Egg immunoglobulins as a plasma replacer

Animal plasma has been widely used in piglet feeding, not only as a protein source, but also as a tool to reduce gastrointestinal disorders after weaning.
Drs FELLIPE BARBOSA and INGE HEINZL consider a safe alternative in order to keep animals healthy and*

to avoid loss of performance.

The recent developments surrounding the health risks associated with using animal plasma as a piglet feed ingredient is growing serious concerns in China. After the reported cases of African swine fever (ASF) commencing in August 2018, the Chinese government decided to ban the use of pig blood (and its by-products) in animal feed for some time.

The reason for the temporary ban of pig blood ingredients: African swine fever.
ASF is a viral disease of pigs and wild boars. The virus causes a lethal hemorrhagic disease in pigs. In some cases, the death of infected animals can occur during one week after the infection. There are no vaccines against the ASF Virus. When it hits the herd it is virtually impossible to stop its spread contaminating all animals.
Spreading of the virus occurs as follows:
• contact with contagious pigs from infected areas,
• contact with contaminated materials, being fed with kitchen waste and
• non-trusted animal origin feed ingredients.

Table 1: Performance of pigs weaned at 19 days of age fed for 15 days post-weaning a diet containing different plasma or fractions.

	Casein	Plasma	Albumin	IgG*	LMW**
Weight gain (g/day)	19[a]	134[b]	78[ab]	158[c]	50[a]
Feed intake (g/day)	181[a]	262[b]	244[ab]	273[b]	191[a]

Gatnau *et al.*, 1995
*Immunoglobulins; **Low molecular weight
rows with different superscripts are significantly different $p<0.05$

There is a risk of pig blood carrying different types of viruses like ASF virus. Therefore, from time to time the use of ingredients based on blood is questioned by pig producers. To minimise this risk, the use of ingredients derived from pig slaughterhouses (including animal plasma) in pig feed is no longer allowed in China. This measure will cause not only a protein deficit in piglet feeds but also reduced protection of weaned piglets when intestinal disorders are concerned.

Immunoglobulins from animal plasma and its benefits on reducing post-weaning diarrhea (PWD)
The use of animal plasma has a positive effect on post-weaning performance of piglets. It is generally known that as a palatable ingredient, animal plasma stimulates feed intake. This results in better growth and a higher post-weaning performance in piglets. However, a closer inspection on the mode of action of spray dried plasma reveals its properties as an immune-ingredient and shows its supporting effect on the overall health status of the animals. Scientific publications showed that the positive influence on growth when feeding plasma to piglets is mainly due to its “immunoglobulin fraction”. This assigns to plasma a specific role in nutrition of weaned pigs to prevent PWD and to reduce the need for antibiotics.

Egg immunoglobulins: a natural way of protecting weaned piglets
Globigen® Jump Start (EW Nutrition GmbH) is a functional and standardized product based on whole egg powder. It contains natural immunoglobulins (IgY – “immunoglobulins from yolk”) mixed with a carrier. IgY are cells of the immune system from birds similar to the IgG in mammals. They have the main function of identifying and neutralizing harmful substances in the body. IgYs are obtained through a non-invasive process and are natural ingredients from eggs. There is no connection with blood and slaughter by-products and therefore no risk of carrying animal diseases.
Globigen® Jump Start is used to support piglets during critical stages of life, as long as their natural immunity is not completely developed. Scientific data confirmed that the IgY present in egg powder are capable of supporting intestinal health and growth performance of newly weaned piglets. More recently, also the possibility of using immunoglobulins as alternatives to zinc oxide (ZnO) and in-feed antibiotics (Hedegaard et al., 2017; Li at al. 2015) were evaluated with promising results.

Table 2: Effect of IgY against diarrhea caused by bacterial pathogens in piglets.

Items			%		Outcome measured considered mortality (M) or diarrhea (D)
Prophylatic effect			Intervention	Control	
Reference	Pathogens	Piglet age			
Imberechts *et al.*	F18 + ETEC	Weaned (21-28d old)	33	66	D
			25	75	D
			0	25	M
Marquardt *et al.*	K88 + ETEC	Neonatal (3d old)	12.5	62.5	M
		Weaned (21-28 d old)	0	30	M
		Weaning (14-18 d old)	1.9	3.9	D

Adapted from Li *et al.*, 2015

Better results than plasma IgG: understanding the antigens causing post-weaning diarrhea

Animal plasma is a by-product of the meat industry. The animals slaughtered were possibly exposed to various diseases over their whole life. It cannot be considered as a standardized product in terms of immunoglobulins (either quantity nor quality). The Ig contained could be useful but also totally useless, depending on the pathogens the animals have been confronted with. As a source of immunoglobulins Globigen Jump Start is a costefficient and effective alternative to replace plasma in piglets' diets. Its IgY content will have the same protection effect in the gut as IgG, but the nutritionist will have the possibility of choosing different protein sources in the market, either because of price or availability of raw materials. Our recommendation is that 40kg of plasma can be replaced by 2kg of Globigen Jump Start supplied with different high digestible protein sources.

