Sustainability: The Road Ahead

Conference Report

Nowadays, climate change is an omnipresent topic. Extreme weather events, such as high temperatures and heavy rainfall, are becoming more frequent, and there has been a rapid increase in greenhouse gas concentrations since the 1850s. Climate change will also have consequences for the pig industry. Dr. Jan Fledderus, Schothorst Feed Research, discussed upcoming issues for the pig industry at EW Nutrition's Swine Academy.

Shift in mycotoxin-producing fungi

Climate change is likely to expand the geographical range of mycotoxin-producing fungi, exposing new crops and areas previously considered low risk to higher contamination levels. For instance, regions in South and Eastern Europe have reported increased occurrences of aflatoxins due to hotter and drier conditions favoring *Aspergillus flavus* over *Fusarium* species.

European Green Deal

The European Commission has adopted the European Green Deal, a comprehensive policy initiative to address climate change and promote sustainability within the European Union (EU). It sets ambitious targets and outlines a roadmap for reducing greenhouse gases by at least 55% by 2030, compared to 1990 levels, and achieving climate neutrality by 2050. The EU's primary goal is to ensure food security while reducing environmental and climate footprint.

The EU regulation on deforestation-free products includes soybeans and palm oil. The objective is to guarantee that the products EU citizens consume do not contribute to deforestation or forest degradation worldwide. Effective 1 January 2026, all imported soy must be free of deforestation. This means soybeans must be from areas not deforested since 1 January 2021.

The Green Deal will affect pig production

While it is still early to fully assess the impacts of the European Green Deal on pig farmers, it is clear that regulatory changes, economic pressures, and shifts in consumer behavior will shape the future of pig farming in the EU. Several potential consequences are still being assessed, including:

- Halving nutrient losses, particularly nitrogen, influences the eutrophication of natural areas and surface water, which will likely require pig farmers to adjust their feeding strategies and potentially reduce herd sizes.
- The use of food waste and by-products, such as wheat bran, in pig diets will be encouraged, promoting a circular economy approach that minimizes waste and enhances resource efficiency.
- Costs (notably related to feed) are likely to increase due to manure management and a reduction in crop production due to stricter environmental regulations.
- Farmers may need to invest in more sustainable practices and technologies to comply with new regulations, which could strain finances unless supported by subsidies or compensatory payments.
- Reduced supply and higher consumer prices for pigmeat products.
- Encouraging a shift towards plant-based diets in humans, which may reduce demand for pork (and other animal proteins).
- There may be opportunities for the pig industry to develop premium products that meet sustainability criteria or cater to specific consumer preferences.

Defining sustainability

It is necessary to apply a uniform method to calculate sustainability parameters and define objectives for “sustainable pig feed.” The Global Feed LCA Institute (GFLI) is the global standard for raw material parameters. It gives data by different methods to calculate carbon dioxide (feed/food), with detailed data per country of origin, including peat oxidation. It includes 16 environmental impact categories.

Climate-neutral pig production

How does this impact pig production? Firstly, feed contributes 50-70% of CO_2 equivalents/kg of pigmeat. Secondly, it is essential to have a uniform method to calculate the CO_2 equivalents/kg of pigmeat. Currently, there are no financial benefits for pig farmers to improve sustainability.

Based on scenario calculations, Dr. Fledderus concluded that it is challenging to realize ‘zero emissions’ and that improving on all environmental impact parameters is not realistic. Formulating pig diets to reduce CO2 equivalents to produce ‘green pork’ increases feed costs. The obvious question is, who will pay for this?

EW Nutrition’s Swine Academy took place in Ho Chi Minh City and Bangkok in October 2024. Dr. Jan Fledderus, Product Manager and Consultant at the S&C team at Schothorst Feed Research, one of the founders of the Advanced Feed Package and with a strong focus on continuously improving the price/quality ratio of the diets for a competitive pig sector, was a reputable guest speaker in these events.

Immunoglobulins – Novel solutions for swine health

Conference Report

Unlike humans and most mammals, piglets do not receive any maternal immunoglobulins (antibodies) via the placenta. Therefore, it is vital for piglets to receive maternal antibodies via the colostrum within 24 hours of birth. Otherwise, they are more vulnerable to illnesses in their early stages of life. In situations where piglets do not receive enough colostrum, such as due to large litter sizes or weak sows following a prolonged farrowing — supplemental colostrum or IgY products can provide essential immune protection.

In the following, Dr. Shofiqur Rahman describes the innovative role of IgY – yolk immunoglobulins in enhancing swine health.

IgY – modes of action

IgY is an antibody found in egg yolk. It is an entirely natural product; each egg contains approximately 100 mg of IgY. These egg-derived antibodies primarily function in the gut through several mechanisms:

- Adherence inhibition – IgY antibodies bind to specific structures on the surface of pathogens (such as fimbriae, flagella, and lipopolysaccharides), preventing them from adhering to the intestinal mucosa and blocking the initial stages of infection. This is particularly significant for enterotoxigenic *E. coli* (ETEC), which causes piglet diarrhea by attaching to intestinal cells.
- Neutralization – IgY can neutralize toxins produced by pathogens, preventing them from exerting harmful effects on host cells.

- Agglutination – IgY promotes the clumping of pathogens by binding them together, effectively immobilizing them, and facilitating their removal from the animal's gut.
- Cell damage – IgY can damage the integrity of bacterial cell walls leading to cell lysis and reduced bacterial viability.

