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.

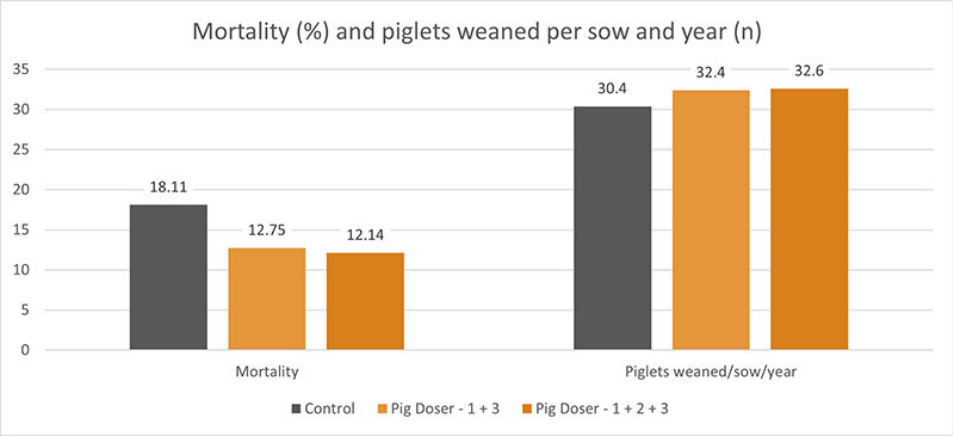
The answer was provided by Felix Klemperer (1893), a German internist researching immunity. He found that hens coming in contact with pathogens produce antibodies against these agents and transfer them to the egg. It is unimportant if the pathogens are relevant for chickens or other animals. In the egg,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

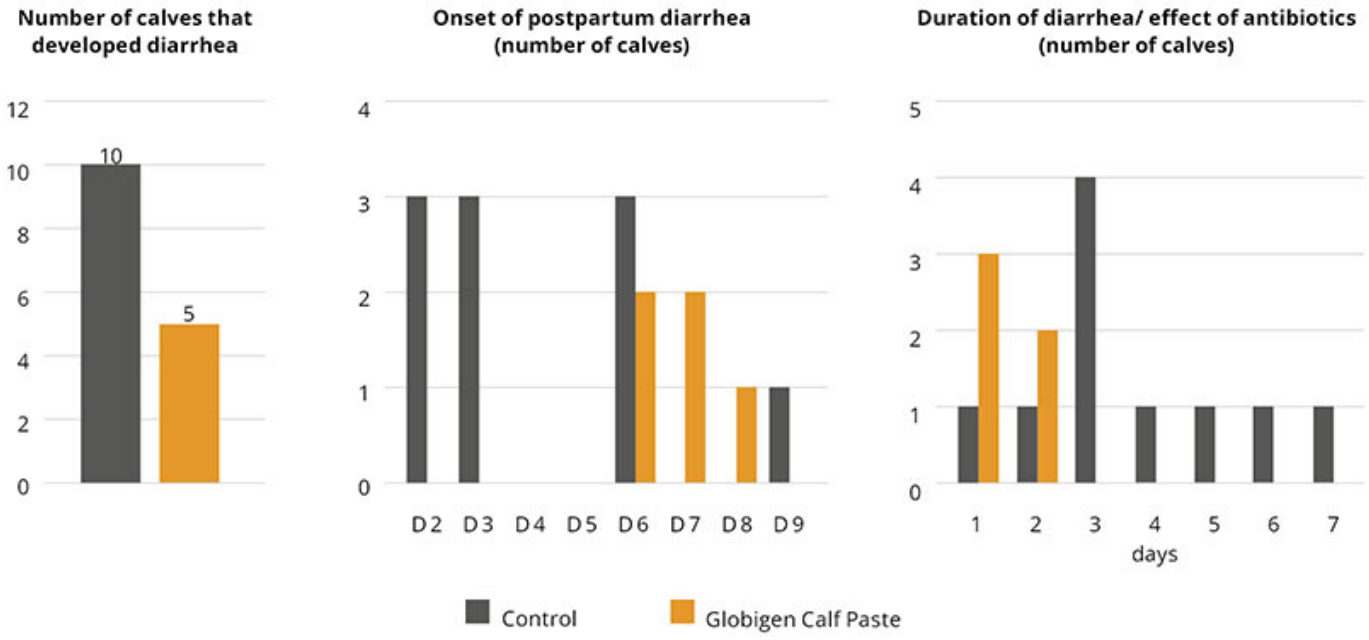
Trial proves high efficacy of egg immunoglobulins in piglets

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.

