Mycotoxins in dairy cattle: What we know and what we can do

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Abstract
Mycotoxins are secondary fungal metabolites which are identified in a broad range of food and feed ingredients worldwide. These metabolites have been shown to limit animal health, performance and reproduction through a variety of negative effects including depressed feed intake, diarrhea and compromised immune function. Ruminants are often considered to be less susceptible to mycotoxins compared with monogastric species due to natural detoxification by rumen microbiota, but the extent of degradation is dependent on the type of mycotoxin present and is influenced by other factors including toxin concentration, co-occurrence, duration of exposure and specific conditions in the rumen such as ruminal pH. Therefore, a variety of negative effects associated with mycotoxin exposure have been reported in dairy cattle. Although much research related to mycotoxins has been conducted since the mid-20th century when aflatoxins were first identified, there are still many unknowns when it comes to these toxic fungal metabolites and their consequences in animals, especially ruminants. However, mycotoxicology, the study of mycotoxins and mycotoxicoses, or diseases produced by mycotoxins, is a growing area of research that has continued to expand what we know and provide better options for mitigating mycotoxin challenges throughout various stages of dairy production.

Keywords: mycotoxins, mycotoxicosis in dairy cows, trichohecenes, zearalenone

Introduction
Many molds exist that lead to crop diseases and contaminate feed, but relatively few types of molds are known to produce toxic secondary metabolites referred to as mycotoxins. Such metabolites have been detected in a vast array of food and feed ingredients worldwide including cereal grains, forages, grain by-products, as well as fruits, vegetables and even tree nuts.29,66, 69 Due to their potential to harm humans and animals, regulations have been put in place in many countries to limit exposure to certain mycotoxins, including aflatoxins, deoxynivalenol (DON, colloquial term “vomitoxin”) and fumonisins (FUM).7,39,48 Mycotoxins result in vast economic consequences which arise from food and feed losses, analytical costs, mitigation expenditures and health and performance losses in livestock, and are estimated to average over $1 billion annually in the U.S. alone.7 Although the toxic effects of mycotoxin consumption resulting in ergotism have been recorded since at least the Middle Ages,77 understanding mycotoxins as a causative agent of disease took much longer to be realized since advanced analytical techniques are required to detect and quantify these toxic compounds. Modern mycotoxicology began with the discovery of aflatoxins in the 1960s after an outbreak of a non-infectious disease, referred to as Turkey “X” disease, killed more than 100,000 birds in England, and for which aflatoxins were identified as the etiologic agent.59 Since then, much mycotoxin-related research has been conducted, but there are still many unknowns when it comes to these fungal metabolites and their consequences in animals, especially ruminants.

Mycotoxin effects can be subclinical or may present with non-specific signs which could be attributed to various causes, often complicating diagnosis of mycotoxicoses or their potential contribution to challenges on farm.8,62 Some complications associated with mycotoxin consumption in dairy cattle include toxic metabolites in milk (aflatoxin M1, AfM1) depressed feed intake, diarrhea, decreased milk production, infertility and neurological signs including staggerers or tremors.21,46,62 The objective of this paper is to highlight what is known about the major mycotoxins associated with health, performance and reproductive concerns in dairy cattle and provide insight about what can be done to mitigate these challenges.

What we know
Mycotoxins and mycotoxicoses are complex
A multitude of factors influence the occurrence of mycotoxins and contamination can originate in the field prior to harvest or occur once a feed is in storage, making complete prevention of contamination difficult.34,48 Determining the presence and concentration of mycotoxins in feed samples through laboratory analysis is also a challenge due to the heterogenous distribution of toxins in crops and feeds which is further complicated by the fact that mycotoxins occur in low concentrations, often measured in parts per million (ppm) or parts per billion (ppb).83 Therefore, much care is needed in order to collect a representative sample for analysis since toxins may develop at any time point from pre-harvest through feeding and can occur in isolated “hot spots” within a lot of feed.34,83

Dairy rations are complex, consisting of combinations of diverse ingredients which may expose cattle to multiple sources and types of contamination.17,62 Combinations of mycotoxins can result in even poorer performance than would be expected if an individual toxin was present.26,71 Additionally, the development of mycotoxicosis is dependent on a complex interplay of factors including those inherent to the mycotoxin as well as factors specific to the animal itself and its environment.5,6,15 These factors, in addition to others, complicate the establishment of definitive mycotoxin risk threshold recommendations and diagnosis of mycotoxicosis.5,62,85

