

Review Article

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Aflatoxine Effect on Livestock Health: A Review

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ABSTRACT

Aflatoxins have been the cause of numerous deaths in livestock and it also the cause for economic losses. Aflatoxins belong to a group of mycotoxins that are produced by fungi species (molds) as they grow on their substrates. The major ones are aflatoxins B1, B2, G1 and G2, thus named depending on their fluorescence under blue and green light. *Aspergillus parasiticus* can synthesize AFB1, AFB2, AFG1, and AFG2. AFB1=AFM1>AFG1>AFB2=AFM2>AFG2 from strongest to weakest in terms of toxicity. Pigs so affected became lethargic, did not eat, and eventually became hypothermic, icteric, and had blood in their feces. Acute aflatoxicosis is characterized by an acute hepatotoxic disease that manifests itself with depression, anorexia, jaundice, hemorrhages, edema of the lower extremities, abdominal pain and vomiting. Chronic exposure leads liver cancer. The major target organ for aflatoxins in animals is the liver. Aflatoxins are probably not major causes of livestock disease and low productivity, but are contributing factors which are likely to become more important as livestock production intensifies. The animal feeds most likely to be contaminated are maize, cottonseed, and groundnuts. These feeds are at high risk for aflatoxin contamination. Aflatoxins cannot be detected by sight or smell in contaminated food or feed. Aflatoxins are not eliminated by boiling, cooking, or by processing into compound feeds. Animal source foods, especially milk, may also contain aflatoxins if animals eat contaminated feeds. This is often the case with milk; carry-over rates are relatively high, consumption is high, and milk is often given to infants and young children who are most at-risk for negative health outcomes related to aflatoxin exposure. Affected animals may exhibit reduced feed consumption, weight loss, and reduction in production. The more significant effects in cattle may occur when animals consume lower levels of aflatoxins and chronic effects appear such as reduced reproductivity, immunosuppression, and reduced feed efficiency. An increase in dietary protein protects against adverse effects of the toxin. Feeding of extra vitamins, A and K could also decrease the detrimental effects of aflatoxins. The prevention ways are removing the sources; promotes better agricultural and storage techniques; have good resources for testing and early diagnosis; strict food quality standards; General awareness and personal protection; Better livestock feeding & management.

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Introduction

Livestock makes an important contribution to the economic livelihoods and nutritional wellbeing of people throughout. Aflatoxins have been the cause of numerous deaths in livestock and it also the cause for economic losses. The economic significance occurs in feeds and foods is through lowered productivity including meat and eggs, reduced weight gain, reduced feed efficiency, increased incidence of disease because of immunosuppression, and subtle damage to vital organs. Aflatoxin is transferred into animal tissue and dairy products [1].

Aflatoxins belong to a group of mycotoxins that are produced by fungi species (molds) as they grow on their substrates. The main fungi responsible for producing aflatoxins are *Aspergillus flavus* and *Aspergillus parasiticus*. Other species of fungi also produce aflatoxins but at lower concentrations. The fungi occur naturally in the soil in tropical regions and infect crops while on the farm (preharvest) and after harvest during storage (postharvest) and processing. The crops most infected include maize, groundnut, cassava, cotton, spices, dried and farmed fish, oilseeds, beans and nuts, and dried fruits. Eighteen different types of aflatoxin are

known. The major ones are aflatoxins B1, B2, G1 and G2, thus named depending on their fluorescence under blue and green light. Aflatoxin B1 and B2 fluoresce under blue light while G1 and G2 fluoresce under green light. Aflatoxin M1 and M2 are breakdown products of aflatoxin B1, B2, or G1 and G2 formed in the liver and excreted in the milk and urine of mammals exposed to aflatoxin B1, B2, G1, and G2. All animals are affected by aflatoxin. Pigs are highly susceptible; dogs, calves, and sheep are moderately susceptible; chickens and cattle are relatively resistant. Fish vary from highly susceptible to resistant, and honey bees are relatively resistant [2].