A piglet trial was conducted with the objective of evaluate the efficacy of egg immunoglobulins on performance parameters of weaned piglets and to evaluate it as a substitute for animal plasma. Piglets were challenged with F4 and F18 entertoxic E. coli (ETEC) strains and feed either 2kg of Globigen Jump Start (GJS) or 40kg of spray dried plasma (SDP) in the weaner diet. The comparison was also done to a negative group (NG – microbiological challenge and no protection in the diet); and a positive group (PG – no microbiological challenge and antibiotics + ZnO in the diet).

Piglets from NG had lower feed intake, weight gain, and feed efficiency than animals from PG. The same was observed for piglets from GJS and SDP group. However, the impact of bacterial challenge on weight gain was lower for GJS piglets than for SDP (-14% and -52% when compared to PG); whereas feed intake was similar for both groups (-13% and -14% when compared to PG). The results showed that piglets receiving GJS where more efficient on converting feed into growth even when challenged when compared to SDP animals.

Table 3: Effect of IgY compared to plasma on performance of challenged piglets.

Parameters	1 to 7 days after adaption period								
	NG	GJS	SDP	PG	NG ← → PG	NG ← → GJS	SDP ← → GJS	SDP ← → GJS	SDP ← → PG
Feed intake (kg)	1.46^{a}	2.16^{ab}	1.93^{ab}	2.47^{b}	-41%	-32%	-13%	-11%	-14%
Weight gain (kg)	0.78^{a}	1.88^{bc}	1.04^{ab}	2.19^{c}	-64%	-58%	-14%	-44%	-52%
Feed efficiency (kg weight gain / kg of feed)	0.39^{a}	0.80^{ab}	0.45^{ab}	0.89^{b}	-56%	-52%	-10%	-44%	-49%

different superscripts within the row are significantly different $p<0.05$

Trial conclusion

In this trial, the product based on egg immunoglobulins showed better influence on the performance of piglets than blood plasma. This may be due to the fact that the quality of the plasma depends on the animals slaughtered and on their contact with diseases, determining how much and which antibodies are available in this feed.

Additionally, blood plasma includes the danger of infectious diseases.

Safe and standard: free of swine related diseases and ruminant material
EW Nutrition clearly understands the importance of maintaining standardisation. It is a key factor for the customers to have a product that they can depend on every day.
Therefore, trough specific steps during the production of Globigen products, EW Nutrition ensures product quality. During production, all eggs are pasteurised and dried to a whole egg powder. In between steps include microbiological analysis, Salmonella, and avian disease controls to ensure the final product is free of the mentioned threats. Furthermore, as Globigen products are originated from laying hen farms there is no risk of contamination with any swine disease, like the devastating ASF. Finally, Globigen products do not contain any raw materials produced from, or substances derived from ruminants nor do the products come in contact with risk materials during the whole process (not be at risk for carrying transmissible spongiform encephalopathy or bovine spongiform encephalopathy – BSE).

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Understanding the dangers of mycotoxins for breeder hens

Breeding hens are a valuable asset for the poultry industry, as they produce the hatching eggs and day-old chicks. It is therefore important to manage contamination as well as possible. Mycotoxin management is part of that.

As the producers of hatching eggs and day-old chicks, breeding hens are the backbone of the poultry industry. Hence it is common practice to pay particular attention to this valuable asset's feed, selecting raw materials of high nutritional quality and safety. However, in any feed formulated for animals in production and reproduction, studies show that it is almost inevitable to find a certain level of mycotoxin contamination.

Mycotoxins exert toxic effects mainly on the gastrointestinal tract, liver, and kidneys and can accumulate in some tissues but also in the eggs. Mycotoxin contamination in breeding birds rations does not always

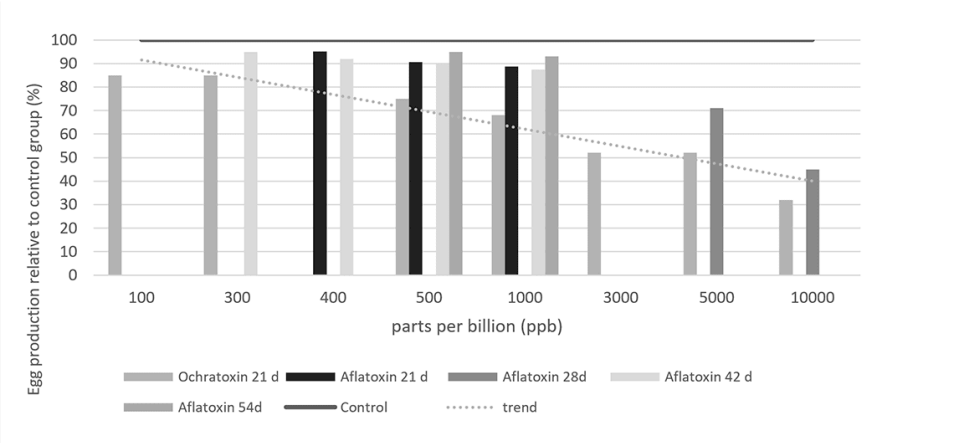
lead to visible symptoms, such as when trichothecenes cause oral lesions. However, it may influence productivity, egg quality, hatchery performance, as well as chick quality and immunity. Mycotoxin risk management is thus an essential part of managing breeder hens.

