Role of Mycotoxins in the Food Chain and their Implications of Human Health

CHAPTER 13

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Introduction

It has been estimated that 25 of the world's crops are affected by mould or fungal growth [1]. Fungal corruption of crops can have serious profitable consequences and goods may be defiled with poisonous fungal secondary metabolites known as mycotoxins. Mortal exposure to mycotoxins may affect from consumption of factory deduced foods that are defiled with poisons, the carryover of mycotoxins and their metabolites into beast products similar as milk, meat and eggs or exposure to air and dust containing poisons Mortal food can be defiled with mycotoxins at colourful stages in the food chain and the three most important rubrics of mycotoxigenic fungi are Aspergillus, Fusarium and Penicillium. The top classes of mycotoxins produced by these rubrics are aflatoxins (Aspergillus), ochratoxins (Aspergillus and Penicillium) and trichothecenes and fumonisins (Fusarium). The complaint performing from mycotoxin exposure is a mycotoxicosis. Deoxynivalenol (DON) is the trichothecene most frequently encountered in the field [4]. Fumonisins and aflatoxin B1 are

carcinogenic [5][6]. There is now inviting epidemiological evidence that aflatoxin B1 consumption contributes significantly to the high prevalence of mortal liver cancer in numerous developing countries, especially in individualities infected with hepatitis B or C contagion [7][8]. Ochratoxin A is nephrotoxic and a possible cause of urinary tract excrescences and Balkan – aboriginal nephropathy [6]. There are a number of other mycotoxins that beget complaint and these include zearalenone (Fusarium), an oestrogenic mycotoxin and ergot alkaloids produced on cereal grains (Claviceps) or by endophytic fungi (Neophytodium) [9][10]. The medium (s) of action of these mycotoxins is generally well characterised [11].

There has been a major transnational exploration trouble, aimed at the identification and quantification of mycotoxins and evaluation of their natural goods in humans and creatures. The motivation for the trouble is the reports of acute mycotoxicoses in humans, the recrimination of mycotoxins in habitual mortal complaint, especially cancer and the negative profitable goods of beast mycotoxicoses and crop losses due to mycotoxin impurity [12]. Still, the mycotoxins that are likely to be encountered by mortal populations differ between countries. This reflects different crops, agronomic practices and climatic conditions which mandate the fungi that are present in a husbandry system. Two recent books give a good overview of the significance of mycotoxins in different regions of the world and in European countries [13][14]. This review describes the impact of mycotoxin impurity of the mortal food chain.

Mycotoxin exposure and discovery

A wide range of goods can be defiled with mycotoxins (Table 1) both pre-and post- crop [3]. Aflatoxins are plant in sludge and peanuts as well as in tree nuts and dried fruits. Ochratoxin A is plant substantially in cereals but significant situations of impurity may also do in wine, coffee, spices and dried fruits. Fumonisins are plant substantially in sludge and sludge grounded products. Tricothecenes are primarily associated with grain as is zearalenone. Available substantiation suggests that towel accumulation of mycotoxins or their metabolites is veritably low and that remainders are excreted in many days.

The hydroxylated metabolite of aflatoxin B1, aflatoxin M1 is excreted into milk from 1 to 6 of salutary input. Ochratoxin A has been detected in blood, feathers, liver, and muscle towel from gormandizers in several European countries Remainders of cyclopiazonic acid (CPA), aco-contaminant with aflatoxin, have been plant in meat, milk and eggs [19]. After an expansive review of the literature, Pestka concluded that trace situations of mycotoxins and their metabolites may carry over into the comestible towel (meat) of food producing creatures. Still, he concluded that to date there is no substantiation to suggest that the situations of transmitted mycotoxins pose a trouble of acute toxin [20].

Immaculately determination of exposure and opinion of a mycotoxicosis should depend upon the absence of other readily diagnosed conditions and the finding of a mycotoxin in questionable food [21]. It isn't enough to have insulated the fungus as one must be suitable to demonstrate the presence of biologically effective attention of the poison. One difficulty in counting upon chemical analysis of food is that of carrying a sample representative of the food which was consumed. Another major

difficulty is analysis because of the vast array of chemical composites that are mycotoxins. Discovery of numerous of these composites requires veritably sophisticated and precious laboratory outfit and veritably professed logical druggists [22]. Operation of immunological styles to mycotoxin analysis still, has seen the development of immunoassays which are rapid-fire, unremarkable and sensitive. Mycotoxins are non-antigenic, but an antibody response can be inspired to the poison after conjugation to a protein or polypeptide carrier. The vacuity of antibodies to a number of mycotoxins has allowed the development of enzyme-linked immunosorbent assays (ELISA) for the discovery of poisons in food goods and residual mycotoxins or metabolites in body fluids or apkins [23]. Marketable ELISA accoutrements, which are suitable for field use, have come available for aflatoxins, zearalenone, deoxynivalenol, ochratoxins and fumonisins.

