Supporting the immune system of piglets

This paper was presented at the
feedQC Pig Feed Quality Conference
Ho Chi Minh City 9-10 April 2015

Piglets with insufficient immunity cannot cope well with stressful situations as they are more prone to pathogen infection, most likely causing diarrhoea. It is not only that cost and mortality increase when piglets get sick, but also and perhaps most importantly, their full performance potential for growth cannot be achieved. FELLIPE FREITAS BARBOSA and INGE HEINZL* report that strengthening the immune system by supplying natural egg immunoglobulins is a feasible alternative in swine production.

Fellipe Freitas Barbosa

Inge Heinzl

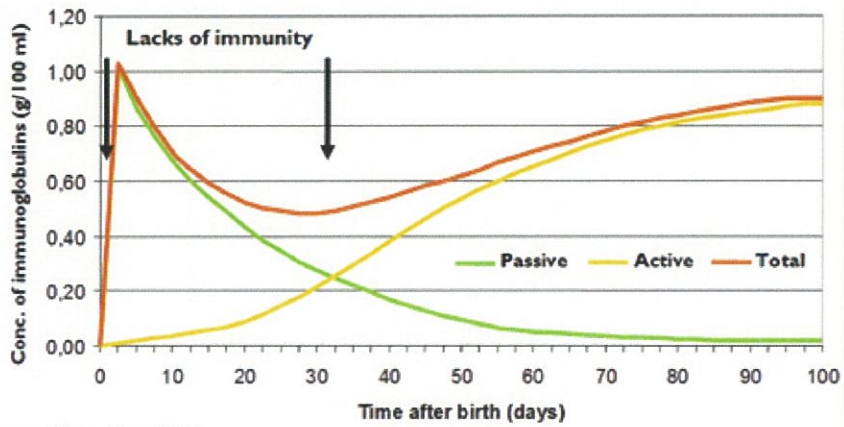
The immune system is extremely organised and consists of different cells acting according to specific functions. Some cells of the immune system have to 'identify' that there's a foreign substance in the organism and show it to the rest of the complex system; some others are tasked to receive or send commands of attack; and finally there are those made to kill and/or neutralise the 'enemy' or the toxins produced by the enemy. As part of this defensive force, there is a group of proteins extremely efficient and considered as the most powerful line of defense against pathogens. Their role is to identify and neutralise foreign substances in the animals' body, such as bacteria, viruses, and protozoa. These proteins called immunoglobulins are natural globular proteins produced by animals as part of their own immune system. Facing an 'invasion' the body produces immunoglobulins against specific pathogens, to disable these potential harmful substances.

The dominant class of immunoglobulins circulating in the blood of mammalians is IgG's. The functional equivalent immunoglobulins to IgG in birds are immunoglobulins of the IgY class, which constitute the majority of the circulating immunoglobulins. IgY is selectively transferred from the serum into the developing egg to passively protect the chick embryo from harmful substances or pathogens, similar to the transplacental transfer of maternal antibodies to mammalian foetuses. Although functionally equivalent, IgG and IgY are markedly different in structural and physiochemical properties, which might explain the variability, comparing their effectiveness against different antigens.

Immunity in young animals

Young mammalians are protected against diseases by specific antibodies. These are provided by their mother through milk (passive immunity) or they are produced by the organism after contact with a pathogen (active immunity). Unlike to what happens with humans, the maternal barrier between the foetus and the womb of some animals impedes the transference of parental immunity to the progeny (epitheliochorial placenta). Therefore, in many cases young animals are born without an own immune protection. The supply of

Figure 1: Development of immunity in young animals.



Source: Sieverding, 2000

antibodies from colostrum (passive immunisation) shortly after birth is therefore of vital importance. However, the colostrum quality and the quantity available per piglet, especially with the increase of piglets/sow, can be quite variable and not always the whole litter will have enough colostrum (and passive immunisation) coming from the sow. In addition, it is well known that the IgG level in the sow colostrum decreases rapidly during the first hours after farrowing and milk IgG level is quite low. The maternal protection therefore is getting weaker during lactation. This is a too short period of time for the piglet to completely develop its own immune system.