Type of mycotoxin and exposure time determine effect on egg production

Mycotoxicosis in hens can cause reduced egg production, most likely because it causes a decrease in protein synthesis. A lower synthesis of albumin results from a degeneration of the liver tissue due to aflatoxin, ochratoxin, T2 and DON exposure. The liver then may look pale, friable and occasionally shows superficial haemorrhages.

The contamination levels at which these effects can be observed are as low as 100ppb in feed, for example during a 21 day exposure to ochratoxin (*Figure 1*). With increasing levels of the toxin, production further decreases. A similar effect is observed when breeder hens are exposed to aflatoxins.

Figure 1 – Effect of mycotoxins on egg production, compared to non-contaminated control (=100 %).



Egg production, however, is not the only parameter that is affected when breeding hens are exposed to mycotoxins. Earlier on in the reproductive cycle they already impact on embryonic mortality and hatchability. These effects are potentially more severe and may even occur without any noticeable change in the number of eggs produced.

Mycotoxins' insidious consequences for eggshell quality and embryonic mortality

The eggshell is important to protect the progeny: thin and fragile shells can increase embryonic mortality, lower embryonic weight gain and decrease hatchability. Egg shell quality is a function of the hen's calcium and vitamin D3 metabolism. The bioavailability of calcium and of vitamin D3 depends on intestinal integrity and on the production of enzymes and transporters that aid in feed metabolism. These processes can be adversely affected by aflatoxins, DON, T2, and Fumonisins.

The gastrointestinal tract is not the only site of mycotoxin action, however. Mycotoxins such as aflatoxins and ochratoxins have nephrotoxic effects, affecting calcium metabolism and increasing its excretion via the urine, while lowering its levels in blood serum.

Moreover, mycotoxins damage the liver, which plays a central role in egg production, being responsible for vitamin D3 metabolism and the synthesis of the lipids that make up the yolk. Moreover, the synthesis of

transporters for lipids, calcium and carotenoids – important components of the egg– also takes place in liver. When liver function is impaired, the internal and external quality of the egg declines, which, in the end, affects the production of day-old chicks.

Figure 2 – Effects of mycotoxins on eggshell quality and embryonic mortality.

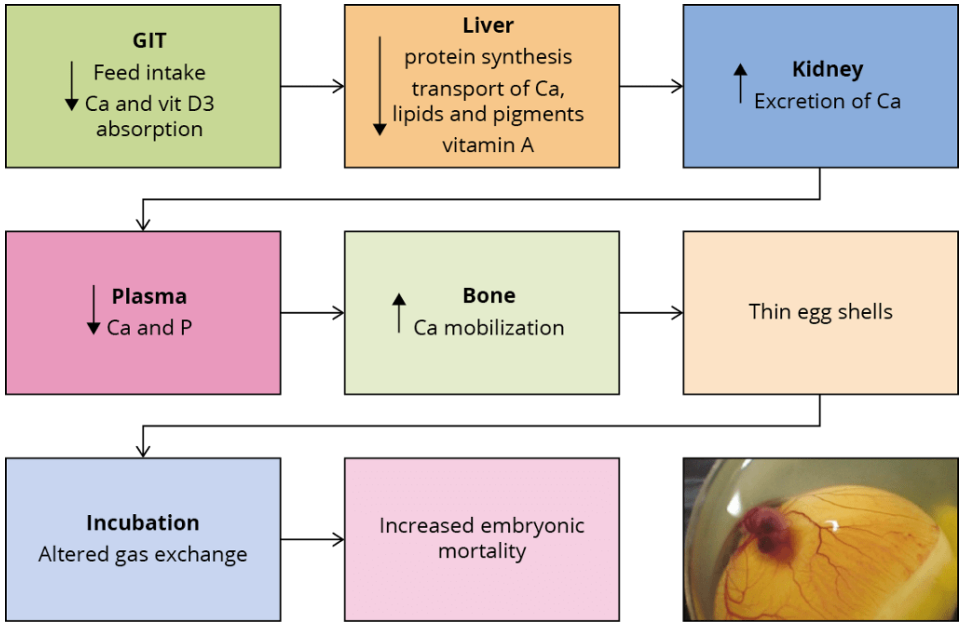


Figure 2 summarises the possible ways in which mycotoxins can negatively affect eggshell quality and, as a consequence, increase embryonic mortality. If a hen's intestinal integrity is compromised, the utilisation of nutrients decreases. Liver and kidney damage leads to a diminished availability of calcium and other nutrients necessary for egg formation. The birds' calcium (and phosphorus) levels in the plasma are then lower and may lead to a greater mobilisation of calcium from the bones. However, this response cannot be maintained and the eggs get a thinner shell.

