Department of Animal Science

NECROTIC ENTERITIS IN BROILER CHICKENS

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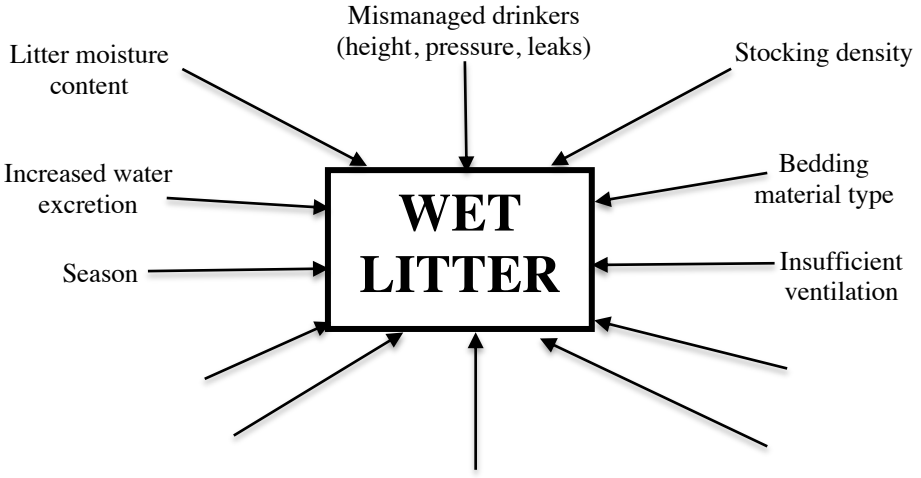
Necrotic enteritis (NE) is a major enteric poultry disease that has a huge detrimental effect on profitability in the broiler industry (Bansal et al., 2021; Salem et al., 2021), in either the clinical or subclinical form. Necrotic enteritis is caused by *Clostridium perfringens*, a ubiquitous (found everywhere) spore-forming, anaerobic, Gram-positive bacterium, found in the environment and in the gastrointestinal tract of humans and animals (Songer, 1996; Van Immerseel et al., 2004). It is one of the most common causes of foodborne illnesses in humans (Caly et al., 2015), but it also poses an important threat to animals (Uzal et al., 2010; Grass et al., 2013). A survey by Van der Sluis (2000) estimated that the cost of subclinical NE can be as high as five cents per bird, and NE outbreaks have the potential to cost the global broiler industry approximately $2 billion per year (Abd El-Hack et al., 2022). Furthermore, Timbermont et al. (2011) estimated the annual cost to the global poultry industry to be approximately $6 billion, including the cost of output losses and control measures. Restrictions on the use of subtherapeutic doses of antimicrobials as antibiotic growth promoters (AGPs) in the broiler industry have led to the reappearance of enteric diseases such as NE (Fathima et al., 2022). The decrease in antimicrobial use is being driven by the increasing occurrence of antimicrobial resistance, as well as pressure from consumers to reduce antibiotic use in livestock production. Increasing cases of NE are also being driven by a reduction in ionophore use, which, besides their activity against coccida, also show efficacy against clostridia. With increasing use of anticoccidial live vaccines, use of ionophores is not possible, and clostridia and NE increase (Williams, 2005).

Necrotic enteritis and broiler chickens

The causative agent of NE, *Clostridium perfringens*, was first called *Bacillus welchii* and then renamed *Clostridium welchii*, which was isolated from intestinal lesions of Black Orpington pullets in Australia (Bennetts, 1930). Over the past several decades, following the discovery of what was termed "necrotic enteritis" by Parish in England (Parish, 1961), several preventive measures have been attempted for disease prevention and control, with dietary inclusion of AGPs in poultry feed being the most widely used approach worldwide (Elwinger et al., 1998). However, the ban on preventive use of in-feed antibiotics in the European Union countries (Levy, 2014), United States and Canada has resulted in substantial economic losses to the poultry industry due to the re-emergence of once well-controlled diseases, including NE (M'Sadeq et al., 2015).

