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Antibiotic-Free and Reduced Antibiotic Use in Broiler Production: *Gut Health*

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Introduction

Since the discovery of antibiotics in 1928 by the Scottish scientist Sir Alexander Fleming, the use of antibiotics to treat bacterial diseases in humans and animals has become mainstream. In the 1940s and 1950s, researchers found that low (sub-therapeutic) doses of antibiotics exhibited a growth-promoting effect in chickens. Consequently, using low doses of antibiotics for growth promotion became common as large-scale poultry production became more widespread.

Over the last few decades, there have been notable surges in antibiotic-resistant bacteria in human and animal medicine, such as methicillin-resistant *Staphylococcus aureus* (MRSA), *Clostridioides difficile* (*C. difficile*), vancomycin-resistant Enterococci (VRE), and extended-spectrum B-lactamase (ESBL) *Escherichia coli* (*E. coli*). The increased prevalence of antibiotic-resistant bacteria (or “superbugs”) has been highlighted as a significant risk to human health. It has resulted in comprehensive shifts in the judicial use of antibiotics in human and animal medicine. The risk of antibiotic resistance is not a new phenomenon; the risk of antimicrobial resistance was highlighted in 1945 by Fleming as penicillin-resistant bacteria were observed within a year of the first commercial penicillin being released. Resistance occurs when a bacterium can resist the mode of action of an antibiotic (e.g., producing an enzyme that destroys the antibiotic or having a mutation that makes its cell wall stronger). Increased antibiotic-resistant bacterial populations occur when the antibiotic creates a natural selection pressure for the resistant bacteria, allowing it to dominate. Fortunately, research within livestock populations has shown that once antibiotic use is reduced, antibiotic-resistant bacteria in the environment are reduced as they lose their competitive advantage.

The focus was placed on the livestock industries as a source of antibiotic-resistant bacteria, resulting in the appeal for reduced antibiotic use. Subsequently, the poultry industry has rapidly reduced the use of both therapeutic and sub-therapeutic antibiotics over the last few decades. In 1999, a ban on “growth-promoting” antibiotics (AGPs) was implemented in Europe and became fully effective in 2006 (EC Regulation No. 1831, 2003); many other countries soon followed suit to phase out AGPs and reduce therapeutic antibiotics. Consequently, some poultry operations no longer use antibiotics in rearing their birds, instead opting for alternative strategies for promoting bird health and growth. Reducing the use of antimicrobials within the poultry industry aims to reduce the incidence of antibiotic-resistant bacterial populations.

Promoting Gut Health in Antibiotic-Free and Reduced Antibiotic Use Poultry Production

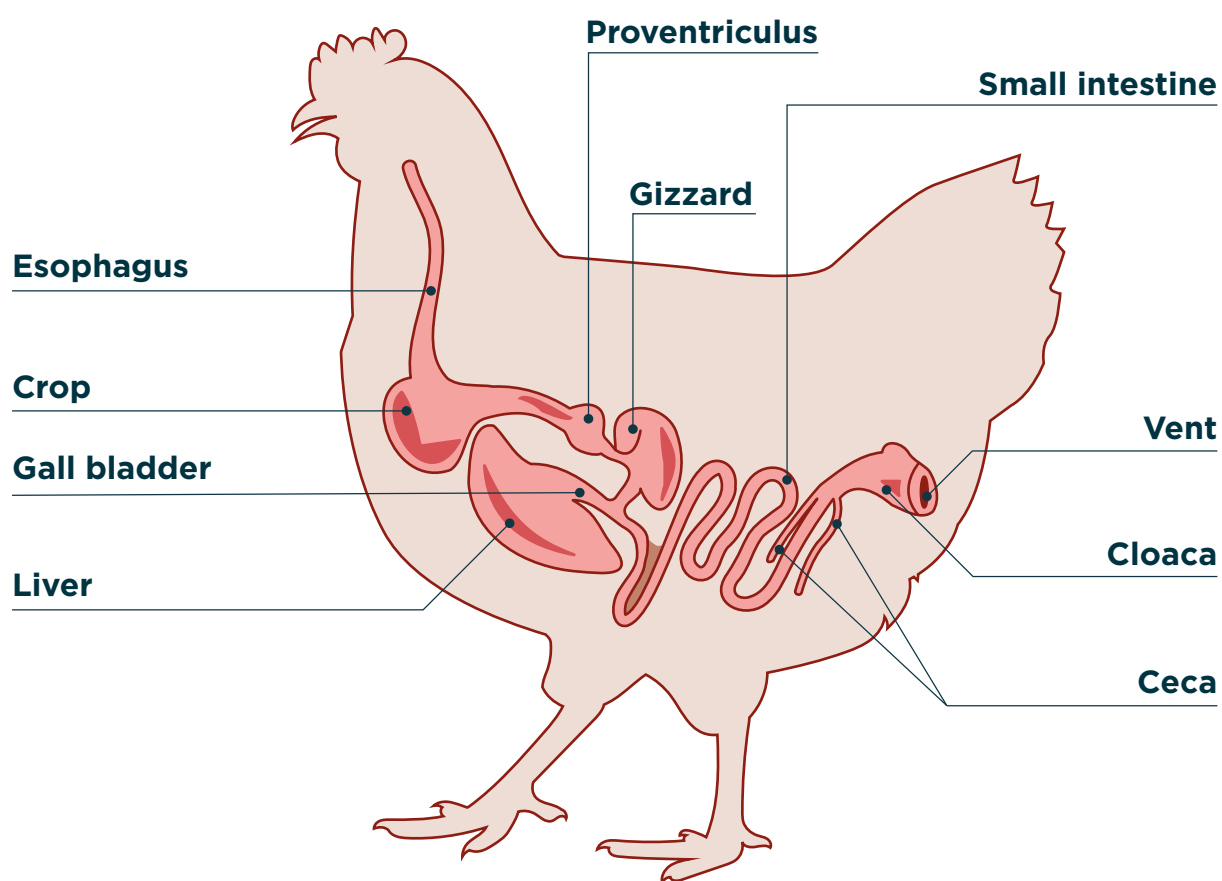
Antibiotics provide a very effective means of controlling gut pathogens and enhancing the growth and efficiency of chickens. When AGPs were first removed from poultry flocks across Europe, there was a surge in gut-related diseases such as dysbacteriosis and necrotic enteritis, resulting in wet litter and higher levels of hock burn and pododermatitis. The short-term consequence was an increase in the use of therapeutic antibiotics that highlighted the need to focus on new strategies for rearing chickens in an antibiotic-free and reduced antibiotic-use era. Research into how AGPs promoted gut health and growth showed a range in the modes of action of the AGPs. Some AGPs simply inhibited the growth of pathogens, some reduced the overall amount of bacteria in the intestinal tract, and others acted like anti-inflammatories. While natural products for promoting gut health have been around for centuries, removing AGPs from poultry flocks triggered a massive investment in research to find natural alternative products that performed like AGPs. These “alternatives to antibiotics” products are selected for their ability to promote bird health and performance by controlling specific pathogens, stimulating the gut tissues and gut immune system, reducing intestinal inflammation, and enhancing digestion. While these alternative products are very successful in promoting gut health, their use could be inconsistent; it soon became apparent that these products do not offer a “silver bullet,” and more had to be done to promote gut health in an antibiotic-free and reduced antibiotic-use age.

Gut Function and Physiology

The first step to promoting gut health is understanding gut function and physiology and how they relate to a bird's overall health and well-being. The gut's fundamental function is converting feed into its basic components and then absorbing all the nutrients for the host to use for growth and maintenance. In its simplest form, the intestinal tract is a tube that starts at the beak and ends in the cloaca. This tube is separated into five distinct regions (**Figure 1**):

