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## Aflatoxin contamination of foodstuffs: Its health implications in Sub-Saharan Africa

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### ABSTRACT

Aflatoxins are both toxic and carcinogenic. They are produced by *Aspergillus flavus* and *Aspergillus parasiticus*. Food contamination by these toxins has become a serious health issue. In Africa, some of the factors responsible for it include favorable weather condition; temperature of between 24°C and 35°C and moisture level of about 7% in many parts, poverty, ignorance, drought and social problems. Aflatoxin production may occur during harvest, storage and food processing, although pre-harvest food contamination has also been reported. The presence of these toxins modulates the metabolism and status of many important micronutrients such as Zn, Se, vitamin A and vitamin E; vital ingredients in maintaining healthy immune system and normal development, making the relationship between aflatoxin contamination of food and immune suppression and stunted growth quite understandable. The association between aflatoxin in food and some of the foremost risk factors (under-weight, Zn, Fe & vitamin A deficiencies) described by World Health Organization to contribute to burden of disease in disability-adjusted life years in Africa makes this problem a probable factor, responsible for the short lifespan prevailing in this region. Some other health implications include delay in recovering from protein malnutrition and hepatocellular carcinoma. Moreover in several nations in the sub-region, HBV (hepatitis B virus) & HCV (hepatitis C virus) affect about 20% of the population, their co-occurrence with aflatoxins have been identified to increase aflatoxin potency by about 30 times and the risk of HBV infection which results in hepatocellular carcinoma from 5 to 60. The objective of this review is to examine the magnitude of this problem by identifying its causes, attending effects and proffer possible intervention strategy which may be of assistance in bringing aflatoxin contamination of food to a tolerable level in the sub-Saharan Africa.

**Key words:** aflatoxin; immunosuppression; malnutrition; cancer; infectious diseases.

### INTRODUCTION

Sub-Saharan Africa is a geographical term that describes the area of Africa that lies south of the Sahara, which may include African countries that lie fully or partially south of the Sahara. It is a region faced with diverse socio-economic problems due to a low gross domestic product (GDP), wars and a number of health problems. The health problems prompted the World Health Organization (WHO) to convene a conference - the Bamako initiatives in 1987: the focus of this conference was to reshape the health policy of Sub-Saharan Africa. Although this conference was able to greatly increase accessibility to health care through community-based health care reform,

thereby improving access to health care and create a more efficient provision of health services yet two decades later some aspects of preventive medicine, which address food contamination and safety, remain largely unattended to [1-3].

The problem or adverse health effect of mycotoxin contamination of foods is not new; it has been on for centuries. It was indeed a world-wide problem, but this has largely been addressed in the developed world, where modern agricultural practices and legislation against unregulated food processing and marketing system have enormously reduced aflatoxins contamination of food leading to eradication of many of the health effects associated with it. Shepherd [4] in complete agreement with this observation stated that even though sale of food exceeding maximum tolerated levels of aflatoxins have been legislated against in a number of countries, many of the developing countries to which many Africa countries belong are not included in this group. This is so because they do not have laws against food safety compliance and most of this unsafe food are locally consumed by the producers or sold at the local market where these laws may not be enforced.

The serious health implication which can arise from the consumption of produce contaminated by aflatoxin was demonstrated by damage caused by aflatoxins exposure to human and other animals in 2004 in the Eastern part of Kenya, where over 125 deaths as well as 319 hospitalization were recorded as a result of an outbreak of aflatoxicosis [5,6]. This occurrence as well as data obtained from other studies revealed that unsafe food consumption is still a problem in sub-Saharan African and a lot of resources (material & human) as well as political will may be needed to address this problem. This review therefore sets out to highlight some of the health implications associated with aflatoxin contamination of food and proffer some methods which can be applied to eradicate this problem. This review may be timely as many of these countries are faced with health systems that lack capacity to adequately address the health issues that might arise from mycotoxin contamination of food. Moreover, the predisposing factors to aflatoxin contamination of food such as drought, soil type and insect activities are commonly found in this sub-region [7-14].

