Mycotoxins and reproduction in domestic livestock

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Mycotoxins and Reproduction in Domestic Livestock

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ABSTRACT: Molds are parasitic plants that are ubiquitous in livestock feedstuffs. Even though molds themselves reduce the quality of grains, their synthesis of chemical substances termed mycotoxins causes the greatest monetary loss to the animal industry. Five major mycotoxins that impair growth and reproductive efficiency in North America are aflatoxins, zearalenone, deoxynivalenol, ochratoxin, and ergot. Aflatoxins are produced by Aspergillus flavus and Aspergillus parasiticus. Consumption of grains containing aflatoxins by swine affects reproduction indirectly by reducing feed intake and growth. In swine, aflatoxins impair liver and kidney function, delay blood clotting, increase susceptibility to bruising, and interfere with cellular humoral immune systems. Ruminants are comparatively resistant to aflatoxicosis, but presence of aflatoxins in milk of dairy cows is closely monitored for human safety.

Depending on environmental conditions, Fusarium roseum can produce either zearalenone or deoxynivalenol. Days 7 to 10 postmating seem to be a critical period of gestation for zearalenone to exert its detrimental actions on early embryonic development. Presence of deoxynivalenol in swine feedstuffs decreases feed intake, causes feed refusal, and induces occasional vomiting. Several species of Penicillium and Aspergillus produce ochratoxin, a mycotoxin that causes necrosis of kidney tissue. Ergot alkaloids produced by Claviceps purpurea on wheat can cause reproductive problems and are associated with lactational failure in swine. Various methods have been developed to remove mycotoxins from infected feedstuffs. Chemical analyses in laboratories as well as diagnostic kits suitable for use at the elevator or farm can be used successfully to identify which mycotoxins are present in suspect feedstuffs.

Key Words: Reproduction, Aflatoxins, Zearalenone, Deoxynivalenol, Ochratoxins, Ergot


Introduction

Molds are parasitic plants that thrive on common livestock feedstuffs. Not only do molds themselves reduce the quality of grains, but production of chemical substances called mycotoxins impairs growth and reproductive efficiency. Outbreaks of mycotoxin contamination occur sporadically but are somewhat predictable if attention is paid to growing conditions of the plant in the field or to storage conditions of the harvested crop.

Molds capable of synthesizing mycotoxins have been identified on corn, wheat, oats, barley, cottonseed, and peanuts. A comprehensive list of mycotoxins that affect animals can be found in a Task Force Report No. 116 from the Council for Agricultural Sciences and Technology (CAST, 1989). Five major mycotoxins that impair livestock performance in North America are aflatoxins, deoxynivalenol (DON), ergot, ochratoxin, and zearalenone (ZEN). Of these mycotoxins, ZEN affects reproduction of livestock most seriously because it possesses estrogenic activity. The other mycotoxins affect reproduction in livestock via indirect means such as reduced feed intake or reduced growth or by damaging other vital organs of the body (Shull and Cheeke, 1983). This review will examine the conditions necessary for molds to produce mycotoxins and how these mycotoxins affect reproductive performance of livestock, with the greatest emphasis on ZEN in swine.
Molds

Plants and animals serve as excellent hosts for molds. Spores from molds are primarily spread by water and air and come into contact with plants in the field or with grain in storage facilities. Factors that influence whether grain is invaded by the spores or the degree of infestation are moisture, temperature, and availability of oxygen. Other factors such as insect population, physical condition of grain, or susceptibility of certain hybrids to mold growth also influence whether molds will proliferate under a given set of environmental conditions.

Each species of mold has an ideal set of atmospheric conditions in which it will grow and reproduce. These conditions vary even within the same genera. For example, suitable relative humidity for growth of *Aspergillus glaucus* is approximately 10% lower than for *Aspergillus flavus*. Although a few molds can grow at extremely high or low temperatures, most proliferate at moderate temperatures and cannot grow without at least 1 to 2% oxygen.

Environmental conditions sufficient for mold growth in the field are usually found during the growing season and thus are difficult to control. Conditions for optimal mold growth, however, can be controlled after crops are harvested and in storage. In general, mold growth can be inhibited by maintaining the following conditions in the storage bin: 1) relative humidities < 70%, 2) moisture content of grains < 14%, 3) temperatures < -2.2°C, and 4) oxygen < .5%. If these conditions are met, most molds will cease to grow. If suboptimal conditions are present the mold may grow slowly and eventually change the environment to a more favorable one for itself or other molds. If enough heat or moisture is produced, the environmental conditions may then be conducive for rapid growth to occur. For this reason, bins must be routinely monitored to ensure that storage conditions have not changed over time.

Even though mold growth in storage can be controlled through refrigeration, drying, or application of mold inhibitors, total inhibition of mold growth is very difficult and expensive. Controlling mold growth can be profitable if a higher market price for the grain is obtained, the handling properties of the feedstuff are improved, and/or more industrial uses are realized. In general, the consumption of moldy feedstuffs by livestock is not harmful. Fortunately, most moldy grain is not toxic because 1) a toxic species must compete with a nontoxic species to grow, 2) a toxic isolate of the species does not exist by itself because only a portion of the mold is producing toxins, and 3) suitable environmental conditions for mold growth do not coincide with conditions suitable for toxin production. Even though quality of the grain can be reduced by mold infestations, the problems with livestock consuming moldy grain are usually manifested through the presence of mycotoxins.

