The control of coccidiosis in poultry

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Coccidiosis is still considered one of the main diseases affecting the performance of poultry reared under intensive production systems. The estimated cost per bird produced is €0.05, resulting in a worldwide cost of €2.3 billion. Still, with currently available diagnostic methods such as oocyst counts and lesion scoring, an interpretation of the impact of (subclinical) coccidiosis is not easy. Another problem that is difficult to address with currently available tools is the interpretation of the efficacy of an anticoccidial programme.

Anticoccidial sensitivity testing is the only reproducible method available today, but interpretation is far from easy. Therefore, although coccidiosis is not perceived as a major problem in poultry production, economical impact of coccidiosis is most probably underestimated and optimisation of anticoccidial programmes might be advantageous to the broiler industry.

In addition to this, a link between subclinical coccidiosis and bacterial enteritis complicates choosing the right tools and strategy for poultry producers. Sound shuttle and rotation programmes can be part of the answer in order to control not only clinical, but also subclinical, coccidiosis.

Coccidiosis is a disease that is caused by protozoan parasites of the genus Eimeria, developing within the intestine of most domestic and wild animals and birds.

Seven species of Eimeria (E. acervulina, E. brunette, E. maxima, E. mitis, E. necatrix, E. praecox and E. tenella) are recognised species infecting chickens. Although coccidiosis has been known for many years, it is still considered the most economically important parasitic condition affecting poultry production worldwide.

An estimate of the cost of coccidiosis in poultry in Sweden is €0.023 per kg live weight. Based on a compartmentalised model, one can estimate that the worldwide impact of coccidiosis, assuming 50 billion broilers of 2kg live weight are produced annually, is more than €2.3 billion.

It should also be noted that Swedish poultry production is at a high standard and coccidiosis is not considered an issue.

Importantly, almost 70% of this cost is subclinical due to its impact on weight gain and feed conversion rate. The reasons for these remarkable findings might be a difficult diagnosis of subclinical coccidiosis preventing the industry from evaluating the best possible strategies for coccidiosis control.

For the control of coccidiosis in chicken and turkeys, a number of preventive medications have been approved for use worldwide, but reduced sensitivity and resistance are increasingly important as no new anticoccidial compounds are known to be under development.

Live attenuated and non-attenuated vaccines are available, but next to cost reasons, the fact that live vaccines need host cells to replicate and instigate an active immunity, cause them to allow subclinical levels of coccidiosis. This is associated with a diminution of performance and in the absence of growth promoters even attenuated vaccines are considered by many producers to be associated with a higher incidence of bacterial enteritis. Still, live vaccines are significant and important in the anticoccidial arsenal, as will be explained in this article.

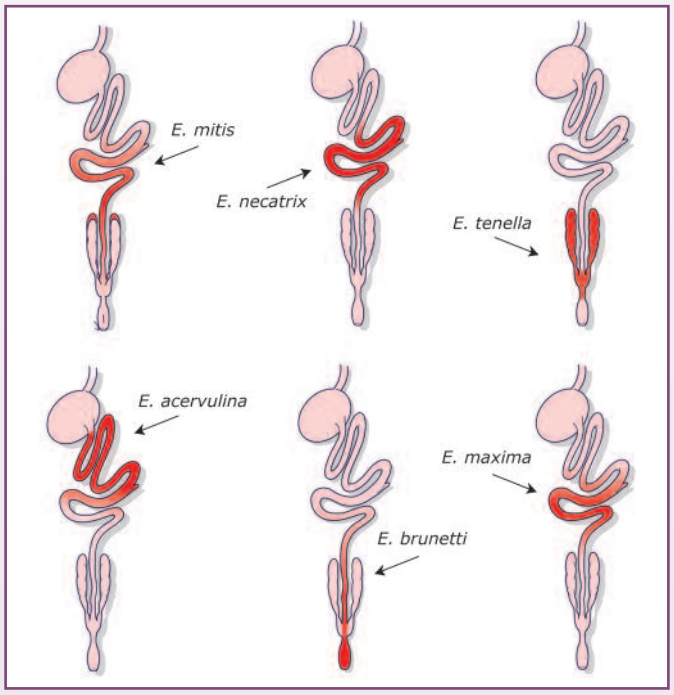
New approaches, such as vaccination of breeders with conferring maternal immunity or recombinant vaccines are not popular in practice or not yet available.