## BACKGROUND

Aflatoxins are produced principally by three strains of aspergillus: *A. flavus*; *A. nomius* and *A. parasiticus* [15-17]. They are relatively stable and toxic and include B1, B2, G1, G2, M1 and M2. Aflatoxin B1 is the most common and most potent of them all. *A. flavus* produces B1 and B2, these are widely distributed while B1, B2, G1, G2 are produced by *A. parasiticus* and are restricted to the Americas and Africa. Humans are exposed to aflatoxins [18,19] at nanogram to microgram levels daily through dietary staples like groundnut, and corn [20]. Exposure to AFM1 and M2, hydroxylated metabolites of B1 and B2 is through milk and its products in animals as well as humans [21].

The toxic effects of aflatoxin was discovered in 1960 in Britain when thousand of young turkeys, ducklings and chicks died of an unknown disease simply called "Turkey - X" disease. Histological examination showed this agent to be hepatotoxic in nature [22,23]. Seventeen compounds which make up the aflatoxins, most are metabolites of B1 and only four occur naturally (AFB1, B2 G1 and G2). The elucidation of its structure revealed that they all have basic bisfurocoumarine structure. Shortly after its discovery, aflatoxins were found to be hepatocarcinogenic as well since it could bind to and alter deoxyribonucleic acid (DNA).

## TOXICOLOGY

Metabolic activation of aflatoxin B1 from its pro-carcinogenic to carcinogenic state is essential before it can damage DNA [24-27], to achieve this, the epoxide reacts with guanine to form some adducts. These adduct or their metabolic derivatives cause heritable genetic changes which may propel a cell toward malignant transformation. Although there are various types of DNA adducts formed, the mutational spectrum of the toxin favors only one dominant genetic change which is a GC to TA transversion. It is assumed that these mutations are as a result of the guanine adduct formed since nearly all aflatoxin adducts occur at this base [28]. Cytochrome (CYP) iso-enzymes convert AFB1 to its 8, 9-epoxide, an electrophilic compound which reacts readily with DNA. The initial and predominant product (adduct) is AFB1- N7-Gua which is readily converted or depurinated to the AP (apurinic) due to unstable glycoside bond. AFB1 - N7 Gua can also suffer opening of its imidazole ring to produce chemically and biologically stable formamidopyrimidine adducts (AFB1-FAPY) [26- 31].

Of the three adducts formed, AFB1-N7 Gua is the most abundant in vivo, which correlates with many of the clinical presentations of aflatoxin exposure. This is so more for cancer formation, it is presumed, and therefore that adducts either individually or collectively is responsible for the genetic effects of AFB1. There are other adducts formed but

at a much lower levels compared to the three. AFB1 is not only converted to DNA adducts but to AFB1 - albumin adducts as well. Aflatoxin - albumin (AFB1 - alb) used an index of exposure has been reported to be related to growth faltering on one hand [27, 27, 32] and immune suppression on the other among the children.

Another important factor; genetic polymorphism of glutathione - S-transferase (GSH), the enzyme which detoxifies the epoxide by conjugating GSH to 8, 9 - epoxide has been reported to play a role in the clinical presentation of AFB1 exposure. Different subjects within same population group and same exposure level have been reported to present differently to AFB1 exposure, as a result of different expression level of this enzyme. Giving evidence to this observation in human subject is the observation made by Bailey *et al.*[31] that the mouse which has GST which is three to five times that the human is known to be resistant to AFB1.

Moreover, the microsomal mixed function enzymes, the CYP450, not only convert AFB1 to the unstable but highly reactive 8,9- epoxide, but to other reduced and oxidized products. In human the intra-species variation which has been described may result from different isoenzymes formed, expression levels as well as activities of these enzymes. In human CYP1A2, 3A4, 3A5, 3A7 have been reported to metabolize AFB1, some of the metabolic products include AFM1, AFQ1 (hydroxylated metabolites), AFB1 (demethylated metabolites) and others. Many of these are rather less toxic than AFB1. The reaction of aflatoxin - 8,9 exo epoxide to N7- guanine of DNA produces trans 8,9 - dihydro - (N-guanyl) - 9-hydroxy 1 - aflatoxin B1 (AFB1-N7-Gua), the adducts which is the biomarker that best reflects the oxidative damage to DNA by aflatoxin. Therefore the carcinogenicity of AFB1 is highly related to the level of this adduct in vivo [33] and this adduct was found also to be linearly correlated to AFB1 doses (mg/kg/day).