Molds and their associated mycotoxins
Over 400 mycotoxins have been identified, but relatively few are well-understood, especially when it comes to their potential negative effects in livestock. Some of the most studied mycotoxins are those which are frequently detected and likely to cause harm. These toxins are often grouped into 6 major categories including aflatoxins, trichohecenes such as DON and T-2 toxin, FUM, zearalenone (ZEN), ochratoxins and ergot alkaloids.7,29,60 Additional mycotoxins occur, but are not routinely screened for, so their occurrence is currently unclear. However, improvements in analytical techniques have helped increase awareness of these so-called “emerging mycotoxins” including enniatins, beauvericin, fusaric acid, alternariol and mycophenolic
acid,23,28 and further research is expected to advance understanding of their toxic effects in humans and animals.

Many factors influence mold growth and mycotoxin formation including temperature, water availability and moisture content, oxygen levels, pH, substrate, other stressors like physical damage to the crop, as well as various agronomic practices.34,48,73 Complete prevention of contamination is difficult, especially since critical factors such as weather conditions are beyond human control, and mycotoxins can be produced while the plant is in the field or once the feed is in storage.

Mycotoxigenic molds are roughly categorized based on where they infect the substrate and produce mycotoxins: in the field pre-harvest or in storage post-harvest.34,85 Three key genera are associated with mycotoxin production including Fusarium (field) as well as Aspergillus and Penicillium (storage).48,73 Exceptions occur which enable storage fungi to contaminate crops in the field and field fungi may continue to produce mycotoxins post-harvest if storage conditions support their growth and biosynthesis of metabolites. For instance, certain climatic conditions (e.g., high temperature) support field growth and contamination associated with Aspergillus and Penicillium.48,73,84 Mycotoxigenic molds are capable of producing a variety of mycotoxins in combination, so co-occurrence or the presence of multiple types of mycotoxins is common.26,29,66 Fusarium spp. are associated with production of trichothecenes, FUM, ZEN, enniatins, beauvericin, fusaric acid and a variety of other mycotoxins.6,7,73 Aspergillus spp. can produce a range of mycotoxins as well, most notably aflatoxins, ochratoxins, sterigmatocystin, and cyclopiazonic acid.7,73 The broadest array of mycotoxin classes is produced by the genus Penicillium and includes ochratoxins, mycophenolic acid (MPA), patulin (PAT), citrinin (CIT), roquefortine C (ROQ) and penicillic acid (PA).51,67,73 Additional mycotoxigenic genera include Claviceps, Neotyphodium, Stachybotrys and Pithomyces, among others.57

Global concerns regarding the impact of mycotoxins on human and animal health have focused primarily on understanding mycotoxin challenges in cereals and foods relevant to human nutrition. However, many of those mycotoxins are also found in forages and unique features of ensiled feeds (e.g., high moisture content) can result in complex mycotoxin profiles beyond what are found in other commodities.60,69,85 Molds that are capable of surviving in environments with low pH and limited oxygen availability are of concern in silages. A variety of Penicillium spp. produce mycotoxins in silages including CIT, ochratoxin A (OTA), PAT, ROC, PR toxin, MPA and PA.51,67,85 Aspergillus fumigatus is another silage-associated mold which produces gliotoxin.58,85 Monascus ruber is also identified in silages in North America and is reported to produce CIT.21,23 Most commercial laboratories do not routinely screen feeds for these silage-associated toxins. Therefore, the occurrence of silage-associated mycotoxins has not been well-described in field settings, but scientific studies have provided more insight into these toxins23,60 including several review articles focused on mycotoxins in forages.21,51,67,68 Additionally, a variety of mycotoxins including ZEN, DON, NIV, T-2 toxin and various ergot alkaloids have been identified in pasture grasses24,25,38 and that contamination can persist in harvested hays and other fermented grass-based feeds.21,69

Occurrence of mycotoxins
Monitoring of mycotoxins in feed is needed to understand their frequency of occurrence as well as their corresponding levels of contamination in order to gauge potential risk to livestock consuming those mycotoxins. Testing is required as visual inspection is not a reliable indicator of mycotoxin presence.81 Furthermore, mold counts are not a reliable proxy for mycotoxin levels33,42,75 for a variety of reasons as described in the “What can we do” section of this article. Several reports are published each year describing mycotoxin contamination levels in different feed ingredients in various regions around the world.

