LIVESTOCK DEVELOPMENT NOTES: NO 6

MYCOTOXICOSIS: II - RISK OF MYCOTOXINS TO ANIMAL HEALTH AND PRODUCTIVITY

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ABSTRACT

Mycotoxins are frequent contaminants of commodities destined for use as animal feed. Some of the severe health and productivity issues in animals which may arise following ingestion of feed containing mycotoxins are discussed, and those considered to be of some importance to Papua New Guinea livestock agriculture are highlighted.

***Key words**: fungi, mycotoxins, mycotoxicosis,* Alternaria *toxins,* Fusaria *toxins,* Aspergilli *toxins,* Penicillia *toxins*

INTRODUCTION

Mycotoxicosis (mould poisoning) results from consumption of food or feedstuffs "laced" with toxins "excreted" by the moulds. In natural conditions, however, the levels of mycotoxins produced are usually low, and as a consequence the effects they cause may be difficult to detect. This is highlighted by the fact that low levels of some mycotoxins (e.g. aflatoxin) suppress the immune system before they have any other discernible effect on the animal. In such circumstances a secondary infection would be taken as the cause of the disease when the actual cause is due to ingestion of mycotoxin(s).

This communication intends to highlight some of the toxic effects mycotoxins can cause, and describe problems associated with those which may contaminate feedstuffs in Papua New Guinea (PNG).

NATURE OF MYCOTOXIN-RELATED PROBLEMS

Acute and chronic toxicity

Mycotoxins are chemical compounds, many of which cannot be destroyed by normal cooking processes. Their toxic effect depend on their chemical properties, susceptibility of the animal, level of toxins include increased susceptibility to infectious diseases through impairment of immune system, and increase carcass bruising through loss of tissue strength and intergrity and impaired blood coagulation.

When mycotoxins are ingested and absorbed from the digestive tract, they exact their effects by injuring vital organs or parts of the body or disrupting a metabolic pathway. Many mycotoxins are specific in their effects and will injure particular organ(s) of the body when ingested (*Table 1*). Acute intoxication is due to extensive injury to these parts of the body, as a result of ingesting feed containing moderate to high levels of the toxin(s). Deaths often occur during acute intoxication. But, as stated earlier, natural levels of mycotoxins in food or feedstuffs are likely to be low and therefore chronic rather than acute intoxication is likely to be encountered in the field.

Low levels of mycotoxins in rations are likely to cause different types of disturbances to various metabolic systems and may go unnoticed. In most instances, these disturbances are difficult to detect because they can be expressed in many ways: including a reduction in growth rate,

Table 1: **Grouping of mycotoxins based on the toxic effects they cause.**

Target Tissue/Function Affected	Mycotoxin
Liver toxins	Aflatoxin, spordesmin, rubratoxin B, sterigmatocyin, trichothecenes, ochratoxin A, phomopsin A
Kidney toxins	Ochratoxin A, citrinin, aflatoxin, oxalate
Nerve toxins	Trichothecenes, slaframine, peritrem A, ochratoxin A (in poultry only), ergot alkaloids, lupinosis (ammonia accumulation)
Genital toxins	Zearalenone, ergot alkaloids
Lung toxins	Furanoterpenoids (4-ipomeanol, 1-ipomeanol)
Skin toxins	Trichothecenes
Photosensitizing agents	Spordesmin (facial eczema)
Cancer-causing toxins	Aflatoxin, T-2 toxin, ochratoxin A, sterigmatocyin, luteoskyrin, patulin, penicillic acid
Malformation toxins	Aflatoxin, ochratoxin A
Immune system suppressants	Aflatoxin, trichothecenes (T-2 toxin), ochratoxin A, gliotoxin, fusaric acid
Blood toxins	Dicoumarol, aflatoxin, trichothecenes
Brain toxins	Fumonisins
Bone toxins	Fusarochromanone

Table 2: **Toxicity of Alternaria isolated from different cereal grains assessed by a chick bioassay**

Cereal	Number of Isolates	Mortality* (No)	Weight Gain (No.)	Feed Conversion (No.)
Wheat	45	5	32	34
Barley	57	9	44	46
Sorghum	95	12	47	53
Rice	3	-	2	1
Total	200	26	125	134

*Number of isolates that caused deaths, or reduced weight gain and feed conversion efficiency

egg production (including increased cracked or thin shelled eggs), feed conversion efficiency, reproductive efficiency and in milk yield. Other notable effects include increase susceptibility to infectious diseases through impairment of immune system, and increase carcass bruising through loss of tissue strength and intergrity and impaired blood coagulation.

