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Science & Solutions

Endotoxins a Hidden Danger

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More Sow Milk for Piglet Performance

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What's Wrong with My Pigs?

Part 5: Rectal Prolapse

Editorial

A Fruitful Reminder

When low pork prices persist, pig producers quickly turn to cost reduction, focusing on nutritional costs. Feed cost represents approximately 70% of the total production cost. Since feed additives have the higher cost per weight of product, at first glance constraining feed additive use seems to be an obvious strategy. But is it the right one?

No. The common mistake is to calculate expenditures for feed additives without considering the many benefits. When chosen and implemented wisely, additives have the potential to maintain health, promote growth, improve feed efficiency and finally increase profitability. Even with low prices, we regularly see return on investment that justifies the expense. Moreover, withdrawal may pose a threat to animal well-being by, for example, allowing pathogens to thrive. A higher pathogen load and more health issues can compromise performance that requires a huge effort to regain by the time prices recover.

In this issue of **Science & Solutions** we reveal the hidden threat of endotoxins, their negative effects on animals and humans, and risk mitigation tips. Then we focus on one crucial bottleneck for pig production –milk yield– that can limit the growth of modern, large litters. We demonstrate the benefits that Digestarom® –a phytogenic feed additive– can bring in terms of milk production and pathogen control. Finally, this issue introduces the fifth installment of the differential diagnosis series, this time covering the multifactorial rectal prolapse.

Enjoy the reading and do not forget: Unlock the hidden profits!

Kostantinos SARANTIS
Technical Sales Manager Swine

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The Hidden Dangers of Lipopolysaccharides

By **Diego Padoan** DVM, BIOMIN Swine Technical Sales Manager EMA

Lipopolysaccharides pose a serious and often overlooked risk to pigs. Several tips can help limit their negative impacts.

