Fighting antimicrobial resistance with immunoglobulins

*By **Lea Poppe**, Regional Technical Manager On-Farm Solutions Europe, and **Dr. Inge Heinzl**, Editor*

One of the ten global public health threats is antimicrobial resistance (AMR). Jim O'Neill predicted 10 million people dying from AMR annually by 2050 (O'Neill, 2016). The following article will show the causes of antimicrobial resistance and how antibodies from the egg could help mitigate the problem of AMR.

Global problem of AMR results from the incorrect use of antimicrobials

Antimicrobial substances are used to prevent and cure diseases in humans, animals, and plants and include antibiotics, antivirals, antiparasitics, and antifungals. The use of these medicines does not always happen consciously, partially due to ignorance and partially for economic reasons.

There are various possibilities for the wrong therapy

1. The use of antibiotics against diseases that household remedies could cure. A recently published German study (Merle et al., 2023) confirmed the linear relationship between treatment frequency and resistant scores in calves younger than eight months.
2. The use of antibiotics against viral diseases: antibiotics only act against bacteria and not against viruses. Flu, e.g., is caused by a virus, but doctors often prescribe an antibiotic.
3. Using broad-spectrum antibiotics instead of determining an antibiogram and applying a specific antibiotic.
4. A too-long treatment with antimicrobials so that the microorganisms have the time to adapt. For a long time, the only mistake you could make was to stop the antibiotic therapy too early. Today, the motto is “as short as possible”.

Let’s take the example of neonatal calf diarrhea, one of the most common diseases with a high economic impact. Calf diarrhea can be caused by a wide range of bacteria, viruses, or parasites. This infectious form can be a complication of non-infectious diarrhea caused by dietary, psychological, and environmental stress (Uetake, 2012). The pathogens causing diarrhea in calves can vary with the region. In Switzerland and the UK, e.g., rotaviruses and cryptosporidia are the most common pathogens, whereas, in Germany, E. coli is also one of the leading causes. To minimize the occurrence of AMR, it is always crucial to know which pathogen is behind the disease.

Prophylactic use of antibiotics is still a problem

1. The use of low doses of antibiotics to promote growth. This use has been banned in the EU now for 17 years now, but in other parts of the world, it is still common practice. Especially in countries with low hygienic standards, antibiotics show high efficacy.
2. The preventive use of antibiotics to help, e.g., piglets overcome the critical step of weaning or to support purchased animals for the first time in their new environment. Antibiotics reduce pathogenic pressure, decrease the incidence of diarrhea, and ensure the maintenance of growth.
3. Within the scope of prophylactic use of antimicrobials, also group treatment must be mentioned. In veal calves, group treatments are far more common than individual treatments (97.9% of all treatments), as reported in a study documenting medication in veal calf production in Belgium and the Netherlands. Treatment indications were respiratory diseases (53%), arrival prophylaxis (13%), and diarrhea (12%). On top, the study found that nearly half of the antimicrobial group treatment was underdosed (43.7%), and a large part (37.1%) was overdosed.

However, in several countries, consumers request reduced or even no usage of antibiotics (“No Antibiotics Ever” – NAE), and animal producers must react.

Today’s mobility enables the spreading of AMR worldwide

Bacteria, viruses, parasites, and fungi that no longer respond to antimicrobial therapy are classified as resistant. The drugs become ineffective and, therefore, the treatment of disease inefficient or even impossible. All the different usages mentioned before offer the possibility that resistant bacteria/microorganisms will occur and proliferate. Due to global trade and the mobility of people, drug-resistant pathogens are spreading rapidly throughout the world, and common diseases cannot be treated anymore with existing antimicrobial medicines like antibiotics. Standard surgeries can become a risk, and, in the worst case, humans die from diseases once considered treatable. If new antibiotics are developed, their long-term efficacy again depends on their correct and limited use.

Different approaches are taken to fight AMR

There have already been different approaches to fighting AMR. As examples, the annually published MARAN Report compiled in the Netherlands, the EU ban on antibiotic growth promoters in 2006, "No antibiotics ever (NAE) programs" in the US, or the annually published "Antimicrobial resistance surveillance in Europe" can be mentioned. One of the latest approaches is an advisory "One Health High-Level Expert Panel" (OHHLEP) founded by the Food and Agriculture Organization of the United Nations (FAO), the World Organization for Animal Health (OIE), the United Nations Environment Program (UNEP), and the World Health Organization (WHO) in May 2021. As AMR has many causes and, consequently, many players are involved in its reduction, the OHHLEP wants to improve communication and collaboration between all sectors and stakeholders. The goal is to design and implement programs, policies, legislations, and research to improve human, animal, and environmental health, which are closely linked. Approaches like those mentioned help reduce the spread of resistant pathogens and, with this, remain able to treat diseases in humans, animals, and plants.

On top of the pure health benefits, reducing AMR improves food security and safety and contributes to achieving the Sustainable Development Goals (e.g., zero hunger, good health and well-being, and clean water).

Prevention is better than treatment

Young animals like calves, lambs, and piglets do not receive immunological equipment in the womb and need a passive immune transfer by maternal colostrum. Accordingly, optimal colostrum management is the first way to protect newborn animals from infection, confirmed by the general discussion on the Failure of Passive Transfer: various studies suggest that calves with poor immunoglobulin supply suffer from diarrhea more frequently than calves with adequate supply.

Especially during the immunological gap when the maternal immunoglobulins are decreasing and the own immunocompetence is still not fully developed, it is crucial to have a look at housing, stress triggers, biosecurity, and the diet to reduce the risk of infectious diseases and the need for treatments.

Immunoglobulins from eggs additionally support young animals

Also, if newborn animals receive enough colostrum in time and if everything goes optimally, the animals suffer from two immunity gaps: the first one occurs just after birth before the first intake of colostrum, and the second one occurs when the maternal antibodies decrease, and the immune system of the young animal is still not developed completely. These immunity gaps raise the question of whether something else can be done to support newborns during their first days of life.

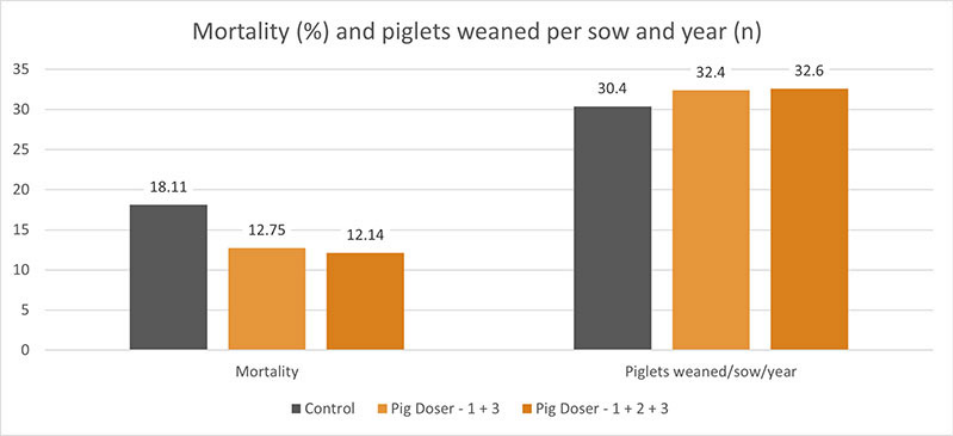
The answer was provided by Felix Klemperer (1893), a German internist researching immunity. He found that hens coming in contact with pathogens produce antibodies against these agents and transfer them to the egg. It is unimportant if the pathogens are relevant for chickens or other animals. In the egg, the immunoglobulins usually serve as an immune starter kit for the chick.

Technology enables us today to produce a high-value product based on egg powder containing natural egg immunoglobulins (IgY – **i**mmuno**g**lobulins from the **y**olk). These egg antibodies mainly act in the gut. There, they recognize and tie up, for example, diarrhea-causing pathogens and, in this way, render them ineffective.

The efficacy of egg antibodies was demonstrated in different studies (Kellner et al., 1994; Erhard et al., 1996; Ikemori et al., 1997; Yokoyama et al., 1992; Marquart, 1999; Yokoyama et al., 1997) for piglets and calves.

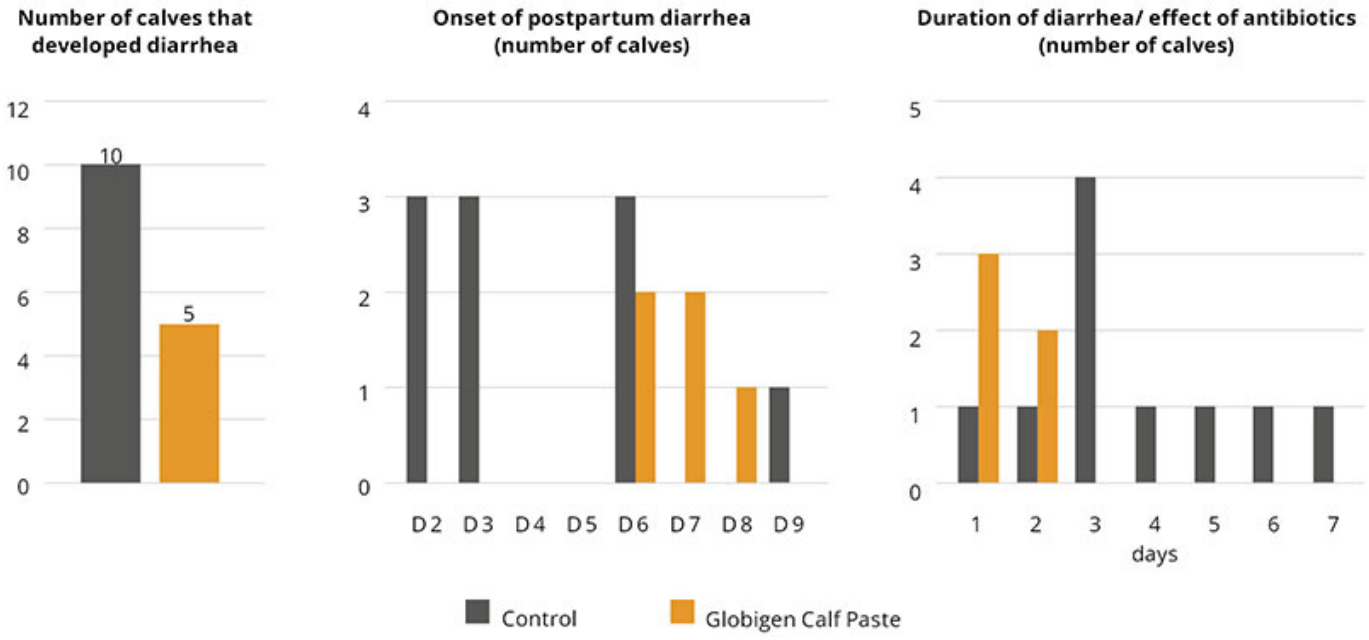
Trial proves high efficacy of egg immunoglobulins in piglets

One trial conducted in Germany showed promising results concerning the reduction of mortality in the farrowing unit. For the trial, 96 sows and their litters were divided into three groups with 32 sows each. Two of the groups orally received a product containing egg immunoglobulins, the EP -1 + 3 group on days 1 and 3 and the EP – 1 + 2 + 3 group on the first three days. The third group served as a control. Regardless of the frequency of application, the egg powder product was very supportive and significantly reduced mortality compared to the control group. The measure resulted in 2 additionally weaned piglets than in the control group.



Egg immunoglobulins support young dairy calves

IgY-based products were also tested in calves to demonstrate their efficacy. In a field trial conducted on a Portuguese dairy farm with 12 calves per group, an IgY-containing oral application was compared to a control group without supplementation. The test product was applied on the day of birth and the two consecutive days. Key observation parameters during a two-week observation period were diarrhea incidence, onset, duration, and antibiotic treatments, the standard procedure on the trial farm in case of diarrhea. On-farm tests to check for the pathogenic cause of diarrhea were not part of the farm's standards.



In this trial, 10 of 12 calves in the control group suffered from diarrhea, but in the trial group, only 5

calves. Total diarrhea and antibiotic treatment duration in the control group was 37 days (average 3.08 days/animal), and in the trial group, only 7 days (average 0.58 days/animal). Additionally, diarrhea in calves of the Globigen Calf Paste group started later, so the animals already had the chance to develop an at least minimally working immune system.

The supplement served as an effective tool to support calves during their first days of life and to reduce antibiotic treatments dramatically.

Conclusion

Antimicrobial reduction is one of the biggest tasks for global animal production. It must be done without impacting animal health and parameters like growth performance and general cost-efficacy. This overall demand can be supported with a holistic approach considering biosecurity, stress reduction, and nutritional support. Feed supplements such as egg immunoglobulins are commercial options showing great results and benefits in the field and making global animal production take the right direction in the future.

References upon request.

Cryptosporidia in calves – chickens can help

*By **Lea Poppe**, Regional Technical Manager, EW Nutrition*

Diarrhea due to infestation with cryptosporidia is one of the most pressing problems in calf rearing. These

protozoa, along with rotaviruses, are now considered the most common pathogens in infectious calf diarrhea. Due to their high resistance and thus limited possible control and prevention measures, they have now overtaken other pathogens such as coronaviruses, salmonellae, and *E. coli*.

Cryptosporidia show complex development

Cryptosporidia are single-celled intestinal parasites. In calves, Cryptosporidium parvum and Cryptosporidium bovis are most commonly found. C. bovis is normally considered nonpathogenic. Accordingly, the disease known as cryptosporidiosis is caused by C. parvum. The rapid tests for determining the diarrheal pathogens, which are increasingly widespread, are usually unsuitable for distinguishing between the individual strains, which can lead to false positive results.