The thickness of the eggshell influences the egg's moisture loss and exchange with the environment during the incubation period. An eggshell of optimal quality does not allow the loss of nutrients and prevents bacterial contamination. Thinner eggshells are less able to fulfil these functions, leading to higher embryo mortality.

Figure 3 – Effects of mycotoxins on embryonic mortality

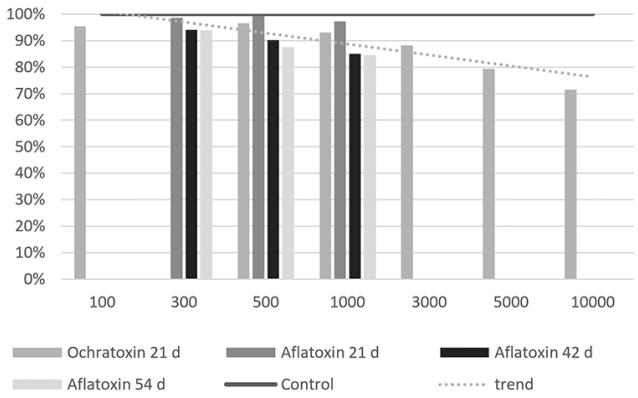


Figure 3 shows the effect of different mycotoxins on embryonic mortality. Incremental levels of ochratoxin

or aflatoxin heighten embryonic mortality in a range from 1.5 to 7.5 times the embryonic mortality of the control group. In some cases, embryos are affected even when the hens received feed contaminated with mycotoxin levels that are within the guidelines suggested by the EFSA.

For example, an exposure to 4900ppb of DON for ten weeks increases the number of embryos with abnormalities. The causes are not entirely clear, as only traces of DON can be found in the egg. However, we do know that this mycotoxin can affect the protein synthesis at the level of the hen's liver and therefore compromise the deposition of nutrients into the egg.

Mycotoxins' effects on the progeny may cause long-term damage

Ochratoxin and aflatoxin can be transferred into the egg, where they exert toxicity on the embryos. This does not necessarily result in mortality. However, the chicks can suffer from a compromised immune function due to two reasons: lower transmission of antibodies from the hen and lower viability of the chickens' immune cells, accompanied by a lower relative weight of the bursa of Fabricio and the thymus.

When both aflatoxin and ochratoxin are present in the feed, the effect on these parameters is synergistic. As a consequence of mycotoxin contamination, the animals' immune response is impaired, which makes them more susceptible to infection. The final result could be an increased early chick mortality due to a higher incidence of bacterial and viral infections.

The transmission of other mycotoxins into the egg is minimal. While this means that a direct effect on the progeny is unlikely to occur, mycotoxin contamination still has a snowball effect: we have to consider the indirect effect of a lower deposition of nutrients on chick quality.

Prevention is key: mycotoxin risk management for breeder hens

The best approach to manage mycotoxin risk is to implement an integrated strategy that includes good crop and grain storing practices, regular raw material sampling and mycotoxin evaluation and analysis. Management tools (such as MasterRisk) can help to evaluate mycotoxin interactions and to choose the best strategy for dealing with specific mycotoxin challenges.

The results of mycotoxin analyses can be used to take decisions regarding the inclusion levels of raw materials and in choosing feed additives that counteract mycotoxins. Products based on plant extracts, yeast cell walls and clay minerals can help to stabilise a digestive system challenged by mycotoxins. They support the barrier function in the intestine, preventing the passage of mycotoxins into the bloodstream.

Phytomolecules are another piece of the puzzle: thanks to their antimicrobial, anti-inflammatory and antioxidant properties, they support liver function. This is particularly important for long-living animals prone to accumulating mycotoxins in their body tissues.

For a long time the "deleterious effects" of mycotoxins on breeder hens and "their repercussions on progeny health status and performance have not received from a scientific point of view as much attention"(Calini and Sirri, 2007) as they ought to have. However, now that the dangers of mycotoxins for breeder hens' welfare, health and performance are better understood, it is clear that mycotoxin risk evaluation and management is central to successful poultry production.

Read Mycotoxins: Their effect in breeder hens, the full article

ALL ABOUT FEED, Mycotoxins, Background, 31.October.2018