 90: 1269-1278.

151. Navi SS, Bandyopadhyay R, Reddy RK, Thakur RP, Yang XB. Effects of wetness duration and grain development stages on sorghum grain mold infection. Plant Dis 2005; 89: 872-878.

152. Naiker S, Odhav B. Mycotic keratitis: profile of *Fusarium* species and their mycotoxins. Mycoses 2004; 47: 50-56.

153. Nelson BD, Hansen JM, Windels CE, Helms TC. Reaction of soybean cultivars to isolates of *Fusarium solani* from the Red River Valley. Plant Dis 1997; 81: 664-668.

154. Nelson PE, Toussoun TA, Cook RJ. *Fusarium*: Disease, Biology and Taxonomy. University Park, Pennsylvania State University Press, 1981.

155. Nucci M, Aiaissie E. Cutaneous infection by *Fusarium* species in healthy and immunocompromised hosts: implications for diagnosis and management. Clin Infect Dis 2002; 35: 909-920.

156. Nwabuisi C, Ologe FE. The fungal profile of otomycosis patients in Ilorin, Nigeria. Niger J Med 2001; 10: 124-126.

157. Ono EYS, Sugiura Y, Homechin M, Kamogae M, Vizzoni E, Ueno Y, Hirooka EY. Effect of climatic conditions on natural mycoflora and fumonisins in freshly harvested corn of the state of Paraná, Brazil. Mycopathologia 1999; 147: 139-148.

158. Okoye JOA, Gugnani HC, Okeke CN. Pulmonary infections due to *Aspergillus fumigatus* in turkey poults and gooselings. Mycoses 1989; 32: 336-338.

159. Okoye JOA, Gugnani HC, Okeke CN. Clinical and pathological features of *Aspergillus fumigatus* infection in poultry in Southern Nigeria. Rev Elev Vet Pays Trop 1990; 42: 153-154.

160. O'Neil CE, McCants ML, Salvaggio JE, Lehrer SB. *Fusarium solani*: prevalence of skin reactivity and antigenic allergenic analysis. J Allergy Clin Immunol 1986; 77: 842-849.