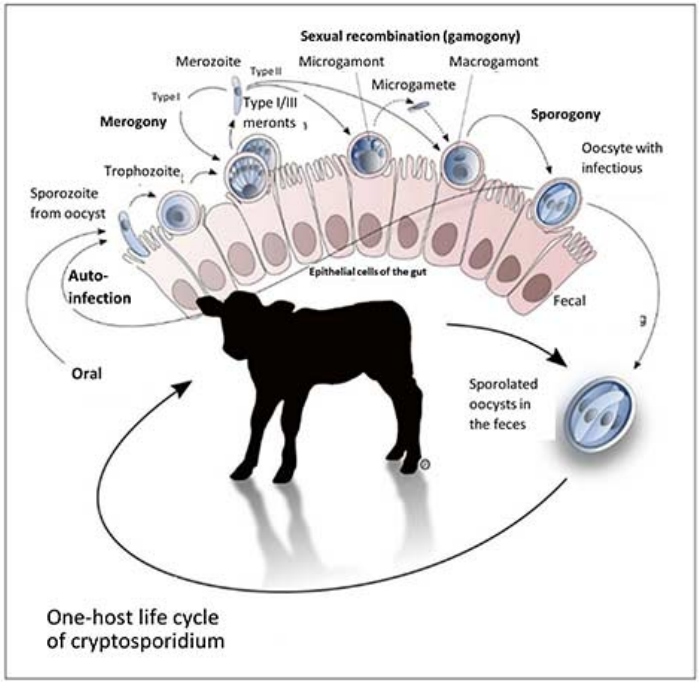


Figure 1 (Olias et al., 2018): Life cycle of cryptosporidia: ingested oocysts release four sporozoites that invade host enterocytes (intestinal epithelial cells). There, they develop into trophozoites before asexual and sexual reproduction ensues, and thin- and thick-walled oocysts are formed. Thick-walled 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.

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.

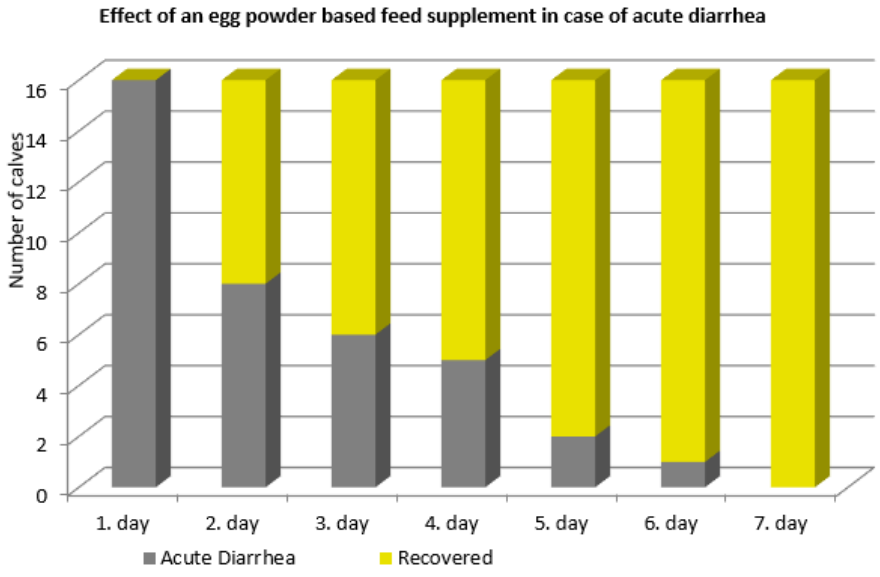
4. Calves need their special feed

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%).