Furthermore, because these pathogens are bound in complexes with IgY and eliminated through feces in an inactivated form, IgY helps prevent environmental re-infection through manure.

IgY and IgG – functional differences

Both IgY and Immunoglobulin G (IgG) (IgG, the most abundant immunoglobulin in mammals) are antibodies. They, however, exhibit significant differences due to their distinct structural characteristics. "IgY, for instance, does not activate the complement system, a key function of IgG that enhances immune responses against infections. Additionally, IgY promotes more rapid phagocytosis and reduces inflammation compared to IgG. These effects contribute to energy conservation, thereby facilitating improved animal growth performance," he explained.

IgY is more hydrophobic than IgG, which increases its stability and resistance to proteolytic degradation. This property is beneficial for maintaining its functionality in the gastrointestinal tract.

Production and quality control

IgY develops in hens in response to the pathogens they encounter, regardless of their relevance to the hens themselves. For instance, hens immunized with an infectious pathogen affecting pigs can produce IgY, effectively preventing the disease caused by that pathogen.

There are different methods of IgY production. One possibility is to hyperimmunize the hens simultaneously with multiple antigens. This method seems convenient, but it does not produce products with standardized levels of immunoglobulins for each antigen.

Another approach involves immunizing different groups of hens, each with a single antigen (e.g., transmissible gastroenteritis virus, rotavirus, *E. coli*) that commonly challenges piglets during the first weeks of life. The immunoglobulin content is then quantified, and the resulting egg powders are spray-dried, pasteurized, and mixed. This process yields an IgY product with standardized amounts of specific immunoglobulins that exhibit high affinity for the target pathogens.

One health application in swine

“The benefits of IgY have been demonstrated through extensive trials and commercial experiences, highlighting its potential for various applications not only in swine but also in other animals and humans,” said Dr. Rahman.

Due to concerns about antibiotic resistance, regulatory and consumer scrutiny increased over the use of in-feed antibiotics. IgY can serve as an effective and natural alternative for improving overall gut health, reducing the incidence and severity of diarrhea, reducing morbidity during the critical pre- and post-weaning periods, and, thereby, increasing performance.

Unlike antibiotics, which can indiscriminately kill both harmful and beneficial bacteria, IgY selectively targets specific pathogens. This selective action helps maintain a balanced gut microbiome, which is crucial for overall health and digestion in piglets. Disruption of the gut microbiota by antibiotics can lead to issues such as antibiotic-associated diarrhea and increased susceptibility to opportunistic infections due to the loss of beneficial microbes.

In contrast to antibiotics, IgY targets multiple antigenic sites on pathogens, requiring various genes for their protection, thereby avoiding resistance issues among pathogenic microorganisms. Additionally, IgY is effective not only against bacteria but also demonstrates significant efficacy against viruses and coccidia.

Conclusion

Dr. Rahman concluded that “the use of IgY as a passive immunization strategy, incorporated into a holistic approach to reducing piglet diarrhea, offers a safe and natural alternative to traditional antibiotics, particularly in the light of rising antibiotic resistance and the need for effective treatments also for viral diseases.”

EW Nutrition’s Swine Academy took place in Ho Chi Minh City and Bangkok in October 2024. Dr. Shofiqur Rahman, Senior Researcher at the Immunology Research Institute Gifu (IRIG) in Japan was one of the highly experienced speakers of EW Nutrition. Originally a microbiologist, Dr. Rahman focuses on researching and developing IgY products for Human, Animal, Pet, Fish, Plant, and Environmental health.

Managing heat stress in pigs in Asia

Conference Report

Heat stress poses a significant challenge to pig production, particularly in Asia, due to the region's warm and humid climate. In the following, Dr. Merideth Parke, Global Application Manager Swine at EW Nutrition, discusses effective management strategies to mitigate the adverse effects of heat stress on pig health and productivity.

Understanding Heat Stress

Pigs are particularly vulnerable to heat stress due to their limited ability to dissipate heat. "This is because they lack functional sweat glands, have relatively small lungs, a thick subcutaneous fat layer, and a narrow thermoneutral zone. The pigs' thermoneutral or 'comfort' zone varies by age and weight. For instance, sows require 18-22°C, grow-finish pigs less than 25°C, while newborn piglets need a much warmer 35°C," she explained.

Furthermore, today's lean and efficient pigs have higher metabolic demands and produce more body heat, making them more susceptible to heat stress than pigs from the 1980s.

Symptoms of heat stress include:

- Increased respiration rates (>50/minute)
- Elevated rectal temperature (>39.5 oC)
- Decreased feed intake
- Reduced growth rates
- Lower reproductive performance
- Lower reproductive performance

Pigs naturally reduce their feed intake as a response to heat stress, which is a mechanism to decrease metabolic heat production from digestion. For example, research on sows has shown that for each 10°C increase between 25-27°C at 50-60% relative humidity, they reduce their feed intake by 214 g/day.

Managing Heat Stress

Managing heat stress is complex. It requires a combination of solutions specific to each production system. Additionally, it must be considered that heat stress is not only about temperature. Its impact can be exacerbated by relative humidity, which hinders heat dissipation through evaporation. The heat index chart below demonstrates the relationship between temperature, humidity, and comfort levels for a grow-finish pig. Pigs require an environment where the heat index is within the thermoneutral zone, enabling them to shed heat and maintain efficient feed utilization and growth.