Moreover, in field situations there is every chance for food or feedstuffs to contain a number of mycotoxins. Such situation can arise as a result of either, the activity of one or more moulds in a commodity or in different commodities which have been mixed. Under such circumstances, the toxicity and clinical signs observed may differ greatly from effects observed in a single intoxication in the laboratory. For example, it has been shown that aflatoxin causes fatty livers in chickens (a presumptive diagnostic feature of aflatoxicosis), but this will not occur if ochratoxin A (a mycotoxin produced by *Aspergillus* and *Penicillium* sp.) is also ingested (Huff and Doerr 1981). Undoubtedly, this makes diagnosis of mycotoxin-related problems in the field difficult unless the presence of mycotoxins is detected.

Recognizing mycotoxic diseases in the field

There are several common features of mycotoxic diseases which can be taken as a useful guide in recognizing diseases of mycotoxin origin. These include:

- the disease must be feed related,
- no known disease causing microorganisms are present or have been isolated,
- the disease is not being passed from the parents to their offspring (contagious),
- the disease is not infectious nor, is it transferable,
- the animals recover or show signs of improvement when the feed (contaminated) is withdrawn,
- feeding some of the contaminated feed to other healthy animals of the same species reproduces the disease.

However, as can be noted from the above and later discussions, the task of distinguishing mould poisonings from other diseases is not easy, especially, in view of the large number of toxins and the signs they can cause and the influence of animal and environment factors on the expression of the disease symptoms. It is therefore of no suprise that even the veterinarians and the physicans have difficulty in recognizing mycotoxic diseases - even those acute ones.

Further, it is worth noting that mycotoxic poisonings occur sporadically, usually seasonally and geographically that it is difficult in having in place an organized diagnostic response or strategy.

MYCOTOXINS OF SOME CONCERN AND THEIR TOXIC EFFECTS

Alternaria toxins

The genus *Alternaria* is a common plant pathogen. It is responsible for causing spoilage of many commercially important commodities in the field (e.g. potato leaf blight and black point disease of grains) and during handling and storage (e.g. black rot of tomato). Some of the toxins it produces, about 70 compounds in total, can poison cells and the developing foetus, and increase mutations and malformation of body tissues (King and Schade 1984).

There is now a growing evidence that the genus may pose a significant threat to animal health and productivity. This stems from the fact that:

- *Alternaria* is one of the most common plant pathogens and isolates obtained from numerous commodities intended for animal consumption are highly toxigenic,
- *Alternaria* toxins can be naturally produced in feedstuffs, and can co-occur with toxins such as zearaleone, a metabolite of *Fusarium* species,
- Feedstuffs containing *Alternaria* toxins have been suspected to be responsible for losses in productivity in livestock.

Cereal grains, the main energy feed sources used in modern pig and poultry production, can habour potentially highly toxigenic *Alternaria* isolates. For instance, our recent work on barley, wheat, sorghum and rice produced in east-

Table 3: **Selected *Fusaria, Aspergilli* and *Penicillia* mycotoxins and their resulting effects on animals and humans**

Mycotoxin	Affected Animal Species	Pathological Effects
	Fusaria Mycotoxins	
Trichothecenes* (eg.T-2 toxin, HT-2 toxin,DAS,DON, nivalenol,fusareno-, nX neosolaniol)	ducks, chickens, cats, quails, pigs, cattle, rats, dogs, horses & humans	digestive disorders (feed refusal, vomiting, diarrhoea), edema, oral lesions, dermatitis & blood disorders (leucopenia)
Zearalenone	ducks, chickens, pigs turkeys, dairy cattle, sheep, rats & guinea pigs	estrogenic effects (reddening of vulva, prolapse of vagina, enlargement of uterus, atrophy of testicles & ovaries, enlargement of mammary glands & abortion)
Fumonisins	horses, donkeys & mules	brain damage (disintegration of white matter), neurological disorders
Furanoterpenoids	cattle, pigs & humans (?)	Lung damage (haemorrhages, alveolar and interstitial emphysema)
	Aspergilli and *Penicillium* Mycotoxins	
Aflatoxins	ducks, chickens, pigs, quails, cattle, sheep, cats, trouts, monkeys & humans	liver damage (hepatotoxic), bile-duct hyperplasia, heamorrhage of intestinal tract & kidneys and liver tumors (carcinogenic)
Ochratoxin A	pigs, poultry, dogs, rats & human	kidney damage (nephrotoxic), porcine nephropathy, mild liver damage, enteritis, teratogenesis & kidney tumors (carcinogenic)
Cyclopiazonic acid	pigs, poultry, guinea pigs & humans(?)	muscle necrosis, intestinal haemorrhages, edema & oral lesions
Citrinin	pigs, dogs, guinea pigs rats & rabbits	kidney damage (nephrotoxic) & porcine nephropathy
Patulin	poultry, cattle, cats, rats & rabbits	edema (brain & lungs), haemorrhage (lungs), convulsions, paralysis of motor nerves & carcinogenic