Mycotoxins

Most mycotoxins that are of economic importance in the livestock industry are produced by the genera *Penicillium*, *Aspergillus*, *Claviceps*, and *Fusarium*. *Penicillium* molds are beneficial to the livestock industry because they produce penicillin. However, several species of *Penicillium* as well as *Aspergillus* produce ochratoxin, a mycotoxin that damages kidney tissue. Two distinct species of *Aspergillus* produce aflatoxins, a mycotoxin that primarily affects animal performance by reducing feed intake and growth. Ergot alkaloids synthesized by *Claviceps purpurea* augment vasomotor activity and affect lactation in swine.

*Fusarium roseum* produces two mycotoxins, DON and ZEN, that reduce livestock performance. Consumption of corn or wheat containing DON causes decreased feed intake or feed refusal and occasionally vomiting. Zearalenone disrupts reproductive processes because it mimics the action of estradiol-17β. Each of these mycotoxins will be discussed in more detail in the remainder of this review.

Aflatoxin

Aflatoxins are mycotoxins produced primarily by *Aspergillus flavus* and *Aspergillus parasiticus*. Although these molds are abundant in the southeastern United States, drought-stressed corn in Indiana and Illinois in 1983 contained aflatoxins. In 1988, *Aspergillus* was observed on corn plants in the Midwest but production of aflatoxins was scant.

Several closely related aflatoxins are produced by *A. flavus* and *A. parasiticus*. Four aflatoxins were isolated initially and were identified as B1, B2, G1, and G2 based on their blue or green fluorescence properties and migration patterns during chromatography. The potency and carcinogenicity of these aflatoxins are dependent on the species, dose of intake, duration of intake, age of animal, and nutritional state, but it is generally agreed that B1 is the most potent of the aflatoxins (Pier, 1981). Additional aflatoxins such as M1, M2, B2a, H, D, G, and parasitic01 have been identified but characterization studies are incomplete.

Aflatoxins affect all livestock to some degree but swine are the most sensitive. Consumption of feedstuffs contaminated with aflatoxins does not
seem to impair reproduction directly, but rather indirectly through other physiological systems. Nutritional responses in young animals during their growing phase have been examined in most trials using aflatoxin-infested grain. Few studies have addressed the effects of aflatoxins on animals of specific reproductive states. Signs of aflatoxicosis include liver and kidney damage, decreased tissue strength, delayed blood clotting, and susceptibility to bruising. Aflatoxins also decrease resistance to bacterial, fungal, viral, and parasitic diseases in swine by interfering with cellular and humoral immune systems (Pier et al., 1979). In addition, vaccinations against various agents are less effective in pigs exposed to aflatoxins, potentiating the problems of environmental heat and cold stress.

Overall, aflatoxins impair swine performance by reducing feed efficiency and rate of growth. The majority of studies with aflatoxin have used barrows from 6 to 12 wk of age. For the few studies that have used gilts, the effects of aflatoxins have not been studied beyond 12 wk of age. Effects of aflatoxin on performance in barrows have not been reported. Therefore, the direct effects of aflatoxin on reproduction have not been determined.

Most experiments examining the effects of aflatoxins on swine performance have used corn and soybean diets that have been supplemented with aflatoxin that was produced through fermentation of rice by Aspergillus. Rice powder is then mixed into diets to give the desired aflatoxin contamination. As shown in Table 1, impairment of performance of young barrows and gilts is manifested through a reduction in ADG. In most cases, concentrations of aflatoxin > 500 ppb resulted in reduced growth. In an experiment in which a diet of 18% CP was spiked with purified aflatoxin, a reduction in ADG was observed with 182 ppb (Coffey et al., 1989) but ADG was not affected if aflatoxin was added to a diet with 20% CP. Feed efficiency or feed intake was not always measured but the response was variable among experiments.

Ruminants seem to be more resistant to aflatoxicosis than swine, but clinical signs of acute aflatoxicosis such as reduced feed intake, decreased milk production, and liver damage have been observed in cattle. In addition, chronic exposure to aflatoxin has lowered feed efficiency, depressed the immune system, and reduced reproductive efficiency (Guthrie, 1979; Bodine and Mertens, 1983). Aflatoxin alters ruminal function by decreasing cellulose digestion, volatile fatty acid formation, proteolysis, and motility (Dvorak et al., 1977; Cook et al., 1986). Ruminal fluid or bacteria from the rumen of sheep or cattle did not convert aflatoxin into other metabolites (Kiessling et al., 1984), but the predominant metabolite of aflatoxin B1 is M1, which is found in greatest quantities in milk. Close monitoring of milk for aflatoxins is necessary by the Food and Drug Administration because of the potential for carcinogens to enter the human food chain.

Ochratoxin

Ochratoxin A is the best-characterized of several structurally related mycotoxins produced by Aspergillus ochraceus and Penicillium viridicatum. Ochratoxin A has been found on a variety of feedstuffs grown on the southeastern coast of the United States as well as in the blood of pigs slaughtered in western Canada (Marquardt et al., 1988). Ochratoxin A primarily disrupts renal function when animals are exposed to naturally occurring concentrations of the mycotoxin (Krogh, 1977; Rutqvist, 1978). When 3- to 4-wk-old pigs ingested feed containing 5 to 10 ppm of ochratoxin, extrarenal effects were observed. Ingestion of 28 ppm of ochratoxin resulted in death within 3 wk (Szczech et al., 1973). When barrows ingested feed containing 2,000 ppm of ochratoxin from 7 to 11 wk of age, they gained poorly and their kidney weight and function was altered (Harvey et al., 1989a). That the kidney is a main target for ochratoxin is demonstrated by selective uptake of ochratoxin by the proximal tubules of pig kidney cortex (Friis et al., 1988). Overall, the occurrence of ochratoxin in feedstuffs in the United States is low and poses little threat to our food supply.