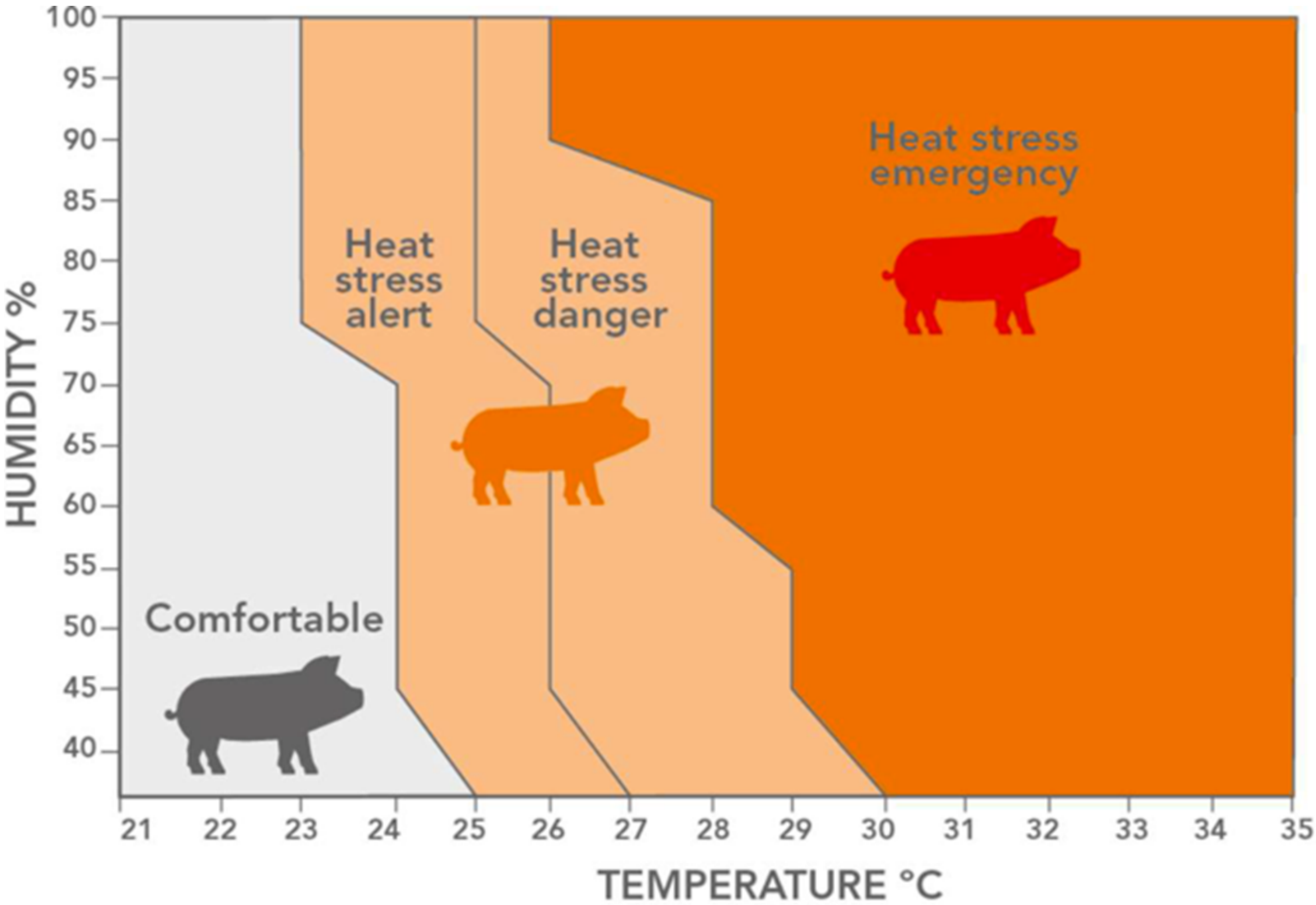


Figure 1: Heat stress index chart *(kepro.nl)*

While we often initially look to nutritional interventions, such as reducing dietary crude protein levels, increasing fats, or adding feed additives such as betaine, the effectiveness of these heat mitigation strategies is limited if the pigs are not eating well. Therefore, we must first focus on environmental management to reduce external heat absorption and increase heat load shedding. Pigs with the highest metabolic demands – lactating and gestating sows and finisher pigs – are especially susceptible to heat stress and should be given priority.

Several strategies to effectively manage heat stress can be used:

1. ## Misters and sprinklers

   Misters or sprinklers can help cool pigs through evaporation. However, these should be used strategically – running them for short periods followed by breaks – to maximize cooling effects without creating excessive moisture and wet conditions that could lead to other health issues, such as skin lesions or respiratory problems.

   However, water-based cooling systems can inadvertently raise the heat index in humid environments. When water is sprayed into a humid environment, it will further increase the moisture levels in the air, exacerbating the heat stress situation. If humidity is too high, alternative cooling methods, such as evaporative cooling pads or high-pressure fogging systems, may be more effective.

Snout and flank drip systems deliver water directly onto the pig's body, mainly targeting areas more sensitive to heat. This localized approach enables heat dissipation without excessively increasing humidity in the surrounding environment.

2. Ventilation and airflow

Increased air movement, combined with misting or sprinkling (in low-humidity environments), can enhance the cooling effect by enhancing evaporative and convective heat loss. This combination helps reduce the temperature the pigs 'feel', making them more comfortable.