161. O'Quinn RP, Hoffman JL, Boyd AS. *Colletotrichum* species as emerging opportunistic fungal pathogens: A report of 3 cases of phaeohyphomycosis and review. J Am Acad Dermatol 2001; 45: 56-61.
162. Otani H, Kodama M, Kohmoto K. Physiological and molecular aspects of *Alternaria* host-specific toxin and plant interactions. Chapter 22. In: Mills D, Kunoh H, Keen NT, Mayama S (Eds.) Molecular Aspects of Pathogenicity and Resistance: Requirement for Signal Transduction. St. Paul, APS Press, 1996: 257-267.
163. Pagano L, Offidani M, Fianchi L, Nosari A, Candoni A, Piccardi M, Corvatta L, D'Antonio D, Girmenia C, Martino P, Del Favero A. Mucormycosis in hematologic patients. Haematologica 2004; 89: 207-214.
164. Palanee T, Dutton MF, Chuturgoon AA. Cytotoxicity of aflatoxin B_1 and its chemically synthesized epoxide derivative on the A549 human epitheliod lung cell line. Mycopathologia 2000; 151: 155-159.
165. Panda A, Sharma N, Das G, Kumar N, Satpathy G. Mycotic keratitis in children: epidemiologic and microbiologic evaluation. Cornea 1997; 16: 295-299.
166. Parry DW, Jenkinson P, McLeod L. *Fusarium* ear blight (scab) in small grain cereals – A review. Plant Pathol 1995; 44: 207-238.
167. Patovirta RL, Reiman M, Husman T, Haverinen U, Tiovola M, Nevalainen A. Mould specific IgG antibiodies connected with sinusitis in teachers of mold damaged school: a two-year follow-up study. Int J Occup Med Environ Health 2003; 16: 221-230.
168. Paulose KO, al Khalifa S, Shenoy P, Sharma RK. Mycotic infection of the ear (otomycosis): a prospective study. J Laryngol Otol 1989; 103: 30-35.
169. Payne GA. Aflatoxins in maize. Crit Rev Plant Sci 1992; 10: 423-440.
170. Peraica M, Radiç B, Luciç A, Pavloviç M. Toxic effects of mycotoxins in humans. Bull World Health Org 1999; 77: 754-766.
171. Peltroche-Llacsahuanga H, Manegold E, Kroll G, Hasse G. Case report. Pathohistological findings in a clinical case of disseminated infection with *Fusarium oxysporum*. Mycoses 2000; 43: 367-372.
172. Pereiro M, Perreiro Ferreiros MM, De Hoog GS, Toribio J. Cutaneous infection caused by *Alternaria* in patients receiving tacrolimus. Med Mycol 2004; 42: 277-282.
173. Perkel VS, Miura Y, Magner JA. Brefeldin-A inhibits oligosaccharide processing of glycoproteins in mouse hypothyoid pituitary tissue at several subcellular sites. Proc Soc Exp Biol Med 1989; 190: 286-293.
174. Perelman B. Infectious diseases and preventative medicine during the hatching and rearing period. Warsaw, Proc World Ostrich Congress. Sept. 26-29, 2002: 69-82.
175. Pestka J, Bondy GS. Immunotoxic effects of mycotoxins. In: Miller JD, Trendholm HL (Eds.) Mycotoxins in Grain. St. Paul, Eagan Press, 1994: 339-358.
176. Pestka JJ, Smolinski AT. Deoxynivalenol: toxicology and potential effects on humans. J Toxicol Environ Health B Crit Rev 2005; 8: 39-69.
177. Pettersson H, Hedman R, Engstrom B, Elwinger K, Fossum O. Nivalenol in Swedish cereals – occurrence, production and toxicity towards chickens. Food Addit Contam 1995; 12: 373-376.
178. Pettersson H, Hedman R. Toxicity and metabolism of nivalenol in farm animals. Cereal Res Commun 1997; 25: 423-427.
179. Pitt JI. Toxigenic fungi: which are important? Med Mycol 2000; 38(Suppl1): 17-22.
180. Polis MA, Kovacs JA. Fungal infections in patients with acquired immunodeficiency syndrome. In: DeVita VT Jr, Hellman S, Rosenberg SA. (Eds) AIDS: Biology, Diagnosis, Treatment and Prevention. 4th ed. Philadelphia, Lippincott-Raven, 1997: 231-244.
181. Pumhirun P, Towiwat P, Mahakit P. Aeroallergen sensitivity of Thai patients with allergic rhinitis. Asian Pac J Allergy Immunol 1997; 15: 183-185.
182. Roháãik T, Hudec K. Influence of agro-environmental factors on *Fusarium* infestation and population structure in wheat kernels. Ann Agric Environ Med 2005; 12: 39-45.
183. Rementeria A, López-Molina N, Ludwig A, Vivanco AB, Bikandi J, Pontón J, Garaizar J. Genes and molecules involved in *Aspergillus fumigatus* virulence. Rev Iberoam Micol 2005; 22: 1-23.
184. Richardson MD, Warnock DW. Fungal infection: diagnosis and management. Oxford, Blackwell Scientific Publications, 1993.
185. Riley RT, Wang E, Schroeder JJ, Smith ER, Plattner RD, Abbas H, Yoo HS, Merrill AH Jr. Evidence for disruption of sphingolipid metabolism as a contributing factor in the toxicity and carcinogenicity of fumonisins. Nat Toxin 1996; 4: 3-15.
186. Rinaldi MG, Phillips P, Schwartz JG, Winn RE, Holt GR, Shagets FW, Elrod J, Nishioka G, Aufdemorte DB. Human *Curvularia* infections: report of five cases and review of the literature. Diag Microbiol Infect Dis 1987; 6: 27-39.