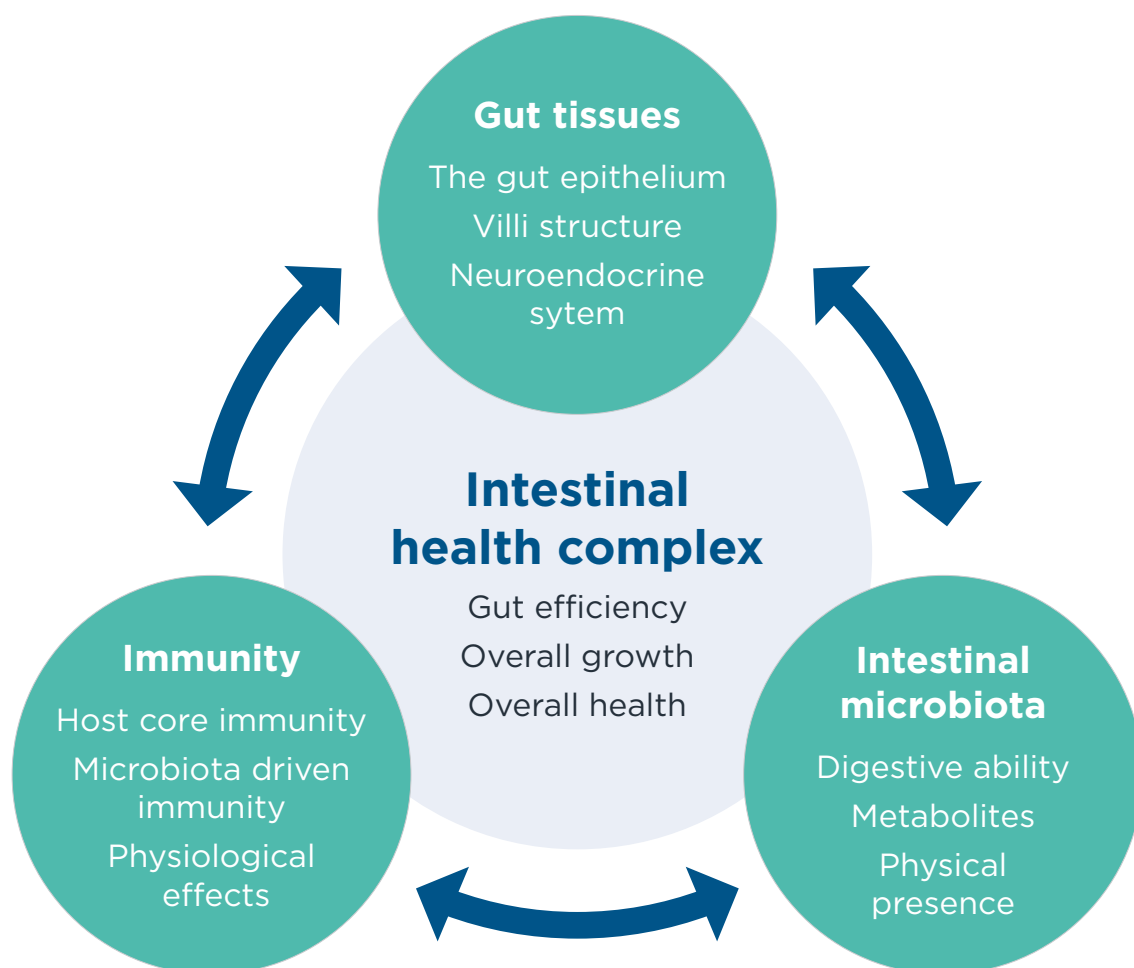
- Crop
- Proventriculus
- Gizzard
- Small intestine (duodenum, jejunum, and ileum)
- Large intestine (ceca, colon, and rectum)

Figure 1. Diagram of the gut.



The most straightforward view of gut health relies on each gut region's ability to fulfill its specific role to ensure proper digestion and absorption of nutrients. However, looking deeper into gut health reveals that it is an intricate and complex subject, combining nutrition, microbiology, immunology, and physiology (**Figure 2**).

Figure 2. The gut health complex.



The feed enters the crop, is stored briefly, and is partially fermented by the resident bacteria. It then enters the proventriculus and mixes with acid and pepsin—an enzyme responsible for breaking down protein—before moving on to the gizzard. The gizzard acts like a grinding mill to break feed into smaller particles, releasing it to the small intestine once the particles are small enough. While the gizzard grinds the feed, it is mixed with the acid and enzymes secreted by the proventriculus. This process allows the breakdown of whole proteins into smaller peptides that precipitate out to be further digested in the small intestine into amino acids for absorption. Within the small intestine, carbohydrates and fats are also broken down to be absorbed and used by the bird. During the normal digestion process, by the time the digesta reaches the last part of the ileum, all the digestible fractions of proteins, fats, and carbohydrates should have been absorbed, leaving behind the non-digestible components of the feed (e.g., cellulose and non-starch polysaccharides). This material has two fates; it is either passed out in the feces or taken up by the ceca, where bacteria ferment these materials to form organic acids, short-chain fatty acids, and vitamins that the bird can absorb for extra nutrition. At the end of digestion, chickens produce two types of droppings—a cecal and a fecal, which look very different (**Figure 3**).

Figure 3. Normal cecal dropping (left) and fecal (right) from a broiler chicken.



When any part of the gut is compromised, digestion and nutrient absorption are affected, resulting in a potentially detrimental effect on feed conversion, leading to economic loss and a greater susceptibility to further disease.

The Gut Health Complex

The gut tissues, microbiota, and immune system have an intricate relationship. Each component relies on the other for the development of the gut and subsequent gut function. If one fails, all three will fail. Supporting each of these components is the cornerstone of gut health management.

Gut Tissues

One of the most critical aspects of optimal gut function and health is the correct development and maintenance of the gut tissues. Correct incubation conditions are essential, as gut development starts in the egg. The last 3 days of incubation are critical for developing the gut tissues *in ovo*. Research has shown that overheating the eggs during this time can inhibit the final stages of embryonic gut development that are still occurring in the newly hatched chick. Inhibiting this growth can be detrimental to the next stage of gut development in the chick during brooding. Post-hatch, once the chicks have access to food and water on the farm, the gut starts to develop rapidly. It has been estimated that the gut develops four times faster than the rest of the bird during brooding, making it the most critical period of gut development in the bird's life.

One of the key stages of development of the intestinal tissues post-hatch is the development of the villi; these are the projections along the small intestine that increase the gut's surface area to ensure optimal nutrient absorption (**Figure 4**). During the brooding period, the villi quickly elongate due to the high concentration of rapidly dividing cells along the body and at the base of the villi (**Figure 5**). These cells are most active during the first 4-10 days of life, making this the period where the most villi development occurs. After the brooding period, villi growth slows as the cells along the body of the villi stop dividing with new gut cells, leaving villi growth to occur only at the base. This phenomenon is important because if optimal villi growth does not happen during brooding, there is no compensatory growth, meaning a chick with poorly developed villi will always have shorter villi.

Figure 4. Villi.

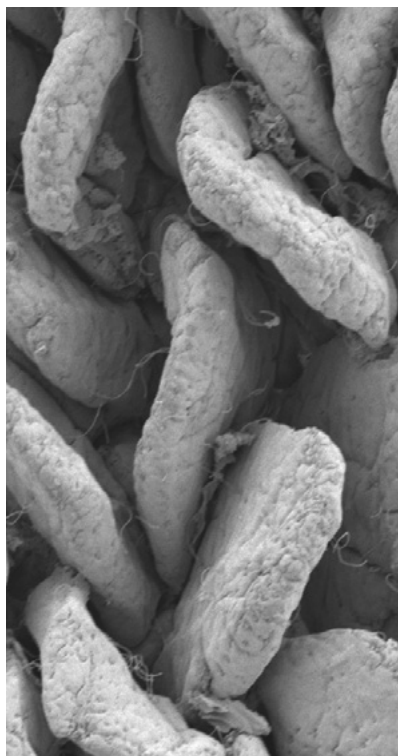
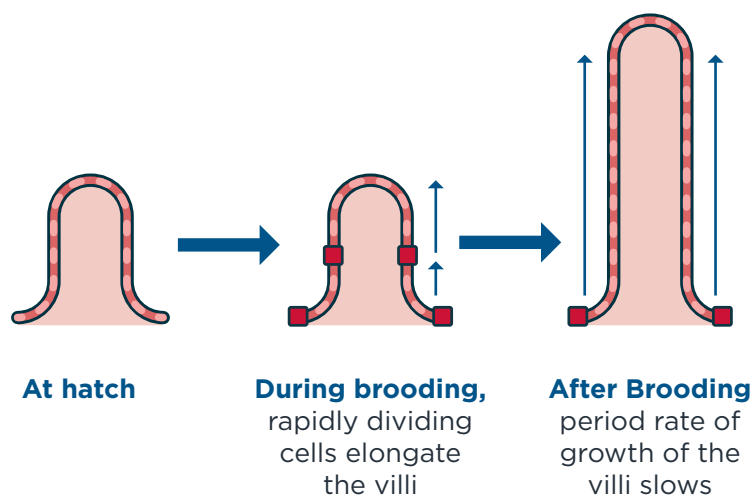


Figure 5. Villi development.