Results of a 10-year global mycotoxin survey investigating contamination in various feed and raw ingredients (e.g., corn, wheat, soybean) reported that 88% of the samples in the data set (74,821 total samples collected from 100 countries between 2008 and 2017) were contaminated with at least one mycotoxin and 64% of samples were contaminated with ≥ two mycotoxins.29 In North America (n = 5,471) DON was the most frequently detected mycotoxin in 64.1% of samples at an average contamination level of 505 ppb. The next most frequently detected toxins were FUM (47.7% positive; average 929 ppb) and ZEN (31.7% positive; average 102 ppb). Variation in contamination levels and types were observed year-to-year and across different regions. A recent 7-year survey of corn grain (n = 711) and corn silage (n = 1,117) collected from the United States Between 2013 and 2019 reported DON was the most frequently occurring major mycotoxin in both data sets, occurring at 75.7% and 82.7%, respectively.82 Routine monitoring and surveillance is ongoing with more publications anticipated, reporting on occurrence and contamination levels in a variety of ingredients from different regions.

Mycotoxicoses in dairy cows
The topic of ruminant mycotoxicosis has been reviewed in detail.18,21,33,46,62 Factors that influence the manifestation of negative effects due to mycotoxins include animal health and nutrition status, species, sex, production stage, management factors on farm such as overcrowding, weather conditions (e.g., heat stress) and the type, dose and duration of mycotoxin exposure.15,85 Additionally, combinations of mycotoxins are reported to result in even poorer performance than would be expected if an individual toxin was present due to toxicological interactions.26,73 Many of these combinations and relationships are not fully understood, but it is common to see animal health and performance impacted in the field at toxin concentrations below the tolerance levels described in research studies.28 Unfortunately, co-occurrence of mycotoxins is frequently identified.29,66,71 Furthermore, oral bioavailability and metabolism pathways of mycotoxins vary by the type of mycotoxin and across species; these topics are beyond the scope of this article, but have been reviewed.10,80,87 Animals suffering from mycotoxicosis may exhibit a few or many signs and most are non-specific or may be secondary effects.15,62 All of these factors combined, hinder diagnosis of mycotoxicosis and complicate the ability to establish definitive mycotoxicosis risk thresholds and hinder prediction of the outcome of consumption of contaminated feeds.15,62,76 In addition to regulatory levels, risk threshold recommendations for various mycotoxins are available in literature and industry publications.50,55,61 These guidelines vary by species and can be useful in the interpretation of analytical results. However, when assessing results as compared with risk recommendations, attention should be paid to the units (ppb or ppm) as well as the basis on which results and guidelines were reported (as-received or dry matter).55
The effects of mycotoxins have been studied more extensively in monogastric species as ruminants have long been reported to be less sensitive to mycotoxins due to natural detoxification by rumen microbiota, but the extent of degradation and subsequent protection is dependent on the type and concentration of mycotoxin present. Furthermore, there is evidence that natural detoxification in the rumen is limited by increased passage rate in high-producing cows and low ruminal pH conditions (pH 5.8) reduced disappearance of DON, nivalenol (NIV) and enniatin B. As such, some mycotoxins pass through the rumen and retain their biological activity (e.g., aflatoxin B1),33 the toxicity of some mycotoxins is amplified by ruminal metabolism (e.g., ZEN to α-zearalenol),30 some mycotoxins are degraded to less toxic metabolites to a high degree (e.g., ochratoxin A to ochratoxin α),45 while inconsistent results are reported in literature for some mycotoxins such as FUM. The primary mechanism of action of the major mycotoxin groups are outlined in Table 1.

