PHYSIOLOGICAL IMPLICATIONS OF MYCOTOXICOSES IN HUMANS AND LIVESTOCK

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Preamble

Mycotoxins could be defined as highly toxic substances produced from the secondary metabolites of low molecular weights, by naturally occurring fungi like those belonging to the *Aspergillus, Fusarium* and *Penicillium* genera etc, which may contaminate agricultural commodities. Mycotoxins are known to be hardy, survive both processing and ingestion thus, finding their ways into processed foods, meat and milk products, posing health threat to humans. Currently, studies have identified about 300 types of mycotoxins that have been shown to cause mycotoxicoses in livestock and humans. But, Scientists' interests have been drawn to those that can produce toxins in agricultural commodities with potential negative impacts on health in particular and the economy at large. For example, human exposure to fumonisins alone was estimated in Canada to be 0.017-0.089µg/kg, USA 0.08 µg/kg, Switzerland 0.030 µg/kg, The Netherlands 4-220 µg/kg and South Africa 14-440 µg/kg body weight per day. Similarly, livestock exposure was exceptionally high as much as 330, 70, 38, 9 and 2 mg/kg diet in USA, Italy, Brazil, South Africa and Thailand respectively. These exposure estimates could vary considerably due to the agricultural commodities tested, source, extent of consumption and prevalence of the fungi in the areas. In each case, mortality and morbidity were suspected and recorded (WHO, 2000). In a related trend, if the fumonisins standard (safe level) of 0.5mg/kg in agricultural commodity was adopted worldwide, total export losses may exceed $300m annually.

More so, export losses from aflatoxins in groundnut alone may exceed $450m/annual (Guerzoni, 2008).

The commonest of these mycotoxins that are prevalent in Nigeria vis-à-vis Africa are:

i. **Aflatoxins.** They are metabolites produced by *Aspergillus flavus* and *A. parasiticus* They are the most potent hepatocarcinogenic substances that have been proved to be genotoxic by several Scientists;

ii. **Fumonisins.** These are produced by *Fasarium* species particularly *F. verticillioides.* They are carcinogenic, hepatotoxic and immunosuppressive;

iii. **Zearalenone.** This is produced by various species of *Fusarium* especially, *F. culmorum* and *F. graminearum.* It is significantly toxic to the reproductive system with oestrogenous action probably due to its similarity in chemical structure to the female sex hormones-oestrogen;

iv. **Deoxynivalenol.** This is also referred to as Vomitoxin and it is produced by several species of *Fusarium.* It has been associated with the outbreak of acute gastrointestinal illness in humans;

v. **Ochratoxins.** They are produced by *Penicilluim verrucosum* and *A. ochraceus.* They are carcinogenic and nephrotoxic;

vi. **Tricothecenes.** These are group of metabolites produced by *Fusarium, Stachybotrys* and *Cephalosporium* species. This group notably causes dermotoxicity, immunotoxicity and gastrointestinal disturbances;

vii. **Citrinin.** This is a nephrotoxin produced by *Penicillium* and *Aspergillus* species. Renal damage, vasodilatation and bronchial constriction are some of the health effects associated with this toxin;

viii. **Satratoxin H.** This is a macrocyclic tricothecene produced by *Stachybotrys chartarum, Trichoderma viridi* and other fungi. High doses or chronic low doses are lethal. This toxin is abortogenic in animals and is believed to alter immune system function and makes affected individuals more susceptible to opportunistic infection;

ix. **Gliotoxin.** This is an immunosuppressive toxin produced by species of *Alternaria, Penicillium* and *Aspergillus*;

x. **Patulin.** This is a mycotoxin produced by *Penicillium, Aspergillus* and a number of other genera of fungi. It is believed to cause hemorrhaging in the brain and lungs and is usually associated with apple and grape spoilage and

xi. **Sterigmatocystin.** is a nephrotoxin and a hepatotoxin produced by *Aspergillus versicolor*. This toxin is also considered to be carcinogenic.

