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REVIEW ARTICLE

Enteric Diseases of Poultry with Special Attention to *Clostridium perfringens*

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ABSTRACT

The enteric health of growing poultry is imperative to success of the production. The basic role of poultry production is turning feed stuffs into meat. Any changes in this turning process, due to mechanical, chemical or biological disturbance of digestive system (enteric disorders) is mostly accompanied with high economic losses due to poor performance, increased mortality rates and increased medication costs. The severity of clinical signs and course of the disorders are influenced by several factors such as management, nutrition and the involved agent(s). Several pathogens (viruses, bacteria and parasites) are incriminated as possible cause of enteric disorders either alone (mono-causal), in synergy with other micro-organisms (multi-causal), or with non-infectious causes such as feed and /or management related factors. In addition, excessive levels of mycotoxins and biogenic amines in feed lead to enteric disorders. Also factors such as high stocking density, poor litter conditions, poor hygiene and high ammonia level and other stressful situation may reduce the resistance of the birds and increases their susceptibility to infections. Under field conditions, however, it is difficult to determine whether the true cause of enteric disorders, is of infectious or non-infectious origin. In recent years and since the ban of use of antimicrobial growth promoters in several countries the incidence of intestinal disorders especially those caused by clostridial infection was drastically increased. The present review described in general the several factors involved in enteric disorders and summarized the available literatures about *Clostridium perfringens* infection in poultry.

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INTRODUCTION

The basic role of poultry production is turning feed stuffs into meat. Broilers and meat turkeys are very efficient at both growth and feed conversion rate. Any slight alteration from the optimal condition is mostly accompanied by disruption of the growth process and all over performance. To reach the maximal potential of development, considerable demands should be placed on good intestinal health.

Enteric disorders are one of the most important groups of diseases they affect poultry and are continuing to cause high economic losses in the many areas world-wide due to increased mortality rates, decreased weight gain, increased medication costs, and increased feed conversion rates. Several pathogens (viruses, bacteria and parasites) are incriminated as possible causes of enteric disorders either alone (mono-causal), in synergy with different other microorganisms (multi-causal) or with non-infectious causes such as feed and /or management related factors (Table 1). Under field conditions, however, it is difficult to determine weather the true cause of enteric disorders in poultry is of infectious or non-infectious origin (Hafez, 2001).

Since the first report of Moore *et al*. (1946), it is generally known, that supplementation of poultry feed with antibiotic growth promoters (AGPs) improves performance of livestock. The effect of AGP on gut flora results in improvement of digestion, better absorption of nutrients, and a more stable balance in the microbial population. As consequence this is accompanied with reduced intestinal disorders. However, AGP can also increase the prevalence of drug-resistant bacteria.

Based on "Precautionary Principle" and experiences made in Sweden, Denmark, Germany and the Netherlands, the EU has decided to ban the use of growth-promoting antibiotics in feed of food producing animals completely by January 2006. The first step was taken in

1997 by the ban of avoparcin, followed by spiramycin, tylosin phosphate, zinc bacitracin and virginiamycin in 1998 and carbadox and olaquindox in 1999. Field observations in several countries in Europe showed that poultry industry faced several problems after the ban of AGPs. The impact of the ban has been seen on the performances (body weight and feed conversion rate) as well as on the rearing husbandry (wet litter and ammonia level), animal welfare problem (foot pad dermatitis) and general health issues on the birds (enteric disorders due to dysbacteriosis and clostridial infections) (Hafez, 2008).

The present paper reviews the currently most important causes of enteric disorders of poultry and their economic impacts with special attention to clostridial infections.