The difficulty of counting on logical data for determining mycotoxin exposure of mortal populations is the miscellaneous distribution of mycotoxins in food goods the time pause between poison input and the development of habitual complaint and the inaccuracies of salutary questionnaires for determining food input data. A further dependable and applicable index of individual exposure can be handed by biomarkers which can be determined in urine or blood. Biomarkers include parent composites and metabolites or macromolecular adducts. An understanding of aflatoxin metabolism has allowed the development of a number of biomarkers, especially the aflatoxin albumen adduct that is measured in serum [24]. This marker has been used considerably to assess mortal exposure in epidemiological studies. Lately there has been demonstration of a specific mutation in the TP53 gene and this has contributed significantly to the identification of aflatoxin B1 as a mortal carcinogen [24].

Table 1. *Some human diseases in which mycotoxins have been implicated.*

Disease	Mycotoxin source	Fungus
Akakabio-byo	Wheat, barley, oats, rice	*Fusarium spp.*
Alimentary toxic aleukia	Cereal grains (toxic bread)	*Fusarium spp.*
Balkan nephropathy	Cereal grains	*Penicillium spp.*
Cardiac beriberi	Rice	*Aspergillus spp., Penicillium spp.*
Celery harvester's disease	Celery (Pink rot)	*Sclerontinia*
Ergotism	Rye, cereal grains	*Claviceps purpurea*
Hepatocarcinoma	Cereal grains, peanuts	*Aspergillus flavus, A. parasiticus*
Kwashiorkor	Cereal grains	*Aspergillus flavus. A. parasiticus*
Neural tube defects	Maize	*Fusarium verticillioides, F.proliferatum*
Oesophageal tumors	Corn	*Fusarium verticilloides, F.proliferatum*
Onyalai	Millet	*Phoma sorghina*
Reye's syndrome	Cereal grains (grain dust)	*Aspergillus*
Stachybotryotoxicosis	Cereal grains, (grain dust)	*Stachybotrys atra*

Mycotoxins and mortal complaint

Mycotoxins have been associated with a number of mortal conditions, some acute and others habitual and a number of these conditions are listed in Table 1. Although mycotoxins have been intertwined in this mortal ails, only infrequently has a direct connection been established and much remains to be done to establish the aetiology of numerous questionable mortal mycotoxicoses. Beardall and Miller have given a veritably detailed account of mortal ails that have been associated with mycotoxin ingestion [25].

The numerous interacting factors in the pathogenesis of a mycotoxicosis (Fig 1) make opinion delicate as does attesting mycotoxin exposure. Habitual input is the widest form of mycotoxin exposure and the consequences of this for mortal health are bandied below. Throughout history there are cases, especially following deluge, shortage and war, when acute mycotoxicosis have devastated mortal populations [26].

Acute complaint occurrences have passed lately following high situations of mycotoxin ingestion. Acute liver complaint has been reported in India, Malaysia and Kenya following aflatoxin

consumption [27][28][29]. Bhat et al. reported gastrointestinal pain and diarrhoea in an outbreak of food borne complaint associated with high fumosin input in India [30]. Gastrointestinal symptoms including vomiting were apparent in humans after high situations of DON input in China [31]. An analogous outbreak was observed in India when original townlets consumed rain damaged wheat that contained DON and other trichotheces [32]. There have been suggestions that zearalenone caused unseasonable menarche in youthful girls in South America but these reports haven't been substantiated [9]. Since the middle periods there have been occurrences of ergotism reported in mortal populations in Europe and North America [26]. The most recent outbreak of gangrenous ergotism was in Ethiopia in1978 [33].