Although the precise mechanism of carcinogenesis of AFB1 is not fully understood the oncogenes and tumor suppressor genes have been implicated to be the critical molecular targets by AFB1, specifically these are the P53 tumor suppressor gene and ras protooncogenes. It is known that in some parts of Sub-Sahara Africa (Southern Africa), about 50% of hepatocellular carcinoma (HCC) patients where there is high aflatoxin exposure, the P53 of their liver tissue harbor a codon 249 G to T transversion which is consistent with in vitro mutagenic activity of AFB1 [34]. The P53 a transcriptional activator regulates cell cycle, plays a role in apoptosis [26, [26,35, 36] and is responsible for some types of DNA repairs.

The combine exposure to both AFB1 and HBV may act together or separately leading to selection of the hallmark P53 mutation and ultimately to HCC. HBV is one of the risk factors associated with increase incidence of HCC and liver cancer is four times more common in a patient with HBV. It has also been reported that gene products of HBV, HBX binds to and inactivates the p53 protein [37,38] thereby inhibiting P53 induced apoptosis [39]. Smela *et al.* [40] on the other hand stated that no direct interaction between P53 and HBX exists, but that this may be due to direct effect of HBX on the cell.

In another study carried out to determine the risk of individuals to HCC, using aflatoxin exposure and hepatitis B infection as risk factors, patients with positive urinary AFB1 - guanine- antigen are 3 times more likely to develop HCC, this increases to 7 times in patients with positive HBV surface antigen (HbsAg) whereas patients with the combination of both factors (AFB1-N7-guanine antigen and HbsAg) are 60 times more likely to develop HCC. Both aflatoxin exposure and hepatitis B infections are serious health issues in sub-Saharan Africa.

The hepatitis BX protein has been observed to inhibit nucleotide excision repair either by binding to repair protein or to the damage DNA itself making it possible for AFB1 adduct to persist in patients exposed to both HBV and AFB1. Some of the base excision repair enzymes occur in several polymorphisms e.g. XRCCI and subjects with 399 Gln allele have increase levels of AFB1 adducts [41]. The synergistic effect of HBV infection on AFB1 may also be due to increase aflatoxin metabolism [41]. In HBV transgenic mice, liver injury is associated with increase expression of CYP enzymes and decrease GST activity in human liver in HBV infected patients have been reported. The importance of these studies in experimental animals clearly point out the danger of unregulated aflatoxin exposure especially in an area like Sub- Saharan Africa where incidence of hepatitis B infection is also high [42]. The effects of aflatoxin on hematological parameters have also been reported [43].

#### **MAGNITUDE OF THE PROBLEM**

Due to its high potency, AFB1 is classified by international agency for research in cancer (IARC) as a group 1 carcinogen, being highly toxic (carcinogenic) not only to many animal species but humans as well [44,45]. Although

extensive reports about the contaminating effect of aflatoxins in peanuts and grains (rice and corn) worldwide, the situation is more serious in sub-Saharan Africa, where contamination is endemic [46]. It is known to contaminate various dietary staple of the sub-Saharan Africans, such as guinea corn, sorghum, millet, beans, cottonseed, melon, etc [47-49]. Aflatoxins are commonly found in improperly stored food, such that improper storage has therefore been identified as the principal cause of aflatoxin contamination of food [2,50]. Other causes such as high day or night temperature as well as high relative humidity may also encourage aflatoxin contamination of corn especially during growing season [50,51].

In addressing this issues the Joint FAO / WHO expert committee on food Additives (JECFA) has put in place risk analysis in dealing with issues of food safety. Its component parts being, risk assessment, risk management and risk communication. In Africa, the risk assessment for aflatoxins B1 contamination of food stuff was conducted using the carcinogenic potency. Data obtained showed, that there was significant health consequence as a result of intake of high exposure to contaminated foods. Although in some communities where the level of contamination is intermediate, serious health issues have also arisen as a result of high level of consumption. In West Africa, for example growth retardation and immune suppression have been identified as some of the health issues in the human populations [3]. Wagacha and Mathomi [4] are also of the opinion that agricultural produce contamination by mycotoxin in Africa is not a post - harvesting problem only but may occur prior to harvesting. And that a number of factors apart from processes involved in food production may contribute greatly to this problem especially in this sub- region. These are environmental as well as socio - economic factors. Some of the environmental causes - high humidity and high day or night temperatures are common occurrences in many parts of sub- Africa, the Northern part of this region especially is known for high temperatures for many months within a year due to the effect/impact of the Sahara Desert.