Significant accumulations of these mycotoxins in agricultural commodities depend on favourable climatic conditions such as humidity and temperature, geographic factors, seasonal variations and the agricultural practices adopted. Interestingly, no mater the strict adherence to the agronomical practices of these agricultural commodities, they would still be infected in one way or the other. But the quantity might not be able to illicit pathological and physiological changes when such commodities are consumed. For instance, maize has been reported to be the only commodity that contains significant amounts of fumonisins both in the field and storage. In a like manner, aflatoxins are considered ubiquitous in groundnut and to some extent maize. Essentially, both of these agricultural commodities are staple foods for man and feed ingredients for livestock. Thus, the possibility for their occurrences in foods and feeds is amply high with frightening deleterious health hazards.

Consequently, their global occurrence is considered to be a major risk factor, especially as much as about 25% of the world's agricultural commodities are annually infected with significant financial losses as well as serious repercussions on human and livestock health. Based on these, mycotoxins risk assessment and management agencies all over the world, developed uniform regulations worldwide for food- and feed-borne mycotoxin contamination. Such regulations stipulated maximum tolerant levels for aflatoxins and fumonisins, which are believed to be the most prevalent mycotoxins in human foods and livestock feeds.

Table 1: National Maximum Tolerated Levels for Aflatoxins in Human Foods

Nation	Total Aflatoxins standard in food (µg/kg)
Australia	5.0
China	20
EU (Harmonized)	4.0
Germany	4.0
Guatemala	20
India	30
Ireland	30
Kenya	20
Taiwan	50

Source: CAST, 2003.

Table 2: Recommended Maximum Tolerated Levels for Fumonisins in Human foods

Product	Total Fumonisins standard in food (ppm/kg)
Degermed dry milled corn products with < 2.25% fat content	2.0

Whole or partially degermed dry milled corn products with ≤ 2.25% fat content	4.0
Dry milled corn bran	4.0
Cleaned corn intended for masa production	4.0
Cleaned corn intended for popcorn	3.0

Source: FDA, 2001.

Table 3: Recommended Maximum Tolerated Levels for Fumonisins in Livestock Feeds

Corn and corn-products intended for:	Total Fumonisins Standard in Feed (ppm/kg)
Equids and Rabbits	5.0 (Not more than 20% of diet)
Swine and catfish	20 (Not more than 50% of diet)
Lactating ruminants, minks and laying birds	30 (Not more than 50% of diet)
Broilers	100 (Not more than 50% of diet)
Other species of livestock including pets	10 (Not more than 20% of diet)

Source: FDA, 2001.

Unfortunately, these mycotoxins have been shown to be stable to food or feed processing methods, which undoubtedly would be consumed and present health hazards. In Africa therefore, it becomes a pitiable scenario as poverty keeps compelling some households to consume potentially mycotoxin-containing foods rather than food grading and discarding the unwholesome ones. This threat becomes worse off when feed manufacturers utilize these stale feed ingredients in livestock feed production. That is, humans will be exposed to mycotoxins directly from the infected foods and indirectly through the livestock products. Although mycotoxin accumulation in livestock products like eggs, tissues, milk, carcass and others could be insignificant, its gradual consumption and residual accumulation may be high enough to illicit symptoms characterized by pathological and physiological changes.

Symptoms of Mycotoxicoses

Mycotoxicoses could be defined as a disease outbreak that is commonly associated with the ingestion of mycotoxins or inhalation of spores produced by fungi. The appearance of mycotoxicoses symptoms depends on the level of contamination, length of exposure, type of mycotoxin, degree of combination with several other mycotoxins, individual differences, species-specific resistance, sex, pre-existing pathological and physiological status of the victim. The synergistic effects associated with several other factors such as genetics, diet, and interactions with other toxins have been poorly studied. Therefore, it is possible that vitamin deficiency, caloric deprivation, alcohol abuse, and infectious disease status can all have compounded effects with mycotoxins. In turn, mycotoxins have the potential for both acute and chronic health effects through ingestion, skin contact and inhalation. These toxins can enter the blood stream and lymphatic system and inhibit protein synthesis, damage macrophage systems, particle clearance of the lung and increase sensitivity to opportunistic infections. If symptoms appear within a short period of less than 7 days of contamination, it is termed "acute mycotoxicoses" but, if the interval between contamination and appearance of the symptoms persist longer, it is termed "chronic mycotoxicoses". In acute cases, victim may die if adequate treatment measures are not taken whereas, in chronic cases, the victim may live longer though with protracted illnesses. In any case, the victim should consult medical or veterinary doctor for prompt diagnosis based on the observed symptoms.

