Fungal Spores: Hazardous to Health?

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Fungi have long been known to affect human well being in various ways, including disease of essential crop plants, decay of stored foods with possible concomitant production of mycotoxins, superficial and systemic infection of human tissues, and disease associated with immune stimulation such as hypersensitivity pneumonitis and toxic pneumonitis. The spores of a large number of important fungi are less than 5 μm aerodynamic diameter, and therefore are able to enter the lungs. They also may contain significant amounts of mycotoxins. Diseases associated with inhalation of fungal spores include toxic pneumonitis, hypersensitivity pneumonitis, tremors, chronic fatigue syndrome, kidney failure, and cancer. *Key words*: mold, fungi, mycotoxin, lung disease, toxic pneumonitis. — *Environ Health Perspect* 107(suppl 3):469–472 (1999).
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Background

Fungi are heterotrophic, filamentous organisms that by virtue of their dependence on external sources of organic carbon and their rigid cell walls are confined to a saprobic and/or parasitic lifestyle in which they absorb soluble nutrients through the cell membrane. The fungi, together with the bacteria, are responsible for decay of organic matter and the fungi have been estimated to comprise approximately 25 % of the biomass of the earth (*1*). As such, they are among the principal microorganisms involved in biodeterioration and are found universally in human habitations and occupational settings. The possible role of airborne microorganisms in indoor air health problems as a result of energy-saving measures was accentuated by Tobin et al. (*2*) and a number of studies have noted a strong relationship between mold growth in homes and respiratory symptoms (*3–5*). When one considers that urban residents typically spend more than 90% of their time indoors (*6*), it is readily recognized that very large numbers of people, both adults and children, are potentially exposed to indoor air contaminants. Although spore concentrations are usually much lower in homes than in agricultural workplaces, concentrations as high as 450,000 colony-forming units/m^3 have been reported (*7*). In some of these homes, the toxigenic *Stachybotrys chartarum* (= *Stachybotrys atra*) was prominent on the walls and in the air. This article focuses on health effects due to mycotoxins, but fungi in general also cause other diseases such as infections, allergy, and inflammation.

Mycotoxins and Mycotoxigenic Fungi

Excluding mushroom toxins, approximately 350 to 400 fungal metabolites are considered to be toxic. Most of these are relatively small molecules of greater than 200 and the majority are less than 500 mass units (*8*). Perhaps the most important mycotoxins in agriculture are the aflatoxins, the 12,13-epoxytrichothecenes, the fumonisins, and ochratoxin. Species belonging to the genera *Aspergillus, Penicillium,* and *Fusarium* are common contaminants of agricultural commodities, and some of the mycotoxins produced by these species are produced by fungi common in house dust (*2*). In addition, some toxigenic fungi produce many different mycotoxins. For example, the *Penicillium verrucosum* complex (*P. verrucosum, P. aurantiogriseum, P. viridicatum, P. crustosum,* and *P. solitum*) produce nearly 20 different mycotoxins (*9*) and *S. chartarum* produces several trichothecenes including the highly potent macrocyclic trichothecenes as well as a variety of other mycotoxins (*10*). Other toxigenic fungi include species of *Alternaria, Paecilomyces, Rhizopus, Trichoderma,* and *Trichothecium.* All of these fungi occur commonly in soil, agricultural products, grain dust, and house dust (*2*).

