# Mycotoxins and their Effects on Dairy Cattle

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## Introduction

In the early 1960's, **aflatoxin (AF)** was discovered as the factor causing disease and death in turkeys which had been labeled "Turkey-X Disease" (Detroy, et al., 1971). Aflatoxin was found to be a carcinogen and its presence in dairy cattle feeds and in milk became regulated by the Food and Drug Administration. In the 1970, a number of *Fusarium* produced mycotoxins such as **zearalenone (ZEN)** and **deoxynivalenol (DON)** were found to occur in feedstuffs and associated with poor performance and disease in livestock. "Moldy corn disease" that often resulted in the death of horses was found to be caused by **fumonisin (FB)** , another *Fusarium* produced mycotoxin discovered in the late 1980's (Marasas, et al., 1988). Hundreds of mycotoxins are known to exist naturally and many are known to affect livestock.

A priority list of mycotoxins was subjectively produced by a survey of mycotoxicologists worldwide (Hesseltine, 1986a). Such information would suggest that the mycotoxins of greatest concern for dairy cattle consuming stored feeds include: aflatoxin, fumitremorgens, and sterigmatocystin, which are primarily produced by *Aspergillus* molds; DON, ZEN, **T-2 toxin (T-2)**, **diacetoxyscirpenol (DAS)**, and FB, which are produced by *Fusarium* molds; and **ochratoxin (OT)**, PR toxin, and roquefortine primarily produced by *Penicillium* molds. Several other mycotoxins, produced by these and other molds, are known to be prevalent at times, including derivatives of those listed.

## Mycotoxin Occurrence.

Mycotoxin production is often related to weather extremes (causing plant stress or excess hydration of stored feedstuffs), to inadequate storage practices, to low feedstuff quality, and to faulty feeding conditions. Molds can grow and mycotoxins can be produced pre-harvest or post-harvest, during storage, processing, or feeding. Mycotoxins occur in most all types of feedstuffs. Various mycotoxins have been found in silage (McDonald et al., 1991).

The warm, humid climate of the southern U.S., results in a considerably higher incidence of AF in feeds. From 1975 to 1980, 34% of corn grain in **North Carolina (NC)** contained more than 20 ppb of AF. Corn samples from the Midwestern U.S. representing the 1988 season (severe drought) showed 8% with AF levels above 10 ppb, 3% positive for ZEN above 1 ppm, 3% positive for DON above 1 ppm and 7% positive for T-2 above 500 ppb (Russel et al., 1991).

Analysis results, from feed samples submitted by North Carolina farmers during a nine-year period and representing more than 2400 samples, were summarized (Whitlow, Hagler and Hopkins, 1998). Percentage of corn silage and corn grain samples testing positive were for aflatoxin ≥10 ppb, 8% and 9%; DON ≥500 ppb, 51% and 52%; ZEN ≥300 ppb, 17% and 3%; T-2 ≥200, 5%



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and 4% and FB ≥1 ppm, 37% and 60%, respectively. Occurrence was variable by year.

**Mycotoxin effects.**

Mycotoxins can increase disease incidence and reduce production efficiency. They exert their effects through three primary mechanisms: (1) alteration in nutrient content, absorption and metabolism, (2) changes in the endocrine and neuroendocrine function, and (3) suppression of the immune system (CAST, 1989). The resulting nonspecific symptoms may therefore be perplexing and make diagnosis difficult. Hesseltine (1986b) and Schilfer (1990) discussed some of the problems encountered in diagnosing a mycotoxicosis which include: (1) a lack of research reports especially concerning some mycotoxins (2) symptoms which are not specific or unique for the mycotoxin, (3) interaction of mycotoxins with other mycotoxins or other stress factors, (4) interaction of mycotoxins with immune suppression and thus infectious diseases, (5) lack of feed samples or samples improperly collected, (6) analysis which is complex and expensive.

Until recent years, it was thought that mycotoxins were harmless to mature cattle because mycotoxins are partially destroyed in the rumen. It is now known that mycotoxins occur frequently in dairy cattle feedstuffs and in general affect production, reproduction, and health of dairy cattle. However, we need a better understanding of why mycotoxins occur, when to expect them, how to prevent their occurrence and how to deal with their presence. We need to better understand their toxicity to dairy cattle, their interactions with other mycotoxins and with other factors such as nutrients, or stresses such as disease organisms or environmental stress. Diagnosis of a mycotoxicosis is difficult and not highly definitive. We need better methods to monitor animal exposures to mycotoxins and to diagnose their contribution to unsatisfactory conditions. And, we must learn how to prevent toxicities and to treat toxicities which do occur.

**Safe Levels of Mycotoxins.**

Hamilton (1984) and Schaeffer and Hamilton (1991) have reviewed the topic of safe levels of mycotoxins. They conclude that epidemiological studies coupled with laboratory studies to elaborate the underlying principles may be the best approach to determining safe levels. They state that any level of mycotoxin carries a risk of loss with it and that it is impossible to define a safe level under laboratory conditions that will be accurate under field conditions, primarily because of three reasons: (1) difficulties in conceptualizing and executing experiments to investigate multiple interacting factors simultaneously; (2) the unappreciated fact that the frequency and level of contamination with aflatoxin and other mycotoxins vary unpredictably under field conditions; and (3) animal facilities currently available to investigators do not permit experiments under controlled conditions with the number of animals commonly at risk under field conditions. Establishing usable or tolerable levels of mycotoxins may be acceptable when all concerned parties are aware of levels and the risks associated.