Habitual goods of mycotoxins in mortal populations

In numerous regions of the world, salutary masses, especially cereal grains contain low situations of mycotoxins. The impact of regular low- position input of mycotoxins on mortal health is likely to be significant with a number of possible consequences including disabled growth and development, vulnerable dysfunction and the complaint consequences of differences in DNA metabolism.

Growth and development

Multitudinous beast studies have shown that one of the first goods of mycotoxin ingestion is reduced feed input and growth [34]. Gong et al. conducted across-sectional epidemiological Check in West Africa in which they determined the aflatoxin exposure of children between 9 months and 5 times of age and examined their growth, development and height against a WHO source population [35]. The study revealed a veritably strong association between exposure to aflatoxin in the children and both suppressing and being light. Both conditions reflect significant malnutrition and exposure of the children to aflatoxin in utero and latterly after birth

[35]. The children were also co-exposed to a number of contagious conditions and it's likely that the exposure to complaint and aflatoxin would significantly compromise growth and development through reduced food input and also the repartitioning of nutrients to maintain an upregulated vulnerable system and down from growth and development [36]. There are reports linking kwashiorkor, a complaint of malnutrition, to aflatoxin exposure Still, it has not been established if the advanced circumstance of aflatoxin adducts in children suffering from kwashiorkor is a cause or a consequence of the complaint.

Immunosuppression

Aflatoxin, trichothecenes, ochratoxin A, sterigmatocystin, rubratoxin, fumonisins, zearalenone, patulin, citrinin, wortmannin, fusarochromanone, gliotoxin and ergot alkaloids have been shown to beget immunosuppression and increase the vulnerability of creatures to contagious complaint [3]. Substantial substantiation exists that mycotoxin can be immunotoxic and ply goods on cellular responses, humoral factors and cytokine intercessors of the vulnerable system. The goods on impunity and resistance are frequently delicate to honor in the field because signs of complaint are associated with the infection rather than the poison that fitted the individual to infection through dropped resistance and/ or reduced vaccine or medicine efficacity [40]. Also, in beast models, immunosuppressant goods of poisons occur at lower situations of input than do the poison's goods on other parameters of toxin similar as feed input and growth rate.

Recent studies in Gambian children and in Ghanaian adults show a strong association between aflatoxin exposure and reduced immunocompetence suggesting that aflatoxin ingestion decreases resistance to infection in mortal populations [41][42]. Studies by Pestka and his colleagues have shown that DON can both stimulate and suppress the vulnerable system [43]. This has been

demonstrated with the effect of DON on dysregulation of IgA and the development of order complaint in beast models that nearly resembles mortal glomerulo-nephritris IgA nephropathy.

Carcinogenicity, mutagenicity, and teratogenicity

There has been extensive evaluation of the capacity of mycotoxins to interact with DNA and modify its action [11]. Mycotoxins may be carcinogenic (eg. fumonizins), carcinogenic and teratogenic (eg. ochratoxin) or carcinogenic, mutagenic and teratogenic (eg. aflatoxin) [11]. When it was first appreciated some 40 years ago that aflatoxin was a potential carcinogen, it was this finding that gave significant impetus for the research that has subsequently been conducted to define the role of mycotoxins in human and animal disease. Wild and Turner have extensively reviewed the mechanism of toxicity and carcinogenicity of aflatoxins [24].

There is now a significant body of evidence demonstrating human exposure in utero to a number of mycotoxins but the relevance of this exposure to birth defects or impaired embryonic developed has received relatively little attention. Cawdell-Smith et al. were able to identify some 40 mycotoxins that had been shown to be teratogenic and/or embryotoxic in animal models [44]. However, most of these mycotoxins have only been evaluated in rapid screening assays that did not seek to delineate their potential teratoenicity during early pregnancy. Aflatoxin B1, ochratoxin A, rubratoxin B, T-2 toxin, sterigmatocystin and zearalenone have been shown experimentally to be teratogenic in at least one mammalian species. Recent epidemiological investigations of human populations in Texas, China, Guatemala and southern Africa that rely on foods prepared from maize, which is often contaminated with fumonisins, found a significantly higher incidence of neural tube defects in babies [45]. Interestingly, fumonisins perturb folate metabolism46 and folate deficiency is a known cause of neural tube defects in human embryos.

