Controlling the oxido-inflammatory cycle in coccidial infections

Over the past few years, in any forum, conference or seminar relating to monogastric animal nutrition, intestinal health has been a common topic of discussion, or, rather, discussing it has become a must.

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It is an issue of particular interest from a nutritional, health, scientific and, of course, commercial point of view, due to the immense importance that has finally been accorded to the central organ of livestock production and, for many, the most important organ of all.

The intestine is the organ with the largest surface area in contact with the external environment, even more so than the skin if we take into account each and every one of the intestinal villi.

The intestine is a great barrier which limits the entry of pathogenic micro-organisms and harmful substances contained in foodstuffs, whilst also intervening in the absorption of nutrients and the secretion of waste products from the organism's different metabolic processes.

Thus, an extremely diverse microbiome exists in the intestinal mucosa and lumen, which plays an important defence function: preventing colonisation by pathogenic micro-organisms through competitive exclusion. It also helps to regulate immune responses and to supply metabolites such as volatile fatty acids, which are important for nutrition and the balance of the intestinal microbiota.

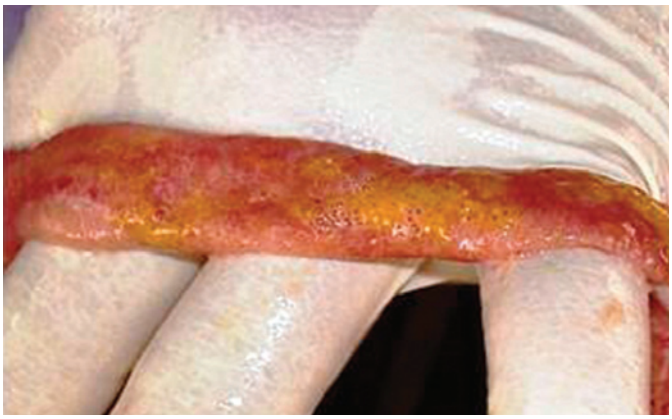
The intestinal epithelium has a vast network of Pattern Recognition Receptors (PRRs) which recognise pathogens, and a large number of terminals connected to the central and peripheral nervous systems that generate effector and inhibitory responses to modulate the immune response, the organ's homeostasis and multiple physiological functions of the animal.

When any kind of imbalance occurs between the functions or the components of the intestinal epithelium, inflammation is generated as a response. The extent and duration of the inflammation generated will be proportional to the type of pathogenic agent or harmful substance triggering it.

Depending on the intensity and the type of potentially damaging agent, the inflammation can be physiological, pathological or nutritional.

A physiological inflammation is controlled and tolerated without an overt defence reaction from the innate immune system up until a certain point, beyond which any stimulus is capable of triggering a cascade response by the cellular defence system.

In contrast, when infectious agents such as bacteria or protozoa exceed maximum tolerance levels, pathological inflammation occurs. In this case, severe inflammation develops due to the release of pro-inflammatory mediators. This can give rise to an imbalance in the organism's antioxidant defence system (ADS).



Inflammation and enteritis due to Eimeria maxima infection.

Finally, nutritional or sterile inflammation can occur, originating from antinutritional factors present in raw ingredients or foodstuffs which cause chronic inflammation with equally extensive and severe damage, and with immune responses just as complex as those which occur with pathological inflammation.

Coccidiosis is an intestinal infection caused by intracellular protozoan parasites of the Eimeria genus and one of the most economically damaging diseases in poultry production. When a bird has a coccidial intestinal infection, their immune system generates an immediate response.

Although Eimeria spp. infection promotes both a humoral and a cellular immune response, the latter (mediated by CD4 and CD8 LT cells, NK cells and macrophages among others) is the most relevant in terms of resisting and containing said infection, causing pathological inflammation.

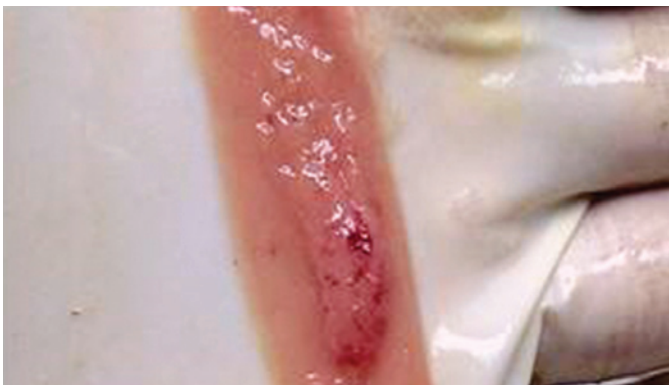
The different species of Eimeria spp. induce the activation of macrophages, which are the main inflammatory effector cells involved in an infectious process.