* DON- deoxynivalenol; DAS- diacetoxyscirpenol

ern Australia revealed that a number of *Alternaria* isolates from these grains are highly toxic in a chick bioassay system (Bakau *et al.* 1997; *Table 2*). The majority however, were chronically toxic, and cause reduced growth and feed conversion efficiency rates. Unlike other mycotoxins, *Alternaria* toxins have not been observed to target any specific organ or tissue when ingested. It is therefore difficult to pinpoint their involvement during natural intoxication from the signs exhibited by the animals. In chickens known to have consumed feed naturally contaminated with *Alternaria* toxins for instance, reduced feed intake, growth and feed conversion efficiency and increased "helicopter" feathering and culls were some of the signs that have been noted (Bryden *et al.* 1984).

Fusaria toxins

Like *Alternaria*, the genus *Fusarium* is also a common plant pathogen. It is also responsible for causing plant diseases such as stalk and cob rots in maize (*Figure 1*), and basal stalk rot and head blight of sorghum. There is an increased interest in this genus because of its involvement in causing some of the most severe and fatal cases of poisonings involving both animals and humans. Of numerous *Fusaria* mycotoxins, the trichothecenes, zearalenone, fumonisins and furanoterpenoids will be considered here, as these toxins have been frequently found in commodities intended for animal consumption, and are more likely to be of some concern to PNG.

a) Trichothecenes

This group consists of about 148 chemically related mycotoxins. Besides *Fusarium*, other genera such as *Trichoderma, Stachybotrys, Myrothecium* and *Cephalosporium* also produce trichothecenes. Cereal grains, particularly, maize, wheat and sorghum are frequently contaminated with these toxins and are the main cause of disease outbreaks in animals in the field. Different trichothecenes cause different types of toxic effects. Some of the general signs which can be attributed to the toxicity of this group of compounds in animals are weight loss, decreased feed conversion efficiency, feed refusal, vomiting, bloody diarrhoea, severe skin lesions (*Figure 2*), haemorrhages, decreased egg production, abortion and death (*Table 3*). Of the animals, pigs are particularly susceptible to trichothecenes in the diets, especially, T-2 toxin, diacetoxyscirpenol and deoxynivaenol trichothecenes (Bryden *et al.* 1987). They will refuse to eat feed containing these toxins, probably a mechanism of the animal to protect itself because of its susceptibility. However, if they are forced to eat contaminated feed, they will more likely develop stomach problems and may vomit, grind their teeth and salivate excessively.

b) Zearalenone

This mycotoxin produced primarily by *F. gaminearum*, a frequent mould affecting cereal grains; is often found along with the trichothecenes - a biomarker for the presence of trichothecenes in the commodities. Zearalenone possesses a strong estrogenic activity (*Table 3*). When sufficient amount is consumed, it will cause severe reproductive and infertility problems. It is interesting to note that zernaol, a synthetically produced anabolic nonsteriod used as a growth promoter in beef cattle and sheep, was based on the chemical structure of this toxin. Animals treated with zernaol will also show signs of hyperes-trogenism.

Again, pigs are most sensitive to this toxin and hence, most field cases of zearalenone toxicity have involved pigs. Swelling and reddening of the vulva (vulvovaginitis) is the most common feature of zearalenone intoxication (*Figure 3*). In young males, the toxin can cause female -like syndrome, usually characterized shrunken testes and enlarged mammary glands. Whilst in boars, it affects sperm quality and the desire to copulate (libido) but has no infuence on the pregnancy rate (Bryden *et al.* 1987). It appears there is no safe level of zearalenone in the diet for pigs. Levels as low as 1 gram of zearalenone in a tonne (1 part per million) of feed can cause a zearalenone-toxicity.

In cattle and sheep, signs of hyperestrogenic syndrome can be expressed as restlessness, udder enlargement, mucoid vaginal discharge, diarrhoea, decreased milk yield and abortion.