Strategies for reducing mycotoxin risk

In addition to the genetic capacity of the fungus, mycotoxin production depends on many factors. Moisture and temperature are two factors that have a crucial effect on fungal proliferation and toxin elaboration. In the preharvest period, crops that have experienced significant stress whether it be from drought or insects can succumb to fungal invasion. Prior to harvest, preventive measures begin with good agronomic practices including cultivating to improve plant vigour, the judicious use of insecticides and fungicides to reduce insect and fungal infestation, irrigation to avoid moisture stress, harvesting at maturity and breeding programmes to improve genetic resistance to fungal attack [47]. During the post-harvest period, control of moisture and temperature of the stored commodity will largely determine the degree of fungal activity [48]. Moisture content depends mostly on water content at harvest and can be modified by drying, aerating, and turning of the grain before or during storage. Apart from methods that modify the fungal environment many compounds are available that will inhibit mould growth. Organic acids, especially propionic acid, form the basis of many commercial antifungal agents used in the animal feed industry [47]. Once formed, mycotoxins are very stable but many processing practices reduce the level of contamination as food commodities are processed prior to packaging for human consumption [3].

Approaches to detoxification of mycotoxin contaminated grain have included physical, chemical, and biological treatments [3][49]. Methods include dehulling, washing, density segregation of contaminated from noncontaminated kernels, food processing practices and treatment with chemicals including sodium bisulfite, ozone, and ammonia. A diverse variety of substances have been investigated as potential mycotoxin-binding agents including

synthetic cation or anion exchange zeolites, bentonite, hydrated sodium calcium aluminosilicate (HSCAS) and yeast cell wall preparations [50][51]. HSCAS is a high affinity adsorbent for aflatoxins, capable of forming a very stable complex with the toxin and hence reducing its bioavailability and thereby diminishing the adverse effects and tissue accumulation of the toxin A yeast cell wall-derived glucomannan prepared from Saccharomyces cerevisiae has been shown to efficiently adsorb aflatoxins, zearalenone and fumonisins [52][53]. A feed additive that is a stabilised bacterial species of Eubacterium can detoxify trichothecenes by removal of the epoxide group in vivo and is a novel approach to mycotoxin decontamination [54].

The foregoing discussion highlights the need to develop strategies that minimise the production of mycotoxins in food commodities both before and after harvest. A knowledge of fungal ecology, toxicgenicity and food and animal production systems are required. Such an interdisciplinary understanding supports the principles of the HACCP (Hazard Analysis and Critical Control Points) approach for mycotoxin management [55]. However, in developing countries, these processes may not be economically feasible in many high-risk regions and that is why it is often more prudent to look for other intervention strategies. In many African countries the mycotoxin problem is related to insufficient food and the reliance on a single crop (eg. maize) [29]. In these situations, with high daily intake of the cereal, only moderate mycotoxin contamination levels are required to exceed recommended tolerable intake for mycotoxins. It has been demonstrated in animal studies and in some human studies that oltipraz is an effective agent in blocking aflatoxin adduct formation and it is believed that this predominantly reflects induction of aflatoxin detoxifying enzymes [24]. Nevertheless, the multi-phase and long-term development of hepatocellular carcinoma (HCC) may limit the

effectiveness of chemotherapeutic agents It was the considered view of WHO that because of the interaction of aflatoxin with hepatitis B virus in the development of HCC, the most cost-effective approach to intervention is vaccination against viral infection [8].