Resistant in the environment, active in the animal

In the environment, cryptosporidia are distributed as oocysts. The oocysts are only about 5 µm in size and have a very resistant shell. They can remain infectious for up to 6 months in high humidity and moderate temperatures. Drought and extreme temperatures (below -18°C and above 65°C) cause the oocysts to die.

After oral ingestion, the oocysts are reactivated by conditions in the gastrointestinal tract (low pH and body temperature): As sporozoites, the parasites attach to the posterior small intestine, causing diarrhea symptomatology. There, they surround themselves with a special protective membrane, and the complex life cycle continues. Only a few days after infection, reproductive forms are detectable in the calf's intestine, and excretion of infectious oocysts in the feces begins.

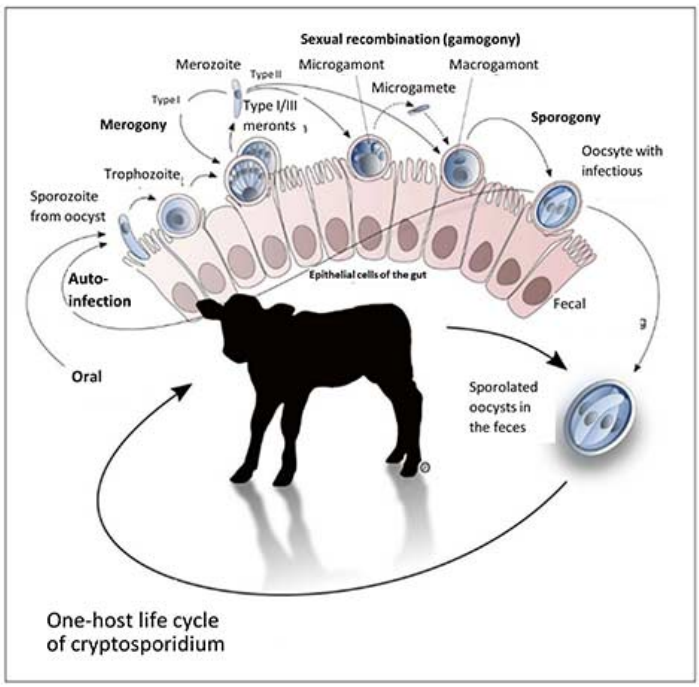


Figure 1 (Olias et al., 2018): Life cycle of cryptosporidia: ingested oocysts release four sporozoites that invade host enterocytes (intestinal epithelial cells). There, they develop into trophozoites before asexual and sexual reproduction ensues, and thin- and thick-walled oocysts are formed. Thick-walled oocysts are excreted through the intestine. Thin-walled oocysts may break apart, and the sporozoites may infect other enterocytes, resulting in relapse or prolonged diarrhea. Infestation of the cells leads to their destruction, resulting in villi atrophy or fusion.

Oocysts bring the disease to the animal

Cryptosporidiosis is transmitted either by direct contact of calves with feces from infected animals or indirectly by ingesting contaminated feed, bedding, or water. Each gram of feces excreted by calves showing symptoms may contain up to 100 million oocysts. According to experimental studies, as few as 17 orally ingested oocysts are sufficient to trigger infection. In addition, some multiplication forms can infect other intestinal cells directly within the intestine and thus further advance the disease by autoinfection.

Cryptosporidiosis caused by cryptosporidia often presents with typical diarrhea symptoms and occurs primarily in calves up to 3 weeks of age. Older calves may also be infected with cryptosporidia but usually show no symptoms. Pathogen excretion and, thus, the spread of disease within the herd is nevertheless likely due to the minimal infectious dose.

Damage to the intestinal wall leads to retardation of growth

Attachment of cryptosporidia to the intestinal wall is associated with an inflammatory reaction, regression and fusion of the intestinal villi, and damage to the microvilli. As a result, nutrient absorption in the small intestine is impaired, and more undigested nutrients enter the colon. The microflora starts a fermentation process with lactose and starch, leading to increased lactate levels in the blood and, thus, hyperacidity in the calf. Faintness, unwillingness to drink, recumbency, and growth disorders are the consequences.

Diarrhea often occurs late or not at all and, accordingly, is not considered the main symptom of cryptosporidiosis. When diarrhea occurs, it lasts about 1-2 weeks. The feces are typically watery, greenish-yellow, and are often described as foul-smelling. Due to diarrhea, there is a loss of electrolytes and dehydration.

Studies show: Cryptosporidia are the most prevalent diarrheal pathogens

Several studies in different regions, which examined calf diarrhea and its triggers in more detail, came to a similar conclusion: Cryptosporidia are one of the most common causes of calf diarrhea. In addition, mixed infections often occur.

Country or region	Number	Age/Health status	% Crypto-sporidia	% Rota viruses	Combined infections with crypto-sporidia	Others (%)	Source
Switzerland		2 – 21 DL Ill and healthy	43	46		1 case of E. coli	Luginbühl et al., 2012
Switzerland	63	1 – 4 DL Ill and healthy ———– 7 – 20 DL ———– 26 – 49 DL	34.4 ———– 54.0 ———– 33.3	3.1 ———– 28.6 ———– 13.3	2 EP – 1.6 4 EP – 3.2 ———– 2 EP – 19 3 EP – 3.2 4 EP – 0 ———– 2 EP – 30 3 EP – 11.7 4 EP – 6.7	Corona 4.7 E. coli 4.7 Giardia 1.6 ———– Corona 0 E. coli 3.2 Giardia 6.3 ———– Corona 0 E. coli 15 Giardia 35	Weber et al., 2016 Weber et al., 2016 EN
Switzerland	147	Up to 3rd WL; Diarrhea	55	58.7		5.5 % Rota 7.8 % BCV	Lanz Uhde et al., 2014
Sweden	782	1 – 7 DL Diarrhea	25.3		Detected with Giardia, E. coli, Rota, Eimeria		Silverlås et al., 2012
USA (East coast)	503	Pre-weaning	50.3				Santin et al., 2004

USA	30	2 weeks old 1-8 weeks old 3-12 months 12-24 months	96.7 45.8 18.5 2.2				Santin et al., 2008
Germany	521		32	9			Losand et al., 2021
Ethiopia	360		18.6				Ayele et al., 2018
Argentina	1073	n.m. / Ill and healthy	25.5				Lombardelli et al., 2019
UK	n.m.	Ill ??	37	25	20	Coccidia 8 E. coli 4 Corona 3 Co infections not including Crypto-sporidia 3	APHA, SRUC, Veterinary investigation diagnosis analysis (VIDA) report (2014)

DL = days of life WL = weeks of life n.m. = not mentioned EP = enteropathogen

Cryptosporidia reduces profit

Infection with cryptosporidia and sometimes subsequent diarrhea entails treatment of the animals and generates costs (veterinarian, medication, electrolyte drinks). In addition, poorer feed conversion, lower growth, and animal losses result in lower production efficiency.

A Scottish study shows 34 kg less gain in the first six months of life compared to healthy calves in beef calves that experienced severe cryptosporidiosis in the first three weeks of life. Similar results are described in lambs, also a susceptible species to cryptosporidia. These studies suggest a long-term negative effect of cryptosporidia on growth performance and production efficiency.

Here’s how you can support your calves against cryptosporidia

High resistance of the pathogens to environmental influences, a very low necessary infection dose combined with an elevated excretion of infectious oocysts, and the possibility of autoinfection make cryptosporidia tough opponents. This is also reflected in their worldwide distribution.

What is the treatment?

Suitable drugs for the treatment of cryptosporidiosis are currently unavailable on the market. The only medicine that can be used in case of cryptosporidiosis infestation may only be administered to calves that have had diarrhea symptoms for 24 hours or less. Accordingly, this agent is usually used only for prevention. Scientific studies on its effectiveness are contradictory; some suggest that it merely delays the onset of the disease. In addition, it is not always easy to use due to the exact dosage that must be followed. Doubling the dose (sometimes happening already due to incorrectly observed intervals between doses) can lead to a toxic overdose.

Accordingly, only the symptoms of the disease – diarrhea with its accompanying symptoms – can be treated. Electrolyte and water losses must be continuously compensated with the help of a high-quality electrolyte drink. The buffer substances contained also reduce the hyperacidity of the blood caused by faulty fermentation in the intestines. For successful treatment, the electrolyte drink should be given in addition to the milk drink. Under no circumstances should the feeding of milk or milk replacer be discontinued because the sick calf urgently needs energy and nutrients. Opinions to the contrary are outdated.

As always: prevention is better than treatment

To make it more difficult for cryptosporidiosis to spread from the outset, it is worth looking at the risk factors. These include direct contact with other calves and general herd size. Furthermore, organic farms seem to have more problems with cryptosporidia. Weather also influences calves born during warmer and, at the same time, wetter weather periods (temperature-humidity index) often get sick.

Due to the limited possibilities for treatment, prevention is of greater importance. For other diarrheal pathogens such as rotavirus, coronavirus, and *E. coli*, it has become established practice to vaccinate dams to achieve better passive immunization of the calf. However, commercial vaccination against cryptosporidia is not currently available, making dam vaccination as unavailable as calf vaccination.

Accordingly, optimal colostrum management is the first way to protect the calf from cryptosporidia infection. This also confirms the general discussion on the Failure of Passive Transfer: various studies suggest that calves with poor immunoglobulin supply suffer from diarrhea more frequently than calves with good supply, although a concrete link to cryptosporidia itself cannot always be established with certainty.

Furthermore, it is essential to break the chain of infection within farms. In addition to the separate housing of the calves, it is necessary to ensure consistent hygiene. One should take advantage of the pathogen's weakness as well as its sensitivity to high temperatures and ensure that the water temperature is sufficiently high when cleaning the calf pens and calving area. When disinfecting afterward, it is crucial to consider the spectrum of activity of the agent used, as not all are effective against cryptosporidia.

Egg immunoglobulins support animals against cryptosporidia

Egg immunoglobulins were initially designed to help chicks get started. In this process, hens form antibodies against pathogens they are confronted with. As studies have shown, this also works with cryptosporidia. Cama and Sterling (1991) tested their produced antibodies in the neonatal mouse model and achieved a significant ($P \leq 0.001$) reduction in parasites there. Kobayashi et al. (2004) registered decreased binding of sporozoites to the intestinal cell model and their decreased viability in addition to oocyst reduction.

In the IRIG Research Institute (2009, unpublished), feeding egg powder with immunoglobulins against cryptosporidia (10 g/day) to 15 calves reduced oocyst excretion. Before administration, calves excreted an average of 106.42 oocysts/g of feces. After administration of egg powder, only two calves still showed 103.21 oocysts/g feces, and the other 13 of the 15 calves showed no oocyst excretion. All these results are confirmed by positive customer feedback on IgY-based feed supplements.

Egg immunoglobulins and optimal colostrum management as a key solution

Since there are no effective drugs against cryptosporidia, animals must be prophylactically protected against this disease as much as possible. In addition to optimal colostrum management, which means feeding high-quality colostrum (IgG≥50g/L) to the calf as soon as possible after birth, we have products with egg immunoglobulins available to support the calf as a prophylactic against cryptosporidia infestation and thus prevent significant performance losses, especially during rearing.

References

Brainard, J., Hooper, L., McFariane, S., Hammer, C. C., Hunter, P. R., & Tyler, K. (2020). Systemic review of modifiable risk factors shows little evidential support for most current practices in Cryptosporidium management in bovine calves. *Parasitology research 119*, 3572-3584.

Cama, V. A., and C. R. Sterling. “Hyperimmune Hens as a Novel Source of Anti-Cryptosporidium Antibodies Suitable for Passive Immune Transfer.” University of Arizona. Wiley-Blackwell, January 1, 1991. https://experts.arizona.edu/en/publications/hyperimmune-hens-as-a-novel-source-of-anti-cryptosporidium-antibo .

Kobayashi, C, H Yokoyama, S Nguyen, Y Kodama, T Kimata, and M Izeki. “Effect of Egg Yolk Antibody on Experimental Infection in Mice.” *Vaccine* 23, no. 2 (2004): 232–35. https://doi.org/10.1016/j.vaccine.2004.05.034.

Lamp, D. O. (25. Januar 2020). Rinder aktuell: Kälberdurchfall durch Kryptosporidien – Hartnäckig und weitverbreitet. *BAUERNBLATT*, S. 52-53.

Losand, B., Falkenberg, U., Krömker, V., Konow, M., & Flor, J. (2. März 2021). Kälberaufzucht in MV – Alles im grünen Bereich? 30. Milchrindtag Mecklemburg-Vorpommern.

Luginbühl, A., K. Reitt, A. Metzler, M. Kollbrunner, L. Corboz, and P. Deplazes. “Feldstudie Zu Prävalenz Und Diagnostik Von Durchfallerregern Beim Neonaten Kalb Im Einzugsgebiet Einer Schweizerischen Nutztierpraxis.” *Schweizer Archiv für Tierheilkunde* 147, no. 6 (2005): 245–52. https://doi.org/10.1024/0036-7281.147.6.245.

Olias, P., Dettwiler, I., Hemphill, A., Deplazes, P., Steiner, A., & Meylan, M. (2018). Die Bedeutung der Cryptosporidiose für die Kälbergesundheit in der Schweiz. *Schweiz Arch Tierheilkd, Band 160, Heft 6, Juni 2018*, 363-374.

Santín, M., Trout, J. M., Xiao, L., Zhou, L., Greiner, E., & Fayer, R. (2004). Prevalence and age-related variation of Cryptosporidium species and genotypes in dairy calves. *Veterinary Parasitology 122*, 103-117.

