Interfacing Immunity, Gut Health and Performance

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CONTEXT

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Future challenges in poultry meat production

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Introduction

The poultry meat industry has undergone remarkable change and growth over the last 30 yrs, and it seems that this will continue in the next 10-20 years. The meat industry has undoubtedly been the most successful, yet the egg industry is now making strides in new product development. Today, we see 4 kg male broilers at 49 d of age. There is often debate about there being an end point to this increased genetic potential, yet the geneticists indicate that selection pressure will be little reduced in the foreseeable future.

The modern broiler chicken continues to show increased yearly genetic gains, that equates to almost 1 d reduction in time taken for males to achieve 2.5 kg live weight. This increased growth potential (Figure 1) has meant that we are continually increasing our global consumption of broiler meat, since bird numbers are also increasing annually.

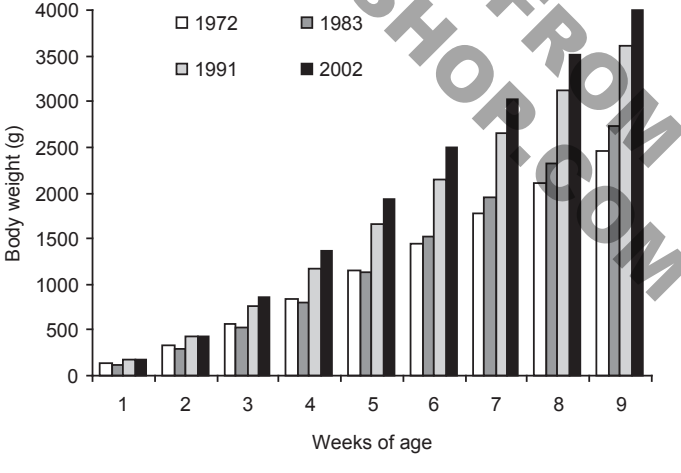

Figure 1. Male broiler growth over the past 30 years.

Early gut development: the interaction between feed, gut health and immunity

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Introduction

The following paper examines the morphological development of the gut, its hydrolytic and absorptive capacity, development of microbial populations and the development of an immune system responding to the contents of the gastrointestinal tract.

Gastrointestinal development

Gross development

As incubation progresses embryonic small intestinal weight increases at a much greater rate than body weight close to hatching. During the last three days of incubation the ratio of small intestinal weight to body weight increases from approximately 1% on day 17 of incubation, to 3.5% at hatch. The morphology of the small intestine also changes rapidly with villi developing in at least three phases, with different sized villi found at hatch (Uni et al,et al., 2003).

In the immediate post-hatch period intense changes occur in the small intestines of chicks, as they continue to increase in weight more rapidly then the whole body mass. This rapid relative growth of the small intestines is maximal at 6-8 d in the turkey poult and at 6-10 d in the broiler chick. In contrast, other digestive tract organs such as gizzard and pancreas do not show parallel-enhanced changes in relative size (Uni et al., 1999). The preferential early growth of the small intestine occurs both in the presence and in absence of feed although in the absence of exogenous feed both absolute and relative growth is lower (Noy and Sklan, 1999). In the 'held' bird the substrates for this growth apparently originate from the yolk indicating the high priority for intestinal growth post-hatch. Temporal increases in intestinal weight and length are not identical

Interaction of nutrition with intestinal microbial communities

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Introduction

When focussing on bacteria, the overall process of digestion in the gastrointestinal tract of monogastric animals is commonly described as occurring in either the small intestine or the hindgut. For example, catalytic enzyme activity and other factors produced by the host are active in the small intestine, and conversions of remaining nutrients by bacterial activities are restricted to the hindgut. This is true with regard to major nutrient conversions. However, it is known that bacteria are present in the chyme and epithelia along the digestive tract of pigs. The significance of bacterial metabolic activities in precaecal sections is already visible in the small intestine and can be shown by partial degradation of non-starch-polysaccharides (NSP) like pectins, 1-3,1-4 ß-glucans or arabinoxylans; by formation of bacterial metabolic products like lactate and short chain fatty acids as well as by deconjugation of bile acids.