Producers should assess their ventilation systems and consider modifications to improve air circulation. This can be achieved by installing additional fans. However, the fans must be maintained – clean fan blades and louvers can increase efficiency by 30%. Furthermore, it must be evaluated if there are dead spots and drafts at the pig level, not along the walkways.

Using suspended ceilings can effectively reduce the airspace that needs cooling and can lead to lower energy costs for cooling systems.

3. Housing and surroundings

Adding insulation to roofs and walls can help reduce heat transfer inside the pig housing. Applying reflective coatings (such as white paint) to rooves and walls can help deflect solar radiation, reducing heat accumulation inside the shed by several degrees.

Dense vegetation surrounding a piggery can provide shade and reduce reflective heat. However, it can also obstruct airflow and trap moisture, increasing local humidity and exacerbating the pigs' heat index and heat stress.

4. Drinking water

Providing fresh, chilled drinking water (10°C) is a highly effective method for mitigating heat stress in pigs and increasing feed intake to improve overall performance. Insulating header tanks and water pipes can help to maintain cool temperatures.

Regular checks on water supply systems are essential to ensure they function correctly and provide adequate flow rates to the end of the line. For example, lactating sows need a flow rate of 4 L/minute.

5. Stocking density and body condition

Higher stocking densities can exacerbate heat stress in pigs. Increased animal density leads to higher ambient temperatures due to the combined metabolic heat produced by the animals and reduced airflow at the pig level. Lower stocking densities can allow pigs to manage their body temperature better.

Pigs with higher body condition scores (more body fat) may be more susceptible to heat stress. Excess fat can hinder effective heat dissipation, making it more difficult for these pigs to regulate their body temperature during hot weather.

6. Monitoring and evaluation

Continuous monitoring of temperature, humidity levels, and airflow is vital to adjust cooling strategies as necessary. A common mistake when monitoring the pigs' thermal environment is placing sensors in walkways at head height for workers because they are easier to read than at pig level in the pens. Sensors should be positioned in several locations throughout the shed. Regardless of sensor readings, stockpersons need to observe behavioral changes that provide immediate insights into the welfare and comfort of pigs during high-temperature periods.

7. ## Husbandry

Pigs must be regularly observed for signs of heat stress, such as rapid breathing, reduced activity and feeding, lateral recumbency, and changes in vocalization. Aggressive behaviors may increase among pigs during heat stress as they compete for cooler spaces and water. Early detection of behavioral changes allows for timely interventions.

"Schedule feeding during cooler parts of the day, such as early mornings or late evenings. This practice helps minimize additional heat production from digestion during peak temperatures", according to Dr. Parke.

"When moving pigs, especially pregnant sows, to the farrowing room, do so during the coolest times of the day and allow them to walk at their own pace."

Conclusion

In conclusion, in the first run, each aspect of a production system must be critically evaluated, and existing housing or husbandry procedures must be modified to reduce the severity of the adverse effects of high temperatures on pig health and performance.

EW Nutrition's Swine Academies took place in Ho Chi Minh City and Bangkok in October 2024. Dr. Merideth Parke, Global Application Manager, Swine, was one of the highly experienced speakers of EW Nutrition. She is a veterinarian who strongly focuses on swine health and preventive medicine.

The Science Behind Phytogenics

Conference Report

Essential oils, secondary plant compounds, phytogenics – all these expressions can be found in the context of animal feed. In the following, Dr. Sabiha Kadari, Regional Technical Director Southeast Asia/Pacific at EW Nutrition, will show the difference between essential oils and phytomolecules and the science behind phytogenics.

Essential oils and phytomolecules– not the same

Let us first show what are essential oils using the example of oregano oil. Essential oils are extracted from plants and unpurified mixes of different phytomolecules. The raw oregano oil extract contains carvacrol, thymol, P-cymene, and several other phytomolecules. The concentration and composition of these phytomolecules can vary significantly, depending on factors such as geographical origin, seasonal variations, plant part, plant growth stage and harvest time, extraction methods, and post-harvest processing. As a result, there can be significant batch-to-batch variations, resulting in differences in animal performance. Furthermore, there is the potential for the presence of undesirable contaminants.

In contrast, **phytomolecules** are the active ingredients in essential oils or other plant materials. They are clearly defined as one active compound (IUPAC name/CAS number) by their unique chemical structures, such as carvacrol. By focusing on specific active compounds, standardized products don’t have batch-to-batch variation, enhancing consistent animal performance.

Stringent screening processes

To yield the best phytogenic formulations for animal production, a rigorous screening process is required:

The initial screening process consists of ensuring the bioactives are generally recognized as safe (GRAS) by the US Department of Agriculture and approved by the European Food Safety Authority (EFSA). This step is crucial to ensure that any compounds used in formulations do not pose health risks to animals or humans.

In addition to being selected for their chemical-physical properties, which play a significant role in determining how well the phytogenics will perform in various applications, and a thorough cost-benefit analysis, the phytogenics are mapped for their following biological activities.

Antioxidant

Phytomolecules exert their antioxidant effects through various mechanisms, including scavenging free radicals. The ORAC (Oxygen Radical Absorbance Capacity) test is widely regarded as a gold standard for measuring the antioxidant potential of phytomolecules. It quantitatively assesses the ability of compounds to scavenge free radicals, providing a reliable comparison against a known standard, specifically Trolox, a vitamin E analog. Trolox has well-documented antioxidant properties, making it a reliable benchmark for evaluating the effectiveness of other antioxidants.

