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Review Article

Public Health Significance of Aflatoxin in Food Industry – A Review

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Abstract: Aflatoxins are a group of related fungal secondary metabolites primarily produced by the fungi, *Aspergillus flavus* and *Aspergillus parasiticus*. *Aspergillus flavus* and *Aspergillus parasiticus* colonize a wide variety of food commodities including maize, oilseeds, spices, groundnuts, tree nuts, milk, peanut and dried fruits. However, production of aflatoxin by these fungi depends on drought stress, rainfall, suitability of crop genotype for its climate, insect damage, agricultural practices and postharvest conditions (storage, transportation and food processing). Four major aflatoxins produced naturally are known as aflatoxin B_1, B_2, G_1 and G_2. Aflatoxin is both a food safety and public health issue because of its toxicity. When it is consumed, it can exert toxicity by altering intestinal integrity or modulate the expression of cytokins which can result to stunted growth in children and/or immune suppression. In the liver, aflatoxin may be transformed by certain p450 enzyme to its DNA reactive form Aflatoxin-8-9-epoxide which binds to liver proteins and lead to their failure, resulting in acute aflatoxicosis or it may bind to DNA, contributing to aflatoxin induced hepatocellular carcinoma (liver cancer). In high doses, aflatoxin can lead to acute liver cirrhosis and death in both human and animals. Aflatoxin exposure is linked to increased risk of liver cancer, immunesuppression, increased susceptibility to diseases such as HIV and malaria and possible compromised vaccine efficacy. Aflatoxin accumulation can be managed by primary interventions involving improved irrigation, use of fungicides, pesticides and insecticides, use of cereal strains resistant to fungal colonization, biocontrol by introduction of competitive non-aflatoxigenic strains of *A. flavus* and genetically modified crops that inhibit fungal colonization and improved storage conditions. Intervention strategies also encompass chemoprevention, using compounds that interfere with the absorption or metabolism of aflatoxins once ingested.

Keywords: Aflatoxin, Public Health, Food, Aflatoxicosis, Hepatocellular Carcinoma

1. Introduction

Aflatoxins are a group of related fungal secondary metabolites primarily produced by the fungi, *Aspergillus flavus* and *Aspergillus parasiticus* [1]. *A. flavus* is a common contaminant in agriculture. *A. bombycis*, *A. ochraceus*, *A. nomius*, and *A. pseudotamari* are also aflatoxin-producing species, but they are encountered less frequently [2]. There are great qualitative and quantitative differences in the aflatoxin-producing abilities displayed by different isolates of each aflatoxigenic species [3].

Four major aflatoxins produced naturally are known as aflatoxin B_1, B_2, G_1, and G_2. “B” and “G” refer to the blue and green fluorescent colors produced under UV light on thin layer chromatography plates, while the subscript numbers 1 and 2 indicate major and minor compounds, respectively [1]. According to [1], Aflatoxin B_1 is the most toxic of the aflatoxins, and has been recognized as the most potent naturally occurring chemical liver carcinogen known. Specific P450 enzymes in the liver metabolize aflatoxin into a reactive oxygen species, aflatoxin-8,9-epoxide, which may then binds to proteins and cause acute toxicity (aflatoxicosis) or to DNA and induce liver cancer [1, 4, 5].

Aflatoxins are naturally occurring contaminants of food. According to [6], aflatoxins have been recognized as significant contaminants by the agricultural production community since the 1960s and control strategies have mostly eliminated harmful exposures in developed countries. The application of these strategies in developing countries is difficult, given differences in technology, agriculture, and trade practices, as well as other issues contributing to occurrence of aflatoxins and incidence of exposure. *Aspergillus flavus and A. parasiticus* colonize a wide variety of food commodities including maize, oilseeds, spices, groundnuts, tree nuts, milk, dried fruit and fig [1, 3, 7]. The production of aflatoxin by these fungi depends on certain factors including, unsuitable geography, drought stress and rainfall, high temperature, suitability of crop genotype for its climate, insect damage, and agricultural practices [5]. Moreso, these fungi can produce aflatoxin in "postharvest" conditions viz: storage, transportation, and food processing. The main predisposing factor in postharvest aflatoxin accumulation in food is poor storage conditions; namely, excessive heat and moisture, pest-related crop damage, and extensive periods of time spent in storage (exceeding several months) [1]. Aflatoxin contamination is a particular problem in maize, oilseeds, spices, peanuts, tree nuts (almonds, pistachios, hazelnuts, pecans, Brazil nuts, and walnuts), milk (in the form of aflatoxin B1's metabolite aflatoxin M1), and dried fruit [1, 8]. Maize and peanuts are the main sources of human exposure to aflatoxin because of high rate of consumption worldwide and susceptibility to aflatoxin contamination [1, 5].

Over 5 billion people in developing countries worldwide are estimated to be at risk of chronic exposure to aflatoxins through contaminated foods [7-9]. The primary and major disease associated with aflatoxin consumption is hepatocellular carcinoma (HCC) or liver cancer. This disease was reported by [10] to be the third-leading cause of cancer death globally, with about 550,000–600,000 new cases each year. 83% of these deaths occur in East Asia and sub-Saharan Africa [7, 11, 12]. Liver cancer has an increasing incidence that parallels the rise in chronic hepatitis B (HBV) and hepatitis C (HCV) infection [13]. Reports have shown that HBV infection and aflatoxin synergize to produce 30-fold higher liver cancer risk in HBV-positive, aflatoxin-exposed persons, as compared to HBV-negative persons [5, 13, 14]. Unfortunately, HBV and HCV rates are high in sub-Saharan Africa as well as in Asia, which means that the risk of liver cancer from aflatoxin consumption is greatly magnified. In addition, aflatoxin has also been linked to stunted growth in children and immune system disorders [15-17. Hence, this paper reviews the public health significance of aflatoxin in food.