The second critical period for a young pig is the time around weaning. The well-known stressful moment of change in piglet's life (feed change, associated with a period of stress and fasting; environmental changes and mixing of litters) normally leads to a reduction in growth, negatively impacting the subsequent performance of the piglets.

Two important moments on piglet's life, when the young animal is lacking immunity and susceptible to intestinal disturbances, diarrhoea and reduced performance must be considered:

- Right after birth, before passive protection provided by colostrum starts working
- The first weeks after weaning, when passive protection decreases and the animals' own immune system is still not developed

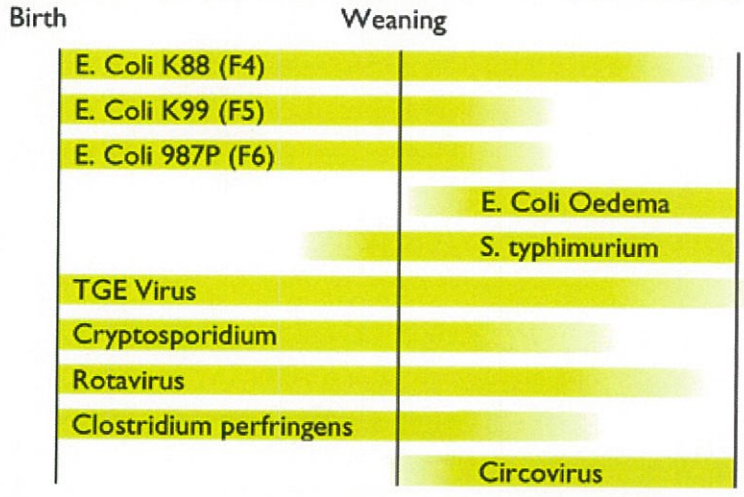
Due to damages in the intestinal villi architecture, the 'new' grain-based diets will not be well absorbed after weaning. Non-digested feed ends up as a substrate for the multiplication of pathogenic bacteria. These harmful bacteria disturb the balance of the microflora by competitive exclusion of beneficial microbes, causing the severe symptoms of diarrhoea. Different strains of enterotoxigenic *E. coli* (ETEC) are associated with diarrhoea in weaned piglets and, as a consequence, with significant losses during the first weeks post-weaning. The fimbrial types F4 and F18 are related to diarrhoea in weaned piglets and the fimbriae from these pathogens will attach to the microvilli surface initiating bacterial colonisation. However, also other pathogens of bacterial, viral and eukaryotic origin must be taken into consideration, when developing efficient strategies to prevent diarrhoea (Figure 2).

During the periods of low immunity, supporting the immune system of the piglets is an important strategy. This can be done by feeding immunoglobulins effective against these potentially harmful pathogens.

Egg immunoglobulins to support the immune system of young animals

The idea goes back to practical experience of farmers who fed eggs to ill or weak animals. An explanation was delivered by Dr. Felix Klemperer in 1893 when he observed that mice fed with eggs from hens confronted with tetanus bacteria didn't get ill when challenged with tetanus. He concluded that hens transferred antibodies against these bacteria into the egg. As we know now, laying hens produce IgY related to the pathogenic challenges they have experienced. Therefore, if hens are challenged with different pathogens they will produce antibodies linked to these pathogens. Based on this knowledge the methodology and processing technologies have been adopted to enable large scale production of antibody enriched egg powders. Laying hens are challenged with antigens to produce eggs with high content of corresponding antibodies. The eggs are then collected, pasteurised and dried to a whole egg powder. During the whole process, strict quality control must be adopted to ensure that the eggs used have no microbiological contamination. Several scientific studies have shown that IgY can bind to bacteria, virus and protozoa like *Clostridium perfringens*, *E. coli*, *Salmonella typhimurium*, *Rotavirus*, and *Cryptosporidium* and therefore can reduce the incidence of diarrhoea in young animals such as

Figure 2: Common pathogens causing diarrhoea in piglets before and after weaning.



piglets and calves.