Ergot

Claviceps purpurea, C. paspalli, and C. fusiformis invade rye, wheat, and barley plants and produce alkaloid toxic agents termed ergots. Ergotism reduces weight gains, lowers reproductive efficiency, and promotes agalactia of several livestock species (Robbins et al., 1986). Signs of ergotism include staggers, convulsions, temporary posterior paralysis, and loss of blood flow to limbs, ears, and the tail, which sometimes leads to gangrene and eventual loss of extremities (Burfening, 1973). Steers consuming a barley diet containing ergot at .5% (wt/wt) exhibited higher rectal temperatures, reduced feed intake, and body weight loss while they were exposed to high summer temperatures (Ross et al., 1989). Documented cases of ergotism are rare in the United States because the cleaning and milling processes remove the ergot-infected grains. Exposure of livestock or humans to ergot alkaloids is most likely in locally grown and consumed grain, but in most cases the concentration of ergot is too low to be of any major consequence.
Table 1. Summary of selected references on aflatoxin and growth performance of swine

<table>
<thead>
<tr>
<th>Source</th>
<th>Location</th>
<th>Aflatoxin, ppb</th>
<th>Sex</th>
<th>Treatment period (age or BW)</th>
<th>Effect</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Groundnut meal in barley/wheat</td>
<td>United Kingdom</td>
<td>260</td>
<td>Barrows, gilts</td>
<td>18-64 kg</td>
<td>↓ADG</td>
<td>Duthrie et al., 1985</td>
</tr>
<tr>
<td></td>
<td></td>
<td>460</td>
<td>Barrows, gilts</td>
<td>13-30 wk</td>
<td>↓FE</td>
<td>Hintz et al., 1987</td>
</tr>
<tr>
<td>Natural contamination</td>
<td></td>
<td>1,005</td>
<td>Barrows, gilts</td>
<td>13-30 wk</td>
<td>↓ADG</td>
<td></td>
</tr>
<tr>
<td>Natural contamination</td>
<td>North Carolina</td>
<td>385</td>
<td>Not stated</td>
<td>53-97 kg</td>
<td>↓ADG</td>
<td>Southern and Clawson, 1979</td>
</tr>
<tr>
<td>Natural contamination</td>
<td></td>
<td>1,480</td>
<td>Not stated</td>
<td>53-80 kg</td>
<td>↓ADG</td>
<td></td>
</tr>
<tr>
<td>Natural contamination</td>
<td>Texas</td>
<td>1,000-4,000</td>
<td>Barrows</td>
<td>6-10 wk</td>
<td>↓ADG</td>
<td>Harvey et al., 1988</td>
</tr>
<tr>
<td>Natural contamination</td>
<td>Georgia</td>
<td>500-600</td>
<td>Miniature boars</td>
<td>18-27 kg</td>
<td>↓ADG</td>
<td>Colvin et al., 1989</td>
</tr>
<tr>
<td>Natural contamination</td>
<td>Texas</td>
<td>2,000</td>
<td>Barrows</td>
<td>7-11 wk</td>
<td>↓ADG</td>
<td>Harvey et al., 1989a</td>
</tr>
<tr>
<td>Natural contamination</td>
<td></td>
<td>750</td>
<td>Barrows</td>
<td>6-9 wk</td>
<td>↓ADG</td>
<td>Harvey et al., 1989b</td>
</tr>
<tr>
<td>Natural contamination</td>
<td></td>
<td>3,000</td>
<td>Barrows</td>
<td>6-10 wk</td>
<td>↓ADG</td>
<td>Harvey et al., 1989c</td>
</tr>
<tr>
<td>Natural contamination</td>
<td>Texas</td>
<td>3,200</td>
<td>Barrows</td>
<td>7-11 wk</td>
<td>↓ADG</td>
<td>Harvey et al., 1989c</td>
</tr>
<tr>
<td>Natural contamination</td>
<td>North Carolina</td>
<td>182</td>
<td>Barrows, gilts</td>
<td>4-8 wks</td>
<td>↓ADG</td>
<td>Coffey et al., 1989</td>
</tr>
<tr>
<td>Natural contaminated</td>
<td>Czechoslovakia</td>
<td>30-300</td>
<td>Not stated</td>
<td>28 days</td>
<td>↓ADG</td>
<td>Drabek et al., 1989</td>
</tr>
<tr>
<td>Natural contamination</td>
<td>Iowa</td>
<td>200-2,000</td>
<td>Barrows, gilts</td>
<td>2-12 wk</td>
<td>↓ADG</td>
<td>Cook et al., 1989</td>
</tr>
</tbody>
</table>

*Unless otherwise indicated, diets consisted of naturally contaminated field corn, or aflatoxin was produced by fermentation of rice and added to achieve desired concentrations.*

*FE = feed efficiency; FI = feed intake.*
Deoxynivalenol

Optimal environmental conditions for *Fusarium roseum* to multiply occur when the corn plant is exposed to cool, wet weather during silking followed by a short drying season. Even though the moisture content of grain may be low enough (13 to 14%) to prevent mold growth when it is put into storage, improper storage may allow the moisture content of the grain to rise to 22 to 23%. At this moisture content, the mold can produce high concentrations of DON as well as ZEN in a relatively short period of time. In naturally molded roseum to multiply occur when the corn plant is infected with *Fusarium roseum*, both DON and ZEN are usually present. In earlier experiments when naturally contaminated moldy corn was used, the specific actions of each mycotoxin could not be discerned. However, addition of purified DON or ZEN to diets has indicated that reduced feed intake or poorer feed efficiency is due to the presence of DON (Table 2), whereas the estrogenic stimulation of reproductive tissues can be attributed to ZEN (Table 3).