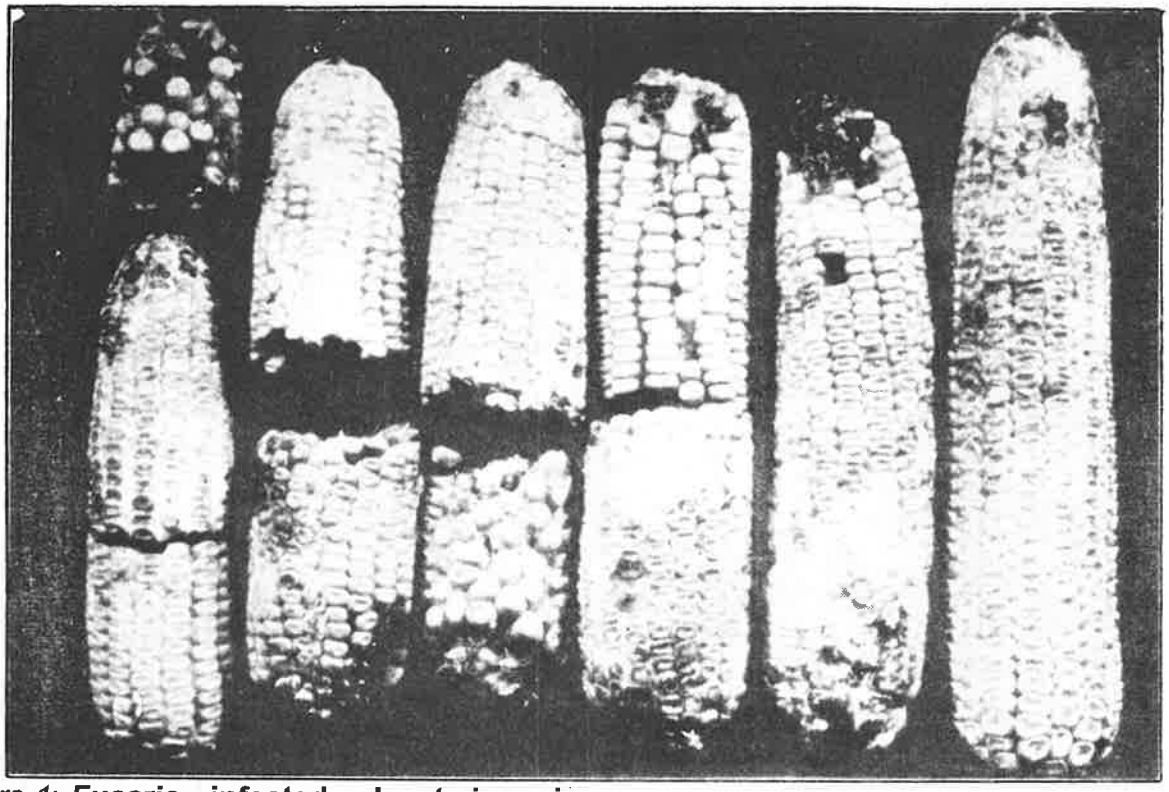

Figure 1: ***Fusaria*** **- infected cob rots in maize.**

Figure 2: **Characteristic ulcerative beak lesions in chickens caused by ingestion of trichotecene (T - 2 toxin) mycotoxins.**