Mycotoxicoses symptoms in livestock as well as humans could persist in the form of:

(i) General body weakness
(ii) Inappetence
(iii) Weight loss
(xii) Cyanosis
(xiii) Oedema
(xiv) Heart hypertrophy

(iv) Immunosuppression (xv) Abortion

(v) Lethargy (xvi) Dyspnoea

(vi) Abdominal pains

(vii) Organ (e.g. brain, kidney, liver etc) lesions/haemorrage

(viii) Diarrhoea (xvii) Convulsion

(ix) Head pressing (xviii) sudden death

(x) Fibrosis (xix) Hyperplasia

(xi) Alimentary Toxic Aleukia

All of these could be diagnosed through the following:

(i) Haematological analyses (v) Autopsy

(ii) Biochemical analyses (vi) Histopathochemical analyses

(iii) Urinalyses (vii) Radiography

(iv) Biopsy (v) Necropsy (viii) Radiochemical analyses

Following detailed diagnosis and clear interpretation of the clinical signs, the case could be referred to as:

(i) Hepatotoxic: when the livers are damaged;

(ii) Nephrotoxic: if it involves the kidneys malfunctioning;

(iii) Cardiotoxic: in relation to heart dysfunctioning;

(iv) Embryotoxic: if mummification, abortion or miscarriage is observed;

(v) Immunotoxic: in cases associated with dysfunctional immune response to stimuli;

(vi) Genotoxic: when there is observed gene (cell) alteration or mutation;

(vi) Leukoencephalomalacia syndrome: when there is observed brain lesion or haemorrage;

(vii) Pulmonary oedema syndrome: if there is observed hypertrophy of the pulmonary arterioles;

(viii) Dermotoxic: when the fur, hair, wool, skin is affected or

(ix) Neurotoxic: if the central nervous system is distorted, resulting in incoordination, convulsion and death of the victim.

These clinical signs could be more complex to diagnose, if there are synergistic mycotoxicity due to the presence of a particular mycotoxin in a food or feed stuff that is simultaneously contaminated with other important agricultural toxins. This phenomenon explains the ambiguity of evaluating human or livestock health risks. Meanwhile, human exposure as demonstrated by the occurrence of some mycotoxins in maize intended for human and livestock consumption is very common worldwide.

However, there will be considerable differences in the extent of human exposure between maize-growing regions especially, when comparing fully developed and developing countries of the world. For instance, human consumption of maize and its products in USA, Canada and Western Europe is modest compared to Africa, South-Central America and Asia. Where many people derive a higher percentage of their calories from maize believed to be highly contaminated. I have only cited examples with maize, same is true with other crops that are suitable medium for fungal growth e.g. groundnut, rye, wheat, barley, oats etc. As a result, there would be high incidences of mycotoxicoses due to high levels of exposure and spread in human foods and livestock feeds.

Incidence of mycotoxicoses

A number of surveys on the natural occurrence of mycotoxin in maize and maize-based foods and feeds showed that 60% of the 5211 samples analysed was contaminated. The highest

incidence of contamination was in Oceania (82% of 82 samples) followed by Africa (77% of 383 samples), Latin America (85% of 266 samples), North America (63% of 1662 samples), Europe (53% of 1918 samples) and Asia (52% of 900 samples). Maize feeds were recorded to be highest (82% of 1112 samples) followed by ground maize products like flour, grits, polenta, semolina and gluten (73% of 517 samples), maize kernels (52% of 2525 samples) and miscellaneous maize foods (40% of 892 samples).

