Gut health: overview of current approaches

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Over the last decade or more, there has been growing global pressure to reduce antibiotic use and adopt a 'One Health' approach to their use. Antibiotics as growth promoters were very useful additives and are typically perceived as the gold standard to help livestock strive to achieve genetic potential. Reducing or eliminating the use of antibiotic growth promoters is, however, often associated with an increased incidence of intestinal disorders. There remains some uncertainty over the precise mode of action of antibiotic growth promoters, but we see changes reported in particular bacterial taxa, mucus-related parameters, and epithelial structure and function, with somewhat less data available on gut immune parameters (Broom, 2018). Understanding the relationships between external influences, the microbiome and host responses should help to reduce antibiotic use while preserving animal performance and welfare.

Various factors have been reported to influence the establishment of the microbiota and subsequent successional phases. Age, diet and drugs are generally considered the most influential factors but breed, biosecurity measures, housing, litter and climate have all been shown to be influential. In a series of 3 experiments, it was demonstrated that contact with an adult hen has a strong influence on the gut microbiota composition of chicks (Kubasova et al., 2019). Work has also shown maternal influence on microbiota composition in pigs (PaBlack et al., 2015), and work suggests that the gut maybe exposed to microorganisms prior to birth in pigs and hatch in poultry (Leblois et al., 2017; Lee et al., 2019.

Generally, early colonisers of the intestine are facultative anaerobes that utilise available oxygen and thus facilitate the proliferation of stricter anaerobes (Kubasova et al., 2019). Bacterial diversity is initially reported to increase in both pigs and poultry. Weaning represents a period when there is a major shift in community structure, which coincides with a transition from the degradation of milk to plant glycans (De Rodas et al., 2018). In chickens, diversity was reported to increase to day 12, with greater stability from day 20. Day 12 to 20 is considered to be a period where there is a considered to be a shift from competitive to environmental/host drivers (Ijaz et al., 2018).

Various taxa have been associated with better or worse health and/or performance. There are some inconsistencies where particular taxa are associated with improved parameters in one study, with the reverse found in another study. *Lactobacillus* is one genera that may having differing effects and has been described as having a 'Marmite effect', whereby they have many positive and negative interactions with other taxa (Zou et al., 2018).

We see various stages to immune development in conventional pigs and chickens, generally occurring in concert with the evolving microbiome, such that relatively mature immune responses are observed in conventional chickens and pigs by 2-4 and 6 weeks, respectively. In germ-free birds, we see delayed IgA and immune cell appearance, as well as a biased repertoire (Broom and Kogut, 2018).

Comparison of animals that are more or less resistant to particular intestinal diseases can provide useful models to attempt to draw out more or less helpful immune responses to the causative pathogens/processes. We compared studies with birds reported to be more or less resistant to coccidiosis or necrotic enteritis. The most consistent features in immune relevant sites were down-regulation of IL-10 and, generally, up-regulation of IFN-γ. This is perhaps not unexpected but, given growth performance where available is used as a distinguisher of phenotypes, it does suggest that sites that maybe relatively more inflammatory could be beneficial during these challenge conditions (Broom and Kogut, 2019). It is also important to note that sampling timepoint can affect the relative changes observed. In addition, various studies reporting greater inflammatory responses are associated with better disease resistance, and perhaps improved growth performance. Studies have also shown that *Campylobacter jejuni* induces a pro-inflammatory response, including heterophil influx, which helps limit bacterial translocation and can occur without tissue pathology. Immunosuppression reduced pro-inflammatory responses and led to faster C. jejuni intestinal colonisation and translocation to the liver (Vaezirad et al., 2017). It is interesting to note, and perhaps surprising, that numerous studies do not show clear relationships between gut damage (e.g., lesion scores) and chicken growth performance.

An on-going question is how do we define gut health? The term 'gut' is clear but defining 'health' is very challenging. Typically, health means the absence of disease. Determining reliable parameters (or biomarkers) that help define gut health, particularly in less invasive ways, is currently a very active area of research. 'Gut health' status results from the dynamic interaction of three main components – the microbiome, immune system and external influences, particularly nutrients, microbes, toxins or drugs. Recently, gut health was defined as 'the ability of the gut to perform normal physiological functions and to maintain homeostasis, thereby supporting its ability to withstand infections and non-infectious stressors' (Kogut et al., 2017).

We can see a number of commercial concepts that are revolving around this topic, as well as a plethora of commercially available products. Key areas that industry is focusing on to help facilitate production in an era of more judicious antibiotic use include; breeder selection; vaccination & health of breeders; Immunosuppressive diseases; robust neonate/optimal immunity; intestinal disorders; nutritionally optimal diets; management practices; greater data recording & analysis (water & feed intake, temp, etc.); Feed and water quality & consistency, including additives .