Interactions with other factors make recommendations difficult. Lillehoj and Ceigler (1975) give an example where penicillic acid and citrinin where innocuous when administered alone but were 100% lethal when given in combination. Fumonisin at 100 ppm has been shown to reduce milk production in dairy cattle (Whitlow, 1999), but to not affect average daily gain in beef cattle fed 148 ppm (Osweiler et al, 1993). AF produced from culture was more toxic to dairy cattle than pure AF added

to diets (Applebaum et al., 1982). In swine, Foster et al. (1986) demonstrated that pure DON added to diets was less toxic than diets with similar concentrations of DON which was supplied from naturally contaminated feeds. Smith and MacDonald (1991) have suggested that fusaric acid may occur along with DON to produce more severe symptoms. Many such interactions are possible since *Fusarium* molds produce many mycotoxins, and it is well documented that several mycotoxins may be found in the same feed (Hagler et al., 1984). Abbas et al. (1989) demonstrated that *Fusarium* species isolated from Minnesota corn produces an array of mycotoxins. Scott (1990) states that screening methods are needed for the *Fusarium* produced mycotoxins and that one approach is to test for DON, DAS, T-2 and nivalenol, because other *Fusarium* mycotoxins seldom occur without one of these four also present. Feeds could then be further tested for other mycotoxins.

There are distinct species differences in tolerance to mycotoxins. Cattle are more tolerant to most mycotoxins than many other animals, probably due to some mycotoxin degradation in the rumen (Kiessling et al., 1984). However, Kiessling et al. (1984) demonstrated that a low rumen pH reduced degradation and that protozoa where the primary rumen microorganism with the ability to degrade mycotoxins. Thus, diet may play an important role in degree of mycotoxin degradation in the rumen. The rat is much more sensitive to both aflatoxin and T-2 than is the mouse (Wannemacher et al., 1991). Other animal factors include sex, age, environmental and production stress. Certainly duration of exposure is important. The known dietary factors which interact with mycotoxins include most nutrients for which rations are formulated including, fat, protein, fiber, vitamins and minerals. Dietary pellet binders (clay) adsorb some mycotoxins reducing exposure of the animal. Thus, many factors and interactions make it difficult to relate field observations to those from controlled research.

**Aflatoxin (AF).**

AF, produced primarily by *Aspergillus flavus* and is commonly found in the southern US. The FDA limits AF in corn grain according to its intended use which for lactating dairy cattle is 20 ppb. AF is excreted into milk in the form of $AFM_1$ with residues approximately equal to 1.7% of the dietary level (Van Egmond, 1989). The FDA limits aflatoxin $M_1$ in milk to no more than 0.5 ppb. Levels of 300 to 700 ppb are considered toxic for beef cattle depending on criteria for toxicity, and other factors affecting toxicity (CAST, 1989). Garrett et al., (1968) showed that with beef cattle, gain and intake were affected at 700 ppb AF, but not at 300 ppb; however, levels of no effect can not be determined from such data with few animals. Trends in the data, especially for increased liver weights, would indicate potential toxicity at levels as low as 100 ppb. Guthrie (1979) showed a decline in reproductive efficiency when lactating dairy cattle in a field situation were consuming 120 ppb AF and an increase in milk production of over 25% when cows were changed to an AF free diet. Patterson and Anderson (1982) and Marsi et al. (1969) also suggest that 100 ppb may reduce milk production. Applebaum et al. (1982) showed that impure AF produced by culture reduced production while equal amounts of pure AF did not.

**Fumonisin (FB).**

Fumonisin $B_1$ ($FB_1$) was isolated by Gelderblom et al. (1988) and shown to be a cancer promoter. $FB_1$ has been shown to cause leukoencephalomalacia in horses (Marasas, et al., 1988), pulmonary edema in swine (Harrison et al., 1990) and hepatoxicity in rats (Gelderblom et al., 1991). A USDA, APHIS

(1995) survey found an average of 6.9% of 1995 corn samples from Missouri, Iowa and Illinois to contain more than 5 ppm $FB_1$. While $FB_1$ is thought to be much less potent in ruminants than monogastrics, work by Kriek et al. (1981) suggested that fumonisin was toxic to sheep. Osweiler et al., (1993) demonstrated that $FB_1$ in large amounts (148 ppm) can cause mild liver damage in cattle even when fed for a short term (31 days), but without an effect on feed intake or weight gain. Whitlow (1999) has demonstrated that $FB_1$ is toxic to dairy cattle. Fed for approximately 7 days prior to freshening and for 70 days thereafter, dietary $FB_1$ at 100 ppm significantly and dramatically reduced milk production (7 kg/cow/day) and increased serum enzymes levels indicative of liver disease. These results strongly suggest that $FB_1$ is toxic to dairy cattle perhaps at levels that are not toxic to beef cattle, or perhaps $FB_1$ interacts with other factors to produce greatly different effects in beef and dairy cattle under different conditions. $FB_1$ carryover from feed to milk is thought to be negligible. Richard et al. (1996) fed fumonisin $B_1$ (about 75 ppm) to dairy cows and with no fumonisin $B_1$ or $B_2$ detectable in milk (detection limit of 5 ng/ml). Scott et al. (1994) have confirmed this observation.