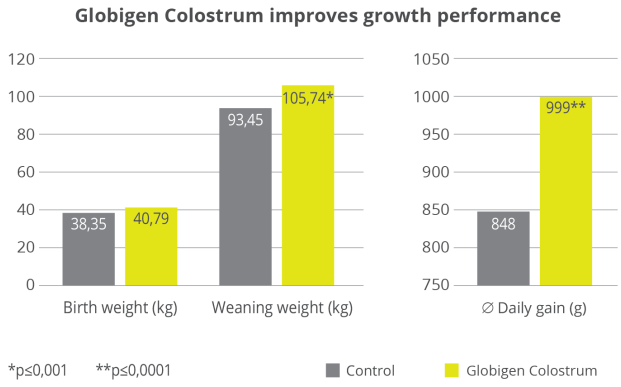
Immunoglobulins from the egg help calves against diarrhea

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

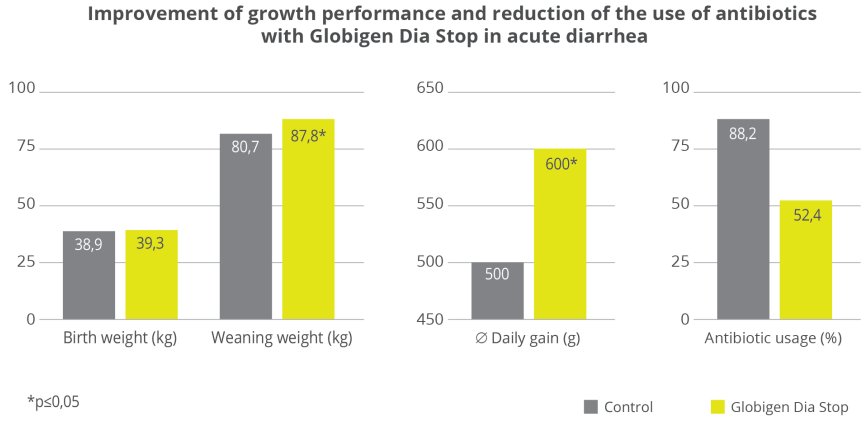
life, the diarrhea incidence per group was checked: while 73% of the calves in the control group had diarrhea, requiring antibiotics, only 1 calf of the trial group had diarrhea, and no antibiotic treatment was needed. On the second farm in the Moscow region, where the groups encompassed 20 calves each 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)

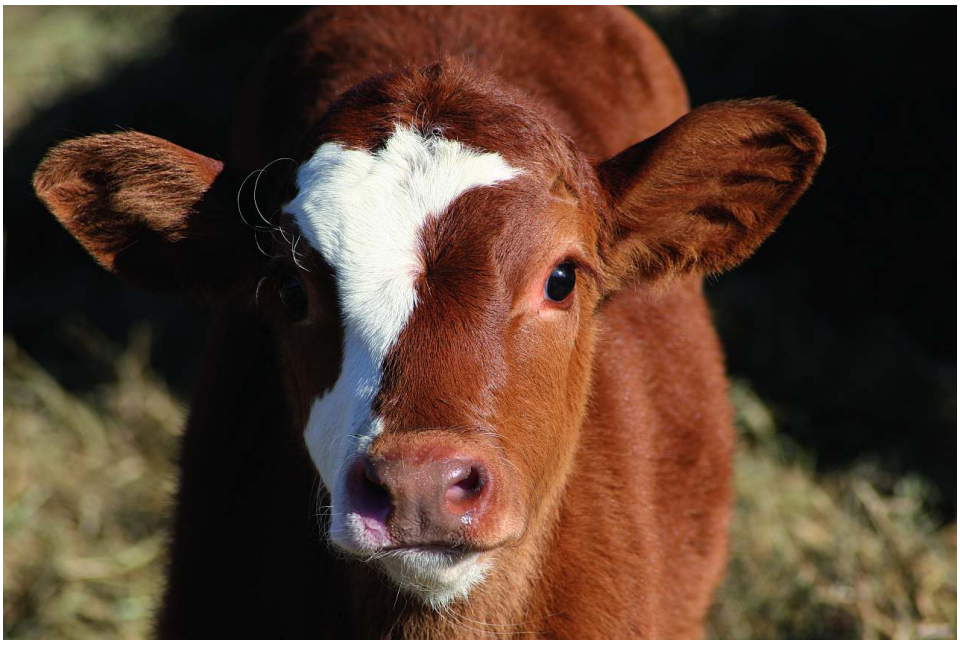
Conclusion: Egg immunoglobulins support gut health

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.