As shown in Table 2, most trials examining the effects of moldy corn containing DON on growth performance in swine have used young, growing pigs whose diets contained DON concentrations from 1 to 20 ppm. If purified DON is added to the diet, usually higher concentrations of the mycotoxin will be ingested by the pig before complete refusal of the feed occurs (Forsyth et al., 1977; Long and Diekman, 1984b). With one exception (Trenholm et al., 1984b), DON impaired growth performance in each experiment in which ADG and feed efficiency were measured (Table 2). No deleterious effects of DON were observed on fetal development when feed containing 8 ppm of purified DON was consumed, even though higher concentrations of DON (< 20 ppm) need to be tested before it can conclusively be stated that DON is not toxic to embryonic development (Long and Diekman, 1984b).

In lambs, consumption of a wheat diet containing DON at 15.6 mg/kg of BW for 28 d did not alter feed consumption, weight gain, or feed efficiency (Harvey et al., 1986). Oral administration of DON revealed that it was rapidly cleared essentially unchanged (> 95%) and was excreted primarily in urine (Prelusky et al., 1986). Incubation of DON with ruminal microorganisms in vitro for 48 h resulted in the partial conversion to deepoxy DON (Swanson et al., 1987). Extremely low amounts of DON (< 4 ng/mL) were transmitted to milk after a single oral dose of 920 mg to a dairy cow (Prelusky et al., 1984).

Zearalenone

Estrogenic compounds naturally produced by plants are commonly referred to as phytoestrogens. Phytoestrogens are of three general classes: 1) isoflavones, 2) coumestans, and 3) resorcylic acid lactones (Stob, 1983). Zearalenone and zearalenol are both estrogenic resorcylic acid lactone compounds produced by the fungi *Fusarium* spp. Mycotoxins produced by *Fusarium* spp. are of two general types: 1) the nonestrogenic trichothecenes, including DON, nivalenol, T-2 toxin, and diacetoxyscirpenol, and 2) the mycoestrogens, including ZEN and zearalenol.

Although an estrogenic factor in moldy corn was recognized in the late 1920s (McNutt et al., 1928), Stob and coworkers were the first to isolate a uterotrophic compound from corn contaminated with the fungus *Gibberella zeae* (Stob et al., 1962). This compound was identified as ZEN (Urry et al., 1966). The same metabolite was isolated by Christensen et al. (1965) from corn inoculated with *Fusarium* and named “F-2.” Caldwell and Tuft (1970) screened 110 isolates, belonging to seven species of *Fusarium*, for ZEN production. Thirty-four isolates were found to produce ZEN with a range of production of 0.2 to 230 μg/g of corn.

Despite their structural dissimilarity to the steroidal estrogens, ZEN and several of its derivatives possess estrogenic activity. Patterson (1977) postulated that ZEN undergoes a folding such that hydroxyl or potential hydroxyl groups become appropriately orientated to facilitate binding to tissue receptors that normally bind estrogens. In the immature rat uterus, zearalanol exhibits a binding affinity of 10% for the estrogen receptor when compared to estradiol-17β, whereas ZEN possesses a relative binding affinity of 1.8% to that of estradiol-17β (Katzenellenbogen et al., 1979). Similar affinities for ZEN have been determined for the estrogen receptor in sheep (Shutt and Cox, 1972) and calf uterus (Kiang et al., 1978).