Moreover, the socio-economic problem of most communities may escalate mycotoxin (aflatoxin) contamination of food stuffs. Exposure to aflatoxin is not only through crops, milk and milk products are rich sources of aflatoxin M1 and M2 [52]. Ayalew et al. [2] have reported mycotoxin contamination of barley, sorghum, teff (*Eragrostis tef*) and wheat in Ethiopia, which they also have discovered to occur as a result of improper storage of these grains in the underground pit. A more specific aspect of storage, the effects of storage and agro ecological zone on mould incidence and aflatoxin contamination of maize obtained from traders in Uganda was the focus of the investigation carried out by Kaaya and Kuamuhangire [53]. These workers observed that although maize kernels obtained from dealers (traders) in the three agro ecological zone of Uganda had (mean) moisture content which was within recommended safe storage levels of 15% (with a lower levels found in Highland maize kernels while the higher levels were found in Mid- Attitude (moist) kernels) mycotoxin contamination of food still occurred.

Across all the agro ecological zones the most prominent fungal genera were *Aspergillus*, *Fusarium*, *Penicillium* and *Rhizopus* with *A. flavus* and *A. parasiticus* major producers of aflatoxin being the most common of the *Aspergillus* species. Invariably, aflatoxin contamination was present in all the three zones the level of contamination was highest in Mid-altitude(moist) zone of 88% followed by 78% in Mid- altitude (dry) zone and only 69% in Highland zone. More importantly, levels of aflatoxin contamination increased with storage time to the extent that levels greater than 20ppb was observed in maize samples from both Mid- altitude (dry) and Mid- altitude (moist), stored for over six months. Qualitative analysis showed AFB1, the most potent of all the aflatoxins to be the most common contamination of maize kernel in all the 3 zones.

Fungal infestation of groundnuts in Botswana was reported by Mphande et al. [54]. Raw peanuts obtained from different retail points showed fungi and mycotoxin contamination. Apart from Zygomycetes (*Absidia corymbifera* and *Rhizopus stolonifer*) which constituted about 41% of the isolated fungi present in over 98% of the peanut samples. The most prominent was *Aspergillus* species which accounted for 35% of the isolates of all 120 raw peanut samples examined for total aflatoxins 78% had aflatoxins at concentration range of 12 to 329 mg/kg more than half had concentration above 20 micro/kg, the regularly limit allowed by the World Health Organization.

In another study carried out by Siame et al. [55], the main dietary staple food of Botswana, sorghum and maize were found to be toxin contaminated, this not only reflected in foodstuffs but animal feed as well. Their report as well as others also revealed a high level of contamination of peanut butter in Botswana and Sudan [56]. Therefore the study of Mphande et al. [54] is an indication of lack of commitment of necessary bodies in addressing this issue. Peanut seems to be one of the most common heavily contaminated food in the sub-Saharan Africa. Reports of Atawodi et al. [57] obtained from a study conducted in Nigeria also showed that the contamination level of 1962 ppb (part per

billion) was detected in groundnut cake samples obtained during market survey between 1988 and 1991, during this period some grains and cereals which were of nutrient importance to human and the livestock were also slightly contaminated.

Many survey studies carried out in Nigeria have revealed that mycotoxin contamination of food is a nation-wide problem [57,58]. Ibeh et al. [58] as well as many other report findings showed that garri, yam flour, cassava flour, rice and bean, melon; foodstuffs which are consumed across the country had aflatoxin contamination of 30%, 50%, 40%, 10%, and 20% respectively [59-61].

To show the seriousness of this problem especially in Nigeria, not only locally obtained foods were contaminated but locally processed food as well as industrial products was affected. A report of study conducted in Abeokuta and Odeda Local governments of Ogun State, Nigeria by Atanda et al. [62], using two - dimensional thin layer chromatography, showed aflatoxin M1 of milk and ice cream to be in the range 2.04-4.00 mg/L. The situation in Abeokuta and Odeda Local Governments is serious because a study had earlier put the weighted mean concentration of aflatoxin M1 in milk for Africa diets to be approximately 0.002mg/L. The study of Atanda et al. [62] also revealed that human milk had 4.0 mg/L indicating that exposure to aflatoxin starts early in the Nigerian environment.