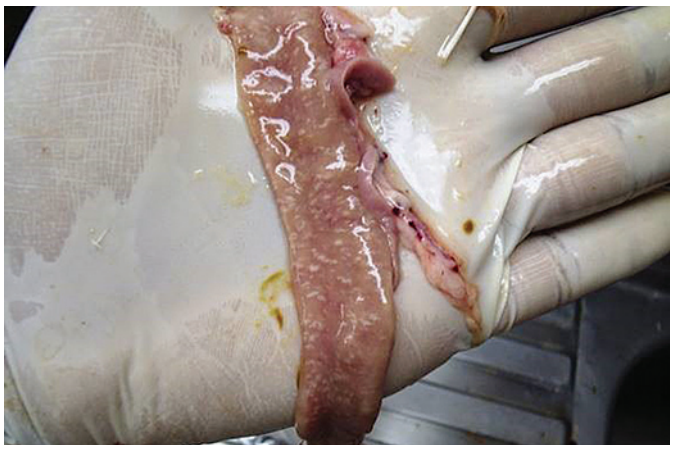
Once the macrophages initiate the

Continued on page 23

Eimeria maxima infection and associated lesions.

Inflammation due to Clostridium perfringens infection.





Eimeria acervulina infection associated with duodenal inflammation.

Eimeria tenella infection. Blind sacs (caeca) of the gut filled with purulent and haemorrhagic material.

Continued from page 21

inflammatory response to Eimeria spp., pro-inflammatory cytokines are released which, in turn, induce the production of free radicals, or 'reactive oxygen species' (ROS), in the macrophages and other defence cells such as intraepithelial lymphocytes (IEL).

This mechanism supports the immune system by generating an unfavourable environment for pathogens which limits their growth and multiplication.

Therefore, the inflammatory processes in the mucosa caused by severe Eimeria spp. infection frequently give rise to an imbalance in the ADS. The ROS released overwhelm the organism's capacity to neutralise the reactive metabolites, and ultimately turn on the organism itself.

The generation of ROS, nitric oxide (NO), reactive nitrogen species (RNS) and NOS is the consequence of the activation of the oxidative enzymes NADPH oxidase (NOX) and nitric oxide synthase (iNOS). These oxidative enzymes are activated by the pro-inflammatory cytokines induced in response to inflammation. The ADS imbalance with high levels of ROS is what we know as oxidative stress.

Once the imbalance in the organism's antioxidant capacity has been triggered, NO, which is released into the intestinal lumen, quickly transforms into nitrate, which favours the growth of nitrate-reducing bacteria such as E. coli.

Likewise, the increase in blood flow to the inflamed intestine increases oxygen concentration. Some authors claim that this leads to the rapid growth of facultative anaerobic bacteria of the Streptococcus genus and the Enterobacteriaceae genus, such as E. coli. Hence, in coccidial infections with their inevitable resulting inflammatory process, the antioxidant balance in the intestine is compromised. As the situation degenerates, the organ usually enters a state of oxidative stress, causing tissue damage. This damage tends to lead to an increase in pathogenic bacteria and a decrease in saprophytic bacteria, causing the imbalance in the microbiota known as dysbiosis.

Therefore, in the comprehensive diagnosis of intestinal health, we often assess and associate the interaction between coccidiosis, inflammation and dysbiosis with a leaky gut and oxidative stress.

To this end, considering and assessing the conditions that lead to oxidative stress is paramount in sustaining a good intestinal health programme. Oxidative stress damages cells. Among the different factors that can trigger this process are:

- Elevated metabolic activity as a result of an intensive production system.
- High production density with low oxygen levels.
- High ammonia levels.
- Heat stress.
- Diet and ingredients used in feed production (antinutritional factors, fat rancidity, etc).
- Coccidiosis and acute bacterial infections which damage the intestinal epithelium.

ROS, which are products of oxidative stress, target cellular macromolecules, DNA, proteins and membrane lipids.

When these free radicals oxidise proteins, the latter can form abnormal enzymes which do not function properly and alter the metabolic pathways in which they participate.

Likewise, during protein oxidisation, the protein structure of the intestinal epithelium's tight junctions is affected, which results in leaky gut syndrome, where absorption and osmotic balance are impaired.

Therefore, in coccidiosis and dysbiosis, the osmotic balance of the intestine is affected not only in terms of the integrity of the tissue itself, but also by the damage done to the tight junctions generated by oxidative stress resulting from the inflammation triggered by Eimeria infection.

Peptasan is a 100% natural polyherbal mixture composed of Saccharum officinarum, Accacia concinna and other plants whose bioactive components such as polyphenols, terpenoids and saponins, among others, act synergistically to promote the balance of the intestinal microbiome and reduce the negative effects of coccidia on the epithelium.

In addition, the high concentration of antioxidant compounds and anti-inflammatories in Peptasan actively decelerate the inflammatory oxidation-reduction cycle generated by oxidative stress, which is a consequence of the antioxidant imbalance brought about by coccidial infection.

Thus, Peptasan promotes improved integrity of cellular membranes, tissue regeneration and intestinal osmotic balance and microbiota.

This ultimately translates into a more effective immunological response to coccidiosis, better intestinal health and higher levels of animals' production performance. ■