Table 1: Some possible causes of enteric disorders in poultry

Non - Infectious	Infectious
Feed	Viral agents
Structure	Reo, Astro, Entero, Rota,
Palatability	Coronavirus enteritis, HE
Energy content	ND, Influenza A
Pellet quality	Bacterial agents
Management	Salmonellas, E. coli,
Available feed space	Clostridia
Available water space	Mycotic agents
Distribution of feeders	Candida
Distribution of waterers	Parasites
Air quality	Coccidia, Histomonas,
Temperature	Hexamitia, Ascaridia
Stocking density	

Non-infectious factors involved in intestinal disorders

Nutrition

Enteric health and nutrition are closely related. Poor enteric health can adversely affect food digestion, gut motility and nutrient absorption by several means. Likewise, poor nutrition and feed quality can either increase the bird's susceptibility to enteric disorders or directly cause them (Ferket, 1996; Hafez, 1998). Nutritional factors that influence gut health include feed intake, palatability, feed ingredient quality, feed formulation and pellet quality. In addition, mistakes in feeding technique, the amount of fibre in the feed, the content and quality of the raw materials as well as sudden feed changes or restriction, can result in changes in the intestinal flora and/or in the enzymatic activity which lead to digestive disorders (Nixey, 1989; Kaldhusdal and Skjerve, 1996; D'Mello, 1997; Corless and Sell, 1999; Annett *et al.*, 2002; Batal and Parsons, 2002; Kocher, 2003; McReynolds *et al.*, 2004). Also, excessive levels of mycotoxins and biogenic amines in feed lead to enteric disorders (Smith and Hamilton, 1970; Burditt *et al.*, 1983; Brown *et al.*, 1992; Dwivedi and Burns, 1986; Hoerr, 2008).

Feed contains a little dust; however, excess dust can adversely affect the palatability and lead to reduction of feed intake. Badly stored feed can contain fungal spores, and fat may go rancid which results in reduction of the feed intake and may negatively affect the content of some vitamins in the feed (Dhand *et al.*, 1998; FAO, 2004). Inadequate feeder space and false distribution can result in competition and stronger birds dominating the feeder with a consequent variation in feed intake within the flock. Feed can contain undesirable substances such as mycotoxins, which adversely affect the immune system, increase the susceptibility of the birds to infectious diseases and cause poor response to vaccine (Uraguchi and Myamazaki, 1978; Campbell *et al.***,** 1981; Burns and Dwivedi, 1986; El-Karim *et al.,* 1991; D'Mello *et al.,* 1993**,** D'Mello and MacDonald, 1998; Devegowda *et al.,* 1998). Proper adjustment of feeder is a factor that should receive constant attention (Hafez, 1998).

Management and environmental factors

Good rearing management is the starting point for healthy, productive and profitable poultry production in agreement with animal welfare. Rearing management mean all factors which influence the birds health include several factors such as house structure, climatic conditions (ventilation, temperature, litter condition), stocking density, feed and water supply, hygienic condition as well as the knowledge's and qualification of the stockman. These factors affect each other and can promote or inhibit the health condition of the flock. In aim to achieve desired performance results, managers of turkey flocks should integrate good environment, husbandry, nutrition and disease control programmes (Sundrum, 1995; Hafez, 1996; 1998). The rearing management must be directed to satisfy the bird's requirements, to promote the production and to prevent diseases condition (Morgen and Avens, 1985). Any disturbance will cause stress, which will reduce the resistance of the birds, increase their susceptibility to infections and reduce their immune-response to vaccines (Sainsbury, 1992; Hafez, 1998).

Infectious diseases

Several infectious agents such as viruses, bacteria, fungus and parasites are involved in intestinal disorders (Fig. 1). These infectious agents can introduce and spread in poultry farms by different routes. It occurs by vertical and/or horizontal route. At early days of age the main disease problems are related to vertically transmitted infections such as salmonella, *E. coli* and improper hatchery management (Hafez, 1999; Hafez, 2005; Bermudez and Stewart-Brown, 2008). Those and other infectious agents can also be transmitted horizontally (laterally) by direct contact between infected and non-infected susceptible birds, and through indirect contact with contaminated feed, water, equipment, environment and dust through ingestion or inhalation (Hafez, 1996; Bermudez and Stewart-Brown, 2008).

