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Original article

Towards the control of necrotic enteritis in broiler chickens with in-feed antibiotics phasing-out worldwide

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ABSTRACT

Poultry production has undergone a substantial increase compared to the livestock industries since 1970. However, the industry worldwide is now facing challenges with the removal of in-feed antibiotics completely or gradually, as the once well-controlled poultry diseases have re-emerged to cause tremendous loss of production. Necrotic enteritis (NE) is one of the most important diseases which costs the industry over two billion dollars annually. In this paper, we review the progress on the etiology of NE and its control through dietary modifications, pre- and probiotics, short chain fatty acids, and vaccination. The other likely measures resulted in the most advances in the toxin characterization are also discussed. Vaccine strategies may have greater potential for the control of NE mainly due to clearer etiology of NE having been elucidated in recent years with the identification of necrotic enteritis toxin B-like (NetB) toxin. Therefore, the use of alternatives to in-feed antibiotics with a better understanding of the relationship between nutrition and NE, and limiting exposure to infectious agents through biosecurity and vaccination, might be a tool to reduce the incidence of NE and to improve gut health in the absence of in-feed antibiotics. More importantly, the combinations of different measures may achieve greater protection of birds against the disease. Among all the alternatives investigated, prebiotics, organic acids and vaccination have shown improved gastrointestinal health and thus, have potential for the control of NE.

1. Introduction

Poultry production has undergone a substantial increase compared to other animal food-producing industries since 1970 (Yegani and Korver, 2008). Improvements in housing, genetic selection for growth rate, and advances in feed formulation achieved by matching nutrient requirements of the birds and nutrient contents of the feedstuffs, have resulted in higher meat yield, improved feed conversion and lower mortality rates (Choct et al., 1999; Cooper and Songer, 2009). As growth rate and feed conversion ratio improve, the birds' nutrition and health care are becoming more demanding (Choct et al., 1999). The nutritional and health status of poultry are interlinked with gut health which includes immune system, gut microbial balance and macro and micro-structural integrity of the gut. The health of the gastrointestinal tract (GIT) affects digestion, absorption and metabolism of nutrients, disease resistance and immune response (Kelly and Conway, 2001; Yegani and Korver, 2008). The disturbances of these processes can result in enteric diseases (Dekich, 1998). This makes it important to pay attention to gastrointestinal health; usually any slight change is mostly accompanied by disruption of gut health and thus overall performance.

Enteric diseases are one of the most important problems in the poultry industry because of high economic losses due to decreased weight gain, increased mortality rates, worse feed conversion ratio, greater medication costs, and increased risk of contamination of poultry products for human consumption (Timbermont et al.,

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2011). Several pathogens including viruses, bacteria, macroparasites and other infectious and non-infectious agents are reported as possible causes of enteric diseases either alone or in synergy (Reynolds, 2003). Many conditions have been associated with gastrointestinal problems such as diarrhea, wet droppings, dysbacteriosis, intestinal colibacillosis, malabsorption syndrome, coccidiosis and necrotic enteritis (NE). Enteric disorders are frequently associated with an overgrowth of *Clostridium perfringens*. Infections with this bacterium in poultry can cause NE, necrotic dermatitis, cholangiohepatitis, as well as gizzard erosion (Hafez, 2011). NE is the most common clostridial enteric disease in poultry, which typically occurs in broiler chickens (Cooper et al., 2013). NE is characterized by necrosis and inflammation of the GIT with a significant decline in growth performance and, in clinical cases, a massive increase in flock mortality. The total cost of NE outbreaks globally is estimated to be over $2 billion annually (Van der Sluis, 2000).

Antibiotics have been used as an effective tool to improve animal performance, by selectively modifying the gut microflora, decreasing bacterial fermentation, reducing thickness of the intestinal wall and suppressing bacterial catabolism. All these are important to improve health, nutrient availability and growth performance (Carlson and Fangman, 2000). Hence, dietary antimicrobials not only improve poultry growth and feed conversion efficiency, but also control enteric disease outbreak (Kim et al., 2011). The use of antibiotics in feed and for treating animals is second only to the medical use (Dahiya et al., 2006). It has been estimated that 11.15 million kg of antibiotics are used in animal feed in the USA alone each year (Union of Concerned Scientists, 2001) and 4.7 million kg or 35% of all antibiotics administered in Europe in 1999 were used in animal feed (European Commission Directorate General XXIV Directorate B, 1999). Hence, antibiotics have come under increasing scrutiny by government regulators, scientists and consumers because of the emergence of antibiotic-resistant “superbugs”. European countries have now prohibited the use of in-feed antibiotics in poultry feed (Van Immerseel et al., 2004). Without the use of in-feed antibiotics, the Animal Health Institute of America has estimated that the USA will require an additional 12 million pigs, 23 million cattle and 452 million chickens to reach the levels of production attained by the current practices (Dahiya et al., 2006).