Gut development starts in the egg



Growth is dependant on the presence of food in the gut



Stimulated by the intestinal bacteria

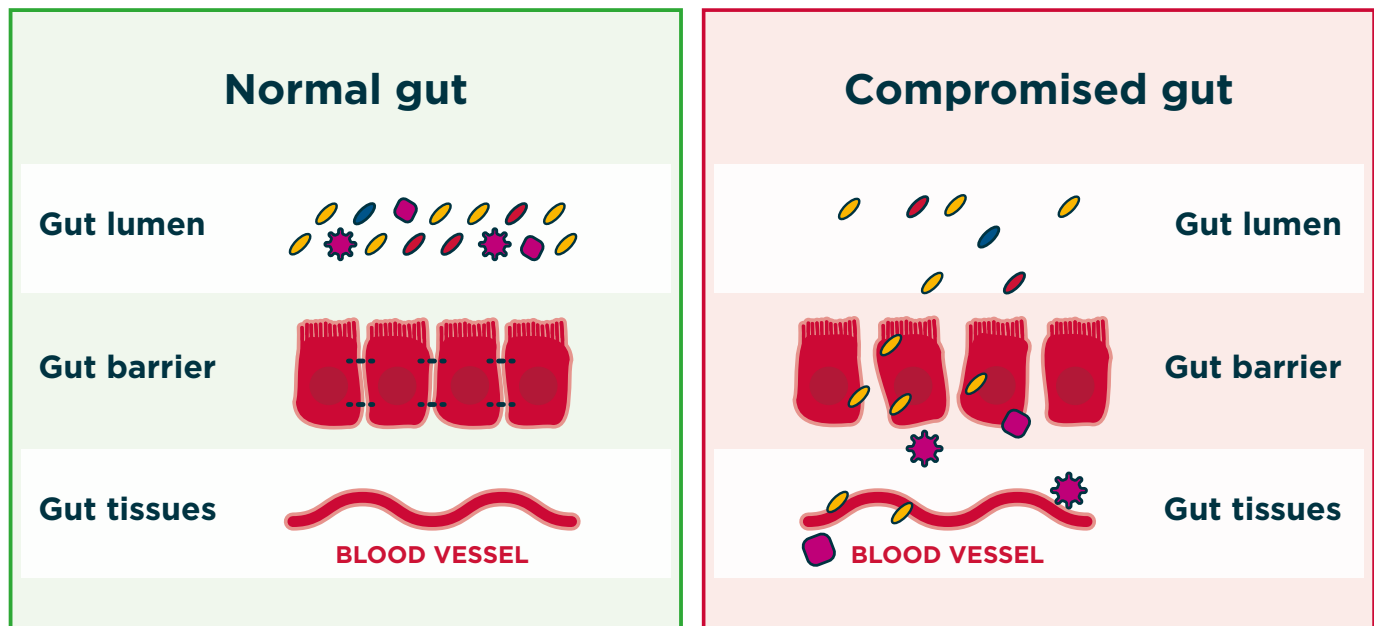


Growth is inhibited by stress

Brooding conditions play a vital role in the development of the villi, as growth depends upon the presence of food and water in the gut and the activity of beneficial bacteria. Any stress factors—such as incorrect temperature or humidity in the poultry house—can inhibit the development of the villi; optimal management during brooding is critical.

The layer of epithelial cells lining the gut is often called the gut barrier, as it protects against pathogens invading the deeper gut tissues. These cells are held together by structures called “tight junctions” or “gap junctions,” which essentially glue the cells together to form this gut barrier (**Figure 6**).

Figure 6. The gut barrier.



Gut health relies on the integrity of this barrier. A failure of the barrier can result in the invasion of the gut tissues by pathogens that can cause localized disease, such as necrotic enteritis. These pathogens can also enter the bloodstream and cause disease in bones and organs, such as bacterial chondronecrosis with osteomyelitis (BCO), peritonitis, or endocarditis. Good brooding helps the establishment of a good gut barrier. Throughout the bird's life, however, the gut barrier's integrity can be affected by poor nutrition, infection (e.g., coccidiosis), heat stress, and mycotoxins.

The gut microbiota

The community of microorganisms in the gut is referred to in many ways:

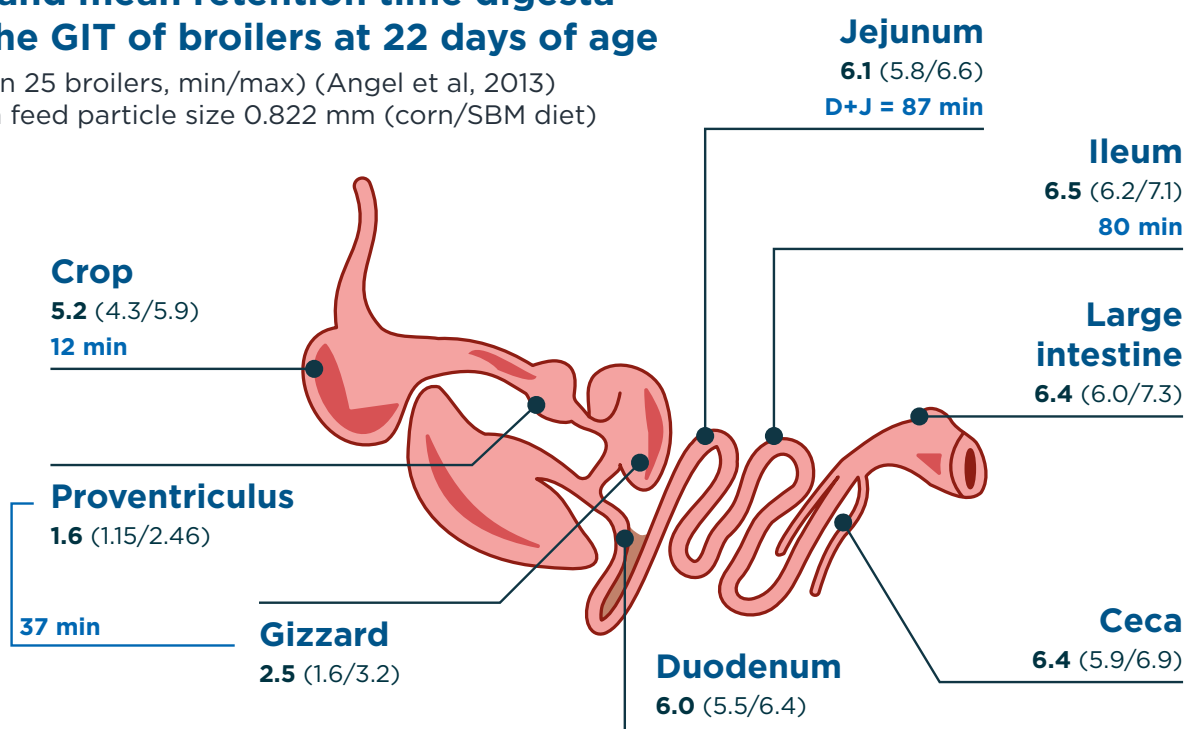
- Friendly bacteria
- Gut flora
- Gut microbiota
- Gut microbiome

It is a diverse community comprised mainly of bacteria, fungi, protozoa, and viruses. Modern DNA-based technologies have given a much more accurate picture of the bacterial species in the gut, and it has become increasingly evident that many bacteria in the gut are currently unknown and unclassified. Recent poultry studies have proposed that a broiler chicken's gastrointestinal tract (GIT) is colonized by an estimated 600–800 species of bacteria. The abundance and diversity of the microbiota vary along the GIT. Predictably, the regions with less tolerable conditions and faster passage of gut contents have lower numbers of bacteria. (**Figure 7**).

Figure 7. Retention time for digesta in the GIT of broilers.

pH and mean retention time digesta in the GIT of broilers at 22 days of age

(mean 25 broilers, min/max) (Angel et al, 2013)
Mean feed particle size 0.822 mm (corn/SBM diet)



Total residence time as affected by age:

10 d = 3h 15 min	(2:32–3:51)	(SEM09)
22 d = 4h 25 min	(3:10–4:42)	(SEM14)
30 d = 4h 44 min	(3:30–5:52)	(SEM19)
42 d = 5h 10 min	(4:09–6:05)	(SEM25)

The developing embryo is not entirely sterile; bacteria can be isolated from the embryonic gut. However, it is generally considered that the development of the adult gut microbiota begins at hatch, where bacteria are picked up from the hatchery and farm environments. The crop is rapidly colonized within 24 hours, and 24 hours post-hatch, the ileum and ceca are both dominated by bacteria. After 3 days, the level of bacteria in the small and large intestines increases tenfold. The first bacteria to enter the GIT can be considered the pioneering bacteria, as they rapidly multiply and colonize the gut environment. The composition of the pioneering bacterial community goes through a succession of changes as the gut develops and oxygen levels fall. It can take up to 3–4 weeks for the microbiota to form the climax (or adult) microbiota. However, during this period, stability is seen in the gut after 7–10 days if chicks are provided with optimal brooding conditions along with good-quality feed and water.

Within the GIT, there are multiple interactions between the host (bird) cells, the intestinal environment, bacterial cells, and feed components. These interactions emphasize the extremely important role of gut microbiota in the health and well-being of the host, and there is still ongoing research on both human and animal species to understand these interactions. One of the most fundamental interactions of the microbiota with the host is the stimulation of the gut tissues. Research has found that beneficial gut microbes stimulate the development of the villi and the integrity of the gut barrier. Furthermore, the beneficial bacteria in the gut stimulate the renewal of the gut cells, which ensures the cells lining the gut are healthy, leading to optimal nutrient absorption and making the gut more resilient against disease.

The gut microbiota forms a protective barrier within the gut, preventing the growth of less favorable or pathogenic bacteria such as *Salmonella spp.*, *Campylobacter jejuni*, *E. coli*, and *Clostridium perfringens*. This principle is most commonly known as competitive exclusion. Theories suggest that the commensal (i.e., friendly) microbiota dominate attachment sites on the gut cells, reducing the opportunity for attachment and colonization by pathogens. Another proposed mechanism is that the intestinal microbiota can secrete compounds, including volatile fatty acids, organic acids, and natural antimicrobial compounds (known as bacteriocins) that either inhibit the growth of or make the environment unsuitable for less favorable bacteria.

