Optimising immunity in broiler production – part two

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In modern production, animals are subjected to stress at certain moments in their life which can affect the defence of the gut associated lymphoid tissue (GALT). These stressors include high stocking density, suboptimal climate, change of diet, nutritional deficiencies and anti-nutritional factors. Lectins are an example of the latter.

They are carbohydrate binding (glyco)proteins that are resistant to proteolytic breakdown in the gut and are also resistant to breakdown by most gut bacteria.

Dietary lectins are taken up by receptor-mediated endocytosis and induce cellular proliferation leading to a reduction in and extensive damage to the absorptive villi with a consequent depression of the absorptive potential of the gut.

Avidly binding lectins (for example, PHA of Phaseolus vulgaris) can be hyperplastic growth factors for the gut epithelium. However, while cell multiplication and migration to the villus tip is increased, cell differentiation is unchanged leading to more immature cells on the villi.

As a result the capacity of nutrient absorption is reduced and bacterial overgrowth may be facilitated. This can lead to excessive inflammation in the intestine and to the development of opportunistic pathogens.

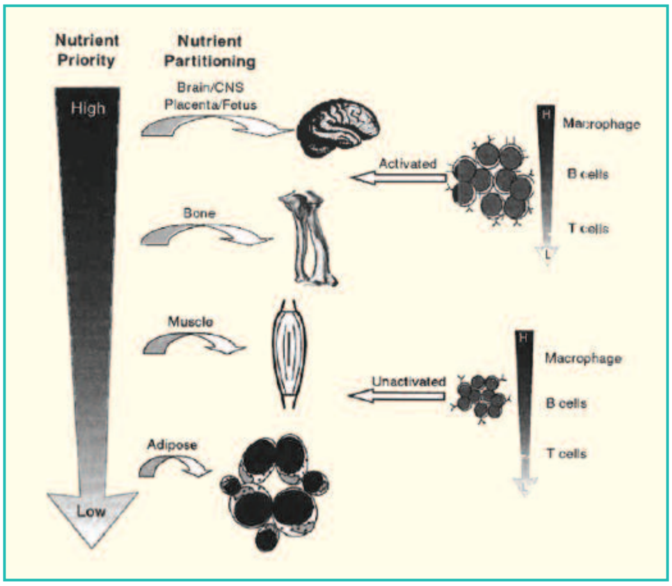

Fig. 4. Priority of nutrient use by various tissues with proposed sites for the immune system and leukocyte populations in their activated and unactivated states (Humphrey and Klasing, 2004).

Kelley referred to experiments of Previte and Berry (1962), to illustrate how climatic conditions can suppress immune functions.

They studied characteristics of virulent and avirulent forms of Staphylococcus aureus (Fig. 3).

As expected, when mice were held at comfortable ambient conditions, virulent staphylococcus aureus caused 70% of the mice to die, but avirulent S. aureus caused a death rate of only 20%. Totally different results were obtained when the mice were maintained at suboptimal air temperature.

Virulent bacteria continued to cause a 70% mortality rate, but the avirulent bacteria somehow turned into virulent bacteria, killing 91% of the mice. Nearly identical results were obtained in similar experiments with virulent and avirulent Salmonella typhimurium. Both examples show how environmental conditions or stress factors can affect the animal's capacity to defend itself against pathogens.

In these conditions it can be worthwhile to give some extra aid to the animal by inclusion of nutrients that support tissue repair or that stimulate development or activity of the immune system.

Immune stimulation

As we all know from experience, disease or excessive inflammation has a negative impact on growth.

Following activation, the immune system becomes anabolic and increases its nutrient demand while at the same time food intake decreases.

Moreover, Humphrey and Klasing showed that the priority of the activated immune system for nutrients is higher than the nutrient priority of bone and muscle growth (Fig. 4).

