Issue 15 • Poultry
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Science & Solutions

Minor threat?

Can low levels of mycotoxins harm the poultry industry?

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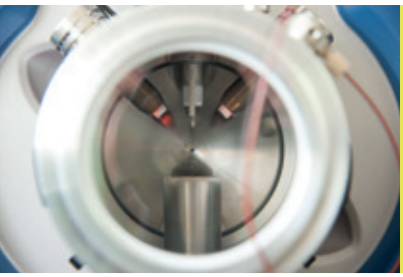

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Editorial

Chicken will win?

Global animal protein food production will double in size by 2050—with poultry and aquaculture set to be the fastest growing markets. Forecasts often depict the poultry industry's future as bright in terms of production development in the coming decades, citing its potential to become the principal animal protein food source worldwide by 2030.

This upward trajectory will be driven by global population growth—expected to reach 9 billion people by 2050—and economic development that puts more disposable income in consumers' pockets. This newfound wealth will foster demand for more varied diets and higher protein consumption, particularly in developing countries.

Yet, the way forward is not without obstacles. The poultry industry will have to face challenges such as: improving production efficiency, zoonosis, pressure regarding the use of antibiotics, climate change, higher mycotoxin presence, environment, food safety, social demands, market variability, the heterogeneity of consumer purchasing power and more.

Optimizing poultry health and performance will be crucial. Alongside biosecurity, genetics, health and farm management, **gut integrity** and **feed conversion efficiency** provide keys to success. At the recent World Nutrition Forum in Munich, leading researchers demonstrated the importance of current and future research in this regard. At Biomin, we are committed to helping identify and supply the best solutions for the poultry industry in terms of mycotoxin risk management and gut performance.

This issue of **Science & Solutions** magazine provides additional elements to address these topics within the poultry industry.

Most of us like to eat eggs, to savor cheese, to cook with milk, to eat a succulent piece of meat, or enjoy a tasty fish. While no one knows for sure whether poultry will win the animal protein battle, we believe that it is important for the industry and Biomin to work together to achieve sustainable poultry production for the next decades and beyond 2050.

Mickaël ROUAULT
Technical and Marketing Director, EMA

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Can low levels of mycotoxins harm the poultry industry?

by Mycotoxin Risk Management

Poultry husbandry is a challenging activity. In spite of the best efforts to keep each production cycle running as smoothly as possible, birds may eventually get sick from one of many variables such as nutrition, water supply and quality, biosecurity, housing, management and the existence of pathogens, to name a few.

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“Mycotoxins’ general effects include impaired nutrient uptake, immune suppression and decreased performance.”

Symptoms of poultry diseases, arising due to lapses in their diets or the farm environment, allow veterinarians and nutritionists to take action and treat the problem accordingly. Often, disease manifestations can be attributed to several causes and thus, understanding the root of the problem can be hard.

In this article, we explore how mycotoxins, toxic metabolites produced by molds, can harm the gastrointestinal tract (GIT), open the gate to infectious agents and/or predispose animals to a number of factors that will reduce performance and cause disease outbreaks.

The gut barrier

The GIT is probably one of the most amazing organs in the body, including that of chickens. It can digest food but it does not digest itself. It is the most extensively exposed surface in the body and therefore the most important barrier between the internal and external environments.

In poultry, the GIT harbors more than 650 different species of bacteria, contains over 20 different hormones, digests and absorbs the vast majority of nutrients, and accounts for 20% of the body’s total energy expenditure while being the largest organ of the immune system.

GIT exposure to mycotoxins

Whenever mycotoxins are discussed at a feed mill or farm, the first question raised usually concerns the mycotoxin level that triggers a symptom of disease. With the (high) limits imposed by regulatory bodies (European Commission in the European Union, and Food and Drug Administration in the USA) for the presence of mycotoxins in animal feed, levels below those thresholds may be dismissed as benign.