Studies using germ-free animals have also shown the importance of intestinal microbiota in stimulating and developing the immune system. The gut microbiota is thought to keep the gut immune system alert, allowing it to react quickly to invading pathogens. The gut microbiota plays an essential role in the overall development and maturation of the immune system. Research has shown that animals lacking gut microbiota are more susceptible to disease and have poorly developed immune tissues. The microbiota development in a young chick is essential for proper immune system development.

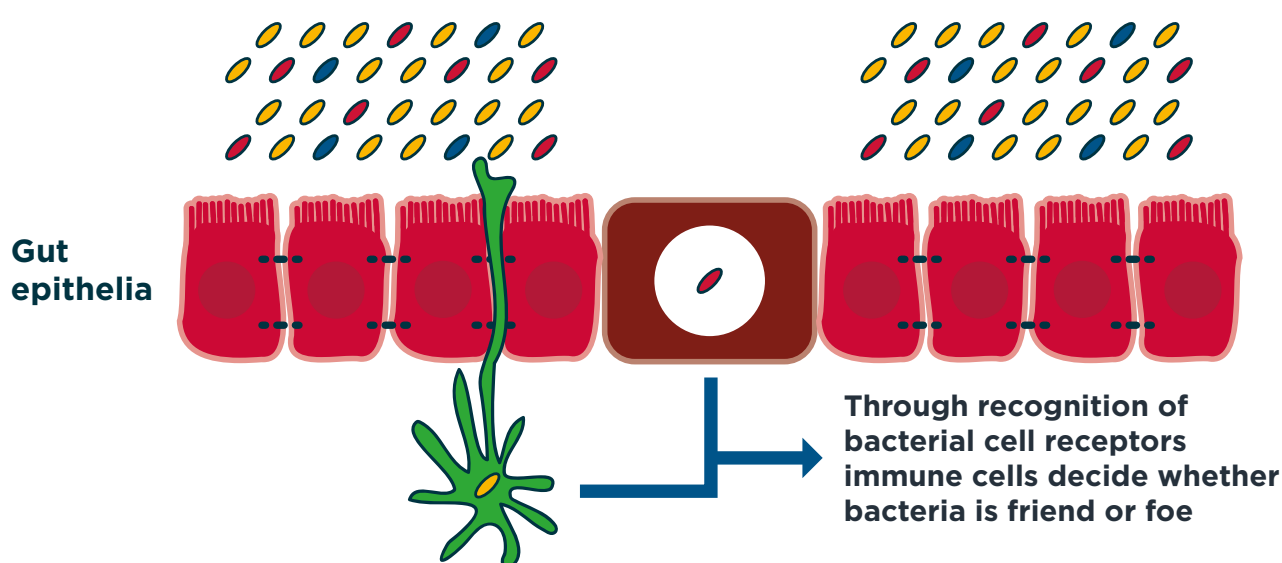
In addition to protecting against disease and stimulating the immune system, the intestinal microbiota can influence host growth rates by producing extra nutrients through the fermentation of indigestible plant fibers and non-digestible carbohydrates that birds cannot digest.

Gut immunity

Another key feature of the gut, often overlooked, is its role as an immune organ. Around 70% of an animal's circulating immune cells are estimated to reside in the gut tissues. Considering the gut as an immune organ makes it one of the primary interfaces of the bird. As such, the ability of a bird to defend against disease is intrinsically linked to the function and activity of the gut.

As previously mentioned, the gut microbiota constantly stimulates the immune system, keeping it alert and ready to react to pathogens. The two primary methods by which the immune system interacts with the gut contents are outlined in **Figure 8**. In simpler terms, the immune cells lining the gut examine the gut contents and process the material to decide if any action needs to be taken.

Figure 8. Immune system interaction with gut contents.



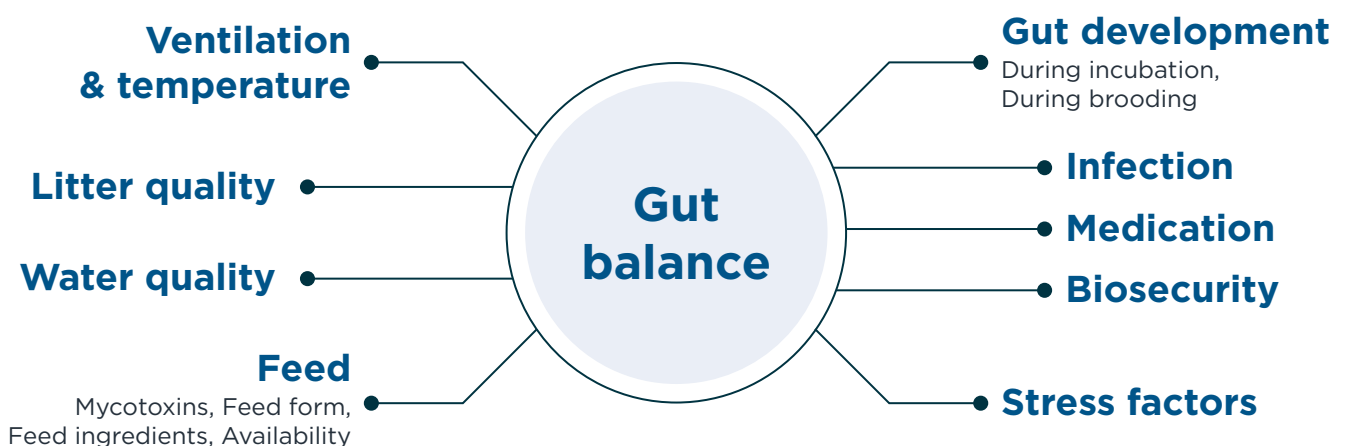
The education of the immune system as to whether a bacterium is a friend or foe happens early in the bird's life when the chick is ingesting many novel bacteria from the environment. Beneficial bacteria, such as *Lactobacilli*, have markers on their cell wall that instruct the bird that they are not a threat. Conversely, the immune cells recognize markers on pathogenic bacteria (e.g., *E. coli*) as a threat. As the chick gets older, the education of the immune system slows, meaning any novel bacteria the host comes into contact with is more likely to be seen as a pathogen, even if it is harmless. For this reason, the development of the microbiota must be supported early in the life of the chick. The use of probiotics during the first week of life is a very effective way to promote the development of the microbiota. In addition, many probiotic species are selected for their ability to interact positively with the immune system.

Another fundamental feature of early immune system development and education of the immune system is the role of maternal antibodies present in the yolk. As the chick absorbs the nutrients from the yolk during the first few days of its life, it also absorbs the maternal antibodies that help promote the immune repertoire of the chick. Consequently, the conditions must be correct to optimize yolk sac absorption and ensure the chick absorbs all the yolk. Several factors can influence yolk sac absorption, but the major two are environmental conditions and access to feed and water. First, if the conditions in the hatchery holding area, during transport, or on the farm are not optimal, the movement of the yolk through the yolk sac is reduced, possibly resulting in a retained yolk sac. Second, full absorption of the yolk sac is stimulated by the presence of feed and water in the gut, which is why feed and water access on the farm are so important. If the chick doesn't get access to enough protein during its first few days of life, the antibodies present in the yolk—which are proteins—may be broken down and used by the chicks as nutrients instead of promoting immunity.

Gut Imbalance

Gut health relies on the balance between all three components of the gut health complex: gut tissues, the gut microbiota, and the gut immune system. An imbalance results in the gut if there is an issue with any of these components; there are many factors that influence gut balance (**Figure 9**). When rearing poultry without antibiotics or with reduced antibiotic use, it is essential that close attention is paid to all of these factors. It is also important to recognize that these factors are additive. Therefore, if there is more than one issue on the farm, the impact on gut health is greater.

Figure 9. Factors influencing gut balance.



Compromised gut balance most commonly manifests as reduced growth rates, poor flock uniformity, wet droppings/litter, and increased mortality (in severe cases). The result of a challenge to the gut is fundamentally the same; there is malabsorption of nutrients that results in more nutrients being available to the microbiota, leading to bacterial overgrowth. Many bacteria that take advantage of the sudden increase in nutrients are not favorable and produce compounds that can cause inflammation in the gut or growth depression if the bird absorbs them. The result is further malabsorption and overgrowth of bacteria, impacting the entire flock as litter conditions deteriorate. Antibiotics worked well to cure most gut problems by helping to rebalance the microbiota. However, unless the initial challenge is not rectified, the imbalance can return once antibiotic therapy is completed. In poultry production, the aim is not to have any gut imbalances, but in antibiotic-free (ABF) production, it is even more important, and care must be taken to ensure optimal management of the birds. Every farm has strengths and weaknesses; therefore, it is important to identify the root cause of gut health issues to resolve the causal factor and offer the birds support accordingly. In the event of a gut imbalance with ABF production, it is important to recognize issues as early as possible to allow for intervention with non-antibiotic strategies to return the gut to its balance.