Health Effects Linked with Inhalation of Mycotoxins

Although extensive literature has been developed since the discovery of the aflatoxins, few studies have been conducted to document the occurrence of these substances in airborne grain or other organic dust or to estimate the inhalation hazard to workers and others exposed to contaminated airborne dust. Several studies have provided evidence for the association of cancer in humans with inhalation of aflatoxin-contaminated dust, e.g., lung cancer (*11–13*) or colon cancer (*14*). Olsen et al. (*13*) noted elevated risks for liver cancer and cancers of biliary tract among animal feed workers that increased by 2- to 3-fold significance after a 10-year latency. Their daily pulmonary exposure was estimated to be approximately 170 ng. Autrup et al. (*15*) used measurements of aflatoxin bound to serum albumin as an index of exposure and showed that 7 of 45 workers exposed to feed contaminated with low levels of aflatoxin B_1 (AFB_1; 0–26 μg/kg) had detectable levels of AFB, bound to serum albumin, confirming systemic exposure. Zarba et al. (*16*) demonstrated that aerosol inhalation is an effective route of exposure to AFB_1 in rats. In their experiments, approximately 2% of the administered dose became bound to liver DNA and the amounts of DNA adducts were statistically different among the treated groups. These workers (*17*) also demonstrated that nose-only aerosol in exposure of rats at an estimated dose of 16.8 μg/kg body weight suppressed alveolar macrophage (AM) phagocytosis, with the effect persisting for approximately 2 weeks. These findings indicate that inhalation exposure to AFB_1 is an occupational hazard where exposure to AFB_1-laden dust is common.

Inhalation exposure to spores of *S. chartarum* has also been associated with episodes of human illness. Andrassy et al. (*18*) reported an outbreak of illness in which workers exposed to hay heavily contaminated with *S. chartarum* unanimously complained of dyspnea, airway obstruction, sore throat, bloody nose or nasal secretions, conjunctivitis, and inflammation of the

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skin on the face and body. Croft et al. (*19*) reported long-term illness, apparently caused by heavy infestation of a water-damaged home in Chicago, Illinois. Between 1993 and 1998, there were 34 cases, including 10 deaths, of idiopathic pulmonary hemosiderosis among infants in Cleveland, Ohio. Incidence of this disease is generally quite low (*20,21*). The vast majority of cases occurred within a very small geographic area of the city. Case homes tended to have a higher prevalence of water damage (*22*) and higher quantities of toxigenic *S. chartarum* (*23*). Strains of *S. chartarum* isolated from both case and control homes were shown to be toxigenic, but there was no correlation between toxigenicity of the isolate and source, i.e., case versus control. The disease seemed to correlate with frequency of occurrence and quantity of the organism rather than with strain (*24*). *Memnoniella echinata*, a close relative of *S. chartarum* with similar biochemical and physiologic characteristics and habitat preferences, was also found in samples from a case home. *M. echinata* produces some of the same toxins as *S. chartarum* (*24,25*) but has smaller spores, although the conidia of both species are small enough to reach the alveoli (*25*). Aqueous rinses of the spores of both species were nearly as toxic as methanolic extracts of the spores themselves (*25*), indicating that these highly potent toxins would be readily released into the microenvironment of the developing lung cells *in vivo*.

Further support for the proposed mycotoxin etiology of infant pulmonary hemosiderosis comes from animal studies in which mice were treated intranasally with both nontoxic and toxic spores of *S. chartarum* (*26*). Severe inflammatory changes, including hemorrhage, were observed in mice receiving toxic spores of this species. Two recent studies report occupational illness associated with chronic, low-level exposure to *S. chartarum* in water-damaged office buildings (*27,28*). Dill et al. (*29*) noted massive development of *S. chartarum* on decomposable flower pots made of recycled paper, which led to the development of very painful inflammed efflorescences at the fingertips followed by scaling of the skin. The symptoms disappeared when gloves were worn to handle the pots and were ascribed to trichothecene mycotoxins. Although respiratory symptoms were not noted in the report, viable spore counts of *S. chartarum* up to 7,500 spores/m^3 were determined when the pots were handled (30–100 spores/m^3 when the pots were not handled).