The general understanding is that in many cases, mycotoxins occur without any symptoms at levels below the regulatory limits and therefore their amounts are not high enough to be absorbed, attack target organs and cause mycotoxicoses. This understanding overlooks the fact that even subclinical levels of mycotoxins can and do cause harm to animals.

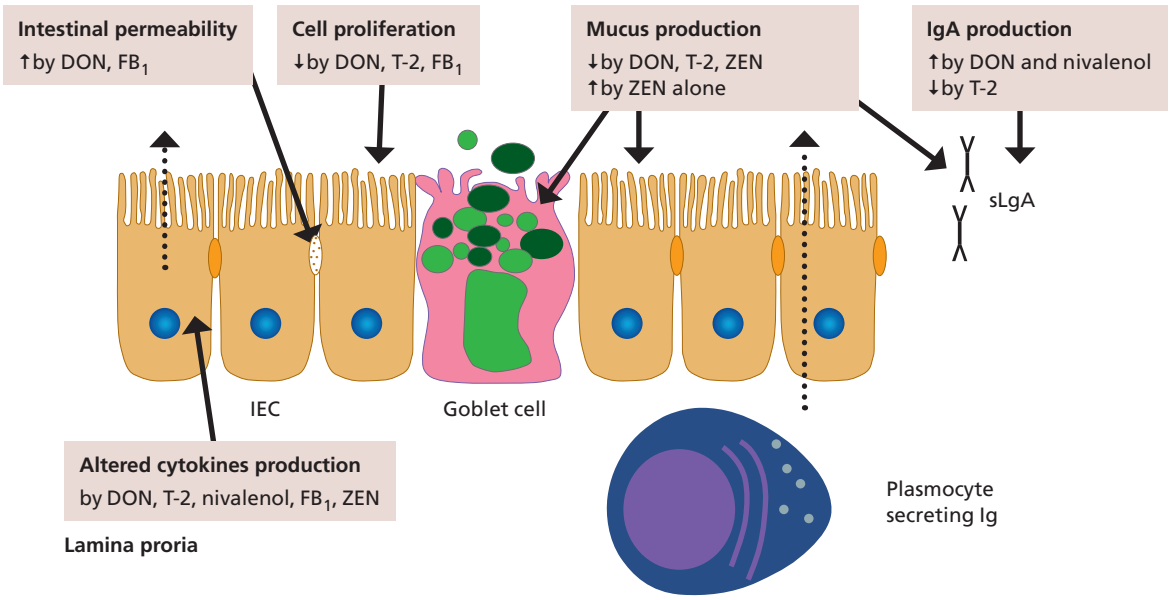
Indeed, it can be argued that not all mycotoxins cross the intestinal barrier; thus, not all mycotoxins will result in mycotoxicoses. Nonetheless, intestinal cells are the first cells to be exposed to mycotoxins and often at higher concentrations than in other tissues. Therefore, the intestinal epithelium and its entire extension can be compromised by non-absorbed toxins before absorption can even begin.

Effects of mycotoxin exposure

There are many studies focusing on the different levels of impact of mycotoxins in the GIT. A meta-analysis published by Grenier and Applegate (2013) thoroughly reviews how mycotoxins can modulate intestinal functions. In terms of morphology of the intestinal villi, studies show that feeding poultry low or moderate levels of deoxynivalenol (DON) alone or combined with other fusariotoxins leads to a reduction in villi height in both the duodenum and jejunum.

> *"Even subclinical levels of mycotoxins can and do cause harm to animals."*

Figure 1. The effect of *Fusarium* mycotoxins on the intestinal epithelium.



A variety of *Fusarium* mycotoxins alter the different intestinal defense mechanisms including epithelial integrity, cell proliferation, mucus layer, immunoglobulins and cytokine production.
IEC – intestinal epithelial cell; FB_1 – fumonisin B_1; Ig – immunoglobulins; sIgA – segregated immunoglobulin A.