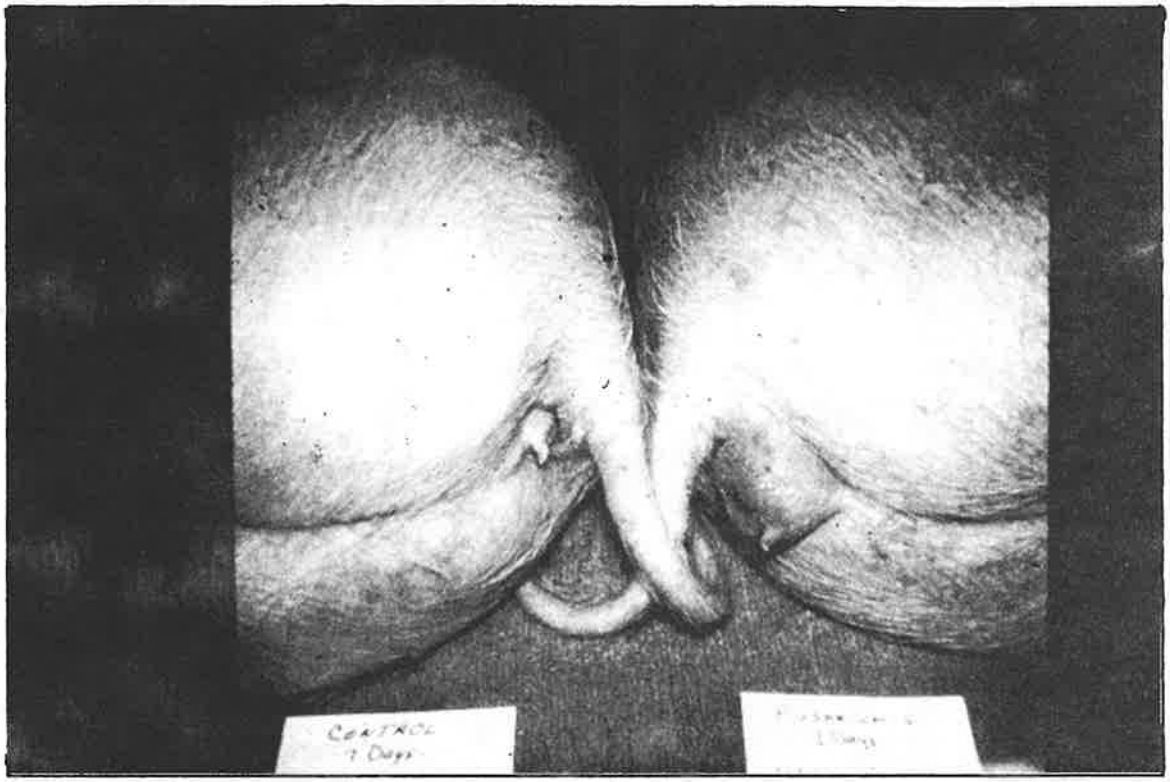

Figure 3: **Characteristic clinical symptom of estrogenic syndrome (vulvovaginitis) in prepuberal pigs resulting from zearalenone intoxication - normal (*left*) and intoxicated (*right*).**