Shaw, H. J., Innes, E. A., Marrison, L. J., Katzer, F., & Wells, B. (2020). Long-term production effects of clinical cryptosporidiosis in neonatal calves. *International Journal for Parasitology 50*, 371-376.

Silverlås, C., H. Bosaeus-Reineck, K. Näslund, and C. Björkman. “Is There a Need for Improved Cryptosporidium Diagnostics in Swedish Calves?” *International Journal for Parasitology* 43, no. 2 (2013): 155–61. https://doi.org/10.1016/j.ijpara.2012.10.009.

Thomson, Sarah, Carly A. Hamilton, Jayne C. Hope, Frank Katzer, Neil A. Mabbott, Liam J. Morrison, and Elisabeth A. Innes. “Bovine Cryptosporidiosis: Impact, Host-Parasite Interaction, and Control Strategies.” *Veterinary Research* 48, no. 1 (2017). https://doi.org/10.1186/s13567-017-0447-0.

Uhde, F., Kaufmann, T., Sager, H., Albini, S., Zanoni, R., & Schelling, E. (2008). Prevalence of four enteropathogens in the feces of young diarrhoeic dairy calves in Switzerland. *Veterinary Record (163)*, 362-366.

Coughing calves? How to save costs and prevent respiratory disease

*By **Judith Schmidt**, Product Manager On Farm Solutions*

There will always be germs in barns. Yet, calves are particularly susceptible to lung viruses and bacteria that attack the respiratory systems. What can we do to prevent calf flu?

Coughing in calves is one of the most obvious signs of illness. It should be taken seriously – calves are important for the profitability of farms. Calf flu not only leads to treatment costs but also has long-term consequences, such as weak daily gains, delayed lactation, lower milk yield, reduced fertility, and increased susceptibility to other diseases.

Respiratory disease in calves: recognize the symptoms and protect their lung health

Calves are much more sensitive to respiratory diseases than many other animals. Why? One major cause is that calves are born with immature lungs. The lungs are only fully developed at about one year of age. In addition, calves generally have small lungs relative to their body size. Furthermore, the immunological gaps around the second month of life are decisive. During this phase, the number of maternal antibodies in the calf´s blood decreases, while the calf´s own immune system is still slowly building up.

Symptoms of calf flu

1) Cough

A very easy-to-recognize sign of a developing calf flu is coughing. Coughing can also be caused by changes in weather, stress, or an unsuitable barn climate, but coughing should always be monitored, and animals should be checked for other symptoms.

2) Respiratory distress

Sick calves breathe heavily and show an increased respiratory rate. Even at rest, this can be more than forty breaths per minute, ranging from a slight acceleration of breathing to severe respiratory distress and breathing through the open mouth. Mouth breathing can be the first indication of lung damage.

3) Eye and nose discharge

Calf flu not only shows its symptoms in the internal respiratory tract but also in the eyes and nose through clear, watery discharge. In later stages, bacterial infections can also cause purulent discharge. The animal's gaze is not clear and rather "sleepy."

4) Body posture

Calf flu often manifests itself by drooping ears or an overall low head posture, as the calves are dull and weak. They are inactive and separate themselves from the group. They also lie down and standing up is delayed.

5) Reduced water and feed intake

Due to their physical condition, animals suffering from flu tend to take in only little feed and water or do not eat and/or drink at all. The logical consequence is a weakening of the animals. In case of doubt, one should actively water and feed the animals.

Economic significance of respiratory disease in calves

Influenza in cattle and calves is a herd disease and often causes serious financial losses. Losses are caused by pronounced performance decreases, developmental disorders of the animals, and treatment costs. Significantly reduced daily gains have been demonstrated for fattening animals.

Next to diarrheal diseases, calf flu causes the highest treatment and follow-up costs for calves. A study by the Chamber of Agriculture of Lower Saxony (Germany) found that farmers had to spend between 83 and 204 euros per sick calf, depending on the severity of the disease.

4 tips to save costs and tackle calf flu with less antibiotics use

1) Offer a stable climate

Warm, damp barns, as well as overcrowded and poorly ventilated ones, weaken the calf´s defense mechanisms. Temperature fluctuations of more than 10°C between day and night also favor the development of calf flu. It is important to keep the calves' environment free of dust and draughts. This can be achieved by adjusting the air exchange rate.

In addition, the humidity in barns without a heating system should be between 60 and 80 percent. Data loggers help to keep an eye on the climate in the barn. They make it possible to check how the outdoor climate and ventilation affect the climate conditions in the barn.

2) Hygiene-sensitive calving management

Attention should be paid to calving management. The long-term health of the animal is already predetermined in the calving pen. If several cows calve at the same time or if calving pens are not mucked out regularly, harmful germs will accumulate. In other words: if a calf is born into a dirty box, it will absorb many germs through its mucous membranes.

3) Avoid stress

It is crucial to minimize stress from causes such as transport, re-housing, feed changes, group formation, dehorning, and weaning. These events should be spaced out as far as possible and should never occur simultaneously.

4) Prevention through supplementary feed

In the winter months, when the weather is cold and damp and constantly changing, calf flu incidence skyrockets. Now, it is imperative to strengthen the calf´s respiratory tract from the beginning. EW Nutrition's Bronchogol Liquid is a herbal concentrate that supports respiration and stabilizes the physiological defense system in the respiratory organs.

Bronchogol liquid supports young calves in stressful situations, such as critical weather transition periods (autumn-winter; winter-spring) and housing changes, and when they suffer from calf flu. The product is based on a proprietary mixture of phytomolecules. By stimulating the cilia in the respiratory tract, the phytomolecules promote the transport of mucus and facilitate expectoration.

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4 steps to improve dairy cow fertility through feeding

*By **Judith Schmidt**, Product Manager On Farm Solutions*

The average pregnancy rate for dairy cows has declined over the past decades. But why is my cow not getting pregnant? Is it because of feeding? These are questions we ask ourselves when things do not quite work out with the offspring in the cowshed. Economic success in the cow barn is closely related to the successful reproduction of our cattle herd.

The maintenance and possible improvement of fertility are becoming increasingly important issues for farm productivity. Infertility is still one of the main reasons for culling on dairy farms. When farmers decide to cull a cow after a few unsuccessful inseminations, they often ask themselves whether this could not have been prevented. There is no “all-encompassing” solution for achieving an optimal fertility rate, which ultimately requires excellent management. Relevant factors include oestrus monitoring and insemination timing, genetic conditions, feeding, hygiene, and climate.

How can I tell if a cow is in heat?

A cow behaves differently than usual during oestrus. She is restless and walks around more. A cow in heat stands next to other cows – head to tail. Sie also quarrels with her herd mates or sniffs at the shame of the other cows. Fertility in cows decreases during late winter and spring; the resulting absence of clear signs of oestrus makes it difficult to recognize the right time for insemination. There are several possible causes which will be reviewed below.

Possible causes of fertility problems in dairy cows

Beta-carotene deficiency

A productive herd needs to receive an optimal mineral and trace element supply. Beta-carotene, in particular, is essential for herd fertility. But why?

Beta-carotene is an orange-yellow plant pigment whose name comes from “carrot” because of its appearance. It is also a precursor of vitamin A. Both as a precursor and as vitamin A itself, it is essential for the organism of humans and animals, particularly when it comes to the fertility of dairy cows. Besides its important function as provitamin A, beta-carotene also exerts an independent effect on the ovary. It influences the quality of the follicle and the corpus luteum. Beta-carotene also protects the corpus luteum. It promotes the synthesis of the pregnancy hormone progesterone and thus enables the fertilized egg to implant successfully in the uterine lining.

A beta-carotene deficiency can lead to the following problems:

- Smaller, not fully functional follicles
- Altered oestrus intervals
- Indistinct signs of oestrus
- Decreased corpus luteum quality

Scientific trials show how much a beta-carotene deficiency influences the fertility process. With a beta-carotene deficiency, the fertilization rate after the first insemination is only 40%, whereas with a normal beta-carotene supply, the fertilization rate is about 70%.

How do I know if my herd is deficient in beta-carotene?

The easiest way is to check the color of the fresh colostrum. If it is a deep yellow to an even orange, the cows are supplied with sufficient beta-carotene. If it looks more ivory, this is a sign of a deficiency. Of course, a poor herd fertilization rate can also indicate a deficiency. If you suspect a beta-carotene deficiency, it is best to test some blood samples from your animal or use a testing device such as a carotene photometer. With such a test kit, you can determine not only the levels in the blood but also in the colostrum and the milk.

Feeding deficiencies

Feeding plays a major role in fertility issues. Too low input rates often have a negative effect on the health of cows. Feed quality and herd management have an impact on how long the cow loses weight after calving and at what point she gains weight again. One must always keep in mind the cows’ feeding, energy balance, and nutrient supply because cows with a negative energy balance often do not show oestrus. It is also important that the silage is of high quality – poor silage inhibits fertility.

Follicle quality

The quality of the follicle is crucial for good fertility. The quality is influenced by the energy supply during the dry period and lactation during the first days. Since the follicles are already formed in the last days of gestation, a lack of energy during this period means that the maturation of the follicles – even with a better supply later on – can no longer proceed optimally and is ultimately inferior. This inevitably leads to a reduction of oestrus symptoms and minimizes the chances of successful insemination.

Prevention is key: 4 steps to improve fertility through feeding

1) Avoid stress in the feeding environment

Well-being and a high feed intake are the basis for high milk and fattening yields as well as healthy and fertile animals. Dry cows and transit cows particularly should only experience low stress. This means no overcrowding and generous feeding space, i.e., each animal should have its own feeding space. Feeding areas that are too narrow prevent the animals from eating, rank fights occur, and feed intake decreases.

Freshly lactating cows should be separated from the group. If the cows are in calving pens or calving stables, they should always have visual contact with the herd.

2) Optimize feed quality and rations

Feed quality and feeding management determine how long the cow loses weight after calving (negative energy balance) and at what point the cow gains weight again (positive energy balance). Optimal fertility performance can only happen when a positive energy balance is achieved.

The cow’s fertility performance is primarily determined by nutrient supply and feeding. At the beginning of the lactation, high-quality basic feed with a high energy concentration should be fed, as feed intake is slow to get going after calving. Nevertheless, this ration should have sufficient structure. The amounts of

concentrate should be divided into several individual portions and carefully increased. For high feed intakes, fresh water should be constantly available to the animals.

3) Treat diseases early to enable feeding

Diseases that lead to a reduced appetite should be treated as early as possible. In particular, attention should be paid to healthy hooves because a cow that has pain or difficulty getting up and walking is much less likely to go to the feed table.

4) Supplement vitamins, minerals, and trace elements

The needs-based supply of vitamins, minerals, and trace elements in every performance phase is a decisive success factor for good herd fertility. A sufficient supply of trace elements, especially selenium, manganese, zinc, as well as vitamin A and beta-carotene, are important for the formation of fertility hormones and optimal insemination success. At the same time, they ensure a high colostrum quality.

EW Nutrition's Fertilgol Bolus is a long-term bolus to support fertility. The high content of beta-carotene has a positive influence on the formation of the corpus luteum, the oestrus cycle, the quality of colostrum and sperm. The release rate of the ingredients beta-carotene, selenium, vitamin A, and other trace elements takes place over at least twenty days. Fertilgol Bolus can be used for female and male breeding animals shortly before and during the breeding or insemination period.

IgY technology: using nature to support antibiotic reduction

*By **Dr**. **Inge Heinzl**, Editor, EW Nutrition*

For a long time now, IgY technology has been used to provide clear benefits in diagnostics, human medicine, and animal production. To give you a deeper insight into this topic, in the following, we will show you some steps of production, the benefits, and the applications of IgY.

IgY – what is it?

IgY (immunoglobulin of the yolk) are immunoglobulins that hens produce to protect their chicks during the first weeks of life against occurring pathogens. They are the equivalent of immunoglobulin G in the colostrum of mammalians. IgY are an entirely natural product; every egg sold in the supermarket contains IgY.

IgY develops in the hen against the pathogens with which the hens are confronted. Thereby, it does not matter if these pathogens are relevant for the hens. They also produce antibodies against, e. g., bovine, porcine, or human-specific pathogens. This fact was already noticed by Vaillard (1891). He saw that the intraperitoneal injection of tetanus bacteria raised immunity against tetanus bacteria in hens' serum.

A short time later, Klemperer (1892) documented that the serum antibodies were also transferred into the egg. For this purpose, he did a similar trial with hens but collected the eggs. He fed mice a solution containing the egg yolk, and afterward, he infected them with tetanus. All mice with a higher dosage of egg yolk remained healthy, the others receiving a low dosage or no egg yolk died.

IgY production is a non-invasive and highly effective process

The “usual” production of antibodies in mammals includes pain and stress-causing procedures such as immunization, bleeding, and sacrifice. The only stress factor in producing egg antibodies is the hyper-immunization with the pathogen or parts of it; the rest -collecting the eggs- is non-invasive (Ikemori et al., 1993). The European Centre for the Validation of Alternative Methods (ECVAM)), one of Europe’s health and consumer protection institutes, strongly recommends egg immunoglobulins as an alternative to mammalian antibodies (Schade et al., 1996).

IgY production is also advantageous in terms of quantitative and qualitative output. Usually, one egg (with 15 mL of yolk) contains about 100-150 mg IgY (Pereira et al., 2019). Assuming that a hen lays about 300 eggs per year, one bird can produce between 30 and 45 g IgY in this period. After the isolation of the IgY from the egg yolk and the extraction from the remaining proteins, a final purification step that includes chromatography could achieve IgY with >90 % purity (Morgan et al., 2021).