Aflatoxins are probably not major causes of livestock disease and low productivity, but are contributing factors which are likely to become more important as livestock production intensifies. The animal feeds most likely to be contaminated are maize, cottonseed, and groundnuts. These feeds are at high risk for aflatoxin contamination. Aflatoxins cannot be detected by sight or smell in contaminated food or feed. Aflatoxins are not eliminated by boiling, cooking, or by processing into compound feeds. Animal source foods, especially milk, may also contain aflatoxins if animals eat contaminated feeds. This is often the case with milk; carry-over rates are relatively high, consumption is high, and milk is often given to infants and young children who

are most at-risk for negative health outcomes related to aflatoxin exposure. Carry over rates of aflatoxins from feed to livestock products are much lower for meat and eggs. Given the relatively low quantities consumed, meat and eggs are not likely to present a major contribution to overall consumption of aflatoxins in the diet. Smoked fish and fermented foods [3].

Aflatoxins have proven to have negative health impacts on animals, which include death from ingesting large amounts; lowered productivity; and immunosuppression. In mammals, aflatoxins mainly damage the liver. Clinically Dairy and beef cattle are more susceptible to aflatoxicosis than the other species. Young animals of all species are more susceptible to the effects of aflatoxins than mature animals. Pregnant and growing animals are less susceptible than young animals but more susceptible than mature animals. Toxicity due to aflatoxins, under natural conditions, is usually sub-acute or chronic, depending on the level of exposure. Occasionally, acute cases are also seen. In general affected animals show reduced growth rate, weight loss, immune suppression, icterus, hemorrhagic enteritis, reduced performance, and ultimately death. Key economic impacts of aflatoxins occur when feed or animal products fail to meet standards and cannot be exported or marketed [4].

Aflatoxin contamination has been the most common cause of acute and chronic mycotoxicosis in animals and humans. Hepatotoxicity, immunosuppression, carcinogenicity and nephrotoxicity are the major effects of aflatoxins. It has gained increasing attention due to their harmful effects on human and animal health and also due to the widespread presence of aflatoxigenic fungi in all the agricultural commodities under field and storage conditions. Aflatoxin occurs worldwide. Chronic aflatoxin consumption has greater economic and health related impacts than acute aflatoxicosis outbreaks. Impacts are likely to worsen as livestock industries intensify in response to growing demand for meat, milk, fish, and eggs. In this review I explain the health impact of aflatoxins on animal health [5].

Literature Review

Meaning of Toxin and Causes of Aflatoxin

A toxin (from Ancient Greek: *toxikon*) is a poisonous substance produced within living cells or organisms. It simply means, it is a biologically produced poison. Aflatoxins are naturally occurring toxins that are produced by species of a fungus called *Aspergillus* types *Aspergillus flavus* and *Aspergillus parasiticus*. *Aspergillus parasiticus* can synthesize AFB₁, AFB₂, AFG₁, and AFG₂. AFB₁ = AFM₁ > AFG₁ > AFB₂ = AFM₂ > AFG₂ from strongest to weakest in terms of toxicity. They survive on many organic nutrient sources like plant debris, tree leaves, decaying wood, animal fodder, cotton, compost piles, dead insects and animal carcasses, stored grains, and even immune compromised humans and animals. The toxins are produced as secondary metabolites by the fungi in temperatures range between 24 and 35°C, within many commodities whenever the moisture content exceeds 7% (10% with ventilation) [1].

Brief Historical Overview

The toxicity of a group of closely related compounds, called aflatoxin in the popular literature and often in the scientific press, was recognized in 1960 following one of the most intensive and productive investigations of unknown toxic factors of natural origin ever pursued. Peanut meal imported to Great Britain from Brazil was quickly targeted as the cause of the deaths of large numbers of turkey poults and ducklings on British farms. Mold hyphae were observed during examination for the presence of

poisonous plants, although attempts at culture were negative. The disease syndrome was subsequently recognized in other domestic animals and in places other than England. The causative mold, *Aspergillus flavus*, which reproduced the animal disease signs and symptoms, was actually isolated from meal associated with a hepatic problem. Fluorescent material that could be estimated visually and corresponded with the toxicity of the samples as determined biologically. The isolation and characterization of the four closely related toxins, aflatoxin B₁, B₂, G₁ and G₂, were first reported by Hartley [6].