**Deoxynivalenol (DON).**

DON is the proper name for a commonly detected *Fusarium* produced mycotoxin often referred to as vomitoxin. Two independent Midwestern studies (Vesonder et al., 1978 and Côté et al., 1984) showed DON to be the primary mycotoxin associated with swine problems including feed refusals, diarrhea, emesis, reproductive failure, and deaths. In cattle, DON has been associated with reduced feed intake (Trenholm et al., 1985). Clinical data from 300 herds representing about 40,000 cow records showed that DON was associated with a loss in milk production but this study did not establish a cause and effect (Whitlow et al., 1991). DON may simply be a marker for problem feeds. Field observations by others help substantiate these observations (Gotlieb, 1997 and Seglar, 1997).

Charmley et al. (1993), demonstrated a 13% (2.85 kg) numerical decrease in 4% fat corrected milk production (statistics not available) utilizing 18 midlactation dairy cows (average 19.5 kg milk) consuming diets shown to contain no common mycotoxins other than DON which was at levels of 2.7 to 6.4 ppm in treatment diets. While the decrease in actual milk production (1.35 kg) was not statistically significant, the decrease in fat test (3.92% *vs.* 3.04%) was significant. Noller et al., (1979) utilized 54 lactating dairy cows in a 21 day feeding experiment using corn grain contaminated with *Gibberella zeae* and containing 500 ppb of zearalenone. DON was probably present, but it was not analyzed directly. Grain harvested earlier from the same field was contaminated with DON at 12 to 13 ppm. Neither dry matter intake nor milk production (average 22.9 kg) were affected by additions of this grain to the diet. However, compared with controls, cows which received this grain at either 10% (about 1.25 ppm DON and 50 ppb ZEN) or 20% (about 2.50 ppm DON and 100 ppb ZEN) of their diet gained significantly less weight during the study (5.8 kg or 8.1 kg, less weight gain for cows consuming the 10% or 20% diets over 21 days). DiCostanzo et al, (1995a) cites results by Ingalls (1994) where lactating dairy cows were fed 0, 3.6 10.9 and 14.6 ppm of DON for 21 days, without an apparent effect on feed intake or milk production which averaged about 30 kg daily.

Beef cattle and sheep appear to tolerate relatively large amounts of DON without obvious deleterious effects (DeHaan et al., 1984, Nelson et al., 1984, DiCostanzo et al.,1995a and 1995b, Boland et al., 1994, and Windels et al., 1995).

**T-2 Toxin.**

T-2 toxin, a *Fusarium* produced mycotoxin, has been associated with gastroenteritis, intestinal hemorrhages (Petrie et al., 1977 and Mirocha et al., 1976) and death (Hsu et al., 1972 and Kosuri et al., 1970). Weaver et al. (1980) showed that T-2 was associated with feed refusal and gastrointestinal lesions in a cow, but did not show a hemorrhagic syndrome. Serum immunoglobulins and certain complement proteins were lowered in calves receiving T-2 toxin (Mann et al, 1983). Gentry et al. (1984) demonstrated a reduction in white blood cell and neutrophil counts in calves. A calf intubated with T-2 developed severe depression, hindquarter ataxia, knuckling of the rear feet, listlessness and anorexia (Weaver et al, 1980). Data with cattle are limited, but, the toxicity of T-2 toxin in laboratory animals is well documented (Wannemacher et al, 1991).

**Zearalenone (ZEN).**

Zearalenone is a *Fusarium* produced mycotoxin which elicits an estrogenic response in monogastrics (Sundlof and Strickland, 1986). However, ZEN is rapidly converted to α- and β-zearalenol in rumen cultures (Kiessling et al., 1984) and has been of less toxicity to ruminants. Ruminal degradation of ZEN was found to be about 30% in 48 hours (Kellela and Vasenius, 1982). A controlled study with cows fed up to 22 ppm ZEN showed no obvious effects except that corpora lutea were smaller in treated cows (Weaver et al., 1986b). In a similar study with heifers receiving about 13 ppm ZEN, conception rate was depressed about 25%; otherwise, no obvious effects were noted (Weaver et al., 1986a). Several case reports have related ZEN to an estrogenic response in ruminants (Khamis et al., 1986; Mirocha et al., 1968; and Roine et al., 1971). Large doses are associated with abortions in cattle (Kellela and Ettala, 1984; and Mirocha et al., 1974). Mirocha et al. (1968) isolated ZEN from hay associated with infertility in dairy cattle. Other cattle responses may include vaginitis, vaginal secretions, poor reproductive performance and mammary gland enlargement of virgin heifers. In a field study, (Coppock et al., 1990) diets with about 750 ppb ZEN and 500 ppb DON resulted in poor consumption, depressed milk production, diarrhea, and total reproductive failure. New Zealand workers (Towers, et al., 1995a, Towers, et al., 1995b, Sprosen and Towers, 1995, and Smith et al., 1995) have related urinary zearalenone and zearalenone metabolites (zearalenone, zearalanone, α- and β-zearalenol and α- and β-zearalanol) which they refer to as "zearalenone" to intake of "zearalenone" and to reproductive disorders in sheep and dairy cattle. In sheep, "zearalenone" was related to lower conception, reduced ovulation, and increased twinning rates. With dairy cattle, herds with low fertility were found to have higher levels of blood and urinary "zearalenone" and consumed pastures containing higher levels of "zearalenone." In addition, within herds, individual cows were examined by palpation and those that were determined to be cycling had lower blood "zearalenone" levels than did cows that were not cycling. Differences in "zearalenone" levels were attributed to selective grazing behavior. The reproductive problems in dairy cattle were noted with "zearalenone" concentrations of about 400 ppb in the pasture samples.