Antimicrobial

Incorporating a comprehensive approach to testing the antibacterial properties of phytogenics is essential for developing effective feed additives. The antibacterial properties should not only be tested against harmful enteropathogenic bacteria, such as *Clostridium perfringens*, *E. coli*, and *Salmonella*. It should also be evaluated if beneficial species such as *Lactobacilli*, *the proliferation of which is wanted*, are preserved.

By evaluating both pathogenic and beneficial bacteria, researchers can ensure that phytogenic formulations support optimal gut health and reduce the reliance on antibiotics.

Anti-inflammatory

Anti-inflammatory properties also help to modulate the gut-associated immune system and mitigate excessive immune response so that animals can allocate more energy towards growth and production. This shift is vital for optimizing feed conversion ratios and overall performance.

Dr. Kadari noted that “EW Nutrition uses nuclear factor kappa beta (NFkß), which regulates the expression of various pro-inflammatory cytokines, and interleukin 6 (pro-inflammatory) and 10 (anti-inflammatory) cytokines as biomarkers, for measuring anti-inflammatory activity. A reduction in NFkß and the ratio of IL-6/ IL-10 indicates a decrease in inflammatory response.”

Anti-conjugation

Conjugation is a common mechanism of horizontal gene transfer that is instrumental in spreading antibiotic resistance between bacteria. “Most resistance genes are found on mobile genetic elements named plasmids and primarily spread by conjugation,” explained Dr. Kadari.

Cell stress of bacteria modulates the conjugation frequency. Among these stressors are antimicrobial phytogenics. The goal is to keep the conjugation frequency below the one that could occur under unchallenged conditions.

Figure 1: High throughput screening allows EW Nutrition researchers to quickly conduct millions of chemical, genetic, or pharmacological tests

Delivery mechanism

Lastly, to optimize the benefit of the selected phytogenics and deliver consistent results, the substances must be protected by, e.g., encapsulation to ensure homogenous distribution in feed and thermostability in pelleted feed. A special delivery system provides for the targeted release of the active ingredients within the organism, specifically ensuring that these compounds are effectively utilized within the body rather than eliminated through the feces. This is crucial for optimizing their benefits in animal production.

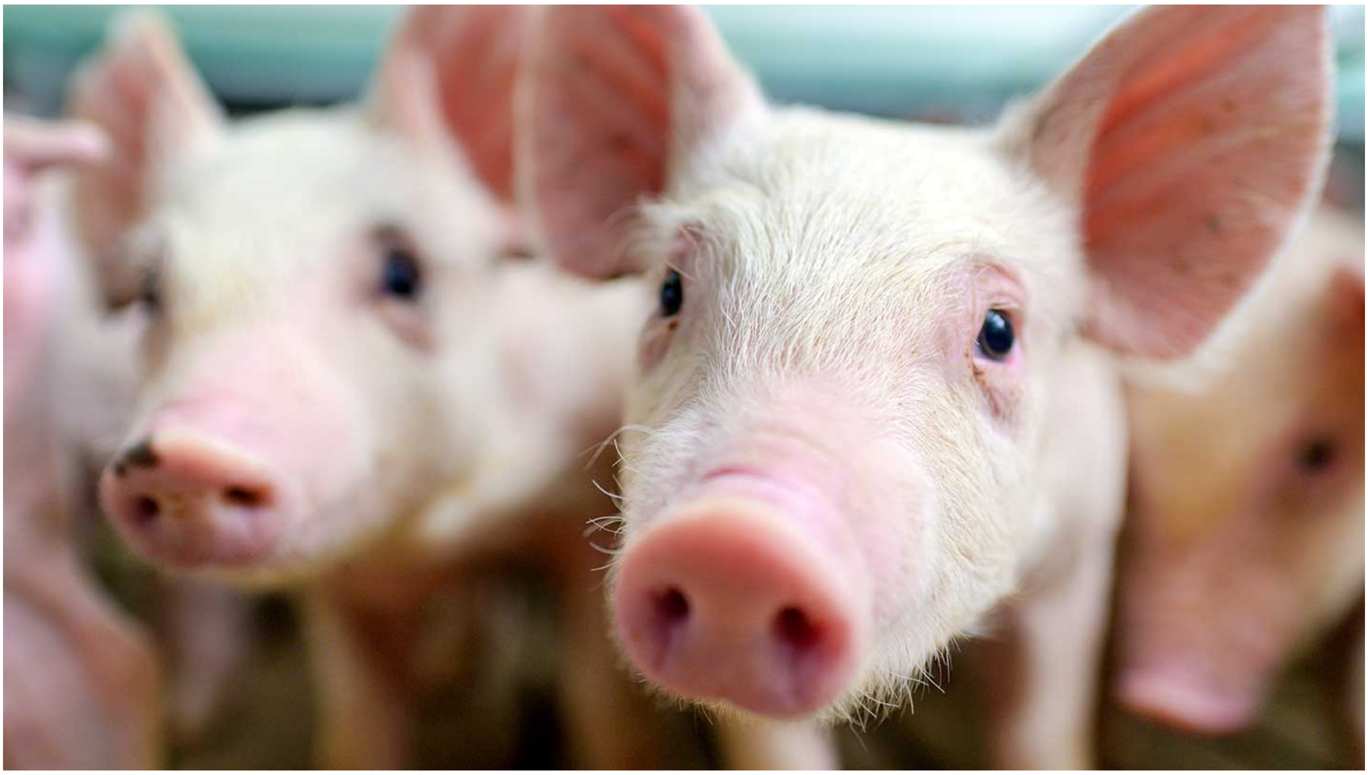
Phytomolecules are an essential support in antibiotic reduction

“Phytogenics are increasingly recognized as effective alternatives in antimicrobial reduction programs. The combination of stringent screening processes alongside rigorous in *vitro* and in *vivo* testing is essential for ensuring that phytogenics deliver optimal and consistent performance in animal production,” noted Dr. Kadari.