2. Factors Affecting Occurrence of Aflatoxin in Foods

Aflatoxins can affect a wide range of commodities including cereals, oilseeds, spices, and tree nuts as well as milk, meat, and dried fruit. The major sources of exposure are maize and groundnuts as these are the foods that are most susceptible to contamination and consumed in the greatest amounts. Developing countries located in the tropical regions, are at greatest risk given their reliance on these commodities as their staple food source [7, 18]. In fact, over 5 billion people in developing countries worldwide are estimated to be at risk of chronic exposure to aflatoxins through contaminated foods [8, 9]. Insufficiency of food and lack of food diversity increases the risk of exposure to aflatoxins among individuals who live in these regions. Insect activity, poor timing of harvest, heavy rains at harvest and post-harvest, and inadequate drying of the crop before storage are also contributing factor to the occurrence of aflatoxins in foods as well as humidity, temperature, and aeration during drying and storage [7, 18].

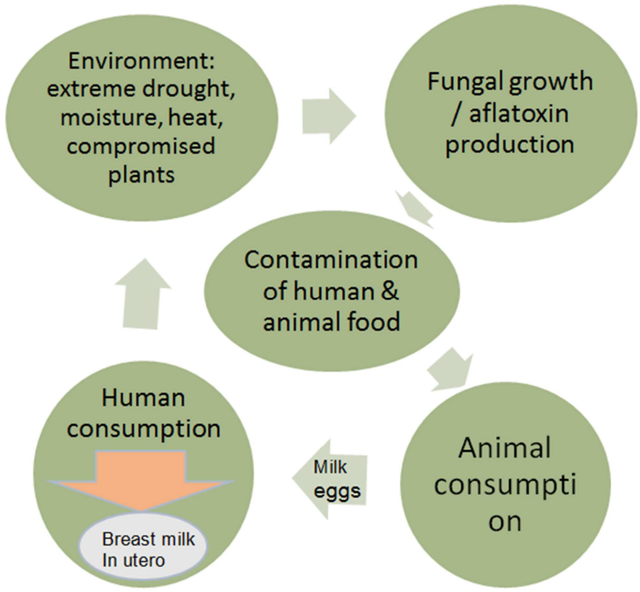

Fig. 1. *Human, Animal, and Environmental Interactions [19].*

Environmental factors such as soil moisture and temperature create the conditions under which *Aspergillus* can grow and produce toxins on crops or food. Animals and humans are exposed to aflatoxins through consumption of contaminated products such as meat [20], dairy products (e.g. milk, cheese, and yogurt) [21], or eggs [22] (Figure 1). Infants can be exposed to aflatoxins through breast milk or in utero [17]. Agricultural practices may contribute to the growth of *Aspergillus* through poor land management and crop storage practices [7].

Many factors affect the growth of *Aspergillus* fungi and the level of aflatoxin contamination in food. Contamination can occur at any stage of food production from pre-harvest to storage [7, 18]. Factors that affect aflatoxin contamination include the climate of the region, the genotype of the crop planted, soil type, minimum and maximum daily temperatures, and daily net evaporation [7]. Aflatoxin contamination is also promoted by stress or damage to the crop due to drought prior to harvest, insect activity, poor timing of harvest, heavy rains at harvest and post-harvest, and inadequate drying of the crop before storage. Humidity, temperature, and aeration during drying and storage are also important factors [18].

3. Aflatoxins and Their Health Consequences

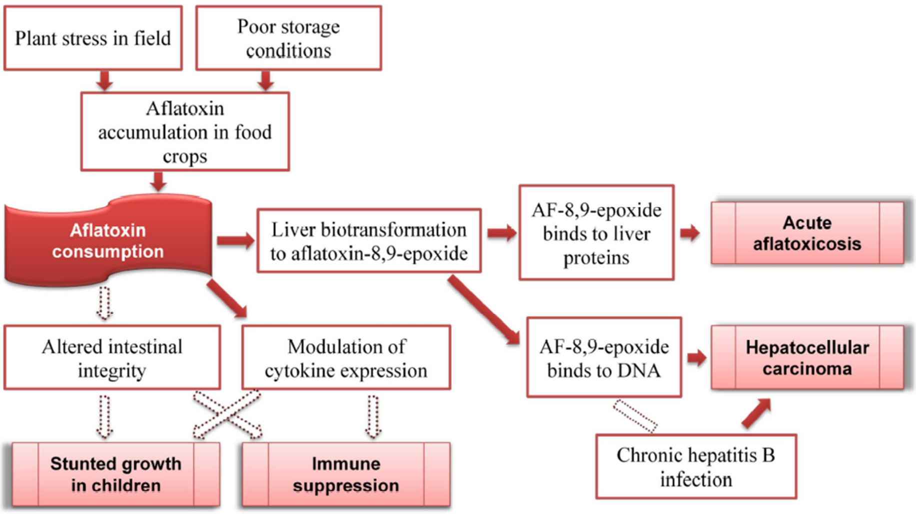

Fig. 2. *Aflatoxin and disease pathways in humans. Source: [23]. The darker arrows indicates link that have been well-established in agricultural and toxicological research, while the white arrows show linkages that have been relatively less well established [23].*

Aflatoxins are associated with both toxicity and carcinogenicity in human and animal populations [18]. Acute aflatoxicosis results in death, whereas chronic aflatoxicosis results in more prolonged pathologic changes, including cancer and immunosuppression [18]. The liver is the primary target organ, and liver damage has been documented in rodents, poultry, and nonhuman primates following ingestion of aflatoxin B1. Aflatoxin contamination is both a food safety and public health issue because of its toxicity. In high doses, aflatoxins can lead to serious illness like acute liver cirrhosis and death in both humans and animals.