187. Robertshaw H, Higgins E. Cutaneous infection with *Alternaria tenuissima* in an immunocompromised patient. Br J Dermatol 2005; 153: 1047-1049.
188. Rodriguez-Herrera R, Waniska RD, Rooney WL. Antifungal proteins and grain mold resistance in sorghum with nonpigmented testa. J Agric Food Chem 1999; 47: 4802-4806.
189. Rohwedder JJ, Simmons JL, Colfer H, Gatmaitan B. Disseminated *Curvularia lunata* infection in a football player. Arch Inter Med 1979; 139: 940-941.
190. Romano C, Paccagnini E, Difonzo D. Onychomycosis caused by *Alternaria* spp. in Tuscany from 1985 to 1999. Mycoses 2001; 44: 73-76.
191. Romero C, Vanzi L, Massi D, Difonzo EM. Subcutaneous alternariosis. Mycoses 2005; 48: 408-412.
192. Rondeau N, Bourcier T, Chaumeil C, Borderie V, Touzeau O, Scat Y, Thomas F, Baudouin C, Nordmann JP, Laroche L. Fungal keratitis at the Centre Hospitalier National d"Ophthalmologie des Quinze-Vingts: restropective study of 19 cases. J Fr Ophtalmolmologie 2002; 25: 890-896. (in French).
193. Roy KW, Lawrence GW, Hodges HH, McLean KS, Killebrew JF. Sudden death syndrome of soybean: *Fusarium solani* as incitant and relation of *Heterodera glycines* to disease severity. Phytopathology 1989; 79: 191-197.
194. Rupe JC. Frequency and pathogenicity of *Fusarium solani* recovered from soybeans with sudden death syndrome. Plant Dis 1989; 73: 581-584.
195. Saberi-Riseh R, Javan-Nikkhah M, Heidarian R, Hosseini S, Soleimani P. Detection of fungal infectious agent of wheat grains in store-pits of Markazi province, Iran. Commun Agric Biol Sci 2004; 69: 541-554.
196. Safdar A. *Curvularia* – favorable response to oral itraconazole therapy in two patients with locally invasive phaeohyphomycosis. Clin Microbiol Infect 2003; 9: 1219-1223.
197. Salas B, Steffenson BJ, Caspar HH, Tacke B, Prom LK, Schwarz PB. *Fusarium* species pathogenic to barley and their associated mycotoxins. Plant Dis 1999; 83: 667-674.
198. Sampathkumar P, Paya CV. *Fusarium* infection after solid-organ transplantation. Clin Infect Dis 2001; 32: 1237-1240.
199. Sargent K, Sheridan A, O'Kelley L, Carnaghan RBA. Toxicity associated with certain samples of groundnuts. Nature 1961; 192: 1096-1097.
200. Saubolle MA. Fungal pneumonias. Semin Resp Infect 2000; 15: 162-177.
201. Schollenberger M, Müller H-M, Rüfle M, Suchy S, Planck S, Drochner W. Survey of *Fusarium* toxins in foodstuffs of plant origin marketed in Germany. Int J Food Microbiol 2004; 97: 317-326.
202. Scott PM. Mycotoxins: review. J Assoc Off Anal Chem 1987; 70: 276-281.
203. Scott PM, Stoltz DR. Mutagens produced by *Alternaria alternata*. Mutat Res 1980; 78: 33-40.
204. Segal BH, Walsh TJ, Liu JM, Wilson JD, Kwon-Chung KJ. Invasive infection with *Fusarium chlamydosporum* in a patient with aplastic anemia. J Clin Microbiol 1998; 36: 1772-1776.
205. Sewram V, Mshicileli N, Shephard GS, Vismer HF, Rheeder J.P, Lee Y-W, Leslie JF, Marasas WFO. Production of Fumonisin B and C by several *Fusarium* species. J Ag Food Chem 2005; 53: 4861-4866.
206. Severns DE, Clements MJ, Lambert RJ, White DG. Comparison of *Aspergillus* ear rot and aflatoxin contamination in grain of high oil and normal oil corn hybrids. J Food Protect 2003; 66: 637-643.
207. Severo LC, Oliveira de Mattos F, Dreher R, Teixeira PZ, Porto ND, Londero AT. Zygomycosis: A report of eleven cases and a review of the Brazilian literature. Rev Iberoam Micol 2002; 19: 52-56.
208. Shah A, Panjabi C. Allergic bronchopulmonary aspergillosis: a review of a disease with a worldwide distribution. J Asthma 2002; 39: 273-289.
209. Shah A, Maurya V, Panjabi C, Khanna P. Allergic bronchopulmonary aspergillosis without clinical asthma caused by *Aspergillus niger.* Allergy 2004; 59: 236-237.
210. Shono K. Disseminated *Fusarium solani* infection in patients undergoing hematopoietic stem cell tranplantation. Nippon Ishinkin Gakkai Zasshi 2003; 44: 187-191.
211. Simmonds JH. A study of the species of *Colletotrichum* causing ripe fruit rots in Queensland. Queensld J Agric Anim Sci 1965; 22: 437-459.
212. Singh A, Prakash D, Singh AB. Sensitization to different species of *Aspergillus* in bakery workers and general atopic population. Asian Pac J Allergy Allergy Immunol 1998; 16: 5-15.
213. Singh AB, Kumar P. Common environmental allergens causing respiratory allergy in India. Indian J Pediatr 2002; 69: 245-250.
214. Singh SM, Naidu J, Pouranik M. Ungual and cutaneous phaeohyphomycosis caused by *Alternaria alternata* and *Alternaria chamidopsora*. J Med Vet Mycol 1990; 28: 275-278.