Water and Feed Quality

Water and feed quality are critical for the gut health management of birds of all ages in ABF production systems, and a range of Aviagen® documents discuss these subjects in depth.

Water and feed can be a source of pathogens that can disrupt gut health and cause disease in the birds; therefore, effective pathogen control and sanitation are essential. The mineral content of water varies from region to region and must be considered when it comes to gut health, as it can impact gut function or the activity of bacteria in the gut. For example, high sodium levels can increase water intake and urine output, causing wetter feces and litter, which can impact gut health. Bacteria such as *E. coli* have a high affinity for iron; thus, iron-rich water can result in increased *E. coli* activity in the gut of birds. Water pH is also important, as a pH greater than 7 can increase the risk of limescale formation in the water lines. It also provides a more advantageous environment for the survival of pathogens such as *E. coli* and *Salmonella spp.*

Gut health is also affected by poor quality feed and feed materials due to direct effects on gut function. For example, high levels of fines result in poor gizzard function and impaired protein digestion, leading to poor nutrient utilization by the bird and bacterial overgrowth. There can also be effects on the gut tissues, such as inflammation and immunosuppression by mycotoxins. Oxidized fats or poor-quality proteins can cause oxidative stress and inflammation in the gut, leading to loss of integrity of the gut barrier.

The gut and stress factors

When an animal has prolonged exposure to stress factors or discomfort, the result can be highly detrimental to gut health.

- Environmental pressures (e.g., heat) can cause the gut barrier to fail, allowing bacteria to invade the gut tissues and cause disease.
- Prolonged exposure to an uncomfortable environment or incorrect management can result in increased levels of stress hormones being released by the birds, which has a dampening effect on the immune system and can inhibit proper immune development in the chick or cause immunosuppression in birds of any age.
- When faced with a challenge at the gut level, certain neurotransmitters are released, which can stimulate specific bacteria, such as *E. coli*, *Enterococcus spp.* and *Campylobacter spp.*, to either increase their growth rates or become more virulent.

Gut Health Monitoring

Daily monitoring of gut health in a chicken flock is an essential component of ABF production. Bird behavior, along with body weights and uniformity, is an easy way to monitor flock performance and gut health. However, if bird behavior indicates disease or if body weights start to drop, it is likely that any gut health issue has been affecting the flock for a few days and is well established in the birds. In ABF production, it is critical that problems are identified and rectified before the gut becomes extensively imbalanced, as restoring balance with non-antibiotic strategies can be more of a challenge in severely affected flocks. As such, it is important to look for other indicators of potential gut health issues, such as:

Water and feed intake

Sudden changes in water and feed intake, whether an increase or decrease, can be a very good indicator of a gut health problem. In the early stages of a gut challenge, water intake may increase, and feed intake may decrease. Even if the change in water and feed intake is not linked directly to gut health (e.g., extreme temperatures in hot weather), any change in feed and water in the gut can disrupt the gut environment if it is not rectified.

Fecal and cecal droppings

As previously mentioned, chickens produce two types of droppings, fecal and cecal, which give an instant insight into the status of the gut at any given time. **Figure 3** shows examples of normal fecal and cecal droppings; if a bird excretes normal droppings, the gut is working correctly, and there is no imbalance. Therefore, when walking through the poultry house, examine the quality of droppings on the floor and look for changes in the consistency and color. If the quality of the droppings starts to deteriorate, there is a possible gut health issue in the birds, and intervention is needed.

Shank color

Shank color is only applicable in regions where birds are fed corn or pigments to increase the yellow color of the birds' skin. The yellow color comes from the deposition of carotenoid pigments, which are responsible for the color of corn and plants such as marigolds. During digestion, the pigments are absorbed along with fats from the diet into the bloodstream, where they are deposited around the body. Therefore, optimal pigmentation of the legs requires optimal fat absorption from the gut. If there is a gut imbalance and fat absorption is impaired, the amount of carotenoid present in the bird starts to decline, and the legs start to become pale. **Figure 10** shows an extreme case of a broiler with pale legs next to a broiler with good pigmentation. The bird on the left suffered from coccidiosis, which caused damage to the gut tissues and reduced fat absorption.

Figure 10. Bird with pale legs (left) compared to a normal broiler (right).

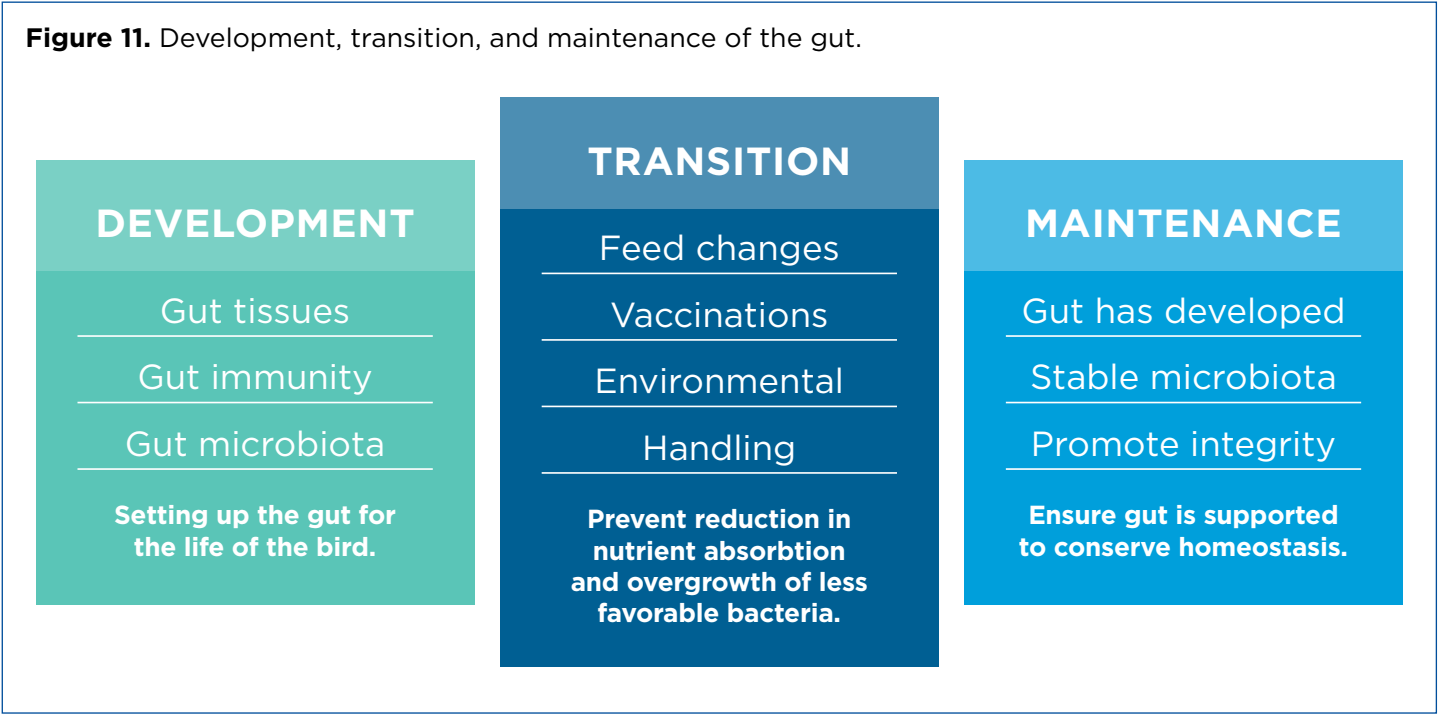


Therefore, leg color can be a very good indicator of the birds’ gut health status and nutrient absorption. If a gut health challenge is suspected, it is recommended to react quickly while an investigation is carried out to ascertain the cause. A quick and straightforward strategy is to start administering a gut health product (e.g., probiotics, organic acids, or plant extracts) to help control bacterial overgrowth and support the gut tissues. There are many gut health additives on the market, and if used correctly, they can help rebalance the gut. In most cases, a minor gut health challenge is resolved around 3–4 days after administration of a gut health product. A time period of 3–4 days is suggested, as this is the time it takes for the cells of the gut barrier to go through complete renewal. It is imperative, of course, that the cause of the gut health challenge is identified to prevent it from causing further issues. However, despite all of the ongoing industry and veterinary efforts to prevent poultry diseases, some flocks may become ill, and antibiotic treatment is then a necessary and justifiable option for the poultry veterinarian.

Gut Health Strategies

Optimal gut health in any poultry production system relies on understanding the needs of the bird throughout its life. This understanding is especially important in ABF production. When it comes to gut health products, there are often discussions about alternatives to antibiotics; however, these products work differently from antibiotics, and it may be better to consider gut health management from the perspective of alternative strategies.

The gut has three predominant stages: development, transition, and maintenance (**Figure 11**).



The gut undergoes different processes through each stage and, therefore, has different requirements. It is also worth noting that there is not one strategy that fits all flocks and farms; this is why understanding the principle of gut development and function is so important to enable the correct approach to be implemented in a given flock.