Abulu et al. [63] even stated that exposure might start earlier than this, showing that the presence of aflatoxin has been detected in cord blood. This very early exposure from intrauterine life which continues in human breast milk, supplement milk, and weaning material may therefore be an indication of the magnitude of the problem [64]. Especially as Gong et al. [65] also revealed that about ninety-nine percent of children between the ages of 9 months and 5 years were found to be aflatoxin exposed using aflatoxin - albumin adducts as index of survey an indication that the degree of contamination and variety of crops contaminated by aflatoxin reflects in the human population.

The relative severity of aflatoxin contamination among crops in the West Africa Sub-region was compared by Bandyopadhyay et al. [66]. They found out that maize, an introduced crop to this region was more heavily colonized by *Aspergillus* species, resulting in higher aflatoxin contamination than other cereals. These workers stated that maize had 4-fold and 8-fold aflatoxin contamination than sorghum (*Sorghum bicolor*) and pearl millet (*Spennisetum glaucum*) respectively. All these grains are commonly consumed in Nigeria.

Atehnkeng et al. [67] carried out their study in three agro-ecological zones (dried savannah, southern savannah in the humid south and the north guinea savannah in the drier north). They studied the incidence of aflatoxin B1 contamination of crops especially maize kernels as well as aflatoxin producing potential of members of *Aspergillus* especially the *flavi* and *Fusarium*. Study result showed that *Aspergillus flavus* (aflatoxin producer) was the most abundant with the L- strains constituting more than 90% in all districts surveyed except Ogbomoso and Mokwa districts in derived savannah and south guinea savannah respectively.

Bankole et al. [68] also confirmed moulds and aflatoxin B1 contamination of melon seeds (*Coloxythis citrullus* L) obtained from many markets in the rain forest (Ogun, Oyo, Osun) and Northern Guinea Savannah (Kaduna, Niger, Bauchi) zones of Nigeria. Field and pre-harvest contamination of maize has also been reported in Nigeria (South Western) by Bankole and Mabekoje [69]. They also reported occurrences of aflatoxin - B1 in dried yam crops in some states in Western Nigeria. Some other food-stuffs in which aflatoxin has been detected include garri (*Manihot utilis* pohl), beans (*Phaseolus lunatus*) and rice (*Oryza sativa*) (Makun et al., 2011). Aflatoxin contamination of cassava and yam chips has also been reported in two agro ecological zones of Benin Togo and Cameroon [70,71].

To compound the problem of aflatoxin contamination of food is the fact that it does not occur alone but is found in association with other mycotoxins. Ayalew et al. [2] have reported mycotoxin contamination of barley, sorghum, teff (*Eragrostis tef*) and wheat in Ethiopia. Samples analysis using high performance liquid chromatography (HPLC) or enzyme linked immunosorbent assay (ELISA) specifically showed aflatoxin (AFB1), ochratoxin (OTA), deoxy nivalenol (OOH) nivalenol (NIV) and zearalenone (ZEN) contamination of these foodstuffs. It was only AFB1 and OTA that were present in samples of all the four crops. Although AFB1 was detected in 8.8% of the 352 samples examined, and sometimes at trace amount, concentration as high as 26 mg/kg were also frequently encountered. The implication of concurrent contamination of other mycotoxin with aflatoxin is that their combined presence in foodstuffs tends to increase of potency of aflatoxin.