Since ruminal processes do not always result in complete degradation of mycotoxins, these toxins can pass into the lower gastrointestinal tract or potentially enter circulation via rumen absorption and have their biological action in cattle, leading to adverse effects and mycotoxicosis. High concentrations of mycotoxins are generally needed for the expression of classical signs of mycotoxicosis, but low to moderate levels can cause problems that are less easily identified, yet result in reduced animal performance and health.15

### Immune function

Mycotoxins disrupt proper immune function through various mechanisms such as impaired cell-mediated immunity, reduced phagocytic cell function, and altered humoral immunity. Alterations in immune function can increase the risk of disease, especially during stressful periods including parturition or weaning. Transition cows and calves are often reported as more susceptible to mycotoxicosis challenges than other mature cows. Many mycotoxins have been reported to affect immune function including trichothecenes and various silage-associated Penicillium mycotoxins. In sows, co-contamination of the diet with DON (5.08 ppm), ZEN (90 ppb), and fusaric acid (FA, 21.6 ppm) resulted in reduced immunoglobulin A (IgA) transfer to colostrum and subsequently reduced serum IgA and IgG in their piglets. Additionally, the natural immune response to vaccinations may be reduced, leaving animals more susceptible to disease despite vaccination. This has not been studied thoroughly in cattle, but is reported in swine consuming DON (3.5 ppm). By inhibiting proper immune function, mycotoxins can serve as predisposing factors to disease.15,54

### Decreased milk production

Another commonly reported complaint in herds exposed to various mycotoxins such as DON, FUM14 and ergot alkaloids is decreased milk production. The exact mechanism(s) of action responsible for lower milk yields have not been confirmed, but it’s suggested poor production may be related to depressed feed intake or feed refusal, altered rumen function through changes in microbial populations (many mycotoxins have antimicrobial properties), decreased microbial protein, decreased nutrient absorption in the intestinal tract, or impaired metabolism which ultimately leads to reduced availability of the precursors needed for milk synthesis.

### Elevated somatic cell count (SCC) and mastitis

Research has reported elevated SCC and increased incidence of mastitis in herds consuming mycotoxin contaminated diets. Mycotoxins may affect udder health by disrupting immune function through various mechanisms such as impaired cell-mediated immunity, reduced phagocytic cell function, altered humoral immunity and compromised gut integrity and function. Mycotoxins can diminish neutrophil function, making the cow’s immune response less effective which in turn can increase the severity and duration of mastitis or other infections. The rate and concentrations at which mycotoxins can reach the mammary epithelium is not known, but in vitro research suggests DON and ZEN exert direct toxic effects on bovine mammary epithelial cells. Further research into the potential negative effects of mycotoxins on SCC and mastitis is warranted.

<table>
<thead>
<tr>
<th>Mycotoxin</th>
<th>Mechanism of action</th>
<th>Citation</th>
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<tbody>
<tr>
<td>Aflatoxins</td>
<td>Bind to guanine (DNA-adduct) following hepatic activation</td>
<td>Bennett and Klich, 2003</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Jouany and Diaz, 2005</td>
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<tr>
<td>Trichothecenes</td>
<td>Inhibit protein synthesis</td>
<td>Pestka, 2010</td>
</tr>
<tr>
<td>(including DON, NIV, T-2 toxin)</td>
<td></td>
<td>Mostrom and Raisbeck, 2012</td>
</tr>
<tr>
<td>Fumonisins</td>
<td>Inhibit ceramide synthase (sphingolipid metabolism)</td>
<td>Wang et al., 2016</td>
</tr>
<tr>
<td>Zearalenone</td>
<td>Bind mammalian estrogen receptors</td>
<td>Seeling and Danicke, 2005</td>
</tr>
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<td></td>
<td></td>
<td>Zinedine et al., 2007</td>
</tr>
<tr>
<td>Ochraotxins</td>
<td>Inhibit protein synthesis</td>
<td>Bennett and Klich, 2003</td>
</tr>
<tr>
<td>Ergot alkaloids</td>
<td>Bind adrenergic, dopaminergic, and serotonin receptors</td>
<td>Klotz, 2015</td>
</tr>
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Altered milk composition and technological properties

Various mycotoxins have been reported to modify milk composition. Depressed butterfat is a common complaint in the field, but there is relatively limited scientific research on this topic.\(^{15,35,37,40}\) and its potential mechanism. Alterations in milk composition and milk quality may be consequences of damage that mycotoxins cause to the immune system and gastrointestinal tract or due to fluctuations in feed intake, all of which can alter the availability of precursors needed for synthesis of various milk components. Altered cheesemaking properties have also been documented including negative effects on curd firmness and curd firming time with known DON and FUM exposure,\(^{12}\) as well as negative effects on curd firmness and curd quality following consumption of multi-mycotoxin contaminated diets.\(^{40}\)

The various effects reported on milk yield, milk composition, milk quality and udder health can negatively affect profitability of dairy producers. Additionally, milk processors can be affected due to alterations in milk composition, quality, and technological properties which can reduce yield and shelf-life of dairy products.