Diarrhea in calves: Causes, consequences, prevention

by Judith Schmidt, ProductManager On Farm Solutions, EW Nutrition

Although diarrhea is called a factor disease, strictly speaking, it is not a disease but a symptom. Diarrhea can be a protective function of the body. With the higher fluid volume in the intestine and its increased peristalsis, pathogens and toxins are excreted.



Common causes of diarrhea

Despite various electrolyte drinks available from the veterinarian or in stores, too many calves still die as a consequence of diarrhea. The economic damage for the farms is immense.

The causes of the occurrence of diarrhea are diverse. Infectious causes such as viruses, parasites, bacteria, fungi, and non-infectious causes such as insufficient colostrum supply, feeding, and housing have a significant influence.

The diet of the newborn calf has a significant influence on scours. The following factors are decisive:

- The immune status of the calves
- Inadequate/incorrect preparation of the liquids
- Inadequate drinking hygiene

The development of diarrhea

In the first three weeks of life, diarrheal diseases are the most common and economically impactful diseases in newborn calves. In the first weeks of life, 75 to 85 % of calf diseases are related to diarrhea. The reason for this is that calves are born without immune protection. Their immunity is primarily built up in the first twelve hours by the supply of colostrum. After that, the intestinal barrier is barely passable for the antibodies.

The four most important pathogens are Rotavirus and Coronavirus, Cryptosporidium, and E.coli. These pathogens damage the intestinal lining, leading to water and minerals not being absorbed from the intestine into the blood. The minerals, instead of being assimilated, are lost and eliminated through feces.

Bacteria such as E.coli attach to the intestinal wall and produce toxins. Viruses, on the other hand, penetrate the intestinal wall in order to multiply. Both of them result in damages to the intestinal wall, which can allow fluids to leak out. The result is diarrhea.

Symptoms of diarrhea

The most important symptoms are:

- Sunken eyes as an expression of dehydration
- Reduced intake of fluids
- Lying down
- Low temperature
- Cold body surface
- Apathy or even coma

Types of diarrhea

There are different types of diarrhea, mainly the secretory and the malabsorptive form. Because of frequent mixed infections, the two forms of scours are often mixed.

Secretory diarrhea

The binding of toxins to the enterocytes' cell surface receptors activates enzyme systems that lead to increased fluid secretion in the intestine. The intestinal lining can no longer absorb this increased fluid influx. The trigger for this can be, for example, an E.coli infection.

Malabsorptive diarrhea

The erythrocytes are destroyed and the villi are reduced in size. There is a loss of the microvilli. The result is a lower enzyme activity and resorption capacity. By this reduction in villi length, less fluid can be absorbed and has to be excreted through the intestine.

Importance of the colostrum supply

Low colostrum intake or a low quality of colostrum at birth results in the failure of passive transfer (FPT) due to the inadequate ingestion of colostral immunoglobulins. FPT is associated with an increased risk of mortality and decreased health status.

Adequate transfer of maternal immunoglobulins is associated with short- and long-term health advantages. These advantages are created by reducing pre- and post-weaning mortality due to infectious diseases, as well as by increasing daily weight gain, feed efficiency, fertility, and milk production in first and second lactation.

Colostrum is the elixir of life for newborn calves. As already mentioned, calves are born without their own active immune protection. Their immune system develops slowly. In order to obtain a first passive immunization, early administration of high-quality colostrum (≥ 50 mg IgG/ml) is of the highest importance.

The colostrum should be administered to calves as early as possible, but latest 4 to 6 hours after birth. The reason for early administration of colostrum is that the amount of immunoglobulins decreases with the passage of time after birth and with an increased milking number.

By the twelfth week, the calf has fully developed its own stable immune system and is therefore able to produce its own antibodies.