Apart from maize and maize products, mycotoxins were also found in other food products such as rice (Abbas *et al.,* 1998), asparagus (Logrieca *et al.,* 1998) beer (Torres *et al.,* 1998 and sorghum (Shetty and Bhat, 1997). Whereas, they were not found in wheat, rye, barley and oat (Meister *et al.,* 1996).

Suspected and recorded cases of mycotoxicoses incidences in humans and livestock have been documented particularly in countries were maize and groundnuts are staple foods. Such countries are China, Italy, Africa, India, Kenya and USA.

Humans

Africa

Available studies showed some relationship between oesophageal cancer rates and occurrence of mycotoxins in Transkei, South Africa (Makaula *et al.,* 1996). The incidence was very high among the black population and was higher in both sexes in Butterworth and Kentani Districts compared to Bizana and Lusikisiki Districts (IARC, 1993).

These incidences could be attributed to both Districts dependence on home-grown maize that ranges between 50 and 100% yearly supply which is supplemented with commercial or imported sources. They consume maize in form of porridge and the adults specifically also drink beer deliberately made from mouldy maize that would have been discarded. Such maize was

found to contain up to 118mg/kg mycotoxins culminating in 30mg/litre of beer made from the wort (Scott *et al.,* 1995).

In some of these cases, synergic mycotoxic activities between fumonisns, deoxynivalenol and zearalenone was observed as *F. graminearum* and *F. verticillioides* were detected by Marasas *et al.* (1979b), in the home-grown maize intended for human consumption.

More recently, a case study conducted by Sydenham *et al.* (1990b) confirmed that deoxynivalenol and zearalenone levels were significantly higher in the home-grown maize. Cancer Registry data according to Makaula *et al.* (1996) showed that Transkei, South Africa have consistently had high rates of oesophageal cancer since 1955.

China

In China, maize is a staple food consumed by many people particularly when processed into varieties of products. This could be possibly why mortality rates recorded among males in Linxian and Cixian in Henan Provinces ranged between 26-36 per 100,000 people in low-risk counties and 76-161 per 100,000 people in high-risk counties (Yoshizawa *et al.,* 1994). Mean values of 0.87mg mycotoxin/kg maize product in high-risk counties and 0.89mg/kg in low-risk counties were discovered. Although Zhen (1984) stated that the mycological data were fragmentary and difficult to evaluate in these areas, it was obvious that there were confirmed oesophageal and liver cancers emanating from mycotoxicoses.

Italy

According to Franceschi *et al.* (1990), Pordenone Province in the Northeast of Italy has the highest mortality rate for oral, pharyngeal and oesophageal cancers in Italy and amongst the highest in Europe. The risk factors identified were alcohol and tobacco use. Significant mortality

associated with maize consumption was found for oral cancer (179 cases), pharyngeal cancer (1970 cases) and oesophageal cancer (68 cases) as well as 505 hospital control cases.

The evaluated risk of upper digestive tract cancer was however limited to those consuming more than 42 weekly drinks of alcohol. The analysis was somewhat restricted to men only and the level of mycotoxin contamination was not available thus, the possibility of bias report can not be excluded in this observatory survey. It is worthy of note that maize is locally produced and eaten as cooked maize meal (polenta) which was reported to contain 0.15 – 3.76mg mycotoxin per kilogram (Pascale *et al.,* 1995).

India

There was a reported case of disease outbreak in India which Bhat *et al.* (1997) stated was characterized by abdominal pains, borborygmi and diarrhoea in a sect of people that were suspected to have consumed food borne mycotoxins.

Kenya

Notably severe cases of aflatoxin ingestion in 2004 in Kenya, 125 people died and nearly 200 others were treated after eating aflatoxin contaminated maize. The deaths were mainly associated with home-grown maize that had not been treated with fungicides or properly dried before storage. Due to food shortages at the time, farmers may have been harvesting maize earlier than normal to prevent thefts from their fields, so that the grain had not fully matured and was more susceptible to infection (Lewis *et al*., 2005).

