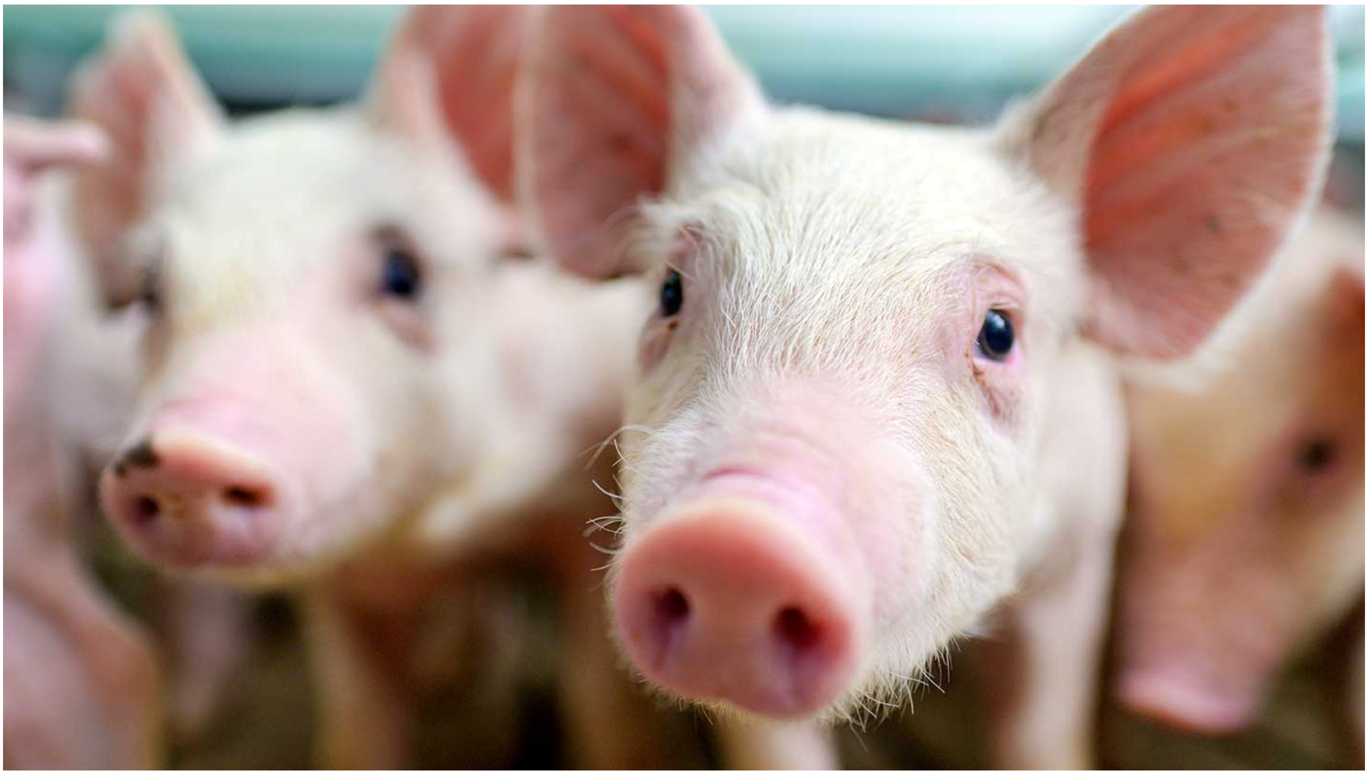
Minimizing Collateral Effects of Antibiotic Administration in Swine Farms: A Balancing Act



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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[10, 9, 16]. The gut-respiratory microbiome axis is well-established in mammals. Gut microbiota health, diversity, and nutrient supply directly impact respiratory health and function[15]. 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[12].

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[3].

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[6]. 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[5].

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[8, 13]. 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, 14].

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 already mentioned before, 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[7] and Salmonella enterica[2] and the carbadox and metronidazole effect on *Brachyspira hyodysenteriae*[16]. Additionally, there is an indication that the zinc resistance of Staphylococcus of animal origin is associated with the methicillin resistance coming from humans[4].

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[11] 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.

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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 specific 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.

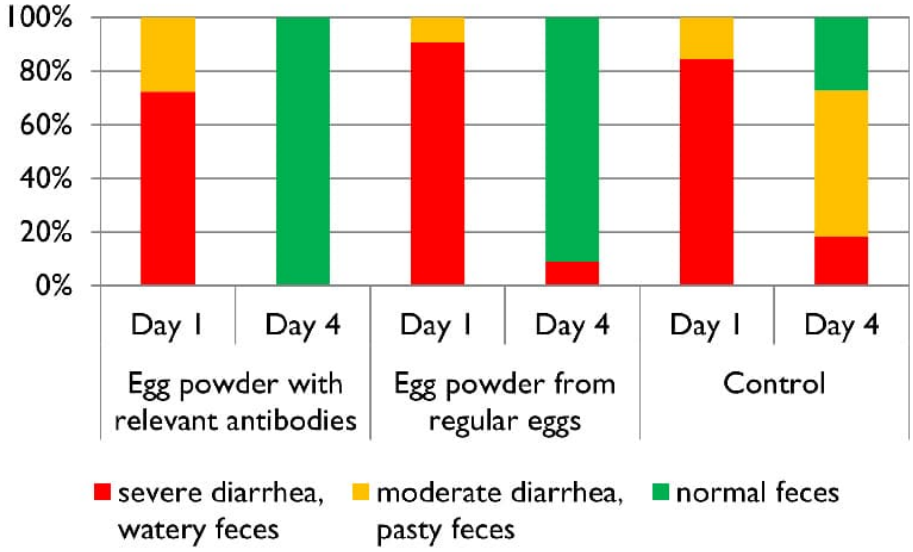

Figure 1: Comparison of eggs originating from regular and hyperimmunized hens

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 specific 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. If the technique is mastered, the production of IgY is not complicated. 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, a.o. 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.

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