Aflatoxicosis of Animals

Aflatoxicosis is the poisoning that results from ingesting aflatoxins. It is exposure related large doses lead to acute illness and death, usually through liver cirrhosis; while chronic low doses have nutritional and immunologic consequences; and all doses have a cumulative effect on the risk of cancer. Acute aflatoxicosis is acute poisoning is characterized by an acute hepatotoxic disease that manifests itself with depression, anorexia, jaundice, hemorrhages, edema of the lower extremities, abdominal pain and vomiting. Chronic exposure leads liver cancer. The major target organ for aflatoxins in animals is the liver. These compounds have been found to be carcinogenic and teratogenic in animals, as well as the cause of impairment of protein formation. Domesticated animals are variably susceptible to aflatoxins. Sheep and cattle appear to be more resistant than most livestock and poultry. Whereas swine, chickens, turkeys, and ducklings are more susceptible. Within a species, there are breed differences; this is best demonstrated in breeds of chickens. Although these factors influence the toxic effects of aflatoxin, other factors to consider are age, sex, exposure (duration and dose), nutrition, environmental stresses, and other chemical exposures including other mycotoxins [7].

Swine Aflatoxicosis

Liver changes in swine with acute aflatoxicosis include centrilobular congestion and hemorrhage with the hepatocyte nuclei showing the margination of chromatin and some pyknosis. These changes were followed by centrilobular necrosis and were concomitant with increases in serum enzymes and prothrombin time and decreased liver function as measured by bromosulphaphthalein clearance. Pigs so affected became lethargic, did not eat, and eventually became hypothermic, icteric, and had blood in their feces. Additional studies have demonstrated that the major change observed in swine aflatoxicosis is damage to the hepatic parenchyma. Aflatoxin had reduced growth rate, feed efficiency and general unthriftiness [8].

Cattle Aflatoxicosis

The acute intoxication of cattle with aflatoxins produces liver lesions similar to those described for swine, although cattle are less susceptible to the aflatoxins. Affected animals may exhibit reduced feed consumption, weight loss, and reduction in milk production. The more significant effects in cattle may occur when animals consume lower levels of aflatoxins and chronic effects appear such as reduced reproductivity, immunosuppression, and reduced feed efficiency. These effects are economically important to the producer. Thus, the general effect of aflatoxin in cattle is liver disease, with specific effects ranging from acute to chronic disease dependent on the dosage given. Milk production in cows appears to be affected even by low levels of dietary aflatoxins that have no other effects on the health of the animals [6].

Poultry Aflatoxicosis

The poultry industry is probably more severely affected than any of the livestock industries because poultry appear to be more

susceptible to the effects of dietary aflatoxins and losses can be quite severe. Susceptibility to aflatoxins varies in chickens, depending on dosage, nutritional status, environmental stress, breed, strain, and sex. Low concentrations of dietary aflatoxins can cause weak chickens with reduced weight gains, feed efficiency, and egg production. The toxicity and carcinogenicity of aflatoxin B1 are influenced by a variety of factors including, among others, diet, microsomal activity, age, sex, and animal species. The recipient of the toxic insult metabolizes or activates the aflatoxins primarily by the microsomal mixed function oxidase system of the liver [9].

Clinicopathological Effect of Aflatoxines

The general effects of aflatoxicosis in animals include decreased feed utilization and efficiency leading to poor weight gain, liver and kidney damage, gastrointestinal dysfunction, embryonic death, teratogenicity, carcinogenesis, suppressed immune functions, reduced productivity, anaemia, jaundice and death. In chicks immunosuppression, reduced growth and production potential are often noticed. Acute liver damage, induction of tumors and immunotoxicities are of much concern. High level of aflatoxin exposure produces alteration in digestion, absorption and metabolism of nutrients. Chronic or subclinical exposure does not lead to visible signs but leads to carcinogenesis, as the metabolites aflatoxins can intercalate into DNA. Over a very long exposure, teratogenic and mutagenic effects can also be observed in livestock. Embryotoxic potential of AFB1 and AFM1 has been evaluated using the frog embryo teratogenesis assay. High doses of aflatoxins may also result in severe hepatocellular necrosis and prolonged low dosages result in reduced growth rate and hepatomegaly. It inhibits the DNA dependent RNA synthesis in nucleus resulting into inhibition of protein synthesis, which results in reduced production of essential metabolic enzymes and structural proteins for growth [4].