**HEALTH IMPLICATION:**

That aflatoxin alone may not be the cause of the health issue associated with aflatoxin exposure is the observation made by Azziz-Braumgartner *et al.* [5]. These workers demonstrated that selected subjects from the 125 deaths and 317 hospitalized patients in 2004 outbreak of aflatoxicosis showed that not only maize contamination but that hepatitis B surface antigen was associated with cases of both mortality and morbidity which occurred during this period. In Latin American an extensive region where maize serves as part of staple food, liver cancer is rare, so also in HBV (hepatitis B virus) infection. Since maize is prone to *Aspergillus* contamination, there is a high aflatoxin exposure. This may also confirm that aflatoxin exposure alone without favorable genetic or environmental factors may not be sufficient for hepatocarcinogenesis. In addition, Campbell *et al.* [72] in a comprehensive survey with a cross sectional set-up to determine risk factors for primary liver cancer observed through a survey which comprised 48 survey sites, with approximate 600 - fold aflatoxin exposure range, 39 fold liver cancer mortality rates, a 28- fold HBV surface antigen (HbsAg+) carrier prevalence and a variety of exposure range for a large number of nutritional, dietary and life-style features that primary liver cancer was unrelated to aflatoxin intake, but was positively corrected with HbsAg prevalence, plasma cholesterol, frequency of liquor consumptions and most especially mean daily intake of cadmium from foods of plant origin. Exposure to alcoholic drinks which the above study has identified to act synergistically with aflatoxin is a common problem among selected groups of people in rural Africa. To compound this problem in Tanzania is that home - made alcoholic beverages offered for sale at commercial places in Dar es Salaam were found to be aflatoxin contaminated: heavy metals content were present in these drinks as well, thereby buttressing another observation by Campbell *et al.* [72], that cadmium is well correlated with incidence of hepatocellular carcinoma in aflatoxin exposed population. In sub-Saharan Africa, exposure to toxins is not limited to foods such as grains, cereals, processed tuber, of all nineteen dietary and 30 medicinal wild plants analyzed by HPLC for aflatoxin B1 and fumonisin B1, many contained detectable levels of aflatoxin B1.

**ADVERSE EFFECTS OF AFLATOXIN IN MAN:**

Apart from hepatocellular carcinoma and many of the health problems that have been highlighted, other effects of AFB1 in human subjects include growth faltering which may eventually lead to stunting. According to Wild [73] exposure to aflatoxin starts early life, the presence of AFB1 - adducts has been reported in cord blood, also activation of AFB1 is not entirely restricted to the hepatocytes, the human placental microsomes also activate AFB1 and its high mutagenic activity has been describe [74]. Moreover, the human placenta allows passage of aflatoxin to the growing fetus. This thereby makes growth faltering a most likely manifestation since high growth rate occurs in the first five years of life.

Another study, with cross-sectional set up, carried out by Egal *et al.* [70] among 480 children between the ages of 9 months to 5 years in 4 agro-ecological zones in Benin and Togo, observed that aflatoxin exposure indicated by blood aflatoxin -albumin adducts was also associated with growth faltering. Moreover, according to Wagacha and Muthoni [3] apart from impaired growth and cancer, immunosuppression which may result in death has also been reported. An indication that some of the common health problems confronting the African countries might have been aggravated by aflatoxin exposure, especially diseases like malaria, kwashiorkor and HIV / AIDS since exposure to this toxin has been reported in many studies to compromise the immune system [75-77]. The interaction between HIV/AIDS goes beyond immune suppression, studies have shown that many of the factors which affect the rate of progression of HIV infection to AIDS are nutritional in nature [77-79] and since aflatoxin interferes with nutritional status of an individual, it is therefore likely it accelerates this rate of progression. The interference at the micronutrient level means that HIV-positive patients have additional protein requirement of about fifty percent, since aflatoxin decreases protein synthesis for up to 5 days after exposure [77, 80].

Another study was that of Turner *et al.* [81], carried out among 472 Gambian children aged 6-9 years in which these subjects were examined for aflatoxin - albumin adducts (as an index of exposure) and immune parameters such as secretory IgA in saliva, cell - mediated immunity (skin), antibody responses to rabies and pneumococcal polysaccharide vaccines. The result of their study revealed that secretory IgA was greatly decreased in children with detectable aflatoxin-albumin adducts and over 93% of these children had detectable adducts with a range of 5-456 pg/mg. Although there was no association between cell mediated immunity responses to tested antigen and aflatoxin shown adducts, the response of antibody to pneumococcal polysaccharide was weakly associated with higher levels of aflatoxin - albumin adducts. These workers were of the opinion that from the results of this study it is clear that impaired infant immune system might be a cause of high mortality from infectious diseases, a common phenomenon in the sub-Saharan Africa. A number of studies have linked exposure to aflatoxins to many other disorders e.g. jaundice, hepatic encephalopathy and human male infertility [26, 82-84].