Numerous university and field studies have demonstrated that IgY's from the egg, fed as an egg powder via the diet, milk replacer or directly as a doser serve as a potent supplement to support the immature immune system of young animals. The IgY's have an important role in filling this 'gap of immunity', attaching to the antigens in the intestine, the same environment where the pathogens causing diarrhoea proliferate and colonise.

Different immunoglobulin sources are available in the market as for instance bovine colostrum, whey protein concentrate/isolate, and spray dried animal plasma. These products in general are not standardised products in terms of immunoglobulins content (quantity and specificity of antibodies). The immunoglobulin fraction of the spray dried plasma, for instance, is mainly responsible for the increased performance of weaned piglets. In conclusion of these results, the inclusion of egg powder to weaning diets may also improve pig performance by promoting better overall health status. Furthermore, mortality and the use of antibiotics to control intestinal disorders can be reduced.

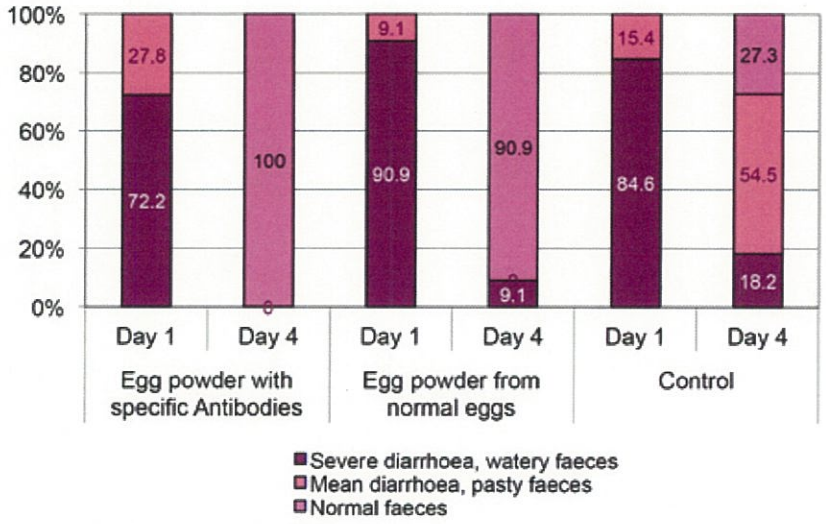
What is the mode of action of these antibodies?

Ideally, diarrhoea causing pathogens should be neutralised directly in the gut to prevent them from binding to the intestinal wall. For this purpose, antibodies with specificity towards the fimbriae (E. coli) or adhesive proteins (Rota and Corona virus), blocking the pathogen's binding site for the intestinal wall, would be a possible solution. Egg immunoglobulins are orally ingested and become available in the gastro-intestinal (GI) tract. Although their mode of action is not yet fully understood, IgY possess some characteristics which allow them to support a healthy animal performance;

Inhibition of bacterial attachment and neutralisation of virus – specific IgY are able to recognise disease-causing pathogens, adhere to them, block the binding sites and thus inhibit the attachment and invasion to the host's gut wall. Shedding of neutralised germs is facilitated, thus decreasing the environment's pathogenic load.

Agglutination – IgYs are able to agglutinate motile antigens, like flagellated bacteria. This immobilisation allows for easier elimination of pathogens by macrophages, which actively remove them by invagination. Via this process the natural immune status of the host is enhanced.

Figure 3: Effects of egg powder with specific antibodies compared to egg powder of normal eggs and to a diet without any egg powder (control) on piglet diarrhoea.



Source: Kellner *et al.*, 1994

Experimental data

The positive effect of normal eggs and the even better effect of eggs from hens hyper-immunised against relevant pathogens is clearly shown in Figure 3. Even powder from normal eggs, which contains a lot of different but not necessarily relevant antibodies, could decrease the duration of diarrhoea. On the first day (beginning of the trial) all animals suffered from diarrhoea. After the application of egg powder with specific antibodies (1st column), on day four, there was no more diarrhoea. In the group of pigs fed with normal eggs, still 9% of the animals suffered from diarrhoea on day four, the rest having been cured. In the control group (no egg antibodies) only 27% were free of diarrhoea, the rest still suffering from heavy- (18%) or medium-intensity (55%) diarrhoea.