The hormonal regulation of this negative correlation between immune activation and growth was illustrated by Kelley. He describes how the immune system, acting in the form of proinflammatory

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Fig. 3. Mice succumb to avirulent Staphylococcus aureus when exposed to cold air temperature (Previte and Berry, 1962).

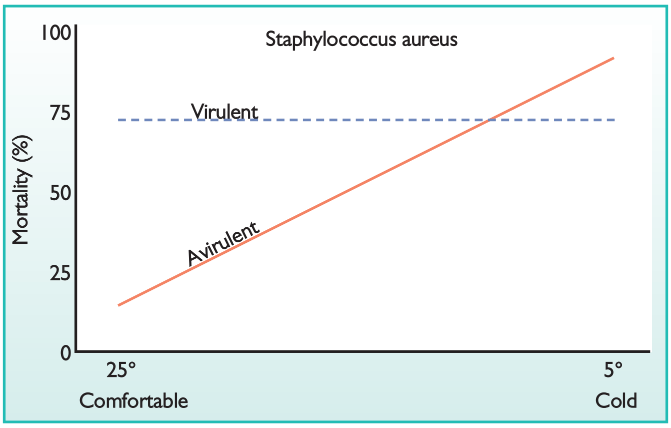
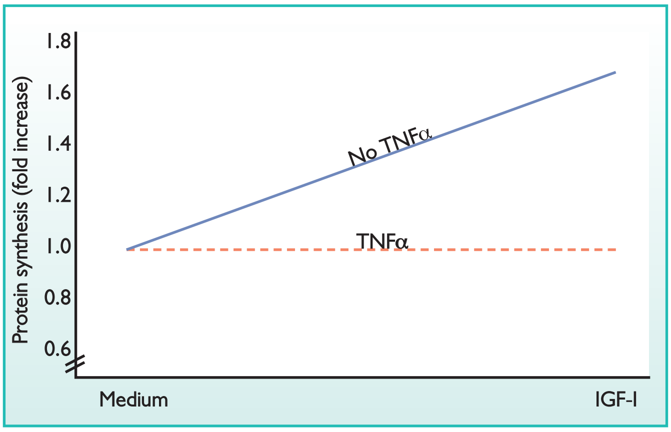


Fig. 5. A hormone (IGF1) and a proinflammatory cytokine (TNFα) interact to regulate protein synthesis in murine myoblasts (Broussard et al. 2003).



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cytokines, interacts with both growth hormone and IGF-I to suppress cell growth and survival. One example is the inhibition of stimulation of protein synthesis in murine muscle myoblasts by IGF-1 when also the pro-inflammatory cytokine TNFa is present in the cell culture medium (Fig. 5). The molecular mechanism by which TNFa impairs sensitivity of the IGF-I receptor is by decreasing the cascade of intracellular events that normally follow activation of the IGF-I receptor.

Their findings indicate that the ability of proinflammatory cytokines to impair IGF-I-induced biological activities is likely to result from intracellular cross-talk between hormone and cytokine receptors expressed on a single cell (Fig. 6).

From this we can conclude that immune stimulation (vaccination or immunostimulating feed additives) should be applied in a strategic way in order to obtain an optimal balance between health and performance in animal production.

Intestinal immune system

Nutritional deficiencies can have a negative impact on the animal's immune status. Not only an adequate energy and protein supply is important in this aspect as micronutrients such as zinc, selenium, iron, copper, b-carotene, vitamins A, C and E and folic acid also influence several components of the non-specific immune system.

In this section however, we assume that minimal nutritional requirements for optimal growth are fulfilled and we will discuss nutrients or feed compounds that can give additional support to the immune system or that can help to sustain or restore intestinal integrity. They can be divided into:

- Blockers of colonisation.
- Immunomodulators.
- Nutrients for tissue repair.

Compounds with a direct antibacterial effect like antibiotics, organic acids or phytoproducts are not considered here.