*Prepubertal Gilts.* Of all domestic species and all stages of maturity, the prepubertal gilt is the most sensitive to ZEN. The genital system of immature gilts exhibits gross and histologic changes after exposure to ZEN. Gross changes include tumefaction of the vulva, increased size and weight of the uterus, and mammary enlargement (Stob et al., 1962; Kurtz et al., 1969; Nelson et al., 1973; Young et al., 1981). In extreme cases, rectal and vaginal prolapses occurred (Young et al., 1981; Blaney et al., 1984). Microscopic changes included edema and thickening of the uterus caused by a combination of hypertrophy and hyperplasia of both the endometrium and myometrium. Although many of the above observations were produced by naturally contaminated feedstuffs, Kurtz et al. (1969) found that the histological changes produced by estradiol-17β-cyclopentyl propionate, purified F-2 (ZEN) extract, and *Fusarium*-inoculated corn were indistinguishable.
<table>
<thead>
<tr>
<th>Source of DON</th>
<th>Location</th>
<th>DON, ppm</th>
<th>Zearalenone, ppm</th>
<th>Sex</th>
<th>Treatment period (age or BW)</th>
<th>Effect</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Purified</td>
<td>Indiana</td>
<td>3.6</td>
<td>1</td>
<td>Not stated</td>
<td>20-24 kg</td>
<td>↓FI 20%</td>
<td>Forsyth et al., 1977</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7.2</td>
<td>1</td>
<td>Not stated</td>
<td></td>
<td>↓FI 44%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>40</td>
<td>1</td>
<td>Not stated</td>
<td></td>
<td>↓FI 90%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Vomiting</td>
<td></td>
</tr>
<tr>
<td>Natural contamination</td>
<td>Ontario</td>
<td>3.6</td>
<td>6.7</td>
<td>Gilts</td>
<td>6.8-11.7 kg</td>
<td>↓ADG 47%</td>
<td>Young et al., 1981</td>
</tr>
<tr>
<td></td>
<td>Ontario</td>
<td>8.7</td>
<td>4.5</td>
<td>Gilts</td>
<td>6.4-8.4 kg</td>
<td>↓FE 23%</td>
<td>Young et al., 1981</td>
</tr>
<tr>
<td></td>
<td>Canada</td>
<td>1.3</td>
<td>0</td>
<td>Not stated</td>
<td>3 wk</td>
<td>↓ADG</td>
<td>Young et al., 1983</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12</td>
<td>.02</td>
<td>Not stated</td>
<td>3 wk</td>
<td>↑FE</td>
<td>Young et al., 1983</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20</td>
<td>.09</td>
<td>Not stated</td>
<td>3 wk</td>
<td>Almost complete feed refusal</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Vomiting</td>
<td></td>
</tr>
<tr>
<td>Natural contamination</td>
<td>Indiana</td>
<td>8</td>
<td>0</td>
<td>Pubertal gilts</td>
<td>Days 2-15 of gestation</td>
<td>No effect on fetuses</td>
<td>Long and Diekman, 1984</td>
</tr>
<tr>
<td>Natural contamination</td>
<td>Ontario</td>
<td>.75-2</td>
<td>.03- .26</td>
<td>Barrows, gilts</td>
<td>3-7 wk</td>
<td>↓FI</td>
<td>Trenholm et al., 1984</td>
</tr>
<tr>
<td>Natural contamination</td>
<td>Illinois</td>
<td>.7</td>
<td>0</td>
<td>Barrows, gilts</td>
<td>9.8-24.0 kg</td>
<td>↓ADG 27-50%</td>
<td>Cote et al., 1985</td>
</tr>
<tr>
<td>Natural contamination</td>
<td>Ontario</td>
<td>10.5</td>
<td>1.1</td>
<td>Barrows</td>
<td>8.4-16.4 kg</td>
<td>↓FE</td>
<td>Lun et al., 1985</td>
</tr>
<tr>
<td>Naturally contaminated wheat</td>
<td>Kansas</td>
<td>6.8</td>
<td>0</td>
<td>Barrows, gilts</td>
<td>3 wk</td>
<td>↑FI</td>
<td>Pollmann et al., 1985</td>
</tr>
<tr>
<td>Naturally contaminated wheat</td>
<td>Ontario</td>
<td>3.7</td>
<td>.4</td>
<td>Boars, gilts</td>
<td>23-53 kg</td>
<td>↓FI 25%</td>
<td>Friend et al., 1986</td>
</tr>
<tr>
<td>Naturally contaminated corn</td>
<td>Ontario</td>
<td>4.2</td>
<td>.2</td>
<td>Boars, gilts</td>
<td>23-53 kg</td>
<td>↓FI 25%</td>
<td>Friend et al., 1986</td>
</tr>
</tbody>
</table>

a) Unless otherwise stated, diets consisted of naturally contaminated field corn, or crystalline deoxynivalenol was added to achieve desired concentrations.
b) ↓FI = feed intake; FE = feed efficiency.
Table 3. Summary of selected references when zearalenone (ZEN) was fed to prepubertal gilts

<table>
<thead>
<tr>
<th>Source of ZEN&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Location</th>
<th>ZEN, ppm</th>
<th>Treatment period</th>
<th>Effect</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Purified</td>
<td>Ontario</td>
<td>10-40</td>
<td>10-20 kg</td>
<td>Uterine enlargement</td>
<td>James and Smith, 1982</td>
</tr>
<tr>
<td>Purified</td>
<td>Missouri</td>
<td>10</td>
<td>163-193 d</td>
<td>↑Age puberty →Length of estrous cycle</td>
<td>Edwards et al., 1987a</td>
</tr>
<tr>
<td>Naturally contaminated milo</td>
<td>Mississippi</td>
<td>1.8</td>
<td>70-115 or 70-160 d</td>
<td>↑Age puberty →Fetuses →Ovulation Rate</td>
<td>Rainey et al., 1990</td>
</tr>
<tr>
<td>Purified</td>
<td>Indiana</td>
<td>10</td>
<td>178-1982 d</td>
<td>→Age puberty →Litter size</td>
<td>Green et al., 1990</td>
</tr>
</tbody>
</table>

<sup>a</sup>Unless otherwise indicated, crystalline zearalenone was added to corn-soya diets to give desired concentrations.

Although the gross and histologic changes that are induced by ZEN are well characterized in prepubertal gilts, little is known about what effect this hyperestrogenism has on puberty or subsequent reproduction. Recently, Edwards et al. (1987a) reported that prepubertal gilts fed 10 ppm of ZEN displayed first estrus later than controls, but the proportion of gilts showing estrus within 60 d of boar exposure was not affected. The length of the first estrous cycle was also not affected by prepubertal exposure to ZEN. In contrast, prepubertal gilts consuming a milo diet contaminated with 1.8 ppm of ZEN exhibited puberty at a younger age without altering conception rates, ovulation rates, or embryonic survival (Rainey et al., 1990).

In a third study, ingestion of 10 ppm of ZEN during prepubertal development did not delay attainment of puberty or alter the proportion of gilts that reached puberty (Green et al., 1990). Even though it is not clear whether ZEN consumption affects the onset of puberty, results from these studies indicate that the estrogenic properties of ZEN are not permanently damaging and that gilts may successfully enter the breeding herd without subsequent reduction in fertility if they are given a 2-wk withdrawal period.

Cycling Gilts. Zearalenone causes multiple reproductive dysfunctions in the mature, cycling gilt (Table 4). Chang et al. (1979) reported that concentrations of 25 to 100 ppm of ZEN (95% pure) fed from weaning continuously throughout the next gestation produced constant estrus, pseudopregnancy, and, ultimately, infertility. Flowers et al. (1987) extended the interval between estrus by administering either 20 mg of ZEN or 2 mg of estradiol benzoate per gilt on d 6 to 10 or d 11 to 15 of the estrous cycle.