Two other recent reports of human disease thought to be due to inhalation of mycotoxins are noteworthy. Di Paolo et al. (*30*) reported acute renal failure in a female agricultural worker exposed to grain dust in an enclosed granary, believed to be due to inhalation of ochratoxin in the spores of *Aspergillus ochraceous*. Ochratoxin was not demonstrated in airborne dust in the granary, but the authors were able to isolate *A. ochraceous* from a sample of wheat from the granary. Ochratoxin A was observed in extracts of ground moldy grains, and Di Paolo and colleagues were able to demonstrate acute kidney failure in experimental animals (rabbits and guinea pigs) exposed for 8 hr to aerosols generated by their natural movement on moldy wheat in their cages.

Gordon et al. (*31*) reported tremorgenic encephalopathy in a young man exposed to high concentrations of grain dust contaminated with several species of fungi known to be capable of producing tremorgenic mycotoxins. Because of the circumstances of exposure, the similarity of his syndrome to that of an animal model, and the lack of an alternative explanation, the authors proposed that his illness may have resulted from inhalation of tremorgenic mycotoxin(s).

Mycotoxins in Spores

Species of fungi in which mycotoxins have been reported in the spores include *Alternaria alternata* (*32*), *Aspergillus fumigatus* (*33–35*), *Aspergillus flavus* and *Aspergillus parasiticus* (*36*), *Fusarium graminearum* (*1*), *Fusarium sporotrichioides* (*1*), and *S. chartarum* (*37*). Several different mycotoxins were demonstrated in these investigations including deoxynivalenol (*1*), fumitremorgen and verruculogen (*35*), fumigaclavine C (*34*), T-2 toxin (*1*), tryptacidin (*33*), alternariol and alternariol monomethylether (*32*), and the macrocyclic trichothecenes satratoxins G and H (*37*). Gliotoxin has been demonstrated in tissues infected by *A. fumigatus* (*38*) and *Candida albicans* (*39*) but was not detected in spores of *A. fumigatus* (*40*). It is likely that mycotoxins occur in spores of toxigenic species much more commonly than is currently appreciated, as they have been found in spores in a high proportion of species in which attempts were made to find them. In a study in Scotland, extracts from spores of 47% of a group of 83 isolates collected from damp public sector housing in Scotland were cytotoxic to the human embryonic hybrid fibroblast lung cell line MRC-5 (*41*).

These findings seem to support earlier findings of health hazards in epidemiologic studies of the inhabitants of damp, moldy houses (*42*). Spores of *P. aurantiogriseum* containing the benzodiazepine metabolite auranthine cause nephrotoxicity and pathology typical of Balkan endemic nephropathy when mixed with feed and fed to rats (*43*). These findings confirm the presence of auranthine in the spores and suggest that workers and others who handle infected grain may be at risk of exposure by inhalation. The vast majority of mycotoxins are nonvolatile and therefore mycotoxin exposure by inhalation is most likely to occur via inhalation of spores.

Effects of Mycotoxins on Alveolar Macrophages and Immune Function

T-2 toxin, patulin, and penicillic acid were shown to be acutely toxic to rat AM *in vitro*, causing membrane damage, inhibition of protein and RNA synthesis, inhibition of phagocytosis, and inhibition of the ability of AM to respond to lymphokines (*44–47*). Ayral et al. (*48*) showed that the trichothecenes diacetoxyscirpenol and deoxynivalenol reduce phagocytosis, suppress microbicidal activity, and inhibit superoxide anion production and phagosome–lysosome fusion of peritoneal macrophages at concentrations that did not affect cell viability. Similarly, Vidal and Mavet (*49*) demonstrated inhibition of phagocytosis of *Pseudomonas aeruginosa* by murine peritoneal macrophages in the presence of 0.001 μM T-2 toxin.