**Other Mycotoxins.**

Many other mycotoxins may affect ruminants but are thought to occur less frequent or be less potent. Fumitremorgens such as fumigaclavine A and B are produced by *Aspergillus fumigatus*, and are

thought to be common in silages of the southeastern US. They can cause anorexia, diarrhea, unthriftiness and irritability (Cole et al., 1977). Sterigmatocystin is primarily produced by *Aspergillus versicolor* and has been observed as a primary mycotoxin produced by *Aspergillus* on cereal grains in western Canada (Mills and Abramson, 1986). While it is thought to be infrequent at toxic levels in the U.S., it was detected in a grain mixture and associated with bloody diarrhea and cow deaths in a field case in Tennessee (Vesonder and Horn, 1985). Diacetoxyscirpenol is a *Fusarium* produced mycotoxin. It may occur along with T-2 toxin and causes similar symptoms. Ochratoxin, produced primarily by a *Penicillium* mold but also by certain *Aspergillus* molds, has been reported to affect cattle (Vough and Glick, 1993), but it is rapidly degraded in the rumen and thus thought to be of little consequence unless consumed by young pre-ruminant calves (Sreemannarayana et al., 1988). However, high-concentrate diets reduce ochratoxin degradation in the rumen. Patulin, a *Penicillium* produced mycotoxin associated with aerobic deterioration of silage has been incriminated as a possible toxin in Europe and New Zealand (Lacey, 1991). PR toxin, produced by *Penicillium roqueforti*, has been found in silage and was the suspected vector in a case study with symptoms of abortion and retained placenta (Still et al., 1972). Roquefortine, produced by *Penicillium requefortii*, is a tremorgen which has been found in silage. Other mycotoxins such as rubratoxin, citrinin, cyclopiazonic acid, and ergotoxins may be of some importance. Many other mycotoxins are possible.

**Mycotoxin Testing.**

Analytical techniques for mycotoxins are improving (Chu, 1992). The costs are decreasing and several commercial laboratories are available which provide screens for a large array of mycotoxins. Collection and handling of representative feed samples is a problem.

**Prevention and Treatment.**

Some additives may be beneficial in reducing mycotoxins because they are effective in reducing mold growth. Ammonia, propionic acid and microbial or enzymatic silage additives have all shown effectiveness as mold inhibitors. It seems reasonable that additives, which enhance fermentation, may be added at ensiling, while those which inhibit mold growth may be added as surface treatments when capping off the silo or daily after silage feed-out to reduce molding of the exposed silage surface. If unacceptably high levels of mycotoxins occur, dilution or removal of the contaminated feed is preferable; however, it is usually impossible to completely replace major forage ingredients. Ammoniation of grains can destroy some mycotoxins, but there is no practical method to detoxify affected forages already in storage. Increasing nutrients such as protein, energy and antioxidant nutrients may be advisable (Brucato et al., 1986, Chandler, 1992). Adsorbent materials such as clays (bentonites) added to contaminated diets fed to rats, poultry, swine and cattle have helped reduce the effects of mycotoxins (Diaz et al., 1997; Galey et al., 1987; Harvey, 1988; Lindemann et al., 1991; Scheideler, 1990; Hayes, 1990 and Smith, 1980 and 1984). In most cases, clay was added to the diet at about 1%. Other absorbent materials such as charcoal (Galvano, et al., 1996), and yeast cell components (Diaz, et al., 1999) have shown effective in reducing aflatoxin in milk.

**References .**

Abbas, H.K., C.J. Mirocha, T.Kommedahl, R.F. Vesonder and P. Golinski. 1989. Production of trichothecenes and non-trichothecene mycotoxins by *Fusarium* species isolated from maize

in Minnesota. Mycopathologia. 108:55.

Applebaum, R.S., R.E. Brackett, D.W. Wiseman, and E.L. Marth. 1982. Responses of dairy cows to dietary aflatoxin: feed intake and yield, toxin content, and quality of milk of cows treated with pure and impure Aflatoxin. J. Dairy Sci. 65:1503.