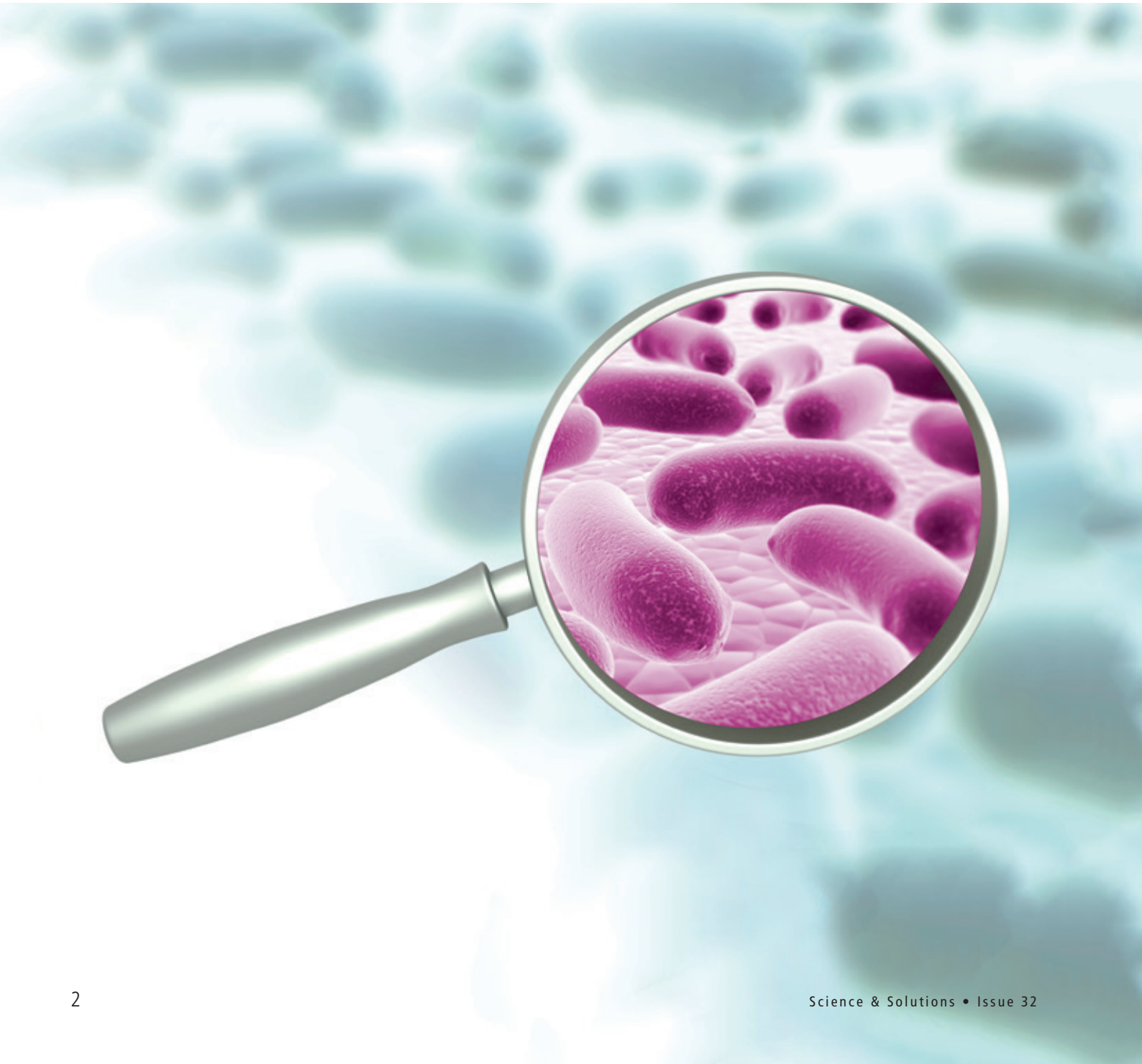
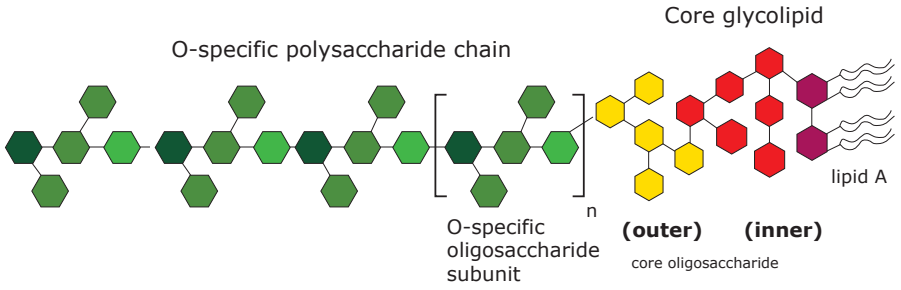


Figure 1. Diagram of a lipopolysaccharide.



Source: BIOMIN

Lipopolysaccharides (LPS) constitute up to 75% of the structure of the cell wall of Gram-negative bacteria, being present at average $2x10^6$ molecules of LPS/bacterial cell. LPS are a prerequisite for bacterial viability; they serve as a potential barrier toward antimicrobials at the outer membrane of Gram-negative bacteria. *Figure 1* illustrates the structure of a lipopolysaccharide containing a pyrogenic lipid part embedded in the bacterial wall, an inner and outer core oligosaccharide, and an O antigen polysaccharide chain.

Also called endotoxins, lipopolysaccharides are released upon bacterial replication or death (lysis). They are present everywhere in the environment including in the ground, air, water and the GI tract.