The trichothecene mycotoxins are immunotoxic in rats and mice, causing acute inhibition of antibody and delay of skin graft rejection (*50,51*). Gliotoxin has antiphagocytic and immunomodulating activity, it is produced by *A. fumigatus* (*52*), and it has been demonstrated in tissues infected by *A. fumigatus* (*38*). Gliotoxin also contributes to the pathogenesis of vaginal candidiasis (*39*). Jakab et al. (*17*) confirmed earlier reports that dietary exposure to AFB_1 impairs innate and acquired host defenses. Subsequent work by these authors also showed that AM phagocytosis was suppressed for approximately 2 weeks following nose-only inhalation exposure to an estimated dose of 16.8 μg/kg. Exposure using intracheal instillation (IT) of AFB_1 also suppressed AM phagocytosis in a dose-dependent manner, but approximately 10-fold higher doses were required for IT than for inhalation. Animals exposed by IT administration also had impaired release of tumor

necrosis factor-α, primary splenic antibody response, and peritoneal macrophage phagocytosis. These studies show that experimental respiratory tract exposure can suppress pulmonary and systemic host defenses and that inhalation exposure to AFB_1 could lead to increased susceptibility to infection. Richard et al. (*53*) used killed spores of *A. fumigatus* as carrier vehicles for AFB_1 in studies of the effect of long-term exposure to aflatoxin. Lung lesions were not observed in unexposed animals, but lesions of varying severity were observed in the lungs of rats exposed to aflatoxin. The authors reported that the general response of the exposed animals appeared to be that of a compromised host.

Although the effects of mycotoxins as a result of dietary exposure is beyond the scope of the present discussion, a number of mycotoxins, especially aflatoxin, the trichothecenes, ochrataoxin A, patulin, citrinin, and zearalenone, experimentally alter immunity, causing inhibition of natural killer cell activity, impaired resistance to pathogenic microorganisms, suppression of antibody response, lymphoid depletion of the thymus associated with delayed hypersensitivity, and functional alteration of bone marrow cells. This subject has been extensively reviewed by Richard et al. (*54*), Thurston et al. (*55*), and Pestka and Bondy (*56,57*).

In studies of the acute inhalation toxicity of T-2 toxin in mice, Creasia et al. (*58*) demonstrated that T-2 toxin, when given by inhalation, was at least 10 times more toxic than systemic administration and at least 20 times more toxic than dermal administration.

Because of technical limitations, it is difficult to accurately assess the role of mycotoxins in human health effects associated with damp environments. For example, demonstration of mycotoxin production in the laboratory does not prove their presence in the environment; we are generally unable to measure mycotoxins in the field at the site of exposure and, with the exception of aflatoxin, there is a general lack of biomarkers of either exposure or effect. In addition, it appears that isolates of many toxigenic species vary in their ability to produce mycotoxins, but it is uncertain to what extent this is due to actual genotypic differences between the isolates or to the effect of the stress of isolation in artificial culture. It is prudent to take the possibility of mycotoxin exposure into consideration whenever known toxigenic species are demonstrated in these environments.