USA

Hendricks (1999) speculated that the consumption of maize from the 1999 maize crop season might be associated with the observed cluster of birth defects among residents in Brownsville, Texas, USA.

It will not be enough to infer that only these countries are most susceptible and exposed to mycotoxins, just that there are little or no available reports on suspected or recorded cases elsewhere. Who knows why the life span of humans all over the world keeps deteriorating? Who can explain why the mortality rate among children worldwide keeps increasing per day? What could be responsible for high infertility rates among human race in the world today?

Therefore, suspected mycotoxicoses cases should be taken to the hospitals or other appropriate health care delivery centers where proper records of the victims, history, hospital diagnosis, treatments procedure adopted and dose responses would be kept. This will elucidate the level of incidences and awareness as a measure to proffer answers to some of the preceding questions raised in this chapter, whose answers could be simply "how mycotoxin-free is what you eat?

To further buttress the possibility of mycotoxicoses incidences through food in humans, non-human primates were deliberately studied by Kriek *et al.* (1981) and recorded 66.7% mortality in baboons fed mycotoxin-containing food. Similarly, vervet monkeys were also investigated and Jaskiewicz *et al.* (1987a) observed various degrees of toxic hepatosis, increase in serum cholesterol, plasma fibrinogen and blood coagulation factor VII at a dose of 0.3mg mycotoxin per kilogram body weight per day. Again, who knows if this dose would be lethal in humans? Since extrapolations could be drawn from such studies because we are all primates.

Livestock

Mycotoxins are known to be consumed by livestock through contaminated feed ingredients. They are probably the causative agents or suspected contributing factors in farm animal diseases. Therefore, efforts are being made by several researchers to understand the

kinetics and metabolism of these mycotoxins in ruminants, avian, swine, equine and rodents among a host of other laboratory animals, plants and some micro organisms.

Ruminant

In a study using beef cattle fed mycotoxin culture materials, Smith and Thakur (1996) found out that the majority of mycotoxin dose was recovered unmetabolised in faeces and only traces were detected in the blood and urine. Similarly, Prelusky *et al.* (1995) did not find mycotoxin or known metabolites in the plasma following a single gavage of 1 to 5mg/kg body weight in cows. This indicates no or very limited bioavailability in ruminants probably due to the rumen metabolic activities involving myriads of micro organisms with high kinetics and metabolism potentials.

In dairy cows, systemic absorption based on plasma levels and accumulation of radiolabelled compounds in tissues was estimated to be less than 1.0% of the original dose (Prelusky *et al.,* 1996a; Vudathala *et al.* 1994; Scott *et al.* 1994). The carry-over rate of mycotoxin into the milk reached maximum of a negligible level of 0.11% when Hammer *et al.* (1996) administered mycotoxin intravenously to lactating cows. On the other hand, no detection of mycotoxin in the cows' milk at all when Richard *et al.* (1996) and Scott *et al.* (1994) conducted similar studies.

However, some studies have demonstrated that feeding highly contaminated feed stuff to ruminants could result in poor performance, with regard to low feed intake and weight gain. Possibly, this could be why a study by Ogunlade *et al.* (2005) suggested that highly Fusarium-infected maize stovers should be avoided in sheep diets.

Avian

Mycotoxins when dosed orally are poorly absorbed by chickens and Prelusky *et al.* (1996a) reported that only trace amounts of mycotoxins were recorded in the tissues and no residues were recorded at all in the eggs. However, injection of purified mycotoxin into fertile chicken eggs resulted in time- and dose-dependent embryopathic and embryocidal effects (Javed *et al.* 1993b). The embryonic changes involved hydrocephalus, enlarged beaks and elongated necks as well as pathological changes noted in most organ systems. But at low mycotoxin dose (0.72μg/ml), stimulation of chick embryo development was observed.

Several studies revealed that mycotoxin-contaminated feed is capable of inducing avian diseases. The clinical signs of such diseases are often diarrhoea, weight loss, increase liver weight, poor performance and immunosuppression.