Today, fundamental research on coccidiosis is focused on improving molecular techniques that might serve improved diagnostics or the development of recombinant vaccines but, until now, have not solved many practical questions on what kind of prevention is adequate for a certain poultry production unit.

Although significant and promising steps have been made in describing the biology, diagnosis, epidemiology and prevention of coccidiosis, a number of issues important to the industry are not sufficiently addressed today.

The purpose of this article is to provide a brief overview and interpretation of the most practically relevant insights on diagnosis, control, prevention and the impact of coccidiosis on the overall gut health of chickens.

Fig. 1. Important species of coccidiosis and their sites of infection in the gut.



Diagnosis and testing

As indicated, one of the main reasons coccidiosis is still a major problem, is the difficult diagnosis. The classical parasitological methods of diagnosis are labour intensive and therefore costly. Oocyst per gram (OPG) counts in faeces or litter have a poor relation with the impact of the parasite on the performance of a flock.

Lesion scoring is an interpretation based on macroscopic visible lesions caused by Eimeria, usually following a scoring system from zero to four.

The individual scores for all the species are usually compiled for a certain number of birds (for example, six) per flock resulting in a Total Mean Lesion Score (TMLS). The method is extremely labour intensive, sometimes subjective and only reliable when performed by skilled people.

The relation between lesion scoring and performance is believed to be stronger than with OPG but there is still a difficult appreciation of the level of lesions towards impact on performance, mainly at subclinical levels. E. mitis, although quite pathogenic, does not cause typical lesions and is mostly disregarded using this method.

Lesion scoring still remains the most frequently applied diagnostic method today. The seven species of Eimeria infecting chickens are not considered equally important.

Usually, the most pathogenic recognised species in broiler chickens are E. acervulina, E. maxima and E. tenella. The latter is, amongst broiler chicken farmers, the best known. It infects the caecum and because of its deep development in the mucosa and subsequent widespread damage with distinct gross

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lesions and loss of blood in the faeces, it is easily recognised by farmers as an important pathogen.

On the other hand, when performing field necropsies on a larger scale, E. tenella will be the least prevalent of the three species mentioned.

Damage is limited to the caecum, a relatively less important part of the gut with regards to digestion and absorption, thus growth and feed conversion rate. Diagnosis of the clinical disease is quite easy and action (therapy in the short term, change of preventive means) is swift.

These facts make its impact on the productivity of the broiler industry relative to the others limited, although many broiler farmers associate coccidiosis only with caecum coccidiosis. This is a good example of perception not being in line completely with the facts. E. acervulina and E. maxima, both more prevalent, are less related to clinical coccidiosis in field conditions.

E. acervulina causes white lesions in the duodenum and in heavier infections also more caudal, interfering even with the ability for E. maxima to develop, E. maxima causes petechiae in the midgut.

Lesion score performance

To assess the levels of coccidiosis of these two species, lesion scores can be performed. An important debate is still ongoing on what levels are to be considered clinical (and requiring treatment) and what levels are subclinical. Some consider lesions higher than 1.5 per species as indicative for clinical disease and levels below as subclinical, not requiring treatment. E. praecox and E. mitis are not scored for and are completely disregarded using the lesion scoring method, although both species are known to cause feed conversion losses and, in the latter case, even morbidity.

Moreover, it has been demonstrated that there is a poor relation between macroscopic and microscopic lesions, emphasising that using macroscopic lesion scoring alone is not suitable to detect all economical relevant coccidiosis infections.

It is frequently disregarded that any macroscopic but also microscopic lesion, even any infection of coccidia, requires an invasion and thus destruction of host cells.

This is both true with a completion of the parasitical life cycle, but also when an intervention of the immune system occurs. In the latter case not only are host cells destroyed, but the activation of the immune system means that nutrients cannot be used for conversion into meat, which is the ultimate goal of broiler production. As a consequence, defining what (sub)clinical levels of coccidiosis are, might be relevant with regards to a decision on treatment. It is important to understand that any level of coccidiosis causes a real, but difficult to quantify, loss in performance.

As coccidiosis is a disease that cannot currently be eliminated, the objective of coccidiosis prevention is to find the economically optimal balance between the cost of diagnosis, prevention and treatment making use of host immunity, while accepting a certain level of subclinical loss.