References and Notes

1. Miller JD. Fungi as contaminants in indoor air. Atmos Environ 26:2163–2172 (1992).
2. Tobin RS, Baranowski E, Gilman AP, Kuiper-Goodman T, Miller JD Giddings M. Significance of fungi in indoor air: report of a working group. Can J Public Health 78:SI–S32 (1987).
3. Brunekreef B, Dockery DW, Speizer FE, Ware JW, Spengler JD, Ferris BG. Home dampness and respiratory morbidity in children. Am Rev Respir Dis 140:1363–1367 (1989).
4. Dales RE, Zwanenburg H, Burnett R, Franklin CA. Respiratory health effects of home dampness and molds among children. Am J Epidemiol 134:196–203 (1991).
5. Dales RE, Miller JD, McMullan E. Indoor air quality and health: validity and determinants of reported home dampness and molds. Int J Epidemiology 26:120–125 (1997).
6. Spengler JD, Sexton K. Indoor air pollution: a public health perspective. Science 221:9–17 (1983).
7. Hunter CA, Grant C, Flannigan B, Bravery AF. Mould in buildings: the air spora of domestic dwellings. Int Biodeterior 24:81–101 (1988).
8. Samson RA. Mycotoxins: a mycologist's perspective. J Med Vet Mycol 30: 9–18 (1992).
9. Frisvad JC, Filtenborg O. Terverticillate penicillia: chemotaxonomy and mycotoxins production. Mycologia 81:837–861 (1989).
10. Jarvis BB, Salemme J, Morais A. *Stachybotrys* toxins 1. Natural Toxins 3:10–16 (1995).
11. Hayes RB, Van Nieuwenhuize JP, Raatgever JW, Ten Kate FJW. Aflatoxin exposures in the industrial setting: an epidemiological study of mortality. Food Chem Toxicol 22:39–43 (1984).
12. Dvorackova I. Aflatoxin inhalation and alveolar cell carcinoma. Br Med J III:691 (1976).
13. Olsen JH, Dragsted L, Autrup H. Cancer risk and occupational exposure to aflatoxins in Denmark. Br J Cancer 58:392–396 (1988).
14. Deger GE. Aflatoxin—human colon carcinogenesis. Ann Intern Med 85:204–205 (1976).
15. Autrup JL, Schmidt J, Seremet T, Autrup H. Determination of exposure to aflatoxins among Danish workers in animal-feed production through the analysis of aflatoxin B_1 adducts of serum albumin. Scand J Work Environ Health 17:436–440 (1991).
16. Zarba A, Hmieleski R, Hemenway DR, Jakab GJ, Groopman JD. Aflatoxin B_1-DNA adduct formation in rat liver following exposure by aerosol inhalation. Carcinogenesis 13:1031–1033 (1992).
17. Jakab GJ, Hmieleski RR, Zarba A, Hemenway DR, Groopman JD. Respiratory aflatoxicosis: suppression of pulmonary and systemic host defenses in rats and mice. Toxicol Appl Pharmacol 125:198–205 (1994).
18. Andrassy K, Horvath I, Lakos T, Toke Z. Mass incidence of mycotoxicoses in Hajdu-Bihar county. Mykosen 23:130–133 (1979).
19. Croft, WA, Jarvis BB, Yatawara CS. Airborne outbreak of trichothecene toxicosis. Atmos Environ 20:549–552 (1986).
20. Kjellman B, Elinder G, Garwicz S, Svan H. Idiopathic pulmonary haemonsiderosis in Swedish children. Acta Paediatr Scand 73:584–588 (1984).