### **BIOMARKERS OF EXPOSURE**

Most of the studies carried out in this sub-region have made use of aflatoxin - albumin adducts to detect the levels of exposure, therefore serving as biomarker of exposure. But a number of other biomarkers are available, which are urinary total aflatoxins, aflatoxin adducts in urine, aflatoxin - DNA adducts in liver as well as genetic polymorphisms of some key genes. AFB1 - albumin adducts has a longer half - life in vivo compared to urinary AFB1 - N7 guanine which reflects exposure in the last 24 hours or so. The albumin adduct can predict and reflect exposures for a longer period of time - between 2-3 months. Scholl *et al.* [85] showed a strong correlation between excretion of urinary aflatoxin nucleic acid and formation of serum albumin adduct. The two markers currently being considered reliable for short-term exposure, but they can neither predict long-term or life - time exposure nor reflect the natural pattern of exposure to aflatoxin *i.e.* seasons, manual sorting of foodstuffs and onset (age) of exposure.

Wild *et al.* [86] stated that aflatoxin-albumin adducts in peripheral blood is a reliable marker of exposure since it correlates well with AFB1 adduct in rodent liver. They therefore proposed AFB1 adduct as a sensitive indicator of risks of liver cancer developments as a result of AFB1 exposure. Therefore, since the aflatoxin-alb is a reliable biomarker, one can deduce that reports of studies emanating from the sub -region which predominantly used aflatoxin-albumin as an index of study point out the seriousness of this health issue especially as it relates to compromised immune response of the infant population. Shephard [87] is also of the opinion that even when the immune suppression is not overtly expressed it may contribute to overall burden of other infections disease facing the continent, signifying that an important way to address health problems in this region will have to include giving adequate attention to food contamination.

### **AFLATOXIN AND THE IMMUNE SYSTEM**

Other studies focused on the effects of aflatoxin on the immune system which are relevant to crop handlers in the sub-region who might be exposure to this toxin by inhalation through the nasal routes are that of Jakab *et al.* [88] and Raisuddin *et al.* [89]. Jakab *et al.* [88] studied immuno suppressive effects of AFB1 in the respiratory tracts of rats (Male Fischer 344) and mice (female Swiss) exposed to aerosol inhalation and intra-tracheal instillation. Aerosol inhalation of AFB1 (in rats) suppressed alveolar macrophage (AM) phagocytosis at dosage as low as 16.8 microgram/kg whereas intra-tracheal instillation equally suppressed AM phagocytosis but at doses in an order of magnitude greater than aerosol inhalation. Some of the other immunosuppressive effects of intra-tracheal administration were; it suppressed the release of tumor necrosis factor alpha from AMs and therefore impaired, both systemic, innate and acquired immune defenses especially suppression of peritoneal macrophage phagocytosis and the primary splenic antibody response. Raisuddin *et al.* [89] on the other hand observed an alteration of the immune response as a result of aflatoxin exposure, that it caused decreased resistance to infectious agents as well as suppression of cellular and humoral immune systems. AFB1 caused induction of thymic aplasia, reduced T- lymphocyte function and number, reduced phagocytic activity as well as decreased complement activity. Specifically in poultry and pigs, aflatoxin contamination of food caused suppression of cell-mediated immune response.

In addition, pigs born to sows fed aflatoxin contaminated feed and sensitized with *Mycobacterium tuberculosis* displayed smaller delayed cutaneous hypersensitivity reaction than pigs not exposed to aflatoxin. In broiler chickens, vitamin status as well as immunity was compromised by aflatoxin in feed.

### **ADVERSE EFFECTS OF AFLATOXIN IN DOMESTIC ANIMALS**

The health effects of aflatoxins are not restricted to men but are evident in animals especially farm animals. Among the livestock, there is a wide range of response to aflatoxin among species and biological factors like age or sex may also play some roles in their level of tolerance. Liver is the target organ among this group of animals and young animals are more susceptible, fertility is not affected in many species and it specially does not cause abortion.

Most of the animals raised on subsistence level in rural Africa have a wide range of susceptibility; the cattle are more tolerant than the swine, with the sheep being the most tolerant of the domestic animals. The young turkeys and ducklings are most sensitive to AFB1 exposure, thereby aggravating the malnutrition problem of many rural communities. The massive loss of farm birds might arise from exposure to mould infested grains or peanuts in feeds. Moreover, one other consequence of exposure of farm animals to contaminated feed is the transmission of aflatoxin in the milk of lactating cattle. And the consumption of processed milk in a variety of products has increased the exposure levels of aflatoxin in the human population in this sub-region. Atanda *et al.* [62] reported aflatoxin M1 (hydroxylated metabolite of B1) contamination of "wara" and "nono" in Abeokuta and Odeda Local Government of Ogun State, Nigeria.