Aflatoxin can exert toxicity in several ways when consumed as shown in figure 2 above. It may alter intestinal integrity [2004] or modulate the expression of cytokines, proteins that "signal" to each other and to immune system components. Both of these effects may result in stunted growth in children and/or immune suppression [1, 23]. Aflatoxin may be transformed by certain P450 enzymes (CYP1A2, 3A4, 3A5, 3A7) in the liver, to its DNA reactive form aflatoxin-8,9-epoxide. This molecule may bind to liver proteins and lead to their failure, potentially resulting in acute aflatoxicosis. Alternatively, it may bind to DNA to form adduct, a step that is a precursor for aflatoxin-induced hepatocellular carcinoma (liver cancer) [1].

The mechanism of aflatoxin-induced carcinogenesis involves tumor promotion or progression as reported by [18]. It has been observed that aflatoxin is involved in the activation of proto-oncogenes and mutations in the tumor suppressor gene p53. Aflatoxin exposure and p53 mutations have been tightly linked in epidemiologic studies in Africa and China. Specifically, aflatoxin has been linked to a p53 mutation whereby there occurs a G-to-T transversion at codon 249 [18, 24]. This biomarker has been used in epidemiologic studies to establish the link between aflatoxins and hepatic cancer and also to show that cofactors such as infection with hepatitis B virus increase the risk of HCC substantially. It has also been suggested that aflatoxin induces various chromosomal aberrations, unscheduled DNA synthesis and chromosomal strand breaks in human cells. Another suggested mechanism for aflatoxin-mediated carcinogenesis is production of mutagenic substances as a result of metabolization of Aflatoxin by hepatic cytochrome p450. However, there may be a synergistic effect between aflatoxin and chronic infection with hepatitis B virus (HBV) that results in significantly higher liver cancer risk [1, 23]. Studies have linked aflatoxin to immune suppression, increased susceptibility to diseases (e.g. HIV and malaria), and possibly compromised vaccine efficacy. With aflatoxin seriously affecting maize production, aflatoxin exposure poses the greatest health risk to populations who rely on maize as their main staple.

It has been hypothesized that kwashiorkor, a severe malnutrition disease, and Reye syndrome, marked by encephalopathy and fatty degeneration of the viscera, represent forms of pediatric aflatoxicosis. Although aflatoxins have been found in the livers of children with kwashiorkor and in Reye syndrome patients, a strong cause-and-effect relationship between aflatoxin exposure and these disease states has not been established [25].

3.1. Acute Exposure to Aflatoxins

Acute aflatoxicosis is associated with high doses of aflatoxin. It is characterized by hemorrhage, acute liver damage, edema, and death in humans. Conditions increasing the likelihood of acute aflatoxicosis in humans include limited availability of food, environmental conditions that favor fungal development in crops and commodities, and lack of regulatory systems for aflatoxin monitoring and control. Several reported cases of acute aflatoxicosis in Africa associated with consumption of contaminated home-grown maize have been documented. These include the outbreaks in Kenya in 1982, in which 12 people died, and in 2004, in which 317 people became ill and 125 people died in the central provinces [1, 7, 26-28].

Acute aflatoxicosis has also been reported in animals. In 1960, more than 100,000 turkeys died on in the United Kingdom within few months, resulting to the name "Turkey X disease". However, investigations revealed that the source of the disease was toxic peanut meal. In 1981, several hundred calves that had been fed on peanut hay died in Australia while in 2007, hundreds of animals died in a chinchilla farm in Argentina which are linked to aflatoxin [1]. In cattle, aflatoxin has been reported to cause decreased rumen motility and function, changes in the gastrointestinal tract physiology and blood coagulation defect (impairment of pthrombin, factors VII and X and possibly factor IV) while in poultry, aflatoxin can result to decreased feed consumption, body weight, testes weight and semen volume and decreased plasma testosterone value and reproduction [29].

3.2. Chronic Exposure to Aflatoxins

Chronic exposure to aflatoxin results to hepatocellular carcinoma (HCC) or liver cancer. HCC as a result of chronic aflatoxin exposure most often present in persons with chronic hepatitis B virus (HBV) infection [1, 14]. According to [14], aflatoxin consumption raises the risk of liver cancer up to thirty-fold for individuals chronically infected with HBV, compared with either exposure alone. Unfortunately, these two risk factors – aflatoxin and HBV – are especially prevalent in poor nations worldwide [13].