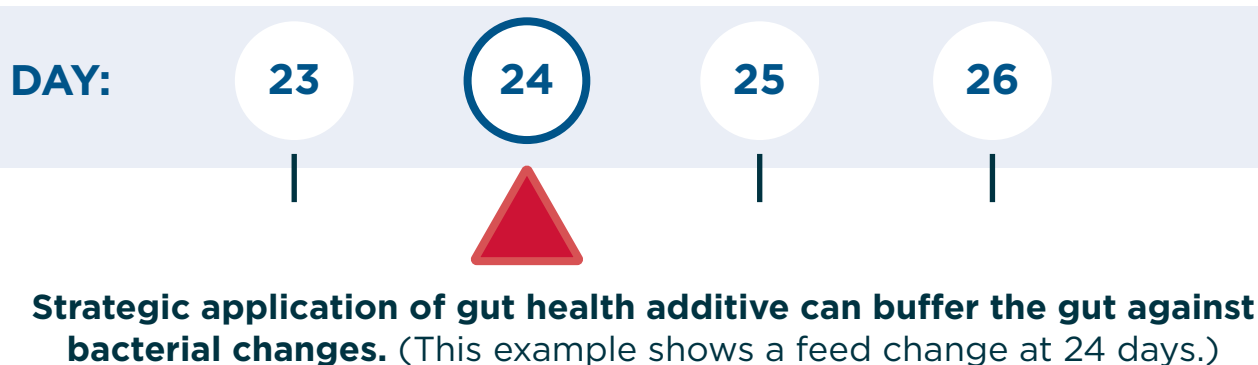
Development

During the development stage, the aim is to stimulate gut tissue and immune development and establish a beneficial microbiota. Therefore, it is essential that brooding conditions are optimal to ensure the chick is comfortable and has good access to feed and water. The establishment of a healthy microbiota can be facilitated during the first week of life by using probiotics that provide pioneering beneficial species (e.g., *Lactobacillus spp.* or *Enterococcus spp.*) that colonize the gut or probiotics that modulate the gut environment to favor colonization by beneficial bacteria from the environment. Organic acids can also be used to aid the colonization of favorable bacteria by reducing the pH in the gut. Whichever method is used to promote the beneficial microbiota must be done from the moment the chicks reach the farm; otherwise, less favorable bacteria may colonize first.

Transition

The transition stage refers to the periods where there are fluctuations in the gut environment in response to impacting factors such as feed change, vaccination, and handling. These events are normal processes during the rearing of poultry; however, they can sometimes cause a change in the intestinal environment and increase the risk of malabsorption and bacterial overgrowth. For example, when there is a feed change, there is an alteration in feed ingredients or nutrient densities; this alters the nutrients available to the bacteria, and there can be a change in the balance of bacterial communities, as they all respond differently to alternations in feed. During vaccination, the immune system has extra work to do, which can result in imbalances in the gut environment. With broiler breeders, there are times when they are handled (e.g., during grading or transport to another farm); these processes can put pressure on the birds, increasing the release of stress-related hormones and neurotransmitters in the birds. Certain bacteria have receptors for these compounds, and when activated, their growth or virulence can increase, resulting in disease. Gut health can be successfully supported through these events by strategically administering gut health additives during the event (**Figure 12**). Another strategy can be limiting the number of bird processes at a given time so that the gut does not get overloaded (e.g., it is not advisable to do a feed change and vaccination on the same day).

Figure 12. Strategic application of gut health additives.



Sudden changes in environmental conditions, such as spikes in environmental temperature, can impact the gut, causing loss of integrity of the gut barrier and bacterial invasion through the gut tissues. Strategies can be implemented to support the gut through the hot periods of the year, such as increased antioxidants in the feed or waterline administration of antioxidants during sudden spikes in temperature. Antioxidants can help limit the impact of heat stress on the gut tissues.

Maintenance

The maintenance stage refers to the period when the gut has stopped developing and reached balance. However, there is still the risk of disruption due to management or pathogen challenges, so it is important to maintain the support of the gut tissues. Optimal bird management is central to maintaining gut health, as is water and feed quality. Regular monitoring of gut health, as mentioned earlier in the document, is essential to ensure that any minor fluctuations in gut health are resolved quickly. Gut health additives may or may not be necessary during this period; it is highly dependent on the farm or flock, and regular monitoring of gut health can dictate the need.

Conclusion

Successful gut health management and optimal bird performance are possible in antibiotic-free and reduced antibiotic-use production systems. Understanding the function and biology of the gut and its components is fundamental to promoting gut health. By focusing on the relationship between the three major components of gut health (tissues, immune system, and microbiota), the needs of the gut can be identified at all points in the bird's life and supported accordingly.

References

- Adedokun SA, Olojede OC. Optimizing gastrointestinal integrity in poultry: the role of nutrients and feed additives. *Frontiers in Veterinary Science*. 2019 Jan 31;5:348.
- Akşit, M., Yalçın, S., Yenisey, C. and Özdemir, D., 2010. Brooding temperatures for chicks acclimated to heat during incubation: effects on post-hatch intestinal development and body weight under heat stress. *British Poultry Science*, 51(3), pp.444-452.
- Amerah AM, Ravindran V, Lentle RG, Thomas DG. Influence of feed particle size and feed form on the performance, energy utilization, digestive tract development, and digesta parameters of broiler starters. *Poult Sci*. 2007 Dec;86(12):2615-23.
- Andersson DI, Hughes D. Selection and Transmission of Antibiotic-Resistant Bacteria. *Microbiol Spectr*. 2017 Jul;5(4). doi: 10.1128/microbiolspec.MTBP-0013-2016. PMID: 28752817.
- Angel R, Kim SW, Li W, Jimenez-Moreno E. Velocidad de paso y pH intestinal en aves: Implicaciones para la digestión y el uso de enzimas. *Proceedings of the XXIX Curso de Especialización FEDNA, Madrid, Spain*. 2013 Nov:6-7
- Backhed, F., R. E. Ley, J. L. Sonnenburg, D. A. Peterson, and J. I. Gordon. 2005. Host-bacterial mutualism in the human intestine. *Science* 307:1915-20.
- Bailey RA, Kranis A, Psifidi A, Watson KA, Rothwell L, Hocking PM, Kaiser P, Stevens MP, Avendano S. Colonization of a commercial broiler line by *Campylobacter* is under limited genetic control and does not significantly impair performance or intestinal health. *Poult Sci*. 2018 Dec 1;97(12)
- Bailey RA. Intestinal microbiota and the pathogenesis of dysbacteriosis in broiler chickens (Doctoral dissertation, University of East Anglia). 2010
- Barekattain R, Chalvon-Demersay T, McLaughlan C, Lambert W. Intestinal Barrier Function and Performance of Broiler Chickens Fed Additional Arginine, Combination of Arginine and Glutamine or an Amino Acid
- Based Solution. *Animals (Basel)*. 2021 Aug 17;11(8):2416. doi: 10.3390/ani11082416. PMID: 34438873; PMCID: PMC8388668.
- Barnes, E. M., G. C. Mead, D. A. Barnum, and E. G. Harry. 1972. The intestinal flora of the chicken in the period 2 to 6 weeks of age, with particular reference to the anaerobic bacteria. *Br Poult Sci* 13:311-26.
- Barton MD: Antibiotic use in animal feed and its impact on human health. *Nutr Res Revs* 13:279-299, 2000.
- Bedford, M. 2000. Removal of antibiotic growth promoters from poultry diets: Implications and strategies to minimise subsequent problems *World Poultry Sci J* 56:347-365.
- Bengtsson-Palme J, Kristiansson E, Larsson DGJ. Environmental factors influencing the development and spread of antibiotic resistance. *FEMS Microbiol Rev*. 2018 Jan 1;42(1):fux053. doi: 10.1093/femsre/fux053. PMID: 29069382; PMCID: PMC5812547.
- Bohorquez DV, Bohorquez NE, Ferket PR: Ultrastructural development of the small intestinal mucosa in the embryo and turkey poult: A light and electron microscopy study. *Poult Sci* 90:842-855, 2011.
- Casewell, M., C. Friis, E. Marco, P. McMullin, and I. Phillips. 2003. The European ban on growth-promoting antibiotics and emerging consequences for human and animal health. *J Antimicrob Chemother* 52:159-61.
- Cebra, J. J. 1999. Influences of microbiota on intestinal immune system development. *Am J Clin Nutr* 69:1046S-1051S.
- Cerf-Bensussan, N., and V. r. Gaboriau-Routhiau. 2010. The immune system and the gut microbiota: friends or foes? *Nat Rev Immunol* 10:735-744.
- Chen J, Tellez G, Richards JD, Escobar J. Identification of potential biomarkers for gut barrier failure in broiler chickens. *Frontiers in veterinary science*. 2015 May 26;2:14.
- Choct M. Managing gut health through nutrition. *Br Poult Sci* 50:9-15, 2009.
- Clavijo V, Flórez MJV. The gastrointestinal microbiome and its association with the control of pathogens in broiler chicken production: A review. *Poult Sci*. 2018 Mar 1;97(3):1006-1021. doi: 10.3382/ps/pex359. PMID: 29253263; PMCID: PMC5850219.
- Corthesy B, Gaskins HR, Mercenier A. Cross-talk between probiotic bacteria and the host immune system. *The Journal of nutrition*. 2007 Mar 1;137(3):781S-90S.
- De Meyer F, Eeckhaut V, Ducatelle R, Dhaenens M, Daled S, Dedeurwaerder A, De Gussem M, Haesebrouck F, Deforce D, Van Immerseel F. Host intestinal biomarker identification in a gut leakage model in broilers. *Veterinary Research*. 2019 Dec;50:1-4.
- Diaz Carrasco JM, Casanova NA, Fernández Miyakawa ME. Microbiota, Gut Health and Chicken Productivity: What Is the Connection? *Microorganisms*. 2019 Sep 20;7(10):374. doi: 10.3390/microorganisms7100374. PMID: 31547108; PMCID: PMC6843312.
- Dibner, J. J., and J. D. Richards. 2005. Antibiotic growth promoters in agriculture: history and mode of action. *Poult Sci* 84:634-43.