A number of other animals native to Africa have been reported to be highly sensitive to aflatoxin, some of the animals in the wild which constitute a great foreign exchange earning for many countries in this region through tourism. The monkey has been reported to possess the same level of sensitivity as human (both are sensitive species), but with a wide range of interspecies sensitivity, among sub human primate. This is especially so for squirrel monkey which develops liver tumors at doses of 200 mg/kg given for a period of 13 months.

### **INTERVENTION STRATEGY**

In conclusion some of the constraints to effective management of mycotoxin contamination in sub-Saharan Africa include non-availability of toxicological data, survey data and standard analytical methods. Apart from these, economic and political factors have been described to be a hindrance in providing solutions to these problems. According to van Edmond [90] only about 77 nations have regulations against mycotoxin contamination while about 50 have no data available, most of these 50 nations are found in Africa.

Shephard *et al.* [4] is of the opinion that the problem of mycotoxin contamination of food in this region is compounded by a favorable climate condition as well as inadequate storage system. Moreover, the farming is subsistence in practice and the local markets largely unregulated, the situation which was responsible for the 2004 outbreak of aflatoxicosis in Kenya [69]. Examining broadly the issues of mycotoxin problem in Africa Wagacha and Muthomi [3] stated that conditions between pre and post harvesting period may contribute to this problem. Some of these conditions are (pre-harvest practices which in many more settings are largely primitive) moisture level, time, handling and processing of crops at harvest. Insect damage, marketing as well as transportation may impact some degree of contamination.

The way forward in addressing this problem may include adopting some of the methods that have worked well in other sub-regions of the world which are early harvesting, proper drying, sanitation, proper storage and management of insect problems. All these will essentially have to be taught to rural/local farmers who in many instances are largely illiterates and have been used to primitive methods and do not know the consequences of aflatoxin exposure. This will invariably reduce mycotoxin contamination of foods. Biological and chemical control decontamination, resistant breed of crops as well as surveillance by health workers may also be effective in Africa. Maternal education which has been described by Egal *et al.* [70] to be associated with decrease level of mycotoxin contamination in maize food may also help in solving this problem in Africa. A more holistic approach not involving food consumers alone but farm workers may also be adopted. A cohort study in countries with rare cases, of liver cancer as well as low aflatoxin exposure e.g. the Nordic countries in Europe (Sweden, Denmark and Netherlands) and the USA, have revealed that aflatoxin exposure is not considered an etiological factor for primary liver cancer except among some population with higher exposure to AFB<sub>1</sub>, a good example is the workers exposed to grain dust in animal feed processing plants. These are known to have higher risks in certain cancers. The expected risk of this population compared to the general population are liver (2.4 times), liver and biliary (2.5 times) lung cancer (1.5 - 3 times). Aflatoxin exposure therefore in farm/crop handlers as a result of occupational hazard may need to be addressed in this category of sub-Saharan Africans especially, so as to offer adequate protection by preventing exposure through inhalation.

### **CONCLUSION**

Aflatoxin contamination of food causes hepatotoxicity, carcinogenicity as well as immunosuppression. It is a serious health problem because factors which encourage the production of these toxins by *Aspergillus flavus* and *Aspergillus parasiticus* abound in Africa. Because their presence in food interferes with micronutrients absorption and status in the body, they therefore affect immunity and development. Due to the devastating effects of these agents on many communities in this sub region -with 90% aflatoxin exposure in Benin and as much as 45% of corn sampled found to be contaminated, there is need for these African nations to utilize scientific and technologic methods as well as political will to eradicate this problem. Since many of these nations are signatories to CODEX Alimentarius (WHO/FAO documents that deal with food quality in traded commodities).

Moreover mechanized food production may be helpful as subsistence production and food insecurity have made the economic enforcement of regulation impractical. Likewise, harvesting with the aid of machinery and efficient drying that does not depend on weather may also be helpful as adverse weather has been reported to cause slow and inadequate drying and subsequently increases the risk of contamination. Establishment of laboratories, equipped to test foodstuffs for the presence of aflatoxin is also encouraged. Insect damage should be controlled by pesticides or



cultural practices; this is because pockets of contamination have been reported to occur due of moisture generated through insect respiration.

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