Antibiotics have been used as growth promoters in various species of farm animals for many years. Benefits include reduced frequency of diarrhoea under certain conditions, and beneficial effects on performance parameters such as body weight gain or feed conversion ratio up to approximately 5 per cent. These effects are explained by the modification of intestinal bacterial populations and their interaction with the host animal. They might include interactions with intestinal epithelial tissues (proliferation and apoptosis of epithelial cells, surface coating – mucin formation and secretion, invasions and lesions) and the immune system (response of the lymphocyte population and of formation and secretion of immunoglobulins).

From the above it is obvious that the intestinal microbiota is not only greatly involved in nutrient conversion along the gastrointestinal tract, but may also affect or support animal health. Thus, modifications

Commensal bacteria and intestinal development: Studies using gnotobiotic pigs

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Introduction

Soon after birth the intestine of the pig is colonized by coliform bacteria followed rapidly by predominantly anaerobic bacteria and becoming more complex with age (Swords *et al.*,1993). Estimates suggest 500 or more bacterial species colonize the adult intestine reaching 10^{11} cfu/g intestinal contents and totalling 10-fold more cells than the number of cells in the pig's body. Furthermore, the aggregate genome of these bacteria represent 2-4 million genes in contrast to only 30 to 40 000 genes present in the host genome (Hooper and Gordon, 2001). Comparisons of conventional and gnotobiotic (germ-free or having a defined microbiota) animals have indicated a marked host response to bacterial colonization of the intestine as evidenced by obvious contrasts in intestinal morphology, immunity and digestive function (Coates *et al.*,1963; Pabst *et al.*,1988; Wostmann, 1996).

Recently, Hooper *et al*. (2001) used genome-wide expression profiling in gnotobiotic rodents to confirm a marked effect of the commensal bacteria and uncovered a tremendous array of intestinal genes regulated by bacterial colonization, including genes involved in nutrient uptake and metabolism (e.g. sodium glucose contransporter (SGLT-1), co-lipase) and mucosal barrier function (e.g. sprr2a, decay accelerating factor). Most interestingly, expression profiling in gnotobiotic animal studies, and the results of *in vitro* studies using bacterial co-culture with intestinal epithelial cell lines indicate that host gene expression responses are specific for different bacteria. As a result, the composition of the commensal bacteria colonizing the neonatal intestine may have significant consequences relative to intestinal development, immunity and the digestion and absorption of nutrients. The following paper reviews bacteria-host interrelationships with particular reference to the impact of the intestinal commensal bacteria on the development and function of the intestine. We will highlight the breadth of the host responses

Regulation of gut function and immunity

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Introduction

European-wide directives are now in place restricting the non-clinical use of production enhancers, chemotherapeutics and heavy metals in animal production. These legislative events have had a major impact on animal production within Europe and the UK, rendering current production systems inappropriate. Similarly in the US, the FDA are now actively promoting alternatives to feed-grade antibiotics. Hence, the animal industry worldwide is now faced with new and demanding challenges. From a practical standpoint, changes in weaning strategies, dietary regimes and rearing environments can be implemented in an attempt to accommodate the withdrawal of antibiotics. However, to address the wider issues of animal welfare, food safety, nutrient and mineral capture, in the context of both economic and environmental sustainability, animal production, once an applied science, needs to move to a more fundamental level.

Bacterial colonisation and immunity and disease resistance

Bacterial colonisation of gut surfaces

Adherence of bacteria to the intestinal mucosa remains a subject of great interest, primarily because the successful colonisation of micro-niches within the gut has been largely attributed to the ability to adhere and because attachment is recognised as an important initial event in the pathogenesis of bacterial infections. The mechanisms involved in bacterial attachment have been difficult to define primarily because the interaction involves a number of complex mechanisms including bacterial motility, chemotactic attraction and both specific and non-specific attachment to the mucus gel and epithelial surface.

Controlling gastrointestinal disease to improve absorptive membrane integrity and optimize digestion efficiency

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Introduction

Many broiler and turkey producers are withdrawing growth-promoting antibiotics in response to retailer and consumer demand. Antibiotics have been an integral part of poultry feed for the past 50 years (Rosen, 1995) and decades of research and field use have established their efficiency as growth promoters or more correctly, 'pronutrients' (Rosen, 1995; Rosen, 1996a).