215. Smith SN, Ebbels DL, Garber RH, Kappelman AJ Jr. *Fusarium* wilt of cotton. In: Nelson PE, Toussoun TA, Cook RJ (Eds.) *Fusarium*: Diseases, Biology and Taxonomy. University Park, Pennsylvania State University Press, 1981: 29-38.

216. Steffenson BJ. *Fusarium* head blight of barley: Epidemics, impact, and breeding for resistance. Tech Quart MBAA 1998; 35: 177-184.

217. Sugiura Y, Barr JR, Barr DB, Brock JW, Elie CM, Ueno Y, Patterson DG, Potter ME, Reiss E. Physiological characteristics and mycotoxins of human clinical isolates of *Fusarium* species. Mycol Res 1999; 103: 1462-1468.

218. Sundaram BM, Badrinath S, Subramanian S. Studies on mycotic keratitis. Mycoses 1989; 32: 568-572.

219. Suter DA, Jackson CAW, Bryden WL, Andrews S, Tobin N, Jay S. *Alternaria* toxins: a potential problem in animal feeds. Aust Microbiol 1984; 5: 142.

220. Syndenham EW, Thiel PG, Marasas WFO, Shephard GS, Van Schalkwyk DJ, Koch KR. Natural occurrence of some *Fusarium* mycotoxins in corn from low and high esophageal cancer prevalence areas of the Transkai, southern Africa. J Agric Food Chem1991; 38: 1900-1903.

221. Tanure MA, Cohen EJ, Sudesh S, Rapuano CJ, Laibson PR. Spectrum of fungal keratitis at Wills Eye Hospital, Philadelphia, Pennsylvania. Cornea 2000; 19: 307-312.

222. Taj-Aldeen SJ, Hilal AA, Chong-Lopez A. Allergic *Aspergillus flavus* rhinosinusitis: a case report from Qatar. Eur Arch Otorhinolaryngol 2003; 260: 331-335.

223. Tarlo SM, Fradkin A, Tobin RS. Skin testing with extracts of fungal species derived from homes of allergy clinical patients in Toronto, Canada. Clin Allergy 1988; 18: 45-53.

224. Thomas PA. Mycotic keratitis: an underestimated mycosis. J Med Vet Mycol 1994; 32: 235-256.

225. Thomas PA. Current perspectives on ophthalmic mycoses. Clin Microbiol Rev 2003; 16: 730-797.

226. Thomas PA. Fungal infections of the cornea. Eye 2003; 17: 852-862.

227. Tomee JF, van der Werf TS. Pulmonary aspergillosis. Neth J Med 2001; 59: 244-258.

228. Tosti A, Piraccini BM, Lorenzi S. Onychomycosis caused by nondermatophytic molds: clinical features and response to treatment of 59 cases. J Am Acad Dermatol 2000; 42: 217-224.