It is clear that producers achieving a better balance will have a competitive advantage over other producers.

An overview of advances in diagnosis of coccidiosis and analysis in genetic variation in Eimeria is given by Morris and Gasser. This review covers both biochemical and molecular methods such as multilocus enzyme electrophoresis, southern blot analysis, pulsed-field gel electrophoresis and several PCR techniques.

These techniques are a major addition for scientific research and more practical applications such as establishing vaccine quality control.

Unfortunately, the lack of a rapid, low cost and especially quantitative test is preventing the broad scale use of these techniques.

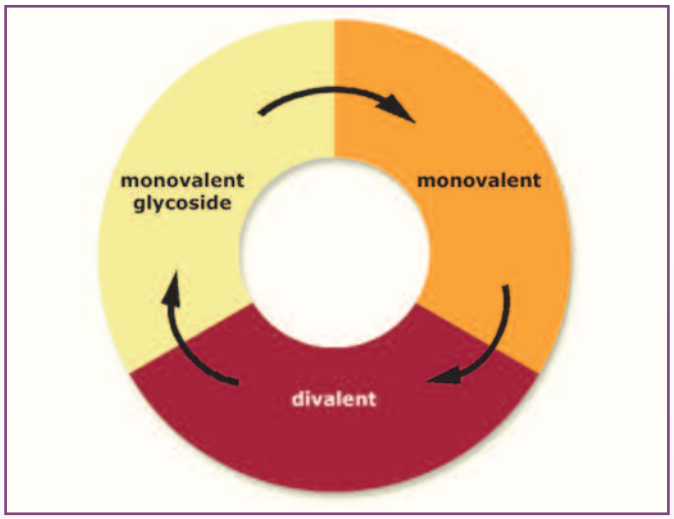
The main application of these techniques for field diagnosticians today is the possibility of defining the presence of species currently disregarded such as E. praecox and E. mitis. Still, the lack of the quantitative aspect of the techniques, certainly with the widespread use of ionophores that allow some multiplication of also sensitive parasites, is preventing an accurate appreciation of different species of coccidiosis.

A very innovative on-line technique is called Coccimorph. This is a computational approach for parasite diagnosis, in this case Eimeria spp. from chicken and rabbit.

Images from sporulated oocysts from a confirmed species were assessed on different features: curvature characterisation, size and symmetry and internal structure characterisation.

Users can upload their digital images from unidentified oocysts and have the programme identify the species concerned. This is very accessible and the low cost is a major advantage.

A disadvantage is only sporulated oocysts can be identified, which limits the use of this technique to litter sample identification only, and no aid for instance in identifying species encountered during necropsy or from fresh faecal samples.



Rotate ionophores by switching from one ionophore class to another.

Regular assessments

Necropsy sessions are performed in co-operation with the pharmaceutical industry in a number of countries. Basically, such systems consist of a planned, organised and benchmarked assessment of the lesions score and gut health on a poultry complex (group of farms on the same anticoccidial programme) basis.

A number of times per year and always at the same laboratory, preferably the same, well trained specialists assess a significant number of poultry houses, thus improving the reproducibility of lesion scoring session, compared to a field lesion scoring session.

This methodology is suitable for assessing the overall efficacy of the anticoccidial programme, including reduced sensitivity and resistance of drugs in use. In order to make firmer conclusions, session data are compared with historical data.

Anticoccidial sensitivity testing (AST) is a well known technique to try to assess resistance of a certain coccidial isolate to different anticoccidial drugs. Although a valid method for a certain isolate, this technique is not routinely used.

The main reason is the long timelines and very high cost associated with the complicated, in vivo character of the test. The short period of testing (usually about six days), without allowing the initially naïve birds to recover from an artificially high infective dose, does not makes interpretation of the results easy.

One way to decrease the cost is sampling different houses in one AST. In this way, a worst case result for the different strains may give good information on what anticoccidials could be effectively used on a large portion of farms in a broiler complex.

By meta-analysing AST results from strains with a known drug history, a better knowledge of how fast resistance is induced, how long it remains established in a certain coccidial population and information on cross resistance amongst drugs, can be obtained.

Prevention and control

There are basically two means of prevention of coccidiosis: chemoprophylaxis and vaccination. Chemoprophylaxis is by far the most popular and it is estimated that 95% of the broilers produced yearly receive drugs – the so-called anticoccidials or anticoccidial products (ACP) in the ration. Sometimes the term 'coccidiostats' are used with regard to ACPs but, in reality, most of the ACPs currently on the market are coccidiocidal and not just static.