Immunosuppression in chickens was observed when Marijanovic *et al.* (1991) fed birds with maize-contaminated mycotoxins. In a related study, Espada *et al.* (1997) observed reduced spleen and bursa weights as well as altered haematological parameters when broiler chicks were fed diets containing 10mg of pure mycotoxin/kg diet. Mycotoxins greater than 1.8 μg/ml, inhibited reagregation and growth of chicken embryo neural retina cells which is commonly used in *in vitro* assay for screening potential developmental toxins (Bradlaw *et al.,* 1994).

Effects of mycotoxins in fertile chicken eggs similar to those reported by Javed *et al.* (1993b) was also discovered by Bacon *et al.* (1995), who in addition reported synergistic toxic response due to co-injection of different mycotoxins. In a more detailed study, Zacharias *et al.* (1996) reported that morphological changes due to direct administration of mycotoxins to chick embryo were correlated with inhibition of glycosphingolipid biosynthesis.

Swine

The first report of a disease outbreak in pigs due to mycotoxicoses was in 1981. The disease was referred to as porcine pulmonary oedema syndrome (Kriek *et al.,* 1981). The clinical signs were classically dyspnoea, weakness, cyanosis and sudden death. In a necropsy examination, the pigs could also exhibit varying degrees of interstitial and interlobular oedema, lung oedema, pulmonary oedema as well as hydrothorax with varying amounts of clear yellow fluid accumulation in the pleural cavity.

In a more complex mycotoxicoses in pigs, toxic hepatosis may occur concurrently with porcine pulmonary oedema, in which case the liver would contain multiple foci of coagulative necrosis that may not show zonal distribution across the three zones of the liver. On the other hand, nodular hyperplasia could be observed. According to Colvin *et al.* (1993), cardiac failure is a well-known physiological mechanism inducing altered pulmonary haemodynamics which could result in pulmonary oedema syndrome. That is, there would be significant changes in oxygen consumption and several haemodynamic parameters emanating from hypoxic vasoconstriction otherwise known as pulmonary hypertension.

Typically in pigs, the tissues that are mostly the targets of mycotoxicoses are liver, lungs, pancreas, heart, kidney, pulmonary intravascular macrophages and oesophagus. In any case, altered growth and changes in selected haematological parameters are bound to be observed. There is a confirmed dose-response relationship between the ratio of free sphinganine to free sphingosine in serum as well as tissues and the amount of mycotoxin ingested by pigs. Based on this, Riley *et al.* (1994c) proposed that the ratio of free sphinganine to free sphingosine and the

presence of elevated levels of free sphinganine in serum, urine and tissue could be used as indicators for ingestion of mycotoxins by livestock.

Equine

In horses, mycotoxicoses has been known to be the cause of equine leukoencephalomalacia syndrome since the 19th century as a sporadically occurring condition. This disease condition is characterized by the presence of liquefactive necrotic lesions in the white matter of the horse's cerebrum. This fatal mycotoxic disease where there is persistent brain lesions or haemorrhage apparently occur only in horses, donkeys and ponies.

Other pathological changes of this disease include lethargy, head pressing, inappetence, convulsion and sudden death. Further diagnostic procedure could reveal elevated serum enzyme levels that are preceded by elevation in the serum sphinganine to sphingosine ratio which could be indicative of liver damage (Wilson *et al.,* 1992). This serum enzymes levels often times return to near normal concentrations in the animal's system probably due to the physiological status and partly due to dosage of the mycotoxin. But would usually increase markedly immediately, prior to or at the onset of behavioral changes.

Besides the outbreak of this syndrome in horses, donkeys and ponies, histopathlogical abnormalities in livers and kidneys have been reported (Caramelli *et al.,* 1993). Equine leukoencephalomalacia syndrome concurrent with significant liver disease has been observed in horses and ponies fed feeds naturally contaminated with mycotoxins at low concentrations (Ross *et al.,* 1993). The development of brain lesions in the absence of major liver lesions does not preclude the biochemical dysfunction in non-brain tissue from contributing to the brain lesions.