Boland, E.W., V.L. Anderson, H.H. Casper, P.T.Berg, and D.V. Dhuyvetter. 1994. The effects of increasing vomitoxin (DON) levels from scab infested barley fed to feedlot steers. Beef Prod. Field Day. Carrington Res. Ext. Ctr. Livestock Unit. North Dakota State University Ag. Expt. Sta. 17:34. (As quoted by DiCostanzo et al., 1995a).

Brucato, M., S. F. Sundlof, J. U. Bell and G. T. Edds. 1986. Aflatoxin B1 toxicosis in dairy calves pretreated with selenium-vitamine E. Am. J. Vet. Res. 47:179.

Chandler, Paul. 1992. Selenium, vitamin E indicate oxidative stress in dairy cattle. Feedstuffs 64(44):10.

Charmley, E., H.L. Trenholm, B.K. Thompson, D. Vudathala, J.W.G. Nicholson, D.B. Prelusky and L.L. Charmley. 1993. Influence of level of deoxynivalenol in the diet of dairy cows on feed intake, milk production and its composition. J. Dairy Sci. 76:3580.

Chu, F.S. 1992. Recent progress on analytical techniques for mycotoxins in feedstuffs. J. Anim. Sci. 70:3950.

Cole, R.J., J.W. Kirksey, J.W. Dorner, D.M. Wilson, J.C. Johnson, Jr., A.N. Johnson, D.M. Bedell, J.P. Springer, K.K. Chexal, J.C. Clardy and R.H. Cox. 1977. Mycotoxins produced by *Aspergillus fumigatus* species isolated from moldy silage. J. Agric. Food Chem. 25:826.

Coppock, R.W., M.S. Mostrom, C.G. Sparling, B. Jacobsen and S.C. Ross. 1990. Apparent zearalenone intoxication in a dairy herd from feeding spoiled acid-treated corn. Vet. Hum. Toxicol. 32:246.

Côté, L.M., J.D. Reynolds, R.F. Vesonder, W.B. Buck, S.P. Swanson, R.T. Coffey and D.C. Brown. 1984. Survey of vomitoxin-contaminated feed grains in Midwestern United States, and associated health problems in swine. J. Am. Vet. Med. Assoc. 184:189.

Council for Agricultural Science and Technology (CAST). 1989. "Mycotoxins: Economic and Health Risks". Task Force Report No. 116. Ames, Iowa.

DeHaan, K., R. Stock, D. Brink, T. Klopkenstein and N. Schneider. 1984. Scabby wheat influence on performance. Nebraska Beef Cattle Report. MP-47:6.

Detroy, R.W., E.b> Lillehoj, and A. Ciegler.1971. Aflatoxins and related compounds. p. 3-178. In: Ajl, S.J., A ciegler, s. Kadis, T.C. Montie, and G. Weinbaum (eds.) Microbial toxins: a comprehensive treatise, vol. 6, Fungal toxins. Academic Press, Inc., New York.

Diaz, D.E., J. T. Blackwelder, W.M. Hagler, Jr., B.A. Hopkins, F.T. Jones, K.L. Anderson and L.W. Whitlow. 1998. The potential of dietary clay products to reduce aflatoxin transmission to milk of dairy cows. J. Dairy Sci. 80(Suppl. 1):261.

Diaz, D.E., W. M. Hagler, Jr., B.A. Hopkins, J.A. Eve and L.W. Whitlow. 1999. The potential for dietary sequestering agents to reduce the transmission of dietary aflatoxin to milk of dairy cows and to bind aflatoxin *in vitro*. J. Dairy Sci. (Abstract) Southern Branch, American Dairy Science Association, February 1, 1999.

DiCostanzo, A., L. Johnston, H. Windels and M. Murphy. 1995a. A review of the effects of molds and mycotoxins in ruminants. Professional Animal Scientist 12:138.

DiCostanzo, A., J.C. Meiske, M. Murphy, R. Epley, L. Felice, L. Johnson, and H. Chester-Jones. 1995b. Effects of feeding vomitoxin-contaminated barley on performance of feedlot steers. Minnesota Cattle Feeders Rep. B-418, St. Paul, MN. (As quoted by DiCostanzo et al.,

