Major Biological Consequences of Aflatoxicosis in Animal Production

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ABSTRACT: Aflatoxins, a family of closely related, biologically active mycotoxins, have been known as a prominent cause of animal disease for 30 yr. The toxins occur naturally on several key animal feeds, including corn, cottonseed, and peanuts. Occurrence of aflatoxin on some field crops tends to spike in years when drought and insect damage facilitate invasion by the causative organisms, Aspergillus flavus and A. parasiticus, which abound in the crop's environment. Acute aflatoxicosis causes a distinct overt clinical disease marked by hepatitis, icterus, hemorrhage, and death. More chronic aflatoxin poisoning produces very protean signs that may not be clinically obvious; reduced rate of gain in young animals is a sensitive clinical register of chronic aflatoxicosis. The immune system is also sensitive to aflatoxin, and suppression of cell-mediated immune responsiveness, reduced phagocytosis, and depressed complement and interferon production are produced. Acquired immunity from vaccination programs may be substantially suppressed in some disease models. In such cases the signs of disease observed are those of the infectious process rather than those of the aflatoxin that predisposed the animal to infection. Mixtures of aflatoxin with other mycotoxins can result in greatly augmented biological responses in terms of rate of gain, lethality, and immune reactivity. Because of its great biological activity, its widespread potential presence in areas where critical feed crops are grown, and its propensity to spike in problem years, aflatoxin promises to be a continuing problem in animal production.

Key Words: Aflatoxins, Aflatoxicosis, Mycotoxicoses, Immunosuppression, Hepatitis

Introduction

The year of this conference (1991) marks the 30th anniversary of our recognition of the aflatoxins and their deleterious effects on animal health. Certainly this family of potent mycotoxins has been with us for a much longer period, but their involvement in a number of acute animal disease outbreaks in 1960 led to the isolation and description of the major members of the toxin group in 1961 (Goldblatt, 1969). These events were typical of mycotoxicoses in general; a seasonal peak in toxin occurrence drew attention to the agents through production of an acute clinical disease. Although these acute intoxications can be dramatic and economically devastating, they constitute only a small fraction of the biological and economic consequences of the more usual chronic intoxications caused by lower levels of toxin (Pier, 1981, 1987).

Aflatoxins in Feedstuffs

Aflatoxins, primarily aflatoxin B₁, occur in a number of important animal feeds. Growth of toxigenic strains of Aspergillus flavus and A. parasiticus on corn, cottonseed, and peanuts often results in injurious levels of aflatoxin B₁, the most biologically active member of the aflatoxin family. These three feedstuffs are the most important sources of aflatoxin in animal feeds (Cheeke and Shull, 1985). The causative molds may occasionally colonize small cereal grains (barley, oats, and wheat) and produce low to moderate levels of aflatoxin. Soybeans do not support appreciable levels of aflatoxin B₁ production (Lillehoj et al., 1991). Ensilage, particularly the silage cap, may also contain aflatoxin, particularly if corn contain-
ing aflatoxin formed in the field is ensiled. A potentially hazardous feed is ground high-moisture corn, unless it is treated with adequate preservatives (e.g., propionates); the moisture content promotes the growth of the toxigenic molds and grinding of the kernel destroys the natural barrier to infestation. Hay (unless it contains a large complement of cereal grain infested in the field) is rarely if ever a source of appreciable aflatoxin (however, hay and forage may be sources of other mycotoxins such as ergot alkaloids, sporodesmin, slaframine, etc.).

Even on the preferred substrates listed above, aflatoxin requires specific conditions of moisture and feed substrate before toxigenic strains of A. flavus or A. parasiticus can produce appreciable levels of toxin. Only about 50% of the strains of these two molds are toxigenic. Moisture content of the feed must be ≥ 15% to support growth of the molds. The fungus must gain access to susceptible parts of the plant (e.g., the corn kernel, cotton seed, etc.) before it grows and elaborates aflatoxins. Seasonal peaks in aflatoxin content are seen in key years when drought-damaged plants or insect-damaged crops are rendered more susceptible to fungal invasion. Wet harvest seasons also may contribute to high levels of aflatoxin in certain crops. Aflatoxin sometimes develops in crops stored at levels of moisture content > 15% or properly dried crops stored in leaky bins. Development of aflatoxin can be prevented in stored grains by good management practices (Christensen and Meronuck, 1988); the occurrence of aflatoxin in field crops, however, is largely a matter of uncontrollable natural events. In these events careful use of blending with clean crops or detoxification through ammoniation, with close attention to existing rules and regulations, may be possible to reduce the toxin content in animal feeds to safe levels (Park et al., 1988; FDA, 1989). Recent information suggests that binding agents fed with aflatoxins may reduce the availability of the toxins and thereby reduce their effects in some animal species (Harvey et al., 1989). In the absence of one of these control procedures the feed should be withheld from animal use.

Effects of Aflatoxins on Animals

Effects of aflatoxin consumption are similar in all animals; the animal's susceptibility to aflatoxin, however, varies by species, age, and individual variation (Table 1; Pier, 1987). In acute clinical aflatoxicosis, signs of acute hepatic injury are seen as coagulopathy, increased capillary fragility, hemorrhage, and prolonged clotting times. Blood pigments may appear in the urine and mucous membranes are icteric. The liver shows gross changes caused by centrallobular congestion and hemorrhage and fatty changes of surviving hepatocytes. Death of the animal may occur within hours or a few days. In chronic aflatoxin poisoning, most of the effects are still referable to hepatic injury, but on a milder scale. The most sensitive clinical sign of chronic aflatoxicosis is reduced rate of growth of young animals. Other signs include prolonged clotting time, increases in serum glutamic oxalacetic transaminase, ornithine carbamyyl transferase, and cholic acid levels. Hepatic pathology includes a yellow to brassy color, enlarged gall bladder, dilute bile, histologic signs of fatty changes in the hepatocytes, and bile duct proliferation. Frequently the signs of chronic aflatoxins are so protean that the condition goes undiagnosed for long periods. Chronic aflatoxin poisoning, however, is the manner in which animals are most frequently affected and the economic consequences are often considerable.

