Advisory

Information from Phibro Technical Services

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Understanding and Managing Mycotoxins in Dairy Cattle Feeds

Introduction

In a perfect world, grains, hays and silages could all be grown, harvested, stored and fed to dairy cattle with no molds or mold metabolites (mycotoxins) present at all. However, based on different environments, weather conditions, farming practices, harvesting and storage conditions, each crop can present challenges for feeding dairy cattle depending on the year. For example, *Fusarium* species of molds begin their contamination of crops in the fields whereas *Aspergillus* and *Penicillium* species of molds produce their toxins on the crops after harvesting (Antonissen et al., 2014).

Whatever the reasons and because molds are everywhere, mycotoxins will be present in all feedstuffs, at one concentration or another (Devegowda and Murthy, 2005). The goal of harvesting and storing of feeds is to minimize the concentrations of mycotoxins that creep into the total mixed ration (TMR) of the dairy cow.

Non-Toxigenic and Toxigenic Molds

The presence of mold indicates the preservation technology applied at harvest or storage has failed or become less effective. Grains may have been harvested and subsequently put in the bin with moisture greater than 15% or silages may have been inoculated with a lactic acid-producing bacterial solution at ensiling but improperly packed or covered, resulting in visible mold formation on the feedstuff. However, detecting mycotoxins goes beyond visually confirming the presence of mold as approximately 67% of the species are non-toxigenic (do not produce mycotoxins) while the remaining 33% are toxigenic or produce mycotoxins (Table 1). When investigating feedstuffs for mycotoxins, oftentimes a mold and yeast enumeration and identification will help pinpoint whether mycotoxins are to be expected or not.

Table 1. Toxicity of Mold Species

Non- Toxigenic Mold Species	Toxigenic Mold Species
Mucor, Trichoderma, Rhizopus, Cladosporin	*Aspergillus, Penicillium, Stenocarpella* (formerly *Diplodia*), *Fusarium sporotrichoides, Fusarium verticillioides, Gibberella zeae (Fusarium graminearum)*

Courtesy of Dr. Lon Whitlow, Professor Emeritus, North Carolina State University, Raleigh, NC

Mycosis or Mycotoxicosis: The Difference

There are two ways in which molds can affect the health and production of dairy cattle; mycosis and mycotoxicosis. Some molds, such as Aspergillus fumigatus, can invade and colonize the respiratory or digestive tracts and enter the circulatory system, spreading to other tissues (Seyedmousavi et al., 2015). This is referred to as a mycosis and there are specific clinical signs observed in dairy cows when this occurs (Bennett and Klich, 2003).

A well-known example of a mycosis is Jejunal Hemorrhagic Syndrome (JHS), also referred to as Hemorrhagic Bowel Syndrome (HBS) of dairy cattle. Aspergillus fumigatus colonizes the gastrointestinal tract as cows ingest contaminated feeds or A. fumigatus can also enter via the respiratory tract when cows inhale the pathogen from spoiled feed at

the bunk (Stanzani et al., 2005) or from deep bedded or tie stalls (Jensen et al., 1992). From there, the pathogen can enter the circulatory system and spread to other organs of the cow, as A. fumigatus DNA has been isolated in the blood of dairy cows (Puntenney et al., 2003). A. fumigatus produces primarily gliotoxin with lesser amounts of fumigaclavines A and C. Gliotoxin causes apoptosis (controlled cell death) of cells lining the G.I. tract (enterocytes), suppresses functional T-cell responses and causes monocyte apoptosis, leading to immune system dysfunction (Stanzani et al., 2005).

Clinical signs for JHS include depression, loss of appetite, low body temperature, abdominal pain, bloating, constipation or bloody diarrhea. Mortality from JHS can range from 77 to 100% (McGuirk, 2014).

At one point, Clostridium perfringens type A isolated from the G.I. tracts of JHS cows was thought to play a role in the syndrome. However, Ewoldt and Anderson (2005) were unable to fulfill Koch's postulate and induce JHS by inoculating the G.I. tracts of dairy cows with C. perfringens type A. In addition, Adaska et al. (2014) reviewed 314 individual cases of JHS and found no causative connection between JHS and Clostridium perfringens type A. The bacterium is often isolated at necropsy and might be considered an artifact.