Given its ubiquitous nature, the main source of *C. perfringens* is the environment (Petit et al., 1999). *Clostridium perfringens* is a natural inhabitant of chickens' intestines. Necrotic enteritis is a multifactorial disease associated with the overgrowth of *C. perfringens* in the intestines. The ubiquitous nature of *C. perfringens* makes it difficult to attribute a single cause to the development of NE. The overgrowth of *C. perfringens* in the intestines and the resulting NE has been suggested to occur because of a combination of events, including damage to the intestinal mucosa, low pH level in the intestine (Baba et al., 1992), breed, sex, and age of bird, and particularly co-infection with coccidia (Prescott et al., 2016). Perhaps the most important of these is the occurrence of coccidiosis (Al-Sheikhly and Al-Saieg, 1980; Craven et al., 2001; Williams, 2005, Si et al., 2007) ahead of the NE. The incidence of NE and the mortality rates are higher when chickens are co-infected with coccidiosis (Shane et al., 1985; Baba et al., 1992).

Numerous researchers have proposed a variety of predisposing factors that might contribute to the development of NE, including thickening of the digesta due to consumption of water-soluble and hard-to-digest carbohydrates (Kocher et al., 2003), damage to the intestinal lining because of rough ration and different farm operations (Craven et al., 2001), and seasonal variation (Kaldhusadal and Skjerve, 1996). Diet composition has a significant impact on the development and pathogenesis of NE, particularly the presence of undigested protein in the lower gut. By leaving undigested proteins in the lower gut, trypsin inhibitors commonly found in soybean meal provide an ideal environment for bacterial development (Clarke and Wiseman, 2007). In addition, the severity of NE in chickens may vary depending on dietary makeup (wheat and barley or fishmeal use, antimicrobial of anticoccidial inclusion and protein content) (Prescott et al., 2016). Environmental factors may also play a role such as wet litter (Figure 1), high stocking density and stress (Hoerr, 2010). Every effort should be made to avoid wet litter.



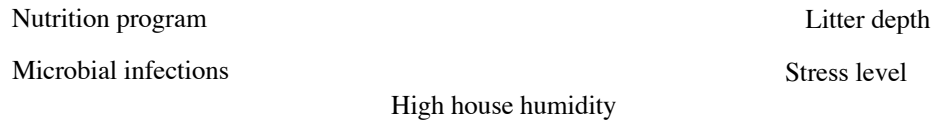


Figure 1. Some key contributing factors to wet litter in commercial broiler flocks. Source: Adapted from Williams (2005).

It is the presence of all or some of these predisposing factors that creates an environment conducive for the proliferation and colonization of *C. perfringens* in chickens. While *C. perfringens* is often found in the intestinal tract of chickens, the number of bacteria may be manageable until predisposing factors cause a proliferation in growth. These predisposing factors play a critical role in NE outbreaks in the field. Predisposing factors can 1) damage the intestinal epithelium, 2) increase mucus secretion, 3) disrupt gut microbiota composition, 4) change gut transit times and 5) alter the immune status of the host (Fathima et al., 2022). The changes in the physical properties of the gut and the immunological status of the birds cause an over-proliferation of *C. perfringens*, resulting in NE (Rodgers et al., 2015; Moore, 2016). An intact intestinal epithelium is essential for absorbing and utilizing nutrients and preventing the entry of pathogens. Chickens are often infected through bacterial cells or spores present in their feed, from contaminated litter or by cross-contamination with infected chickens early in life. Young birds with immature immune systems and no established commensal flora are particularly at risk.

Dealing with necrotic enteritis

In general, NE occurs in broiler chickens that are two to six weeks of age. There are two forms of the disease, a subclinical form, characterized by impaired digestion, reduced growth and poor feed conversion, and a more dangerous clinical form, leading to severe problems and increased flock mortality in a very short time. Necropsy will often reveal ballooned small intestines with a roughened "Turkish towel" mucosal surface, lesions and brownish pseudo-membranes. There will likely be a watery brown, blood-tinged fluid and a foul odor in the intestines. Birds may appear depressed, lethargic and often have diarrhea (leading to wet litter), which will be the most visibly obvious symptom. The rapid death (often within 24 hours) of chickens with NE often prevents treatment of the disease (Caly et al., 2015). In the past, antibiotics were used to keep NE outbreaks in check with great success. However, in recent years, the shift to "No Antibiotics Ever" programs by the poultry industry to address antimicrobial resistance and public demands has meant that alternatives to antibiotics are now essential to prevent NE occurrence and the consequent economic losses for the poultry industry.