Infections with *Clostridium perfringens*

Infections with *Clostridium perfringens* in poultry can cause several clinical manifestations and lesions include necrotic enteritis, necrotic dermatitis, cholangiohepatitis as well as gizzard erosion. However, subclinical infection can take place too. In addition, *C. perfringens* type A has been showed to cause food poisoning in humans (Løvland and Kaldhusdal, 2001; McClane *et al*., 2006; Novoa-Garrido *et al*., 2006).

Etiology

Clostridium perfringens is a Gram-positive, non-motile, spore-forming anaerobic bacterium which is widespread in soils, feed, litter and the intestinal tract of

diseased and healthy birds (Char *et al*., 1986; Frame and Bickford, 1986; Gazdzinski and Julian, 1992; Branton *et al.*, 1997). The optimum growth occurs within temperature range of 12-50°C and pH between 6.0 and 7.0 (Adams and Moss, 1995). Under optimal conditions, 43−47°C, *C. perfringens* grows extremely rapidly, with a generation time of 8-10 min, and growth is accompanied by abundant gas production (Bryant and Stevens, 1997). The bacterial spores are very resistant to heat, desiccation, acids and many chemical disinfectants (Willis, 1977).

C. perfringens is divided into 5 biotypes A, B, C, D, and E based on the synthesis of four major lethal toxins: alpha, beta, epsilon, and iota. Along with these four major toxins, enterotoxin (CPE) and beta2 (CPB2) toxins produced by *C. perfringens* are considered as important toxins for enteric diseases (McDonel, 1986; Songer, 1996; Waters *et al*., 2003, Smedley *et al.,* 2004, McClane *et al*., 2006). However, it is not clear whether CPE and CPB2 are involved in *C. perfringens*-associated avian enteric diseases (Crespo *et al*., 2007).

The infections in poultry are mostly caused by *C. perfringens* type A, and to a lesser extent by type C (Songer and Meer, 1996; Engström *et al.,* 2003). Because *C. perfringens* type A is highly prevalent in the intestines of healthy animals, controversy exists about its real pathogenic role (Smedley *et al.,* 2004; McClane *et al.,* 2006). Additionally, it was shown that strains isolated from necrotic enteritis outbreaks did not produce more alpha toxin compared to isolates from the gut of clinically healthy broilers (Gholamiandehkordi *et al.,* 2006). Timbermont *et al.* (2009) examined the ability of *C. perfringens* isolates from both healthy and diseased poultry, and from calf hemorrhagic enteritis cases, producing different concentrations of alpha toxin in vitro, to induce necrotic enteritis in broilers. The obtained results revealed that induction of necrotic lesions in the broiler gut is not associated with the ability to produce alpha toxin in vitro. Moreover, the results also suggest that the virulence of *C. perfringens* strains is to some extent host specific since two *C. perfringens* strains isolated from calf hemorrhagic enteritis were not able to produce necrotic lesions in chickens.

Keyburn *et al.* (2008) were able to identify a novel toxin (netB) in a *C. perfringens* type A strains isolated from chickens suffering from necrotic enteritis. According to the authors this novel toxin is the first definitive virulence factor to be identified in avian *C. perfringens* strains capable of causing necrotic enteritis. However, netB strain could be also found in healthy chickens and turkeys (Gad *et al*., 2011a) as well as in other animal species such bovine (Martin, 2010). On the hand, Martin (2010) reported that the majority (58%) of chickens with NE were caused by *C. perfringens* isolates that were NetB positive. Under experimental condition they found that only strains that possess NetB were capable of producing NE regardless of the source of the isolate. NetB negative strains including those isolated from cases of NE were unable to produce NE in the disease model. Martin and Smyth (2009) also found a strong correlation between the detection of the cpb2 gene and netb gene. However, when interpreting the results it has to be kept in mind that the presence of the gene of a toxin does not necessarily mean, that the toxin is produced, as it was shown for netb toxin (Abildgaard *et al*., 2010) or cpb2 (Crespo *et al*.,2007).