Source: Adapted from Antonissen et al.*, 2014*

The practical consequence of this is that there is a smaller absorptive area available for nutrient uptake, with obvious impacts on animal performance. Interestingly, it seems that mycotoxins such as DON and T-2 have a direct effect on glucose transporters in the jejunum. This leads to an anti-nutritional effect (decreased glucose absorption) and may potentially limit water reabsorption resulting in diarrhea.

Several studies have explored the effects of mycotoxins on the intestinal defense against parasitic and bacterial infections. Chicks fed with the mycotoxin Ochratoxin A (OTA) presented more severe lesions and mucosal damage and more *E. acervulina* and *E. adenoeides* oocysts than those not exposed to the toxin.

Studies with a more commonly occurring mycotoxin showed that even at dosages below those regarded safe for poultry, DON modulated the intestinal response and intestinal recovery following a coccidial infection. In particular, the recruitment and stimulation of lymphocytes was inhibited at the site of infection, which delays the clearance of the parasitic infection.

Other factors that might explain coccidial outbreaks in the field despite the use of coccidiostats were explored in experiments in which the efficacy of lasalocid was reduced in broiler diets contaminated with T-2.

Experiments dealing with Afla and T-2 contamination of poultry feeds and birds' increased susceptibility to diseases were so far unable to establish a correlation

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Table 1. Summary of the literature on the effect of mycotoxins in poultry.

Author(s), Year	Mycotoxin	Type of trial	Effect in poultry
Awad *et al*., 2009; Awad *et al*., 2010	DON (alone or combined with other fusariotoxins)	*In vivo*	Reduction in villi height in both the duodenum and jejunum
Awad *et al*., 2005	T-2	In vitro and *in vivo*	Decreased glucose absorption
Koynarski et al., 2007	OTA	*In vivo*	Increased lesions, mucosal damage and more oocysts after cocci infection
Girgis *et al*., 2010a; Girgis *et al*., 2010b; Girgis *et al*., 2008	DON	*In vivo*	Slow intestinal response and recovery after cocci infection
Varga & Vanyi, 1992	T-2	*In vivo*	Reduced coccidiostat effect
Fukata *et al*., 1996	Afla and T-2 combination	*In vivo*	Increased *Salmonella typhimurium* CFU in duodenal and cecal contents
Grenier & Applegate, 2013 (review)	DON	*In vitro* and *in vivo* (several species)	Up-regulation of pro-inflammatory cytokines in the GIT
Grenier & Applegate, 2013 (review)	FUM	*In vitro* and *in vivo* (several species)	Altered barrier function of the gut epithelium
Antonissen *et al*., 2014 (review)	Subclinical concentrations of various mycotoxins	*In vitro* and *in vivo* (several species)	Increased susceptibility to infectious diseases and reduced efficacy of vaccines and other medication

between *Salmonella typhimurium* colonization and mycotoxin levels. For other mycotoxins, such as OTA, this interaction has been proven and the number of colony forming units (CFU) found in the duodenal and cecal contents increased when animals ingested OTA-contaminated feed.

More studies are available showing that DON in particular increases the intestinal inflammatory response to *S. typhimurium* and leads to a significant increase in both the invasion and epithelial translocation of *Salmonella* in swine. Similar observations were obtained when FUM were present concomitantly with *E. coli* in swine diets—prolonged intestinal infection, increased intestinal colonization and translocation of bacteria and dissemination into the lungs, liver and spleen were observed.

As research in this field develops, the subclinical effects of mycotoxins can be more confidently addressed. Gunther Antonissen, a researcher from Ghent University, presented his research findings at the 2014 European Poultry Conference, adding to the above-mentioned effects the negative impact of subclinical concentrations of mycotoxins on the uptake and efficiency of vaccines and other medication. His review published in 2014 summarizes decades of mycotoxin research on the susceptibility to infectious diseases.