When it comes to a mycotoxicosis, a prime example would be aflatoxicosis. Aflatoxin mycotoxicosis causes tissue damage in the liver and kidney as well as immunosuppression in dairy cattle and decreased milk production (Riet-Correa et al., 2013). Aflatoxin mycotoxicosis is of particular importance because dietary aflatoxins (Aflatoxin B1) can be converted to active mycotoxins in milk (Aflatoxin M1). Hence, the FDA has limited dietary aflatoxin concentrations for lactating dairy cows to 20 ppb. If greater levels are fed, aflatoxins then pass into the milk, creating problems for humans consuming the milk.

Impact of Mycotoxins on the Cow

When mycotoxin-contaminated feeds are consumed by the cow, mycotoxins interact with other dairy cow stressors to produce numerous clinical signs. These clinical signs are often non-specific and reflect the organ systems affected by the toxins. Clinical signs include lower dry matter intakes, intermittent diarrhea and other digestive upsets, unthriftiness, rough hair coat, reproductive dysfunction, early embryonic mortality (irregular heat cycles), and decreased milk production and milk components. Because of immune suppression, mycotoxins often cause an increase in infectious disease and death rate (Antonissen et al., 2014). Thus, the observed clinical signs reported in a mycotoxicosis may well result from occurrence of opportunistic diseases such as salmonellosis, colibacillosis and necrotic enteritis.

Diaz et al. (2000) reported a fumonisin mycotoxicosis when dry cows were fed diets containing 100 ppm fumonisin 1 week prior to calving through 70 days in lactation. The cows fed fumonisin produced 13.2 lbs. per day less milk at peak compared to controls, demonstrating how economically important it is to diagnose and manage a mycotoxicosis.

Chronic toxicity resulting from long term, low level consumption of mycotoxins is more likely than acute toxicity (Marin et al., 2002). However, ruminants are somewhat protected from acute toxicity because the rumen microorganisms destroy a substantial portion of many mycotoxins. While in the rumen, multiple mycotoxins in feedstuffs may lead to rumen upsets. These mycotoxins bring about rumen upsets by exerting anti-microbial effects on rumen microorganisms, altering microbial populations, changes in volatile fatty acids and reduced protein and fiber digestibility (Zain, 2011).

Some mycotoxins escape ruminal degradation and some derivatives formed in the rumen maintain toxicity and in the case of zearalenone, metabolites cause even greater toxicity. Regardless, sufficient amount of mycotoxins can flow from the rumen and cause chronic toxicity (Grenier and Applegate, 2013).

How Mycotoxins Affect the Gut

The epithelial cells lining the digestive tract are first exposed to ingested mycotoxins, usually at higher concentrations than other cells. Aflatoxin is very bioavailable and passes through the G.I. tract into the circulation in the upper G.I. Other mycotoxins, such as fumonisins, are less well absorbed and spend more time in the digestive tract, impacting cells lower in the tract (Grenier and Applegate, 2013). As the Fusarium mycotoxins deoxynivalenol (DON), T-2 toxin

(T-2), zearalenone (ZEN) and fumonisin B1 (FB1) pass down the G.I. tract, they modify the physiology of the epithelial cells by loosening the tight junctions between cells, decreasing mucus production in the goblet cells and decreasing replacement enterocyte proliferation. This tissue damage in the cells lining the gut allows intestinal contents to "leak" into the supportive tissues of the gut (Bouhet and Oswald, 2005). However, within the enterocytes, mycotoxins inhibit protein synthesis, increase lipid peroxidation which in turn induces oxidative stress and more cell damage, eventually leading to cell death (Broom, 2015). This tissue destruction has a negative impact on the cow's ability to absorb nutrients and explains why dairy cows lose performance when exposed to mycotoxins (Riet-Correa et al., 2013). It also increases the maintenance requirements for energy and protein in the cow by having to spend those resources repairing the tissues.