1995a).
Foster, B.C., H.L. Trenholm, D.W. Friend, B.K. Thompson and K.E. Hartin. 1986. Evaluation of different sources of deoxynivalenol (vomitoxin) fed to swine. Can. J. Anim. Sci. 66:1149.
Galey, F.D., R.J. Lambert, M. Busse and W.B. Buck. 1987. Therapeutic efficacy of superactive charcoal in rats exposed to oral lethal doses of T-2 toxin. Toxicon 25:493.
Garrett, W.N., H. Heitman, Jr. and A.N. Booth. 1968, Aflatoxin toxicity in beef cattle. Proc Soc. Exp. Biol. Med. 127:188.
Gentry, P.A., M.L. Ross and P.K-C Chan. 1984. Effect of T-2 toxin on bovine hematological and serum enzyme parameters. Vet. Hum. Toxicol. 26:24.
Gelderblom, W.C.A., K. Jaskiewicz, W.F.O. Marasas, P.G. Thiel, R.M. Horak, R. Vleggaar and N.P.J. Kriek. 1988. Fumonisins: Novel mycotoxins with cancer-promoting activity produced by *Fusarium moniliforme*. Appl. Environ. Microbiol. 54:1806.
Gelderblom, W.C.A., N.P.J. Kreik, W.F.O. Marasas, and P.G. Thiel. 1991. Toxicity and carcinogenicity of the *Fusarium moniliforme* metabolite, fumonisin $B_1$, in rats. Carcinogenesis 12:1247.
Gotlieb, A. 1997. Causes of mycotoxins in silages. pp. 213, In: "Silage: Field to Feedbunk", NRAES-99, Northeast Regional Agricultural Engineering Service, Ithaca, NY.
Guthrie, L.D. 1979. Effects of Aflatoxin in corn on production and reproduction in dairy cattle. J Dairy Sci. 62 (Suppl. 1):134.
Hagler, W.M., K. Tyczkowska and P.B. Hamilton. 1984. Simultaneous occurrence of deoxynivalenol, zearalenone and aflatoxin in 1982 scabby wheat from the Midwestern United States. Appl. Environ. Microbiol. 47:151.
Hamilton, P.B. 1984. Determining safe levels of mycotoxins. J. Food Prot. 47:570.
Harrison, L.R., B.M. Colvin, J.T. Greene, L.E. Newman, and R.J. Cole. 1990. Pulmonary edema and hydrothorax in swine produced by fumonisin $B_1$, a toxic metabolite of *Fusarium moniliforme*. J Vet. Diagn. Invest. 2:217.
Harvey, R. B., L. F. Kubena, T. D. Phillips, W. E. Huff, and D. E. Corrier. 1988. Approaches to the prevention of aflatoxicosis. Pp. 102-107. Proc. Maryland Nutr. Conf.
Hayes, S.M. 1990. Counteracting aflatoxin in livestock feed. In: "Agricultural Research", USDA, ARS, Washington, D.C. 38(2):18.
Hesseltine, C.W. 1986a. Global significance of mycotoxins. In: P.S. Steyn and R. Vleggaar. (Eds). "Mycotoxins and Phycotoxins." Elsevier Scientific Publishing Co., Amsterdam.
Hesseltine, C.W. 1986b. Resumé and future needs in the diagnosis of mycotoxins. IN: J.L. Richard and J.R. Thurston, (Eds.) "Diagnosis of Mycotoxicoses." Martinus Nijhoff Publishers, Dordrecht, The Netherlands.
Hsu, I.C., C.B. Smalley, F.M. Strong and W.E. Ribelin. 1972. Identification of T-2 toxin in moldy corn associated with a lethal toxicosis in dairy cattle. Appl. Microbiol. 24:684.
Ingalls, J. R. 1994. Influence of DON on feed consumption by dairy cows. In Proc. Western Nutr. Conf. P 129. Winnipeg, MB, Canada.
Kellela, K. and E. Ettala. 1984. The oestrogenic *Fusarium* toxin (zearalenone) in hay as a cause of early abortions in the cow. Nord. Vet. Med. 36:305.
Kellela, K. and L. Vasenius. 1982. The effects of rumen fluid on the content of zearalenone in animal fodder. Nord. Vet. Med. 34:336.
Khamis, Y., H.A. Hammad and N.A. Hemeida. 1986. Mycotoxicosis with oestrogenic effect in cattle. Zuchthyg. 21:233.

Kiessling, K.H., H. Patterson, K. Sandholm, and M. Olsen. 1984. Metabolism of aflatoxin, ochratoxin, zearalenone, and three trichothecenes by intact rumen fluid , rumen protozoa and rumen bacteria. Appl. Environ. Microbiol. 47:1070.

Kosuri, N.R., M.D. Grave, S.G. Yates, W.H. Tallent, J.J. Ellis, I.A. Wolff and R.E. Nichols. 1970. Response of cattle to mycotoxins of *Fusarium tricinctum* isolated from corn and fescue. J. Am. Vet. Med. Assoc. 157:938.

Kriek, N.P.J., T.S. Kellerman, and W.F.O. Marasas. 1981. A comparitive study of the toxicity of *Fusarium verticilloides (F. moniliforme)* to horses, primates, pigs, sheep, and rats. Onderspoort J Vet. Res. 48:129.

Lacey, J. 1991. Natural occurrence of mycotoxins in growing and conserved forage crops. In: J. E. Smith and R. E. Henderson (eds.), "Mycotoxins and Animal Foods," CRC Press, Boca Raton, Florida.

Lillehoj, E.B., and A. Ciegler. 1975. Mycotoxin synergism. Pp. 344-358. *In* D. Schlessinger (ed.) Microbiology -- 1975. American Society of Microbiology, Washington, DC.

Lindemann, M.D. and D.J. Blodgett. 1991. Various clays provide alternative for dealing with Aflatoxin. Feedstuffs 63:15.

Mann, D.D., G.M. Buening, B. Hook and G.D. Osweiler. 1983. Effects of T-2 mycotoxin on bovine serum proteins. J. Am. Vet. Med. Assoc. 44:1757.