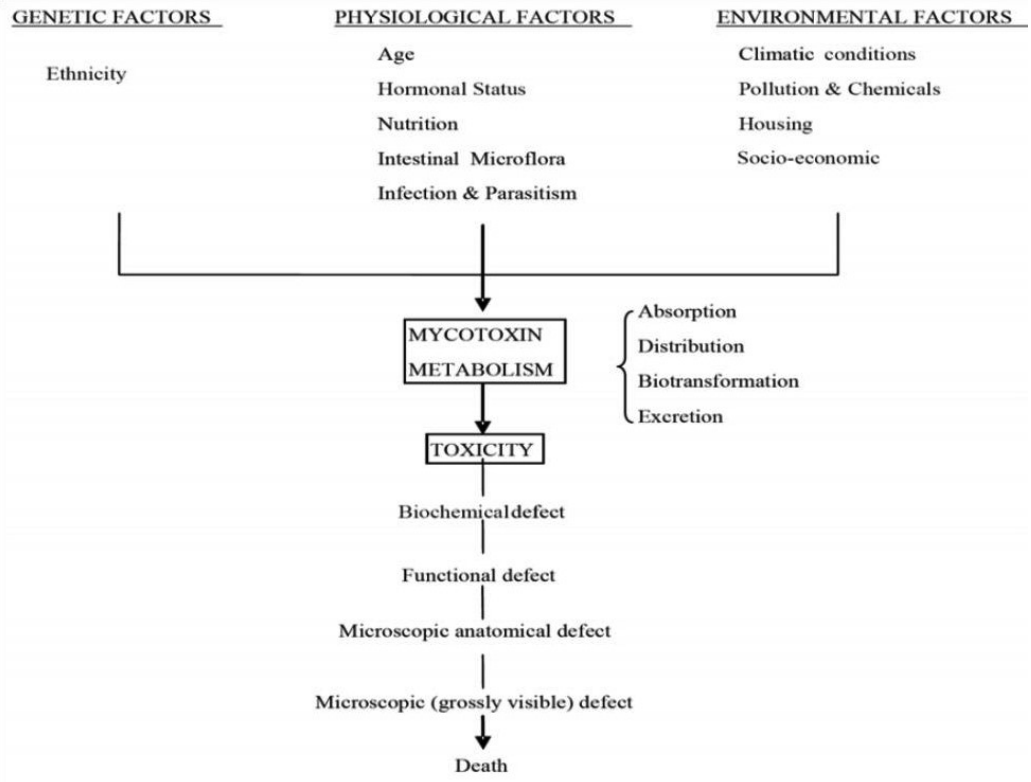

Figure 1. *A simplified representation of some general relationships in a mycotoxicosis.*

Economic impact

Mycotoxin contamination of the food chain has a major economic impact. However, the insidious nature of many mycotoxicoses make it difficult to estimate incidence and cost [47]. In addition to crop losses and reduced animal productivity, costs are derived from the efforts made by producers and distributors to counteract their initial loss, the cost of improved technologies for production, storage and transport, the cost of analytical testing, especially as

detection or regulations become more stringent and the development of sampling plans [56]. There is also a considerable cost to society as a whole, in terms of monitoring; extra handling and distribution costs; increased processing costs and loss of consumer confidence in the safety of food products. It is estimated that in developing countries, the greatest economic impact is associated with human health [12]. Delineating economic impact reflects the complexity of a mycotoxin contamination within the food chain.

A comprehensive risk and economic analysis of lowering the acceptable levels for fumonisins and aflatoxin in world trade demonstrated that the United States would experience significant economic losses from tighter controls [57]. The developing countries, China and Argentina were more likely to experience greater economic losses than sub-Sahara Africa. The disturbing outcome of this detailed analysis was that tighter controls were unlikely to decrease health risks and may have the opposite effect [57]. In other words, very stringent international trade regulations could lead to the situation were exporting countries, especially developing countries, would retain higher risk commodities which would subsequently be available for their own populations; communities which are already exposed to higher levels of mycotoxins than consumers in developed countries.

Conclusion

Mycotoxins are a food safety risk globally. International risk assessments have been performed by JECFA for aflatoxin B1, aflatoxin M1, DON, fumonisins, ochratoxin A, T-2 toxin and HT-2 toxin [58][59]. These analyses indicate that health risks from mycotoxins are generally orders of magnitude lower in developed countries that for populations from developing regions. The scope

of the mycotoxin problem is readily understood when it is appreciated that there are many thousand secondaries fungal metabolites, the vast majority of which have not been tested for toxicity or associated with disease outbreaks [60]. In developing countries, it is likely that consumers will be confronted with a diet that contains a low level of toxin and in many cases, there may be other toxins present. For example, aflatoxins, fumonisins, DON and zearalenone may occur together in the same grain; many fungi produce several mycotoxins simultaneously, especially Fusarium species [61]. Co-occurrence of mycotoxins is of special concern, for instance, in the case of fumonisins (a potent cancer promoter) and aflatoxin (a potent human carcinogen) where a complimentary toxicity mechanism of action occurs [11]. In Africa and Asia, the co-occurrence of these mycotoxins is common and a significant percentage of the population is infected with for Hepatitis B or C which leads to the conclusion that mycotoxins in these regions can have devastating human health effects. Implicit with these conclusions are the existence of syndromes of apparently unknown aetiology and epidemiology that may involve mycotoxins and the difficulty of establishing "no effect" levels for mycotoxins.

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