229. Tournas VH. Spoilage of vegetable crops by bacteria and fungi and related health hazards. Crit Rev Microbiol 2005; 31: 33-44.

230. Tsuda S, Kosaka Y, Murakami M, Matsuo H, Matsusaka N, Taniguchi K, Sasaki Y F. Detection of nivalenol genotoxicity in cultured cells and multiple mouse organs by the alkaline single-cell gel electrophoresis assay. Mutat Res 1998; 415: 191-200.

231. Ueno Y, Iijima K, Wang S-D, Sugiura Y, Sekijima M, Tanaka T, Chen C, Yu S-Z. Fumonisins as a possible contributory risk factor for primary liver cancer: A 3-year study of corn harvested in Haimen, China by HPLC and ELISA. Fd Chem Toxicol 1997; 35: 1143-1150.

232. Updahyay MP, Karmacharya PC, Koirala S, Tuladhar NR, Bryan LE, Smolin G, Whitcher JP. Epidemologic characteristics, predisposing factors, and etiologic diagnosis of corneal ulceration in Nepal. Am J Ophthalmol 1991; 111: 92-99.

233. Van der Westhuizen L, Shephard GS, Snyman SD, Abel S, Swanevelder S, Gelderblom WC. Inhibition of sphingolipid biosynthesis in rat primary hepatocyte cultures by fumonisin B1 and other structurally related compounds. Food Chem Toxicol 1998; 36: 497-503.

234. Van Vleet TR, Klein PJ, Coulombe RA Jr. Metabolism and cytotoxicity of aflatoxin B_1 in cytochrome P-450-expressing human lung cells. J Toxicol Environ Health A 2002; 65: 853-867.

235. Vennewald I, Schönlebe J, Klemm E. Mycological and histological investigations in humans with middle ear infections. Mycoses 2003; 46: 12-18.

236. Verma J, Singh BP, Sridhara S, Gaur SN, Arora N. Purification and characterization of a cross-reactive 45-kD major allergen of *Fusarium solani*. Int Arch Allergy Immunol 2003; 130: 193-199.

237. Versonder R, Haliburton J, Stubblefield R, Gilmore W, Peterson S. *Aspergillus flavus* and aflatoxins B_1, B_2, and M_1 in corn associated with equine death. Arch Environ Contam Toxicol 1991; 20: 151-153.

238. Vieira MR, Milheiro A, Pacheco FA. Phaeohyphomycosis due to *Cladosporium cladosporioides*. Med Mycol 2001; 39: 135-137.

239. Visconti A. Fumonisins in maize genotypes grown in various geographic areas. In: Jackson LS, De Vries JW, Bullerman LB (Eds.) Fumonisins in Food. New York, Plenum Press, 1996: 193-204.

240. Visconti A, Sibilia A. *Alternaria* toxins. In: Miller JD, Trenholm HL (Eds.) Mycotoxins in Grains, Compounds Other Than Aflatoxins. St. Paul, Eagan Press, 1994: 315-336.

241. Vismer HF, Marasas WF, Rheeder JP, Joubert JJ. *Fusarium dimerum* as a cause of human eye infections. Med Mycol 2002; 40: 399-406.

242. Walsh TJ. Emerging fungal pathogens: evolving challenges to immunocompromised patients. In: Scheld WM, Armstrong D, Hughes JM. (Eds.) Emerging Infections 1. Washington, American Society for Microbiology Press, 1998: 201-214.

243. Walsh TJ, Groll A, Hiemenz J, Fleming R, Roilides E, Anaissie E. Infections due to emerging and uncommon medically important fungal pathogens. Clin Microbiol Infect 2004; 10(Suppl. 1): 48-66.