Necrotic enteritis (NE)

NE is an acute disease caused by *Clostridium perfringens* when proliferates to high numbers in the small intestine and produces toxins responsible for damaging the intestinal lining (Long and Truscott, 1976; Shane *et al.,* 1985). It was firstly described by Parish (1961). The disease has been observed in several domestic and wild birds world wide. Recently several reviews were published (Van Immerseel *et al*., 2004; Williams, 2005; Wilson *et al.,* 2005; McDevitt *et al.,* 2006; Opengart, 2008). Beside clinically manifested disease, subclinical infections may take place and are mostly accompanied with reduction of performance.

Mode of infection

The most important source of infection in poultry appears to be contaminated feed, litter, water and the environment (Wijewanta and Seneviratna, 1971; Komnenov *et al.,* 1981; Craven *et al.,* 2001a). In addition, some reports about the possible vertical transmission have been published (Köhler et al., 1974a, b; Shane *et al.*, 1984; Craven *et al.*, 2001b, 2003). Recently, Martin (2010) were able to demonstrate under experimental condition, that factors such as co-infection with Eimeria species, genotype of chicken and the strain of *C. perfringens* were the most critical factors involved in disease development, while other factors such as age of chickens, contact with litter and protein content of the diet played a lesser role.

Clinical signs and lesions

After experimental infection, the first mild clinical signs are evident approximately 24 to 36 hours after administration of a pure *C. perfringens* culture to broiler chickens (Bains, 1968; Helmboldt and Bryant, 1971; Balauca *et al.,* 1976; Al-Sheikhly and Truscott, 1977; Balauca, 1978). The clinical signs appear suddenly; apparently healthy birds may become acutely depressed and die within hours (Long, 1973; Tsai and Tung, 1981; Shane *et al.,* 1985). Mortality ranges between 2 and 10%. Affected birds show ruffled feathers, marked depression, in-appetence, tendency to huddle, watery droppings and diarrhoea (Long, 1973; Porter, 1998; Gazdzinski and Julian, 1992).

The presence of *C. perfringens* in the intestinal tract or inoculation of the animals with high doses of *C. perfringens*, however, does generally not lead to the development of necrotic enteritis. One or several predisposing factors may be required to elicit the clinical signs and lesions (Shane *et al.,* 1984; Cowen *et al.,* 1987; Kaldhusdal *et al.,* 1999). It appears that some dysfunctions of the alimentary tract are necessary predisposing cause of infection. Intestinal stasis, intestinal distension, coccidiosis, salmonellosis, crop mycosis and haemorrhagic enteritis (HE) may predispose the birds to infection (Al-Sheikhly and Al-Saieg, 1980; Shane *et al.,* 1985; Baba *et al.,* 1992, Williams, 2005). Factors predisposing the intestinal tract to overgrowth by clostridia organisms may also be the consumption of diets high in energy, protein and fish meal as well as the

consumption of high fibre litter and wheat based diet (Branton *et al.,* 1987; 1997; Kaldhusdal and Skjerve, 1996; Ficken and Wages, 1997; Kocher, 2003). Panneman (2000) demonstrated that the proximal intestine of normal birds has very low levels of bacteria, whereas birds affected with dysbacteriosis have substantially higher bacterial counts. *Clostridium spp*. has been shown to contribute to this overgrowth. Dysbacteriosis is defined as the presence of a qualitatively and/or quantitatively abnormal flora in the small intestine causing a clinical disorder and/or malabsorption. It is seen in broilers after 21 days of age with wet faeces and a reduction in feed intake (Fabri, 2004). Furthermore, Siegel *et al.* (1993) reported that genetic susceptibility could be an additional factor, which can influence the course of infection, since a significant difference in mortality rate between different major histocompatibility complex genotypes was observed. An outbreak of necrotic enteritis occurred in chickens that were B13B13 or B21B21 at the MHC in sublines of lines selected for high (HA) and low (LA) antibody response to sheep erythrocytes. Percentage mortality and hen-day egg production, although similar for both background genomes, were different for MHC genotypes. Mortality was 6% for B21B21 and 15% for B13B13 types. Although hen-day egg production for both types declined from about 76 to 50%, the decrease occurred earlier but recovery of survivors was faster in B13B13 than in B21B21 pullets (Siegel *et al.,* 1993).