How Mycotoxins Affect the Immune System

One of the more important chronic effects of mycotoxins is suppression of immunity (Oswald et al., 2005). Most importantly, mycotoxins initiate changes in cytokine production in innate immune cells in the tissues below the enterocytes (Antonissen et al., 2014). Cytokines are small proteins secreted by a broad range of cell types (i.e. monocytes, macrophages, neutrophils) and are important in cell to cell communication. There are pro-inflammatory cytokines (i.e. IL-1ß, IL-6 and TNF-α) produced predominantly by activated macrophages and helper T cells (Zhang and An, 2009). There are also anti-inflammatory cytokines (i.e. IL-4, IL-10, IL-11 and IL-13) produced by immune cells to control inflammation (Zhang and An, 2009).

The mycotoxin DON has been shown to cause an increase in the pro-inflammatory cytokines IL-6 and TNF-α in mice, with a subsequent decrease in growth hormone production and lower weight gain (Amuzie et al., 2009). Aflatoxins have been shown to suppress IL-1ß and TNF-α pro-inflammatory cytokines and increase the anti-inflammatory cytokine IL-10 (Marin et al., 2002). Gliotoxin inhibits production of TNF-α (pro-inflammatory cytokine) and IL-8 (a chemokine or "chemotactic"-directing protein produced by macrophages and other immune cells) adding more supportive documentation on how mycotoxins impact the immune system (Fitzpatrick et al., 2000). If the signaling pathways are negatively influenced by mycotoxins, it becomes obvious how immune-suppression results. Producers will see more cases of respiratory and digestive diseases leading to decreases in milk production and altered milk components.

In summary, mycotoxins commonly occur in feeds and adversely affect dairy cattle. Mycotoxins may not be apparent due to difficulties in sampling and detection of mycotoxins. Because mycotoxins suppress immunity, clinical signs may be indirect, resulting in opportunistic diseases. Chronic effects may develop over an extended time period, also making diagnosis difficult. As a result, mycotoxin exposure may be undiagnosed, but a key reason for herd problems.

Managing Around Mycotoxins

Prevention and treatment starts in the field with practices to reduce plant stress, such as plant varieties with fungal resistance, timely planting, proper tillage, soil fertility, irrigation, insect control, fungicides, and timely harvest (Mansfield et al., 2005). Mold growth and mycotoxin formation can be further controlled with feed harvest and storage practices to reduce trash and broken kernels in grain and to manage correct levels of moisture, heat and air.

Because molds and mycotoxins can damage the gut, liver and other body tissues, it becomes obvious how mycotoxins can rob cows of production and efficiency. It also becomes clear why producers need to implement management practices that ensure high quality feeds are produced and minimize mold and mycotoxin impacts on their cows.

The Need for a Mycotoxin Mitigation Strategy

Regardless of how diligent harvest practices are, in some instances, there is no escaping the appearance of high levels of mycotoxins in the TMR. Based on the sheer tonnages of hays, silages and grains, it becomes impractical to discard feedstuffs that contain mycotoxins. Depending on what the mycotoxin load is will dictate how involved a mycotoxin mitigation program should be. In order to reduce the presence and effects of mycotoxins, an effective mycotoxin mitigation strategy could include: feed treatments to reduce mycotoxin content, adsorbents to prevent animal absorption, use of immune modulators to rescue immune system function, added nutrients and incorporation of antioxidants in the TMR (Whitlow and Hagler, 2005).

REFERENCES

Amuzie, C. J., J. Shinozuka and J.J. Pestka. 2009. Induction of suppressors of cytokine signaling by the trichothecene deoxynivalenol in the mouse. Toxicol. Sci. 111:277–287.

Adaska, J.M., S.S. Aly, R.B. Moeller, P.C. Blanchard, M. Anderson, H. Kinde and F. Uzal. 2014. Jejunal hematoma in cattle: a retrospective case analysis. J. Vet. Diagn. Invest. 26:96-103.

Antonissen, G., A. Martel, F. Pasmans, R. Ducatelle, E. Verbrugghe, V. Vandenbroucke, S. Li, F. Haesebrouck, F. Van Immerseel and S. Croubels. 2014. The Impact of Fusarium Mycotoxins on Human and Animal Host Susceptibility to Infectious Diseases. Toxins 6:430-452.

Bennett, J.W. and M. Klich. 2003. Mycotoxins. Clin. Microbiol. Rev. 16:497-516.

Bouhet, S. and I.P. Oswald. 2005. The effects of mycotoxins, fungal food contaminants, on the intestinal epithelial cell-derived innate immune response. Vet. Immunol. Immunopathol. 108:199-209.