Blockers of colonisation are those feed compounds that interfere with the attachment of the pathogens to the intestinal wall, an essential step for intestinal colonisation. Mannan oligosaccharide or MOS is one of the best known examples of this class.

Mannan oligosaccharide

Feed additives containing MOS are derived from yeast or yeast cell wall. These blockers interfere with the interaction between adhesion molecules of the pathogen (for example, F4-fimbriae of E. coli) and their receptor on the intestinal wall (Fig. 7).

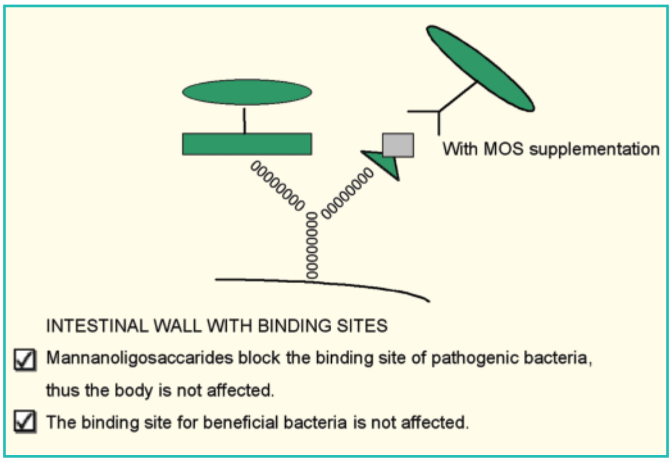


Fig. 7. Intestinal colonisation with MOS supplementation.

	Immune response	Test
Non-specific	Phagocytosis	Superoxide and O-radicals
	Pro-inflammatory signals	Cytokines
Specific	Stimulation and multiplication of B and T cells	B and T cell proliferation
	Antibody production	Antibody production

Table 2. Different steps in a local immune response in the intestinal mucosa and corresponding in vitro tests (Laboratory of Immunology, Faculty of Veterinary Sciences, Ghent University).

They thus reduce attachment and increase the clearance of the pathogens out of the intestinal tract.

Glucans are a well known example of immunomodulators. They interact with receptors on the cells of the mucosal immune system leading to the release of cytokines and modulation of the immune response.

It is not clear yet whether the immunomodulators only interact with macrophages or if they also have receptors on other cells of the mucosal immune system (for example, dendritic cells, IELs or IECs).

The origin, structure and molecular size of glucans determine their biological activity. While many different glucan products are on the market, most of them derived from yeast cell walls, they are very different in purity, glucan concentration and size of the glucan molecules.

Since the relation between purity, size or chemical structure of glucans and their biological activity is not known a set of in vitro tests has been developed at the Laboratory of Immunology of the University of Ghent (Faculty of Veterinary Sciences). With these tests the effect of immunomodulators on different levels of the generation of an immune response can be studied (Table 2).

The effect that can be expected from the use of glucans in poultry feed is illustrated by a very nice experiment of Huff et al (2006).

In their experiment on broilers (Cobb, mixed sexes) they worked with two challenges (800cfu of a non-motile E. coli strain in the airsac on day seven and Control (no challenge) and three feed treatments (Control and 20g/ton glucans in the feed during 7 or 25 days). Body weight and feed intake were registered at 25 days of age.

The test was run under optimal hygienic and climatic conditions.

Their results show that glucans had a negative impact on growth when the birds were not challenged in this condition (Fig. 8). This illustrates the negative relation between stimulation of the immune system and growth as described above.

The supporting effect of glucans on the immune system is clear when the birds were challenged with E. coli: the negative effect of the challenge on growth and feed conversion is significantly reduced when glucans were added to the feed.

In the challenged groups the highest growth was realised by the group that received glucans during seven days.