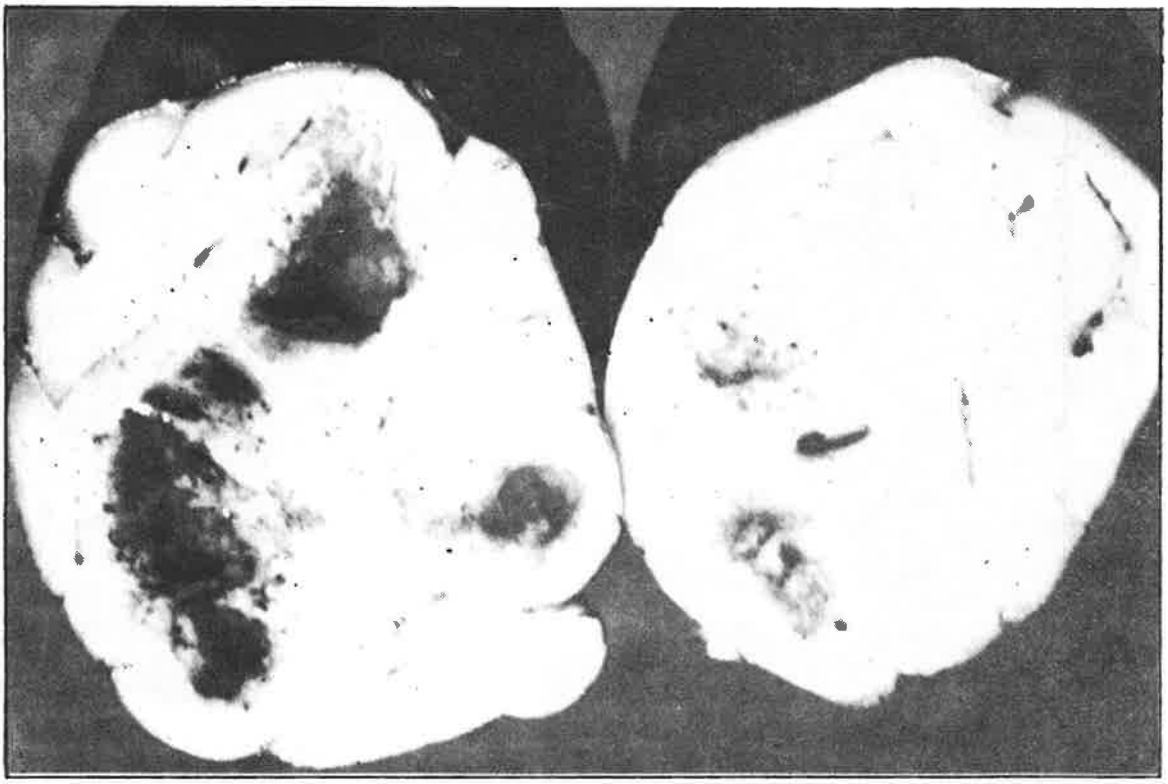

Figure 4: **Characteristic damage (hemorrhagic cavities) of the white matter of the brain by fumonisin mycotoxins - intoxicated (*left*) and normal (*right*).**

Young heifers can also become sterile after ingesting this toxin.

c) Fumonisins

There are six compounds (Fumonisin A1-2 and B1-4) in this group produced mainly by *F. moniliforme*, although *F. proliferatum* and *F. nygamai* also produce these toxins. *F. moniliforme* is commonly associated with maize, and therefore most cases of field intoxication have been due to consumption of maize contaminated with these toxins.

Fumonisin B1, the most potent of the fumonisins, causes extensive damage to brain tissues, especially the white matter part of the brain (*Figure 4*). Horses, mules and donkeys are particularly susceptible to these toxins and hence, the disease is often referred to as equine leukoencephalomalacia. Pigs could be equally affected by these toxins, but more work is needed to confirm this. Initial signs of the disease are characterized by animals having no interest in food or in eating (apathy) and reduced feed consumption. After these, the animals begin to show signs of neurological disorders such as lack of muscular coordination, facial paralysis, abnormal head movement, aimless walking or circling, unilateral blindness and increased excitability (*Figure 5*). As these disorders progress, lameness and recumbency may occur, and finally seizures and death. If sufficient amount is consumed, death can occur within few hours from the time the first signs appear.

d) Furanoterpenoids

This group of compounds (4-ipomeanol, 1-ipomeanol, ipomeanine and 1,4-ipomeadiol) are produced mostly by *F. solani* and are associated with brown storage rot of sweet potato tubers (*see Part I of this Note - series for more details*). Although limited work has been done on these toxins, it is likely to be of some concern for the pigs in PNG (Low *et al.* 1993).

Aspergilli and *Penicillia* toxins

These fungi are also most common in the nature - others being *Alternaria*, *Fusarium* and *Cladosporium*. It is fitting to consider the two genera together because each has species which have the capacity to produce similar metabolites (mycotoxins). For example, Ochratoxin A, a cancer - causing mycotoxin, can be produced by *P. verrucosum* var. *cyclopium* as well as *A. alutaceus* - previously known as *A. ochraceus* (Cole and Cox 1981). *Table 3* contains some of the details on some of the important mycotoxins produced by these genera, namely; aflatoxins, ochratoxin A, citrinin, cyclopiazonic acid and patulin. Only aflatoxin will be considered here as I feel it is the most important mycotoxin of the group in PNG. For more details on other mycotoxins, the reader is referred to the recommended Further Reading list.

Aflatoxins

Aflatoxins basically refer to aflatoxin B1, B2, G1 and G2 produced by *A. flavus* and *A. parasiticus*; B stangs for blue and G for blue - green fluorescent spots under ultraviolet light. Aflatoxin M1 and M2 are slightly less toxic compounds derived from aflatoxin B1 and B2 respectively, and are secreted in the milk - hence, M stands for "milk toxin". The most toxic member of the aflatoxin-group is aflatoxin B1. However, own its own it is not toxic. It requires the digestive system of the animal to convert it to a more active form (2,3 -epoxy -aflatoxin B1) before it can unleash its harmful effects. It was first associated with contaminated (imported) Brazilian peanut meal and the deaths of thousands of turkey poults (Turkey "X" disease) in Great Britain in 1960s (Blount 1961). Since then, there has been considerable interest in this mycotoxin because there is a strong case suggesting it could be involved in causing primary human liver cancer and hepatitis B virus infections in human populations.