Hyperimmunized hens provide more effective IgY

The targeted confrontation of the animal with specific pathogens or antigens leads to the production of specific antibodies. In a field trial with piglets, Kellner et al. (1994) compared three groups of piglets suffering from diarrhea on day 1 of the test. One group received egg powder originating from hens hyperimmunized with diarrhea-causing pathogens, the second group egg powder from regular eggs, and the third didn’t receive any egg powder. The following results they achieved in one of two farms. The trial shows that, after applying egg powder with selected antibodies, the animals completely recovered within three days. In the group receiving egg powder of regular eggs, still, 9.1% suffered from severe diarrhea and in the control group without any egg powder, only 27.3 % recovered.

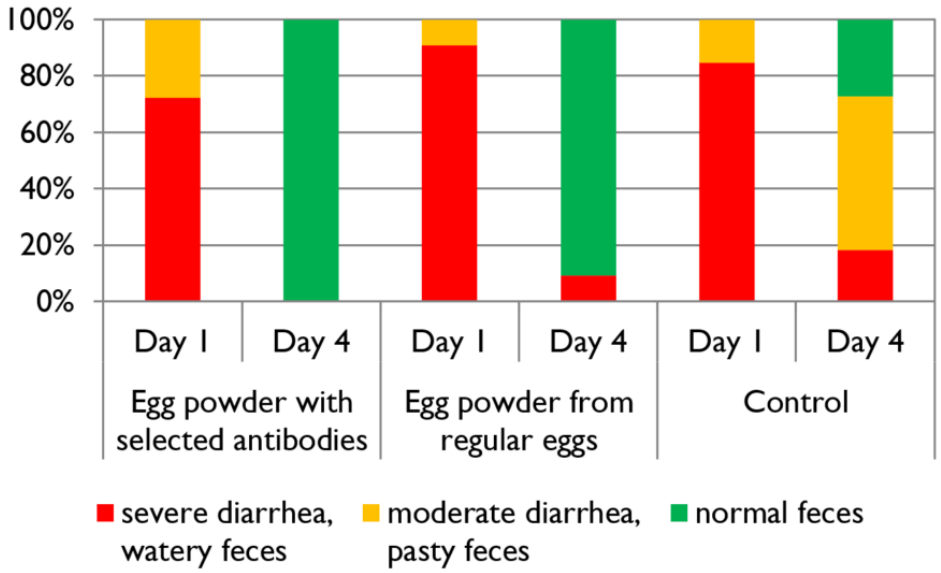


Figure 1: Comparison of eggs originating from regular and hyperimmunized hens

Preconditions for and benefits of industrially produced IgY

A process must meet specific requirements to be suitable for industrial production. In the case of IgY production, the crucial preconditions are that…

- hens produce antibodies also against pathogens non-specific to them
- the antibodies produced and transferred to the egg also are effective in mammals (Yokoyama et al., 1993)
- due to their phylogenetic distance from mammals, hens can produce antibodies even against structurally highly conserved proteins, which is not always possible in rabbits, guinea pigs, and goats (Gassman and Hübscher, 1992).

Industrially produced IgY can target selected pathogens, e.g., enteric bacteria or viruses, respiratory pathogens, SARS-COV-2, etc. As the antibodies act not only in birds but also in other animals, such as mammals including humans, they can be used to prevent disease or support persons/animals in the case of illness. IgY is safe for animals and humans.

Concerning the economic benefits of IgY production, it can be said that it is a cost-effective method due to the high concentration of IgY in the egg yolk and the relatively simple process of the purification of the antibodies. Additionally, feeding and handling are easier and more cost-effective for hens than for many other animals.

Not all IgY products are the same

There are different methods of IgY production. One possibility is to hyperimmunize the hens simultaneously with multiple antigens. This method seems to be convenient but does not deliver standardized products concerning the content of immunoglobulins.

The other possibility is the immunization of different groups of hens, each with one antigen (e.g., Rotavirus, Salmonella, E. coli). The content of immunoglobulins is determined, and the different egg powders are mixed. The result is an IgY product with standardized amounts of specific immunoglobulins.

Where can we use IgY?

There are different application areas for IgY or IgY products. In human medicine, egg immunoglobulins can be used against the toxin of rattlesnakes or scorpions, or Streptococcus mutans bacteria, causing dental caries (Gassmann and Hübscher, 1992) Egg immunoglobulins are important for diagnostic tests such as radioimmunoassay (RIA) and enzyme-linked immunoassay (ELISA).

A further application area is animal nutrition. Young animals, such as calves or piglets, but also young dogs or cats, are born with immature immune systems. If they, additionally, are deprived of maternal colostrum in adequate quantity and/or quality, they suffer from immunity gaps during their first weeks of life and are susceptible to pathogens in their environment.

Antibiotics have been used prophylactically for a long time to protect young animals in this critical phase. With increasing antibiotic resistance, this procedure is not allowed anymore.

Products based on egg immunoglobulins against enteric pathogens, e.g., support young animals against newborn or weaning diarrhea (e.g., Yokoyama et al., 1992; Ikemori et al., 1992; Ikemori et al., 1997, Yokoyama et al., 1998).

IgY – a fascinating technology that should be better recognized

IgY technology is an animal-friendly technology with high output. Its various applications make IgY a helpful tool for human medicine as well as animal production. To get the best results, attention must be paid to quality, meaning, amongst others the standardization of the products.

IgY is an optimal tool to help young animals such as calves and piglets cope with pathogenic challenges in early life. Consequently, IgY technology enables us to limit (preventive) antimicrobial use in critical periods of animal rearing and, therefore, reduce antimicrobial resistance.

References:

Gassmann, M., and U. Hübscher. “Use of Polyclonal Antibodies from Egg Yolk of Immunised Chickens .” ALTEX – Alternatives to animal experimentation 9, no. 1 (1992): 5–14.

Ikemori, Yutaka, Masahiko Kuroki, Robert C. Peralta, Hideaki Yokoyama, and Yoshikatsu Kodama. “Protection of Neonatal Calves against Fatal Enteric Colibacillosis by Administration of Egg Yolk Powder from Hens Immunized with K99-Piliated Enterotoxigenic Escherichia Coli.” Amer. J. Vet. Res. 53, no. 11 (1992): 2005–8. https://doi.org/PMID: 1466492.

Ikemori, Yutaka, Masashi Ohta, Kouji Umeda, Faustino C. Icatlo, Masahiko Kuroki, Hideaki Yokoyama, and Yoshikatsu Kodama. “Passive Protection of Neonatal Calves against Bovine Coronavirus-Induced Diarrhea by Administration of Egg Yolk or Colostrum Antibody Powder.” Veterinary Microbiology 58, no. 2-4 (1997): 105–11. https://doi.org/10.1016/s0378-1135(97)00144-2.

Ikemori, Yutaka, Robert C. Peralta, Masahiko Kuroki, Hideaki Yokoyama, and Yoshikatsu Kodama. “Research Note: Avidity of Chicken Yolk Antibodies to Enterotoxigenic Escherichia Coli Fimbriae.” Poultry Science 72, no. 12 (1993): 2361–65. https://doi.org/10.3382/ps.0722361.

Kellner, J., M.H. Erhard, M. Renner, and U. Lösch. “Therapeutischer Einsatz Von Spezifischen Eiantikörpern Bei Saugferkeldurchfall – Ein Feldversuch.” Tierärztliche Umschau 49, no. 1 (January 1, 1994): 31–34.

Klemperer, Felix. “Ueber Natürliche Immunität Und Ihre Verwerthung Für Die Immunisirungstherapie.” Archiv für Experimentelle Pathologie und Pharmakologie 31, no. 4-5 (1893): 356–82. https://doi.org/10.1007/bf01832882.

Pereira, E.P.V., M.F. van Tilburg, E.O.P.T. Florean, and M.I.F. Guedes. “Egg Yolk Antibodies (Igy) and Their Applications in Human and Veterinary Health: A Review.” International Immunopharmacology 73 (2019): 293–303. https://doi.org/10.1016/j.intimp.2019.05.015.

Schade, R., C. Staak, C. Hendriksen, M. Erhard, H. Hugl, G. Koch, A. Larsson, et al. “The Production of Avian (Egg Yolk) Antibodies: IgY,” 1996. https://www.researchgate.net/publication/281466059_The_production_of_avian_egg_yolk_antibodies_IgY_The_report_and_recommendations_of_ECVAM_workshop_21.

Schade, R., C. Staak, C. Hendriksen, M. Erhard, H. Hugl, G. Koch, A. Larsson, et al. “The Production of Avian (Egg Yolk) Antibodies: IgY. The Report and Recommendations of ECVAM Workshop 21.” ATLA (Alternatives to Laboratory Animals) 24 (1996): 925–34. https://doi.org/https://www.researchgate.net/publication/281466059_The_production_of_avian_egg_yolk_antibodies_IgY_The_report_and_recommendations_of_ECVAM_workshop_21.

Yokoyama, H, R C Peralta, R Diaz, S Sendo, Y Ikemori, and Y Kodama. “Passive Protective Effect of Chicken Egg Yolk Immunoglobulins against Experimental Enterotoxigenic Escherichia Coli Infection in Neonatal Piglets.” Infection and Immunity 60, no. 3 (1992): 998–1007. https://doi.org/10.1128/iai.60.3.998-1007.1992.

Yokoyama, Hideaki, Robert C. Peralta, Kouji Umeda, Tomomi Hashi, Faustino C. Icatlo, Masahiko Kuroki, Yutaka Ikemori, and Yoshikatsu Kodama. “Prevention of Fatal Salmonelosis in Neonatal Calves, Using Orally Administered Chicken Egg Yolk Salmonella-Specific Antibodies.” Amer. J. Vet. Res. 59, no. 4 (1998): 416–20. https://doi.org/PMID: 9563623.

Yokoyama, Hideaki, Robert C. Peralta, Sadako Sendo, Yutaka Ikemori, and Yoshikatsu Kodama. “Detection of Passage and Absorption of Chicken Egg Yolk Immunoglobulins in the Gastrointestinal Tract of Pigs by Use of Enzyme-Linked Immunosorbent Assay and Fluorescent Antibody Testing.” American Journal of Veterinary Research 54, no. 6 (1993): 867–72. https://doi.org/PMID: 8323054.

Zhang, Xiao-Ying, Ricardo S. Vieira-Pires, Patricia M. Morgan, Rüdiger Schade, Xiao-Ying Zhang, Rao Wu, Shikun Ge, and Álvaro Ferreira Júnior. “Immunization of Hens.” Essay. In IGY-Technology: Production and Application of Egg Yolk Antibodies. Basic Knowledge for a Successful Practice., 116–34. Cham, Switzerland: Springer Nature, 2021.

Zhang, Xiao-Ying, Ricardo S. Vieira-Pires, Patricia M. Morgan, Schade Rüdiger, Patricia M. Morgan, Marga G. Freire, Ana Paula M. Tavares, Antonysamy Michael, and Xiao-Ying Zhang. “Extraction and Purification of IgY .” Essay. In IGY-Technology: Basic Knowledge for a Successful Practice, 135–60. Cham: Springer International Publishing AG, 2021.

Zhang, Xiao-Ying, Ricardo S. Vieira-Pires, Patricia M. Morgan, Schade Rüdiger, Patricia M. Morgan, Xiao-Ying Zhang, Antonysamy Michael, Ana Paula M. Tavares, and Marga G. Freire. “Extraction and Purification of IgY (Chapter 11).” Essay. In IGY-Technology: Basic Knowledge for a Successful Practice, 135–60. Cham: Springer International Publishing AG, 2021.

Calf diarrhea: types, causes, solutions

By Dr. Inge Heinzl, Editor, EW Nutrition

Diarrhea causes a higher workload, increased costs for treatment, losses, and, of course, lower benefits for the farmer. But not all diarrheas are equal. How do they differ, where do differences come from, and what can you do to protect your animals?

Diarrhea is a protective measure of the organism

In general, diarrhea is characterized by more liquid being secreted than being resorbed. However, diarrhea is not a disease but only a symptom. Diarrhea has a protective function for the organism: the higher liquid volume in the gut increases motility, and pathogens and toxins are more readily excreted.

Diarrhea can occur for several reasons. It can result from inadequate nutrition but also the reaction to an infection by pathogens such as bacteria, viruses, and protozoa.

Where does the fluid come from?

Depending on how the accumulation of fluid in the gut is generated, there are different kinds of diarrhea:

- In the case of secretory diarrhea, as the name says, the fluid accumulation comes from an increased secretion into the gut caused by toxins activating enzyme systems. The gut mucosa can no longer resorb this higher amount of liquid.
- When the animals suffer from malabsorptive diarrhea due to destroyed enterocytes and shortened villi, the enzyme activity and absorption capacity are reduced. Less liquid can be absorbed and has to be excreted via the gut.
- When inflammatory diarrhea occurs, the gut mucosa is damaged. Higher amounts of mucus, protein, and blood are released into the gut lumen.

Due to multiple infections, diarrhea often is a mixture of different forms.

Multiple causes can be responsible

For the occurrence of diarrhea, different causers can be a possibility. Besides infectious pathogens, also the feed must be considered.

1. Bacteria often produce toxins

E. coli is a common agent of the gut microflora and in general it is harmless. However, *E. coli* can also be the cause of different types of diarrhea, depending on the virulence factors. Virulence factors of *E.coli* are, e.g., fimbria for the attachment to intestinal receptors or the ability to produce toxins influencing the secretion of ions and liquids. Example: enterotoxic *E. coli* (ETEC) F5 and F41 occurring during the first days of life.