Generally, two groups of anticoccidials are considered, ionophorous antibiotics or 'ionophores' and synthetically produced drugs, also denominated as 'chemicals'.

Chemicals were the first type of drugs being used in the treatment and later in the prevention of coccidiosis. In 1948, sulphaquinoxaline was the first drug continuously administered in the feed at low doses.

Other chemicals followed in the years after, allowing the poultry industry to expand and increase production. Most of these chemicals have now disappeared from the marketplace. The main reason for this is the rapid selection for resistant coccidian when these chemicals were used, requiring a judicious use of chemicals, with switching to another drug before resistance had built up.

This limits the commercial potential and in combination with increasingly high costs associated with registration of anticoccidials explains the short life cycles of some chemicals. There are a couple of chemicals that are marketed today, such as nicarbazin, robenidin, diclazuril, zoalene, decoquinate and halofuginone. The fact that they are still being marketed is a demonstration of their value to the poultry industry and

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thus an indication of the more limited potential for resistance compared to the previous ones.

The resistance status of chemicals can be assessed using AST.

Chemicals are often used in order to reduce the infection pressure of coccidiosis, a so-called clean up programme.

Clean up programmes and, consequently, the reduced (subclinical) infection pressure is expected to have a positive impact on performance. To achieve this, chemicals are preferably used during a complete grow out in a so-called full programme. In order to limit the risk of resistance, some producers do not use chemicals in a full programme but switch from one chemical to another in the same grow out, in a so called shuttle programme.

Switching after a certain grow out from one anticoccidial to another or to a shuttle programme is called rotation.

Introduction of ionophores

The most popular ACPs are true carboxylic ionophores. The ionophores are subdivided into different classes, The main reason for their success is the relatively limited risk for complete resistance to ionophores, at least compared to the risk for resistance towards chemicals.

Indeed, after the introduction of the first ionophore, monensin, in the 1970s it is remarkable to see that these drugs are still predominant in the prevention of coccidiosis. An explanation for this slow acquisition of resistance to ionophores is the leakage of sensitive oocysts while chickens are being fed adequate levels of ionophores.

In combination with an immune response corresponding with the age of the birds, this makes the resistance selection less stringent than with chemicals. The mode of action of the different ionophores is similar. Owing to their lipophilicitic character they are able, while carrying cations, to be incorporated in cell walls, thus facilitating ion transport across the cell membrane.

This causes ionic gradient and content modifications with parasite cell death as a final consequence. Based on their cation selectivity, transport rate capacity and structure, three classes can be identified, monovalent, monovalent glycoside and divalent ionophores.

The ones registered and marketed worldwide are monensin, salinomycin, narasin (monovalent), maduramicin, semduramicin (monovalent glycoside) and lasalocid (divalent).

One of the main debates still ongoing amongst coccidiologists is the ability to acquire resistance to one drug by the use of another drug, so-called cross resistance.

There is strong evidence of incomplete cross resistance within a certain ionophore class in the fact that, after years of use of the monovalent ionophore monensin, resistance to narasin in the United States was encountered before the product was commercially launched.

Several papers indicate this cross resistance is less obvious between products of different classes, for instance between maduramicin and monovalent ionophores or between lasalocid and monovalent ionophores. The debate is of particular importance when defining rotation programme. In the strictest sense rotating between one monovalent drug to another can be considered rotation, but taking into account incomplete cross resistance within a class of ionophores, the relevance of this type of rotation should be questioned.

Therefore, relevant or true rotation for anticoccidials is suggested to be between classes of ionophores or chemicals. Some producers do not use rotation programmes, although a majority has accepted this principle as valuable in order to maintain and safeguard the efficacy of anticoccidials.

Chapman pointed out that one of the reasons producers can afford limited rotation, thus working with not fully effective drugs, is the importance of immunity towards coccidiosis. This is true when drugs are used to prevent clinical coccidiosis, but to control subclinical coccidiosis this might be an inadequate strategy.

As solid flock immunity is only achieved at six to seven weeks of age in built up litter conditions, it is likely that subclinical levels will cause economical damage, in direct relation to the level of subclinical coccidiosis.