Most animals including humans are susceptible to aflatoxins (*Table 3*), with males being the most susceptible of the gender. In cattle, pigs and poultry the first signs of acute aflatoxicosis are reduced feed intake, weight gain and general unthriftiness. Death is usually high. Often the signs of lack of muscular coordination and convulsions can also be observed during aflatoxin -

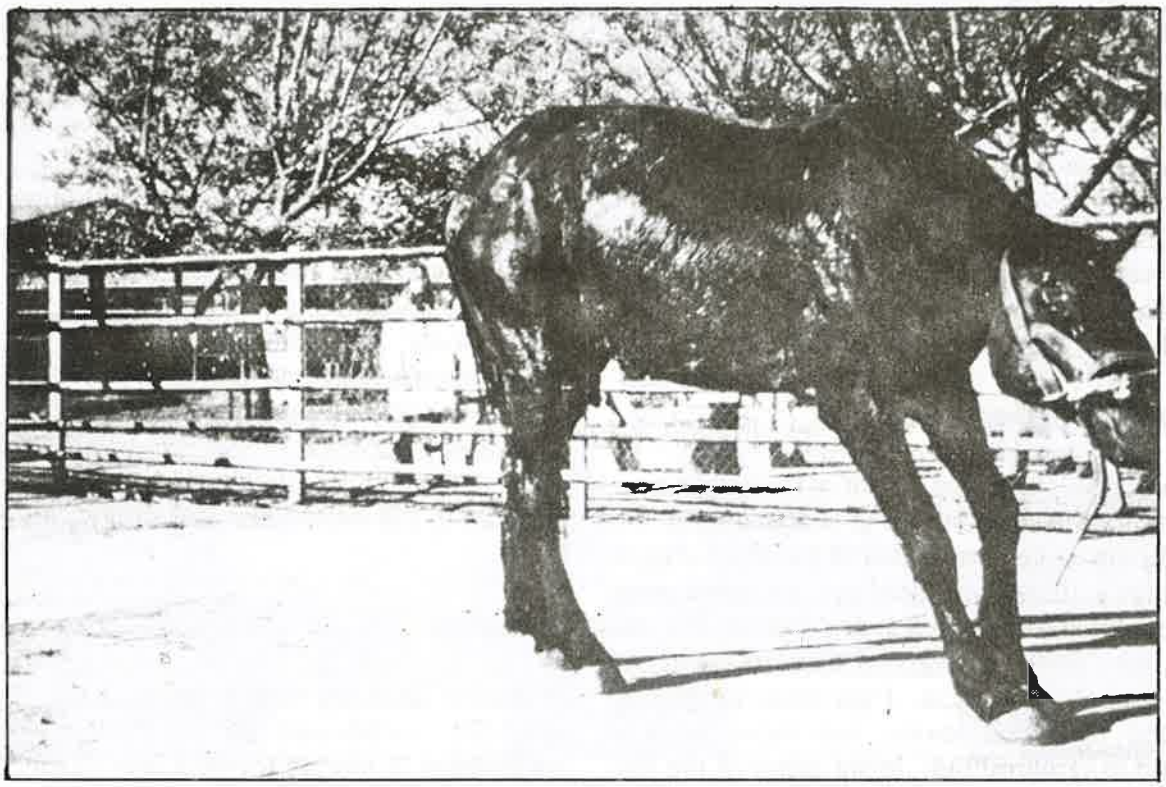

Figure 5: **A typical sign of a terminal stage of leukoencephalomalacia in horses - the animal lacks muscular coordination, is extremely sensitive and blind.**