21. Ohga S, S, Takahashi K, Miyazaki S, Kato H, Ueda K. Idiopathic pulmonary haemosiderosis in Japan: 39 possbile cases from a survey questionaire. Eur J Pediatr 154:994–995 (1995).
22. Montana E, Etzel RA, Allan TM, Hogan TE, Dearborn DG. Environmental risk factors associated with pediatric idiopatahic hemosiderosis in a Cleveland community. Pediatrics 99:117 (1997).
23. Etzel RA, Montana E, Sorenson WG, Kullman GJ, Allan TM, Olson DR, Jarvis BB, Miller JD, Dearborn DG. Acute pulmonary hemorrhage in infants associated with exposure to *Stachybotrys atra*. Arch Pediatr Adolesc Med 152:757–762 (1998).
24. Jarvis BB, Sorenson WG, Hintikka E-L, Nikulin M, Zhou Y, Jiang J, Wang S, Hinkley S, Etzel RA, Dearborn D. Studies of toxin production by isolates of *Stachybotrys atra* and *Memnoniella echinata* isolated from homes associated with pulmonary hemosiderosis in infants. Appl Environ Microbiol 64:3620–3625 (1998).
25. Sorenson WG, Jarvis BB, Zhou Y, Jiang J, Wang S, Hintikka E-L, Nikulin M. Toxine im Zusammenhang mit *Stachybotrys* und *Memnoniella* in Häusern mit Wasserschaden. In: 18. Mykotoxin Workshop (Gareis M, Scheuer R, eds). Kulmbach, Germany:Institut für Mikrobiologie und Toxikologie der Bundesanstalt für Fleischforschung, 1996; 207–214.
26. Nikulin M, Reijula KE, Jarvis BB, Veijalainen P, Hintikka E-L. Effects of internasal exposure to spores of *Stachybotrys atra* in mice. Fundam Appl Toxicol 35:182–188 (1997).
27. Johanning E, Biagini R, Hull D, Morey P, Jarvis BB, Landsbergis P. Health and immunology study following exposure to toxigenic fungi (*Stachybotrys chartarum*) in a water-damaged office environment. Int Arch Occup Environ Health 16:207–218 (1996).
28. Hodgson MJ, Morey P, Leung W-Y, Morrow L, Miller D, Jarvis BB, Robbins H, Halsey JF, Storey E. Building associated pulmonary disease from exposure to *Stachybotrys chartarum* and *Aspergillus versicolor*. J Occup Environ Med 40:241–249 (1988).
29. Dill D, Trautmann C, Szwzyk R. Massenentwicklung von *Stachybotrys chartarum* auf kompostierbaren Pflanztöpfen aus Altpapier. Mycoses 40:110–114 (1997).
30. Di Paolo N, Guarnieri A, Loi F, Sacchi G, Mangiarotti AM, Di Paolo M. Acute renal failure from inhalation of mycotoxins. Nephron 64:621–625 (1993).
31. Gordon KE, Maotti RE, Waddell WR. Tremorgenic encephalopathy: A role of mycotoxins in the production of CNS disease in humans? Can J Neurol Sci 20:237–239 (1993).
32. Häggblom P. De novo synthesis of alternariol in conidia of *Alternaria alternata*. J Gen Microbiol 133:3527–3529 (1987).
33. Parker GF, Jenner PC. Distribution of trypacidin in cultures of *Aspergillus fumigatus*. Appl Microbiol 16:1251–1252 (1968).
34. Palmgren MS, Lee LS. Separation of mycotoxin-containing sources in grain dust and determination of their mycotoxins potential. Environ Health Perspect 66:105–108 (1986).
35. Land CJ, Rask-Andersen A, Lundström H, Werner S, Bardage S. Tremorgenic mycotoxins