Extended cycles were also reported in gilts that ingested 5 to 10 ppm of ZEN between d 5 and 20 of the estrous cycle (Edwards et al., 1987b). Luteal function was maintained as shown by a high serum progesterone concentration on d 19 to 21 for those gilts that had extended cycles. These persist-
ent corpora lutea spontaneously regressed 30 d after ZEN was removed from the diet.

A diet that contained 3.6 to 4.3 ppm ZEN was fed to gilts from puberty to mating (Etienne and Jemmali, 1982). Forty-five percent of these gilts ingesting ZEN did not return to estrus within 30 d after puberty. These gilts were confirmed to be pseudopregnant at slaughter; corpora lutea were present on both ovaries, but no corpora albicantia were found. Similar results were obtained by Young and King (1986a) in pubertal gilts that consumed 6 to 9 ppm of ZEN starting the day after first estrus. Induced retention of corpora lutea by ZEN was similar to that which occurs when sows are given exogenous estrogen on d 11 to 12 of the estrous cycle (Kidder et al., 1955; Gardner et al., 1963).

**Pregnant Gilts or Sows.** Numerous observations of *Fusarium*-contaminated feedstuffs causing stillbirths, neonatal mortality, fetal mummification, splay-leg of pigs, abortion, abnormal return to estrus, and other abnormalities have been reported (Sharma et al., 1974; Shreeve et al., 1975; Mirocha et al., 1977; Christensen, 1979). However, the exact role that ZEN played in each of these situations was not well characterized. In many cases, moldy feedstuffs were not assayed for ZEN (Sharma et al., 1974) and conclusions were made from field observations rather than from controlled experiments. Therefore, it is possible that other mycotoxins besides ZEN or possible synergistic actions between several mycotoxins may be involved in these effects. Zearalenone added to the diet of pregnant sows at 25 to 50 ppm caused them to farrow smaller litters with smaller offspring (Chang et al., 1979; Table 5). Miller et al. (1973) injected 5 mg of “purified” F-2 toxin intramuscularly into a sow and a gilt each day during the last month of pregnancy. Of the 12 pigs farrowed by the sow, three were stillborn and five had splay-leg. All eight of the pigs farrowed by the gilt had severe splay-leg. Four sows that consumed 100 ppm of purified ZEN from breeding until expected parturition failed to maintain their pregnancy (Christensen, 1979; Table 5). Etienne and Jemmali (1982) reported that ZEN did not affect weight of corpora lutea, number of abnormal fetuses, or embryonic mortality in gilts fed 3.6 to 4.3 ppm during gestation. Similarly, Long and Diekman (1984a) reported that gilts fed 5 to 30 ppm of ZEN from d 2 to 15 postmating had normal embryonic development. However, gilts that received 60 or 90 ppm had no fetuses at d 40 to 43 postmating, but remnants of fetal membranes were present in the uterus. No differences in the secretary pattern of serum LH, FSH, or prolactin were detected during ZEN feeding or at 40 to 43 d postmating. Steroid hormone concentrations were decreased at 4 wk postbreeding in gilts fed 60 and 90 ppm of ZEN (Long and Diekman, 1984a).

*Fusarium roseum*-contaminated corn added to a gestation diet to provide 7, 38, and 64 ppm of ZEN and .5, 2.5, and 4.5 ppm of DON inhibited fetal development in seven of eight gilts given the two higher dosages from 3 to 34 d after breeding (Long et al., 1982). Corpora lutea persisted and produced normal levels of progesterone, but serum concentrations of estradiol-17β were decreased in the higher dosage groups. Embryos recovered on d 14 from gilts fed 60 ppm of ZEN from d 7 to 10 postbreeding were fragmented, whereas those from control gilts were filamentous (Diekman and Long, 1989). Secretory patterns of gonadotropins were altered during d 10 and 14 after mating but pituitary gland weight, pituitary concentrations of gonadotropins (Long and Diekman, 1986a), or blastocyst migration and elongation were unaffected by ZEN (Long et al., 1988). Administration of progesterone to sows receiving ZEN from d 7 to 10 postmating failed to neutralize the detrimental actions of ZEN on early pregnancy (Green et al., 1991). Apparently, premature estrogenic stimulation by ZEN interrupts the proper secretory responses that normally occur during d 11 to 12 after breeding (Morgan et al., 1987).

**Boars.** McNutt et al. (1928) first linked moldy corn to reproductive disturbances in pigs. Boars that consumed moldy corn showed inflammation of the prepuce. Immature boars that consumed *Fusarium roseum*-contaminated corn containing 500 to 600 ppm of ZEN had testes weights that were 30% lower than those of boars on the control ration (Table 6; Christensen et al., 1972). Testes, epididymis, and vesicular gland weights were reduced in boars that received 100 ppm of ZEN (Palyusik, 1977). Vanyi and Szeky (1980) found that boars caused a cessation of spermatogenesis, but boars generally returned to normal when the contaminated feed was removed. In vitro culture of swine testes with ZEN resulted in degenerative changes (Vanyi and Szailer, 1974). Bristol and Djurickovic (1971) observed reduced libido in boars fed moldy corn. Similarly, Berger et al. (1981) also reported reduced libido in boars fed 40 ppm of ZEN from 14 to 18 wk of age. Plasma concentrations of testosterone were also suppressed during consumption of ZEN. However, at 36 wk of age, testicular weights, epididymal weight, spermatid production, seminiferous tubule, and Leydig cell characteristics were similar to those of control boars. In contrast, Ruhr et al. (1983) found no effect of ingestion of 60 ppm of ZEN for 8 wk on serum concentrations of testosterone, libido, or semen characteristics.