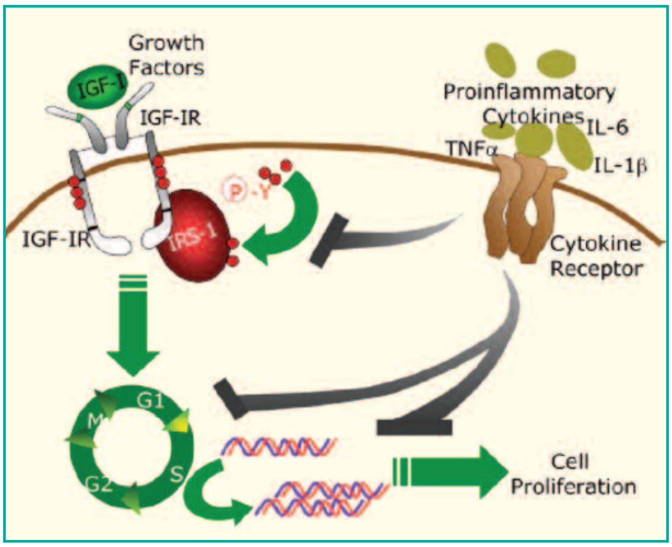
The intermediate result of the group that received glucans during 25 days could again be due to the negative correlation between stimulation of immunity and growth.

Probably the pathogen was cleared before the end of the 25 day period. These data support the idea to use immunostimulants in periods where stress or suboptimal conditions for the animals can be expected.

While intestinal integrity is also very important it can be worthwhile to add nutrients in the feed that can support tissue repair in periods of stress.

Nucleotides and butyric acid are two examples of such nutrients. Nucleotides are essential for tissues with a high intensity of renewal and cell division like the intestinal epithelium. Positive effects of nucleotides on mucosal immunity and intestinal integrity have been shown by various authors.

Fig. 6. Hormone and cytokine receptors, when expressed on a single cell, can regulate downstream receptor signalling events of one another (Kelley, 2004).



Butyric acid

Butyric acid is an excellent source of energy for the intestinal epithelium and stimulates cell proliferation and growth of the villi. It thus helps to maintain the integrity of the intestinal wall at periods of stress.

The positive effect of butyrate on animal performance has been demonstrated for piglets, layers and

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broilers. Due to its positive effect on cell proliferation and on the growth of the villi, butyrate might enhance tissue repair when the intestinal integrity is affected.

This was illustrated by Arnouts and Vandendriessche who included 7.5% raw kidney beans in starter diets of broilers and evaluated the effect on growth and feed intake.

The incorporation of kidney beans clearly reduced growth of broilers leading to a final body weight that was about 4% lower compared to the control group.

This negative effect of kidney beans on growth could be reduced when butyric acid was incorporated in the starter and grower diet at 250g/T.

Final body weight was only 1% lower than the control group when butyric acid was included as compared to the growth reduction of 4% without addition of butyrate.

Reduced growth in diets with kidney beans is probably due to damage in the intestinal wall caused by the lectins. This stress effect could be counteracted by the use of sodium butyrate.