Marasas, W.F.O., T.S. Kellerman, W.C.A. Gelderblom, J.A.W. Coetzer, P.G. Thiel, and J.J. van der Lugt.1988. Leukoencephalomalacia in a horse induced by fumonisin $B_1$ isolated from *Fusarium moniliforme.* Onderstepoort J Vet Res 55:197.

Marsi, M.S., V.C. Garcia and J.R. Page. 1969. The aflatoxin $M_1$ content of milk from cows fed known amounts of aflatoxin. Vet. Rec. 84:146.

McDonald, P., A.R. Henderson and S.J.E. Heron. 1991. The Biochemistry of Silage, 2nd Edition, Chalcombe Pub., Marlow, Bucks, Great Britain.

Mills, J.T. and D. Abramson. 1986. Production of sterigmatocystin by isolates of *Aspergillus versicolor* from western Canadian stored barley and rapeseed/canola. Can. J. Plant Pathol. 8:151.

Mirocha, C.J., J. Harrison, A.A. Nichols and M. McClintock. 1968. Detection of fungal estrogen (F-2) in hay associated with infertility in dairy cattle. Appl. Microbiol. 16:797.

Mirocha, C.J., S.V. Pathre, B. Schauerhamer and C.M Christiansen. 1976. Natural occurrence of *Fusarium* toxins in feedstuffs. Appl Environ. Microbiol. 32:553.

Mirocha, C.J., B. Schauerhamer and S.V. Pathre. 1974. Isolation, detection and quantitation of zearalenone in maize and barley. J. Assoc. Off. Anal. Chem. 57:1104.

Nelson, M., N.R. Schneider, A. R. Doster, M.P. Carlson, and T. Klopfenstein. 1984. Vomitoxin-contaminated wheat-pathology, toxicity in cattle. Nebraska Beef Cattle Report MP-47:3.

Noller, C.H., M. Stob, and J. Tuite. 1979. Effects of feeding *Gibberella zeae*-infected corn on feed intake, bodyweight gain and milk production of dairy cows. J. Dairy Sci. 62:1003.

Osweiler, G.D., M.E. Kehrli, J.R. Stabel, J.R. Thurston, P.F. Ross and T.M. Wilson. 1993. Effects of fumonisin-contaminated corn screenings on growth and health of feeder calves. J. Anim. Sci. 71:459.

Patterson, D.S.P. and P.H. Anderson. 1982. Recent aflatoxin feeding experiments in cattle. Vet. Rec. 110:60.

Petrie, L., J. Robb and A.F. Stewart. 1977. The identification of T-2 toxin and its association with a hemorrhagic syndrome in cattle. Vet. Rec. 101:326.

Richard, J.L., G. Meerdink, C.M. Maragos, M. Tumbleson, G. Bordson, L.G. Rice, and P.F. Ross. 1996. Absence of detectable fumonisins in the milk of cows fed *Fusarium proliferatum (Matsushima) Nirenberg* culture material. Mycopathologia 133:123.

Roine, K., E.L. Korpinen and K. Kallela. 1971. Mycotoxicosis as a probable cause of infertility in dairy cows. Nord. Vet. Med. 23:628.

Russel, L., D.F. Cox, G. Larsen, K. Bodwell, and C.E Nelson. 1991. Incidence of molds and mycotoxins in commercial animal feed mills in seven Midwestern states, 1988-89. J. Anim. Sci. 69:5.

Schaeffer, J.L., and P.B. Hamilton. 1991. Interactions of mycotoxins with feed ingredients. Do safe levels exist? In: J. E. Smith and R. S. Henderson (Eds.) "Mycotoxins and Animal Foods." CRC Press. Boca Raton, Florida.

Scheideler, S.E. 1990. Aluminosilicates in poultry rations. Feed Management 41(1):22.

Schilfer, H.B. 1990. Mycotoxicosis of domestic animals and their diagnosis. Can. J. Physiol. Pharmacol. 68:987.

Scott, P.M. 1990. General referee reports: Mycotoxins. J. Assoc. Off. Anal. Chem. 73:98.

Scott, P.M., T. Delgado, D. B. Prelusky, H.L. Trenholm, J.D. Miller. 1994. Determination of fumonisin in milk. J. Environ. Sci. Health. B29:989.

Seglar, B. 1997. Case studies that implicate silage mycotoxins as the cause of dairy herd problems. pp. 242, In: "Silage: Field to Feedbunk", NRAES-99, Northeast Regional Agricultural Engineering Service, Ithaca, NY.

Smith, J., C. Wesselink, J. Parr, J.M. Sprosen, E.A. Fowke, N.R. Towers, and D. Laboyrie. 1995. Effect of zearalenone on ewe pregnancy rates. In: "Toxinology and Food Safety." Toxinology and Food Safety Research Group, Ruakura Research Centre, Hamilton, New Zealand.

Smith, T.K. 1980. Influence of dietary fiber, protein and zeolite on zearalenone toxicosis in rats and swine. J. Anim. Sci. 50:278.

Smith, T.K. 1984. Spent canola oil bleaching clays: potential for treatment of T-2 toxicosis in rats and short term inclusion in diets for immature swine. Can. J. Anim. Sci. 64:725.