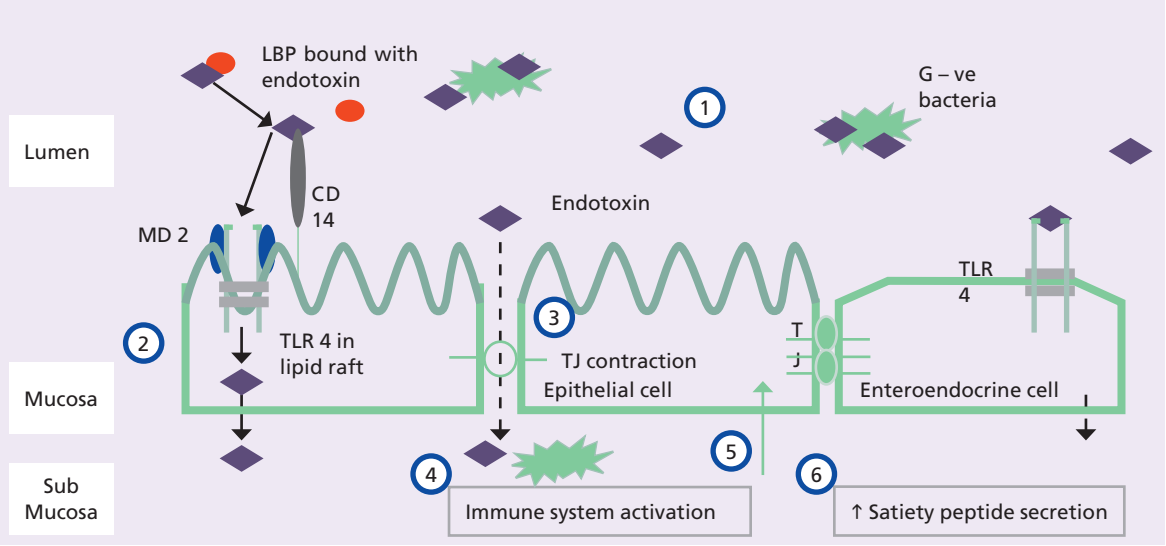
Pigs are continuously exposed to them throughout their lives. In healthy animals, the intestinal and other epitheliums such as skin or lungs, represent an effective barrier that prevents their passage into the bloodstream. Once there, however, endotoxins can elicit strong immune responses, weakening immune systems and impairing performance. Severely pronounced immune response can lead to septic shock.

In swine, endotoxins are known to cause dose-dependent increases in body temperature of 1°C to 1.5°C, reduced levels of activity/movement, lower feed intake, and severe anorexia. More frequent vomiting, salivation and chewing have also been reported.

Effects on gut

The gut is the first line of defense against endotoxins and, if compromised via nutrition, stress or metabolic state, can result in increased endotoxin transport. Heat stress, for example, increases gut permeability. LPS can be absorbed through the intestinal epithelium to the general circulation through either the said paracellular or the transcellular pathway, being the first the most frequent. Transcellular transport happens trough receptor mediated endocytosis or diet fat micellar assisted permeation (*Figure 2*).

Figure 2. Enterocytes with tight junctions structure and actin filament supporting structure.



Source: Mani et al, 2013

> **“A synergistic effect was recently found between deoxynivalenol and lipopolysaccharides”**

Table 3. Higher inflammation and lower growth.

Inflammation processes in the intestinal tract are costly	
Lipopolysaccharides (Endotoxins, LPS)	= inflammatory stimulus
IL-1ß and PGE2 (Factors of inflammatory reactions)	= scale of inflammation
Cortisol (Catabolic factor, immunosuppressant	= body´s reaction on burden
IGF-1 (Insulin-like growth factor 1, growth mediator)	= scale of possible growth

Inflammation markers measured in the blood	- LPS	+ LPS
IL-1ß	32	114
PGE2	490	1.285
Cortisol	55	206
IGF-1	182	101
Daily gain (d 14-28) (g/d)	604	525
Daily feed intake d (14 28) (g/d)	962	838
Feed conversion d (14-28)	1.59	1.59

Source: Lieu et al., 2003

Negative effects

LPS is transported in the blood by LPS binding protein (LPB), synthesized in liver and gut epithelial cells as acute phase reactant, at lower extent transported by albumins; once bound is able to activate the specific receptor TLR4 and initialize the kinase cascade and the NF-κB transcription factor complex, this way several hundreds of genes are transcribed to start inflammatory response.

Once in the bloodstream, endotoxins are transported to the liver through the portal vein where a major portion of the detoxification process occurs. If the amount of endotoxin entering the gastrointestinal tract overwhelms the detoxification capacity of the liver, endotoxemia ensues.

Endotoxins cause an inflammatory cascade that increase a pig's maintenance requirements (due to fever) that, coupled with reduced feed intake, means less energy is available for growth. One research study found that LPS-challenged piglets had a 13% lower average daily gain (*Table 3*) compared to the control group.

Endotoxins also impair feed efficiency. A recent study of common challenges in pig farms reported a reduction in feed intake of 3% due to parasitic infections, 4.1% due to poor housing conditions, 10.2% due to digestive bacterial infections, 17.3% because of respiratory diseases, 25.2% due to mycotoxicoses (mycotoxin-induced diseases) and 26.8% due to lipopolysaccharides.