Several human studies have shown evidence of immunomodulation [30-32] following exposure to aflatoxin, though the actual outcomes of such immunomodulation have yet to be characterized in humans. Aflatoxin's immunotoxicity may be one explanation for the stunted growth in children that appears to follow a dose-response relationship with aflatoxin exposure [5, 30]. The mechanism by which aflatoxin may result in growth impairment is not yet known as reported by [15], however, one possible explanation may be altered intestinal integrity through cell toxicity or immunomodulation [15]. Similarly, animal studies have revealed that chronic exposure to aflatoxins in animals can also cause growth inhibition and immune suppression [17]. Nursing animals may be affected, and aflatoxin M1 may be excreted in the milk of dairy cattle and other dairy animals. This in turn poses potential health risks to both animals and humans that consume that milk. Chronic aflatoxin exposure in animals can result in impaired reproductive efficiency, reduced feed conversion efficiency, increased mortality rates, reduced weight gain, anemia, and jaundice. Aflatoxicosis causes an enlarged fatty liver and lowered egg production in laying hens [33].

Over 5 billion people in developing countries worldwide are estimated to be at risk of chronic exposure to aflatoxins through contaminated foods [7-9]. The consumption of aflatoxin results to hepatocellular carcinoma (HCC) or liver cancer. This disease was reported by [10] to be the third-leading cause of cancer death in the world, with about 550,000–600,000 new cases each year (Figure 3).

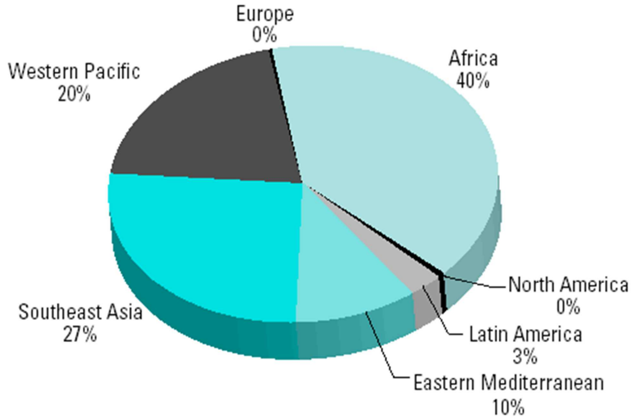

Fig. 3. *Distribution of HCC cases attributable to aflatoxin in different regions of the world [13].*

Aflatoxins in human have been reported to cause digestive system effect (diarrhea, vomiting, intestinal hemorrhage, liver necrosis and fibrosis) and toxic encephalopathy (loss of balance, recent memory decline, headaches, insomnia, and loss of coordination). Moreso, it has been implicated as potential factors in the increased incidence of human gastrointestinal and hepatic neoplasms in Africa, Philippines and China. Exposures to chronic aflatoxin contaminated foods have been reported to result to higher aflatoxin concentrations in the semen of infertile men. In Nigeria, about 37% of the infertile had aflatoxin in their blood and semen [29].

4. Populations at Risk

The most vulnerable population to the risk of aflatoxin are children and individuals with hepatitis B virus (HBV) and Hepatitis C virus (HCV) infections.

4.1. Children

It is well established that dietary aflatoxins reduce the rate of growth and other measures of productivity in animals [1]. However, children have more immature neurologic and immune systems and so are more prone to develop complications and with their low body weights, doses of environmental toxins that might not affect adults may induce illness in children. The epidemiologic studies of [15] in West Africa on the effects of aflatoxin exposure on growth in humans revealed a striking association between exposure to aflatoxin in children and both stunting (a reflection of chronic malnutrition) and being under weight (an indicator of acute malnutrition). Aflatoxin exposure has also been shown to be a factor in modulating the rate of recovery from kwashiorkor in children [18, 25]. Stunting growth in children has been linked to aflatoxin exposure through consuming contaminated food is common. However, the exact mechanisms underlying these effects of aflatoxins have not been elucidated [15, 29].

In developing countries, many people subsist largely on cereal diets. Nutritional deficiencies are very prevalent in populations consuming high levels of cereals [34], particularly children. Additionally, many children in the developing world are also exposed to high levels of mycotoxins in their diets.

4.2. Individuals with Hepatitis B and C Viral Infections

The risk of liver cancer in individuals exposed to chronic hepatitis B virus infection and aflatoxin is up to 30 times greater than the risk in individuals exposed to aflatoxin alone [13, 14]. Aflatoxin and hepatitis B virus are two HCC risk factors which are prevalent in poor nations worldwide. Within these nations, there is often a significant urban-rural difference in aflatoxin exposure and hepatitis B virus prevalence, with both these risk factors typically affecting rural populations more strongly than the urban populations [13, 18].

Aflatoxin also appears to have a synergistic effect on hepatitis C virus-induced liver cancer, although the quantitative relationship is not as well established as that for aflatoxin and hepatitis B virus in inducing HCC [4, 13]. Studies have also shown that the genetic characteristics of the virus, and the age and sex of the infected person may play a role in increasing the risk of aflatoxin induced HCC [18].

5. Preventive Measures and Intervention Strategies

5.1. Role of Politics

The political will at a national level to address the issue of aflatoxin exposure is probably the most important factor in reducing the health hazards associated with aflatoxins in poor countries. Aflatoxin regulatory programs are already in place in most countries. On the export side these regulatory programs are strictly enforced to protect the export market of agricultural commodities, otherwise the importing countries would reject the commodities resulting in a loss of valuable foreign exchange earnings. On the other hand, domestic regulatory measures on aflatoxins have received very little attention and are rarely enforced, without incentives given for the aflatoxin free produce and no heavy penalty on the violators of aflatoxin regulations as asserted by [18].