Broom, L. 2015. Mycotoxins and the intestine. Animal Nutrition 1:262-265.

Devegowda, G. and T.N.K. Murthy. 2005. Mycotoxins: Their adverse effects in poultry and some practical solutions.

In: Diaz, D.E., editor. The Mycotoxin Blue Book. Nottingham University Press, Nottingham, UK. p. 25-56.

Diaz, D.E., B.A. Hopkins, L.M. Leonard, W.M. Hagler, Jr. and L.W. Whitlow. 2000. Effect of fumonisin on lactating dairy cattle. J. Dairy Sci. 83(abstr.):1171.

Ewoldt, J.M. and D.E. Anderson. 2005. Determination of the effect of single abomasal or jejunal inoculation of Clostridium perfringens Type A in dairy cows. Can. Vet. J. 46:821-824.

Fitzpatrick, L.R., J. Wang and T. Le. 2000. In vitro and in vivo effects of gliotoxin, a fungal metabolite: efficacy against dextran sodium sulfate-induced colitis in rats. Dig. Dis. Sci. 45:2327-2336.

Grenier, B. and T.J. Applegate. 2013. Modulation of intestinal functions following mycotoxin ingestion: Meta-analysis of published experiments in animals. Toxins 5:396-430.

Jensen, H.E., B. Aalbaek, A. Basse and H.C. Schonheyder. 1992. The occurrence of fungi in bovine tissues in relations to portals of entry and environmental factors. J. Comp. Path. 107:127-140.

Mansfield, M.E., E. D. De Wolf and G. A. Kuldau. 2005. Relationships between weather conditions, agronomic practices, and fermentation characteristics with deoxynivalenol content in fresh and ensiled maize. Plant Disease 89:1151-1157.

Marin, D.E., I. Taranu, R.P. Bunaciu, F. Pascale, D.S. Tudor, N. Avram, M. Sarca, I. Cureu, R.D. Criste, V. Sutta and I.P. Oswald. 2002. Changes in performance, blood parameters, humoral and cellular responses in weanling piglets exposed to low doses of aflatoxins. J. Anim. Sci. 80:1250-1257.

McGuirk, S.M. 2014. Hemorrhagic Bowel Syndrome: Update and Observations. Proceedings, Four-State Dairy Nutrition and Management Conference, Dubuque, IA. pp. 128-130.

Oswald, I.P., D.E. Marin, S. Bouhet, P. Pinton, I. Taranu and F. Accensi. 2005. Immunotoxicological risk of mycotoxins for domestic animals. Food Addit. Contam. 22:354-360.

Puntenney, S.B., Y. Wang and N.E. Forsberg. 2003. Mycotic infections in livestock: recent insights and studies on etiology, diagnostics and prevention of hemorrhagic bowel syndrome. In: Southwest Animal Nutrition and Management Conference Proceedings. pp. 49–62.

Riet-Correa, F., R. Rivero, E. Odriozola, M. de Lourdes Adrien, R.M. T. Medeiros and A. Lucia Schild. 2013. Mycotoxicoses of ruminants and horses. J. Vet. Diagn. Invest. 20(10):1-17.

Seyedmousavi, S., J. Guillot, P. Arné, G.S. de Hoog, J.W. Mouton, W.J.G. Melchers and P.E. Verweij. 2015. Aspergillus and aspergilloses in wild and domestic animals: a global health concern with parallels to human disease. Medical Mycology 53:765-797.

Stanzani, M., E. Orciuolo, R. Lewis, D.P. Kontoyiannis, S.L.R. Martins, L.S. St. John and K.V. Komanduri. 2005.Aspergillus fumigatus suppresses the human cellular immune response via gliotoxin-mediated apoptosis of monocytes. Blood. 105:2258-2265.

Whitlow, L.W. and W.M. Hagler, Jr. 2005. Mycotoxins in dairy cattle: occurrence, toxicity, prevention and treatment. Proc. Southwest Nutr. Conf. p. 124-138.

Zain, M.E. 2011. Impact of mycotoxins on humans and animals. J. Saudi Chem. Soc. 15:129-144.

Zhang, J.M. and J. An. 2009. Cytokines, inflammation and pain. Int. Anesthesiol. Clin. 45:27-37.