Environment and endotoxin exposure

While the main route for lipopolysaccharide exposure in swine is the gastrointestinal tract, the concentration of endotoxins in the air and dust should not be overlooked: endotoxins are a major component of biological dust.

Air endotoxin levels are an important issue not only for the animals, but also for workers. A survey of pig production facilities has registered airborne lipopolysaccharide concentrations from 40.4 to 1.144 nanograms per cubic meter of air (*Table 1*).

This reinforces the importance of good management regarding hygiene and dust levels on farms, and specific measures to protect workers such as wearing a fine dust mask.

Table 1. Total endotoxin air contamination in pig production facilities, stationary sampling.

Country	Number of samples	Mean ng/m³	Range ng/m³
Canada	46	1144	43.8-4131
Netherlands	168	130	31-343
Canada	8	40.4	21.5-56.9
US	54	200	
Europe	110	52.3-186.5	
Europe	64	338.9-860.4	

Source: Øyvind Omland, 2002

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Photo: haveseen

The potential presence of airborne endotoxins reinforces the need for good management regarding hygiene and dust levels on farms, and specific measures to protect workers such as wearing a fine dust mask.

Aggravation of endotoxin exposure

Major detoxification process for LPS is through a lipase present in macrophages, dendritic cells, neutrophils, liver cells and renal cortical tubule cells. Intestinal alkaline phosphatase, or IAP, is a brush–border enzyme that detoxifies directly lipopolysaccharides. IAP is modulated by presence in the diet of saturated or unsaturated fatty acids, with saturated increasing its presence. High caloric and high fat diets increase serum endotoxin concentrations and induce acute low-grade inflammation. Starvation, stress or disease can depress the expression and function of IAP—particularly in early weaning piglets—and result in high pro-inflammatory cytokine expression.

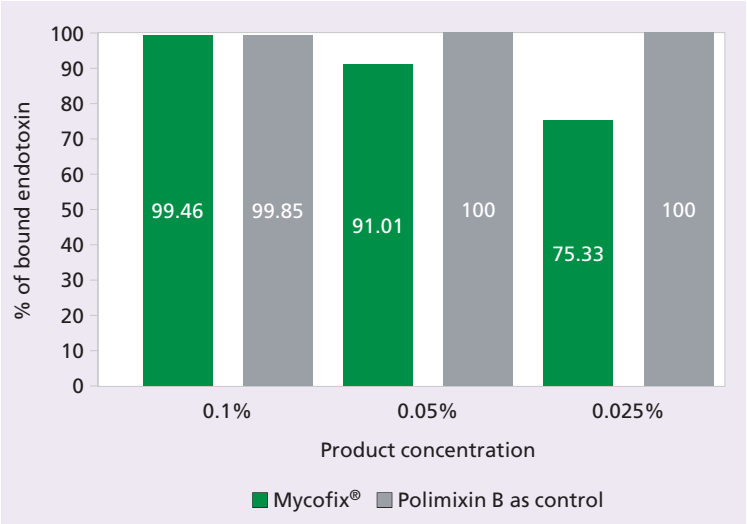
Mycotoxin magnifiers

Lipopolysaccharides are able to increase a pig's sensitivity to deoxynivalenol, a major mycotoxin that can cause feed refusal, vomiting, diarrhea, splay legs and weakened immune function. A synergistic effect was recently found between deoxynivalenol and lipopolysaccharides in induction of pro-inflammatory cytokines TNF-α and IL-1β in porcine alveolar macrophages. Endotoxins reduced the minimum dose of deoxynivalenol needed to induce cytokine response, increased its toxic effects, increased organisms' sensitivity to the toxin and magnified the effects of even low concentrations.

Table 2. Tips to reduce the risk of endotoxins.

1. Avoid the introduction of pathogens through robust biosecurity
2. Limit stressors linked to leaky gut, and conditioned diseases such as *Pasteurella, Haemophilus, E. coli, Salmonella, Brachyspira, Lawsonia,* etc.
3. Provide proper nutrition, balancing appropriate protein and energy (fats)
4. Avoid fasting after weaning
5. Avoid mycotoxin contamination
6. Use an effective endotoxin and mycotoxin deactivator

Figure 4. Mycofix® counteracts endotoxins at low doses.