**Lactating Sows.** The lactating sow is also susceptible to ZEN. Sows fed 50 to 100 ppm of ZEN for 2...
Table 5. Summary of selected references when zearalenone (ZEN) was consumed by mated gilts or sows

<table>
<thead>
<tr>
<th>Source of ZENa</th>
<th>Location</th>
<th>ZEN, ppm</th>
<th>Treatment period</th>
<th>Effect</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Natural contamination</td>
<td>England</td>
<td>2.2</td>
<td>Days 2-114 gestation</td>
<td>No effect on reproduction</td>
<td>Shreeve et al., 1978</td>
</tr>
<tr>
<td>Purified</td>
<td>Minnesota</td>
<td>25-200</td>
<td>Weaning to gestation</td>
<td>Decreased litter wt, Constant estrus, Pseudopregnancy, Infertility</td>
<td>Chang et al., 1979</td>
</tr>
<tr>
<td>Purified</td>
<td>Minnesota</td>
<td>100</td>
<td>Mating to parturition</td>
<td>No effect on reproduction</td>
<td>Christensen, 1979</td>
</tr>
<tr>
<td>Natural contamination</td>
<td>Indiana</td>
<td>64</td>
<td>Days 3-33 gestation</td>
<td>No fetuses</td>
<td>Long et al., 1982</td>
</tr>
<tr>
<td>Purified</td>
<td>Indiana</td>
<td>30</td>
<td>Days 2-15 gestation</td>
<td>Normal fetuses</td>
<td>Long and Diekman, 1984a</td>
</tr>
<tr>
<td></td>
<td></td>
<td>60</td>
<td></td>
<td>No fetuses</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>90</td>
<td></td>
<td>No fetuses</td>
<td></td>
</tr>
<tr>
<td>Purified</td>
<td>Indiana</td>
<td>60</td>
<td>Days 2-8</td>
<td>Normal fetuses</td>
<td>Long and Diekman, 1986</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Days 7-10</td>
<td>No fetuses</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Days 11-15</td>
<td>Normal fetuses</td>
<td></td>
</tr>
<tr>
<td>Purified</td>
<td>Indiana</td>
<td>60</td>
<td>Days 7-10</td>
<td>No effect on blastocyst migration or E2 synthesis</td>
<td>Long et al., 1988</td>
</tr>
<tr>
<td>Purified</td>
<td>Ontario</td>
<td>5-10</td>
<td>Lactation</td>
<td>Increased postweaning estrus interval</td>
<td>Young et al., 1990</td>
</tr>
</tbody>
</table>

aUnless otherwise indicated, crystalline zearalenone was added to corn-soya diets to give desired concentrations.

Table 6. Summary of selected references when zearalenone (ZEN) was consumed by boars

<table>
<thead>
<tr>
<th>Source of ZENa</th>
<th>Location</th>
<th>ZEN, ppm</th>
<th>Reproductive state</th>
<th>Treatment period</th>
<th>Effectb</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Natural contamination</td>
<td>Ontario</td>
<td>Not stated</td>
<td>Mature</td>
<td>Not stated</td>
<td>↓Libido</td>
<td>Bristol and Djurickovic, 1971</td>
</tr>
<tr>
<td>Natural contamination</td>
<td>Minnesota</td>
<td>500-600</td>
<td>Immature</td>
<td>6-15 wk</td>
<td>↓Testes wt 30%</td>
<td>Christensen et al., 1972</td>
</tr>
<tr>
<td>Natural contamination</td>
<td>Hungary</td>
<td>100</td>
<td>Miniature</td>
<td>18.5-20 kg</td>
<td>↓Testes wt, ↓Epididymis wt</td>
<td>Palyusik, 1977</td>
</tr>
<tr>
<td>Purified</td>
<td>Indiana</td>
<td>40</td>
<td>Immature</td>
<td>14-18 wk</td>
<td>↓Libido, ↓Serum testosterone</td>
<td>Berger et al., 1981</td>
</tr>
<tr>
<td>Purified</td>
<td>Iowa</td>
<td>20-200</td>
<td>Mature</td>
<td>8 wk</td>
<td>↓Libido, ↓Spermatogenesis</td>
<td>Ruhr et al., 1983</td>
</tr>
<tr>
<td>Purified</td>
<td>Ontario</td>
<td>9</td>
<td>Immature</td>
<td>Days 32-145 or 32-312</td>
<td>↓FI, FE, ↓Libido, ↓Sperm motility</td>
<td>Young and King, 1989b</td>
</tr>
</tbody>
</table>

aUnless otherwise indicated, crystalline zearalenone was added to corn-soya diets to give desired concentrations.
bFI = feed intake, FE = feed efficiency.
wk before weaning and for 63 d after weaning exhibited constant estrus. Ovaries were atrophied and uterine horns were tortuous (Change et al., 1979). Edwards et al. (1987a) extended the weaning-to-estrus interval by feeding sows a diet that contained 10 ppm of ZEN during the last 14 d of lactation. However, fertility at the first postweaning estrus was not adversely affected. Similarly, Young et al. (1982) reported that low levels of ZEN (2.1 to 4.8 ppm) fed throughout pregnancy and lactation had no effect on postweaning rebreeding.