5.2. Information Dissemination

Considerable information is available on the health hazards of aflatoxin exposure and conditions that lead to mold growth and aflatoxin contamination during growing, harvesting and storage of crops. Several steps that can be followed to avoid or minimize contamination have been developed. Also, information is available on safe storage, handling and transportation practices of agricultural commodities. However, this information is rarely communicated to farmers, traders and all those who need to be informed. Much could be done if the value of different interventions is communicated and the information is disseminated in an appropriate and accessible manner [4]. As an example, during an outbreak in Kenya in 2005, individuals who received information on maize drying and storage had lower serum aflatoxin levels than those who did not receive this information [18].

5.3. Agricultural Strategies

Agricultural interventions are methods or technologies that can be applied either in the field ("pre-harvest") or in drying, storage, and transportation ("post-harvest") to reduce aflatoxin levels in food [5]. The presence and growth of *Aspergillus* on pre-harvested crops is dependent on the environment. Agricultural practices including proper irrigation and pest management can reduce aflatoxin contamination [7]. Pre-harvest interventions include choosing crops with resistance to drought, disease, and pests and choosing strains of that crop which are genetically more resistant to the growth of the fungus and the production of aflatoxins [7]. Elimination of inoculum sources such as infected debris from the previous harvest may prevent infection of the crop [18]. Before storage, crops should be properly dried to prevent the development of aflatoxins. Sorting and disposing of visibly moldy or damaged kernels before storage has proven to be an effective method for reducing the development of aflatoxins [7, 18]. During storage, moisture, insect, and rodent control can prevent damage to the crop and reduce aflatoxin development. Aflatoxin contamination of maize is influenced by the facilities used for storage, storage time, and the form of maize stored [7, 18]. A community-based intervention study in Africa showed that simple and inexpensive measures such as thorough drying and proper storage of groundnuts can have a significant impact on aflatoxin levels [18].

Farming and storage practices play an important role in the growth of aflatoxin-producing fungi. As mentioned, environmental conditions such as temperature, humidity and insect damage can affect fungal growth in the field and the level of aflatoxin contamination in the final commodity. Preventive strategies targeting safe pre-harvest, harvest, and post-harvest practices can reduce contamination. Farmers can begin preventive measures by monitoring weather patterns for conditions favoring aflatoxin production. Pre-harvest interventions incorporate planting at the appropriate time and managing pests, including insects (particularly soil insects), weeds, plant disease and nematodes. Testing soil samples for levels of nutrients and alternating fertilizers or rotating crops to improve conditions can help. Irrigation reduces the levels of *Aspergillus* infection when applied during pollination [35]. Harvesting when the crop is mature helps prevent fungus growth.

Finally, increased dietary diversity in areas where aflatoxin-prone foods such as corn and groundnuts are staples can improve outcomes. Research is ongoing to discover which particular substances protect against aflatoxin toxicity. Other proposed methods of aflatoxin mitigation include thermal inactivation, irradiation, microbial inactivation and fermentation. Fermentation may reduce aflatoxin absorption because Lactobacillus binds to aflatoxin B1 [36].

Bioengineering has been used as a mechanism to implement new, technologically-based solutions. Genetic modification to develop crop resistance to *Aspergillus* is being explored.

Additionally, certain strains of *Aspergillus* are atoxigenic and are able to be introduced into the agricultural environment to prevent production of aflatoxin. The "biopesticide" Aflasafe™ is an example of one of these strains. Aflasafe is not a chemically derived pesticide, and trials in the US have shown successful reduction of contamination (in the context of integrated crop management programs). In a case study in Nigeria, provisional registration and use of Aflasafe™ in 2009 allowed farmers to reduce aflatoxin by 80%. Additionally, Aflasafe includes some long-term benefits, as it may not need to be applied every year (depending on the environment) [36].

5.4. Vaccination Against Hepatitis B Virus

Hepatitis B virus infection increases the risk of HCC in individuals exposed to aflatoxins exponentially. Vaccination against hepatitis B virus in infancy is an effective approach to prevent HCC, particularly in developing countries where both incidence of hepatitis B virus and exposure to aflatoxins are high [18, 36, 37]. Although the vaccine itself has no impact on actual aflatoxin levels in diets, it reduces aflatoxin-induced HCC by lowering hepatitis B virus risk, thereby preventing the synergistic impact of hepatitis B virus and aflatoxin in inducing liver cancer [36]. Those who already have chronic hepatitis B virus infection would not benefit from the vaccine, which is why vaccination should be offered in infancy [36]. Hepatitis B vaccination in infancy has been shown to be safe and effective [36, 37]. Hepatitis B vaccination does not affect aflatoxin exposure itself, but it can dramatically lower liver cancer rates in endemic areas [36].

It is preferable to avoid aflatoxin consumption all together, however, there are various ways to minimize the risk of negative health effects for those whose diets contain foods likely to be contaminated with aflatoxins. Certain compounds reduce absorption of aflatoxins when they are consumed simultaneously. One promising intervention is the use of NovaSil™ clay (sodium calcium aluminosilicate), which adsorbs aflatoxin in the intestine and prevents its uptake. It has been effective in animal models and has been shown to be safe in phase I and II clinical trials in humans [14, 38]. However, while initial results are promising, further research is needed to ensure it is not also binding to and preventing absorption of important nutrients [39, 40].