Table 1 provides a summary of the literature on the effects of mycotoxins on poultry.

"Yes, even low levels of mycotoxins can harm the poultry industry."

Mycotoxin researcher Bertrand GRENIER joins Biomin

Bertrand GRENIER
PhD, Scientist, Biomin Research Center

In early October, Bertrand Grenier joined Biomin's microbiology research team at the research center in Tulln. He co-authored two studies on the the effects of mycotoxins, both published in 2013. One of the findings suggest that preliminary data provide some evidence that birds might be more sensitive to intestinal pathogens following the ingestion of feed containing fumonisins. Although birds were reported to be more tolerant to fumonisins, the interaction of this toxin and Eimeria, responsible for coccidiosis, resulted in more lesions, inflammation and parasite excretion.

Bertrand obtained his PhD at INRA, France where his PhD project focused on the effects of mycotoxins on the immune and intestinal responses of pigs, and on the efficacy of FUMzyme®. He did his post-doctoral research at Purdue University in the United States on the effects of mycotoxins on intestinal health in poultry research and FUMzyme®.

Intestinal inflammation

Since the intestinal mucosal surface is heavily exposed to foreign materials, it is widely recognized that this surface usually presents itself in a normal state of reactivity and mild inflammation. Controlling this inflammation is of utmost importance, not only to reduce the energy and protein required to overcome inflammation, which could otherwise be directed towards performance, but also to avoid any escalation into disease outbreaks.

Antibiotic growth promoters (AGPs) seem to improve animal performance through their action and efficacy towards reducing inflammation, amongst other effects. With increasing pressure to reduce AGPs in animals exported to markets that have banned their usage, such as the EU, birds may now be more exposed to the risks of mycotoxins and other inflammatory agents.

Several studies on different animal species, including humans, clearly show that the fusariotoxin DON leads to an up-regulation of pro-inflammatory cytokines in the gut epithelium, promoting a rapid mucosal inflammatory response, especially when present at low concentrations in feed. It is important to keep in mind that tight junction proteins are regulated by such cytokines.

Similarly, FUM seem to alter the barrier function of the gut epithelium due to their well-known effect on sphingolipids, which play a crucial role in the maintenance of the tight junction barrier. From a practical standpoint, these events can lead to intestinal disorders and disease outbreaks among farmed animals as increased intestinal permeability allows the entry of antigens which would otherwise be restricted to the gut lumen.

Conclusion

Mycotoxins' general effects include impaired nutrient uptake, immune suppression and decreased performance. They can compromise several key functions of the GIT including decreased surface area available for nutrient absorption, modulation of nutrient transporters, and/or loss of barrier function. Several mycotoxins act as inhibitors of protein synthesis; many specifically target rapidly dividing and activated cells which are predominant in the gut epithelium. Others increase the persistence of intestinal pathogens and potentiate intestinal inflammation.

Yes, even low levels of mycotoxins can harm the poultry industry. This is especially so when several mycotoxins co-occur in feeds, when exposure to several different pathogens are often not adequately controlled by biosecurity measures and when the usage of by-products in feeds further contributes to the total load of inflammatory agents to which animals are exposed.

Mycotoxin risk management tools are available to mitigate the negative impacts of mycotoxins in animal health and performance. Due to its long-standing R&D commitment, Biomin is the first, and so far, only feed additive company to have successfully registered in the EU a technological feed additive that is capable of reducing the negative impacts of mycotoxins in animals.

Poultry highlights from the World Nutrition Forum 2014

by Andrew Robertson • Poultry Technical Manager & Fernando Lima • Poultry Technical Manager

The Poultry Breakout Session brought together leaders in poultry research and production to discuss the current problems facing the industry, ways to mitigate them and how two of the world's leading poultry producers have developed their businesses with sustainability in mind.

