Introduction
Mycotoxins are secondary metabolites of moulds that exert toxic effects on animals and humans. The toxic effect of mycotoxins on animal and human health is referred to as mycotoxicosis: The severity of which depends on the toxicity of the mycotoxin, the extent of exposure, age and nutritional status of the individual and possible synergistic effects of other chemicals to which the individual is exposed. The chemical structures of mycotoxins vary considerably, but they are all relatively low molecular mass organic compounds.

The untoward effect of moulds and fungi was known already in ancient times. (Vergilius, P.M., 1994) In the seventh and eighth centuries BC the festival “Robigalia” was established to honour the god Robigus, who had to be propitiated in order to protect grain and trees. It was celebrated on 25 April because that was the most likely time for crops to be attacked by rust or mildew (Ovidius, P.N., 1845).

In the Middle ages, outbreaks of ergotism caused by ergot alkaloids from *Claviceps purpurea* reached epidemic proportions, mutilating and killing thousands of people in Europe. Ergotism was also known as ignis sacer (sacred fire) or St. Anthony’s fire, because at the time it was thought that a pilgrimage to the shrine of St. Anthony’s would bring relief from the intense burning sensation experienced. The victims of ergotism were exposed to lysergic acid diethylamide (LSD), a hallucinogen, produced during the baking of bread made with ergot-contaminated wheat, as well as to other ergot toxins and hallucinogens, as well
as belladonna alkaloids from mandragora apple, which was used to treat ergotism (Van Dongen PWJ, De Groot ANJA, 1995). While ergotism no longer has such important implications for public health, recent reports indicate that outbreaks of human mycotoxicoses are still possible (Schneider DJ et al, 1996).

Some mycotoxicoses have disappeared owing to more rigorous hygiene measures. For example, citreoviridin-related malignant acute cardiac beriberi ("yellow rice disease" or shoshin-kakke disease in Japanese) has not been reported for several decades, following the exclusion of mouldy rice from the markets. Citreovirdin is a metabolic product of Pencillium citreonigrum, which grows readily on rice during storage after harvest (Uraquchi, K., 1969), especially in the colder regions of Japan (Ueno, Y. 1985). Another mycotoxicosis not seen for decades is alimentary toxic aleukia, common in the 1930s and 1940s in the USSR. This disease was caused by trichothecenes produced by Fusarium strains on unharvested grain. General interest in mycotoxins rose in 1960 when a feed-related mycotoxicosis called turkey X disease, which was later proved to be caused by aflatoxins, appeared in farm animals in England. Subsequently it was found that aflatoxins are hepatocarcinogens in animals and humans.

There is a long history of the use of certain moulds in the production of cheese and salami and in the fermentation of beer and wine. Moulds are also used in the production of drugs (antibiotics). The classification of mould metabolites as antibiotics or mycotoxins is based on their toxicity or beneficial effect in treating diseases. Some mould metabolites that were initially
considered to be antibiotics (e.g., citrinin) were subsequently found to be highly toxic (Reiss, J. 1978), and are currently classified as toxins. Ergot alkaloids are still used, inter alia, in the treatment of parkinsonism, as prolactin inhibitors, in cerebrovascular insufficiency, migraine treatment, venous insufficiency, thrombosis and embolisms, for the stimulation of cerebral and peripheral metabolism, in uterine stimulation, as a dopaminergic agonist (Flieger M. Wurst M, Shelby R. 1997).

The toxic effects of mycotoxins (e.g. ochratoxins, fumonisins, zearalenone, etc.) are mostly known from veterinary practice. Mycotoxicoses, which can occur in both industrialized and developing countries, arise when environmental, social and economic conditions combine with meteorological conditions (humidity, temperature) which favour the growth of moulds.

Involvement of mycotoxins in disease causation should be considered in instances when a disease appears in several persons, with no obvious connection to a known etiological agent, such as microorganisms. Given current trade patterns, mycotoxicoses resulting from contaminated food, locally grown or imported, could occur in developing and developed countries alike. Strict control of food and feed and appropriate public health measures are therefore of considerable importance in reducing the risks to human and animal health.
Aflatoxins and Aflatoxicosis:

Aflatoxicosis is poisoning that result from ingestion of aflatoxin in contaminated food or feed. The aflatoxins are a group of structurally related toxic compounds produced by certain strains of the fungi Aspergillus flavus and A. parasiticus. Under favorable conditions of temperature and humidity, these fungi grow on certain foods and feeds resulting in the production of aflatoxins. The most pronounced contamination has been encountered in tree nuts, peanuts and other oil seeds including corn and cotton seeds. The major aflatoxins of concern are designated B1, B2, G1 and G2. These toxins are usually found together in various foods and feeds in various proportions; however, aflatoxin B1 is usually predominant and is the most toxic when a commodity is analyzed by thin layer Chromotagrophy, the aflatoxins separate into the individual components in the order given above; however, the first two fluoresce blue when viewed under ultra violet light and the second two fluoresce green. Aflatoxin M a major metabolic product of aflatoxin B1 in animals and is usually excreted in the milk and urine of dairy cattle and other mammalian species that have consumed aflatoxin-contaminated food or feed.