6. Safe Level of Exposure

There is no "safe" level of exposure to aflatoxin, however, the U.S. government considers aflatoxins to be contaminant of food that cannot be avoided and acknowledges that low levels may be present. U.S. food safety regulations include a limit of 20 µg/kg for total aflatoxins (B, B2, G1 and G2) in all foods except milk and a limit of 0.5 µg/kg for M1 in milk. Higher limits apply for animal feeds [41]. The European Union also regulates the amount of aflatoxin permitted in foodstuffs and sets lower contamination levels. In the EU, the highest permissible concentration for food intended for direct human consumption is 10 µg/kg, but only 0.05 ppb for M1 in milk [42]. At least 99 countries had regulations, a 30% increase from 1995 [43]. However, there still in exists a lack of regulations in lesser-populated countries and no clear regulation in many other developing countries.

The United States Food and Drug Administration sets the maximum allowable levels of aflatoxin in food for direct human consumption at 20 ppb (Table 1) and also regulates allowable aflatoxin levels in feeds for various agricultural animals (Table 2) to protect human and animal health as reported by [19].

Table 1. *Allowable Aflatoxin Levels in Human Foods.*

Amount	Food type
20 ppb	Foods in general
0.5 ppb (aflatoxin M1)	Milk
20 ppb	Peanuts and peanut products
20 ppb	Pistachio nuts
20 ppb	Brazil nuts

Table 2. *Allowable Aflatoxin Levels in Animal Feeds [19].*

Amount	Food Type
20 ppb	For corn and other grains intended for immature animals (including immature poultry) and for dairy animals, or when its destination is not known
20 ppb	For animal feeds, other than corn or cottonseed meal;
100 ppb	For corn and other grains intended for breeding beef cattle, breeding swine, or mature poultry
200 ppb	For corn and other grains intended for finishing swine of 100 pounds or greater
300 ppb	For corn and other grains intended for finishing (i.e., feedlot) beef cattle and for cottonseed meal intended for beef cattle, swine or poultry

7. The One Health Approach

Aflatoxin contamination of foodstuffs and its effects on human and animal health is a complex issue. Therefore, by understanding its epidemiology, holistic solutions can be found. A One Health understanding of aflatoxicity considers how human behaviors influence the environment to promote or inhibit aflatoxin production. A One Health approach recognizes that human impacts on the environment play an important role in *Aspergillus* growth and the production of aflatoxins. By understanding and educating stakeholders on the interconnectedness of humans, animals, and the environment, it becomes possible to find solutions that address each of the contributing factors. [19, 44].

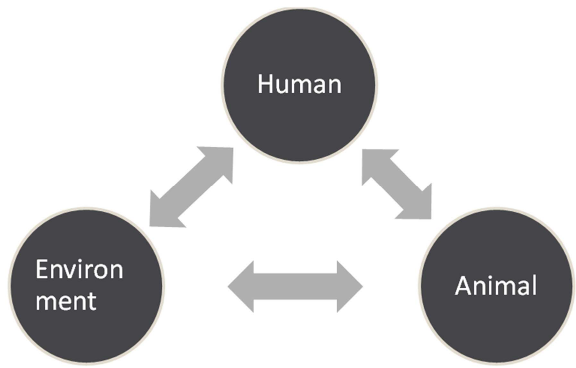

Fig. 3. *Interconnectedness of humans, animals, and the environment [19].*

8. Recommendations/Conclusions

In crop production, irrigation and pest management help reduce stress on plants that can leave them more vulnerable to *Aspergillus* growth and aflatoxin contamination. Agricultural practices such as crop rotation and appropriate harvest timing could be useful. It is important to assure proper pre-harvest drying and post-harvest sorting in a controlled environment [19, 44]. Dietary modification can help in prevention of aflatoxin. Certain food preparation techniques such as fermentation may reduce the intestinal absorption of aflatoxins. Education regarding the sources of aflatoxin can help consumers avoid foods that are most likely to be contaminated. In addition to preventing aflatoxin exposure, another public health strategy to minimize the adverse health effects is Hepatitis B vaccination. This can be widely implemented by governments. However, primary prevention to r*educe* aflatoxin exposure is the best public health strategy [19].

References

[1] Wu, F., Narrod, C., Tiongco, M. and Liu, Y. (2011). The health economics of Aflatoxin: global burden of Disease. *Aflacontrol, 4*: 1-14.

[2] Klich, M. A., Mullaney, E. J., Daly, C. B. and Cary, J. W. (2000). Molecular and physiological aspects of aflatoxin and sterigmatocystin biosynthesis by *A. tamari* and *A. ochraceoroseus*. *Applied Microbiology and Biotechnology, 53*: 605-609.

[3] Reddy, K. R. N., Salleh, B., Saad, B., Abbas, H. K. Abel, C. A. and Shier, W. T. (2010). An overview of mycotoxin contamination in foods and its implications for human health. *Toxin Reviews, 29* (1): 3–26.

[4] Wild, C. P. and Gong, Y. Y. (2010). Mycotoxins and human disease: a largely ignored global health issue. Carcinogenesis 31:71-82.

[5] Wu, F., and Khlangwiset, P. (2010). Health economic impacts and cost-effectiveness of aflatoxin reduction strategies in Africa: Case studies in biocontrol and postharvest interventions. *Food Additives and Contaminants 27*:496-509.

[6] Guo, B., Widstrom, N. et al. (2000). Control of preharvest aflatoxin contamination in corn: Fungus-plant-insect interactions and control strategies. *Recent Research Developments in Agricultural and Food Chemistry, 4*: 165-176.