Source: BIOMIN

Treatment

Biosecurity and hygiene can greatly help decrease the lipopolysaccharide challenge in farm animals, together with the awareness that a certain amount of endotoxin is always present. Some healthy behaviors can greatly help to reduce the risk of endotoxin challenge on the farm (*Table 2*).

In addition, the use of a selected feed additive that offers endotoxin protection can help mitigate the risks of a lipopolysaccharide challenge. Mycofix® is a multi-strategy mycotoxin and endotoxin deactivating feed additive that uses adsorption as a mode of action to effectively bind and prevent endotoxins from entering the bloodstream, mitigating the risk to animals. *Figure 4* shows that even at low doses, Mycofix® is able to efficiently adsorb or bind a considerable percentage of endotoxin in the gut lumen, greatly decreasing its passage into the bloodstream. Other research has demonstrated this mode of action to be effective even in the presence of adsorbable mycotoxins such as aflatoxins.

More Milk Production for Better Piglet Performance

By **Richard Markus**, Assistant to Development Director and **Christine Hunger**, Product Manager Phytogenics

Getting better piglet performance starts with higher quantity and quality milk production. Phytogenic feed additives can support both.

Modern sows with adequate genetics and nutrition can produce approximately 10 to 12 kilograms of milk per day. Piglets' growth rate during the pre-weaning period relies considerably on the quantity and quality of the milk production.

Sow nutrition during gestation and lactation will influence the litter size and weight at farrowing and weaning, with a direct impact on animal health and breeder's profitability. Up to 30% of early piglet mortalities can be attributed to a lack of adequate nutrition that could be due to inadequate sow milk production. In order to maximize milk production in sows, several factors have to be take into account. *Table 1* provides a number of tips to reach this goal.

Phytogenics promote milk quality, quantity

Phytogenic feed additives (PFAs) or botanicals, are functional feed additives of plant origin derived from herbs, spices, essential oils and their extracts. Since phytogenics enhance palatability and improve nutrition digestibility, they can support the subsequent milk and reproduction performance of sows through enhanced feed intake and improved body condition.

Figure 1 illustrates how Digestarom® — a phytogenic feed additive — has been shown to reduce sow weight loss during lactation. This improvement in body condition stems in part from better protein digestibility, as indicated by a lower urea content of the milk in *Figure 2*.

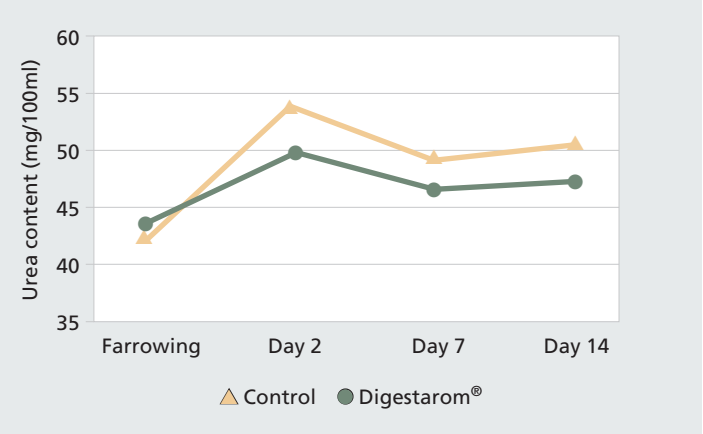
Table 1. Tips for sow milk production.

Correct water intake
Maintain appropriate temperature
Maintain body condition
Support feed intake
Address inflammation (energy loss)
Use Digestarom®

Figure 1. Digestarom® reduces weight loss during lactation.

Source: Khon Kaen University, Thailand, 2008 (Trial 286)

Figure 2. Lower urea content in sow's milk with Digestarom®.