Aflatoxins can induce mutagenesis by alkylation of nuclear DNA, leading to carcinogenesis and teratogenesis. Aflatoxin B1 is one of the most potent hepato carcinogenic substances known and no animal species is immune to its acute toxic effects. The active metabolite of AFB1, the 8, 9, -epoxide (previously referred to as 2, 3-epoxide), is a potent carcinogen and named as proximal carcinogen. It is extremely reactive, and induces chromosomal aberrations and cell toxicity. Evidence suggests that this epoxide can also induce mutations. Aflatoxin G1 is an active carcinogen but aflatoxins B2 and G2 are very less carcinogenic. Aflatoxin M1 has 2, 3- vinyl ether double-bond, which exerts the carcinogenic effects [2].

Prevention and Detoxification Strategies

Prevention would be the most effective means of reducing aflatoxin contamination but needs much improvement in agricultural storage methods, practices in harvesting and handling of crops. Processes such as dry and wet milling can also result in the distribution of aflatoxin residues into less utilized fractions in the commodity. Biological detoxification is another strategy in which degradation of aflatoxins is done by biological means or by using genetically modified plants or non-toxicogenic strains of *Aspergillus* to reduce aflatoxin contamination by competitive inhibition [10].

Modified glucomannans, derivative of yeast cell wall, has also been found beneficial in binding to higher levels of aflatoxins at a lower inclusion rate. Recently, *Saccharomyces cerevisiae* and lactic acid bacteria were found to be effective biological detoxifying agents. Similarly, nutritional approaches can also

modify the toxicity of aflatoxins in animal body. An increase in dietary protein protects against adverse effects of the toxin. Adding methionine to broiler diet improved the weight gains and reduced the adverse effects of AFB1 by increasing liver glutathione levels. Feeding of extra vitamins A and K could also decrease the detrimental effects of aflatoxins [9].

Aflatoxins in Animal Source Foods

Aflatoxins and their metabolites are present in animal source, this is most important in the case of milk. Carry over rates are much lower for meat and eggs. Given relatively low quantities of animal source food consumed, meat and eggs are unlikely to present a major contribution to overall consumption of aflatoxin in the diet. Meat consumption may vary among different groups within a country, so the relative contribution of meat is likely to be higher in wealthier and urban populations. However, the main risk of aflatoxin exposure would continue to come from cereals. Aflatoxins in milk are of concern because milk consumption is often higher among infants and children, who are also more vulnerable [10].

Higher yielding animals consuming large amounts of feed concentrates typically show higher levels in their milk (up to 7 percent of the aflatoxin ingested). Some studies have indicated that mastitis may increase levels of aflatoxins, while other studies were unable to find such an association. Aflatoxins may also be present in sheep milk as well. Aflatoxins in milk are around three times higher in soft cheese and five times higher in hard cheese. Aflatoxin may also be present in yogurt and other dairy products. Recent studies have suggested that another toxic metabolite (aflatoxicol) may also be excreted in significant amounts in milk [4].

Detection of Aflatoxins in Animal Feeds

Aflatoxins are difficult to detect because standards often require the detection of very low levels and because the toxins are not distributed evenly in food or feed. Protocols for sampling and analysis are available and should be used. Quality assurance and laboratory networks have an important role in ensuring accuracy of results. Molds multiply in raw and processed materials under suitable conditions, on the one hand, they change the quality and quantity of the product and cause it to deteriorate, on the other hand, they create toxic substances that are more or less harmful to humans and animal health. A number of tests are available with differing costs, advantages, and disadvantages. Since mycotoxins can't be completely prevented in the crops, regulations are needed to prevent highly contaminated crops from entering the food chains. However, regulations are not enough. Also needed are reliable and affordable tests for aflatoxins, incentives for complying with regulations, and systems to deal with the contaminated products. Testing for aflatoxins is considered in more depth in the technical package on standards for animal feeds. Generally, the difficulty of obtaining a representative sample is recognized as the major cause of inaccuracy in aflatoxin testing. However, laboratories and laboratory methods vary, too. Most methods require a correct extraction and clean-up of samples; how this is done may affect the outcome [7].