Both acute and chronic aflatoxin poisoning can impair immune responses and native defense mechanisms (Pier and McLoughlin, 1985; Pier 1986, 1991). In addition to the liver, the thymus is also a target organ for aflatoxin; thymic involution results with loss of cortical thymocytes. It is primarily the cell-mediated immune responses that are affected by aflatoxin; prominent among these are diminished responses in delayed cutaneous hypersensitivity, graft-vs-host reaction, leukocyte migration, and lymphoblastogenesis. Aflatoxin also reduces phagocytic activity in a dose-related manner; this is important not only to the phagocytic clearance of invading organisms but also to presentation of antigens to other components of the immune system. Some humoral components are diminished by aflatoxin, including complement (C₄), interferon, IgG, and IgA, but not

<p>| Table 1. Comparative susceptibility of food-producing animals and livestock to aflatoxin* |</p>
<table>
<thead>
<tr>
<th>Approximate susceptibility level</th>
<th>Age</th>
<th>Approximate single oral LD₅₀, mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Highly susceptible</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rabbits</td>
<td>3 mo</td>
<td>.30</td>
</tr>
<tr>
<td>Ducks</td>
<td>1 d</td>
<td>.36</td>
</tr>
<tr>
<td>Swine Weaning</td>
<td></td>
<td>.62</td>
</tr>
<tr>
<td>Moderately susceptible</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Horse Adult</td>
<td></td>
<td>6–1.0b</td>
</tr>
<tr>
<td>Calves 1 mo</td>
<td></td>
<td>1.0–1.5b</td>
</tr>
<tr>
<td>Turkeys 3 wk</td>
<td></td>
<td>1.36</td>
</tr>
<tr>
<td>Sheep Adult</td>
<td></td>
<td>2.0</td>
</tr>
<tr>
<td>Relatively resistant</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chickens 1 wk</td>
<td></td>
<td>6.5</td>
</tr>
</tbody>
</table>


bEstimated LD₅₀ from response to experimental doses.
IgM. Usually only dramatically high levels of aflatoxin will affect antibody titers and gut-associated lymph tissue or the bursa or Fabricius in poultry.

Immunity acquired through vaccination procedures is impaired in fowl cholera and porcine erysipelas, but not Newcastle disease in chickens. Similarly, susceptibility to some infectious agents (e.g., Salmonella, Candida, Treponema, Eimeria, and infectious bursal disease virus) is increased, but not all infectious processes seem to be affected (Pier and McLaughlin, 1985). Of considerable potential economic consequence is the fact that aflatoxin can suppress the immune system of young animals by in utero transfer across the placenta of the pregnant dam (Pier et al., 1985). In these cases the affected newborn animals lack resistance to infection and cannot respond well to vaccines. These are reactions of considerable consequence in colonized animals in which we rely on elective vaccination procedures in disease prevention.

Several of the major mycotoxins exert their effects through different organ systems and different biological pathways. Aflatoxin, ochratoxin, and T-2 toxin all interfere with protein formation, but each does so in a different manner; aflatoxin binds to both RNA and DNA and blocks transcription. T-2 toxin blocks initiation of translation, and ochratoxin blocks phenylalanine-tRNA synthetase, and thus blocks translation. Each toxin causes different effects on globulin formation; aflatoxin reduces IgG and IgA but not IgM and usually does not reduce antibody titers, ochratoxin reduces IgG and IgM and regularly reduces antibody responses, T-2 reduces IgM and IgA but usually not IgG and often reduces antibody response. Both aflatoxin and T-2 effect reduced complement activity, but in different ways; aflatoxin reduces C₄ activity, whereas T-2 reduces C₃ activity. Thus, one might expect that when mixtures of mycotoxins are encountered in feed mixtures that some interaction of these toxins might be apparent. Experiments combining aflatoxin and T-2 toxin show a synergistic effect on lethality, but only additive suppression was seen on weight gain and selected immunologic traits (Pier et al., 1986). Another mycotoxin mixture (aflatoxin and cyclopiazonic acid) was studied in guinea pigs (Pier et al., 1989). This was an interesting mixture because these two toxins appear together in nature; some strains of A. flavus are capable of producing both toxins in corn and other substrates. Synergistic interaction was seen on lethality, weight gain, and histopathologic changes in the liver. However, an interesting observation was that cyclopiazonic acid overcame the immunosuppressive effects of aflatoxin on cell-mediated immune responses. From these and other studies it is apparent that the immune system is a sensitive register for the effects of various mycotoxins and that mixtures of mycotoxins can profoundly affect the animal organism.

Implications

The economic consequences of aflatoxicosis on young growing animals are substantial and varied. Aflatoxins cause clinical illness and death when consumed in high quantity; at lesser levels they reduce the growth rate and feed efficiency of young animals and they reduce the animals' ability to cope with infections. Undoubtedly we will recognize yet other effects of the aflatoxins on animal and human health as investigations continue. Because of their exceptional biological activities and their propensity to peak in essential field crops during problem years, aflatoxins promise to be a continuing problem in animal production.

Literature Cited