In general, *Salmonella* plays a secondary role in calf diarrhea. Of the *Salmonella serovars*, mainly *S. Typhimurium* and *S. Dublin* are found in calves. *Salmonella* produces enterotoxins that attack the intestinal wall.

Clostridia infections belong to the most expensive ones in cattle farming globally. In herbivores, *clostridia* are part of the normal flora of the gastrointestinal tract; only a few types can cause severe disease. In calves, the necrotizing toxin-producing *Clostridium perfringens* can lead to enterotoxaemia manifesting in acute bloody diarrhea.

2. Viruses cause lesions in the gut

Rotavirus, which occurs mainly during the 5th -15th day of life, is the most common viral pathogen causing

diarrhea in calves and lambs. If more enterocytes are destroyed than regenerated by the organism, the resorption surface in the gut decreases. With increasing age, animals develop immunity against this pathogen.

Coronavirus usually attacks calves at the age of 5 – 21 days (mainly correlated with the decreasing concentration of antibodies in maternal milk). They cause similar lesions in the intestine as rotavirus but additionally lead to necrosis of the crypts in the large intestine. The digestive and absorptive function is lost, resulting in reduced reabsorption of fluids. 3 to 20 % of diarrhea arising in calves is caused by Coronavirus.

3. Protozoa can lead to malabsorptive diarrhea

Cryptosporidium parvum (mainly 1-2 weeks after birth) belongs to the coccidia and is presumed to be the most common pathogen to cause diarrhea (prevalence up to more than 60 %) in calves. Cryptosporidium is transmitted via oocysts found in feces and on the farm equipment. Cryptosporidia destroy the microvilli in the gut, the function of the gut mucosa is reduced, the resorption area decreases. Consequence: loss of enzyme activity and, therefore, an insufficient breakdown of sugar and protein, resulting in malabsorption.

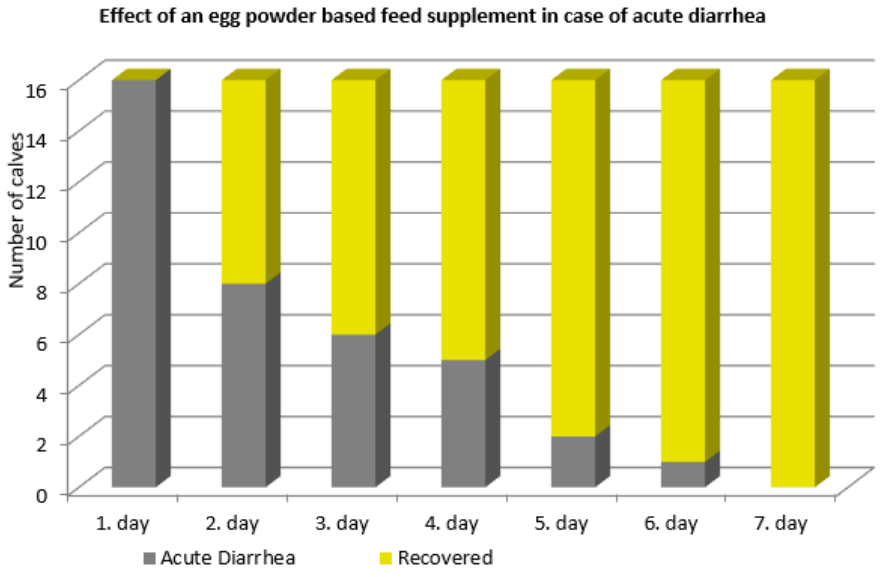
4. Calves need their special feed

In general, raw materials which cannot be well digested by the calf (mainly soya products, often used in milk replacers) or which cause allergy can cause diarrhea in calves. Also, antibiotics can lead to an imbalance of the intestinal flora, destruction of the villi, and malabsorptive diarrhea.

Trial shows promising results in the field

A field study with the egg powder-based product Globigen Dia Stop was conducted with 16 calves suffering from diarrhea. They were fed twice daily 50 g of Globigen Dia Stop stirred into the milk replacer.

Result (fig. 1): already one day after the first application of Globigen Dia Stop, 50 % of the calves recovered. After seven days, all calves overcame diarrhea. On average, one calf needed 2,4 treatments to show a full recovery from diarrhea (≙ 1,25 treatment days).



Egg immunoglobulins support against diarrhea

Egg immunoglobulins can effectively support calves in their fight against diarrhea. Immunoglobulins can act against bacteria, parasites, and viruses, not only against bacteria as antibiotics do. With egg immunoglobulin-based products, the farmer has a tool at his disposal that is easy to handle and does not require a withdrawal period. As there is no danger of the generation of resistance, these products are ideal for reducing the use of antibiotics in animal production.

Article initially published in NutriNews

IgYs support calves in case of diarrhea

By Lea Poppe, Technical Manager – Europe, EW Nutrition

Humans and animals protect themselves against diseases with specific antibodies (immunoglobulins). They receive antibodies from their mother or a vaccination (passive immunity) or produce them themselves after contact with a pathogen (active immunity). To be protected by a high passive immunity during the first weeks of life, a calf must receive high-quality colostrum with a sufficient amount of farm-specific antibodies as early as possible after

birth.

Undersupply with immunoglobulins lowers later performance

In 2015, the Ludwig Maximilian University of Munich examined the immunoglobulin supply of 1,242 newborn calves. This study showed that more than half of the calves were undersupplied: 23% severely (<5mg IgG / ml blood serum) and 36% slightly undersupplied (5-10mg IgG/ml). The supply situation was only satisfactory in 41% of the calves (> 10 mg IgG/ml).

Undersupply results in higher susceptibility to disease, higher mortality, and lower daily weight gain. This entails increased rearing costs. Besides, only healthy calves can achieve their full potential as adult animals. For example, when a calf experiences even mild diarrhea, it is expected to produce 344 kg less milk the first lactation (Welsch, 2016). Possible causes of diarrhea are infectious factors such as viruses (rota, coronaviruses), bacteria (*E. coli*) and parasites (cryptosporidia), but also non-infectious factors such as poor husbandry and feeding errors.

Survey confirms: Calves lack sufficient amounts of immunoglobulins

In December 2020, EW Nutrition conducted a telephone survey among 55 dairy cattle consultants and veterinarians from Spain, Germany, France, Poland, and Great Britain to review calves' passive immunity.

This survey confirmed that calves lack sufficient amounts of immunoglobulins: 69.1% of respondents thought that calves were undersupplied. 76.4% of them saw a clear connection between early-occurring

diarrheal diseases and calves' insufficient passive immunity. Respondents came to these conclusions even though more than half of them thought that colostrum quality had not deteriorated during the last years (56.4%).

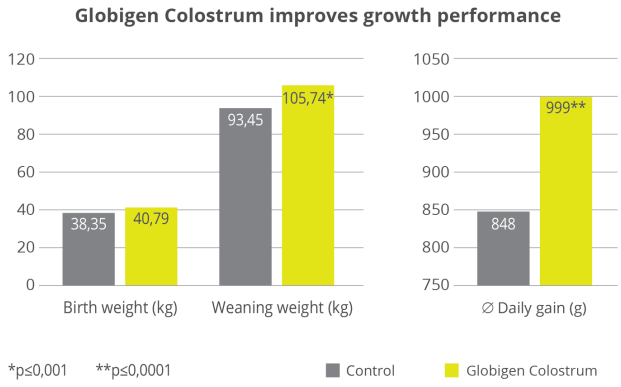
Immunoglobulins from the egg help calves against diarrhea

Egg immunoglobulins offer one way to support calves in case of diarrhea. Chickens form antibodies (IgY from "**I**mmuno**g**lobulins in **Y**olk") against all disease pathogens they encounter and release them into the egg as an immunological starting aid for the chick. It does not matter whether the disease is relevant to poultry or cattle.

These antibodies can be used to improve poor-quality colostrum or to support the calf during acute diarrhea. Studies show that egg immunoglobulins act in calves' intestines, where they can bind and block diarrhea pathogens (Ikemori et al., 1992).

IgY add value to colostrum

A feeding study with 39 female newborn calves took place on an 800-cow dairy farm in Brandenburg, Eastern Germany. The objective was to examine whether the IgY-containing complementary feed Globigen Colostrum effectively supports calves during the first critical period. For the experiment, all calves were given high-quality colostrum (4L within 2 hours after birth). During the first 5 days of life, the 19 calves in the test group additionally received 100g of the complimentary feed stirred into the colostrum (day 1) or the mixed colostrum (days 2 – 5).



Result: The daily weight gain for the test group was 18% higher than in the control group (+ 151g). This resulted in 13% higher weaning weights (see above).

Three calves in the control group had mild diarrhea; in the test group, only one calf. However, antibiotics did not have to be used to treat the diarrhea.

IgY to reduce neonatal diarrhea

The IgY-based product Globigen Calf Paste was tested on two dairy farms in Russia. These trials focused on reducing neonatal diarrhea, which occurs in the first 2 to 3 weeks of life. The product, a 30ml oral syringe with a dosing ring, was administered at a rate of 10ml per day for the first three days of life. On the first farm in the Belgorod region, the trial and control groups consisted of 11 calves each. On the 10th day of

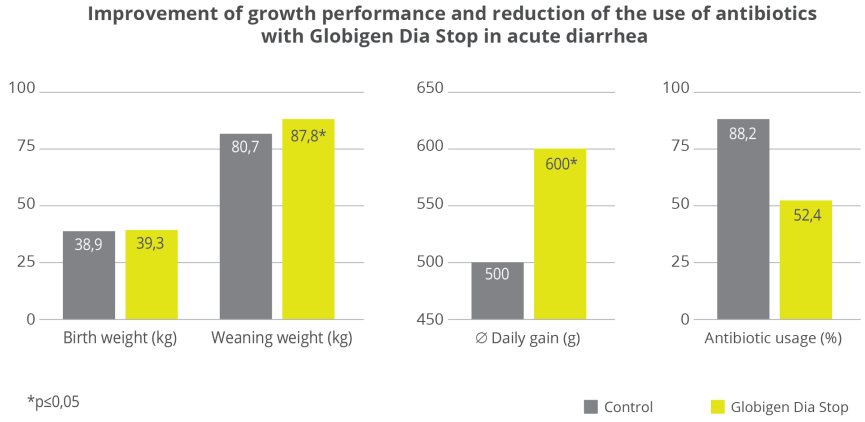
life, the diarrhea incidence per group was checked: while 73% of the calves in the control group had diarrhea, requiring antibiotics, only 1 calf of the trial group had diarrhea, and no antibiotic treatment was needed. On the second farm in the Moscow region, where the groups encompassed 20 calves each and observations took place on the 5th day of life, results were similar: 75% of the control animals suffered from diarrhea, but just 3 calves in the trial group showed signs of diarrhea.

IgY support calves with acute diarrhea

In another trial, carried out with 38 calves on a dairy farm with 550 cows in North Rhine-Westphalia, Western Germany, the dietetic feed supplement Globigen Dia Stop was tested. This product is also based on egg immunoglobulins.

Only calves showing newborn diarrhea were used for this experiment. When diarrhea occurred, the 21 calves in the test group received 50g Globigen Dia Stop twice a day in addition to their milk drink. The diseased calves in the control group (17 calves) were given a rehydration solution, stirred into water, twice a day.

If the diarrhea could not be stopped after four days in the calves of either group, the animals were treated by a veterinarian.

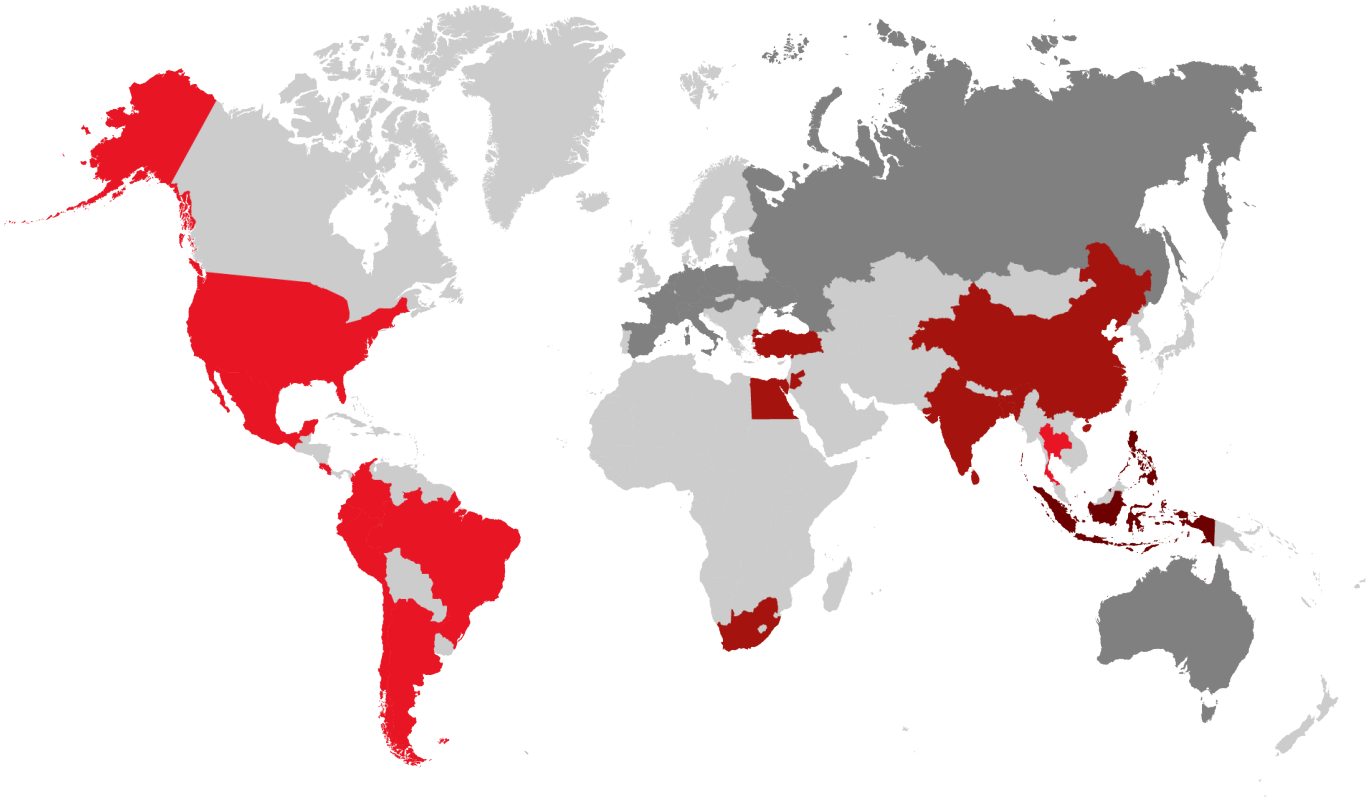


Result: In the test group, 100g (+ 20%) and thus significantly higher daily gains were achieved, which led to a 9% higher weaning weight. Furthermore, over 40% fewer calves had to be treated with antibiotics in the Globigen Dia Stop group than in the control group. (see above)

Conclusion: Egg immunoglobulins support gut health

The results of these studies indicate that the administration of egg antibodies (IgY) to calves supports intestinal health and has a positive effect on calves' performance. Globigen supplementation can likely reduce diarrhea incidence and severity, especially in the critical first phase of the calves' life – thus ensuring high performance in the long term.