Source: Slov. Center of Agriculture, Nitra, 2007

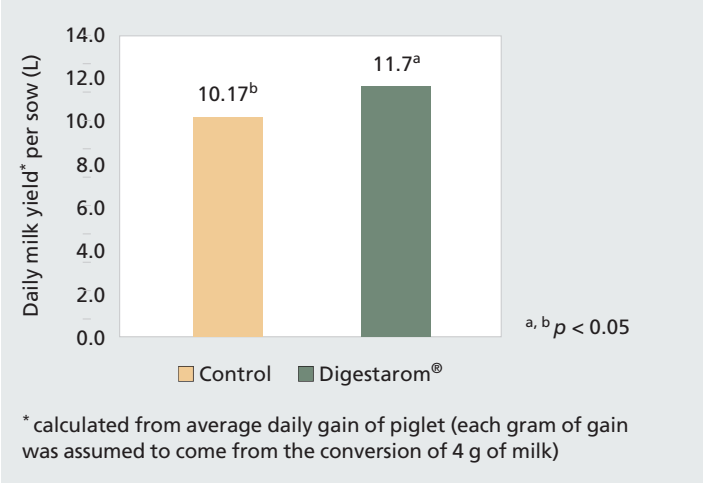
Coping with greater reproduction demands

In general, sow farms have been increasing total born and are weaning large litters with heavier pigs. With litter size continuing to improve and lactation length increasing to around 21 to 28 days, milk production must rise to meet this increasing demand.

Studies have often shown that sows' weight loss has a negative effect on future lactation results, litter size and farrowing rate. In addition, low parity sows are expected to gain weight and grow over the first two parities. It is important to maintain the body condition of the sow at weaning, since it influences wean to estrus

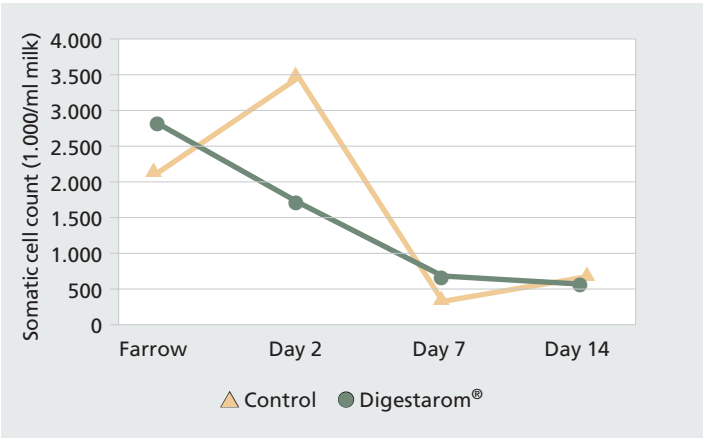
Piglets' growth rate during the pre-weaning period relies considerably on the quantity and quality of the milk production.

Figure 3. Digestarom® improves milk yield.



Source: Khon Kaen University, Thailand, 2008 (Trial 286)

Figure 4. Improved Milk Quality.



Source: Slov. Center of Agriculture, Nitra, 2007

interval, number of services per conception and subsequent litter size. Furthermore, sow body condition in early gestation has an impact on heterogeneity of piglet birth weight as well. The success of Digestarom® in improving daily milk yield per sow is shown in *Figure 3*.

Addressing inflammation

The economic loss through lower feed intake, decreased nutrient digestibility and high energy requirement of inflammatory processes resulting from different diseases can take a toll on sows. One study noted a productivity loss amounting to 10% of the nutrient use during an acute phase immune response: resources which otherwise would have gone towards performance. Other researchers have estimated the nutrient cost of ongoing inflammatory processes to be 1.3 times that of maintenance or a daily cost of 0.27 g ideal protein per kg body weight.

The antimicrobial and anti-inflammatory properties of phytogenics can reduce inflammation along the gastrointestinal tract (GIT). The somatic cell count can provide an indication of the level of activity of inflammatory processes in the mammary tissues. *Figure 4* shows that Digestarom® fed sows had a lower somatic cell count –improved milk quality— over the course of two weeks.

Temperature

Lactating sows at high ambient temperatures reduce their feed intake as part of the response to regulate body heat production, thereby losing more weight during lactation. With a comfort temperature (Tc) of around 15 degrees, a room temperature of 25°C (effective critical temperature of lactating sows) will reduce the feed intake of a 200 kg lactating sow by 2 kg.