The lowest mycotoxin dose that has resulted in this disease syndrome is 22mg/kg diet (Wilson *et al.,* 1992). In a controlled study, analysis of feeds from confirmed cases of this

disease greater than 10mg/kg diet, was associated with increased risk of development of the syndrome whereas, a concentration less than 6mg/kg diet was not (Ross, 1994).

In a study by National Veterinary Services Laboratory of the US Animal and Plant Health Inspection Agency in 1995, horses fed 15mg mycotoxin/kg diet did not exhibit any clinical signs or altered serum biochemical parameters after 150 days. A similar result was observed when Wang *et al.* (1992) fed ponies with a diet containing the same concentrations. Consequently, the minimum toxic dose in equine appears to be less than 22 mg/kg diet but greater than 15mg/kg diet.

Rodents

Rabbits seem apparently insusceptible to micro doses of mycotoxins especially when dosed orally for a relatively short period. But, Idahor *et al.* (2008) observed gradual decrease in sperm production rates, final live weights, feed consumption and body weight gain concomitantly with increasing mycotoxin concentration of 1.7, 1.8 and 1.9ppm per kg diet. In another study, Idahor *et al.* (2008) reported that there were no evidences of mycotoxins at 1.9mg/kg diet crossing the placenta to cause developmental abnormalities in the foetuses examined at the first trimester. It was speculated that there might have been some damages on the physiological status of the rabbits and possibly gradual accumulation of the mycotoxins in the carcasses. This might in turn pose residual health hazard to humans when consumed. In a similar study, Ogunlade *et al.* (2004) reported sufficient evidences of carcinogenicity and toxicity at micro doses of 1650-1990μg mycotoxin per kg diet. But, did not elicit any negative effects on the rabbit's blood cellular components, serum protein metabolism and serum enzymes activities. On the other hand, Ewuola *et al.* (2003) demonstrated that micro doses of mycotoxins can induce physiological and pathological damages in rabbits by reducing the feed intake with

resultant effects on body weight gain. The report stated that at 1.69, 1.82 and 1.90 ppm mycotoxins in diets, there were observed mild carcinogenic effects on the livers, kidneys and causing mucosal erosion as well as cell proliferation of the stomach, small intestinal and caecal tunica mucosa. Pregnant New Zealand White rabbits are speculated to be very sensitive to the toxic effects of mycotoxins and that maternal toxicity was observed at daily gavage doses of 0.25mg/kg body weight.

In mice, dose-dependent increase in apoptosis both in the livers and kidneys were observed at 0.25-6.25mg mycotoxin per kg body weight. Also, there were observed effects of mycotoxicoses on bone marrow and adrenals at 1-75mg mycotoxin per kg body weight. On the contrary however, US NTP (1999) confirmed the report of Voss *et al.* (1995) that only the liver was a target organ in mice. It is believed that mice are not as sensitive to mycotoxicoses as rats and that female mice are more affected at lower doses than the males. Gross *et al.* (1994) observed maternal toxicity and foetal developmental abnormalities between gestation days 7 and 15 at more than 12.5mg mycotoxin per kg body weight.

Unlike in mice, rat kidneys are also a target organ and the male rats are more susceptible to mycotoxins at lower doses than the females (Voss *et al.,* 1993). Renal lesions, significant depression in body weights as well as feed consumption, hydropic swelling, hyaline droplet accumulation, fibrosis, bile duct proliferation, single cell necrosis and increased mitotic figures are the most prevailing physiological and pathological changes that could be observed in rats following mycotoxins ingestion. At the mean time, it is believed that mycotoxins do not cause reproductive, developmental and neonatal toxicity in rats even if it crosses the blood-brain barrier.

Other Species

In some studies involving catfish and trout, mycotoxins were found to illicit elevated sphinganine levels and ratios in tissues including serum. In all the cases where toxicity was obvious, livers, kidneys or homologous organs were involved (Meredith *et al.,* 1998; Goel *et al.,* 1994; Brown *et al.,* 1994).