Highly reliable methods include liquid chromatography mass spectroscopy and high (or ultra-high) performance liquid chromatography; these often serve as references for other methods. Various immunoassays have also been developed, such as enzyme linked immunosorbent assays (ELISA), which are easy and cost effective. A number of rapid tests provide a result over or under a certain limit. These may be used directly at the location of millers

and producers, or in markets. After aflatoxin B1 is consumed by lactating animals, it is metabolised to aflatoxin M1, which is excreted into the milk. As a consequence of aflatoxin influence on the general condition of animals, together with the excretion into the milk, the effects on milk quality, including changes in some milk components concentration could be considered as possible. Reduction of body weight, decreased food consumption, increased concentrations of aspartate aminotransferase and probably of alanine aminotransferase, extensive liver damage are seen in animals after exposure [11].

Economic Losses from Aflatoxins

There are few studies quantifying the economic loss associated with aflatoxins. Given that animal feeds are typically co-contaminated with several mycotoxins, and the variety of different genetics, ages, species, and management practices at farm level, it may be hard to disaggregate and estimate its impact. However, as livestock production increases across Africa, especially under intensive and semi-intensive systems, and these systems tend to use concentrates, aflatoxin related impacts are likely to rise. Chronic aflatoxin exposure in livestock certainly has a larger impact on livestock production than acute aflatoxicosis. The impact on trade both within countries and in the region has yet to be quantified. The impact of aflatoxin consumption and livestock production on food security in vulnerable regions and populations is also yet to be quantified. However, considering the levels of aflatoxins shown in different studies and the ubiquitous exposure in animals, aflatoxins probably cost the livestock sector in East Africa tens of millions of dollars each year while adding aflatoxin exposure to humans [12].

The costs of mycotoxins in the feed chain include research, production practices, testing, and regulation enforcement to prevent the toxins from appearing in feed products of affected commodities. Mycotoxin losses result from lowered animal production and any human toxicity attributable to the presence of the toxin, the presence of the toxin in the affected commodity which lowers its market value, as well as secondary effects on agriculture production and agricultural communities. Although the effects of acute aflatoxicosis can be dramatic, the impact on production and thus economics are even higher for chronic exposure [13].

However, it is often difficult to diagnose chronic mycotoxicosis due to the diffuse symptoms and the fact that feed commonly contains more than one kind of mycotoxin. This makes it difficult to estimate the true economic cost of aflatoxicosis. Several estimates for the costs of mycotoxins have been made, but estimates do not always distinguish between livestock sector and other costs. For an individual producer, economic losses depend on the relative costs of feed, livestock products, and compliance; the levels of aflatoxin contamination; and other factors that either reduce or exacerbate the impact of aflatoxin [14].

For the topic of economic impact, additional questions considered the type of economic impact studied (trade-related, farm level, or health effect) and the method used to estimate the economic impact. Finally, for the topic of mitigation measures, additional questions considered the economic operators characteristics, production stage, and type of mitigation. Measure (cultural, biological, chemical and others), and types of outcomes described [8].

Treatment and Prevention

The source should be eliminated immediately; Levels of protein and vitamins A, D, E, K and B should be increased; Secondary infections must receive immediate attention and treatment; Good management alleviates stress practice. The prevention ways are remove the sources; Promotes better agricultural and storage techniques; Have good resources for testing and early diagnosis; Strict food quality standards; General awareness and personal protection; Better livestock feeding & management [15].

Mycotoxin producing fungi contaminate food and feeds before, during and after harvest. Aflatoxins are important mycotoxins and aflatoxin B1 (AFB1) is a class 1 human carcinogen (definitely carcinogenic). Aflatoxin M1 (AFM1) is a class 2B (possible) human carcinogen. Aflatoxin B1 in feeds can decrease milk production, reduce fertility and increase susceptibility to infections. So preventive mechanisms must be done [16].