In a study to evaluate whether it is possible to support the immune system of piglets during the first weeks of life by feeding egg immunoglobulins, six litters were divided into an experimental group (three litters; ø 10.97 piglets/litter) and a control group (three litters; ø 10.94 piglets/litter). Piglets of the control group, besides routine prophylactic program applied in the farm, did not receive any preparations, while piglets of the

Table 1: Hematological parameters measured in piglets after prophylactic application of an egg powder based product (EP)

Investigated parameter	Unit	Day 0	Average values ± SD 7th day of life EP	Control
Erythrocytes	10^{12}/L	4,77 ±0,77	4,90 ± 1,61	4,56 ± 0,18
Haemoglobin	mmol/L	9,15 ± 1,57	9,47 ± 2,71	9,55 ± 1,63
Leukocytes	10^9/L	7,97 ± 3,41	11,73[2] ± 2,08	7,05[2] ± 0,64
Lymphocytes	10^9/L	2,62 ± 0,73	7,03[2] ± 1,97	3,1[2] ± 0,57
	%	36 ± 6,00	60[2] ± 5,77	45[2] ± 4,24
Monocytes	10^9/L	0,85 ± 0,24	1,63[2] ± 0,15	0,95[2] ± 0,21
	%	10,75 ± 2	13 ± 1,57	13 ± 1,44

[1] Statistical significance $\alpha \leq 0.01$; [2] $\alpha \leq 0.05$; 3) $\alpha \leq 0.1$

Table 2: Incidence of diarrhoea and mortality.

	Piglets showing diarrhoea symptoms			Piglets dead due to diarrhoea	
	Number/litter	N / litter ø	%	N / litter ø	%
Egg Powder	10.97	1.95	18.76	0.37	3.37
Control	10.94	2.94	27.21	0.59	5.39

experimental group preventively received a product based on egg powder during the first three days of life at doses recommended by the manufacturer (2 mL/piglet during the first 12 hours of life, 1 mL/piglet on the second and on the third day of life, respectively). The product was orally administered to all individual animals. Blood samples of both groups were collected on day 0 (before administration of egg powder product to the experimental group), on day 7, 14 and 28 of life. Total count of leucocytes, counts of lymphocytes, neutrophils and other immune system parameters were evaluated. Furthermore incidence of diarrhoea symptoms and mortality due to intestinal problems were evaluated. In the group treated with egg powder, immune cells in the peripheral blood were significantly elevated compared to the control group at the 7th day of life (Table 1). The amounts of lymphocytes and monocytes – indicators for specific immunological defense – were significantly increased as well at day 7 whereas the total amount of granulocytes – indicator for innate, unspecific immune defense - remained constant. The piglets fed with the egg powder product hence showed a higher level of specific immune defense already within the first days compared to the animals undergoing the normal prophylaxis.

In addition, supporting the observed improvement of immune status, the piglets of the control group showed a nearly 1.5 fold higher incidence of diarrhoea and 1.6 fold higher rate of mortality (Table 2). From these data we can extrapolate that one of the most beneficial modes of action of egg immunoglobulins is their pathogen neutralising capacity directly in the gut that prevents them those from causing diarrhoea.

Conclusion

Due to the application of egg antibodies, piglets can start in good immunological condition shortly after birth and therefore obtain a good resistance against the commonly occurring diseases. This leads to a decrease of diarrhoea, costs for medical treatment, and mortality rates. At the end, a healthier piglet will always have the potential to perform to its full capacity resulting in higher output, lower costs, and therefore higher profit. AP

Fellipe Freitas Barbosa (fellipe.barbosa@ew-nutrition.com) Globigen Product Manager and Inge Heinzl (inge.heinzl@ew-nutrition.com) Technical Manager, Marketing Department are with EW Nutrition GmbH, Germany. A list of references is available from the first author on request.