Disease Symptoms:

Aflatoxin produce acute necrosis and carcinoma of the liver in the number of animal species: no animal species is resistant to the acute toxic effect of aflatoxin: hence it is logical to assume that humans may be similarly affected. A wide variation in LD50 values has been obtained in animal species tested with single doses of aflatoxins. For most species, LD50 value ranges from 0.5 to
10mg per Kg. body weight. Animal species respond differently in their susceptibility to the chronic and acute toxicity of aflatoxin. The toxicity can be influenced by environmental factors, exposure level, and duration of exposure, age, health and nutritional status of diet. Aflatoxin B1 is very potent carcinogen in many species, including nonhuman primates, birds, fish and rodents. In each species the liver is the primary target organ of acute injury. Metabolism plays a major role in determining the toxicity of aflatoxin B1: studies show that this aflatoxin requires metabolic activation to exert its carcinogenic effect, and these effects can be modified by induction or inhibition of mixed function oxidase system.

Aflatoxicosis in human has rarely been reported: however such cases are not always recognized. Aflatoxicosis may be suspected when a disease outbreak exhibits the following characteristics.

- The cause is not readily identifiable.
- The condition is not transmissible.
- Syndromes may be associated with certain batches of food.
- Treatment with antibiotics or other drugs has little effect.
- The outbreak may seasonal, i.e., weather conditions may affect mold growth.

The adverse effects of aflatoxins in animal (and presumably in humans) have been categorized in two general forms.

A. (primary) acute aflatoxicosis is produced when moderate to high levels of aflatoxins are consumed. Specific, acute episodes of disease ensue
may include haemorrhage, acute liver damage, edema, alteration in digestion, absorption and/or metabolism of nutrients, and possibly death.

B. (Primary) Chronic aflatoxicosis results from ingestion of low to moderate levels of aflatoxins. The effects are usually sub clinical and difficult to recognize. Some of the common symptoms are impaired food conversion and slower rates of growth with or without the production of an overt aflatoxin syndrome.

Course of Disease & Complications:

In well-developed countries, aflatoxin contamination rarely occurs in foods at levels that cause acute aflatoxicosis in humans: Studies on human toxicity from ingestion of aflatoxins have focused on their carcinogenic potential. The relative susceptibility of humans to aflatoxins is not known, even though epidemiological studies in Africa and South-East Asia, where there is a high incidence of hepatoma, have revealed an association between cancer incidence and the aflatoxin content of the diet. These studies have not proved a cause-effect relationship, but the evidence suggests an association.

One of the most important accounts of aflatoxicosis in humans occurred in more than 150 villages in adjacent districts of two neighboring states in northwest India in the fall of 1974. According to one report of this outbreak, 397 persons were affected and 108 persons died. In this outbreak, contaminated corn was the major dietary constituent and aflatoxin levels of 0.25 to 15 mg/kg were found. The daily aflatoxin B1 intake was estimated to have been at least 55
μg/kg body weight for an undetermined number of days. The patients experienced high fever, rapid progressive jaundice, edema of the limbs, pain, vomiting and swollen livers. One investigator reported a peculiar and very notable feature of the outbreak: the appearance of signs of disease in one village population was preceded by a similar disease in domestic dogs, which was usually fatal. Histopathological examination of human showed extensive bile duct proliferation and periportal fibrosis of the liver together with gastrointestinal hemorrhages. A 10 year follow-up of the Indian Outbreak found the survivors fully recovered with no ill effects from the experience.

A second outbreak of aflatoxicosis was reported from Kenya in 1982, there were 20 hospital admissions with a 60% mortality: daily aflatoxin intake was estimated to be at least 38 μg/kg body weight for an undetermined number of days.

In a deliberate suicide attempt, a laboratory worker ingested 12 μg/kg body weight of aflatoxin B1 per day over a 2-day period and 6 months later, 11 μg/kg body weight per day over a 14 day period. Except for transient rash, nausea and headache, there were no ill effects; hence, these levels may serve as possible no-effect levels for aflatoxin B1 in humans. In a 14-year follow-up, a physical examination and blood chemistry, including tests for liver function were normal.
Ochratoxins:

The Aspergillus genus includes a species (A. ochraceus) that produces ochratoxins, a property it shares with at least two Pencillium species. Ochratoxin A (OA) and ochratoxin B are two forms that occur naturally as contaminants, with OA being more ubiquitous, occurring predominantly in cereal grains and in the tissues of animal reared on contaminated feed. Another mycotoxin, citrinin, often co-occurs with ochratoxin.

The microbiology of animal feeds emerged as an important issue in the wake of the Salmonella, E.coli O517, Campylobacter. Fungal contamination of animal feeds is a regular occurrence on a worldwide scale and detrimental effects have been observed in all classes of farm animals due to the production of mycotoxins by certain species and strains of moulds.