Toxic residues in milk

Aflatoxins are the greatest concern for carry-over into milk and are reported to be transferred as AFM1 at 1.8 to 6.2 percent of the aflatoxin content of the diet.\(^{17,33,79}\) Carry-over rate is reported to increase with increasing dietary aflatoxin content and increasing milk yield per cow per day.\(^{79}\) Aflatoxins are reported to appear in milk within 12 hours following oral administration and disappear from milk 4 days after cessation of oral administration.\(^{15}\) Aflatoxins are carcinogenic and most countries set strict limits on allowable levels in milk as this is a human health concern. In the U.S., AFM1 is restricted to 0.5 ppb in milk and in order to help limit potential milk contamination, feeds destined for lactating dairy cows also have strict regulations, limited to 20 ppb total aflatoxins.\(^{7,50,85}\) Feed-to-milk transmission of other mycotoxins is reported to be negligible.\(^{17}\)

Gastrointestinal effects

Many mycotoxins negatively impact the gastrointestinal tract including aflatoxins, trichothecenes, FUM and various combinations of metabolites.\(^{2,27,60}\) The intestinal epithelium has two key roles: 1) to absorb nutrients and 2) to act as a barrier to prevent harmful substances from entering blood circulation. Both of these functions can be disrupted by various mycotoxins, leading to reduced nutrient uptake and increased passage of toxins and pathogens into circulation. Nutrient digestibility and uptake can be affected, gastrointestinal microbial populations can be altered, and mucosal immunity can also be compromised.\(^{27}\) Some potential downstream consequences of compromised gut integrity and function include poor growth rates, reduced milk yield and altered milk composition, as well as increased risk of disease due to pathogens entering the bloodstream or as a result of immune dysfunction. Disruption of the intestinal mucosa can also lead to diarrhea due damage to the intestinal epithelium and to water malabsorption. The cells lining the intestines are continuously being renewed and are especially sensitive to the effects of trichothecenes which inhibit protein synthesis.\(^{47,56}\)

Reproductive effects

Zearalenone is generally the first mycotoxin thought of in regard to reproductive issues as it’s recognized as an endocrine disrupter and causes estrogenic effects.\(^{2,62,67}\) Reported effects in ruminants include vaginitis, early embryonic death, abortions, irregular heat cycles, cystic ovaries, infertility and premature mammary gland development in virgin heifers.\(^{16,33,68,85}\) In addition to ZEN, ergot alkaloids can negatively affect reproductive function by disrupting normal endocrine function, lower conception rates, and can negatively affect fetal growth, leading to reduced birth weight.\(^{58}\) Male reproduction has also been reported to be negatively impacted by mycotoxins.\(^{16}\)

Other mycotoxoses

Diverse clinical signs have been associated with mycotoxin consumption in dairy cows. Mycotoxoses often present with non-specific signs such as depressed feed intake, diarrhea, emesis (which may present as discarded cud boluses), unthriftness, laminitis, increased incidence of metabolic disorders, impaired thermoregulation, elevated liver enzyme levels, neurological signs, skin lesions, rough hair coats and death, when levels are extreme.\(^{15,21,33,46,62}\) Tall fescue toxicity as well as perennial ryegrass staggers and paspalum staggers are additional well-recognized mycotoxicoses in ruminants associated with ergot alkaloids.\(^{18,38}\) Further information can be found in various reviews\(^{18,33,46,62}\) and Figure 1.

What we can do

Mycotoxins are persistent and stable, therefore, once they’re produced, they tend to remain in feeds through the time of feeding. Various physical, chemical and biological mycotoxin mitigation methods have been described with reported variable efficacies depending on the method utilized and the mycotoxin being addressed.\(^{33,34,65}\) Although chemical treatments have been described, these can result in toxic residues, may reduce palatability and nutritive value of feeds, and have variable efficacies.\(^{7,34}\) Therefore, physical and biological methods are focused on in this paper. Mycotoxin decontamination refers to methods that neutralize or remove mycotoxins from contaminated feeds while mycotoxin detoxification is the elimination of the toxic properties of mycotoxins.\(^{53}\) The first step in addressing mycotoxin contamination is understanding what type(s) and level(s) of mycotoxins are present.