On autopsy dehydration is the most common finding. Breast muscles are dark red and gizzards are full of litter. Severe inflammation in the duodenum and jejunum is the most predominant finding, but in some instances the entire length of the intestinal tract is involved (Bains, 1968; Helmboldt and Bryant, 1971; Long *et al*., 1974; Tsai and Tung 1981; Ficken and Berkhoff, 1989). The intestine is distended thin walled and filled with gas and contains dark offensive fluid (Broussard *et al.,* 1986). The mucosa is covered with green or brown diphteroid membrane, which can be easily separated from the lining (Fig. 1). Varying degrees of sloughing of the intestinal mucosa could also be observed (Fig. 2). As the condition progresses, areas of necrosis can be recognized from outside of the intestine (Helmboldt and Bryant, 1971; Long *et al.,* 1974; Balauca, 1978; Shane *et al.,* 1985).

Initial microscopic lesions develop at the apices of villi and are characterized by sloughing of epithelium and colonization of the exposed lamina propria with bacilli, accompanied by coagulation necrosis. Progression of lesions usually occurs from villi apices to crypts. Necrosis may extend into the submucosa and muscular layers of the intestine (Fig. 3) (Nairn and Bamford, 1967; Helmboldt and Bryant, 1971; Long *et al.,* 1974; Tsai and Tung, 1981; Opengart, 2008). Large numbers of gram-positive bacilli can be seen (Fig. 4 and 5) within the necrotic debris (Randall, 1991). In per acute cases there is little inflammatory cell infiltrate although, if the animal survives, there is a progression to heterophil and mononuclear cell infiltration followed by fibrosis (Shane *et al.,* 1985; Ficken and Wages, 1997).

Cholangiohepatitis

Cholangiohepatitis causes severe economic losses due to high liver condemnation rate on the processing and downgraded of the slaughtered carcasses. *Clostridium perfringens* is usually isolated in association with the disease. The hepatitis characterized by an enlarged firm liver sometimes with a slightly knobby surface and a medium tan colour. Histopathological lesions consist of hyperplasia of the bile duct, fibrinoid necrosis, cholangitis and occasionally focal granulomatous inflammation (Onderka *et al.,* 1990; Løvland and Kaldhusdal, 1999; Sasaki *et al.,* 2000). Onderka *et al.* (1990) experimentally reproduced the condition by either tying off the bile ducts or injecting *C. perfringens* into the bile duct. It seems that the presence of *C. perfringens* in many of the gall bladders of affected livers suggested some involvement of either the bacterium or its toxin which interfere with the liver function.

Gizzard erosions

Gizzard erosions has been observed in commercial broiler chickens and several non-infectious factors such as mycotoxin-contaminated feed, vitamin B6 and E deficiency, inadequate levels of sulphur-containing dietary amino acids, high levels of dietary copper, pelleted feed as well as inclusion of certain fish meals in the diets and were discriminated as possible cause. Ono *et al.* (2003) reported on Outbreaks of adenoviral gizzard erosion in slaughtered broiler chickens in Japan and Novoa-Garrido *et al.* (2006) found a significant association between gizzard lesions and increased caecal *C. perfringens* counts in broiler chickens.