Economic consequences of diarrhea

The consequences of diarrhea and the associated costs should not be underestimated. Even a mild form of diarrhea costs the farmer money:

	Course of diarrhea			
	Heavy diarrhea		Light diarrhea	
	In €	In %	In €	In %
Costs for Vet Costs for drugs, electrolytes	75 € 72 €	56	45 € 30 €	69
Additional rearing days Additional rearing costs	9 days 30,60 €	12	4 days 13,60 €	13
Mortality rate Costs for mortality	13 % 48 €	18	2 % 7,40 €	7
Additional labor farmer Additional costs for labour	2,5 h 37,50 €	14	0,8 h 12 €	11
Overall costs	**263,10 €**		**108,00 €**	

How to avoid diarrhea in calves

It is primarily essential that the calf is protected from fluid losses and that active diarrhea is avoided. Measures can be taken in advance to prevent the newborn calves from diarrhea:

- Cleaning the calving pen after each calving
- Bringing the calves into cleaned and disinfected boxes
- Regularly checking the quality of colostrum

But the most important basic requirement for a healthy start into life is to give 2 to 4 liters of colostrum within the first six hours of life. In addition to the timing, the quality of the colostrum is crucial. To that end, EW Nutrition developed a colostrum enhancer that improves colostrum management.

IgY can bind foreign substances like bacteria or viruses in the gut, which improves gut health and increases weight gain. The natural egg immunoglobulins act like maternal colostrum and bind to the pathogen epitopes. After that, the blocked pathogens cannot bind to the intestinal wall, preventing damage to the intestinal wall. Field studies prove the product's efficacy, showing an 18 % higher daily weight gain and a 13 % higher weaning weight compared to the control group. Additionally, the IgG contained in Globigen Colostrum help you avoid a failure of passive transfer (FPT).

The application of Globigen Colostrum is very user-friendly and simple, as it can be mixed directly into the colostrum of the mother cow.

Higher profit through improved calf performance

The benefits of Globigen Colostrum are:

- Improved calf performance
- Lower incidence of diarrhea
- Improved weight gain
- Higher profit

The timely and adequate supply of colostrum is the most important factor in preventing infection-related calf diseases. Therefore, it is necessary to ensure that calves receive sufficient antibodies from the cow's colostrum in the first days after birth.

References available upon request

Diarrhea? Egg powder to the rescue

Another tool to reduce the use of antibiotics is the use of immunoglobulins from eggs. Trials showed that this product is effective to support a calf's start in life and also to offer support when challenged by various forms of diarrhoea.

The main cause for calf losses during the first two weeks of life is diarrhea. In general diarrhoea is characterised by more liquid being secreted than that being resorbed. However, diarrhoea is not a disease, but actually only a symptom. Diarrhea has a protective function for the animal, because the higher liquid volume in the gut increases motility and pathogens and toxins are excreted faster. Diarrhoea can occur for several reasons. It can be caused by incorrect nutrition, but also by pathogens such as bacteria, viruses and protozoa.

Bacteria in the gut
E. coli belong to the normal gut flora of humans and animals and can be mainly found in the colon. Only a fraction of the serotypes causes diseases. The pathogenicity of *E.coli* is linked to virulence factors. Decisive virulence factors are for example the fimbria used for the attachment to the gut wall and the bacteria's ability to produce toxins.

Salmonella in general plays a secondary role in calf diarrhea, however, salmonellosis in cattle is a notifiable disease. Disease due to *Clostridia* is amongst the most expensive one in cattle farming globally. In herbivores, clostridia are part of the normal gastro-intestinal flora, only a few types can cause serious disease. In calves, *Clostridium perfringens* occurs with the different types A, C, and D. *Rotaviruses* are the most common viral pathogens causing diarrhoea in calves and lambs. They are mainly found at the age of 5 to 14 days. *Coronaviruses* normally attack calves at the age of 5 to 21 days. *Cryptosporidium parvum* is a protozoa and presumed to be the most common pathogen causing diarrhoea (prevalence up to more than 60 %) in calves.

Undigested feed and incorrect use of antibiotics
Plant raw materials (mainly soy products) are partly used in milk replacers as protein sources. These products contain carbohydrates, that cannot be digested by calves which can lead to diarrhea. The transition from milk to milk replacer can also be a reason.

An early application of tetracyclines and neomycin to young calves can lead to a change in the villi, malabsorption and therefore to slight diarrhoea. Longer therapies using high dosages of antibiotics can also lead to a bacterial superinfection of the gut. The problem is that in a disease situation, antibiotics are often used incorrectly. The use of antibiotics only makes sense when there is a bacterial diarrhea and not due to viruses, protozoa or poor feed management. To keep the use of antibiotics as low as possible, alternatives need to be considered.