Fungal Contamination of concentrates and forages:

Fungal contamination of cereal grains, oil-seed meals and forages continues to represent a major animal health risk throughout the world and particularly in the humid tropics. The risks arise primarily from the ability of particular species and strains of fungi to produce harmful compounds known as mycotoxins. These substances arise from the secondary metabolism of fungi in response to a wide range of genetic and environmental factors. Mycotoxin contamination of forages and cereals frequently occurs in the field following infection of plants with specific pathogenic fungi or with symbiotic endophytes. In addition, contamination may occur during processing and storage of harvested
products and feed whenever environmental conditions are appropriate for spoilage fungi. Moisture content and ambient temperature are key factors affecting fungal colonization of and mycotoxin production in concentrates and compound feeds. Inhalation of fungal spores or consumption of mycelia may cause conditions collectively known as ‘mycoses’. An example of such a condition is mycotic abortion arising from the systemic transmission and delivery of fungal material to the placenta.

Classification:

It is conventional to subdivide toxigenic fungi into ‘field’ (or plant pathogenic) and ‘storage’ (saprophytic/spoilage) organisms. Claviceps, Fusarium and Alternaria are classical representatives of field fungi while Aspergillus and Pencillium exemplify storage organisms. Mycotoxigenic species may be further distinguished on the basis of geographical prevalence, reflecting specific environmental requirements for growth and secondary metabolism. Thus, Aspergillus flavus, Aspergillus parasiticus and Aspergillus ochraceus readily proliferate under warm, humid conditions whereas P. expansum and P.verrucosum are essentially temperate fungi. Consequently, the Aspergillus mycotoxins predominate in plant products emanating from the tropics and other warm regions. While the Penicillium mycotoxins occur widely in temperate foods, particularly cereal grains. Fusarium fungi are more ubiquitous but even this genus contains toxigenic species which are almost exclusively associated with cereals from tropical and sub-tropical countries. The distribution of the important fungi in concentrates and forages is shown below.
### Fungi Occurrence Mycotoxins

<table>
<thead>
<tr>
<th>Fungi</th>
<th>Occurrence</th>
<th>Mycotoxins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspergillus flavus</td>
<td>Peanut meal, cotton seed cake, palm kernel cake, maize, compound feeds</td>
<td>Aflatoxins</td>
</tr>
<tr>
<td>A. parasiticus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A. flavus</td>
<td>Oilseed meals, compound feeds</td>
<td>Cyclopiazonic acid</td>
</tr>
<tr>
<td>A. ochraceus; Penicillium viridicatum; P. cyclopium</td>
<td>Barley and wheat grains</td>
<td>Ochratoxin A</td>
</tr>
<tr>
<td>P. citrinum; P. expansum</td>
<td>Cereal grains</td>
<td>Citrinin</td>
</tr>
<tr>
<td>P. citreo-viride</td>
<td>Cereal grains</td>
<td>Citrioviridin</td>
</tr>
<tr>
<td>Fusarium culmorum; F. graminearum</td>
<td>Cereal grains</td>
<td>Deoxynivalenol</td>
</tr>
<tr>
<td>F. sporotrichioides; F. poae</td>
<td>Cereal grains</td>
<td>T-2 toxin</td>
</tr>
<tr>
<td>F. sporotrichioides</td>
<td>Cereal grains</td>
<td>Diacetoxysscirpenol</td>
</tr>
<tr>
<td>F. graminearum; F. sporotrichioides</td>
<td>Cereal grains</td>
<td></td>
</tr>
<tr>
<td>F. culmorum; F. graminearum; F. sporotrichioides</td>
<td>Cereal grains</td>
<td>Zearalenone</td>
</tr>
<tr>
<td>F. moniliforme</td>
<td>Maize kernels</td>
<td>Furmonisins; moniliformin; fusaric acid</td>
</tr>
<tr>
<td>Neotyphodium Coenophialum</td>
<td>Grasses</td>
<td>Ergopeptine alkaloids</td>
</tr>
<tr>
<td>N. lolli</td>
<td>Grasses</td>
<td>Lolitrem alkaloids</td>
</tr>
<tr>
<td>Claviceps purpurea</td>
<td>Cereal grains</td>
<td>Ergot alkaloids</td>
</tr>
<tr>
<td>Phomopsis leptostromiformis</td>
<td>Lupin stubble</td>
<td>Phomopsins</td>
</tr>
</tbody>
</table>

### Aspergillus species:

The *Aspergillus* genus dominates all other fungi in respect of mycotoxin production in cereals and oil seeds. For example, Dhand et al. (1998) observed that Aspergillus was the most significant genus in diary and other feeds.
in the tropics. Three species are responsible for virtually all mycotoxin production by this genus. *Aspergillus flavus*, *Aspergillus parasiticus* and *Aspergillus ochraceus*. *A.flavus* and *A.parasiticus* synthesise the aflatoxins, while *A.ochraceus* produces the ochratoxins.