Cattle. Although cattle are not as sensitive to ZEN as swine, a few experiments have been done to determine whether ZEN affects performance of cattle. Infertility, reduced milk production, and hyperestrogenism in cows have been reported in association with ZEN or Fusarium spp. that produce ZEN (Mirocha et al., 1974). Hay containing 14 ppm of ZEN caused infertility in cattle (Mirocha et al., 1988). Roine et al. (1971) also reported infertility in dairy cows fed hay from which two Fusarium species that produced ZEN were isolated. Holstein cows that consumed 25 or 100 ppm of ZEN for 42 consecutive days exhibited swollen and hyperemic external genitalia but had estrous cycles of normal lengths and normal ovulations (Mirocha et al., 1978). Similarly, enlarged mammary glands that exhibited secretory activity were reported in prepubertal heifers that consumed moldy corn (Bloomquist et al., 1982). Subsequent analysis detected ZEN in this corn. Dairy cattle fed a ration that contained 385 to 1,925 ppb of ZEN for 7 wk had normal milk production. No ZEN residues were found in the milk, urine, serum, or tissues (Shreeve et al., 1979). Noller et al. (1979) also reported that Gibberella zeae-invaded corn that contained 500 ppb of ZEN had no effect on milk or butterfat production. Virgin dairy heifers fed 250 mg of purified ZEN for three estrous cycles had an average conception rate of 62%, compared with 87% in control heifers (Weaver et al., 1986a). Nonlactating, nonpregnant dairy cows given 500 mg of ZEN daily for two estrous cycles had normal serum concentrations of progesterone, normal mating behavior, and normal genital tracts (Weaver et al., 1986b).

Detection and Control of Mycotoxins

To aid in the diagnosis of feedstuffs contaminated with mycotoxins, it is imperative that accurate quantification tests be available. Chemical analysis such as thin-layer chromatography, gas and high performance liquid chromatography, and mass spectrometry accurately detect the concentrations of mycotoxin in properly collected and prepared samples. The development of rapid and easy-to-use tests for use at grain elevators and on the farm will allow more effective monitoring programs in detection of mycotoxin-contaminated crops. Commercially available kits that identify specific mycotoxins are listed in the CAST Task Force Report. A popular and effective on-farm qualitative test to detect mycotoxin-contaminated diets is to closely monitor a small group of 4-mo-old prepubertal gilts. Reduction in feed intake or gain or the presence of swollen vulvas would indicate that aflatoxin, DON, or ZEN is present in the diet.

After mycotoxins have been identified in feedstuffs, it is usually desirable to remove the mycotoxin from the feed. Mold growth can be inhibited in feedstuffs by the application of mold inhibitors (Tindall, 1983), but the user must be aware that existing mycotoxins remain unaffected. Many chemicals have been evaluated for their ability to structurally degrade or inactivate mycotoxins. Among acids, bases, aldehydes, and gases that have been studied, ammoniation resulted in reduced concentrations of aflatoxin in several grains (Dollear et al., 1968; Gardner et al., 1971; Brekke et al., 1977). Commercially, aflatoxin in cottonseed meal and peanut meal is currently being detoxified by ammoniation. Ammoniation of high-moisture corn coupled with low drying temperatures has been successful on a small scale, but the cost-effectiveness for commercial purposes has remained inconclusive (Van Cauwenberge et al., 1982).

Kernels of corn infected with Fusarium roseum can be separated from sound kernels by floating because infected kernels are of lighter test weight. Moreover, most mycotoxins are water-soluble and the acceptance of Fusarium-infected corn by swine was improved after the corn was washed (Forsyth et al., 1976). However, washing large quantities of corn is very expensive and time-consuming. Heating or roasting corn to 160 to 180°C reduced concentrations of aflatoxin in corn, but concentrations of lysine and methionine were also reduced (Hale and Wilson, 1979).

Various factors such as fat, protein, vitamins, trace metals, antibiotics, and preservatives have been added to feedstuffs to modify effective concentrations of mycotoxins. Consumption of swine diets with 15% alfalfa neutralized ZEN activity without altering feed efficiency (James and Smith, 1982). Increasing the dietary protein or amino acids above the normal requirement for optimal performance of weanling swine prevented decreased performance due to aflatoxin (Coffey et al., 1989). Addition of 5% hydrated sodium calcium aluminosilicate to swine diets formulated with aflatoxin-contaminated corn alleviated the reduced feed intake and daily gain associated with
aflatoxin-contaminated corn alone (Colvin et al., 1989; Harvey et al., 1989c). Additional work needs to be done to determine whether the aluminosilicates are effective in neutralizing other mycotoxins that affect performance in livestock.

At the present time, most producers or grain brokers blend mycotoxin-contaminated grain with clean grain in such a proportion that the animals will consume it without any obvious adverse effects on growth or reproduction. However, economic losses that occur with blended grain are unknown because low concentrations of several mycotoxins may interact to reduce performance in ways that are very difficult to detect.

Implications

Synthesis of mycotoxins by molds in livestock feedstuffs decreases animal performance via impaired growth and reproductive efficiency. Five major mycotoxins that affect the livestock industry in North America are aflatoxin, ochratoxin, ergot, deoxynivalenol, and zearalenone. Accurate diagnostic tests are available to detect most mycotoxins, but the development and use of rapid diagnostic tests at grain elevators and on the farm will allow more effective monitoring programs for mycotoxin-contaminated crops.

Literature Cited


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Green, M. L., M. A. Diekman, J. R. Malayer, A. B. Scheidt, and Gardner, J. K., Friis, C., R. Brinn, and B. Hald. 1626 DIEKMAN AND GREEN