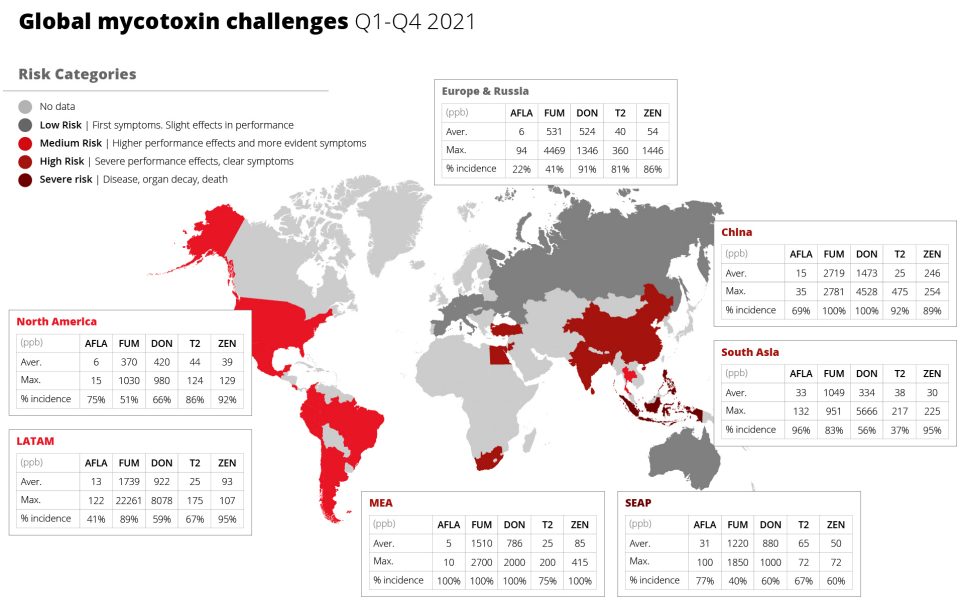
Global mycotoxin challenges: 2021 report



By Marisabel Caballero, Global Technical Manager Poultry, EW Nutrition

Climate around the globe has changed, increasing atmospheric temperatures and carbon dioxide levels. This change favors the growth of toxigenic fungi in crops and thus increases the risk of mycotoxin contamination. When contaminating feed, mycotoxins exert adverse effects in animals and could be transferred into products such as milk and eggs.

***** Please download the full article for detailed information**



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Mycotoxins: a worldwide challenge in 2021

Amongst naturally occurring mycotoxins, the five most important ones are aflatoxin, ochratoxin, deoxynivalenol, zearalenone, and fumonisin. Their incidence varies with the different climates, the prevalence of plant cultures, the occurrence of pests, and the handling of harvest and storage. Worldwide, farmers faced various and sometimes extremely high mycotoxin contamination in their feed materials in 2021. In the following, we show the major challenges in five main regions.

Asia faced high aflatoxin contamination

In Asia, high temperatures and humidity favor Aspergillus growth in grains. As a result, 95 % of the samples in South Asia and three-quarters of the samples in the China and the SEAP region (Indonesia, Philippines, Vietnam) showed aflatoxin contamination. The average contamination being higher than the threshold for all farm animals represents an increased risk for their health and performance.
In China and the SEAP region, also DON and T-2 were highly prevalent. Showing an incidence of more than 60%, they pose a severe risk when combined with aflatoxin.

Fumonisins afflicted the LATAM region

In Mexico, Central and South America, fumonisin contamination prevailed with an incidence of almost 90% at average levels that can be considered risky for swine and dairy. Together with incidence levels of around 60% found for DON and T2, fumonisin may act synergically in the animals, raising the risk for health and performance.
The Fusarium species linked to these mycotoxin contaminations occur in the grains on the field. Amongst others, insect damage, droughts during growing, and rain at silking favor their development.

Trichothecenes prevailed in North America

Contamination with trichothecenes (DON and T2) is the rule in the United States. The interaction of these mycotoxins is at least additive. The damage they cause to the gut opens the door to dysbiosis and disease, decreasing performance and profitability.
Also in this case, the responsible molds for the contamination are Fusarium species that develop when grains are in the field. As with fumonisins, the molds are favored by insect damage, moderate to warm temperatures and rainfall.

Fusarium toxins contaminated grain in the MEA region

Fusarium toxins such as Fumonisin, DON, and T2 prevail in the region of Egypt, Jordan, and South Africa. In combination, these mycotoxins have additive effects at the intestinal level, which increases the risk of

dysbiosis in poultry.

A challenging year with long-term repercussions

Since mycotoxin contamination affects animal health, measures must be taken to provide the best protection. Besides improving agricultural practices in the field, smart in-feed solutions and mold inhibitors can be used in stored grain. These measures help producers preserve feed quality after a troubled year for crops around the world.

EW Nutrition achieves PCAS Certification in Australia

Singapore – November 1, 2021 – EW Nutrition has successfully passed an external audit conducted by the Cattle Council of Australia (CCA) and achieved Pasturefed Cattle Assurance System (PCAS) certification for three products: Activo Premium, Mastersorb Gold, and Prote-N.

The PCAS is a certification program that enables grassfed cattle producers to prove claims relating to pasturefed or grassfed production methods. EW Nutrition also achieved two optional modules under the PCAS Standards relating to the freedom from antibiotics and hormone growth promotants (HGPs). As a

certified supplier, EW Nutrition is able to provide feed products to the industry to support pasturefed or grassfed production methods.

“We are pleased to receive the certification for our solution offerings in Australia. The qualification of these products is a testament of our commitment to work together with the industry to mitigate the impact of antimicrobial resistance. By pursuing our objectives in animal nutrition, our work contributes to increasing the efficacy of human healthcare.” said David Sherwood, Commercial Director Oceania with EW Nutrition.

The PCAS certified products are:

Activo Premium
Activo Premium contains standardized amounts of selected phytomolecules.

Mastersorb Gold
Mastersorb Gold is part of EW Nutrition’s Toxin Risk Management Program, which also includes services, on-site advice, and expert consultancy.

Prote-N
Prote-N is a slow-release source of nonprotein nitrogen (NPN).

About EW Nutrition

EW Nutrition offers animal nutrition solutions to the feed industry. The company’s focus is on gut health, supported by other product lines. EW Nutrition researches, develops, produces, sells and services most of the products it commercializes. In 50 countries, key accounts are served directly by EW Nutrition’s own personnel.

For more information, please visit https://ew-nutrition.com.
For more information about PCAS, please visit https://pcaspasturefed.com.au/

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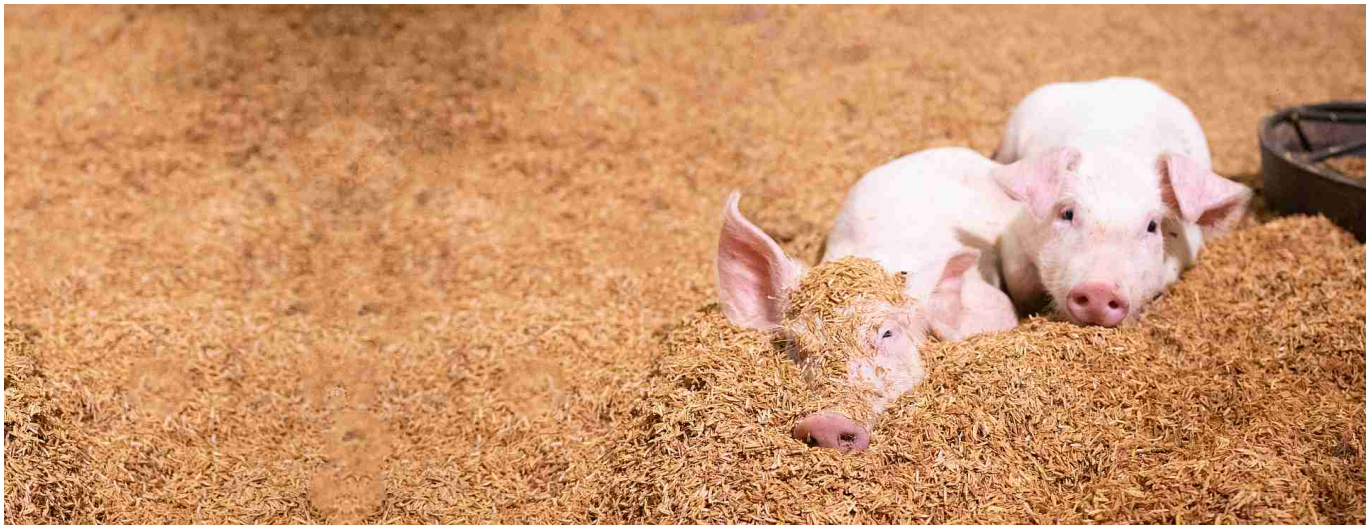
Rising feed costs? Focus on the FCR



by **Inge Heinzl**, Editor, and **Marisabel Caballero**, Global Technical Manager Poultry, EW Nutrition

What is your most crucial key feed performance indicator? We posted this question on an online professional platform and got more than 330 answers from professionals in the industry:

- 55 % of the respondents considered feed efficiency or feed conversion rate (FCR) the key indicator, and
- 35 % listed feed cost / kg produced as their most important indicator.

As feed represents 60-70 % of the total production costs, feed efficiency has a high impact on farm profitability – especially in times of high feed prices. Furthermore, for the meat industry, an optimal FCR is essential for competitiveness against other protein sources. Finally, for food economists, feed efficiency is connected to the optimal use of natural resources (Patience et al., 2015).

In this article, we explain the factors that influence feed efficiency and show options to support animals in optimally utilizing the feed – directly improving the profitability of your operation.

How to measure the feed conversion rate

The FCR shows how efficiently animals utilize their diet for maintenance and net production. In the case of fattening animals, it is meat production; for dairy cows, it is milk, and for layers, it is egg mass (kg) or a specific egg quantity.

The feed conversion rate is the mathematical relation obtained by dividing the amount of feed the animal consumed by the production it provided. The FCR is an index for the degree of feed utilization and shows the amount of feed needed by the animal to produce one kg of meat or egg mass, or, e.g., 10 eggs.

$$\text{FCR} = \frac{\text{Feed weight (kg)}}{\text{Production (kg weight gain, kg milk, or \# of eggs)}}$$

When comparing the FCRs of different groups of animals (e.g., from different houses or farms), some considerations are important:

- Feed consumed is not feed disappeared: Due to differences in feeder design and feeder adjustment, these two values can differ by 10-30 %. If FCR is calculated for economic purposes, the wasted feed must be included, as it causes costs and must be paid by the farmer. However, if FCR is calculated for scientific purposes (e.g., a performance trial), only the feed consumed should be included.
- Even if they are same-aged animals, individuals or groups differ in weight. Hence, they have different requirements for maintenance and also diverging quantity left for production. To avoid mistakes, weight-corrected FCR can be used.
- Nutrient utilization also depends on genotype and sex; thus, comparisons should consider these factors as they also influence weight gain and body composition (Patience et al., 2015).