EW Nutrition’s Swine Academies took place in Ho Chi Minh City and Bangkok in October 2024. Dr. Sabiha Kadari, Regional Technical Director at EW Nutrition SEAP, was one of the highly experienced speakers of EW Nutrition. With expertise in feed cost optimization, feed additive management, audits, and lab support, she provides customized technical solutions and troubleshooting challenges for customers.

Minimizing Collateral Effects of

Antibiotic Administration in Swine Farms: A Balancing Act



*By **Dr Merideth Parke** BVSc, Regional Technical Manager Swine, EW Nutrition*

We care for our animals, and antibiotics are a crucial component in the management of disease due to susceptible pathogens, supporting animal health and welfare. However, the administration of antibiotics in pig farming has become a common practice to prevent bacterial infections, reduce economic losses, and increase productivity.

All antibiotic applications have collateral consequences of significance, bringing a deeper consideration to their non-essential application. This article aims to challenge the choice to administer antibiotics by exploring the broader impact that antibiotics have on animal and human health, economies, and the environment.

Antibiotics disrupt microbial communities

Antibiotics do not specifically target pathogenic bacteria. By impacting beneficial microorganisms, they disrupt the natural balance of microbial communities within animals. They reduce the microbiota diversity and abundance of all susceptible bacteria – beneficial and pathogenic ones… many of which play crucial roles in digestion, brain function, the immune system, and respiratory and overall health. Resulting microbiota imbalances may present themselves in animals showing health performance changes associated with non-target systems, including the nasal, respiratory, or gut microbiome [7, 8, 14]. The gut-respiratory microbiome axis is well-established in mammals. Gut microbiota health, diversity, and nutrient supply directly impact respiratory health and function[13]. In pigs specifically, the modulation of the gut microbiome is being considered as an additional tool in the control of respiratory diseases such as PRRS due to the link between the digestion of nutrients, systemic immunity, and response to pulmonary infections[11].

The collateral effect of antibiotic administration disrupting not only the microbial communities throughout the animal but also linked body systems needs to be considered significant in the context of optimal animal health, welfare, and productivity.

Antibiotic use can lead to the release of toxins

The consideration of the pathogenesis of individual bacteria is critical to mitigate potential for direct collateral effects associated with antibiotic administration. For example, in cases of toxin producing bacteria, when animals are medicated either orally or parenterally, mortality may increase due to the associated release of toxins when large numbers of toxin producing bacteria are killed quickly[2].

Modulation of the brain function can be critical

Numerous animal studies have investigated the modulatory role of intestinal microbes on the gut-brain axis. One identified mechanism seen with antibiotic-induced changes in fecal microbiota is the decreased concentrations of hypothalamic neurotransmitter precursors, 5-hydroxytryptamine (serotonin), and dopamine[5]. Neurotransmitters are essential for communication between the nerve cells. Animals with oral antibiotic-induced microbiota depletion have been shown to experience changes in brain function, such as spatial memory deficits and depressive-like behaviors.

Processing of waste materials can be impacted

Anaerobic treatment technology is well accepted as a feasible management process for swine farm wastewater due to its relatively low cost with the benefit of bioenergy production. Additionally, the much smaller volume of sludge remaining after anaerobic processing further eases the safe disposal and decreases the risk associated with the disposal of swine waste containing residual antibiotics[4].

The excretion of antibiotics in animal waste, and the resulting presence of antibiotics in wastewater, can impact the success of anaerobic treatment technologies, which already could be demonstrated by several studies[6, 11]. The degree to which antibiotics affect this process will vary by type, combination, and concentration. Furthermore, the presence of antibiotics within the anaerobic system may result in a population shift towards less sensitive microbes or the development of strains with antibiotic-resistant genes[1, 12].

Antibiotics can be transferred to the human food chain

Regulatory authorities specify detailed withdrawal periods after antibiotic treatment. However, residues of antibiotics and their metabolites may persist in animal tissues, such as meat and milk, even after this period. These residues can enter the human food chain if not adequately monitored and controlled.

Prolonged exposure to low levels of antibiotics through the consumption of animal products may contribute to the emergence of antibiotic-resistant bacteria in humans, posing a significant public health risk.

Contamination of the environment

As mentioned, the administration of antibiotics to livestock can result in the release of these compounds into the environment. Antibiotics can enter the soil, waterways, and surrounding ecosystems through excretions from treated animals, inappropriate disposal of manure, and runoff from agricultural fields. Once in the environment, antibiotics can contribute to the selection and spread of antibiotic-resistant bacteria in natural bacterial communities. This contamination poses a potential risk to wildlife, including birds, fish, and other aquatic organisms, as well as the broader ecological balance of affected ecosystems.

Every use of antibiotics can create resistance

One of the widely researched concerns associated with antibiotic use in livestock is the development of antibiotic resistance. The development of AMR does not require prolonged antibiotic use and, along with other collateral effects, also occurs when antibiotics are used within recommended therapeutic or preventive applications.