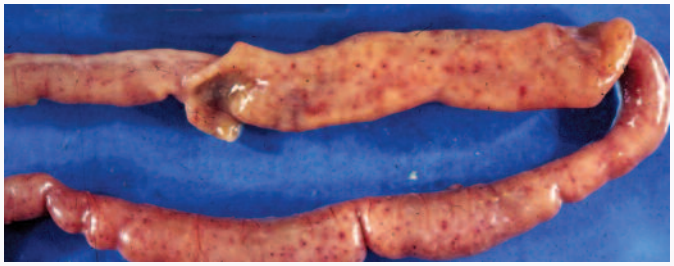
Logically, a more efficient anticoccidial will cause lower levels of subclinical coccidiosis, thus less economical damage. Subclinical damage is, therefore, considered by some coccidiologists today to be the most important reason for rotation programmes.

Live vaccination, as previously indicated, is less important in broiler production. Two types of vaccines are available – attenuated and virulent. Attenuated vaccines lack a part of the life cycle (less asexual reproductive cycles) of the original strain they were derived from and, as a consequence, have a lower reproductive and pathogenic potential.

This is a major advantage towards performance of coccidial vaccines, but because of the lower reproductive potential, production costs are significantly higher.

Some vaccines consist of anticoccidial sensitive strains and others are made of more or less resistant strains. The main advantage of the live ACP sensitive vaccines is their ability to alter the level of resistance in a certain coccidial population.

There are several reports on this very interesting feature of vaccines, but many questions still remain on how many consecutive grow-outs with each vaccine available should be applied to respectively overcome or prevent resistance to the different anticoccidials marketed.



E. necatrix lesions.

Also, the stability of these resensitised populations are not well known. However, the approach of live vaccination to optimise the efficacy of anticoccidials might become increasingly important and, next to simple resting of anticoccidials, is the only method known to help reduce the portion of resistant parasites in a given coccidial population.

Designing programmes

When designing anticoccidial programmes, the above aspects of resistance and restoration of sensitivity may be used to optimise rotation and shuttle programmes. A first consideration is the definition of shuttle and rotation programmes.

Strictly speaking, changing from one drug to another is enough to talk about shuttle or rotation but, in view of the cross resistance described, a more narrow definition would suggest rotation and shuttle to be more valid if switching from one class of drug to another.

Indeed, no proof exists that a shuttle between two monovalent ionophores will slow down resistance development; therefore no indication exists to perform this type of shuttle. Another consideration is resting anticoccidials as proven by Chapman and McFarland. Resting monovalent ionophores is advantageous to the anticoccidial efficacy pattern of a coccidial population, but cross resistance might invalidate this rest.

Therefore, in order to also substantially control subclinical losses, the prudent use of anticoccidials might include a concentration of ionophores from the same class in the same shuttle or in the full programme and after this use of a class, rotating away, ideally to chemicals or vaccines, but practically another class of ionophores will also be considered. However, a lot of research is still needed to better validate these, at first sight, obvious ideas.

Microbial intestinal flora

During recent years, interesting research models have been developed to study impaired gut health in the absence of growth promoters. Indeed, one of the main concerns for poultry integrations is the vast majority of flocks suffering from several degrees of gut disorders.

These disorders are not well defined, variable in aetiology, severity and appearance. Nomenclature is very diverse but some popular terms to describe this condition of impaired gut health are dysbacteriosis, bacterial enteritis (BE), small intestinal bacterial overgrowth, clostridiosis and wet litter.

Signs during necropsy associated with all of these conditions are:

- Poor intestinal strength.
- Ballooning of the gut.
- Hyperaemia of the mesenteric blood vessels and blood vessels on the intestines.
- Thinning of the gut wall, often with translucency of the gut wall.
- Flaccid gut edges after section.
- Watery or foamy contents.
- Poorly digested feed at the end of the gastro intestinal tract (GIT).
- Multi-coloured oily aspect of the gut contents in contact with the mucosa.

During a visit in a typically affected poultry house, the following signs are frequently encountered:

- Acidic smell.
- Wet litter, initially in patches under drinking or feeding lines or in places where condensation is typical. In more severe cases wet litter is generalised.
- The wet litter is greasy.
- When inspecting the litter, droppings with poorly digested feed particles are common.
- Initially feed consumption is reduced, while water consumption shows a daily increase following breeding standards, causing an increased water/feed ratio (WFR).