Diagnosis

A presumptive diagnosis may be made from the case history, clinical signs, lesions and staining fresh smears of upper part of the intestinal tract with Gram stain showing an abundant number of clostridia organisms (Ficken and Wages, 1997; Hafez and Jodas, 1997). This should be confirmed by the isolation of the causative agent. For isolation several media are available such as sheep blood agar supplemented with neomycin or tryptose-sulfite-cycloserine agar (TSC). The identification can be carried out using biochemical tests. Most of isolates ferment lactose, glucose, maltose, hydrolyze gelatin, and reduce nitrate. This bacterium is non-motile, indole and catalase negative (Ficken and Berkhoff, 1989). In addition, PCR was developed to detect of alpha toxin (Heikinheimo and Korkeala, 2005) as well as a real-time PCR for quantitative detection of *C. perfringens* in gastrointestinal tract of poultry (Wise and Siragusa, 2005). Also ELISAs for direct detection of *C. perfringens* major toxins and enterotoxin are commercially available.

Treatment

Treatment with antibiotics such as penicillin, amoxicillin, ampicillin, erythromycin, dihydrostrepto-mycin and tetracyclin provided a satisfactory clinical response. Penicillin's are known to be particularly active against *C. perfringens*. Resistance to penicillin is very rare and β-lactamase has not been demonstrated. Three days is the minimum duration of treatment, however longer applications may be required. Recently, Gad *et al*. (2011b) were determined the minimum inhibitory concentrations of 16 antibiotics for 100 *Clostridium perfringens* isolates collected between 2008 and 2009 from commercial turkey

flocks using a commercially available broth micro-dilution test kit. No isolates were resistant against β-lactam antibiotics (amoxicillin, oxacillin, and penicillin), lincospectin, tylosin, doxycyclin, tetracycline, enrofloxacin, trimethoprim/sulfamethoxazole, lincomycin, and tilmicosin. A low frequency of resistance was detected against erythromycin and tiamulin with 5 and 20%, respectively. Spectinomycin, neomycin and colistin showed the highest incidence of resistance with 74, 94 and 100%, respectively.

According to Brennan *et al.* (2000) administration of dietary Tylan® for seven consecutive days following

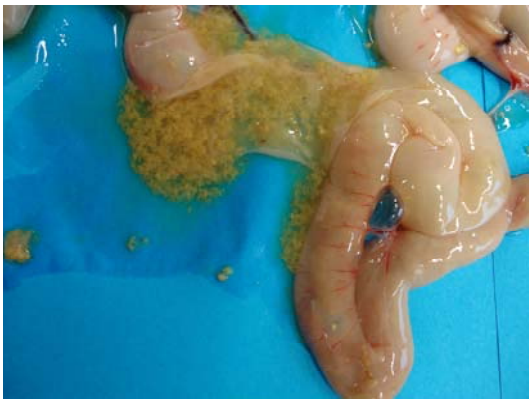

Fig. 1: Necrotic enteritis: The mucosa is covered with green or brown diphtheroid membrane, which can be easily separated from the lining.

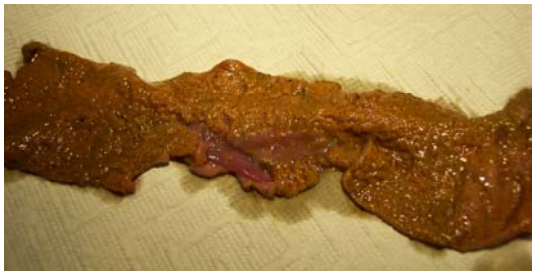

Fig. 2: Severe necrotic enteritis with necrotic pseudomembrane covering the intestinal mucosa.