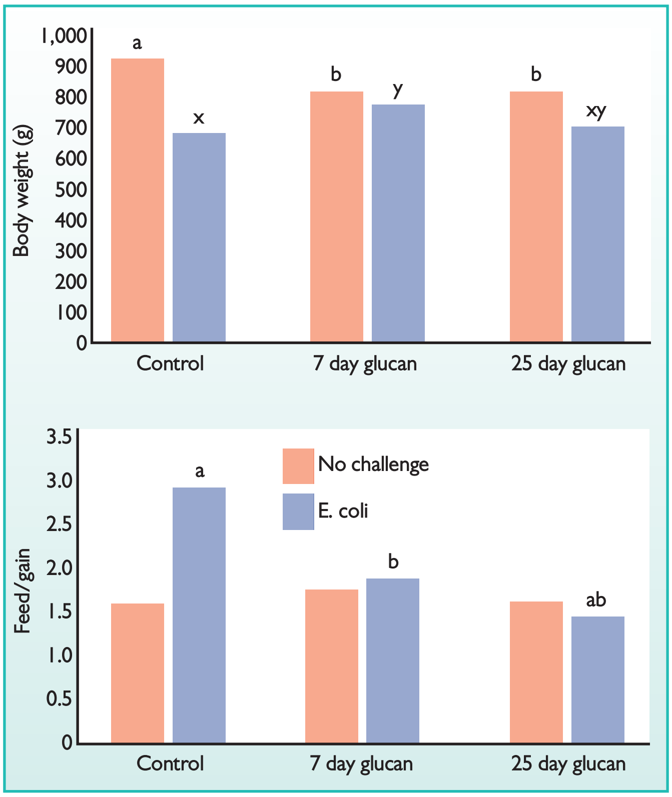

Fig. 8. Effect of feed supplementation with glucans fed for either seven days prior to challenge or for 25 days and respiratory challenge with Escherichia coli at seven days on body weight and feed conversion (Huff et al. 2006).

Conclusions

The gastrointestinal tract creates a continuous flow of nutrients to the body, like a river brings water and food to the land.

This flow however, also contains exogenous challenges including antinutritional factors, pathogens and soluble antigens.

Like the banks of a river are fortified with dykes at some critical points, the gut associated lymphoid tissue including Peyer's patches, intraepithelial lymphocytes and M cells protects the body from invasion of these pathogens into the blood circulation.

The cost for energy and nutrients to maintain a proper local immunity in the intestine is much lower than the cost of a systemic immune response that must be generated when a pathogen was able to pass the intestinal defence system. At hatch the GALT of the broiler is still immature and further develops during the first two weeks of life.

This is thus a critical period as the young broiler gets in contact with its environment and with pathogens from day one.

Next to proper cleaning and farm management we can also support the young broiler during the starter period via the feed.

Antibiotics, organic acids or phytoproducts can be used to reduce the pathogenic load of the intestinal contents.

Next to that we have seen that we can also interfere with the attachment of the pathogens to the intestinal wall.

Blockers like MOS interfere with the interaction between adhesion molecules of the pathogen (for example, F4-fimbriae of E. coli) and their receptor on the intestinal wall.

They thus reduce attachment and increase the clearance of the pathogens out of the intestinal tract.

Another prophylactic measure is the stimulation of the development of the GALT (young birds) or of the activity of the immune system (mature birds) by oral addition (feed or drinking water) of immunomodulators.

The advantage of this approach is that they enable the animal to defend itself against all the pathogens it is confronted with while the other additives, like antibiotics or organic acids, are directed against only a limited spectrum of pathogens.

Immune activation however, also costs energy and nutrients and may have a negative impact on growth and overall performance.

The goal is thus to find a balance between optimal protection and maximal performance. Animals that live in perfect climatic and hygienic conditions and of which all nutritional requirements are met will not profit from extra stimulation of their immune system.

In that case the use of nutrients for the extra stimulation will be a drain that reduces performance.

However, environmental conditions are not always ideal in industrial animal production and animals are often confronted with stress that has an immunosuppressive effect.

In these periods of stress it can be worthwhile to give extra support to the mucosal immune system in order to avoid that opportunistic bacteria can profit from this stress period to invade the host.

Examples of such stress periods in poultry production are hatch, change of diet, vaccination, high stocking density in the finisher phase, suboptimal climatic or nutritional conditions, specific infections or parasitic load and many others.

In these periods of stress the cost for extra support of the immune system is well considered in view of the risk for a general breakthrough of pathogens. Immune stimulation can then also be complemented with other nutrients like nucleotides that can help the animal to maintain its intestinal integrity.

In conclusion, we can state that immunomodulation should not be applied continuously in animal production as the cost of energy and nutrients will then be too high.

Modulating mucosal immunity should, however, be part of an integral health management strategy, including nutrition and vaccination, to optimise gut health. ■

References are available from the author on request