Egg powder to add immunoglobulins
In order to achieve optimal results in calf rearing two approaches are possible. Firstly, the prophylaxis approach. This is the method of choice as diarrhoea can mostly be prevented. Therefore, it is necessary to supply the calf with the best possible equipment. As antibodies are one crucial but limiting factor in the colostrum of the “modern” cow, this gap needs to be minimised. A study conducted in Germany in 2015 demonstrated that more than 50% of the new-born calves had a deficiency of immunoglobulins in the blood. Only 41% of the calves showed an adequate concentration of antibodies in the blood (>10 mg IgG/ml blood serum). Immunoglobulins contained in hen eggs (IgY) can partly compensate for poor colostrum quality and serve as a care package for young animals. A trial was conducted with an egg powder product* on a dairy farm (800 cows) in Brandenburg, Germany. In total 39 new-born calves were observed until weaning (65th day of life). Before birth, the calves were already divided into control and trial group according to the lactation number of their mother cow. All calves were fed the same and received four litres of colostrum with ≥ 50 mg IgG /ml on the first day of life.

Control (n=20): no additional supplementation
Trial group (n=19): day 1 – 5: 100 g of the egg powder product per animal per day mixed into the colostrum or milk.

It was shown that the calves in the trial group showed a significantly higher (13%) weaning weight (105.74 kg compared to 93.45 kg in the control group) and 18% higher average daily gain (999 g compared to 848 g in the control group) *(Figure 1 and Figure 2).*

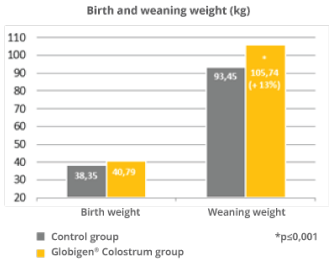


Figure 1: Effect of an egg powder product on weaning weight (kg)

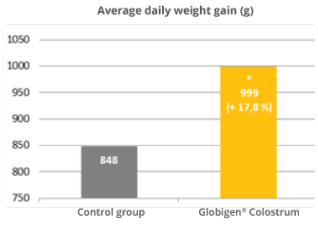


Figure 2: Effect of an egg powder product on ADG (g)

Support during acute diarrhea
When diarrhea occurs, the calf has to be treated. So the second approach is to find the best and quickest solution. It is not always necessary to use antibiotics, as they do not work against virus or protozoa. Egg antibodies can be an answer when combined with electrolytes as the following trial shows. On a dairy farm (550 cows) in Germany a feeding trial with a product based on egg powder and electrolytes** was conducted from December 2017 to May 2018. Two groups of calves were used. Before birth the animals were allocated into the two groups according to the calving plan and were examined from day one until

weaning (77th day of life). All calves suffering from diarrhea (38 in total, 17 in the control and 21 in the trial group) were treated as follows:

Control (n=17): Application of electrolytes
Trial group (n=21): 50 g of the egg powder and electrolytes product twice daily, stirred into the milk replacer until diarrhea stopped.

If the diarrhea did not stop or even got worse, the animals were treated with antibiotics. It was shown that in the control group the antibiotic treatment necessary was nearly twice as long as needed in the trial group (Figure 3). This means also that nearly twice the amount of antibiotics were used. This leads to the conclusion that calves in the trial group had an improved health status compared to calves in the control group. A further result from the improved health status was an increase in performance in the trial group (Figure 4).

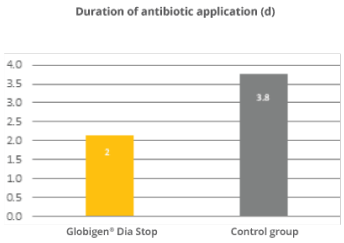


Figure 3: Duration of antibiotic application (d)

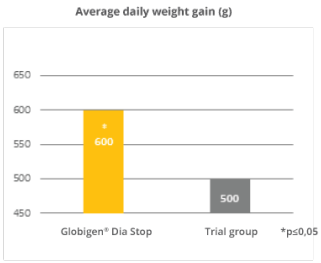


Figure 4: Effect on average daily weight gain (g)

The average daily weight gain of the trial group was 20% higher than in the control (600 vs. 500 g per day) leading to a significantly higher weaning weight (87.8 kg) than in the control (80.7 kg).

By Dr. Inge Heinzl, Editor EW Nutrition
Published in Dairy Global (Online and Printed), 10/2018