Gene mutations can supply bacteria with abilities that make them resistant to certain antibiotics (e.g., a mechanism to destroy or discharge the antibiotic). This resistance can be transferred to other microorganisms, as seen with the effect of carbadox on Escherichia coli[5] and Salmonella enterica[2] and the carbadox and metronidazole effect on *Brachyspira hyodysenteriae*[15]. Additionally, there is an indication that the zinc resistance of Staphylococcus of animal origin is associated with the methicillin resistance coming from humans[3].

Consequently, the effectiveness of antibiotics in treating infections in target animals becomes compromised, and the risk of exposure to resistant pathogens for in-contact animals and across species increases, including humans.

Alternative solutions are available

To successfully minimize the collateral effects of antibiotic administration in livestock, a unified strategy with support from all stakeholders in the production system is essential. The European Innovation Partnership – Agriculture[9] concisely summarizes such a process as requiring…

1. Changing human mindsets and habits: this is the first and defining step to successful antimicrobial reduction
2. Improving pig health and welfare: Prevention of disease with optimal husbandry, hygiene, biosecurity, vaccination programs, and nutritional support.
3. Effective antibiotic alternatives: for this purpose, phytomolecules, pro/pre-biotics, organic acids, and immunoglobulins are considerations.

In general, implementing responsible antibiotic stewardship practices is paramount. This includes limiting antibiotic use to the treatment of diagnosed infections with an effective antibiotic, and eliminating their use as growth promotors or for prophylactic purposes.

Keeping the balance is of crucial

importance

While antibiotics play a crucial role in ensuring the health and welfare of livestock, their extensive administration in the agricultural industry has collateral effects that cannot be ignored. The development of antibiotic resistance, environmental contamination, disruption of microbial communities, and the potential transfer of antibiotic residues to food pose significant challenges.

Adopting responsible antibiotic stewardship practices, including veterinary oversight, disease prevention programs, optimal animal husbandry practices, and alternatives to antibiotics, can strike a balance between animal health, efficient productive performance, and environmental and human health concerns.

The collaboration of stakeholders, including farmers, veterinarians, policymakers, industry and consumers, is essential in implementing and supporting these measures to create a sustainable and resilient livestock industry.

References

1. Angenent, Largus T., Margit Mau, Usha George, James A. Zahn, and Lutgarde Raskin. “Effect of the Presence of the Antimicrobial Tylosin in Swine Waste on Anaerobic Treatment.” *Water Research* 42, no. 10–11 (2008): 2377–84. https://doi.org/10.1016/j.watres.2008.01.005.
2. Bearson, Bradley L., Heather K. Allen, Brian W. Brunelle, In Soo Lee, Sherwood R. Casjens, and Thaddeus B. Stanton. “The Agricultural Antibiotic Carbadox Induces Phage-Mediated Gene Transfer in Salmonella.” *Frontiers in Microbiology* 5 (2014). https://doi.org/10.3389/fmicb.2014.00052.
3. Cavaco, Lina M., Henrik Hasman, Frank M. Aarestrup, Members of MRSA-CG:, Jaap A. Wagenaar, Haitske Graveland, Kees Veldman, et al. “Zinc Resistance of Staphylococcus Aureus of Animal Origin Is Strongly Associated with Methicillin Resistance.” *Veterinary Microbiology* 150, no. 3–4 (2011): 344–48. https://doi.org/10.1016/j.vetmic.2011.02.014.
4. Cheng, D.L., H.H. Ngo, W.S. Guo, S.W. Chang, D.D. Nguyen, S. Mathava Kumar, B. Du, Q. Wei, and D. Wei. “Problematic Effects of Antibiotics on Anaerobic Treatment of Swine Wastewater.” *Bioresource Technology* 263 (2018): 642–53. https://doi.org/10.1016/j.biortech.2018.05.010.
5. Köhler, Bernd, Helge Karch, and Herbert Schmidt. “Antibacterials That Are Used as Growth Promoters in Animal Husbandry Can Affect the Release of Shiga-Toxin-2-Converting Bacteriophages and Shiga Toxin 2 from Escherichia Coli Strains.” *Microbiology* 146, no. 5 (2000): 1085–90. https://doi.org/10.1099/00221287-146-5-1085.
6. Loftin, Keith A., Cynthia Henny, Craig D. Adams, Rao Surampali, and Melanie R. Mormile. “Inhibition of Microbial Metabolism in Anaerobic Lagoons by Selected Sulfonamides, Tetracyclines, Lincomycin, and Tylosin Tartrate.” *Environmental Toxicology and Chemistry* 24, no. 4 (2005): 782–88. https://doi.org/10.1897/04-093r.1.
7. Looft, Torey, Heather K Allen, Brandi L Cantarel, Uri Y Levine, Darrell O Bayles, David P Alt, Bernard Henrissat, and Thaddeus B Stanton. “Bacteria, Phages and Pigs: The Effects of in-Feed Antibiotics on the Microbiome at Different Gut Locations.” *The ISME Journal* 8, no. 8 (2014a): 1566–76. https://doi.org/10.1038/ismej.2014.12.
8. Looft, Torey, Heather K. Allen, Thomas A. Casey, David P. Alt, and Thaddeus B. Stanton. “Carbadox Has Both Temporary and Lasting Effects on the Swine Gut Microbiota.” *Frontiers in Microbiology* 5 (2014b). https://doi.org/10.3389/fmicb.2014.00276.
9. Nasralla, Meisoon. “EIP-Agri Concept.” EIP-AGRI – European Commission, September 11, 2017. https://ec.europa.eu/eip/agriculture/en/eip-agri-concept.html.
10. Niederwerder, Megan C. “Role of the Microbiome in Swine Respiratory Disease.” *Veterinary Microbiology* 209 (2017): 97–106. https://doi.org/10.1016/j.vetmic.2017.02.017.
11. Poels, J., P. Van Assche, and W. Verstraete. “Effects of Disinfectants and Antibiotics on the Anaerobic Digestion of Piggery Waste.” *Agricultural Wastes* 9, no. 4 (1984): 239–47. https://doi.org/10.1016/0141-4607(84)90083-0.
12. Shimada, Toshio, Julie L. Zilles, Eberhard Morgenroth, and Lutgarde Raskin. “Inhibitory Effects of the Macrolide Antimicrobial Tylosin on Anaerobic Treatment.” *Biotechnology and Bioengineering* 101, no. 1 (2008): 73–82. https://doi.org/10.1002/bit.21864.
13. Sikder, Md. Al, Ridwan B. Rashid, Tufael Ahmed, Ismail Sebina, Daniel R. Howard, Md. Ashik Ullah, Muhammed Mahfuzur Rahman, et al. “Maternal Diet Modulates the Infant Microbiome and Intestinal Flt3l Necessary for Dendritic Cell Development and Immunity to Respiratory Infection.” *Immunity* 56, no. 5 (May 9, 2023): 1098–1114. https://doi.org/10.1016/j.immuni.2023.03.002.
14. Slifierz, Mackenzie Jonathan. “The Effects of Zinc Therapy on the Co-Selection of Methicillin-Resistance in Livestock-Associated Staphylococcus Aureus and the Bacterial Ecology of the Porcine