With a ban of in-feed antibiotics in European countries, the incidence of NE has increased on the broiler farms of these countries (Casewell et al., 2003; Hofacre et al., 2003). At the same time, the focus on alternative strategies has increased to secure animal health and thus the efficiency of livestock production. These alternative strategies include modulation of gut microflora, augmentation of immune response and pathogen reduction through management, vaccination, nutritional strategies and feed additives.

2. Necrotic enteritis in broiler chickens

2.1. Epidemiology

NE has a high mortality rate with severe economic losses. The disease has been reported in many countries, including the United Kingdom (Parish, 1961), Australia (Nairn and Bamford, 1967), Canada (Helmboldt and Bryant, 1971) and France (Casewell et al., 2003). The primary causative agent of NE is *C. perfringens* and the source of *C. perfringens* is ultimately the chickens themselves (Cooper and Songer, 2009). Outbreaks of NE in poultry, past and present, have been associated with *C. perfringens* contamination of the chickens' feed (Eleazer and Harrell, 1976; Hofacre et al., 1986; Nairn and Bamford, 1967). Occurrences of NE are also affected by season (Kaldhusdal and Skjerve, 1996), dietary restriction (Olkowski et al., 2006), bedding on high fiber litter (Branton et al., 1997) and management-related stress (Craven, 2000).

NE usually occurs in broiler chicks at 2–6 weeks of age (Cooper and Songer, 2010). Generally, NE is not typically known as a seasonal disease, although the occurrences of NE between different latitudes appear to contradict this. Kaldhusdal and Skjerve (1996) suggested that univariate regression analysis in south-eastern Norway indicated that NE occurred more often during the months October–March than during the months April–September, whilst in Canada it mostly appeared in July–October (Long, 1973). In the United Kingdom, the peak incidence of NE is during winter with a lower incidence during the warmer seasons (Hermans and Morgan, 2007).

2.1.1. C. perfringens as a causative agent of NE

C. perfringens is a Gram-positive, spore forming anaerobic bacterium, able to produce several enzymes and toxins responsible for NE symptoms and lesions (Van Immerseel et al., 2004). *C. perfringens* can be found in poultry litter, feces, soil, dust and in healthy bird intestinal contents (Dahiya et al., 2005). It is expected that small numbers of *C. perfringens* are resident, transiently or permanently, in the GIT of most bird species (Cooper and Songer, 2009). When poultry meat is analyzed for *C. perfringens*, in some cases up to 84% of meat samples are positive (Craven et al., 2001b). It is reported that colonization or contamination of poultry by *C. perfringens* occurs during the early life of the animal, and can commence in the hatchery environment (Van Immerseel et al., 2004). *C. perfringens* is found in eggshell, paper pads and chicken dander in the hatchery (Craven et al., 2001a). Craven et al. (2003) indicated that the *C. perfringens* contamination found in broiler carcasses can begin in the breeder hen, and be transmitted through the hatchery and growing area. Free-living birds such as crows have high counts of *C. perfringens* in their intestinal droppings, which indicate that wild birds also suffer from NE (Asaoka et al., 2004). Craven et al. (2001b) found that swabs taken from poultry farms showed an incidence of *C. perfringens* from a variety of sources, including live flies, walls, dirt outside the entrance, fans, floor, nipple-drinker drip-cups, water pipes, litter material, chick delivery-tray liners and boots of farm staff before chicks were placed. Even feed samples taken after 2 weeks following bird placement had an incidence of *C. perfringens*. This indicates that different sources and strains of *C. perfringens* can colonize in the birds and produce NE. Additionally, NE has been reported in a variety of wild birds including ducks (Chakrabarty et al., 1983), wild geese (Wobeser and Rainnie, 1987), Laysan albatross (Work et al., 1998), mute swan (Duff et al., 2011), bobwhite quail (Shivaprasad et al., 2008) and wild crows (Asaoka et al., 2004; McOrist and Reece, 1992). With the gradual move from caged or housed chicken raising to free range worldwide, occurrence of NE in free range flocks becomes a major concern as the domestic chickens are prone to be infected through wild birds. This poses eminent challenge in the management and care of free range chickens which may be less than when they are raised in housed conditions.

2.1.2. Toxins to produce NE

C. perfringens is able to produce several types of toxins, while individual strains only produce a subset of these toxins (Van Immerseel et al., 2008). *C. perfringens* strains (A, B, C, D and E) are classified according to the production of four major extracellular toxins alpha (α), beta (β), epsilon (ε) and iota (ι), while various strains can also produce other toxins, including β 2 toxin, perfringolysin O [θ-toxin], collagenase [κ-toxin], enterotoxin, theta toxin etc. (Petit et al., 1999). Type A produces α-toxin, type B produces α, β and ε toxins, type C produces α and β toxins, type D