It might interest you to know that mycotoxins are suspected to be phytotoxic and virulent in plants. They were discovered to reduce chlorophyll synthesis in duckweed fronds *Lemma minor* (Vesonder *et al.,* 1992), cause photobleaching in Jimsonweed leaves *Datura stramonium* (Abbas *et al.,* 1993), cause leaf necrosis, shoot and root lengths reduction as well as dry mass in tomato seedlings (Lamprecht *et al.,* 1994) and reduce radicle elongation, seed amylase production, shoot and root lengths as well as dry mass in maize (Doehlert *et al.,* 1994). Mycotoxins were found to disrupt the synthesis of sphingolipids in all the plants and played an important role in the pathogenicity of maize in particular.

More interestingly were the reports of mycotoxicoses in micro organisms. There were evidences of genotoxicity in *Vibrio fischeri* at 5-20µg of mycotoxins per milliliter (Sun and Stahr, 1993).

At 25-100mg/litre, Kaneshiro *et al.* (1992) observed altered sphingolipid precursors in *Pichia ciferri,* depressed growth in *Rhodotorula* species. While Wu *et al.* (1995) recorded cell growth inhibition in *Saccharomyces cerevisiae.*

Meanwhile, Becker *et al.* (1997) using 36-72mg/litre did not observe growth inhibition of some Gram-positive and Gram-negative bacteria. Similarly, Bothast *et al.* (1992) reported that mycotoxin did not affect ethanol production by *S. cerevisiae* in maize distillers wash. It was speculated that some micro organisms can metabolise these mycotoxins in diverse ways. Thus, assuring mankind of natural cleansing mechanisms of the environment. Little wonder the Bini

tribe (Edo) in Nigeria believes that "the naturality of man's environment determines his longevity"… so, safe guard your environment against mouldy foods and feeds for your healthy living!

NOTE:

Despite all these suspected and recorded cases of the incidences of mycotoxicoses in humans and others, many researchers still believe that there are no confirmed acute fumonisin, aflatoxin, ocratoxin etc toxicity in humans. They speculated that there are no available biomarkers for human exposure to mycotoxins. Especially as several studies confirmed that mycotoxins are not significantly transferred into meat, eggs, milk etc.

Furthermore, there are no reports on the kinetics and metabolisms of mycotoxins as well as absorption through inhalation or dermal exposure in humans so far. However, WHO (2000) stated that occupational inhalation exposure could be a problem due to the dusty nature of the substrates (particularly agricultural commodities), high levels of spores and mycelia production capability of the fungi (Tejada-Simon *et al.,* 1995).

Therefore, data should be collected on air-borne levels of mycotoxins during harvesting, processing and handling of agricultural commodities, epidemiological indices and environmental fate in our ecosystems.

Incidences of mycotoxicoses have led to the recruitment of several Scientists such as Chemists, Public Health Officers, Nutritionists, Laboratory Attendants, Technologists, and Researchers with Multidisciplinary background. A great deal of improvements have also been achieved in laboratory animal breeding and handling techniques.

Essentially, the assistance of research granting bodies like WHO, UNICEF, FAO, USAID, World Bank etc have not only proffer solutions to mycotoxicoses incidences but have

led to serendipitous discoveries of some useful mycotoxins in the fields of Human and Veterinary Medicine, Pharmacology, Food Science and Technology as well as Energy Generation for the sustenance of man.

Brain Teaser

1. List five animal species that are susceptible to mycotoxicoses and briefly discuss the physiological implications? (25 marks)
2. Define mycotoxicoses and stress the symptoms? (25marks)
3. Enumerate the various diagnostic procedures and write concisely on five principles? (25 marks)
4. Describe in detail what mycotoxins are? (25 marks)

Some Useful Books for Further Studies

1. Environmental Health criteria 219. Monographs on fumonisins by World Health Organisation.
2. Books of Abstracts by Nigeria mycotoxin Awareness and Study Network.
3. Mycotoxins in Grains by Miller J. D. and Trenholm H. L.

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