Ducatelle R, Goossens E, Eeckhaut V, Van Immerseel F. Poultry gut health and beyond, *Animal Nutrition Journal*, <https://doi.org/10.1016/j.aninu.2023.03.005>.

Dunlop MW, Moss AF, Groves PJ, Wilkinson SJ, Stuetz RM, Selle PH. The multidimensional causal factors of 'wet litter' in chicken-meat production. *Science of the Total Environment*. 2016 Aug 15;562:766-76.

Freestone PPE, Sandrini SM, Haigh RD, et al: Microbial endocrinology: how stress influences susceptibility to infection. *Trends in Microbiology* 16:55-64, 2008

Fuller, R. 1978. Epithelial Attachment and Other Factors Controlling the Colonization of the Intestine of the Gnotobiotic Chicken by Lactobacilli. *J Appl Microbiol* 45:389-395

Garcia-Gutierrez E, Mayer MJ, Cotter PD, Narbad A. Gut microbiota as a source of novel antimicrobials. *Gut Microbes*. 2019;10(1):1-21. doi: 10.1080/19490976.2018.1455790. Epub 2018 May 22. PMID: 29584555; PMCID: PMC6363078.

Geyra A, Uni Z, Sklan D. The effect of fasting at different ages on growth and tissue dynamics in the small intestine of the young chick. *British Journal of Nutrition*. 2001 Jul;86(1):53-61.

Ghafourian S, Sadeghifard N, Soheili S, Sekawi Z. Extended Spectrum Beta-lactamases: Definition, Classification and Epidemiology. *Curr Issues Mol Biol*. 2015;17:11-21. Epub 2014 May 12. PMID: 24821872.

Gustafson, R. H., and R. E. Bowen. 1997. Antibiotic use in animal agriculture. *J Appl Microbiol* 83:531-41.

Heilbronner S, Krismer B, Brötz-Oesterhelt H, Peschel A. The microbiome-shaping roles of bacteriocins. *Nat Rev Microbiol*. 2021 Nov;19(11):726-739. doi: 10.1038/s41579-021-00569-w. Epub 2021 Jun 1. PMID: 34075213.

Hirn J, Nurmi E, Johansson T, Nuotio L. Long-term experience with competitive exclusion and salmonellas in Finland. *Int J Food Microbiol*. 1992 Mar-Apr;15(3-4):281-5. doi: 10.1016/0168-1605(92)90059-c. PMID: 1419533.

Hooper LV, Gordon JI: Commensal host-bacterial relationships in the gut. *Science* 292:1115-1118, 2001.

Hooper LV, Littman DR, Macpherson AJ. Interactions between the microbiota and the immune system. *Science* 336:1268-1273, 2012.

Hooper LV: Bacterial contributions to mammalian gut development. *Trends Microbiol* 12:129-134, 2004 Han GG, Kim EB, Lee J, Lee JY, Jin G, Park J, Huh CS, Kwon IK, Kil DY, Choi YJ, Kong C.

Huyghebaert G, Ducatelle R, Van Immerseel F. An update on alternatives to antimicrobial growth promoters for broilers. *Vet J*. 2011 Feb;187(2):182-8.

Johnston AM: Animals and antibiotics. *Int J Antimicrob Agents* 18:291-294, 2001.

Joshi S, Shallal A, Zervos M. Vancomycin-Resistant Enterococci: Epidemiology, Infection Prevention, and Control. *Infect Dis Clin North Am*. 2021 Dec;35(4):953-968. doi: 10.1016/j.idc.2021.07.002. PMID: 34752227.

Khan KA, Khan SA, Aslam A, Rabbani M, Tipu MY. Factors contributing to yolk retention in poultry: a review. *Pakistan Veterinary Journal*. 2004;24(1):46-51.

Khan S, Moore RJ, Stanley D, Chousalkar KK. The Gut Microbiota of Laying Hens and Its Manipulation with Prebiotics and Probiotics To Enhance Gut Health and Food Safety. *Appl Environ Microbiol*. 2020 Jun 17;86(13):e00600-20. doi: 10.1128/AEM.00600-20. PMID: 32332137; PMCID: PMC7301851.

Kizerwetter-Świda M, Binek M: Bacterial microflora of the chicken embryos and newly hatched chicken. *Journal of Animal and Feed Sciences* 17:224-232, 2008

Lakhundi S, Zhang K. Methicillin-Resistant *Staphylococcus aureus*: Molecular Characterization, Evolution, and Epidemiology. *Clin Microbiol Rev*. 2018 Sep 12; 31(4):e00020-18. doi: 10.1128/CMR.00020-18. PMID: 30209034; PMCID: PMC6148192.

Libby, D. A., and P. J. Schaible. 1955. Observations on growth responses to antibiotics and arsonic acids in poultry feeds. *Science* 121:733-4.

Lobanovska M, Pilla G. Penicillin's Discovery and Antibiotic Resistance: Lessons for the Future? *Yale J Biol Med*. 2017 Mar 29;90(1):135-145. PMID: 28356901; PMCID: PMC5369031.

Lutful Kabir SM: The role of probiotics in the poultry industry. *Int J Mol Sci* 10:3531-3546, 2009.

Maes S, Vackier T, Nguyen Huu S, Heyndrickx M, Steenackers H, Samplers I, Raes K, Verplaetse A, De Reu K. Occurrence and characterisation of biofilms in drinking water systems of broiler houses. *BMC microbiology*. 2019 Dec;19:1-5.

Maharjan P, Clark T, Kuenzel C, Foy MK, Watkins S. On farm monitoring of the impact of water system sanitation on microbial levels in broiler house water supplies. *Journal of applied poultry research*. 2016 Jun 1;25(2):266-71.