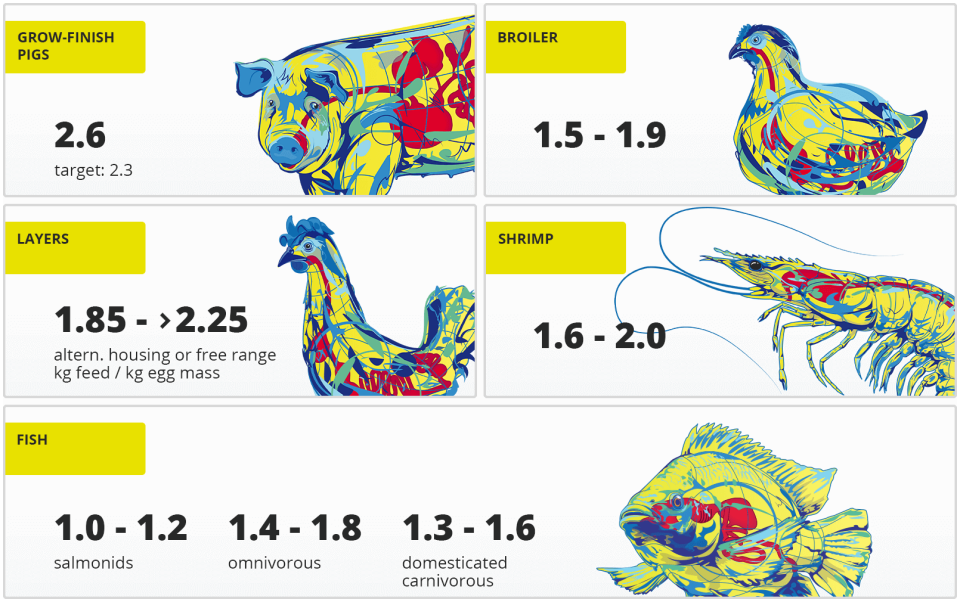
Many factors influence the FCR

There are internal and external factors that influence feed efficiency. Internal factors originate in the animal and include genetics, age, body composition, and health status. In contrast, external factors include feed composition, processing, and quality, as well as the environment, welfare enrichment, and social aspects.

1. Species

Different species have different body sizes and physiology and, therefore, vary in their growth and maintenance requirements, impacting their efficiency in converting the feed.

Table 1: FCRs of different species



Compared to terrestrial animals, for example, fish and other aquatic animals have a low FCR. Being poikilothermic (animals whose body temperature ranges widely), they don't spend energy on maintaining their body temperature if the surrounding water is within their optimal range. As they are physically supported by water, they also need less energy to work against gravity. Furthermore, carnivorous fish are offered highly digestible, nutrient-dense feed, which lowers their requirements in quantity. Omnivorous fish, on the other hand, also consume feedstuffs not provided by the producer (e.g., algae and krill), which is not considered in the calculation. Broilers are the only farm animals achieving a similar FCR.

2. Sex, age, and growth phase

Sex determines gene expression related to the regulation of feed intake and nutrient utilization. Males have a better feed conversion and put on more lean meat than females and castrates, which grow slower and easier run to fat.

Young animals have a fast growth rate and are offered nutritionally dense feed; hence, their FCR is lower. When the animal grows and gains weight, its energy requirement for maintenance increases and its growth rate and the feed nutrient density diminish.

Table 2: FCR during different life phases of pigs (based on Adam and Bütfering, 2009)

	Age / weight / phase	**FCR**
Piglet	0 – 2 weeks	1.1 – 1.2
	3 – 6 weeks	1.6 – 1.8
Grower-finisher	30 – 120 kg	~ 2.6
	End of fattening	4 – 5

3. Health and gut health

Health decisively impacts feed conversion. An animal that is challenged by pathogens reduces its feed intake and, thus, decreases growth. Additionally, the body needs energy for the immune defense, the replacement of damaged or lost tissue, and heat production, in case of fever. As many immune components are rich in protein, this is the first nutrient to become limited.

An imbalance in the gut microbiome also impacts feed conversion: pathogenic microorganisms damage tissues, impair nutrient digestion and absorption, and their metabolic products are harmful. Furthermore, pathogens consume nutrients intended for the host and continue to proliferate at its expense.

4. Environment

The environment influences the way the animals spend their maintenance energy. According to Patience (2012), when a 70 kg pig is offered feed *ad libitum*, 34 % of the daily energy is used for maintenance. For each °C below the thermoneutral zone, an additional 1.5% of feed is needed for maintenance. In heat stress, each °C above the optimum range decreases feed intake by 2%. Therefore, the feed needs to be denser to fulfill the requirement, or the animal will lose weight. Social stress also influences animal performance, especially chronic stress situations. Keeping the animals in their thermoneutral zone and mitigating the impact of stressors means more energy can go towards performance.

5. Feed quantity, composition, and quality

The feed is the source of nutrients animals convert into production. So, it's natural that its quality and composition, and the availability of nutrients affect feed efficiency.

Better FCR by increasing nutrient density and digestibility

Higher energy content in the diet and better protein digestibility improve FCR. Saldaña et al. (2015) assert that increasing the energy content of a diet led to a linear decrease of the average daily feed intake but improved FCR quadratically. The energy intake by itself remained equal. However, these diet improvements also increase costs, and a cost-benefit analysis should be conducted.

Feed form and particle size play an important role

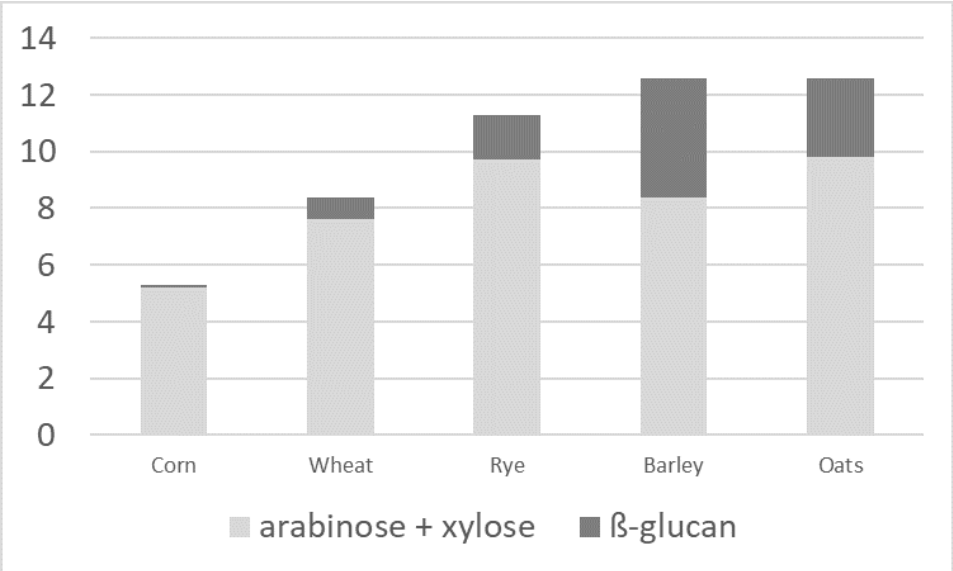
Feed processing can improve nutrient utilization. Particle size, moisture content, and whether the feed is offered as pellets or mash influence feed efficiency. Reducing the particle size leads to a higher contact surface for digestive enzymes and higher digestibility. Chewning et al. (2012) tested the effect of particle size and feed form on FCR in broilers. They found that pellet diets enable better FCRs than mash diets – one reason is the lower feed waste, another one the smaller feed particle size in the pelleted feed. Comparing the different tested mash diets, the birds receiving feed with a particle size of 300 µm performed better than the birds getting a diet with 600 µm particles.

Richert and DeRouchey (2015) show that pigs' feed efficiency improved by 1.3 % for every 100 µm when the particle size was reduced from 1000 µm to 400 µm , as the contact surface for the digestible enzymes increased. In weaning piglets of 28-42 days, the increase of particle size from 394 µm to 695 µm worsened FCR from 1.213 to 1.245 (Almeida et al., 2020). There is a flipside to smaller particle size as well, however: high quantities of fines in the diet can lead to stomach ulceration in pigs (Vukmirović et al., 2021).

Non-starch polysaccharide (NSP)-rich cereals worsen FCR

The carbohydrates in feedstuffs such as wheat, rye, and barley are not only energy suppliers, and if not managed well, the inclusion of these raw materials can deteriorate feed conversion. Vegetable structural substances such as cellulose, hemicellulose, or lignin (e.g., in bran), are difficult or even impossible to utilize as they lack the necessary enzymes.

Figure 1: Contents of arabinoxylan and ß-glucan in grain (according to Bach Knudsen, 1997)



Additionally, water-soluble NSPs (e.g., pectins, but also ß-glucans and pentosans) have a high water absorption capacity. These gel-forming properties increase the viscosity of the digesta. High viscosity reduces the passage rate and makes it more difficult for digestive enzymes and bile acids to come into contact with the feed components. Also, nutrients' contact with the resorptive surface is reduced.

Another disadvantage of NSPs is their "cage effect." The water-insoluble NSPs cellulose and hemicellulose trap nutrients such as proteins and digestible carbohydrates. Consequently, again, digestive enzymes cannot reach them, and they are not available to the organism.

Molds and mycotoxins impair feed quality, but also animal health

Molds reduce the nutrient and energy content of the feed and negatively impact feed efficiency. They are dependent on active water in the feed and feed ingredients. Compared to bacteria, which need about 0.9-0.97 Aw (active water), most molds require only 0.86 Aw.

Table 3: Comparison of 28-day-old chicks performance fed not-infested and molded corn

	Weight gain (g)	FCR
Non-infested corn	767 [a]	1.79 [a]
Molded corn	713 [b]	1.96 [b]

Besides spoiling raw materials and feed and reducing their nutritional value, molds also produce mycotoxins which negatively impact animal health, including gut health. They damage the intestinal villi and tight junctions, reducing the surface for nutrient absorption. In a trial with broiler chickens, Kolawole et al. (2020) showed a strong positive correlation between the FCR and the exposure to different mycotoxins. The increase in levels of toxin mixtures resulted in poor FCR. Williams and Blaney (1994) found similar results with growing pigs. The animals received diets containing 50 % and 75 % of corn with 11.5 mg nivalenol and 3 mg zearalenone per kg. The inclusion of contaminated corn led to a deterioration of feed efficiency from 2.45 (control) to 3.49 and 3.23.

Oxidation of fats also affects feed quality

DDGS (distiller's dried grains with solubles), by-products of corn distillation processes, are often used as animal feed, especially for pigs. The starch content is depleted in the distillation process and thus removed. The fat, however, is concentrated, and DDGS reach a similar energy content as corn.

Pigs also receive fats from different sources (e.g., soybean or corn oil, restaurant grease, animal-vegetable blends), especially in summer. Due to heat, the animals eat less, so increasing energy density in the feed is a possibility to maintain the energy intake. The high fat content, however, makes these feeds

susceptible to oxidation at high temperatures.

The oxidation of feedstuffs manifests in the rancidity of fats, destruction of the fat-soluble vitamins A, D, and E, carotenoids (pigments), and amino acids, leading to a lower nutritional value of the feed.

Use adequate supplements to enhance FCR

The feed industry offers many solutions to improve the FCR for different species. They usually target the animal's digestive health or maintain/enhance feed quality, including increasing nutrient availability.

1. Boost your animals' gut health

Producers can improve gut health by preventing the overgrowth of harmful microorganisms and by mitigating the effects of harmful substances. For this purpose, two kinds of feed additives are particularly suitable: phytomolecules and products mitigating the impact of toxins and mycotoxins.

Phytomolecules help stabilize the balance of the microbiome

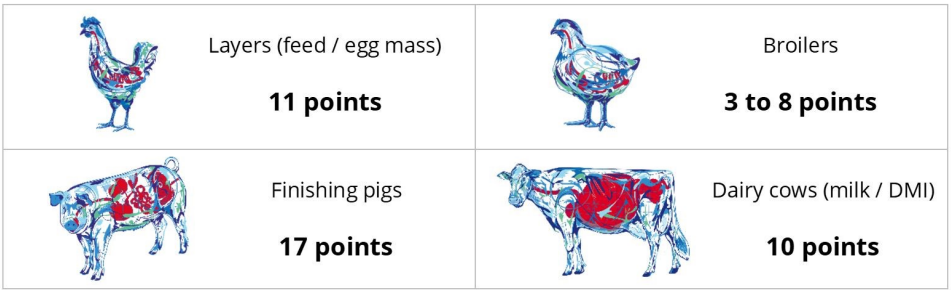
By preventing the proliferation of pathogens, phytomolecules help the animal in three ways:

1. They prevent pathogens from damaging the gut wall
2. They deter and mitigate inflammation
3. By inhibiting the overgrowth of pathogens, they promote better nutrient utilization by the animal

Only a healthy gut can optimally digest feed and absorb nutrients.