and gliotoxin in conidia of *Aspergillus fumigatus*. In: International Workshop. Health Implications of Fungi in Indoor Environments (Samson RA, Flannigan B, eds). Amsterdam: Elsevier, 1994;317–324.
36. Wicklow DT, Shotwell OL. Intrafungal distribution of aflatoxin among conidia and selerotia of *Aspergillus flavus* and *Aspergillus parasiticus*. Can J Microbiol 29:1–5 (1983).
37. Sorenson WG, Frazer DG, Jarvis BB, Simpson J, Robinson VA. Trichothecene mycotoxins in aerosolized conidia of *Stachybotrys atra*. Appl Environ Microbiol 53:1370–1375 (1987).
38. Bauer J, Gareis M, Bott A, Gedek B. Isolation of a mycotoxin (gliotoxin) from a bovine udder infected with *Aspergillus fumigatus*. J Med Vet Mycol 27:45–50 (1989).
39. Shah DT, Larsen B. Clinical isolates of yeast produce a gliotoxin-like substance. Mycopathologia 116:203–208 (1993).
40. Land CJ, Sostaric B, Fuchs R, Lundstrom H, Hult K. Intratracheal exposure of rats to *Aspergillus fumigatus* spores isolated from sawmills in Sweden. Appl Environ Microbiol 55:2856–2860 (1989).
41. Smith JE, Anderson JG, Lewis CW, Murad YM. Cytotoxic fungal spores in the indoor atmosphere of the damp domestic environment. FEMS Microbiol Lett 79:337–343 (1992).
42. Strachan DP, Sanders CH. Damp housing and childhood asthma: respiratory effects of indoor air temperature and relative humidity. J Epidemiol Community Health 43:7–14 (1989).
43. Macgeorge KM, Mantle PG. Nephrotoxicity of *Penicillium aurantiogriseum* and *P. commune* from an endemic nephropathy area of Yugoslavia. Mycopathologia 1122:139–145 (1990).
44. Gerberick GF, Sorenson WG. Toxicity of T-2 toxin, a *Fusarium* mycotoxin, to alveolar macrophages *in vitro*. Environ Res 32:269–285 (1983).
45. Gerberick GF, Sorenson WG, Lewis DM. The effects of T-2 toxin on alveolar macrophage function *in vitro*. Environ Res 33:246–260 (1984).
46. Sorenson WG, Simpson J, Castranova V. Toxicity of the mycotoxin patulin for rat alveolar macrophages. Environ Res 38:407–416 (1985).
47. Sorenson WG, Gerberick GF, Lewis DM, Castronova V. Toxicity of mycotoxins for the rat pulmonary macrophage *in vitro*. Environ Health Perspect 66:45–53 (1986).
48. Ayral AM, Dubech N, Le Bars J, Escoula L. *In vitro* effect of diacetoxyscirpenol and deoxynivalenol on microbicadal activity of murine peritoneal macrophages. Mycopathologia 120:121–127 (1992).
49. Vidal D, Mavet S. *In vitro* and *in vivo* toxicity of T-2 toxin, a *Fusarium* mycotoxin, to mouse peritoneal macrophages. Infect Immun 57:2260–2264 (1989).
50. LaFarge-Frayssinet C, Lespinats G, Lafont P, Loisillier F, Mousset S, Rosenstein Y, Frayssinet C. Immunosuppressive effects of *Fusarium* extracts and trichothecenes: blastogenic response of murine splenic and thymic cells to mitogens. Proc Soc Exp Biol Med 160:302–311 (1979).
51. Rosenstein Y, Lafarge-Frayssinet G, Lespinats G, Loisillier F, Lafont P, Frayssinet C. Immunosuppressive activity of *Fusarium* toxins: effects on antibody synthesis and skin grafts of crude extracts, T-2 toxin and diacetoxyscirpenol. Immunology 36: 111–117 (1979).
52. Eichner RD, Al Salami M, Wood PR, Mullbacher A. The effect of gliotoxin upon macrophage function. Int J Immunopharmacol 8:789–797 (1986).
53. Richard JL, Cheville NF, Songer JR, Thurston JR. Exposure of rats to aerosols of aflatoxin-containing particles. In: Proceedings 8th International Congress of Human and Animal Mycology (Baxter M, ed). Palmerstown, New Zealand:Massey University Press, 1983; 464–468.
54. Richard JL, Thurston JR, Pier AC. Effects of mycotoxins on immunity. In: Toxins: Animal, Plant and Microbial (Rosenberg P, ed). New York:Pergamon Press, 1978:801–817.
55. Thurston JR, Richard JL, Peden WM. Immunomodulation in mycotoxicoses other than alfatoxicosis. In: Diagnosis of Mycotoxicoses, (Richard JL, Thurston JR, eds). Martinus Nijhoff:Boston, 1986;149–161.
56. Pestka JJ, Bondy GS. Alteration of immune function following dietary mycotoxin exposure. Can J Physiol Pharmacol 68:1009–1016 (1990).
57. Pestka JJ, Bondy GS. Immunotoxic effect of mycotoxins. In: Mycotoxins in Grain. Compounds other Than Aflatoxin (Miller JD, Trenholm HL, eds). St. Paul, MN:Eagan Press, 1994;339–358.
58. Creasia DA, Thurman JD, Jones LJ, Nealley ML, York CG, Wannemaker RW, Bunner DL. Acute inhalation toxicity of T-2 mycotoxin in mice. Fundam Appl Toxicol 8:230–235 (1987).