Different alternatives to antimicrobials in feed have been suggested and are being utilized across the poultry industry today. Alternatives include phenolic compounds in herbal extracts, prebiotics, probiotics, essential oils, various plant extracts, phytogenic feed additives, hen egg antibodies, feed enzymes, vaccination, diet formulation with specific ingredient selection, cereal type, feed processing and dietary protein level (Caly et al., 2015). Alternatively, preventative treatments can take the form of actions on predisposing factors, such as coccidiosis prevention or improving overall cleanliness and hygiene. Strict hygienic management practices on the farm, in the hatchery and at the feed mill are critical in today's antibiotic-free environment. Careful selection of feed ingredients for ration formulation and the use of antibiotic alternative feed

additives are important in maintaining broiler efficiency and animal welfare and help increase the profitability of broiler production.

Farm management is considered one of the key factors that contribute to the incidence of *C. perfringens* in poultry flocks (Tsiouris, 2016). Increasing evidence indicates that environmental stressors, such as heat and cold stress, vaccination, processing at the hatchery, transportation to the farm, wet litter, poor ventilation and high stocking density, can disturb the homeostasis of the intestine and negatively impact the immune system of chicks, thereby increasing the incidence and severity of NE in chickens (Hangalapura et al., 2004; Hirakawa et al., 2020). For example, high stocking density increases the risk of horizontal transmission of *C. perfringens* between chickens by spreading spores through the air or by direct contact, and it is often associated with a substantial accumulation of litter, supporting *C. perfringens* sporulation (McDevitt et al., 2006; Guardia et al., 2011). In addition, other environmental factors such as reduced ventilation, high humidity and poor litter condition can also significantly influence the immune systems of birds and predispose them to NE (Dunlop et al., 2016; Hofacre et al., 2018). Biosecurity practices are also important to prevent potential horizontal transmission of infections, including *C. perfringens* within the flock or to other flocks (Tsiouris, (2016).

Numerous criteria must be considered when seeking antibiotic alternatives or preventive treatments for the animal industry. The financial cost is a major consideration, especially for small animals like chickens, with a low individual market value. Also, it is important to consider that the gastrointestinal tract of the chicken is a complex environment that includes the interaction of multiple bacterial species which may affect the efficacy of antibiotic alternatives, perhaps yielding a different response from one animal to the next. In addition, *C. perfringens* and other bacteria have proven to be very highly adaptable microorganisms. Therefore, it is wise to develop and use products in a rational manner to slow and limit the development of resistant bacterial strains which we have seen in recent years with conventional antibiotics.

Summary

The shift to antibiotic-free or “No Antibiotics Ever” production programs by the commercial poultry industry has been associated with reduced performance and increased mortality (Mot et al., 2014; Van Waeyenberghe et al., 2016). This has had a negative effect on the health of commercial chickens and has incurred substantial costs to the poultry industry and its contract producers. This substantial economic burden and the broiler health and welfare concerns raised by subclinical and clinical NE demand additional research into the pathogenesis of this multifactorial disease. There is a critical need for effective antibiotic alternatives to control NE infection after the recent industry shift away from antibiotic usage. Probiotics, prebiotics, symbiotics, herbal extracts, essential oils, enzymes, organic acids and protective vaccines are efficient antibiotic alternatives that could be used along with increased biosecurity practices to mitigate the negative effects of NE in broilers. None of these alternatives has proven to be a consistent “ideal” replacement for antibiotics but each alternative has beneficial properties that has proven useful to the poultry industry in various situations. Optimization of nutritional and on-farm management practices in addition to application of antibiotic alternatives and new generation vaccines offer preventative strategies to control NE in broiler chickens.

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