According to reports, each 1°C increase in ambient temperature above 20°C decreased daily feed intake of sows by 0.17 kg. (For more on overcoming heat stress through nutrition, see Science & Solutions #20.)

Water intake

Water is important element in animal feeding, because on the one hand it is used to excrete metabolism wastage via urine, on the other it is needed for growth, digestion and milk production since it is the major component of milk.

Water intake can be very low (10 liter/day) in some sows during the first 24 hours following parturition. After this period of transition, water intake increases gradually to reach 20 to 35 liters per day during lactation. Increased water intake can reduce relative body weight loss of sows and is positively correlated with the weaning weight of piglets.

Cut & Keep Checklist

What's Wrong with My Pigs? Part 5: Rectal Prolapse

Rectal prolapse can look quite ordinary but can have a serious impact on animal health. It can prevent removal of metabolites produced during the digestive process, cause pain, encourage biting by pen-mates – thus leading to infection and even bacteraemia – and, if left alone, can cause necrosis.

The last part of the gut, the rectum, has a huge unselective absorbtion capacity, meaning that if elimination does not happen regularly, together with water, a number of toxins can enter the bloodstream causing intoxication, liver burden and discomfort.

Rectal prolapse can have many causes, the most common is constipation with hard to release stools that adhere to the gut walls, such that pushing to get rid of them culminates in projection of the last segment of the rectum outside the anus.

Similarly it can happen when swine are coughing as the sudden rise in inner pressure is able to bring protrusion. It can also happen in overcrowding situations when pen-mates step on one another's bellies.

Generic diarrhoea such as enterocolitis and some gut worms can also result in prolapse. A more specific cause can be stricture of the anal sphincter, called tenesmus. Less well known is salmonella two months after diarrhoea and local inflammations affecting the last part of the urogenital tract (vaginitis, urethritis, etc).

Then come the factors which are able to cause relaxation of keeping the rectal structure in situ, the most classic being ageing. In young animals it may be caused by mycotoxins such as zearalenone that also have swelling effects similar to those of phytoestrogens.

The most common treatment is to isolate the animal to avoid pen mates biting and then waiting until the protruded segment necrotises and falls. However, in the process lower feed intake, constipation and bacteraemia often occur, and this is quite commonly associated with high weight loss.

Surgical treatment, cutting and sewing with the tobacco bag technique, requires expert skill, is considered expensive and does not always allow for a complete recovery. It is therefore better to focus on prevention, through providing adequate water, providing fibre in the correct amount and quality according to the production phase, and ready treatment for fever. Prevention and treatment of gut and urogenital tract diseases, along with toxic agents, are reported in the table.

Check list	Corrective action
Potential cause: MYCOTOXINS	
• Vulvovaginitis, vaginal and/or rectal prolapse • Reproductive issues; stillbirth, splay leg, low litter size • Carry-over in sow milk	Prevent mold growth • Purchase clean raw materials • Use Mycofix®
Potential cause: MANAGEMENT	
• Water intake/constipation • Overcrowding • Cough • Transport • Seasonality • Tail docking, tail biting • Sudden diet changes, soft faeces, ingestion of wood shavings	• Control water flow per minute and pressure as well as drinker efficiency • Increasing space • Control fibre content of feed, avoid sudden diet changes
Potential cause: PATHOGENS	
• ELISA • PCR • Flotation procedure of faeces samples	• According to etiology
Potential cause: AGE	
• Average sow population • Number of farrowings	• Replacement rate
Potential cause: GENETICS	
• Control of heterosis effect • Avoid overconsumption/overfeeding/ excess of feed	• Discuss with genetic company
Potential cause: NUTRITION	
• Check fibre content and fibre sources • Too high levels of barley (β-glucanase) • Grinding fineness • Control feed intake • High sodium or potassium levels	• Check feed formulation and grinding fineness

References are available on request

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

DISCLAIMER: This table contains general advice on poultry-related matters which most commonly affect swine and may be related to the presence of mycotoxins in feed. Swine diseases and problems include, but are not confined to the ones present in the table. BIOMIN accepts no responsibility or liability whatsoever arising from or in any way connected with the use of this table or its content. Before acting on the basis of the contents of this table, advice should be obtained directly from your veterinarian.

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