[7] Strosnider, H., Azziz-Baumgartner, E., Banziger, M., Bhat, R. V., Breiman, R., Brune, M., DeCock, K., Dilley, A., Groopman, J., Hell, K., Henry, S. H., Jeffers, D., Jolly, C., Jolly, P., Kibata, G. N., Lewis, L., Liu, X., Luber, G., McCoy, L., Mensah, P., Miraglia, M., Misore, A., Njapau, H., Ong, C., Onsongo, M. T. K., Page, S. W., Park, D., Patel, M., Phillips, T., Pineiro, M., Pronczuk, J., Schurz Rogers, H., Rubin, C., Sabino, M., Schaafsma, A., Shephard, G., Stroka, J., Wild, C., Williams, J. T. and Wilson, D. (2006). Workgroup Report: Public Health Strategies for Reducing Aflatoxin Exposure in Developing Countries. *Environmental Health Perspectives, 114*: 1889-1903.

[8] Shephard, G. S. (2008). Risk assessment of aflatoxins in food in Africa. *Food Additives & Contaminants: Part A: Chemistry, Analysis, Control, Exposure & Risk Assessment 25,* (10): 1246–1256.

[9] Williams, J. H., Phillips, T. D., Jolly, P. E., Stiles, J. K., Jolly, C. M. and Agarwal, D. (2004). Human aflatoxicosis in developing countries: a review of toxicology, exposure, potential health consequences, and interventions. *American Journal of Clinical Nutrition, 80*: 1106-1122.

[10] WHO (2008). World Health Statistics (2008). WHO Press, Geneva, http://www.who.int/whosis/whostat/EN_WHS08_Full.pdf.

[11] Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. CA Cancer J Clin 2005; 55 (2): 74-108.

[12] Kirk, G. D., Bah, E. and Montesano, R. (2006). Molecular epidemiology of human liver cancer: Insights into etiology, pathogenesis and prevention from The Gambia. *Carcinogenesis, 27*: 2070-2082.

[13] Liu, Y. and Wu, F. (2010). Global Burden of Aflatoxin-Induced Hepatocellular Carcinoma: A Risk Assessment. *Environmental Health Perspectives 118*: 818-24.

[14] Groopman, J. D., Kensler, T. W. and Wild, C. P. (2008). Protective Interventions to Prevent Aflatoxin-Induced Carcinogenesis in Developing Countries. *Annual Reviews in Public Health 29*:187-203.

[15] Gong, Y., Hounsa, A. and Egal, S. (2004). Postweaning exposure to aflatoxin results in impaired child growth: a longitudinal study in Benin, West Africa. *Environmental Health Perspective 112*: 1334-38.

[16] Jolly, P., Jiang, Y., Ellis, W. O., Wang, J. S., Afriyie-Gyawu, E. and Phillips, T. D. (2008). Modulation of the human immune system by aflatoxin. *In*: Mycotoxins: Detection Methods, Management, Public Health and Agricultural Trade. Leslie, J. F.B. R. and Visconti, A. (ed). CAB International, Oxfordshire, UK., 41-52.

[17] Khlangwiset, P., Shephard, G. S. and Wu, F. (2011). Aflatoxins and growth impairment: a review. *Critical Reviews in Toxicology, 41* (9):740-55.

[18] Magnussen, A. and Parsi, M. A. (2013). Aflatoxins, hepatocellular carcinoma and public health. *World Journal of Gastroenterology, 19* (10): 1508-1512.

[19] Giezendanner, E. and Budd, B. (2012). Aflatoxin: In Search of One Health Solutions. North Carolina One Health Collaborative, 1-31.

[20] Olufunmilayo, G. O. and Oyefolu, A. B. (2010). Natural occurrence of aflatoxin residues in fresh and sun-dried meat in Nigeria. *Pan African Medical Journal*, *7*: 14.

[21] Prandini, A., Tansini, G., Sigolo, S., Filippi, L., Laporta, M., and Piva, G. (2009). On the occurrence of aflatoxin M1 in milk and dairy products. *Food Chemical Toxicology.* 47 (5): 984-991.

[22] Pandey, I. and Chauhan, S. S. (2007). Studies on production performance and toxin residues in tissues and eggs of layer chickens fed on diets with various concentrations of aflatoxin AFB1. *British Poultry Science, 48* (6): 713-723.

[23] Wu, F (2010). The global burden of disease caused by foodborne aflatoxin. WHO Commissioned Report, Foodborne Di sease Burden Epidemiology Reference Group (FERG).

[24] Soini, Y., Chia, S. C., Bennett, W. P., Groopman, J. D., Wang, J. S., DeBenedetti,,V. M., Cawley, H., Welsh, J. A., Hansen, C., Bergasa, N. V., Jones, E. A., DiBisceglie, A. M., Trivers, G. E., Sandoval, C. A., Calderon, I. E., Munoz Espinosa, L. E. and Harris, C. C. (1996). An aflatoxin-associated mutational hotspot at codon 249 in the p53 tumor suppressor gene occurs in hepatocellular carcinomas from Mexico. *Carcinogenesis 17*: 1007-1012.

[25] Mahoud, B. (2001). Aflatoxin and kwashiorkor. *Acta Paediatrics, 90*: 103.

[26] Azziz-Baumgartner, E., Lindblade, K., Gieseker, K., Schurz Rogers, H., Kieszak, S., Njapau, H., Schleicher, R., McCoy, L. F., Misore, A., DeCock, K., Rubin, C. and Slutsker, L. (2005). Aflatoxin Investigative Group (2005). Case-Control Study of an Acute Aflatoxicosis Outbreak, Kenya, 2004. *Environmental Health Perspectives 113*: 1779-1783.