- Maiorka A, Santin E, Dahlke F, Boleli IC, Furlan RL, Macari M. Posthatching water and feed deprivation affect the gastrointestinal tract and intestinal mucosa development of broiler chicks. *Journal of Applied Poultry Research*. 2003 Dec 1;12(4):483-92.
- Manning L, Chadd SA, Baines RN. Key health and welfare indicators for broiler production. *World's Poultry Science Journal*. 2007 Mar;63(1):46-62.
- Marchini CF, Café MB, Araújo EG, Nascimento MR. Physiology, cell dynamics of small intestinal mucosa, and performance of broiler chickens under heat stress: a review. *Revista Colombiana de Ciencias Pecuarias*. 2016 Sep;29(3):159-68.
- Matijašić M, Meštrović T, Paljetak HČ, Perić M, Barešić A, Verbanac D. Gut Microbiota beyond Bacteria-Mycobiome, Virome, Archaeome, and Eukaryotic Parasites in IBD. *Int J Mol Sci*. 2020 Apr 11;21(8):2668. doi: 10.3390/ijms21082668. PMID: 32290414; PMCID: PMC7215374.
- Mead GC. Microbes of the avian cecum: types present and substrates utilized. *J Exp Zool Suppl* 3:48-54, 1989.
- Mehdi Y, Létourneau-Montminy MP, Gaucher ML, Chorfi Y, Suresh G, Rouissi T, Brar SK, Côté C, Ramirez AA, Godbout S. Use of antibiotics in broiler production: Global impacts and alternatives. *Anim Nutr*. 2018 Jun;4(2):170-178. doi: 10.1016/j.aninu.2018.03.002. Epub 2018 Apr 3. PMID: 30140756; PMCID: PMC6103476.
- Moore, P. R., A. Evenson, T. D. Luckey, E. McCoy, C. A. Elvehjem, and E. B. Hart. 1946. Use of sulfasuxidine, streptothricin, and streptomycin in nutritional studies with the chick. *J. Biol. Chem*. 165:437-441.
- Niewold TA. The nonantibiotic anti-inflammatory effect of antimicrobial growth promoters, the real mode of action? A hypothesis. *Poult Sci*. 2007 Apr;86(4):605-9. doi: 10.1093/ps/86.4.605. PMID: 17369528.
- Onrust L, Ducatelle R, Van Driessche K, De Maesschalck C, Vermeulen K, Haesebrouck F, Eeckhaut V, Van Immerseel F. Steering Endogenous Butyrate Production in the Intestinal Tract of Broilers as a Tool to Improve Gut Health. *Front Vet Sci*. 2015 Dec 17;2:75. doi: 10.3389/fvets.2015.00075. PMID: 26734618; PMCID: PMC4682374.
- Oviedo-Rondón EO. Holistic view of intestinal health in poultry. *Animal Feed Science and Technology*. 2019 Apr 1;250:1-8.
- Paraskeuas V, Mountzouris KC. Broiler gut microbiota and expressions of gut barrier genes affected by cereal type and phytogenic inclusion. *Anim Nutr*. 2019 Mar;5(1):22-31. doi: 10.1016/j.aninu.2018.11.002. Epub 2018 Dec 19. PMID: 30899806; PMCID: PMC6407073.
- Rahimi S, Grimes JL, et al., Effect of a direct-fed microbial (Primalac) on structure and ultrastructure of small intestine in turkey poult. *Poultry Sci* 88:491-503. 2009.
- Ranjitkar S, Lawley B, Tannock G, Engberg RM. Bacterial Succession in the Broiler Gastrointestinal Tract. *Appl Environ Microbiol*. 2016 Apr 4;82(8):2399-2410.
- Ravindran V, Abdollahi MR. Nutrition and Digestive Physiology of the Broiler Chick: State of the Art and Outlook. *Animals (Basel)*. 2021 Sep 25;11(10):2795. doi: 10.3390/ani11102795. PMID: 34679817; PMCID: PMC8532940.
- Relationship between the microbiota in different sections of the gastrointestinal tract, and the body weight of broiler chickens. *Springerplus*. 2016 Jun 29;5(1):911. doi: 10.1186/s40064-016-2604-8. PMID: 27386355; PMCID: PMC4927549.
- Reygaert WC. An overview of the antimicrobial resistance mechanisms of bacteria. *AIMS Microbiol*. 2018 Jun 26;4(3):482-501. doi: 10.3934/microbiol.2018.3.482. PMID: 31294229; PMCID: PMC6604941.
- Rinttilä T, Apajalahti J. Intestinal microbiota and metabolites—Implications for broiler chicken health and performance. *Journal of Applied Poultry Research*. 2013 Oct 1;22(3):647-58.
- Rostagno MH. Effects of heat stress on the gut health of poultry. *Journal of Animal Science*. 2020 Apr;98(4):skaa090.
- Scanes CG, Dridi S, editors. *Sturkie's avian physiology*. Academic Press; 2021.
- Sholeh, M., Krutova, M., Forouzesh, M. et al. Antimicrobial resistance in *Clostridioides (Clostridium) difficile* derived from humans: a systematic review and meta-analysis. *Antimicrob Resist Infect Control* 9, 158 (2020). <https://doi.org/10.1186/s13756-020-00815-5>.
- Simm R, Slettemeås JS, Norström M, Dean KR, Kaldhusdal M, Urdahl AM. Significant reduction of vancomycin resistant *E. faecium* in the Norwegian broiler population coincided with measures taken by the broiler industry to reduce antimicrobial resistant bacteria. *PLoS One*. 2019 Dec 12;14(12):e0226101. doi: 10.1371/journal.pone.0226101. PMID: 31830083; PMCID: PMC6907784.
- Smith JA. Broiler production without antibiotics: United States field perspectives. *Animal Feed Science and Technology*. 2019 Apr 1;250:93-8.
- Song B, Tang D, Yan S, Fan H, Li G, Shahid MS, Mahmood T, Guo Y. Effects of age on immune function in broiler chickens. *Journal of Animal Science and Biotechnology*. 2021 Dec;12:1-2.
- Suzuki T. Regulation of the intestinal barrier by nutrients: The role of tight junctions. *Animal Science Journal*. 2020 Jan;91(1):e13357.

- Szott V, Reichelt B, Friese A, Roesler U. A Complex Competitive Exclusion Culture Reduces *Campylobacter jejuni* Colonization in Broiler Chickens at Slaughter Age In Vivo. *Vet Sci*. 2022 Apr 11;9(4):181. doi: 10.3390/vetsci9040181. PMID: 35448680; PMCID: PMC9029414.
- Torok VA, Hughes RJ, Mikkelsen LL, Perez-Maldonado R, Balding K, MacAlpine R, Percy NJ, Ophel-Keller K. Identification and characterization of potential performance-related gut microbiotas in broiler chickens across various feeding trials. *Appl Environ Microbiol*. 2011 Sep;77(17):5868-78. doi: 10.1128/AEM.00165-11. Epub 2011 Jul 8. PMID: 21742925; PMCID: PMC3165380.
- Umesaki, Y., H. Setoyama, S. Matsumoto, and Y. Okada. 1993. Expansion of alpha beta T-cell receptor-bearing intestinal intraepithelial lymphocytes after microbial colonization in germ-free mice and its independence from thymus. *Immunology* 79:32-7.
- Uni Z, Tako E, Gal-Garber O, Sklan D. Morphological, molecular, and functional changes in the chicken small intestine of the late-term embryo. *Poult Sci*. 2003 Nov;82(11):1747-54. doi: 10.1093/ps/82.11.1747. PMID: 14653469.
- Uni ZE, Ganot SA, Sklan DA. Posthatch development of mucosal function in the broiler small intestine. *Poultry Science*. 1998 Jan 1;77(1):75-82.
- van der Wagt I, de Jong IC, Mitchell MA, Molenaar R, van den Brand H. A review on yolk sac utilization in poultry. *Poultry Science*. 2020 Apr 1;99(4):2162-75.
- van der Wielen, P. W., D. A. Keuzenkamp, L. J. Lipman, F. van Knapen, and S. Biesterveld. 2002. Spatial and temporal variation of the intestinal bacterial community in commercially raised broiler chickens during growth. *Microb Ecol* 44:286-93
- Van Leeuwen P, Mouwen JM, Van Der Klis JD, Verstegen MW. Morphology of the small intestinal mucosal surface of broilers in relation to age, diet formulation, small intestinal microflora and performance. *British Poultry Science*. 2004 Feb 1;45(1):41-8.
- Ventola CL. The antibiotic resistance crisis: part 1 — causes and threats. *P T*. 2015 Apr;40(4):277-83. PMID: 25859123; PMCID: PMC4378521.
- Verbrugghe E, Boyen F, Gaastra W, et al: The complex interplay between stress and bacterial infections in animals. *Veterinary Microbiology* 155:115-127, 2012
- Wideman RF, et al., A wire-flooring model for inducing lameness in broilers: evaluation of probiotics as a prophylactic treatment. *Poultry Sci* 91:870-83. 2012.
- Williams RB. Intercurrent coccidiosis and necrotic enteritis of chickens: rational, integrated disease management by maintenance of gut integrity. *Avian pathology*. 2005 Jun 1;34(3):159-80.
- Wong EA, Uni Z. Centennial Review: The chicken yolk sac is a multifunctional organ. *Poultry Science*. 2021 Mar 1;100(3):100821.
- Yang Y, Iji PA, Choct M: Dietary modulation of gut microflora in broiler chickens: a review of the role of six kinds of alternatives to in-feed antibiotics. *World's Poultry Science Journal* 65:97-114, 2009.
- Yang Z, Zhang C, Wang J, Celi P, Ding X, Bai S, Zeng Q, Mao X, Zhuo Y, Xu S, Yan H. Characterization of the intestinal microbiota of broiler breeders with different egg laying rate. *Frontiers in Veterinary Science*. 2020 Nov 24;7:599337.
- Zenner C, Hitch TCA, Riedel T, Wortmann E, Tiede S, Buhl EM, Abt B, Neuhaus K, Velge P, Overmann J, Kaspers B, Clavel T. Early-Life Immune System Maturation in Chickens Using a Synthetic Community of Cultured Gut Bacteria. *mSystems*. 2021 May 18;6(3):e01300-20. doi: 10.1128/mSystems.01300-20. PMID: 34006629; PMCID: PMC8269260.
- Zhou A, Yuan Y, Yang M, Huang Y, Li X, Li S, Yang S, Tang B. Crosstalk Between the Gut Microbiota and Epithelial Cells Under Physiological and Infectious Conditions. *Front Cell Infect Microbiol*. 2022 Jan 27;12:832672. doi: 10.3389/fcimb.2022.832672. PMID: 35155283; PMCID: PMC8829037.
- Zhou Q, Lan F, Li X, Yan W, Sun C, Li J, Yang N, Wen C. The Spatial and Temporal Characterization of Gut Microbiota in Broilers. *Front Vet Sci*. 2021 Aug 30;8:712226. doi: 10.3389/fvets.2021.712226.
- Zoetendal, E. G., B. Cheng, S. Koike, and R. I. Mackie. 2004. Molecular microbial ecology of the gastrointestinal tract: from phylogeny to function. *Curr Issues Intest Microbiol* 5:31-47.



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