In trials testing the phytogenic Activo product range, supplemented animals showed the following FCR improvements compared to non-supplemented control groups (Figure 2). Note that phytomolecules also have a digestive effect that contributes to the FCR improvements:

Figure 2: FCR improvements for animals receiving Activo



Products mitigating the adverse effects of toxins

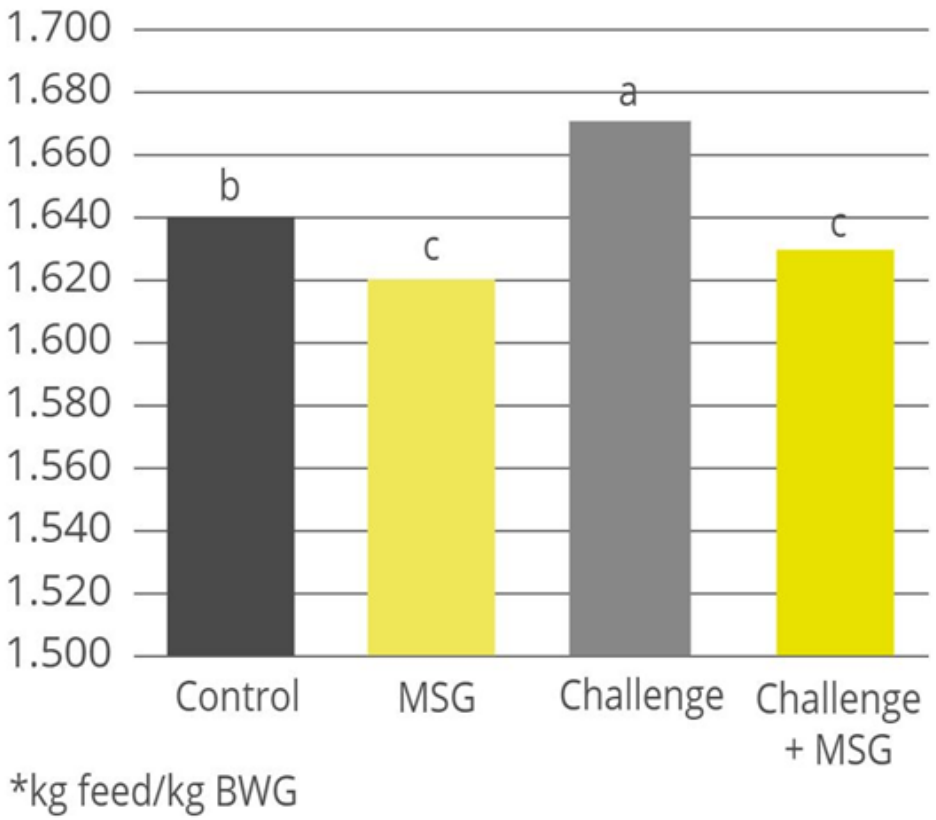
Both mycotoxins and bacterial toxins negatively impact gut health. Mycotoxins are ingested with the feed; bacterial toxins appear when certain bacteria proliferate in the gut, e.g., gram-negative bacteria releasing LPS or *Clostridium perfringens* producing NetB and Alpha-toxin.

Products that mitigate the harmful effects of toxins help to protect gut health and maintain an optimal feed efficiency, as shown with a trial conducted with Mastersorb Gold:

Table 4: Trial design, the impact of Mastersorb Gold on broilers challenged with zearalenone and DON-contaminated feed

	Control	Mastersorb Gold	Challenge	Challenge + Mastersorb Gold
Challenge	—	—	300ppb zearalenone and 6000ppb DON	300ppb zearalenone and 6000ppb DON
Additive	—	MSG (2 kg / MT of feed)	—	MSG (1 kg / MT of feed)

Figure 3: Average FCR for broilers, with or without zearalenone and DON challenge, with or without Mastersorb Gold supplementation



2. Improve nutrient utilization

Maximum use of the nutrients contained in the feed can be obtained with the help of feed additives that promote digestion. Targeting the animal, selected phytomolecules are used for their digestive properties. Focusing on the feed, specific enzymes can unlock nutrients and thus improve feed efficiency.

Phytomolecules support the animal's digestive system

Phytomolecules promote optimal digestion and absorption of nutrients by stimulating the secretion of digestive juices, such as saliva or bile, enhancing enzyme activity, and favoring good GIT motility (Platel and Srinivasan, 2004). FCR improvements thanks to the use of a phytomolecules-based product (Activo) are shown in figure 2.

Enzymes release more nutrients from feed

Enzymes can degrade arabinoxylans, for example. Arabinoxylans are the most common NSP fraction in all cereals – and are undigestible for monogastric animals. Enzymes can make these substances available for animals, allowing for complete nutrient utilization. Additionally, nutrients trapped due to the cage effect are released, altogether increasing the energy content of the diet and improving FCR.

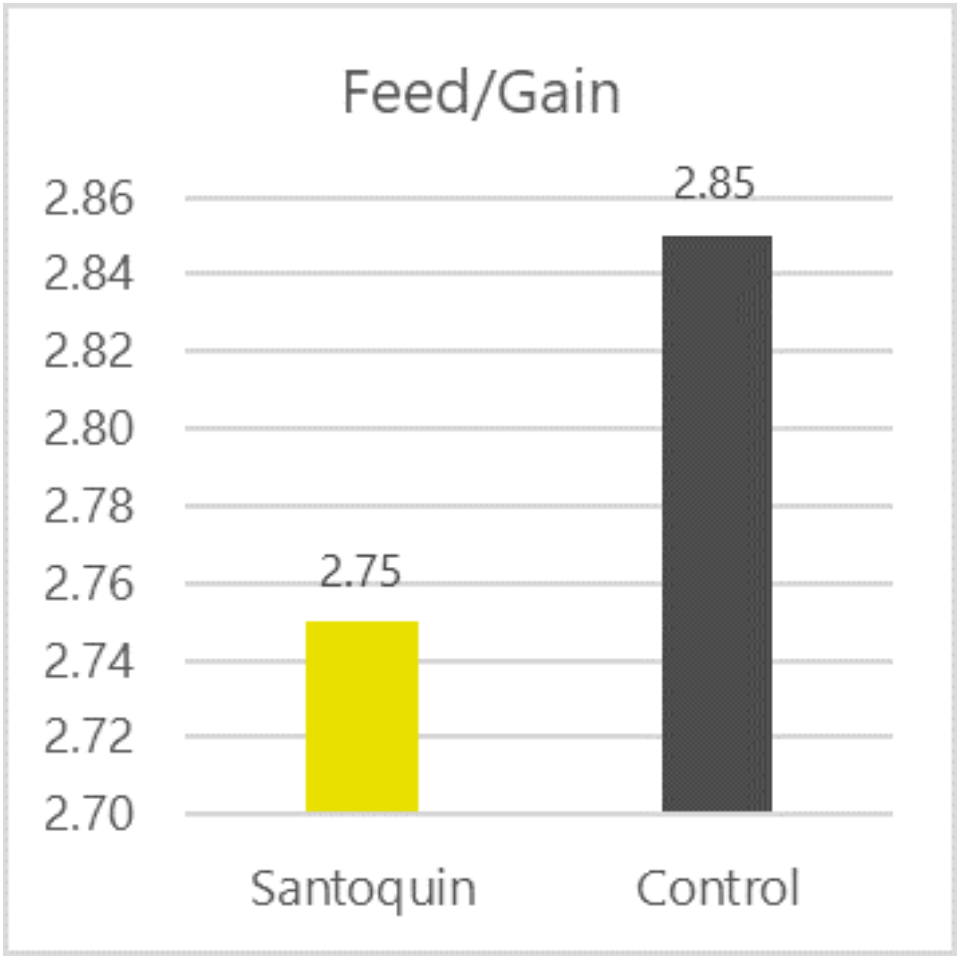
3. Be proactive about preserving feed quality

The quality of feed can deteriorate, for instance, when nutrients oxidize, or mold infestation occurs. Oxidation by-products promote oxidative stress in the intestine and may lead to tissue damage. Molds, in turn, take advantage of the nutrients contained in the feed and produce mycotoxins. Both cases illustrate the importance of preventing feed quality issues. Feed additives such as antioxidants and mold inhibitors mitigate these risks.

Antioxidants prevent feed oxidation

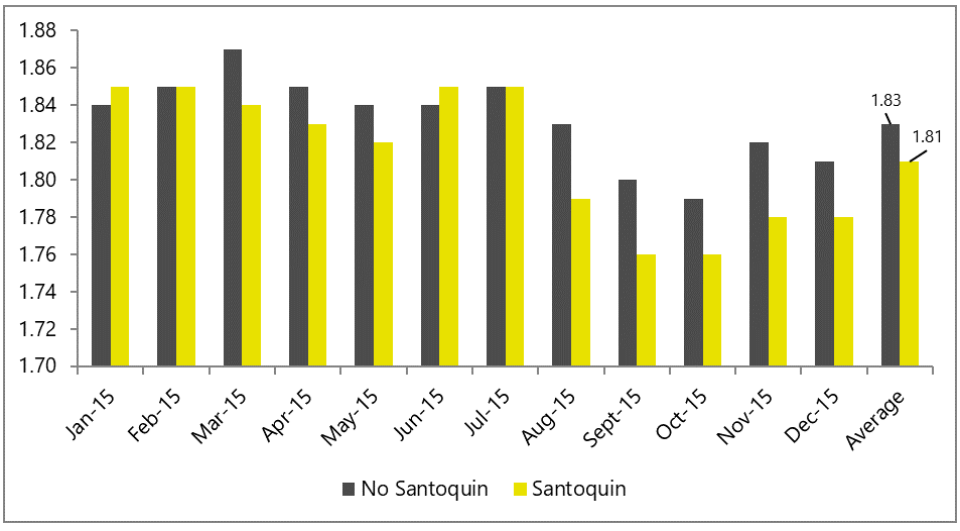
Antioxidants scavenge free radicals and protect the feed from spoilage. In animals, they mitigate the adverse effects of oxidative stress. Antioxidants in pig nutrition can stabilize DDGS and other fatty ingredients in the feed, maintaining nutrient integrity and availability. Figure 4 shows the FCR improvement that a producer in the US obtained when using the antioxidant product Santoquin in pork finisher diets containing 30% DDGS.

Figure 4: FCR improvement in pigs receiving Santoquin (trial with a Midwest pork producer)



In DDGS-free diets, which are more common in poultry production, antioxidants also help optimize FCR, as shown by the results of a comprehensive broiler field study in 2015 (figure 5).

Figure 5: FCR in broilers receiving Santoquin, compared to a non-supplemented control group



Inhibiting molds and keeping feed moisture

To round off the topic of feed quality preservation, one should consider mold inhibitors, which also play an essential role. Used at the feed mill, these products blend two types of ingredients with their different modes of action: surfactants and organic acids. Surfactants bind active water so that the moisture of the feed persists, but fungi cannot survive. Organic acids, on the other hand, have anti-fungal properties, directly acting against molds. Both actions together prevent the reduction of energy in the feed, keeping

feed efficiency at optimal levels.

Conclusion

The improvement of feed efficiency ranks as one of the most, if not the most, critical measures to cope with rising feed costs. By achieving optimal nutrient utilization, producers can make the most out of the available raw materials.

The feed industry offers diverse solutions to support animal producers in optimizing feed efficiency. Improving gut health, mitigating the negative impact of harmful substances, and maintaining feed quality are crucial steps to achieving the best possible FCR and, hence, cost-effective animal production.

References

Adam, F., and L. Bütfering. “Wann Müssen Meine Schweine an Den Haken?” top agrar. top agrar online, October 1, 2009. https://www.topagrar.com/schwein/aus-dem-heft/wann-muessen-meineschweine-an-den-haken-9685161.html.

Almeida, Leopoldo Malcorra, Vitor Augusto Zavelinski, Katiucia Cristine Sonálio, Kariny Fonseca da Silva, Keysuke Muramatsu, and Alex Maiorka. “Effect of Feed Particle Size in Pelleted Diets on Growth Performance and Digestibility of Weaning Piglets.” *Livestock Science* 244 (2021). https://doi.org/10.1016/j.livsci.2020.104364.

Chewning, C.G., C.R. Stark, and J. Brake. “Effects of Particle Size and Feed Form on Broiler Performance.” *Journal of Applied Poultry Research* 21, no. 4 (2012): 830–37. https://doi.org/10.3382/japr.2012-00553.

Gaines, A. M., B. A. Peerson, and O. F. Mendoza. “Herd Management Factors That Influence Whole Feed Efficiency.” Essay. In *Feed Efficiency in Swine*, edited by J. Patience, 15–39. Wageningen Academic, 2012.

Kolawole, Oluwatobi, Abigail Graham, Caroline Donaldson, Bronagh Owens, Wilfred A. Abia, Julie Meneely, Michael J. Alcorn, Lisa Connolly, and Christopher T. Elliott. “Low Doses of Mycotoxin Mixtures below EU Regulatory Limits Can Negatively Affect the Performance of Broiler Chickens: A Longitudinal Study.” *Toxins* 12, no. 7 (2020): 433. https://doi.org/10.3390/toxins12070433.

Patience, J. F. “The Influence of Dietary Energy on Feed Efficiency in Grow-Finish Swine.” Essay. In In *Feed Efficiency in Swine*, edited by J. Patience, 15–39. Wageningen Academic, 2012.

Patience, John F., Mariana C. Rossoni-Serão, and Néstor A. Gutiérrez. “A Review of Feed Efficiency in Swine: Biology and Application.” *Journal of Animal Science and Biotechnology* 6, no. 1 (2015). https://doi.org/10.1186/s40104-015-0031-2.

Platel, K., and K. Srinivasan. “Digestive Stimulant Action of Spices: A Myth or Reality?” *Indian J Med Res, pp 167-179* 119 (May 2004): 167–79. http://www.ncbi.nlm.nih.gov/pubmed/15218978

Richert, B. T., and J. M. DeRouchey. “Swine Feed Processing and Manufacturing.” Pork Information Gateway, September 14, 2015. https://porkgateway.org/resource/swine-feed-processing-and-manufacturing/.

Saldaña, B., P. Guzmán, L. Cámara, J. García, and G.G. Mateos. “Feed Form and Energy Concentration of the Diet Affect Growth Performance and Digestive Tract Traits of Brown-Egg Laying Pullets from Hatching to 17 Weeks of Age.” *Poultry Science* 94, no. 8 (2015): 1879–93. https://doi.org/10.3382/ps/pev145.

Vukmirović, Đuro, Radmilo Čolović, Slađana Rakita, Tea Brlek, Olivera Đuragić, and David Solà-Oriol. “Importance of Feed Structure (Particle Size) and Feed Form (Mash vs. Pellets) in Pig Nutrition – A Review.” *Animal Feed Science and Technology* 233 (2017): 133–44. https://doi.org/10.1016/j.anifeedsci.2017.06.016.