Microbiota," 2016.
15. Stanton, Thaddeus B., Samuel B. Humphrey, Vijay K. Sharma, and Richard L. Zuerner. "Collateral Effects of Antibiotics: Carbadox and Metronidazole Induce VSH-1 and Facilitate Gene Transfer among *Brachyspira Hyodysenteriae*" *Applied and Environmental Microbiology* 74, no. 10 (2008): 2950–56. https://doi.org/10.1128/aem.00189-08.
16. Toledo Castillo, Manuel, Rocío García Espejo, Alejandro Martínez Molina, María Elena Goyena Salgado, José Manuel Pinto, Ángela Gallardo Marín "Clinical Case: Edema Disease – the More I Medicate, the More Pigs Die!" $this->url_servidor, October 15, 2021. https://www.pig333.com/articles/edema-disease-the-more-i-medicate-the-more-pigs-die_17660/.

IgY technology: using nature to support antibiotic reduction

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

IgY – what is it?

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

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

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

IgY production is a non-invasive and highly effective process

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

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

Hyperimmunized hens provide more

effective IgY

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

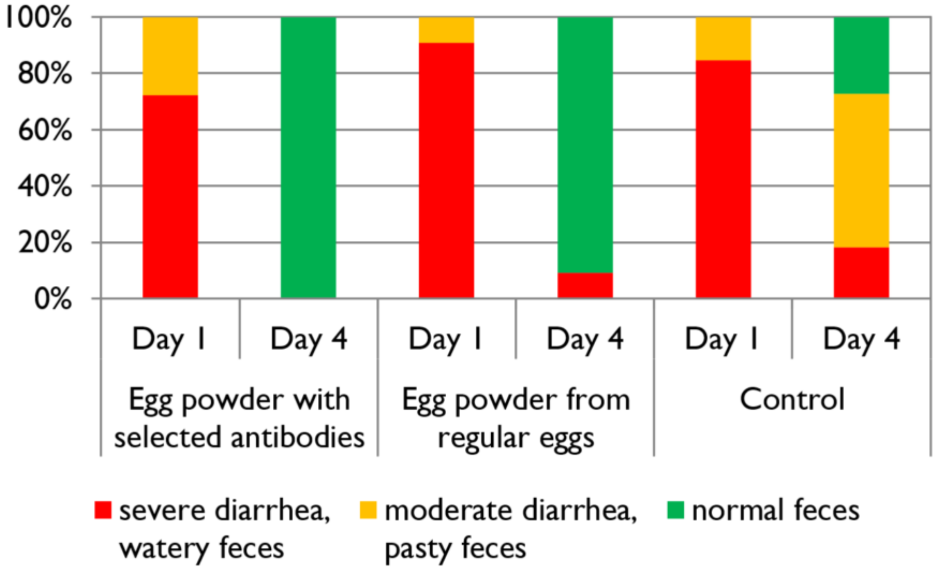

Figure 1: Comparison of eggs originating from regular and hyperimmunized hens

Preconditions for and benefits of industrially produced IgY

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

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

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

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

Not all IgY products are the same

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

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

Where can we use IgY?

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

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

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

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

IgY – a fascinating technology that should be better recognized

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

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

References:

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

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

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

Ikemori, Yutaka, Robert C. Peralta, Masahiko Kuroki, Hideaki Yokoyama, and Yoshikatsu Kodama. “Research

Note: Avidity of Chicken Yolk Antibodies to Enterotoxigenic Escherichia Coli Fimbriae." Poultry Science 72, no. 12 (1993): 2361–65. https://doi.org/10.3382/ps.0722361.

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

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

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

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

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

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

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

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

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

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

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