A typical bacterial enteritis exceeds a WFR of two in normal ambient conditions. In a later phase, water consumption is also reduced.

- Because of the wet litter, the birds appear dirty.
- Feeding and drinking activity is reduced.

As Clostridium perfringens (Cp) has been isolated in much larger numbers and at places in the intestines more cranial than in

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healthy birds, BE is often associated with NE, a condition also associated with Cp. Three predisposing factors are associated with BE: poorly digestible feed, (subclinical) coccidiosis and management.

Most of the research models do combine two of these predisposing factors namely, feed known to instigate BE and subclinical coccidiosis. Models usually combine poorly digestible feed components with a consequent coccidial challenge sometimes with an additional Cp challenge to exacerbate BE. Some researchers claim an as efficient model without the additional Cp challenge as sufficient. Clostridium perfringens is a very common and also in normal situations very abundant bacterial species from the caecum and it is assumed that Cp is able to relocate to more cranial locations in the gut whenever the conditions are appropriate: viscous, poorly digested feed.

It is, however, not yet clear whether Cp is the cause or rather a consequence or indicator of BE. This loophole in the knowledge of BE is a consequence of the lack of knowledge of the exact pathogenesis of the condition, if not the several possible pathogeneses that can lead, in absence of growth promoters, to a similar outcome known as BE.

The well known impairment of the digestive function caused by coccidia is, therefore, probably a main factor in conditioning the gut for Cp to grow. In several models, attenuated Eimeria strains are used, indicating subclinical coccidiosis is sufficient as a predisposing factor.

Still, other factors impairing digestion and absorption of nutrients, such as enzymatic dysfunction, viral infections or mycotoxins are likely to be equally effective as predisposing factors, although in practical conditions and with current knowledge, subclinical coccidiosis is believed by many to be the most important one.

As a consequence, the last commonly recognised predisposing factor, poor management, is probably not so important in inducing the disease, but more important as defining the degree of severity of BE and the subsequent impact on the zootechnical performance of a flock.

A very important debate is ongoing in the role anticoccidial products (ACP) have in the prevention of BE. A publication on the reduction of Cp counts in upper intestinal tract of birds medicated with narasin, a monovalent ionophore, strongly suggest the positive impact ionophore compounds have in reducing the impact of BE.

This reduction of Cp counts is a consequence of the well known antibacterial activity of ionophorous compounds. Minimal Inhibitory Concentrations (MIC) for the different ionophores are given in several publications and are all in the same order of magnitude.

However, as it is not proven that Cp is the main aetiologic agent of BE, or rather an opportunistic, overgrowing bacterium, no conclusions can be made whether ionophores have a direct preventive effect on BE, or more simply reduce the effects of one of the consequences of BE, Cp proliferation.

Prevention of BE

This discussion might seem not so relevant at first sight, but in practice one of the main drivers on selection of ACP in anticoccidial programmes is this presumed effect on BE. A few questions remain unanswered in rightfully assessing the role of ionophores in prevention of BE:

- The vast majority of anticoccidial programmes consist of ionophores. As indicated by the large number of antibiotic treatments through drinking water in growth promotor free production, BE is still considered one of the main problems in poultry production. What would be the number of treatments if ACP with equal anticoccidial but no antibacterial activity? Maybe the number of treatments would be higher in absence of the antibacterial activity exerted by the ionophores, but yet there is neither clear evidence nor numbers.
- As (subclinical) coccidial infections are known to be a predisposing factor of BE, what would be the number of treatments if an ACP existed that had no antibacterial activity but was able to completely suppress coccidial infections?
- Even if assuming Cp is a cause and not a consequence of BE, are the differences in Cp MIC for the different ionophores relevant? As all ionophores are used at concentrations in the gut that approach or largely exceed Cp MIC, there is no inference or even indication that this is a valid hypothesis.
- When using the same ionophores because of the (maybe perceived) important role in preventing BE, is there a risk of installing a vicious circle through the overuse of (certain) ionophores (classes), reduced anticoccidial sensitivity (not resistance), higher coccidial challenge thus a more prominent role of coccidiosis as a predisposing factor for BE?

Coccidiosis, considering the estimated losses mainly due to subclinical coccidiosis, is still one of the most important diseases affecting the poultry industry today. ■

References are available from the authors on request

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