[27] Probst, C., Njapau, H. and Cotty, P (2007). Outbreak of an Acute Aflatoxicocosis in Kenya in 2004: Identification of the Causal Agent. *Applied and Environmental Microbiology,* 2762-2764.

[28] Lewis, L., Onsongo, M., Njapau, H., Schurz-Rogers, H., Luber, G., Kieszak, S., Nyamongo, J., Backer, L., Dahive, A., Misore, A., DeCock, K., Rubin, C. and the Kenya Aflatoxicosis Investigation Group (2005). Aflatoxin Contamination of Commercial Maize Products during an Outbreak of Acute Aflatoxicosis in Eastern and Central Kenya. *Environmental Health Perspective, 113* (12): 1763–1767.

[29] Gong Y, Turner PC, Hall AJ, CP W. 2008. Aflatoxin exposure and impaired child growth in West Africa: An unexplored international public health burden? In: *Mycotoxins: Detection Methods, Management, Public Health and Agricultural Trade*, (Leslie JF, Bandyopadhyay R, Visconti A, eds). Oxfordshire, UK: CAB International, 53-65.

[30] Turner, P. C., Moore, S. E., Hall, A. J., Prentice, A. M., Wild, C. P. (2003). Modification of immune function through exposure to dietary aflatoxin in Gambian children. *Environmental Health Perspective 111* (2): 217-220.

[31] Jiang, Y., Jolly, P., Ellis, W. O., Wang, J. S., Phillips, T. D. and Williams, J. H. (2005). Aflatoxin B1 albumin adduct levels and cellular immune status in Ghanaians. *International Immunology 17* (6): 807-814.

[32] Jiang, Y., Jolly, P., Preko, P., Wang, J. S., Ellis, W. O., and Phillips, T. D. (2008). Aflatoxin-related immune dysfunction in health and in human immunodeficiency virus disease. *Clinical Development in Immunology,* 1-12.

[33] Lubulwa, A. S. G. and Davis, J. S. (1998). Estimating the social costs of the impacts of fungi and aflatoxins in maize and peanuts. Proceedings of the 6th International Working Conference on Stored-Product Protection, Volume 2.

[34] Bankole, S. and Adebanjo, A. (2003). Mycotoxin in food in West Africa: current situation and possibilities of controlling it. *African Journal of Biotechnology, 2* (9): 254-263.

[35] Lawley, R. (2007). Aflatoxins. *Food Safety Watch. N.p.,* http://www.foodsafetywatch.com/public/482.cfm Accessed 6 May, 2014.

[36] Khlangwiset, P. and Wu, F. (2010). Costs and efficacy of public health interventions to reduce aflatoxin-induced human disease. *Food Addit Contam Part A Chem Anal Control Expo Risk Assess*, 27 (7): 998-1014.

[37] Plymoth, A., Viviani, S., Hainaut, P. (2009). Control of hepatocellular carcinoma through hepatitis B vaccination in areas of high endemicity: perspectives for global liver cancer prevention. *Cancer Letter, 286*: 15-21.

[38] Kensler, T. W., Roebuck, B. D., Wogan, G. N. and Groopman, J. D. (2010). Aflatoxin: a 50-year odyssey of mechanistic and translational toxicology. *Toxicology Science, 120* (1): 28-48.

[39] Afriyie-Gyawu, E., Wang, Z., Ankrah, N. A., Xu, L., Johnson, N. M., Tang, L., Guan, H., Huebner, H. J., Jolly, P. E., Ellis, W. O., Taylor, R., Brattin, B., Ofori-Adjei, D., Williams, J. H., Wang, J. S. and Phillips, T. D. (2008). NovaSil clay does not affect the concentrations of vitamins A and E and nutrient minerals in serum samples from Ghanaians at high risk for aflatoxicosis. *Food Additive Contamination Part A Chemical Anall Control Exposure Risk Assess, 25* (7): 872-84.

[40] Marroquín-Cardona, A., Deng, Y., Garcia-Mazcorro, J., Johnson, N. M., Mitchell, N., Tang, L., Robinson, A. 2nd, Taylor, J., Wang, J. S. and Phillips, T. D. (2011). Characterization and Safety of Uniform Particle Size NovaSil Clay as a Potential Aflatoxin Enterosorbent. *Applied Clay Science, 54* (3-4): 248-257.

[41] U.S. Food and Drug Administration (2000). Guidance for Industry: Action Levels for Poisonous or Deleterious Substances in Human Food and Animal Feed. http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/ChemicalContaminantsandPesticides/ucm077969.htm. Accessed July, 4, 2014.

[42] European Union (2006). Commission Regulation (EC) No 1881/2006 of 19 December 2006 setting maximum levels for certain contaminants in foodstuffs. http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:2006R1881:20100701:EN:HTML, Accessed July, 2014.

[43] Takumi, Y. (2006). Mycotoxins and Food Safety Current Situation of Food Contamination, Regulations and Risk Assessment for Mycotoxins. *Foods and Food Ingredient Journal of Japan,* 211-212.

[44] Wagacha, J. M. and Muthomi, J. W. (2008). Mycotoxin problem in Africa: current status, implications to food safety and health and possible management strategies. *International Journal of Food Microbiology*, *124* (1): 1-12.