Smith, T.K., and E.J. MacDonald. 1991. Effect of fusaric acid on brain regional neurochemistry and vomiting behavior in swine. J. Anim. Sci. 69:2044.

Sprosen, J. M. And N.R. Towers. 1995. Urinary zearalenone metabolite concentrations in herds with fertility problems. In: "Toxinology and Food Safety." Toxinology and Food Safety Research Group, Ruakura Research Centre, Hamilton, New Zealand.

Sreemannarayana, O., A.A. Frohlich, T.G. Vitti, R.R. Marquart and D. Abramson. 1988. Studies of the tolerance and disposition of ochratoxin A in young calves. J. Animal Sci. 66:1703.

Sundlof, S.F. and C. Strickland. 1986. Zearalenone and zearalenol: Potential residue problems in livestock. Vet. Hum. Toxicol. 28:242.

Still, P., R.-D. Wei, E.B. Smalley and F.M. Strong. 1972. A mycotoxin from *Penicillium roqueforti* isolated from toxic cattle feed. Fed. Proc. 31:733.

Towers, N.R., J.M. Sprosen, and W. Webber. 1995a. Zearalenone metabolites in cycling and non-cycling cows. In: "Toxinology and Food Safety." Toxinology and Food Safety Research Group, Ruakura Research Centre, Hamilton, New Zealand.

Towers, N.R., C. Wesselink, E.A. Fowke, and J.M. Sprosen. 1995b. Plasma *vs* urinary "zearalenone" concentrations as indicators of "zearalenone" intake. In: "Toxinology and Food Safety." Toxinology and Food Safety Research Group, Ruakura Research Centre, Hamilton, New Zealand.

Trenholm, H. L., B. K. Thompson, K. E. Hartin, R. Greenhalgh and A. J. McAllister. 1985. Ingestion of vomitoxin (deoxynivalenol)-contaminated wheat by nonlactating dairy cows. J. Dairy Sci. 68:1000.

USDA. APHIS. 1995. Mycotoxin levels in the 1995 midwest preharvest corn crop. Veterinary Services Factsheet N195.1295. The National Veterinary Services Laboratory, Ames, Iowa.

Van Egmond, H. P. 1989. "Mycotoxins in Dairy Products." Elsevier Science Pub. Co., Ltd. New York.

Vesonder, R. F., A. Ciegler, R. F. Rogers, K. A. Burbridge, R. J. Bothast and A. H. Jensen. 1978. Survey of 1977 crop year preharvest corn for vomitoxin. Appl. Environ. Microbiol. 36:885.

Vesonder, R.F. and B. W. Horn. 1985. Sterigmatocystin in dairy cattle feed contaminated with *Aspergillus versicolor*. Appl. Environ. Microbiol. 49:234.

Vough, L.R. and I. Glick. 1993. Round bale silage. pp. 117. In: "Silage Production from Seed to Animal", NARES-67, Northeast Regional Agricultural Engineering Service, Ithaca, NY.

Wannemacher, R. W., Jr., D. L. Brunner and H. A. Neufeld. 1991. Toxicity of trichothecenes and other related mycotoxins in laboratory animals. In: J. E. Smith and R. S. Henderson (Eds.), "Mycotoxins and Animal Foods." CRC Press, Inc., Boca Raton, FL.

Weaver, G. A., H. J. Kurtz, J. C. Behrens, T. S. Robison, B. E. Seguin, F. Y. Bates and C. J. Mirocha 1986a. Effect of zearalenone on the fertility of virgin dairy heifers. Am. J. Vet. Res. 47:1395.

Weaver, G. A., H. J. Kurtz, J. C. Behrens, T. S. Robison, B. E. Seguin, F. Y. Bates and C. J. Mirocha. 1986b. Effect of zearalenone on dairy cows. Am. J. Vet. Res. 47:1826.

Weaver, G. A., H. J. Kurtz, C. J. Mirocha, F. Y. Bates, J. C. Behrens, T. S. Robison and S. P. Swanson. 1980. The failure of T-2 mycotoxin to produce hemorrhaging in dairy cattle. Can. Vet. J. 21:210.

Whitlow, L.W. 1999. Effect of fumonisin $B_1$ on dairy cattle. Unpublished.

Whitlow, L.W., W.M. Hagler, Jr., and B.A. Hopkins. 1998. Mycotoxin occurrence in farmer submitted samples of North Carolina feedstuffs: 1989-1997. J. Dairy Sci. 81:(Abstr.)1189.

Whitlow, L.W., R. L. Nebel and W.M. Hagler, Jr. 1991. The association of deoxynivalenol in grain with milk production loss in dairy cows. Pp. 131. *In*: G. C. Llewellyn, W. V. Dashek and C. E. O'Rear. 1994. Biodeterioration research 4. Plenum Press, New York.

Windels, H.F., A. DiCostanzo, and R.D. Goodrich. 1995. Effect of deoxynivalenol from barley on performance and health of large frame crossbred steers. Minnesota Cattle Feeder Rep. B-417. St. Paul, MN. (As quoted by DiCostanzo et al., 1995a).