244. Wang B, Brubaker CL, Burdon JJ. *Fusarium* species and *Fusarium* wilt pathogens associated with native *Gossypium* populations in Australia. Mycol Res 2004; 108: 35-44.

245. Wang B, Jeffers SN. *Fusarium* root and crown rot: a disease of container-grown hostas. Plant Dis 2000; 84: 980-988.

246. Waniska RD, Venkatesha RT, Chandrashekar A, Krishnaveni S, Bejosano FP, Jeoung J, Jayaraj J, Muthukrishnan S, Liang GH. Antifungal proteins and other mechanisms in the control of sorghum stalk rot and grain mold. J Agric Food Chem 2001; 49: 4732-4742.

247. Waterhouse J, Shanmugaratnam K, Muir C, Powell J. Cancer incidence in five continents. Volume 4, No. 82 Lyon, IARC Scientific Publications, International Agency for Research on Cancer, 1982.

248. Webley DJ, Jackson KL, Mullins JD, Hocking AD, Pitt JL. *Alternaria* toxins in weather–damaged wheat and sorghum in the 1995-1996 Australian harvest. Aust J Agric Res 1997; 48: 1249-1255.

249. Wheat LJ, Goldman M, Sarosi G. State-of-the-art review of pulmonary infections. Sem Res Infect 2002; 17: 158-181.

250. Wiederhold NP, Lewis RE, Kontoyiannis DP. Invasive aspergillosis in patients with hematologic malignancies. Pharmacotherapy 2003; 23: 1592-1610.

251. Wilhemus KR, Jones DB. *Curvularia* keratitis. Tr Am Ophthalmol Soc 2001; 99: 111-132.

252. Windstrom NW. The aflatoxin problem with corn grain. Adv Agron 1996; 56: 219-280.

253. Xie L, Dong X, Shi W. Treatment of fungal keratitis by penetrating keratoplasty. Br J Ophthalmol 2001; 85: 1070-1074.

254. Yau YCW, de Nanassy J, Summerbell RC, Matlow AG, Richardson SE. Fungal sternal wound infection due to *Curvularia lunata* in a neonate with congenital heart disease. Case report and review. Clin Infect Dis J 1994; 19: 735-740.

255. Yamanoi T, Shibano K, Soeda T, Hoshi A, Matsuura AG, Yutaka M, Sugiura, Y, Endo K, Yamamoto T. Intracranial invasive aspergillosis originating in the sphenoid sinus: a successful treatment with high-dose itraconazole in three cases. Tohoku J Exp Med 2004; 203: 133-139.

256. Yang GH, Jarvis BB, Chung YJ, Pestka JJ. Apoptosis induction by the satratoxins and other trichothecenes mycotoxins: relationship to ERK, p38 MAPK and SAPK/JNK activation. Toxicol Appl Pharmacol 2000; 164: 149-160.

257. Yao Y, Hausding M, Erkel G, Anke T, Förstermann U, Kleinert H. Sporogen, S14-95, and S-curvularin, three inhibitors of human inducible nitric-oxide synthase expression isolated from fungi. Mol Pharmacol 2003; 63: 383-391.

258. Yiannikouris A, Jouany JP. Mycotoxins in feeds and their fate in animals: a review. Anim Res 2002; 51: 81-99.

259. Yoshizawa T. Red-mold diseases and natural occurrence in Japan. In: Ueno Y (Ed.) Trichothecenes – Chemical, Biological and Toxicological Aspects. Amsterdam, Elsevier, 1983: 195-209.

260. Zahra LV, Mallia D, Hardie JG, Bezzina A, Fenech T. Case report: Keratomycosis due to *Alternaria alternata* in a diabetic patient. Mycoses 2002; 45: 512-514.

261. Zhang N, O'Donnell K, Sutton DA, Nalim FA, Summerbell RC, Padhye AA, Geiser DM. Members of the *Fusarium solani* species complex that cause infections in both humans and plants are common in the environment. J Clin Microbiol 2006; 44: 2186-2190.