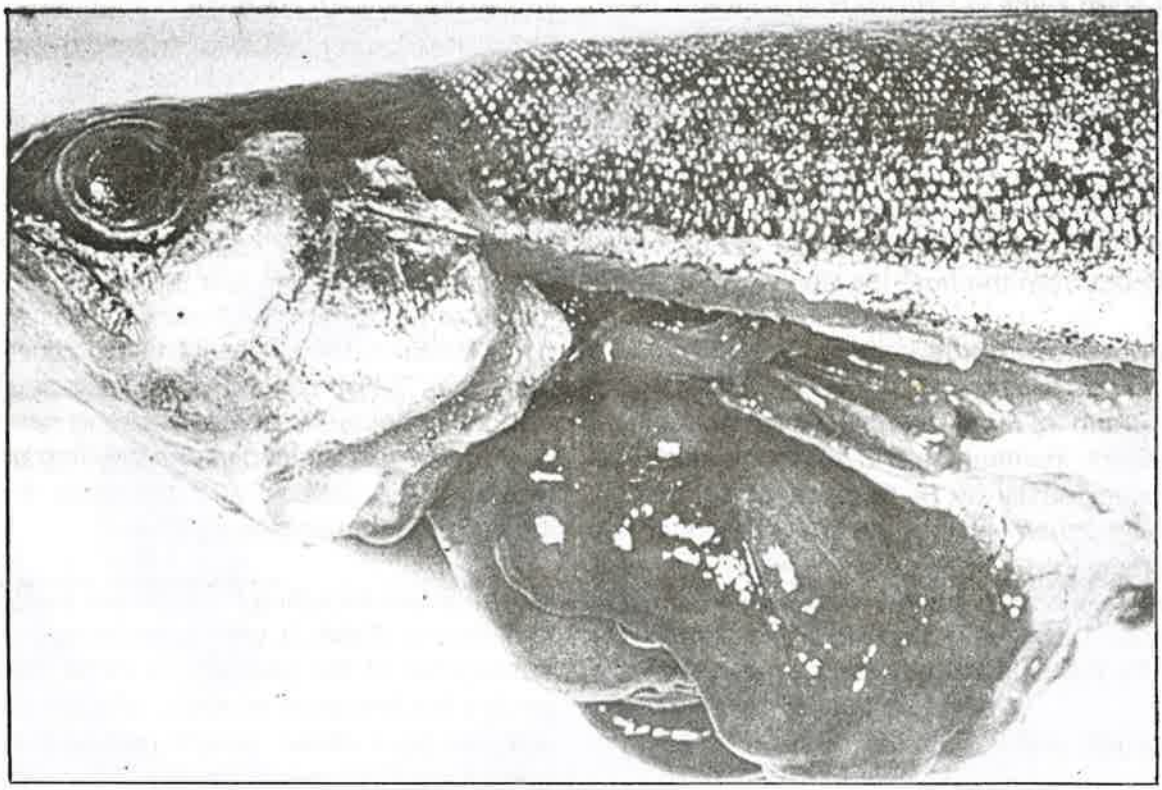

Figure 6: **Liver tumor (cancer) in trouts fed a diet containing 20 parts per billion aflatoxin for 12 months.**

poisoning. From recent findings it appears these are not the signs caused by aflatoxins. Rather, these are indicative signs of intoxication by another toxin called cyclopiazonic acid (Cole 1986). Both aflatoxigenic moulds, *A. flavus* and *A. parasiticus*, also produce this toxin together with or without the aflatoxins.

Of, perhaps, most concern to animal health and productivity viewpoint are the effects from long term exposure to aflatoxin. Other than the straight-forward economic losses through reduced growth rates, egg production and milk yields for instance, chronic exposure may also result in predisposing animals to infectious diseases through impairment of the immune system of the animals. Also, being a liver cancer-causing mycotoxin, such exposure may also result in causing liver cancer in animals; e.g. in hatchery -reared trout (*Figure 6*).

The liver is the main target organ during aflatoxin poisoning and the characteristic pathological changes in the liver include fatty degeneration, necrosis, fibrosis and extensive bile-duct hyperplasia. Because of its implication to human health, it is worth noting that contamination of food and feedstuffs by aflatoxin B1 and its derivative, aflatoxin M1, are also a criteria in international trade of agricultural commodities or their by-products. Many countries, for instance, those of the European Union (EU), United States and Canada have adopted stringent measures in ensuring commodities containing only minimum levels of aflatoxin B1 (e.g. not more than 10 parts per billion (ppb) in EU countries and 20 ppb in United States), and aflatoxin M1 (e.g. not more than 0.5 ppb in United States and 10 ppb in EU countries) are allowed entry into the country.

THE BIG PICTURE

Overall, though, the toxic consequences of mycotoxins take many forms, and since an animal is one complete organism, injury to an organ or disruption to a metabolic pathway will undoubtedly compromise the functions of other organs and therefore the homeostatic network (well being) of the animal. An understanding of when and how they are formed in the field and the effects they cause when ingested is vital in our effort in reducing their impact in the food chain.

Finally, there is enough evidence to suggest that besides aflatoxin, other mycotoxins are also a threat to public health. At the recent international conference (Fungi and Mycotoxins in Stored Products, Bangkok, Thailand, 1991), in which I participated, there appears to be a growing view within the scientific community, Food and Agricultural Organization (FAO) and other food - aid agencies that the issue of mycotoxins and public health should be expanded to include other mycotoxins, especially the trichothecenes. That is to say the importance of mycotoxins in the food chain is not just one country's problem but is rather a global one. Thus the FAO and many scientists working in this field are now looking at ways in which checking for the presence (or the absence) of mycotoxins in the commodities can be standardized worldwide.

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