October saw more than 800 delegates from 86 countries visit Munich for the 2014 World Nutrition Forum hosted by Biomin. The theme for the forum was sustain:ability which reflects tomorrow's challenge of feeding a larger global population (9 billion people by 2050) in the face of resource constraints. Biomin has long been concerned with improving sustainability with its 3-pillar approach – Performance, Profit and Planet.

Improving performance has beneficial impacts on both profit and sustainable use of resources. Gut health and integrity play the major role in achieving efficient performance. The first part of the session discussed the potential causes and effects reducing gut integrity can have. Chaired by Mickaël Rouault, Technical and Marketing Director, EMA at Biomin, the poultry breakout session explored recent research findings and views from academic and industry experts.

Prof. **Siska Croubels** of the Department of Pharmacology, Toxicology and Biochemistry of the University of Ghent described the effects of *Fusarium* mycotoxins on gut integrity in poultry looking at their effects not only on gut morphology and barrier function, but also the way they impact oxidative stress and inflammation affecting performance. There is also a direct effect on the active nutrient transport systems essential for uptake and

Dr. **Phillip SMITH** discussed the focus on meeting customers' needs and sustainable business practices.

Dr. **Raj MURUGESAN** described subclinical challenges to gut integrity and effects on final performance.

Prof. **Elizabeth Santin** presented a method to measure gut integrity, I See Inside (ISI).

Dr. **Robert WIDEMAN** presented how PoultryStar® can reduce the incidence of BCO lameness.

"Improving performance has beneficial impacts on both profit and sustainable use of resources."

the combined effect of DON+FB_1 reducing enrofloxacin absorption in the case of medication.

One of the effects of disrupting the barrier function of the intestine is the absorption of xenobiotics through the intestine. One aspect of this, described by Prof. **Wideman** of the Centre of Excellence for Poultry Science at Arkansas University, is the bacterial translocation of intestinal bacteria via the blood supply to the proximal growth plates of the long bones, particularly the femur and tibia, resulting in bacterial chondronecrosis with osteomyelitis (BCO) as the birds grow to heavier weights. It is suggested that up to 1.5% of heavier birds suffer from BCO. In a model designed to induce BCO, Prof. Wideman showed that PoultryStar® can reduce the incidence of this problem.

Prof. **Elizabeth Santin**, Head of Laboratory of Poultry Pathology at the Department of Veterinary Medicine at Universitade Federal do Paraná in Brazil, gave a short overview of the physiology and morphology of the chicken's gastrointestinal tract. Her team has developed a method to measure gut integrity, I See Inside (ISI). In this method lesion scores are measured (0-3) during necropsy along with a Lesion Severity Factor (LSF) determining a numerical gut health score. The LFS is a system to differentiate the impact on organ function and is scored from 1–3 with necrosis having a greater impact on gut function than inflammation.

Dr. **Raj Murugesan**, Regional Technical and Marketing Director of Biomin America, described the impacts of subclinical challenges to gut integrity and the effects they have on the final performance. Within poultry production, feed costs remain the major expenditure. Under subclinical challenge additional nutrient requirements of between 10-12% are needed to activate the intestinal immune system. He also described how a range of stressors can lead to a subclinical challenge, and that a combination of subclinical conditions can have an additive effect. Phytogenic additives have a proven ability to reduce some of these inflammatory effects.

Dr. **Maarten de Gussem**, Founder and Chairman of Vetworks Belgium, questioned if the current situation of reducing antibiotics in production should be considered an opportunity or a liability. He explained that with the ongoing concerns over resistance in humans the number of available antibiotics licensed for animal use may be severely reduced in the EU. When looking at the causes of dysbiosis in poultry, alternative raw materials and the ban on AGPs, he believes there are areas where feed additives can be used to limit the incidence. This reduces the requirement for antibiotic intervention, resulting in an opportunity not a liability.

With a title for the conference on sustainability, **Juliette Protino**, Scientific Officer for Synalaf, France, described a practical tool to assess sustainability in free range production using a system based on 3 pillars: Economics, Social and the Environment. She then went on to show how sustainability could be improved by reducing dependence on imported soybean meal.