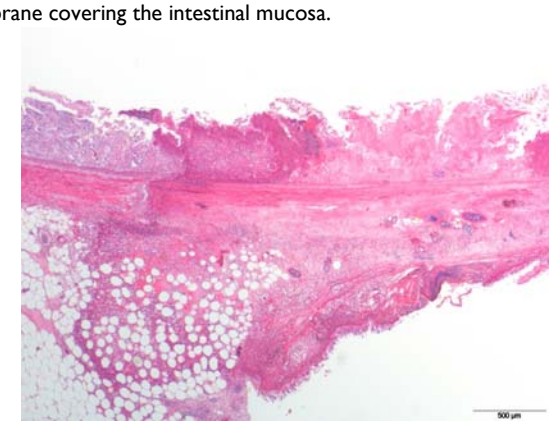

Fig. 3: Severe, acute, necrotizing enteritis with extensive transmural spreading as well as associated, necrotizing and granulomatous steatites/serositis; large number of Gram-Positive bacilli, located multifocal within lesions (H & E 20X) (Courtesy: Dr. Olivia Kershaw, Berlin).

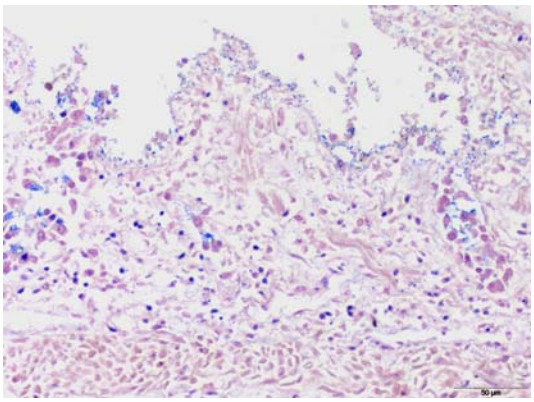

Fig. 4: Necrotic enteritis: note large number of Gram-Positive bacilli, located multifocal on the surface as well as within lesions (Gram X200) (Courtesy: Dr. Olivia Kershaw, Berlin).

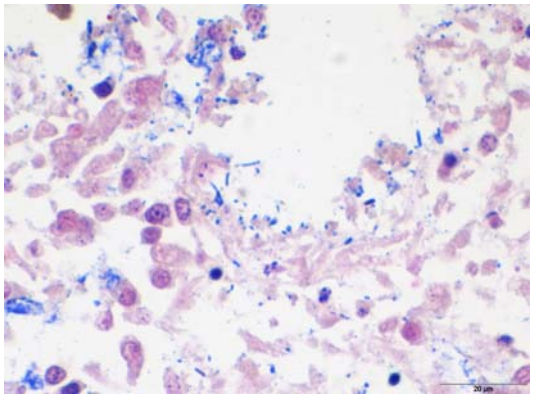

Fig. 5: Necrotic enteritis: note large number of Gram-Positive bacilli, located multifocal on the surface as well as within lesions (Gram X600) (Courtesy: Dr. Olivia Kershaw, Berlin).

confirmation of an NE field outbreak reduced the NE mortality and lesion score and improved overall growth as well as feed conversion in broilers. The optimum dose of Tylan to control NE was 100 ppm.

No resistance to the ionophorous anticoccidial drugs such as Narasin has been found (Watkins *et al.*, 1997; Martel *et al.*, 2004). Brennan *et al*. (2001) reported that Narasin, when administrated at 70 ppm in feed from Day 0 to 41 prevents morbidity, mortality and suppression of growth and feed conversion associated with NE in broilers.

For the commercial poultry industry, controlling the levels of *C. perfringens* is an important issue because of the economic cost of infected flocks. It has been estimated that, worldwide, *C. perfringens* costs the international poultry industry in excess of $US 2 billion per year (Kaldhusdal and Løvland, 2000). In addition, costs to broiler producers associated with subclinical (mild) necrotic enteritis (SNE) were estimated recently by Skinner *et al.* (2010) using published information on impacts on body weight and feed conversion rate (FCR) associated with SNE and costs and revenues associated with broiler production. SNE was estimated to result in a 12% reduction in body weight and a 10.9% increase in FCR compared with healthy birds. For the purposes they considered scenarios involving hypothetical flocks of

20,000 birds raised to final body weights ranging from 4.63 to 7.94 lb. The incidence of SNE was assumed to occur at 20% based on the literature. SNE resulted in a loss to producers ranging from US$878.19 to US$1480.52 per flock. When feed costs required to obtain SNE flocks having a total live body weight equal to equivalent healthy flocks at market age were calculated, the increased cost to producers ranged from US$370.49 to US$739.38 per flock (Skinner *et al.,* 2010).