Conclusion and Recommendation

Conclusion

It is limited for a poor and food insecure population. Its presence in food products and animal feeds is an important problem concerned with food and feed safety. Significant economic losses are associated with their impact on human and animal health. The contamination in food commodities threat does follow the rules of dosage to response and association with health risks in both animals and humans. They also have greater attention than any other mycotoxins because of their potent acute toxicological and carcinogenic effect in susceptible animals and humans, as well as the economic impact drive directly from crops, livestock and their product losses, and indirectly from the cost of regulatory programs designed to reduce risks of animals and humans' health. Lacks of sanitary measures on food commodities usually contaminated with aflatoxins mould growth is an unavoidable and may pass through manufactures and cooking processes.

Consumption of aflatoxins by livestock and fish seriously reduces their productivity. Chronic aflatoxicosis probably has greater economic impacts than acute disease, as acute disease has never been reported but livestock are exposed to uncontrolled aflatoxin through feed. Typically, animals show a worsening in feed conversion ratio, a decrease in average daily gain and decrease in body weight. Different species differ widely in their susceptibility to aflatoxins. The age of the animals also plays an important role. Therefore, management should be differentiated by species; aflatoxins remain as a threat to the health of livestock as well as humans by their continuing intermittent occurrence in both feeds and foods. The finding that aflatoxin contaminated feeds, and eventually purified aflatoxins, were carcinogenic in rats and trout initiated a multitude of studies in search of the role of these toxins in human liver disease, especially cancer. Aflatoxicosis of animals is usually manifested by pathologic changes in the liver, but they have been found to be carcinogenic and teratogenic as well as causing impaired protein formation, coagulation, weight gains, and immunity. The importance of the carcinogenic effect in livestock is diminished because they are not fed contaminated diets for a sufficient time prior to marketing for slaughter. Animals are variably susceptible to aflatoxins, depending on such factors as age, species, breed, sex, nutrition, and certain stresses. Swine, cattle, and poultry are the domestic species of greatest economic concern in terms of aflatoxicosis.

Aflatoxins are considered the primary cause of abnormal health status and productive performances in domestic animals and birds. Aside to this, economic losses arising from aflatoxicoses are enormous. In domestic livestock, aflatoxin causes nutritional interference, there by hampering growth with serious implications on reproductive performances. Aflatoxins cause huge losses to poultry industry by increasing susceptibility to various infections and drastically reducing the production potential of flocks. Aflatoxins present as residues in milk, meat, eggs and other animal products are of much concern to the humans too, as these toxins are much stable to heat treatments. The corner stone to successful mycotoxin reduction in feeds is the control of moisture and temperature, which has a direct bearing on the extent of mould colonization. Suitable detoxifying agents and toxin binders have to be used in order to make sure that the animals are receiving safer feed materials.

On the part of the government, there is a need to educate and supervise the farmers, feed traders and feed manufacturers on the importance of producing crops and feeds with low levels of, or exempt from, aflatoxin and observing good feed storage practices especially during the rainy season. In addition to providing important and novel information on aflatoxins in milk, this study shows that aflatoxin contamination is common in dairy feeds and milk and concentrations may be high. This may contribute to ill health effects in both humans and animals. Therefore, there is need for better understanding of the impacts of aflatoxins in the dairy and feed value chains and, where appropriate, interventions within these value chains to control aflatoxin contamination in animal feeds.

Recommendation

- There should be standards for animal feeds and a monitoring system.
- Concentrates may include many different ingredients. It is important to assess the level of aflatoxins in the total diet rather than individual items.
- Feeds and feed components vary greatly in their susceptibility to aflatoxin contamination. High-risk feeds require more attention. These include maize, oilseeds, groundnut, and commercial concentrate mixes, in this item of feed regulatory rules for controlling must be done.
- Since different species and ages of animals differ widely in their susceptibility to aflatoxins, management and standards should be differentiated by species, age, and other relevant factors.
- Risk assessment should be used to estimate the risk associated with aflatoxins in milk and other animal source foods.
- Milk and traditionally dried or smoked foods have the highest levels of aflatoxin and so should be given the most attention.
- Management of aflatoxins in animal feeds requires: good practices at producer, processor, and retail levels; Appropriate, risk-based legislation and regulations; Monitoring of aflatoxins in feeds and foods; Appropriate management of contaminated feeds.
- Highly contaminated feed or feed ingredients that cannot be safely used should be destroyed.
- A comprehensive set of policies and programs to support the development of forages, pasture, and specific cereal crops for animal feeds should be pursued.

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