The last two speakers provided views from the industry perspective, emphasizing that profitability is essential both through performance to reduce inputs and also to be able to contribute to the social aspects of sustainable production. Dr. **Payungsak Tanagul** of Charoen Pokphand Foods, Thailand, explained the use of a fully integrated business model combining updated technology and best practice to achieve this. Similarly Dr. **Phillip Smith**, Tyson Foods Inc. USA, highlighted the need to produce what the customer wants in order to achieve the returns necessary to maintain the ability to provide the social and environmental aspects.

Cut & Keep Checklist

What's wrong with my birds? Part 3: Fatty Liver

A handy checklist for diagnosing poultry mycotoxicosis that you can cut out and keep with you for reference.

Diagnosing common poultry ailments correctly and precisely can be a challenge even for experienced vets, nutritionists or farm managers. In the case of mycotoxin-related problems, differential diagnosis can be especially difficult as symptoms vary greatly. The following table provides an overview of the potential causes and a checklist of corrective actions; however, please exercise due caution and discretion in use.

MYCOTOXIN RISK MANAGEMENT

	Potential cause	Description of problem	Check list	Corrective actions
NUTRITION	Energy-protein ratio	Excessive energy in diets can cause lipidosis and fatty liver problems.	☐ Carbohydrate level in diet ☐ Energy-protein ratio in diet	☐ Avoid high carbohydrate diets, especially in summer ☐ Adopt proper energy-protein ratio ☐ Apply amino acids in drinking water
	Rancid fats	Peroxides can impair liver activity, creating fatty liver.	☐ Quality of fats in term of: peroxide value, rancidity and free fatty acids	☐ Avoid low quality fats ☐ Use low quality fats in the grower/finisher phases ☐ Replace animal fats with vegetable fats ☐ Apply choline chloride and Vitamin B in feed or water
MYCOTOXINS	Aflatoxins (Afla)	Young animals: fibrosis of liver leads to hardening of the organ. Older animals: hepatic lipidosis, with softening of the organ.	☐ Positive for Afla in raw materials (ELISA) or feed (HPLC) ☐ Raw materials originating from supplier/region with history of aflatoxin contamination ☐ Histopathology: Check other target organs of Afla (ex. Liver) ☐ Overall decline in flock performance	☐ Check average contamination levels ☐ Use Mycofix® at a correct dosage level ☐ Avoid feed bins or feed/water lines that have become contaminated by stale, wet or moldy feed
MANAGEMENT	Hormone status	An over-stimulation of egg production may lead to excessive levels of estrogen in the blood that facilitate fat storage in the liver and the occurrence of fatty liver, especially in layers and breeders.	☐ Management of laying birds	☐ Improve management of laying birds ☐ Correct lighting program
PATHOGENS	Viral hepatitis (IBH – viral inclusion body hepatitis)	Adenovirus causes yellow/hemorrhagic liver and focal necrosis. Symptoms include immunosuppression, diarrhea, anorexia, depression, ruffled feathers, especially in the region of head and neck. Group I is exhibited through inclusion body hepatitis (sudden onset of mortality, typically 10% and rarely up to 30%) or hydro pericardium (same symptoms as IBH, but severe mortality from 20-80%). Usually occurs in chickens older than 3 weeks.	☐ Clinical signs only several hours prior to death: pale comb and wattles, depression and apathy ☐ Up to 30% mortality ☐ Necropsy: Macroscopic lesion is the enlarged, dystrophic liver with yellowish color and crumbly texture and enlarged kidneys ☐ Histopathology: Detection of intranuclear inclusion bodies ☐ Isolation of serotype I or II or III from the lesions by serological assays	☐ Use inactivated vaccines (exist only for group I) ☐ Check the breeding stock and eliminate the affected birds

For more information, visit **www.mycotoxins.info**

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