Sampling and detection

Due to the inherent heterogeneity of mycotoxins in feeds, mycotoxin sampling and detection is challenging.\(^{83}\) Therefore, a highly contaminated sample does not mean the entire crop or lot of feed is bad and a “clean” sample does not guarantee that all of the feed is mycotoxin-free. Additionally, many mycotoxins exist, but relatively few are routinely tested for. Most commercial analytical laboratories can screen samples for several of the major mycotoxin groups. Although limitations exist, mycotoxin analysis of feeds can provide useful information to producers to help guide mycotoxin mitigation approaches and other management decisions. Results can also be helpful when troubleshooting clinical concerns on-farm.

Visible mold growth on feed does not guarantee the presence of mycotoxins, but it does indicate there is potential for contamination. Many molds can infect feeds, but relatively few produce mycotoxins.\(^{86,73}\) Furthermore, mycotoxigenic molds do not constantly produce mycotoxins, so even if the molds are
present, mycotoxins may be absent.\textsuperscript{73} Independent of mycotoxins themselves, molds can reduce feed quality and nutritive value, negatively affect palatability, and molds themselves can cause disease (referred to as mycoses).\textsuperscript{85} Visual inspection may overlook mold growth since it is often very uneven, may not be exposed for viewing, or may be microscopic. Additionally, mycotoxins are more resilient than the molds that produce them, so it’s possible for the mold to die off, but the mycotoxins will persist. Therefore, visual inspection of feed alone cannot positively identify whether mycotoxins are present or not. These reasons also help explain why screening samples for mold counts, although valuable in itself, is not a reliable substitution for mycotoxin testing.\textsuperscript{33,42,75}

Analytical techniques continue to improve with enhanced sensitivity and specificity, leading to greater reliability and better accuracy.\textsuperscript{3,74} Advanced techniques enable screening of complex matrices which is important especially for ruminant feeds including ingredients like corn silage as well as total mixed rations (TMR).\textsuperscript{72} Various mycotoxin testing methods are available with differences in their ease of use, speed, cost, suitability for different matrices as well as their sensitivity and specificity.\textsuperscript{7,8} Lateral flow tests allow rapid identification at a relatively low cost, but have limitations as to what mycotoxins can be screened, potential for cross-reactivity, and are only suitable for use on raw ingredients.\textsuperscript{8} Liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS), is suitable for screening complex feedstuffs and is highly sensitive, but comes at a much higher cost and requires a longer turnaround time.\textsuperscript{8,72} Reviews of the various analytical methods used for the determination of mycotoxins are available.\textsuperscript{8,41}

**Physical mitigation approaches**

Reducing animal exposure to mycotoxins is key to limit negative consequences, but complete substitution is not always possible when feeding livestock due to limitations in various factors such as feed inventories and cost required to purchase other feeds. Additionally, due to sampling difficulties, it is challenging to accurately determine contamination levels and would be costly to discard all feeds that are suspect of being contaminated. Ideally, spoiled feeds with visible mold growth should be discarded and not fed to animals.\textsuperscript{7,85} Since mycotoxin contamination is not visible to the naked eye and requires analysis to confirm the presence of mycotoxins, it is difficult to completely prevent feeding of contaminated feeds. Although visual cues may be present such as mold growth, discolored or misshapen kernels, mustiness or high proportion of damaged kernels, identification of contamination through mycotoxin analysis is needed to confirm the type(s) and concentration(s) of mycotoxins that are present. When suitable, combining feed ingredients may dilute the final mycotoxin contamination levels in the diet offered to cattle and can reduce the risk of toxicity. However, mixing feeds may inadvertently increase contamination levels; caution is warranted when the mycotoxin contamination status of feed ingredients is unknown. In some cases, the practice of dilution is not permitted. Additional physical methods of decontamination include sorting, washing, dehulling and thermal treatment, but their efficacies vary.\textsuperscript{7,34}