In-feed antibiotics have been shown to enhance performance through subtly changing the composition of the normal flora (Rosen, 1995; Anderson *et al.*, 2000). Much of the defining research in this regard was completed prior to the mid 1980s (Anderson *et al.*, 2000). The complexities of the industry have changed considerably in the last 20 years and currently antibiotics are included in meat bird rations primarily to suppress specific pathogens associated with known diseases, such as *Clostridium perfringens*.

In contrast to the direct bacteriostatic or bacteriocidal activity of the gram-positive antibiotics, the alternatives thus far studied often have little if any direct effect on these gram-positive organisms. With the withdrawal of antibiotic growth promoters, clostridial infections with consequential losses from increased mortality and reduced feed conversion efficiency and quality have become a primary concern.

Clostridial enterotoxaemias

Stress that is induced by climatic or management factors leads to a disturbance in the composition of intestinal flora, resulting in selective growth and synthesis of toxins by various Clostridium spp. During the past five years enterotoxemia has resulted in the following conditions:

Impact of mannan oligosaccharide on gut health and pig performance

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Introduction

A healthy digestive system is crucial for optimal animal performance. However, the gut with it's large surface area and heavy microbial load, is a vulnerable site for pathogen entry into the body. This large surface is necessary to optimise nutrient absorption. To allow an efficient transfer of nutrients to the blood, the gut is protected with only one layer of epithelial cells. Unfortunately however, this thin layer does not only facilitate nutrient transfer, but also weakens the ability of the gastro intestinal (GI) tract to prevent pathogens from entering the body.

Therefore, a multitude of additional protection systems exist to minimise the risk of intestinal disease and pathogen entry. Mucins and glycoproteins associated with the intestinal brush border serve as important barriers protecting the delicate absorptive surface from the abrasive action of feedstuffs, bacterial colonisation, and toxins. Endogenous acids, digestive enzymes and bile reduce bacterial growth. Digestive flow and peristaltic movements transport the digesta through the digestive tract, and with it bacteria, thus limiting bacterial attachment and subsequent development. To further optimise gut protection the animal has devoted more than half of its immune cells to protecting the digestive tract. In addition, the GI microflora plays a crucial role in gut defence; through different complex mechanisms beneficial bacteria limit the growth of pathogens, trying to exclude them from the system (Rolfe, 1991).

Profound knowledge of the development and composition of the GI microflora and its regulatory forces is essential to understand the dynamics of the GI microflora as well as interactions with feedstuffs and feed additives.

The potential for immunosaccharides to maximise growth performance – A review of six published meta-analyses on Bio-Mos

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Introduction

The role of indigestible oligo- and polysaccharides as substrates for the microflora in the large intestine of farm animals has been widely discussed in scientific literature. Additionally, it is well-known that the microflora plays a key role in the development of the gut-associated immune system (GALT) (Fioramonti *et al*. 2003). It has further been recognised that sugars on the intestinal surface have an important role in the bacterial attachment to the host (Firon *et al*. 1983; Ofek *et al*. 1977). However, it is only recently that carbohydrates have been recognised as being involved in almost every aspect of biology. Distinct carbohydrate structures can have very specific biological activities. For example, sugars (monosaccharides) combine to form giant molecules such as cellulose; they are already known to regulate hormones, organize embryonic development, direct the movement of cells and proteins throughout the body, and regulate the immune system (Schmidt 2002). Glycobiology or glycomics is defined as the characterisation of the sugars that make up a cell (Newman 2004). Understanding the structure and sequence of individual monosaccharides that form oligo- or polysaccharides is the base for developing new carbohydrate based immune-modulators. Research suggests that we can influence some of the control mechanisms of the immune system through selected dietary carbohydrates or immunosaccharides, as the digestive tract offers a large surface for carbohydrates to interact with intestinal cells and the immune system as well as with bacterial cells. It has been shown that the use of specific immunosaccharides (Bio-Mos®, Alltech Inc.) have a profound effect on animal health and subsequently animal performance. Advantages of adding Bio-Mos® to broiler, turkey, pig and rabbit diets have been evaluated in six individual meta-analyses and have recently been published in scientific journals and trade magazines.

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