Strategies to reduce the incidence of clostridial infections are necessary help to increase the profitability of the poultry production and several further approaches are generally used to combat the infection and as alternatives to AGPs. Investigations indicate that competitive exclusion, prebiotics, probiotics, enzymes and acids can impact the incidence and severity of NE in poultry (Fukata *et al.,* 1991; Elwinger *et al.,* 1992; Hofacre *et al.,* 1998; Kaldhusdal *et al.,* 2001). The data suggest that these products may provide the poultry industry with an alternative management tool that has the potential to promote better intestinal health and decrease monetary losses due to *C. perfringens* (McReynolds *et al.,* 2009).

According to Langhout (2007), these approaches will need adaptations in the feeding program and/or feed production. The practical relevance of these approaches may vary between the different areas in the world. At this moment it is difficult to evaluate novel strategies developed to antibiotic-free feeding concepts. Combination of different approaches is necessary to enhance the performance and reduced health status of the birds such as:

i) Selection of highly digestible feed ingredients to reduce nutrients for microbial degradation.
ii) Improvement in the balance of the essential amino acids resulting in lower total dietary protein levels. This will reduce the risk for clostridium problems, since this bacterium in particular increases during proteolytic fermentation.
iii) Improvement in the physical form of the diet, for example via the inclusion of coarse particles in the diet. Coarse particles will improve the passage rate of the feed through the intestinal tract and as a consequence increase digestion and reduce bacterial fermentation in the intestinal tract.
iv) Introduction of a special prestarter diet in the feeding program. The main objective of this prestarter diet should be to stimulate the development of the immune system and the development of an optimal micro flora.
v) Improvement of climate control in the broiler house to avoid stress in the animal and keeping litter quality in optimal condition.
vi) Improvement of disease control in broilers. This disease control focuses much more on the prevention of health problems than on treatment of diseases.

Vaccination

Active and passive immunity using vaccination against *C. perfringens* and its toxins appears to offer protection. Heier *et al.* (2001) found out that broiler flocks with high titres of maternal antibodies against *C. perfringens* alpha-toxin had lower mortality during the production period than flocks with low tiers. Also Løvland *et al.* (2004) use toxoids vaccines based on *C. perfringens* type A and C toxoids to vaccinate breeder flocks. The IgG responses in vaccinated parent hens were distinct and the levels of antibodies to *C. perfringens* alpha - toxin in progeny of the vaccinated hens was high enough to protect the progeny against subclinical *C. perfringens* associated necrotic enteritis. On the other hand several recent investigations showed that immunity to NE after oral infection using virulent strain and subsequent treatment is much better than using avirulent *C. perfringens* strains and they identified immunogenic secreted proteins apparently uniquely produced by virulent *C. perfringens* isolates and concluded that there are certain secreted proteins beside to alpha-toxin, that are involved in immunity to NE in broiler chickens (Thompson *et al.,* 2006; Kulkarni *et al.,* 2007). Further additional study showed the ability of oral immunisation against *C. perfringens* in broiler chickens using an attenuated *Salmonella* vaccine vector (Kulkarni *et al.,* 2008).

Conclusions

Implementation of several approaches such as improvement of management, feed formulation and use of alternative products to modulate the intestinal flora led to an improvement of the situation. Limiting exposure to infectious agents through biosecurity, vaccination, supportive therapy, cleaning and disinfection are essential. In addition, early recognition in managing the enteric disorders is very important.

Finally, use of an effective anticoccidial drug in the ration is helpful to minimise the effect of enteritis. Since, recent investigations showed that the use of some alternative products might be able to reduce the intestinal colonization with pathogenic bacterial agents. This could be an additional tool to reduce enteric disorders in future.

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