**Biological or in-feed mitigation options**

Since absolute prevention of mycotoxin contamination in feeds is unachievable, there are options available on the market reported to help alleviate challenges despite the fact no products are approved for use by the FDA for control of mycotoxicoses.\textsuperscript{13,43,85} Commercial products are available including inorganic clay minerals (e.g., bentonite, hydrated calcium sodium aluminosilicates, zeolite) and organic products (e.g., yeast, yeast cell wall, algae) which can bind (adsorb) some mycotoxins.\textsuperscript{13} The physical structure and chemical properties of the mycotoxin as well as the binder material itself are critical in whether a toxin can be bound with high efficacy. The pH of the gastrointestinal tract also influences adsorption capacity.\textsuperscript{11} Additionally, binder products vary tremendously in their composition, leading to variability in their effectiveness at adsorbing mycotoxins, especially in vivo.\textsuperscript{19,43,49,57,78} Effective binders should have high adsorption capacity (i.e., high amount of toxin bound per unit of adsorbent), irreversibility of binding (i.e., toxin is bound and remains bound until exiting animal), and specificity of binding (i.e., only mycotoxins are bound, not other nutrients such as vitamins or minerals) and should be non-toxic.\textsuperscript{21}

Much research into feeding non-nutritive adsorbent materials to dairy cows has investigated aflatoxin control.\textsuperscript{13,21,41} Aflatoxins and some ergot alkaloids are reportedly controlled well by binders while other mycotoxins, such as zearalenone and trichotheccenes, are not as readily adsorbed, but other potential detoxification approaches have been identified.\textsuperscript{6,7,65} Options which utilize a combination of tactics are suggested for broad-spectrum control of mycotoxins. Some commercial products can achieve this through utilization of enzymes (or microorganisms that produce enzymes) which deactivate non-adsorbable mycotoxins through alterations of their chemical structure, and convert the parent mycotoxin into essentially non-toxic metabolite(s).\textsuperscript{7,31,65} Additionally, several plant and algal extracts have been identified which can enhance the cow’s natural resistance mechanisms and lessen damage through enhanced gut integrity, immune function support and promotion of liver health. Combination products which utilize binding materials, have degradation capacity and supply protective plant and algal extracts provide more complete mitigation, especially in the presence of co-contamination.

Currently, screening feeds is the most effective way to identify the presence of mycotoxin contamination and potential exposure in field settings. If mycotoxins are detected in feeds, these results can be used in combination with assessment of clinical signs in the herd to guide management decisions. Implementation of a mitigation approach is warranted in order to reduce exposure in the herd whether that be done through complete exclusion of contaminated feed, adjustment of the inclusion rate in the diet, or consideration for the use of another method of decontamination or detoxification. It is recommended that dairy producers consult their nutritionist and veterinarian to develop a mycotoxin mitigation strategy as both dietary and health aspects should be considered.

**Summary and conclusions**

Mycotoxins are fungal metabolites known to negatively impact animal health, performance and reproduction. They are associated with vast economic losses. Mycotoxins are diverse in nature and cause a wide array of effects and clinical signs. The response an animal has following mycotoxin exposure is dependent on a complex interplay of many factors related to the animal itself, its environment, and factors inherent to the mycotoxin. Despite some degree of natural rumen detoxification, mycotoxicoses occur in dairy cattle and often present with non-specific signs. Calves and transition cows appear to be most
susceptible to the negative effects of mycotoxins. Depending on the clinical concerns on-farm, mycotoxins should be considered as a potential cause or contributing factor to health and performance challenges and should be considered when working through a differential diagnosis. Often, mycotoxins are an afterthought when other potential causes have been eliminated or addressed and the problem persists. Proactive screening of feeds can help identify potential mycotoxin challenges early and limit production losses and prevent detrimental health outcomes. Screening feed is a critical step in the development of a comprehensive mycotoxin risk-management strategy. Various mitigation approaches are available including prevention methods that can be implemented in the field prior to mycotoxin formation. However, application of best management practices from planting through the time of feeding cannot guarantee total prevention of contamination as many factors influence mold growth and mycotoxin formation, including weather conditions which are beyond control. Therefore, when mycotoxins are present in feed, use of a research-proven, broad-spectrum mitigation product that provides a combination of adsorption, detoxification and natural ingredients which support gut, immune and liver health should be considered. There is a growing body of literature investigating mycotoxin exposure and subsequent outcomes in ruminants. Although there are still many unknowns in regard to mycotoxins in general, especially in ruminants, more research is warranted to help determine what can be done to maintain dairy cattle health, performance and reproduction in spite of mycotoxin contamination in the diet.

Conflict of interest
The authors are employed by BIOMIN America Inc., a manufacturer of livestock feed additives.

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